Cardiovascular Innovations and Applications

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ABSTRACTS

This Supplement contains the selected Abstracts presented at the Great Wall International Congress of Cardiology, Asian Heart Society Congress, held October 19–25, 2020.

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BASIC AND TRANSLATIONAL MEDICINE

BASIC RESEARCH OF CARDIOVASCULAR DISEASE

GW31-e0016

TREM-2 adenovirus transfection promoted survival of cardiomyocytes in myocardial infarction through PI3K/AKT/mTOR pathway

Cong Fu[1,2], Qiancheng Xu[3], Shengxing Tang[1], Yuhan Cao[2,4]
[1]Department of Cardiology, Yi Ji Shan Hospital Affiliated to Wan Nan Medical College
[2]Key Laboratory of Non-coding RNA Transformation Research of Anhui Higher Education Institution, Wan Nan Medical College
[3]Department of Critical Care Medicine, Yi Ji Shan Hospital Affiliated to Wan Nan Medical College
[4]Department of Nephrology, Yi Ji Shan Hospital Affiliated to Wan Nan Medical College

OBJECTIVES Triggering receptor expressed on myeloid cells-2 (TREM-2) is a cell surface receptor primarily expressed on monocyte-derived cells. Recent years, the organ protecting effect of TREM-2 attracted researchers' attention. However, the role of TREM-2 in other system especially in circulating was still not well demonstrated. If TREM-2 have cardiac protecting effect needed to be further studied. Accordingly, we designed this research to determine the role of TREM-2 in myocardial infarction (MI) and preliminary demonstrated the molecular mechanism.

METHODS Recombinant adenovirus containing the gene coding full-length mouse TREM-2 and EGFP and control vector containing EGFP gene without any transgene were produced using the ViraPower Adenoviral Expression System. The male C57BL6 mice (weight 20–22 g) were anesthetized with intraperitoneal pentobarbital (35 mg/kg) and intubated. The left anterior descending (LAD) coronary artery was ligated proximally with 7-0 silk suture via a left thoracotomy incision. After LAD ligated, animals were randomly divided into three groups: (1) Mice were subjected to LAD coronary ligation; (2) Mice were received 50 μL of intramyocardial injections of 5*105 Ad.Null; (3) Mice were received 50 μL of intramyocardial injections of 5*105 Ad. TREM-2. The injection point was above ligation site. Non-operated control and sham surgery were performed. After 7 days, 2-dimensional echocardiography was performed on the mice using a transthoracic echocardiogram to measure the cardiac function. All the animals were executed by over-dose of intraperitoneal pentobarbital (130 mg/kg) after echocardiography. The expression of GFP and Trem-2 were detected. HE staining, Masson staining and TUNEL staining were performed to detect the pathological changes, infarcted size and cardiomyocytes apoptosis. Western blot was performed to measure the expression of signal protein in myocardial tissue.

RESULTS GFP detection showed that both Ad. TREM-2 and Ad.Null successfully transfected in cardiomyocytes. TREM-2 expressed in cardiomyocytes after Ad. TREM-2 transfection was higher compared to Ad. Null transfection. Cardiac function was evaluated at 10 days after MI. MI group had lower LVEF and LVFS than control and Sham. The LVEF and LVFS were significantly higher in Ad. TREM-2 group than MI and Ad. Null group. Further, the LVIDd and LVIDs were higher in MI group than control and sham. Ad. TREM-2 group had lower LVIDd and LVIDs than MI and Ad.Null. HE staining showed inflammatory cell infiltration, myocardial dissolution and cardiomyocyte apoptosis in MI group compared to control and sham. In the Ad. TREM-2 group, the myocardial injury was significantly alleviated compared to MI and Ad. Nul. Masson staining showed remarkably reduced infarct size in the Ad. TREM-2 group compared to MI and Ad. Null. TUNEL staining showed that apoptotic cardiomyocytes increased markedly in the myocardium tissue in the MI group compared to control and sham. Ad. TREM-2 transfection decreased the number of apoptotic cells compared to MI and Ad. Null. TREM-2 adenovirus transfection significantly activated the phosphorylation of AKT and mTOR compared to MI and Ad.Null transfection.

CONCLUSIONS Over-expression of TREM-2 by recombinant adenovirus transfection after MI alleviated the myocardial injury, decreased the infarcted size and inhibited the cardiomyocytes apoptosis. TREM-2 is a potential therapeutic target in improving heart function after MI.

GW31-e0018

Glycolysis inhibition can alleviate cardiac fibrosis and cardiac fibroblast activation after myocardial infarction

Zhiteng Chen, Haifeng Zhang, Yangxin Chen, Jingfeng Wang
Sun Yat-sen Memorial Hospital

OBJECTIVES Cardiac fibrosis is a common pathophysiological process during different heart diseases, as well as an independent risk factor of heart failure prognosis. Fibroblast is the most important contributor to cardiac fibrosis. In various fibrotic diseases, glycolysis is proved to contribute to fibroblast activation. However, few researches focus on the glycolysis in cardiac fibroblast. As myocardial infarction is the main etiology of heart failure, it is of great significance to study the relationship among glycolysis, cardiac fibrosis and cardiac fibroblast activation.

METHODS *In vivo*, we delivered a glycolysis inhibitor, 2-deoxy-D-glucose (2-DG) or PBS by intraperitoneal injection after mice myocardial infarction and detected the cardiac function by ultrasonic cardiography, fibrosis area by Masson staining, cardiac fibroblast activation by tissue immunofluorescence, and glycolytic and cardiac fibroblast activation markers by western blot at the 28th day after myocardial infarction. *In vitro*, we activated human cardiac fibroblast (HCF) with transforming growth factor-β1 and detected the glycolytic change with Seahorse energy metabolism detector, lactate detection assay, glucose detection assay, and triphosadenine detection assay. We also detected the HCF activation markers with western blot and ELISA to confirm the change of glycolysis and the influence of 2-DG on HCF activation. At last, we also verified the relationship among cardiac fibrosis, cardiac fibroblast activation, and glycolysis in human fibrotic and non-fibrotic heart tissues.

RESULTS *In vivo*, we observe obvious cardiac fibrosis and fibroblast activation accompanied with enhanced glycolysis at the 28th day after myocardial infarction. We found an increase mortality in the 2-DG treated mice compared with the PBS treated mice. Then we delayed our initial administration time to the fourth day after myocardial infarction and lower the dosage of 2-DG to a half. Interestingly, the high mortality decreased, and the fibrosis and fibroblast activation in the heart were inhibited at the 28th day after myocardial infarction but with few benefits for cardiac function. *In vitro*, we uncovered that glycolysis was enhanced when cardiac fibroblast was activated. Glycolysis inhibition can alleviate the activation of cardiac fibroblast. Compared with non-fibrotic heart tissues, we uncovered that glycolysis increased together with fibrosis and fibroblast activation in human fibrotic heart tissues.

CONCLUSIONS Cardiac fibrosis is along with enhanced glycolysis. Glycolysis inhibition at the proper time and dosage can alleviate cardiac fibrosis progress and cardiac fibroblast activation after myocardial infarction.

GW31-e0019

A novel nanoparticles-based layer-by-layer targeted system to deliver miRCombo to fibroblasts in vivor to realize reprogramming into iCMs

Qiaozi Wang, Zheyong Huang, Junbo Ge
Zhongshan Hospital, Fudan

OBJECTIVES Heart diseases are the leading cause of death worldwide every year. Adult mammalian cardiomyocytes hold limited proliferative capacity so that regenerative therapies are needed. The direct reprogramming from fibroblasts into induced cardiomyocytes (iCMs) has shown much potential in the regenerative medicine, whereas its efficiency remains pretty low and latent safety issues may exist. Therefore, noninvasive intravenous delivery of key reprogramming-related factors to the injured heart might be the more ideal route. Fibroblasts within 3 days after acute myocardial infarction are the target cells of direct cardiac reprogramming. In this specific time window, neutrophils hold the strongest chemotaxis ability in the infarct area, as activated fibroblast surface glycoprotein TN-C secretion peaked. Recently nanoparticles have shown great benefit in gene delivery and in vivo targeting strategy. Our study aims to design a novel biomimetic nanoparticles-based layer-by-layer targeted system to deliver miRCombo to fibroblasts in vivo in order to realize reprogramming into iCMs.

METHODS Mesoporous silica nanoparticles (MSNs) were synthesized by chemical solution reaction. Neutrophil membrane protein (Neu) were obtained by ultracentrifugation. We assemble the FH-Neu-LiMSNs/miR by classical thin film hydration. Nanoparticles were injected by tain vein and the mice were killed after 2 weeks to evaluate the therapeutic effect.

RESULTS We successfully finished the package of nanoparticles, which were verified by transmission electron microscope. The core layer is mesoporous silica loaded with microRNAs, while biomimetic nanoliposomes of neutrophils with FH peptide coated outer layer. The nanoparticles were stable after freeze thawing and held relatively long half-life period in vivo. In vitro, the nanoparticles had the capacity of chemotaxis to chemotactic factor and could bind the injured fibroblasts by FH peptide. What's more, these components did not influence the reprogramming effect of miRCombo in vivo. The nanoparticles could target the injured area after tail vein injection of MI model mice, revealed by in-vivo imaging system. After 2 weeks, histologic section fluorescence staining showed that regenerative iCMs could be observed in the infarcted area and had the similar structure with normal cardiomyocytes. Masson staining and echocardiography showed improved cardiac function and decreased fibrotic area.

CONCLUSIONS Our study showed that we successfully designed the novel nanoparticles to target the fibroblasts in the injured heart and could promoted cardiac regeneration and improve cardiac function after MI. Our system provides a new strategy for the regenerative medicine and holds great potential in clinical translation.

GW31-e0025

Interleukin-12p35 knockout aggravates lipopolysaccharide-induced cardiac dysfunction by regulating macrophage polarization

Zhen Wang, Di Ye, Jing Ye, Menglong Wang, Yao Xu, Jianfang Liu, Jishou Zhang, Mengmeng Zhao, Jun Wan
Renmin Hospital of Wuhan University

OBJECTIVES Sepsis-induced cardiac dysfunction is a common complication of sepsis and is associated with decreased survival of septic patients. Previous studies have demonstrated that interleukin (IL)-12p35 knockout regulates the progression of various cardiovascular diseases, such as acute myocardial infarction and hypertension. However, the effects of IL-12p35 on sepsis development remain unclear. Hence, this study aimed to determine the role of IL-12p35 in sepsis-induced cardiac dysfunction and explore its underlying mechanisms.

METHODS Lipopolysaccharide (LPS) was used to induce sepsis and myocardial injury, and the effect of LPS treatment on cardiac IL-12p35 expression was assessed. In addition, IL-12p35 knockout mice were used to determine the role of IL-12p35 in sepsis-induced cardiac dysfunction.

RESULTS First, we observed that LPS treatment significantly increased the cardiac expression level of IL-12p35. In addition, our findings demonstrated that IL-12p35 knockout mice exhibited higher serum and cardiac lactate dehydrogenase (LDH) levels, higher serum and cardiac creatine kinase-myocardial band (CK-MB) levels, and lower survival rates than LPS-treated mice. Moreover, IL-12p35 deletion further increased M1 macrophage differentiation and decreased M2 macrophage differentiation in LPS-treated mice. IL-12p35 deletion also downregulated the activity of AMP-activated protein kinase (AMPK) but increased the levels of phosphorylated p65 (p-p65) and phosphorylated NF-κB inhibitor alpha (p-IκBα).

CONCLUSIONS Knockout of IL-12p35 in mice aggravated LPS-induced cardiac injury and dysfunction by exacerbating the imbalance of M1 and M2 macrophages. These results suggest that IL-12p35 is an attractive target for treating sepsis-induced cardiac dysfunction.

GW31-e0028

Exercise induced peptide TAGLN protects cardiomyocytes from ischemia injury and oxidative stress through regulating PKG-c-Cbl interaction

Zijie Cheng, Lingmei Qian
Department of Cardiology, The First Affiliated Hospital of Nanjing Medical University

OBJECTIVES Recent studies have revealed that proper exercise can reduce the risk of chronic disease and is beneficial to the body. Peptides have been shown to play an important role in various pathological processes, including cardiovascular diseases. However, little is known about the role of exercise-induced peptides in cardiovascular disease. We aimed to explore the function and mechanism of TAGLN peptide in ischemic injury and oxidative stress.

METHODS Cell viability, ROS, LDH, JC-1, TUNEL, Apoptosis were performed to evaluate the function of peptide TAGLN in vitro. Cardiac function, cardiac remodeling, HE staining, infarction size, Masson staining, cardiac markers were investigated to assess the function of peptide TAGLN in vivo. Pull-down, silver staining, Co-IP, Ubiquitination, Half-life and degradation were performed to analyze the mechanism of peptide TAGLN involved.

RESULTS Treatment with TAGLN peptide significantly improved cell viability, the mitochondrial membrane potential, and ROS levels and reduced LDH release, the apoptosis rate and caspase 3 activation in vitro. In vivo, TAGLN ameliorated MI and heart failure induced by I/R or DOX treatment. Pull-down assays showed that TAGLN can bind to PKG. The TAGLN-PKG complex inhibited PKG degradation through the UPS. We also identified cCbl as the E3 ligase of PKG and found that the interaction between these proteins was impaired by TAGLN treatment. In addition, we provided evidence that TAGLN mediated Lys48-linked polyubiquitination and subsequent proteasomal degradation.

CONCLUSIONS Our results reveal that a novel exercise-induced peptide, TAGLN, can inhibit PKG degradation by serving as a competitive binding peptide to attenuate the formation of the PKG-cCbl complex. Treatment with TAGLN may be a new therapeutic approach for MI.

GW31-e0054

Therapeutic targets of rosuvastatin on heart failure and associated biological mechanisms: a study of network pharmacology and an in vivo study

Zheng Lian, Chen Hong
Peking University People's Hospital

OBJECTIVES To explore the potential targets underlying the effect of rosuvastatin on heart failure (HF) by utilizing a network pharmacology approach and animal experiments to identify the results.

METHODS PharmMapper and other databases were mined for information relevant to the prediction of rosuvastatin targets and HF-related targets. Then, the rosuvastatin-HF target gene networks were created in Cytoscape software. Eventually, the targets and enriched pathways were examined by Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis. Furthermore, we constructed an HF animal model and used rosuvastatin to treat them, identifying the changes in heart function and related protein expression.

RESULTS Thirty-five intersection targets indicated the therapeutic targets linked to HF. GO analysis showed that 481 biological processes, 4 cellular components and 23 molecular functions were identified. KEGG analysis showed 13 significant treatment pathways. In animal experiments, rosuvastatin significantly improved the cardiac function of post-myocardial infarction mice and prevented the development of HF after myocardial infarction by inhibiting IL-1β expression.

CONCLUSIONS The therapeutic mechanism of rosuvastatin against HF may be closely related to the inhibition of the expression of apoptosis-related proteins, inflammatory factors, and fibrosis-related genes. However, IL-1β is one of the most important target genes.

GW31-e0055

MicroRNA-21 mediated a positive feedback on angiotensin II induced cardiac fibrosis post myocardial infarction

Dongjiu Li, Chengyu Mao, Changqian Wang
Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine

OBJECTIVES Post myocardial infarction (MI) fibrosis has been identified as an important factor in the progression of remodeling and heart failure. Previous studies have revealed that microRNA-21 (miR-21) played an important role in the pathogenesis of fibrosis. However, the exact role of miR-21 in post-MI fibrosis remains to be elucidated.

METHODS Wild type (WT) and miR-21 knockout (KO) mice were used and subjected to permanent left anterior descending coronary artery ligature.

RESULTS Wild type (WT) and miR-21 knockout (KO) mice were used and subjected to permanent left anterior descending coronary artery ligature. Compared with WT, miR-21 KO mice displayed smaller fibrotic area revealed by Masson's trichrome staining as well as decreased expression of TGF-β, collagen Iα, α-SMA and Fibroblast activation protein (FAP), key markers of fibrotic process. In parallel, angiotensin II (Ang II) induced expression of α-SMA and FAP could be partially downregulated by miR-21 KO in mice primary cardiac fibroblasts (CFs). Mechanistically, we found that the expression of Sprouty1 (Spry1), a previously reported target of miR-21, was markedly elevated in miR-21 KO mice after MI, which could further inhibit the phosphorylation of extracellular-signal-regulated kinase (ERK1/2). In vitro study showed that Ang II promoted the phosphorylation of ERK1/2, activating TGF-β/Smad2/3 pathway. Phosphorylated Smad2/3 (p-Smad2/3) could further enhance the expression of α-SMA and FAP and may promote the maturation of miR-21, thus downregulating Spry1. In vitro knockdown of Spry1 by siRNA could rescue the effects of miR-21 inhibition on ERK/TGF-β/Smad2/3 signaling. Furthermore, in vivo inhibition of Spry1 could rescue the effects of miR-21 KO on cardiac fibrosis.

CONCLUSIONS These findings suggested that miR-21 promoted post MI fibrosis through targeting Spry1. Furthermore, miR-21 mediated a positive feedback on Ang II induced ERK/TGF-β/Smad pathway. Thus, targeting miR-21-Spry1 axis may be a promising therapeutic option for ameliorating cardiac fibrosis post MI.

GW31-e0069

Smooth muscle SIRT1 retards thoracic aortic aneurysm/dissection development in mice

Fang Wang[1], Yimin Tu[1], Yanxiang Gao[1], Houzao Chen[2], Jingang Zheng[1]
[1]Department of Cardiology, China-Japan Friendship Hospital, Beijing, China
[2]State Key Laboratory of Medical Molecular Biology, Department of Biochemistry and Molecular Biology, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

OBJECTIVES Advancing age is the major risk factor of thoracic aortic aneurysm/dissection (TAAD). However, the causative link between age-related molecules and TAAD remains elusive. Here we first report a role of SIRT1, known as Class III histone deacetylase and the best studied member of Sirtuin family relevant to aging and longevity, in the prevention of TAAD *in vivo*.

METHODS Male SIRT1 smooth muscle specific transgenic (ST-Tg) mice, SIRT1 smooth muscle specific knockout (ST-KO) mice and their wild type (WT) littermates with C57BL/6J background were used to establish a TAAD

model by oral administration of 3-aminopropionitrile fumarate (BAPN). The incidence and fatality rate of TAAD were analyzed between different groups. Western blotting and real-time PCR were utilized to examine matrix metallopeptidase 2 (MMP2) expression in aortas or cultured A7r5 cells. To clarify the epigenetic mechanism of MMP2 expression regulated by SIRT1 in vascular smooth muscle cells (VSMCs), chromatin immunoprecipitation (ChIP) assay was performed.

RESULTS BAPN treatment remarkably increased the incidence of TAAD in WT mice, which was attenuated in ST-Tg mice. Moreover, ST-KO promoted the fatality rate of TAAD induced by BAPN in mice. Mechanistically, SIRT1 overexpression reduced MMP2 level after BAPN treatment in both mouse aortas and cultured A7r5 cells. We further found that downregulation of BAPN-induced MMP2 expression by SIRT1 was mediated by deacetylation of histone H3 lysine 9 (H3K9) on *Mmp2* promoter *in vitro*.

CONCLUSIONS We are the first to demonstrate that SIRT1 in VSMCs could be a novel therapeutic target for TAAD management.

GW31-e0100

Co-expression network analysis revealing the potential regulatory roles of lncRNAs in atrial fibrillation

Lishui Shen[1], Xiaofeng Hu[2], Yan Yao[1]
[1]Fuwai Hospital, Chinese Academy of Medical science, Peking Union Medical College
[2]Shanghai Chest Hospital, Shanghai Jiaotong University

OBJECTIVES Atrial fibrillation (AF) is one of the most common heart arrhythmic disorders all over the world. However, it is worth noting that the mechanism underlying AF is still dimness.

METHODS In this study, we implemented a series of bioinformatics methods to explore the mechanisms of lncRNAs underlying AF pathogenesis. The present study analyzed the public datasets (GSE2240 and GSE115574) to identify differentially expressed long non-coding RNAs (lncRNAs) and mRNAs in the progression of AF.

RESULTS Totally, 71 differentially expressed lncRNAs and 390 DEGs were identified in AF. Next, we performed bioinformatics analyses to explore the functions of lncRNAs in AF. Gene Ontology (GO) analysis indicated that differentially expressed lncRNAs were involved in regulating multiple key biological processes, such as cell cycle and signal transduction. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis demonstrated these lncRNAs were associated with the regulation of MAPK and Wnt signaling pathways. Eight lncRNAs (RP5-1154L15.2, RP11-339B21.15, RP11-448A19.1, RP11-676J12.4, LOC101930415, MALAT1, NEAT1, and PWAR6) were identified to be key lncRNAs and widely co-expressed with a series of differentially expressed genes (DEGs).

CONCLUSIONS Although further validation was still needed, our study may be helpful to elucidate the mechanisms of lncRNAs underlying AF pathogenesis and providing further insight into identifying novel biomarkers for AF.

GW31-e0101

Tyrosine kinase inhibitor – relationship mechanism of lapatinib induced cardiotoxicity

Weijie Wang, Yao Zhang
The Second Affiliated Hospital of Harbin Medical University

OBJECTIVES With the development of research and application of anti-tumor drugs, the survival rate of cancer patients has increased year by year, but the cardiovascular disease problems caused by the use of anti-tumor drugs have become increasingly prominent. In recent years, the emerging discipline of oncology and cardiology has received more and more attention. Since the FDA approval in 2006, tyrosine kinase inhibitors (TKIs) have been clinically used to treat many types of cancer. Compared with previous drugs, they have a stronger anti-tumor effect. TKIs act as competitive inhibitors of tyrosine kinase binding to ATP, blocking the signal transduction of cell proliferation. Unlike trastuzumab and other drugs, some of the drugs in TKIs are multi-kinase target inhibitors, and other kinases that are not targeted to specific kinases may cause side effects, such as cardiovascular reactions. The study found that the direct effect of TKIs on cardiomyocytes may lead to heart failure, cardiomyopathy, conduction changes and prolonged QT intervals, leading to malignant arrhythmias until cardiac arrest. Based on the problem of anti-tumor drugs leading to cardiotoxicity, we explored the mechanism of targeting anti-tumor drugs tyrosine kinase inhibitors (TKIs)-lapatinib (cardatin toxicity), especially heart failure.

METHODS Through bioinformatics analysis, we integrated pharmacogenomics and GWAS catalog database to analyze genes related to lapatinib and heart failure. After that, we searched for related downstream targets on the string protein interaction website and predicted related signaling pathways.

RESULTS We integrated analysis of lapatinib and heart failure related genes through pharmacogenomics and GWAS catalog database, and obtained two SNP sites with higher scores, rs14213603 (score 2b, located in EGFR) and rs14145204 (score 3A, located ESR1). Through the String website to search for EGFR-related downstream pathway targets, we found that the proteins that interact most closely with EGFR, such as HRAS and EREG, are related to the ErBb signaling pathway. The specific kinase inhibition target of lapatinib is ErBb2. It is now found that ErBb2 is a molecule related to cardiac regeneration and has a protective effect on cardiomyocytes. Therefore, we believe that lapatinib inhibits EGFR and ErBb signaling pathways, causing off-target effects, inducing cardiomyocyte damage and leading to heart failure.

CONCLUSIONS (1) Lapatinib and human heart failure-related genes share a common SNP site. (2) Lapatinib inhibits EGFR and ErBb signaling pathways, causing off-target effects, inducing cardiomyocyte damage and leading to heart failure.

GW31-e0104

Double checked hub genes and pathways involved in the immune response in calcific aortic valve stenosis

Meng Wang, Haifeng Zhang, Ganglan Fu, Minnan Gao, Lu Zhang, Huiqi Jiang, Jingfeng Wang, Yanqi Yang
Sun Yat-sen Memorial Hospital, Sun Yat-sen University

OBJECTIVES As one of the most common valvulopathies, calcific aortic valve stenosis (CAVS) has profound influence upon the aging population worldwide. Its progression involves complex immunological processes, molecular pathways and genetic factors. This research was conducted to comprehensively analyze the related immune cells and epigenic etiology in this biochemical process.

METHODS The data about CAVS were collected from GEO database and analyzed with R. The fastq files of RNA-sequencing data was processed with kallisto (0.44.0) in Linux and sleuth package (0.30.0) in R. The expression profiles from different platforms were combined to detect the immunological cellular components by using the online tools NetworkAnalyst and Cibersort. The weighted gene correlation analysis (WGCNA) was performed for each individual dataset. Subsequently a consensus network was constructed to identify the significantly altered gene modules. Then the results retrieved from NetworkAnalyst and WGCNA were compared to confirm the overlapped hub genes and enriched pathways. The immune cells infiltration pattern was related to the gene modules.

RESULTS Totally 66 samples in datasets GSE55492, GSE12644, GSE51472, GSE83453 were included and annotated as CAV group (n=33) and NAV group (n=33). In NetworkAnalyst 16,867 genes were matched for all data sets and 1494 different genes were identified. Cibersort showed macrophage M2 constituted 42.8% of all the immune cells in normal valve tissue and drop to 35.4% in calcified valve (P=0.0001). The hub genes FN1, VCAM1, IL7R, VAV1, BTK, PLAU, ARPC1B, CCL5, CDKN2A obtained from both WGCNA and NetworkAnalyst were related to CAVS positively. The hub genes CCL5, CDKN2A were positively correlated with regulatory T cells while negatively with M2 macrophage in calcified valves.

CONCLUSIONS The pathogenesis of CAVS involved extensive participation of immunological responses at cellular and molecular levels. The hub genes FN1, VCAM1, IL7R, VAV1, BTK, PLAU, ARPC1B, CCL5, CDKN2A and Toll-like receptor signaling, NF-kappa B signaling, ECM-receptor interaction, Focal adhesion, hematopoietic cell lineage pathways were closely linked to CAVS.

GW31-e0106

N-cadherin overexpression mobilizes the protective effects of mesenchymal stromal cells against ischemic heart injury through a β-catenin dependent manner

Wenjun Yan[1], Chen Lin[1], Yunlong Xia[1], Xinliang Ma[2], Ling Tao[1]
[1]Department of Cardiology, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, China
[2]Department of Medicine and Department of Emergency Medicine, Thomas Jefferson University, Philadelphia, PA 19107, USA

OBJECTIVES Mesenchymal stromal cells (MSC)-based therapy is promising against ischemic heart failure (IHF). However, its efficacy is limited due to low cell retention and poor paracrine function. A transmembrane protein capable of enhancing cell–cell adhesion, N-cadherin garnered attention in the field of stem cell biology only recently. The current study investigates whether and how N-cadherin may regulate MSC retention and cardioprotective capability against IHF.

METHODS Adult mice-derived adipose tissue-derived MSC (ADSC) were transfected with adenovirus harboring N-cadherin (ADSC-Ncad), T-cadherin (ADSC-Tcad), or control adenovirus (ADSC-con). CM-DiI-labeled ADSC were intramyocardially injected into the infarct border zone at 3 sites immediately

after myocardial infarction (MI) or myocardial ischemia/reperfusion (MI/R). ADSC retention/survival, cardiomyocyte apoptosis/proliferation, capillary density, cardiac fibrosis, and cardiac function were determined. Discovery-driven/cause-effect analysis was employed to determine the molecular mechanisms.

RESULTS Compared to ADSC-con, N-cadherin overexpression (but not T-cadherin) markedly increased engrafted ADSC survival/retention up to 7 days post-MI. Histological analysis revealed that ADSC-Ncad significantly preserved capillary density and increased cardiomyocyte proliferation, and moderately reduced cardiomyocyte apoptosis 3 days post-MI. More importantly, ADSC-Ncad (but not ADSC-Tcad) significantly increased LVEF and reduced fibrosis in both MI and MI/R mice. In vitro experiments demonstrated that N-cadherin overexpression promoted ADSC-cardiomyocyte adhesion and ADSC migration, enhancing their capability to increase angiogenesis and cardiomyocyte proliferation. MMP-10/13 and/or HGF upregulation is responsible for N-cadherin's effect upon ADSC migration and paracrine angiogenesis. N-cadherin overexpression promotes cardiomyocyte proliferation by HGF release. Mechanistically, N-cadherin overexpression significantly increased N-cadherin/β-catenin complex formation and active β-catenin levels in the nucleus. β-Catenin knockdown abolished N-cadherin overexpression induced MMP-10, MMP-13, and HGF expression, and blocked the cellular actions and cardioprotective effects of ADSC overexpressing N-cadherin.

CONCLUSIONS We demonstrate for the first time that N-cadherin overexpression enhances MSC protective effects against IHF via β-catenin mediated MMP-10/MMP-13/HGF expression and production, promoting ADSC/cardiomyocyte adhesion and ADSC retention (Circulation Research. 2020;126:857–874, Cover paper, F1000Prime recommendation).

GW31-e0109

Time-restricted feeding alleviates metabolic inflexibility and cardiac dysfunction induced by simulated microgravity via enhancing cardiac FGF21 signaling

Xinpei Wang, Jiaxin Zhang, Changyang Xing, Xing Zhang, Yunchu Li, Feng Gao, Jia Li
Fourth Military Medical University

OBJECTIVES Dietary restriction has been well-described to improve health metrics, but whether it could benefit pathophysiological adaptation to extreme environment, e.g., microgravity, remains unknown. Here we investigated the effects of a daily rhythm of fasting and feeding without reducing caloric intake on cardiac function and metabolism against simulated microgravity.

METHODS Male rats under *ad libitum* feeding or time-restricted feeding (TRF; food access limited to 8 hours every day) were subjected to hindlimb unloading (HU) to simulate microgravity for 6 weeks. Left ventricular (LV) synchronicity and cardiac function were assessed by two-dimensional speckle tracking echocardiography. Glucose metabolites in the heart and blood were measured by liquid chromatography-tandem mass spectrometry.

RESULTS LV of HU rats displayed increased standard deviations of time to peak strain and maximum opposing wall delay, indicating a disturbed synchronicity compared with control rats. As a result, both cardiac systolic and diastolic function were declined in HU rats. In addition, HU inhibited glucose uptake and glucose oxidation by decreasing GLUT1 expression and inhibiting pyruvate dehydrogenase (PDH) activity in the heart, indicating an impaired cardiac metabolic flexibility. All these were largely rescued by TRF. Furthermore, TRF significantly improved contractile function of cardiomyocytes isolated from HU rats, although it showed no effects on HU-induced loss of cardiac mass. Interestingly, TRF raised liver-derived fibroblast growth factor 21 (FGF21) level and enhanced cardiac FGF21 signaling as manifested by upregulation of FGF receptor-1 expression and its downstream markers including phosphorylation of extracellular signal regulated kinase-1/2 and mRNA expression of *PPARγ coactivator-1α* in HU rats. In isolated cardiomyocytes, FGF21 treatment increased PDH activity, improved glucose utilization, and consequently enhanced cell contractile function. Finally, liver-specific knockdown of FGF21 expression by AAV8 carrying FGF21 shRNA abrogated the cardioprotective effects of TRF in HU rats.

CONCLUSIONS These data demonstrate that TRF ameliorates cardiac metabolic inflexibility and dysfunction induced by simulated microgravity through, at least partially, enhancing cardiac FGF21 signaling. Our data shed new lights on the cardiometabolic regulation of TRF and suggest TRF as a potential protective measurement for cardiovascular adaption to microgravity.

GW31-e0122

CM-4620 attenuates myocardial ischemia-reperfusion injury via inhibiting oxidative stress and macrophages endoplasmic reticulum calcium influx

Bing Xiao, Xiuchun Yang
Department of Cardiology, the Second Hospital of Hebei Medical University, Shijiazhuang 050000, China

OBJECTIVES To explore the effect of STIM1 inhibitor CM-4620 on endoplasmic reticulum (ER) calcium influx in macrophages, and its effect on oxidative stress induced by myocardial ischemia-reperfusion injury.

METHODS An in vivo model of myocardial ischemia-reperfusion (I/R) was established by using 30 C57BL/6J mice, which were divided into sham group, I/R group and CM-4620 group. Before surgery of 24 h, mice in CM-4620 group were treated 2 mM CM-4620 by tail vein injection and rats in sham and I/R groups were given same volume of saline. After surgery of 24 h, heart tissues were obtained. Masson staining was carried out to observe infiltration degree of myocardial tissues. DHE staining was used to detect ROS levels, and Tunel staining was used to detect cell apoptosis. An in vitro model was also established by using bone marrow-derived macrophages (BMDM), which were divided into control group, LPS group and LPS+CM-4620 group. Intercellular Ca^{2+} concentration was determined with Fura-2/AM fluorescent staining. The expression of STIM1, Orail, caspease-3, caspease-9, Bcl-2, Bax, IL-1beta, IL-6, TNF-alpha and IFN-gamma in both myocardial tissues and cells were detected by western blotting.

RESULTS In vivo model, the inflammatory infiltration degree, the ROS levels of myocardial tissues and the cell apoptosis in CM-4620 group were significantly reduced than those of I/R group (P<0.01). The expression of STIM1, orail, caspease-3, caspease-9, Bax, IL-1beta, IL-6, TNF-alpha and IFN-gamma were significantly lower in CM-4620 group than in I/R group (P<0.01), but the expression of Bcl-2 was significantly increased in CM-4620 group than in I/R group (P<0.01). In vitro model, CM-4620 significantly reduced the intercellular Ca^{2+} concentration and the ROS levels in LPS+CM-4620 group than in LPS group (P<0.01). The results of western blotting showed the decreased expression of STIM1, orail, caspease-3, caspease-9, Bax, IL-1beta, IL-6, TNF-alpha and IFN-gamma and the increased expression of Bal-2 in LPS+CM4620 group than in LPS group (P<0.01).

CONCLUSIONS CM-4620 can inhibit oxidative stress injury of myocardial ischemia-reperfusion by inhibiting calcium influx of macrophages endoplastic reticulum.

GW31-e0135

Influence of Dl-3-N-butylphthalide on infarction size in rats with acute myocardial infarction

Yanbo Wang
The Second Hospital of Hebei Medical University

OBJECTIVES To study the influence of dl-3-N-butylphthalide (NBP) on infarction size in rats with acute myocardial infarction (AMI).

METHODS AMI model was established via ligation of left anterior descending artery. A total of 36 healthy male Sprague-Dawley rats (weight, 180±20 g), were randomly assigned to the sham-operation group (SO group, n=12), the model group (n=12) and the NBP group (n=12). The rats in the NBP group were treated with intraperitoneal injection administration of 60 mg/kg/body weight NBP once a day. The rats in the other groups were given distilled water of the same volume. The MI area in each group was detected via TTC staining. The concentrations of CK-MB and LDH were detected. The concentrations of TNF-α, IL-6, MDA and SOD were measured by ELISA.

RESULTS Compared with the SO group, the myocardial infarct sizes in the model group and the NBP group were significantly increased (P<0.001), and the infarct size in the NBP group was lower than that in the model group (28o.6±5.82% vs. 37.74±10.18%, P<0.05). The levels of TNF-α in NBP group and model group were significantly increased compared with that in the SO group (<0.001), while the level of TNF-α in the NBP group was significantly lower than that in the model group (29.01±0.81 pg/mgprot vs. 37.72±0.96 pg/mgprot, P<0.05). The level of IL-6 in the model group and NBP group was significantly higher than that in the SO group, and it was lower than that in the model group (24.13±0.74 pg/mgprot vs. 27.53±1.03 pg/mgprot, P<0.05). The levels of MDA in the model group and the NBP group were significantly higher (<0.001), and the level of NBP group was lower than that in the model group (4.10±0.18 nmol/mgprot vs. 4.77±0.25 nmol/mgprot, P<0.05). The level of SOD in the model group and NBP group were lower (<0.001), and the SOD level in the NBP group was higher than that of the model group (53.49±3.89 U/mgprot vs. 38.06±5.28 U/mgprot, P<0.05).

CONCLUSIONS NBP could reduce the infarction size in SD rats with AMI.

GW31-e0139

Changes of CTRP6 before and after coronary intervention in patients with acute myocardial infarction

Ningkun Zhang, Yu Chen, Li Zhao, Jiangchun He, Lihua Wang, Tianchang Li
Department of Cardiology, The Sixth Medical Center, Chinese PLA General Hospital

OBJECTIVES Investigate the effect of CTRP6 changes before and after coronary interventional surgery on patients with acute myocardial infarction (ami) and related factors of cardiovascular and metabolic disorders.

METHODS Selection of the sixth medical center of PLA general hospital during 2018–2019 in patients with acute myocardial infarction underwent emergency interventional therapy in 80 cases of normal control group selected volunteers check-up blood specimens of 20 cases, preoperative and postoperative patients with acute myocardial infarction (ami) venous blood was drawn, and the normal control group take a physical examination results of normal volunteers a venous blood and 4 c centrifugal 1200 g × 20 min, collect serum, using enzyme-linked immunosorbent assay (ELISA) method to detect CTRP6 level, collect basic data, detection of TC, TG, HDL-C, LDL-C, FBG and biochemical indexes such as, To analyze the correlation between changes before and after emergency intervention of CTRP6 and relevant clinical data.

RESULTS The age of patients with acute myocardial infarction (ami) was (52.7±12.6) years old, 57.8% of male patients and 42.2% of female patients, the smoking rate was 33.4%, the drinking rate was 35.7%, and the normal control group was (29.7±6.5) years old. In patients with acute myocardial infarction, preoperative CTRP6 (135.13±22.52) ng/mL was significantly lower than postoperative CTRP6 (227.44±37.28) ng/mL (P<0.01), and preoperative CTRP6 (135.13±22.52) ng/mL was significantly lower than the normal control group (219.38±31.68) ng/mL (P<0.01). After CTRP6 surgery (227.44±37.28) ng/mL showed no significant change compared with the normal control group (219.38±31.68) ng/mL (P>0.05). Correlation analysis showed that preoperative CTRP6 level was positively correlated with hdl-c; preoperative CTRP6 level was negatively correlated with BMI, TG, and FBG; preoperative CTRP6 level was not correlated with age, gender, smoking, drinking, TC, and ldl-c.

CONCLUSIONS CTRP6 in serum in patients with acute myocardial infarction was significantly reduced, terminate the risk factors in patients with acute myocardial infarction after CTRP6 rise and close to the control group, CTRP6 likely to be involved in the acute myocardial infarction (ami) and its related risk factors of metabolic development process. Studies show that members of the family of CTRP protein similar to adiponectin, members of the family of function CTRP in regulating the protection of cardiovascular disease, inflammation, and sugar play an important role in the regulation of lipid metabolism, the role of different members of the family of CTRP is different also, studies have shown that CTRP6 can significantly reduce the cardiac fibrosis after myocardial infarction, heart after infarction and TGF-β1 processing of fibroblasts, CTRP6 can inhibit myocardial fibroblasts differentiation and the production of extracellular matrix. In vitro knockout fibroblasts, CTRP6 enhanced the differentiation of TGF-TGF-β1 induced cardiac fibroblasts and the expression of various extracellular matrix proteins. In patients with cardiometabolic disorders, this study provides an experimental basis for whether CTRP6 can be used as an independent detection index to assist in the prediction of the occurrence of acute myocardial infarction.

GW31-e0146

NLRP3 inflammasome aggravates cardiac remodeling induced by pressure overload via GSDMD-mediated pyroptosis

Jieyun You[1], Jian Wu[2], Shijun Wang[2], Fangjie Dai[2], Yungzeng Zou[2]
[1]Department of Cardiology, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China
[2]Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital and Institutes of Biomedical Sciences, Fudan University, Shanghai, China

OBJECTIVES NLRP3 inflammation has emerged as an inflammatory cascade trigger contributing to cardiac remodeling induced by pressure overload. NLRP3 inflammasome related pyroptosis is a newly reported programmed cell death. As the pyroptosis executor, gasdermin D (GSDMD) forms pores on the lipid membrane, promotes the release of inflammatory cytokines and triggers inflammatory cascade. But its role remains to be elucidated in cardiac remodeling after pressure unloading.

METHODS By genetic interference with NLRP3 and GSDMD, we investigated the role of NLRP3/GSDMD-mediated pyroptosis on cardiac remodeling in mice subjected to transverse aortic constriction (TAC) for 4 weeks. Left ventricular structure and function were evaluated by echocardiographic, hemodynamic, and histological analyses. Signaling pathways related to pyroptosis, hypertrophy, fibrosis, angiogenesis, and apoptosis were analyzed by histological analysis, western blotting, ELISA, and real-time quantitative PCR.

RESULTS Our found that pressure overload upregulated the expression of NLRP3/GSDMD pathway, accompanied by the activation of inflammatory cytokines, and therefore deteriorated cardiac remodeling at least partially by activation of JNK1/2 and p38 signaling pathways. NLPR3 deficiency reversed the cleavage of GSDMD, leading to attenuation of cardiac remodeling and dysfunction induced by pressure overload. Further studies showed this process was independent of the Akt signaling pathway. On the other hand, overexpression of GSDMD abolished the cardioprotective effect of NLRP3 deficiency.

CONCLUSIONS Our data indicated that pressure overload upregulates NLRP3 to recruit inflammasome, therefore triggers pyroptosis and inflammation in a GSDMD-dependent manner, further activates JNK1/2 and p38 signaling pathways, and plays a critical role in cardiac remodeling induced by pressure overload. This study identified NLRP3/GSDMD as a promising therapeutic target for cardiac remodeling and heart failure.

GW31-e0147

A novel exercise-induced peptide EIP-22 protects cardiomyocytes from myocardial I/R injury through regulating JAK2/STAT3 signalling pathway

Li Zhang, Lingmei Qian
The First Affiliated Hospital of Nanjing Medical University

OBJECTIVES The aim of this study is to elucidate the protective effect and mechanism of exercise-induced peptide EIP-22 in myocardial I/R injury, and to provide a new idea for the clinical treatment of ischemic heart disease.

METHODS We first determined the effect of EIP-22 on hypoxia/reoxygenation (H/R)- or H2O2-induced injury in the neonatal rat ventricular myocytes (NRVMs) via assessing cell viability and lactate dehydrogenase (LDH) level. In addition, TUNEL staining and western blot analysis of apoptosis related proteins were used to detect apoptosis level. Meanwhile, mitochondrial membrane potential (MMP) and reactive oxygen species (ROS) accumulation was assessed by fluorescence microscope. Then we conducted rat I/R model and verified the effect of EIP-22 by measuring cardiac function, evaluating heart pathology and detecting serum LDH, CK-MB and cTnI concentrations. Finally, the main signaling pathway was analyzed by RNA-seq, and the activities of JAK2 and STAT3 were detected via western blot to illuminate molecular mechanism.

RESULTS In vitro, EIP-22 treatment significantly improved cells viability and MMP and attenuated the LDH release level, ROS accumulation, apotosis rate and the activation of apoptosis related proteins in NRVMs. In vivo, EIP-22 distinctly improved cardiac function, ameliorated myocardial infarction (MI) and decreased serum CK-MB and cTnI concentrations in rat I/R model. Mechanistically, JAK/STAT signaling pathway was focused by RNA-seq and we confirmed that treatment with EIP-22 elevated the expression of p-JAK2 and p-STAT3. Moreover, AG490, a selective inhibitor of JAK2/STAT3, eliminated the protective roles of EIP-22.

CONCLUSIONS The results uncovered that a novel exercise-induced peptide EIP-22 protected cardiomyocytes from myocardial I/R injury through regulating JAK2/STAT3 signalling pathway. This study suggested EIP-22 might be a new candidate molecule for the treatment of ischemic heart disease.

GW31-e0158

Adipocyte-derived exosomal lncRNA NBR2 cooperated with hnRNPK/SETDB1 complex promotes diabetic myocardial fibrosis through regulating the IκBα/NF-κB pathway

Yue Guo[1,2], Xingfeng Xu[1,2], Xinxue Liao[1,2]
[1]Department of Cardiology, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou 510080, PR China
[2]NHC Key Laboratory of Assisted Circulation (Sun Yat-sen University), Guangzhou, Guangdong 510080, PR China

OBJECTIVES The activation of NF-κB signaling pathway is regarded as the dominant process that correlates with the pathogenesis of diabetic cardiomyopathy (DCM). Recently, accumulating evidence shows that long noncoding RNAs (lncRNAs) play crucial roles in sustaining the NF-κB signaling pathway. However, the underlying mechanisms remain to be understood. In this study, we identified the upregulated expressed lncRNA NBR2 in adipocyte-derived exosomes (AdEXO) and investigated its regulatory role in diabetic myocardial fibrosis.

METHODS We examined the effect of exosomes from diabetic (db/db) mice-derived adipocytes on ANG-II-induced cardiac fibrosis and function in non-diabetic (C57BL/6J mice). In the in vitro study, HG (33 mmol/L) stimulated AdEXO were cultured with adult human cardiac fibroblasts (aHCFs). Differentially expressed lncRNAs in AdEXO were screened using lncRNA sequencing. The functional role of NBR2 was evaluated by both in vitro and in vivo experiments. Bioinformatics prediction, RNA fluorescence in situ hybridization (RNA-FISH) and immunoprecipitation assays were performed to identify the direct interactions between NBR2 and other associated targets, such as hnRNPK and SETDB1. Chromatin isolation by RNA purification assays were utilized to examine the interaction of NBB2 with IκBα promoter.

RESULTS Intramyocardial injection of diabetic adipocyte exosomes in the non-diabetic heart significantly exacerbated myocardial fibrosis, as evidenced by poorer cardiac function and enhancer collagen deposition. Whereas administration of a exosomes biogenesis inhibitor significantly mitigated cardiac fibrosis in diabetic mice. We identified that lncRNA-NBR2 is a common molecule significantly increased in diabetic Ad-EXO and HG-stimulated non-diabetic Ad-EXO. After four weeks of ANG II infusion, EXO-db/dbWT-injected mice displayed significant fibrosis in the heart; however, interestingly, mice receiving NBR2-deficient db/db-EXO showed a decrease in cardiac fibrosis. Similarly, AdEXO-NBR2 promoted aHCFs proliferation and transformation capabilities in vitro. Mechanistically, NBR2 was loaded to adipocyte-secreted exosomes by directly interacting with heterogeneous nuclear ribonucleoprotein K (hnRNPK). Subsequently, exosomal NBR2 was internalized by aHCFs and epigenetically downregulated IκBα expression by recruitment of hnRNPK/SETDB1 and increasing the H3K9 trimethylation level in the IκBα promoter, ultimately activating the NF-κB pathway.

CONCLUSIONS Our findings suggest that AdEXO-NBR2 provides a novel epigenetic mechanism involved in activation of NF-κB signaling pathway and may represent a new therapeutic target of DCM.

GW31-e0174

Effect of Ginkgolide B on myocardial fibrosis in rats with type 2 diabetes mellitus via TGF-β1/Smad signaling pathway

Sai Ye, Fangjun Guo, Renqiang Yang
Department of Cardiology, the Second Affiliated Hospital, Nanchang University, Nanchang 330006, China

OBJECTIVES To observe the influence of Ginkgolide B on myocardial fibrosis in rats with type 2 diabetes mellitus (T2DM) through the transforming growth factor beta-1 (TGF-β1)/Smad signaling pathway.

METHODS The rat model of type 2 diabetes mellitus was established by intraperitoneal injection of low dose streptozotocin (35 mg/kg) and high fat diet. The Sprague Dawley rats were randomly divided into control group (NC group), T2DM (DM group), and Ginkgolide B treatment group (GB group). GB group was established by intraperitoneal injection of a certain dose Ginkgolide B (10 mg/kg) for 12 weeks after successful model-making. The animals were euthanized, blood and myocardial tissues were collected from rats. Next, blood glucose level and body weight were detected. In addition, histopathological changes of the heart were observed with HE staining. The myocardial collagen volume fraction (CVF) was calculated by Masson staining. Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and Western blotting, which were applied to measure the gene and protein expression levels of important molecules in the proliferation and differentiation of myocardial fibroblasts including alpha-smooth muscle actin (α-SMA), and the relevant pathway TGF-β1, p-Smad2/3. Immunohistochemical method was performed to detect the depositions of collagen extracellular matrix proteins Col-I and Col-III.

RESULTS Compared with NC group, the body weight of the rat in DM group was decreased and the blood glucose was increased significantly ($P<0.05$). However, no statistically difference in blood glucose and body weight between the treatment groups and GB group was observed ($P>0.05$). As compared with NC group, CVF and the protein or mRNA levels of Col-III, TGF-β1, p-Smad2/3 and α-SMA were increased markedly in T2DM group ($P<0.05$). immunohistochemistry showed the expression levels of Col-I, Col-III collagen were increased ($P<0.01$). Moreover, CVF and the protein or mRNA levels of TGF-β1, Col-III, p-Smad2/3 and α-SMA in DM group were higher than treatment groups ($P<0.05$). immunohistochemistry showed the expression levels of Col-I, Col-III collagen in DM group were higher than treatment groups ($P<0.05$).

CONCLUSIONS Ginkgolide B has a protective effect on the myocardium of type 2 diabetes mellitus by inhibiting the TGF-β1/Smad2/3 signaling pathway, Ginkgolide B may be a novel medicine for treating diabetic cardiomyopathy.

GW31-e0208

The role of autophagy in granulocyte colony-stimulating factor-induced anti-apoptotic effects in diabetic cardiomyopathy

Guangyin Shen[1], Yisun Song[2], Kyungsoo Kim[2]
[1]Department of Cardiology, Jilin Central Hospital, Jilin, China
[2]Division of Cardiology, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Republic of Korea

OBJECTIVES Previously, we reported that granulocyte-colony stimulating factor (G-CSF) was shown to reduce cardiomyocyte apoptosis in diabetic cardiomyopathy. However, the underlying mechanisms are not yet fully understood. Therefore, we investigated whether the mechanism of the anti-apoptotic effect of G-CSF was associated with autophagy in a rat model of diabetic cardiomyopathy.

METHODS Diabetic cardiomyopathy was induced in rats by a high-fat diet combined with low-dose streptozotocin and the rats were then treated with G-CSF for 5 days. Rat H9c2 cardiac cells were cultured under high glucose conditions as an in vitro model of diabetic cardiomyopathy. The extent of apoptosis and expression of proteins related to autophagy (Beclin-1, LC3-II/LC3-I ratio, and P62) were determined for both models.

RESULTS G-CSF significantly reduced cardiomyocyte apoptosis (25.12±4.24% vs. 34.51±3.93%, $P<0.05$) in the diabetic myocardium in vivo and led to up regulated expression of Beclin-1 (134.55±25.46% vs. 70.08±21.84%, $P<0.05$), and increased the LC3-II/LC3-I ratio (134.57±26.21 vs. 64.48±11.59, $P<0.05$), and down regulated expression of P62 (110.97±13.85% vs. 169.56±18.14%, $P<0.05$) compared with normal rats. Similarly, G-CSF suppressed apoptosis (17.70±5.41% vs. 29.50±3.93%, $P<0.05$) and up regulated expression of Beclin-1 (75.00±5.37% vs. 50.41±7.86%, $P<0.05$), increased the LC3-II/LC3-I ratio (119.36±14.37% vs. 75.07±5.41%, $P<0.05$), and down regulated expression of P62 (68.57±5.31% vs. 134.46±19.55%, $P<0.05$) in high glucose-induced H9c2 cardiac cells in vitro. These effects of G-CSF were abrogated by 3-methyladenine, an autophagy inhibitor.

CONCLUSIONS Our results suggest that G-CSF might reduce apoptosis through up regulation of autophagy.

GW31-e0221

(Pro)renin receptor involves in myocardial fibrosis and oxidative stress in diabetic cardiomyopathy via PRR-YAP pathway

ShiRan Yu[1], Dong Xuefei[2], Yang Min[2], Cao Xinran[2], Xiong Jie[2], Dong Bo[2]
[1]Department of Cardiology, Center for Cardiovascular Translational Research, Beijing Key Laboratory of Early Prediction and Intervention of Acute Myocardial Infarction, Peking University People's Hospital, Beijing 100044, China
[2]Department of Cardiology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, China

OBJECTIVES In this study, we firstly aim to investigate whether excessive PRR in DCM could active YAP, further mediate downstream factors like CTGF and Smad, involving DCM pathological progression. Secondly, whether activated PRR-YAP pathway could be able to trigger cardiac redox reaction and cardiac fibrosis. Thirdly, whether an intervention targeted PRR-YAP pathway could alleviate these pathological injuries and delay disease's progression.

METHODS Wistar rats and neonatal rat cardiac fibroblasts were respectively used in vivo and in vitro studies. In order to observe the effects of PRR mediated YAP pathway on the pathogenesis of DCM, animal experiments were divided into 3 parts, including the evaluation of PRR overexpression effects part, the assessment of the PRR RNAi silencing effects part and the evaluation of YAP RNAi silencing effects part. Recombinant-adenoviruses-carried-PRR-gene (Ad-PRR), recombinant-adenoviruses-carried-PRR-shRNA (Ad-PRR-shRNA) and lentivirus-carried-YAP-shRNA (LV-YAP-shRNA) were constructed and respectively injected these viruses in each group rats. Evaluating PRR and YAP expression in myocardium by immunohistochemical staining and western blotting to assess the efficacy of virus transfection, as well as the effects of PRR expression on YAP expression. Measured NADPH oxidase activity, MDA and SOD levels to explore the role of PRR-YAP pathway in redox reaction of DCM. Measured type I and III collagen expression by immunohistochemical staining to explore the role of PRR-YAP pathway in cardiac fibrosis of DCM. Measured CTGF and Smad3 expression by western blotting to explore underlying mechanism. In addition, in vitro experiments, using Ad-PRR and Ad-PRR-shRNA, meanwhile, introduce YAP specific inhibitor Verteporfin in cardiac fibroblasts along with PRR overexpression to further demonstrate the impact of PRR-YAP pathway on oxidative stress and myocardial fibrosis at cellular aspect.

RESULTS The results displayed that PRR activated YAP expressions and further exacerbated fibrosis and oxidative stress both in myocardium tissues and cardiac fibroblasts under high glucose condition. However, PRR RNAi silencing has opposite effects. Moreover, the administration of YAP inhibitor Verteporfin in vitro and YAP RNAi silencing in vivo could reverse PRR induced fibrosis and oxidative stress. And these effects may associate with the PRR-YAP pathway activate downstream factors expressions, including Smad3 and CTGF.

CONCLUSIONS We concluded that PRR-YAP pathway plays a key role in the oxidative stress and myocardial fibrosis in DCM and the treatment targeting PRR-YAP pathway may be a novel therapeutic way for DCM.

GW31-e0227

Differential gene expression analysis from left atrial specimens and auricle tissue biopsy to screen for potential biomarkers in atrial fibrillation

Shenjie Sun, Ping Zhang
Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing

OBJECTIVES Owing to the complexity of the clinical phenotype and mechanism, the specific pathogenesis of atrial fibrillation (AF) is still not clear,

especially at the genetic level. In search of etiologically guided solutions to improve diagnosis and treatment, in this study, we focused on the differentially expressed genes (DEGs) in AF using left atrial specimens and auricle tissue biopsy from patients to distinguish AF from sinus rhythm (SR) using bioinformatics approaches.

METHODS Microarray data from patient specimens were downloaded from two Gene Expression Omnibus (GEO) datasets (GSE79768 and GSE31821) to identify DEGs according to a log fold-change of >1 (upregulated genes) or >−1 (downregulated genes) and a P-value <0.05. We identified that the DEGs, the hub and key genes respectively from left atrial and auricle tissue. The DEGs were then used to construct a protein-protein interaction (PPI) network to further identify hub and key genes. Functional annotation of the differentially expressed genes was performed using Gene Ontology biological processes, cellular component, and pathway enrichment tools.

RESULTS Overall, we screened out 488 DEGs in GSE79768 from left atrial specimens, including 427 down-regulated genes and 61 up-regulated genes, and 414 DEGs in GSE31821 from the auricle tissue, including 392 down-regulated genes and 22 up-regulated genes. Function enrichment analysis using DAVID tools indicated that top five GO term plasma membrane, extracellular exosome, integral component of plasma membrane, extracellular region, and extracellular space in GSE79768 and top five GO term protein binding, cytosol, extracellular exosome, extracellular space, and cell surface in GSE31821. Further analysis indicated that the common DEGs were enriched in regulation of angiogenesis, cell surface, extracellular space, extracellular exosome, response to mechanical stimulus, and vasculature development. PPI network analysis mapped 758 nodes and 1516 edges in GSE79768, and 237 nodes and 934 edges in GSE31821. CXCR4, TLR4, and KIT were the top three hub genes in GSE79768 from left atrial specimens, whereas BMP4, CDH2, and BMP2 were the top three hub genes in GSE31821 from the auricle tissue. Finally, there is 16 hub genes is coexisting in GSE79768 and GSE31821. Among these, CXCR4 was identified as a key gene in the network (degree>10), with down-regulated expression in both the GSE79768 and GSE31821. PPI network analysis suggested that CXCR4 is the key gene associated with AF.

CONCLUSIONS The findings of our study suggest that the key gene CXCR4 may be associated with AF recurrence and maintenance and can be further explored as novel biomarkers in AF. Consequently, the top five miRNAs for CXCR4 may act as potential biomarkers or therapeutic targets for AF.

GW31-e0240

The non-coding transcript and a peptide encoded by an annotated long non-coding RNA coordinately regulate smooth muscle plasticity and vascular remodeling

Junyi Yu[1,2,3], Gengze Wu[1,2], Xue Gong[1,2], Hao Luo[1,2], Zaicheng Xu[1,2], Qiao Liao[1,2], Zhi Chen[1,2], Miao Tian[1,2], Jining Yang[4], Chen Gao[3], Bing Zhang[5], Christoph Rau[3], Ye Zhang[1,2], Yibin Wang[3], Chunyu Zeng[1,2]
[1]Department of Cardiology, Daping Hospital, The Third Military Medical University, Chongqing, P. R. China
[2]Chongqing Institute of Cardiology, Chongqing, P. R. China
[3]Division of Molecular Medicine, Departments of Anesthesiology, Physiology and Medicine, David Geffen School of Medicine, University of California at Los Angeles (UCLA), Los Angeles, California, USA
[4]Research Center for Nutrition and Food Safety, Chongqing Key Laboratory of Nutrition and Food Safety, Institute of Military Preventive Medicine, Third Military Medical University, Chongqing, P. R. China
[5]Shanghai Center for Systems Biomedicine, Shanghai Jiao Tong University, Shanghai, China

OBJECTIVES Vascular remodeling is a major pathological feature under chronic hypertension. A subset of mammalian long non-coding RNAs (lncRNAs) are reported to encode functional peptides. Yet, in most cases, the coding products and the non-coding transcripts appear to function independently under unrelated mechanisms. Here we aim to illustrate the function and underlying mechanism of a novel peptide encoded by a lncRNA in vascular smooth muscle (VSMC) phenotype switching and vascular remodeling.

METHODS lncRNA-mRNA microarray was used to identify differentially expressed lncRNAs in aorta tissue from hypertensive vascular remodeling rats model. qRT-PCR and Western Blot were used to test RNA and protein expression respectively. CRISPR-Cas9 was used to construct protein ablation and gene knock-out rats. Carotid artery balloon injury was performed to induce vascular remodeling in vivo. siRNAs and lentivirus were used for gene knock-down, while plasmids and adenovirus were used for gene over-expression in vitro. CCK8 and Ki-67 staining were used to test the proliferation, while trans-well and wound scratching assays were used to test the migration of VSMC. RNA-seq was used to test the transcriptome alteration in VSMC. LC-MS was used to identify and co-IP was used to validate the protein interactions. ChIP-seq was used to test the protein-DNA interaction. ChIRP-seq was used to test the DNA-RNA interaction. RIP-PCR was used to validate the protein-RNA interaction. Dual luciferase assay was used to transcription regulation.

RESULTS We identified a conserved, VSMC enriched gene *Phenotype-Switching-Regulator* (*PSR*), which was previously annotated as a lncRNA. The PSR gene actually produced both a peptide (Arteridin) and a regulatory lncRNA (lncPSR). Arteridin and lncPSR were both necessary and sufficient to induce the transition of VSMCs from contractile to proliferative phenotype. Arteridin and lncPSR mediated VSMC gene regulation involved direct binding to a common transcription factor, YBX1. Arteridin modulates nucleic translocation of YBX1, and lncPSR directs chromatin targeting of YBX1 serving as a molecular scaffold. Intriguingly, the *PSR* gene transcription was also robustly induced by Arteridin, forming an auto-regulated feed-forward loop. Both Arteridin and lncPSR were significantly up-regulated in the remodeled arterial tissue from hypertension patients. Finally, both Arteridin protein ablation and PSR gene knockout attenuated neointima formation induced by carotid artery balloon injury in rats.

CONCLUSIONS This study has uncovered a previously uncharacterized genetic feed-forward regulatory circuit in vascular smooth muscle cell gene regulation that involves coordinated function of a regulatory lncRNA and its encoded peptide through a common transcription factor. Targeting Arteridin protein and lncPSR will provide ultimate therapeutic solution for vascular remodeling as well as other VSMC phenotype switching related diseases.

GW31-e0261

ABCG1 attenuates oxidative stress induced by H_2O_2 through the inhibition of NADPH oxidase and the upregulation of Nrf2-mediated antioxidant defence in endothelial cells

Jiahong Xue, Yuan Li, Fan Jiali, Wu Wenhuan
Department of Cardiovascular Medicine, the Second Affiliated Hospital, Xi'an Jiaotong University

OBJECTIVES Oxidative stress is an important factor that is related to endothelial dysfunction. ATP-binding cassette transporter G1 (ABCG1), a regulator of intracellular cholesterol efflux, has been found to prevent from endothelial activation by decreasing reactive oxygen species (ROS) production in vessel walls. However, the underlying mechanisms of ABCG1 inhibiting generation of ROS are still elusive.

METHODS Human Umbilical Artery endothelial cells (HUAECs) were transfected with specific ABCG1 siRNA or ABCG1 overexpression plasmid. Twenty four hours after transfection, cells were exposed to H_2O_2 to induce oxidative stress. Intracellular ROS production was measured using dihydroethidium, (DHE) fluorescent and malondialdehyde (MDA) was also tested. Prooxidant nicotinamide adenine dinucleotide phosphate (NADPH oxidase) activity was assessed by both lucigenin chemiluminescence assay and translocation of cytosolic p47phox to the membrane. Antioxidant signaling nuclear factor-erythroid 2 (Nrf2)/heme oxygenase 1 (HO-1) were observed by the migration of Nrf_2 from cytoplasm to the nucleus via western blotting. Total intracellular cholesterol were measured with a microenzymatic fluorescence.

RESULTS The results showed that overexpression of ABCG1 by ABCG1 plasmid or To901317 treatment inhibited ROS production and MDA content induced by H_2O_2 in HUAECs. Furthermore, ABCG1 upregulation blunted the activity of prooxidant NADPH oxidase and the expression of Nox4, one of NADPH oxidase subunit. Moreover, the increased migration of Nrf2 from cytoplasm to the nucleus and antioxidant HO-1 were all detected in HUAECs with upregulation of ABCG1. Conversely, ABCG1 downregulation by ABCG1 siRNA increased NADPH oxidase activity and Nox4 expression as well as abrogated the increase at Nrf2 nuclear protein levels. In addition, intracellular cholesterol load interfered with the balance between NADPH oxidase activity and HO-1 expression.

CONCLUSIONS It was suggested that ABCG1 attenuates oxidative stress induced by H_2O_2 in endothelial cells, which might involve in the balance between decreased NADPH oxidase activity and increased Nrf2/OH-1 antioxidant defense signaling via its regulation for intracellular cholesterol accumulation.

GW31-e0263

Impairment of TRPM5 mediates high salt consumption induced hypertension

Yuanting Cui[1,2], Hao Wu[1], Qiang Li[1], Zhiming Zhu[1]
[1]Department of Hypertension and Endocrinology, Center for Hypertension and Metabolic Diseases, Daping Hospital, Army Medical University, Chongqing Institute of Hypertension, Chongqing 400042, China
[2]Department of Cardiology, Southwest Hospital, Army Medical University, Chongqing 400038, China

OBJECTIVES Excessive salt intake is a major risk factor for hypertension and cardiovascular diseases. TRPM5 is a taste transient receptor potential cation channel selectively expressed in tongue epithelium. The aim of this study is to clarify the role of TRPM5 in modulation of salty-taste preference and salt intake.

METHODS The licking behavior of TRPM5 gene knockout (TRPM5KO) and wild-type (WT) mice were tested with a gustometer. The food intake and urinary sodium excretion were measured to estimate salt intake. The neuronal activity of the taste cortex was recorded through fiber fluorometry technique. The ambulatory blood pressure was measured by the telemetry system. The expression of TRPM5 was examined through immunoblotting analysis.

RESULTS TRPM5-induced high-salt taste perception was encoded by neurons in central bitter cortical field of the insula cortex. The expression of TRPM5 was lowered after a long-term high-salt dietary intervention. The mice fed on high-salt diet (HSD) exhibited an increased preference for high salt solutions than the mice on normal diet (ND). The mice on HSD displayed an increased preference for salt diet with 1% and 4% NaCl and a decreased preference for normal diet with 0.25% NaCl compared with the mice on ND. Accordingly, the salt intake and sodium excretion of HSD mice were higher than ND mice. After a long-term HSD administration, the blood pressure of TRPM5KO mice was higher than WT mice, and the secondary cardiac hypertrophy was more severe as well.

CONCLUSIONS These results indicate that the reduced expression of TRPM5 in tongue epithelium is a critical step of enhanced salty preference and hypertension in long-term high salt intake. Administration on TRPM5 may be a novel strategy for reducing high salt intake and blood pressure.

GW31-e0266

Role of Rev-erbα in neointimal hyperplasia after vascular endothelial injury

Xueqing Gan[1,2], Shuang Li[1], Dachun Yang[1]
[1]Department of Cardiology, The General Hospital of Western Theater Command
[2]Department of Cardiology, Xuyong People's Hospital

OBJECTIVES Previous studies suggest that Rev-erbα has important roles in myocardial infarction, ischemia reperfusion, and heart failure, but the mechanism of Rev-erbα in neointimal hyperplasia after vascular endothelial injury remains unclear. We used Rev-erbα agonist SR9011 and antagonist SR8278 to investigate the role of Rev-erbα in neointimal hyperplasia after vascular endothelial injury.

METHODS We used Rev-erbα agonist SR9011 and antagonist SR8278 to investigate the role of Rev-erbα in neointimal hyperplasia after vascular endothelial injury. We also examined the mechanisms of action via *in vitro* experiments. We used angiotensin (Ang) II to induce cellular proliferation in vascular smooth muscle cells (VSMCs). We investigated whether Rev-erbα SR9011 or SR8278 affected cell proliferation.

RESULTS Activation of Rev-erbα with agonist SR9011 suppressed neointimal hyperplasia, whereas antagonist SR8278 treatment promoted neointimal hyperplasia after vascular endothelial injury. *In vitro* experiments, SR9011 induced significant inhibition of cell growth and reduced the expression of Nlrp3 induced by Ang II. SR8278 treatment promoted VSMC proliferation and the expression of Nlrp3. Nlrp3 knockdown reversed Ang II-induced VSMC proliferation, and this effect was not reduced by SR8278. After Nlrp3 knockdown SR8278 did not promote proliferation.

CONCLUSIONS The agonist SR9011 suppressed neointimal hyperplasia and inhibited VSMC proliferation, whereas the antagonist SR8278 promoted neointimal hyperplasia and VSMC proliferation. Rev-erbα has negative regulatory effects on neointimal hyperplasia after vascular endothelial injury and proliferation of VSMCs.

GW31-e0274

CeRNA network analysis in cardiac fibroblast activation during cardiac fibrosis

Qingyuan Gao[1,2], Yangxin Chen[1,2], Haifeng Zhang[1,2], Zhiteng Chen[1,2], Shaohua Wang[1,2], Jingfeng Wang[1,2]
[1]Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong 510120, PRC
[2]Laboratory of Cardiac Electrophysiology and Arrhythmia in Guangdong Province, Guangdong 5101120, PRC

OBJECTIVES Cardiac fibroblast (CF) activation is pivotal in cardiac fibrosis. We predicted and constructed a CF-specific competing endogenous RNA (ceRNA) network. Potential functions related to fibrosis of hub genes in this ceRNA network were explored.

METHODS The Gene Expression Omnibus database was used to search for available datasets. Differentially expressed mRNAs (DE-mRNAs) and lncRNAs (DE-lncRNAs) were identified. microRNAs were predicted and validated. The ceRNA network was constructed and visualized by Cytoscape and ceRNA regulatory mechanisms were validated. Single Gene Set Enrichment Analysis (SGSEA) and comparative toxicogenomics database (CTD) were conducted to analyze the most associated pathways and diseases of DE-mRNAs in the ceRNA network. The functions of hub genes in the ceRNA network were validated by siRNA depletion.

RESULTS Two datasets, which respectively described differentially expressed genes in human CFs and failing ventricles, were used for analysis. Four hundred and twenty DE-mRNAs and 39 DE-lncRNAs, and 369 DE-mRNAs and 93 DE-lncRNAs were identified respectively in the two datasets. Thirteen DE-mRNAs with the same expression tendency were overlapped in two datasets. Expressions of 11 predicted microRNAs were validated differently. Only 2 of the DE-lncRNAs were paired to any one of the 11 microRNAs. Finally, 2 mRNAs (*ADAM19* and *TGFBI*), 3 microRNAs (*miR-9-5p*, *miR-124-3p*, and *miR-153-3p*) and 2 lncRNAs (*LINC00511* and *SNHG15*) constituted a ceRNA network. As shown by SGSEA and CTD, both *ADAM19* and *TGFBI* were closely relative to the TGF-β1 pathway and cardiac fibrosis, respectively. Furthermore, siRNA depletion for 2 mRNAs or 2 lncRNAs can alleviate CF activation.

CONCLUSIONS *ADAM19 and TGFBI* were crucial genes in CF during CF activation and cardiac fibrosis and 2 lncRNAs and 3 microRNAs were involved in their regulations in a ceRNA crosstalk.

GW31-e0282

Knockout of MYOM1 in human embryonic stem cell-derived cardiomyocytes leads to cardiac dysfunction via impairing calcium homeostasis and mimics the phenotype of cardiac atrophy

Chengwen Hang[1], Yuanxiu Song[1], Yanan Li[2], Siyao Zhang[2], Yun Chang[2], Ming Cui[1]
[1]Peking University Third Hospital
[2]Anzhen Hospital

OBJECTIVES Myomesin-1 (encoded by *MYOM1* gene) is a main structural linker of M-band in striated muscle fibrils and participates in sarcomere assembly. Studies have reported that *MYOM1* can also be expressed in nucleus and probably plays a role in transcriptional regulation. Its alternative spliceosome EH-myomesin, a biomarker for dilated cardiomyopathy, has been found to be associated with myotonic dystrophy type 1 (DM1). Mutations of *MYOM1* in familial hereditary hypertrophic cardiomyopathy suggested its potential role in striated muscle disease. Although the structural features of *MYOM1* have been well explained in the past few years, its biological function are little known. Besides, the causal relationship and mechanisms underlying the *MYOM1*-related myopathies (especially in myocardium) still remain unknown. Therefore, it is of great significance to establish a reliable *MYMO1* knockout model to study its biological function.

METHODS The CRISPR/Cas9 gene editing technology was used to establish a *MYOM1* knockout human embryonic stem cell line ($MYOM1^{-/-}$ hESC), which was then induced into cardiomyocytes ($MYOM1^{-/-}$ hESC-CMs) *in vitro*. Immunofluorescence staining and flow cytometry were used to identify the morphological characteristics of hESC-CMs. Calcium imaging and video analysis were utilized to evaluate intracellular calcium and contractile function. RNAseq, RT-PCR and Western Blot were performed to examine the transcriptome differences between $MYOM1^{-/-}$ CMs and WT CMs and elucidate the potential molecular mechanisms of the knockout phenotype. Several drugs were used for early intervention to evaluate its effectiveness on improving the atrophic phenotype caused by myomesin-1 deficiency.

RESULTS *MYOM1* was confirmed to be expressed both in nucleus and cytoplasm of cardiomyocytes at day 30 postinduction. Higher proportion of sarcomere disassembly accompanied with nonuniform sarcomere length was more obvious in KO CMs. The expression of genes anchored to *MYOM1*, including *MYOM2*, *MYOM3*, *TTN*, *OBSCN* and *OBSL1* were significantly upregulated in KO CMs. Moreover, the cell size of KO CMs showed significant reduction compared to WT CMs. Deficiency of myomesin-1 led to increased apoptosis but had no effect on proliferation of cardiomyocytes. Video analysis indicated decreased contraction duration and amplitude, with prolonged time to peak in KO CMs. Calcium imaging showed decreased amplitude, increased duration and higher abundance of Ca^{2+} in sarcoplasmic reticulum, which contributed to contractile dysfunction. Besides, total CaMKII protein was not different between two groups, whereas CaMKIIδ was markedly reduced in KO hESC-CMs. Transcriptome analysis of day 30 cardiomyocytes showed a great difference in calcium signaling pathway between two groups and a molecular signature of anti-muscle atrophy in KO CMs. Interestingly, KO CMs had higher expression of vascular and endothelial-related genes, while WT CMs had predominance of cardiac development-associated genes. More importantly, this knockout phenotype can be partially attenuated by verapamil.

CONCLUSIONS *MYOM1* plays an important role in sarcomere assembly, contractility regulation and cardiomyocytes development. $MYOM1^{-/-}$ hESC-CMs can recapitulate cardiac atrophy phenotype *in vitro* due to calcium disorders. Based on this model, the etiology, pathogenesis, and potential treatments of cardiac atrophy caused by myomesin-1 deficiency can be studied.

GW31-e0284

Necroptosis contributes to CaCl2-Ach-induced atrial fibrillation and acts as a potential target for aerobic exercise-conferred cardioprotection

Yuping Fu[1], Tiannan Jiang[2], Qiangsun Zheng[1]
[1]The Second Affiliate Hospital of Xi'an Jiaotong University
[2]Beijing Friendship Hospital, Capital Medical University

OBJECTIVES Atrial fibrillation (AF) is a highly prevalent arrhythmia in clinical practice, and it is well accepted that aerobic exercise improves AF symptoms and -related quality of life. Necroptosis, a novel programmed cell death, plays a critical role in the development of fibrosis, yet it is largely unknown whether necroptosis contributes to AF and its role in exercise-conferred benefits on AF.

METHODS Mice were administrated with calcium chloride and acetylcholine ($CaCl_2$-Ach) for 3 weeks to establish a model of AF. $CaCl_2$-Ach-treated mice were either sedentary or subjected to 3-week swim training to investigate the effect of aerobic exercise on AF. AF susceptibility, heart structure and function and atrial fibrosis were assessed by electrophysiological examinations, echocardiography, Masson's trichrome staining.

RESULTS Three-week $CaCl_2$-Ach administration enhanced AF susceptibility as evidenced by increased AF frequency and duration time after burst pacing. Echocardiographic and histologic results also showed left atrial enlargement and fibrosis in AF mice, demonstrating apparent atrial structrual remodeling. Moreover, we found key mediators of necroptotic signaling (RIP1, RIP3, MLKL, CaMKII) were markedly activated in the atria of AF mice, while inhibiting necroptosis with necrostatin-1 partly attenuated $CaCl_2$-Ach-induced fibrosis and AF susceptibility, indicating necroptosis plays a critical role in AF pathogenesis. Finally, we found 3-week swim training inhibited necroptotic signaling, thereby decreased $CaCl_2$-Ach-induced AF susceptibility and atrial structural remodeling.

CONCLUSIONS Our findings identify necroptosis as a novel mechanism in AF pathogenesis and highlight that aerobic exercise may confer benefits on AF via inhibiting cardiac necroptosis.

GW31-e0291

Nitric oxide alleviated high salt-induced cardiomyocytes apoptosis and autophagy in rats

Kun Zhao, Peng Li, Yong Li
The First Affiliated Hospital of Nanjing Medical University

OBJECTIVES A high salt diet (HSD) is a key risk factor for hypertension, and nitric oxide attenuates cardiac damage. The present study aimed to explore whether nitric oxide could alleviate high salt-induced apoptosis and autophagy of cardiomyocytes in rats.

METHODS Rats received 8% HSD in vivo. H9C2 cells or primary neonatal rat cardiomyocytes (NRCM) were treated with sodium chloride (NaCl) in vitro.

RESULTS Middle and high doses (50 mM and 100 mM) of NaCl increased the level of cleaved-caspase 3/caspase 3, cleaved-caspase 8/caspase 8, Bax/Bcl2, and LC3 in H9C2 cells. By contrast, 25 mM NaCl and 100 mM mannitol exerted no effect on the levels of cleaved-caspase 3/caspase 3, cleaved-caspase 8/caspase 8, and Bax/Bcl2, or LC3 compared with PBS in H9C2 cells. The endothelial nitric oxide synthase (eNOS) level was increased in the heart of HSD rats and H9C2 cells treated with 100 mM NaCl. Nitric oxide (NO) donor sodium nitroprusside (SNP) reduced the increased levels of cleaved-caspase 3/caspase 3, cleaved-caspase 8/caspase 8, Bax/Bcl2 induced by NaCl (100 mM) in H9C2 cells and NRCM. The levels of cleaved-caspase 3/caspase 3, Bax/Bcl2, and LC3 were increased in the heart of HSD rats. SNP treatment attenuated the increases of cleaved-caspase 3/caspase 3, Bax/Bcl2, and LC3 in the heart of HSD rats.

CONCLUSIONS Overall, our study demonstrated that NaCl increased apoptosis and autophagy of cardiomyocytes, and eNOS/NO alleviated the high salt-induced apoptosis and autophagy of cardiomyocytes.

GW31-e0292

Silencing Mas-related G protein-coupled receptor member D (MrgD) plays a cardioprotective role against angiotension II-induced cardiac remodeling

Kun Zhao, Chuanxi Yang, Peng Li, Wei Sun, Xiangqing Kong
The First Affiliated Hospital of Nanjing Medical University

OBJECTIVES Cardiac fibrosis and hypertrophy, as the major hallmarks of cardiac remodeling involved in the pathophysiological process of hypertensive heart diseases, can result in disturbed function and structure of the myocardium, accompanied by the increased deposition of myocardial collagen. Recent studies have demonstrated that alamandine, the heptapeptide in the Ang-(1-7)//MrgD axis, could alleviate AngII-induced cardiac hypertrophy through binding to its natural receptor Mas-related G protein-coupled receptor member D (MrgD). However, no data to date demonstrates the specific physiological and pathophysiological function of MrgD in the therapeutic effect of alamandine towards AngII induction. Thus, we aimed to investigate the role of MrgD in regulating AngII-induced cardiac hypertrophy in vivo and in vitro.

METHODS In our study, we used AngII to mimic the animal or cell culture models of cardiac hypertrophy and fibrosis. After alamandine treatment, the nucleoproteins were collected to determine the role of alamandine in AngII-induced nuclear import. Pretreatment or intra-myocardial injection of recombinant adenovirus-MrgD (AD-MrgD) or adenovirus-shRNA-MrgD (shRNA-MrgD) were further used to verify the pathophysiological function of MrgD in vivo and in vitro. Then, LIPUS irradiation (0.5 MHz, 77.20 mW/cm^2) was applied for 20 minutes every other day in mice received chronic AngII infusion in vivo. Following that, the levels of cardiac hypertrophy and fibrosis were evaluated by echocardiographic, histopathological, and molecular biological methods.

RESULTS Our results showed the protein and mRNA expression levels, as well as the fluorescence intensities of MrgD were increased after alamandine and/or AngII treatment, while there was no significant difference in those between these two groups. Further, more nuclear import of MrgD was found in cells receiving AngII stimulation by analyzing the results of nucleoproteins compared to those after alamandine treatment alone in vitro. Interestingly, alamandine treatment could reduce AngII-induced MrgD nuclear import by inactivating the phosphorylation of PKA and alleviating oxidative stress, which may account for the beneficial effects of alamandine towards AngII. Then, adenovirus silencing MrgD pre-treatment which reduced the total protein and nuclear protein expressions of MrgD in vitro could mimic the protective role of alamandine, while adenovirus-mediated overexpression of MrgD aggravated the pathological effects induced by AngII in vivo and in vitro. More importantly, we further found that low-intensity pulsed ultrasound (LIPUS) could ameliorate AngII-induced cardiac fibrosis via decreasing MrgD expression in vivo and in vitro.

CONCLUSIONS Taken together, our current study unveiled the promising cardioprotective effect of silencing MrgD expression on alleviating AngII-induced cardiac hypertrophy and fibrosis by reducing its nuclear import, paving the way to develop novel therapeutic apparatus, LIPUS, in the clinical practice of cardiac remodeling in the future.

GW31-e0293

Pellino1 deficiency reprograms cardiac energy metabolism in lipopolysaccharide-induced myocardial dysfunction in vitro

Kun Zhao, Chuanxi Yang, Peipei Huang
The First Affiliated Hospital of Nanjing Medical University

OBJECTIVES Pellino1 has been shown to regulate proinflammatory genes by activating the nuclear factor kappa B (NF-κB) and Toll-like receptor (TLR) signaling pathways, which are important in the pathological development of lipopolysaccharide (LPS)-induced myocarditis. However, it is still unknown whether silencing Pellino1 (si-Pellino1) has a therapeutic effect on this disease. Here, we showed that silencing Pellino1 can be a potential protective strategy for abnormal myocardial energy metabolism in LPS-induced myocarditis.

METHODS We used liquid chromatography electrospray-ionization tandem mass spectrometry (LC-MS/MS) to analyze samples from si-Pellino1 neonatal rat cardiac myocytes (NRCMs) treated with LPS or left untreated. After normalization of the data, metabolite interaction analysis of matched KEGG pathway associations following si-Pellino1 treatment was applied, accompanied by interaction analysis of gene and metabolite associations after this treatment. Moreover, we used western blot (WB) and polymerase chain reaction (PCR) analyses to determine the expression of genes involved in regulating cardiac energy and energy metabolism in different groups.

RESULTS LC-MS-based metabolic profiling analysis demonstrated that si-Pellino1 treatment could alleviate or even reverse LPS-induced cellular damage by altering cardiac energy metabolism accompanied by changes in key genes (Cs, Cpt2, and Acadm) and metabolites (3-oxoocotanoyl-CoA, hydroxypyruvic acid, lauroyl-CoA, and NADPH) in NRCMs.

CONCLUSIONS Overall, our study unveiled the promising cardioprotective effect of silencing Pellino1 in LPS-induced myocarditis through fuel and energy metabolic regulation, which can also serve as biomarkers for this disease.

GW31-e0358

Elabela regulates SIRT3-mediated inhibition of oxidative stress through Foxo3a deacetylation preventing diabetic-induced myocardial injury

Cheng Li, Shudong Wang, Jian Sun, Quan Liu, Yonggang Wang
Department of Cardiovascular Center, The First Hospital of Jilin University, Changchun, Jilin 130021, China

OBJECTIVES Diabetic cardiomyopathy (DCM) – pathophysiological heart failure that occurs in absence of coronary artery disease, hypertension, and/or valvular heart disease, is a common diabetic complication. Elabela, a new

peptide that acts via APJ, has similar functions as Apelin, providing beneficial effects on body fluid homeostasis, cardiovascular health, renal insufficiency, as well as potentially beneficial effects on metabolism and diabetes. The present study sought to reveal the underlying mechanisms of Elabela mediated cardioprotection.

METHODS Six weeks old, male C57BL/6J mice were randomized into 4 groups: (1) Control (Ctrl) group; (2) Ctrl+Elabela group; (3) Diabetes mellitus (DM) group; (4) DM+Elabela group. Type I diabetes model mice was established by intraperitoneally injecting with streptozotocin (150 mg/kg). Elabela (4.5 mg/kg) was administered subcutaneously twice a day for 3 months. Body weight, plasma glucose levels, cardiac function and structure were measured at the end of the experiment. Masson trichrome and TUNEL staining were used to assess myocardial fibrosis and apoptosis, respectively. The expressions of fibrosis, oxidative stress, inflammation, and apoptosis molecules were measured by quantitative PCR and/or Western blot. Furthermore, the expressions of SIRT3, its interaction protein Foxo3a, and its downstream anti-oxidative proteins SOD-2 and MnSOD were also measured.

RESULTS Neither body weight nor plasma glucose levels was affected by Elabela. Cardiac fibrosis, oxidative stress, inflammation, and apoptosis were increased in DM group compared to Ctrl group, all of which were attenuated by Elabela treatment. In addition, the expressions of the SIRT3 and its downstream anti-oxidative proteins SOD-2 and MnSOD were lower than that in Ctrl group, which can be significantly improved by Elabela treatment. Especially, we observed that diabetes significantly increased the level of acetylated Foxo3a while diabetes treated with Elabela decreased acetylated expression.

CONCLUSIONS In this study, Elabela treatment was found to have profound protective effects against diabetes-induced cardiac fibrosis, oxidative stress, inflammation, and apoptosis; these protective effects may depend heavily upon SIRT3-mediated Foxo3a deacetylation. Our findings provide evidence that Elabela has cardioprotective effects for the first time in the diabetic model.

GW31-e0364

Inhibition of cardiac remodeling by mitochondrial-related gene MTFR1L and its mechanism

Yuanxiu Song, Chengwen Hang, Ming Cui
Department of Cardiology, Peking University Third Hospital

OBJECTIVES Cardiac remodeling is the initial factor of heart failure caused by various causes. It is closely related to the abnormal energy metabolism of myocardial cells caused by abnormal mitochondrial dynamics. MTFR1L is a member of the mitochondrial dynamic network, which can promote mitochondrial division. There is no research on the specific physiology of MTFR1L and its pathology related to cardiac remodeling. This study used the combination of iPSC myocardial differentiation and CRISPR/Cas9 gene editing technology to establish a human homozygous knockout cardiomyocyte model of MTFR1L, and explored the relationship between MTFR1L and cardiac remodeling and its molecular mechanism.

METHODS The author combined CRISPR/Cas9 genome editing technology with myocardial differentiation technique of human induced pluripotent stem cells (hiPSCs) to establish the MTFR1L$^{-/-}$ cell line and differentiated into cardiomyocytes. RNA-seq was used to analyze differential genes in wild-type (WT) and MTFR1L$^{-/-}$ (KO) hiPSC-CMs, and key molecules and signaling pathways that MTFR1L regulated cardiac remodeling were screened out. Immunofluorescence staining, electron microscopy and flow cytometry were used to observe the effect of MTFR1L knockout on myocardial cell morphology. Mitotracker and Mitosox fluorescent probes were used to observe the effect of MTFR1L on myocardial mitochondrial number and ROS level. Flou-4/AM probe was used to explore the role of MTFR1L on myocardial cell calcium signal and contractility. Annexin V/APC fluorescence apoptosis detection was used to compare the difference in apoptosis between WT and KO hiPSC-CMs. Western blot and qPCR were used to verify the expression differences of heart failure, fibrosis, ion channels, apoptosis and autophagy-related pathway genes in cardiomyocytes.

RESULTS Compared with WT hiPSC-CMs, the cell volume became smaller, the number of mitochondria decreased, and the length increased ($P<0.05$), indicating that MTFR1L deficiency doesn't affect the differentiation of myocardium, but it can make mitochondrial and cell morphology changes. The knockout of MTFR1L caused the increase of mitochondrial ROS level and the decrease of mitochondrial DNA content ($P<0.05$) in myocardial cells, resulting in mitochondrial damage. QPCR results showed KO hiPSC-CMs ion channel related genes (SCN5A, KCNH2, KCNQ1) expression was significantly reduced, while fibrosis related genes (Col1a, ATP2a) and other cardiac remodeling-related genes increased significantly ($P<0.05$); MTFR1L deficiency caused myocardial calcium activity disturbance ($P<0.05$). RNA-seq results showed that the expression of apoptosis-related pathway genes (caspase8, capase10) and autophagy pathway-related genes (LAMP1, LAMP2, MAPK10) in KO hiPSC-CMs increased significantly. The results of apoptosis detection showed the loss of MTFR1L promotes the level of cardiomyocyte apoptosis.

CONCLUSIONS Mitochondrial division-related gene MTFR1L plays an important role in maintaining mitochondrial morphology and function intact, participating in the maintenance of cardiomyocyte function, and inhibiting cardiac remodeling. This effect is achieved by maintaining mitochondrial division-fusion balance in cardiomyocytes, preventing apoptosis and excessive activation of autophagy. This research helps elucidate the molecular mechanism of heart remodeling and provides new ideas for the prevention and treatment of myocardial mitochondrial energy metabolic diseases.

GW31-e0390

Cryptotanshinone ameliorates doxorubicin-induced cardiotoxicity by targeting Akt-GSK-3β-mPTP pathway

Xiaoping Wang, Yong Wang
Beijing University of Chinese Medicine

OBJECTIVES Doxorubicin (DOX) is an effective first-line chemotherapeutic agent that is widely used in the treatment of various cancers. However, accumulation of DOX can cause side effects with the cardiotoxicity as the most severe one. Oxidative stress and cardiomyocyte apoptosis play a key role in DOX-induced cardiotoxicity (DIC). DOX could induce oxidative stress, which leads to opening of the mitochondrial permeability transition pore (mPTP) and apoptosis in cardiomyocytes. Opening of mPTP is regulated by cyclophilin D (CypD) and glycogen synthase kinase 3β (GSK-3β). Phosphorylation of GSK-3β by AKT could promote its interaction with adenine nucleotide translocator (ANT), inhibit opening of mPTP and prevent apoptosis. Previous studies have shown that cryptotanshinone (Cts) has potential cardioprotective effects, but its role in DIC remains unknown. Our research aimed to explore whether Cts could ameliorate DOX-induced oxidative and apoptosis by targeting Akt-GSK-3β-mPTP pathway.

METHODS A DOX-stimulated H9C2 cell model was established in this study. The effects of Cts on cell viability, reactive oxygen species (ROS) level, superoxide ion accumulation, apoptosis and mitochondrial membrane potential (MMP) were evaluated. Expressions of proteins in Akt-GSK-3β pathway were detected by western blot. Akt inhibitor was applied to treat cells to investigate the effects of Cts on Akt-GSK-3β pathway and mPTP. The effects of Cts on the binding of p-GSK-3β to ANT and the formation of ANT-CypD complex were explored by immunoprecipitation assay.

RESULTS The results showed that Cts could increase cell viability, reduce ROS level, inhibit apoptosis and protect mitochondrial membrane intergrerity. Cts treatment increased phosphorylated levels of Akt and GSK-3β. After cells were co-treated with Akt inhibitor, the effects of Cts on phosphorylation of GSK-3β, ROS, apoptosis and MMP were also abolished. Immunoprecipitation assay showed that Cts significantly increased the GSK-3β-ANT interaction and attenuated DOX-induced formation of ANT-Cyp-D complex, thereby inhibiting opening of mPTP.

CONCLUSIONS In conclusion, Cts is a promising drug for preventing DIC and it ameliorates oxidative stress and apoptosis by acting on Akt-GSK-3β-mPTP pathway.

GW31-e0394

Synergistic effect of vitamin C and endothelin-1 in differentiation of cardiomyocytes from embryonic stem cell

Haifeng Zhang[1,2], Shaohua Wang[1,2], Qingyuan Gao[1,2], Zhiteng Chen[1,2], Guanghao Gao[1,2], Yangxin Chen[1,2], Jingfeng Wang[1,2]
[1]Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong 510120, PRC
[2]Laboratory of Cardiac Electrophysiology and Arrhythmia in Guangdong Province, Guangdong 5101120, PRC

OBJECTIVES To explore the effects of vitamin (Vit)-C in combination with endothelin (ET)-1 on embryonic stem cell (ESC) differentiation into cardiomyocytes and underline mechanism.

METHODS Different Vit-C concentrations and intervention time were tested to optimize Vit-C treatment. After that, Vit-C (100 μmol/L) alone or together with ET-1 (100 nmol/L) were administered to ESC at day 4–9 after differentiation. The beating of embryoid bodies (EBs) was calculated and compared between groups. Expressions of cardiac marker, cTnT, cardiac promotor, Nkx 2.5, GATA-4, and Shox2 were determined. Lentivirus mediated RNA interference was used to knockdown expressions of Nkx 2.5, GATA-4, and Shox2 and EBs beating under Vit-C and ET-1 treatment were observed.

RESULTS Optimal Vit-C treating concentration was 100 μmol/L and day 4–9 after differentiation was the best time to intervene, which increased EBs beating by 11.19% and increased expression of cTnT, Nkx 2.5, GATA-4, and Shox2 expressions at the same time. In combination with ET-1 further increased EBs beating by 11.07% and expression profiles of the above proteins. Knocking down of Shox2 reversed the effects of Vit-C and ET-1 at the greatest extent, reduced EBs beating by 12.94%.

CONCLUSIONS Vit-C plus ET-1 produce more purified cardiomyocytes from ESC differentiation. The up-regulation of Shox2 is the most important underline mechanism.

GW31-e0399

The effects of selenium deficiency on cardiac function and myocardial tissue in SD rats

Yujie Xing, Jing Xu, Shuo Pan, Junkun Wang
Department of Cardiology, Shannxi Provincial People's Hospital, Xi'an, Shaanxi

OBJECTIVES To explore the effects of selenium deficiency on cardiac function and myocardial tissue in SD rats.

METHODS Sixty SD rats were randomly divided into control group, selenium deficiency group and selenium supplement group, with twenty rats in each group. Rats in the control group were fed with standard diet, rats in the selenium deficiency group were fed with selenium deficiency diet and rats in the selenium supplement group were fed with selenium deficiency diet for fourteen weeks and then giving sodium selenite for three weeks. Seventeen weeks later, the levels of blood selenium and BNP were detected. HE staining was used to detect the morphological change of myocardial tissue. The electron microscope was used to detect the myocardial ultrastructure. The cardiac function in rats was detected by the echocardiography.

RESULTS The levels of blood selenium in selenium deficiency group decreased significantly compared with the control group, but after selenium supplement they increased significantly. Compared with the control group, the BNP level of rats in the selenium deficiency group was higher, but the BNP level was significantly decreased after selenium supplement. In the control group the structure of myocardial tissue was normal, but the structure of myocardial tissue in the selenium deficiency group was disordered. There was only mild abnormality in the structure of myocardial tissue in the selenium supplement group. Compared with the control group, the cardiac function of rats in the selenium deficiency group was significantly reduced, but the cardiac function was significantly increased after selenium supplement.

CONCLUSIONS Selenium deficiency can reduce the cardiac function and destroy the normal structure of myocardial tissue. Meanwhile, selenium supplement can improve cardiac function and improve the destruction of myocardial tissue structure in rats.

GW31-e0403

Drp1-induced mitochondrial fission promotes cardiac fibroblast activation and cardiac fibrosis

Qingyuan Gao[1,2], Haifeng Zhang[1,2], Zhiteng Chen[1,2], Shaohua Wang[1,2], Yangxin Chen[1,2], Jingfeng Wang[1,2]
[1]Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong 510120, PRC
[2]Laboratory of Cardiac Electrophysiology and Arrhythmia in Guangdong Province, Guangdong 5101120, PRC

OBJECTIVES The downstream regulators of TGF-β1 are attractive in the studies of cardiac fibrosis and cardiac fibroblast (CF) activation. Imbalanced mitochondrial dynamics were investigated in aged-related diseases and other organ fibrosis. The potential role of Dynamin related protein-1 (Drp1)-induced excessive mitochondrial fission in TGFβ1-stimulated CF activation was explored.

METHODS Mouse CF were isolated from 1–3 days old C57BL/6 neonatal mice that received TGF-β1 (5 ng/mL) or saline. Mitochondrial morphology, expression of the regulatory molecules in mitochondrial fission and fusion, and Drp1-Tom20 interactions were measured. Also, mitochondrial membrane potential and mitochondrial ROS production were measured to reflect mitochondrial damage. The Drp1 inhibitor mitochondrial division inhibitor 1 (Mdivi-1) and mitochondrial fusion promotor M1 (Promotor M1) were added in the TGFβ1-induced group to assess the changes of pro-fibrotic markers, collagen deposition, proliferation, and migration in activated CF. The cell metabolism throughout mitochondrial respiratory and glycolysis were measured by Seahorse XFe96 Analyzer.

RESULTS More mitochondrial fission and less mitochondrial fusion events happened in TGFβ1-induced CF. The expressions of pro-fibrotic markers, collagen secretion and deposition, and CF proliferation and migration can be mitigated throughout inhibiting Drp1-induced mitochondrial fission by Mdivi-1 or promoting mitochondrial fusion by Promotor M1. Besides, this rescuing experiment was accompanied by alleviation in mitochondrial damage. On the other hand, through detecting the level of cell metabolism, Drp1-induced mitochondrial fission in TGFβ1-stimulated CF can lead to impaired mitochondrial respiratory and enhanced glycolysis. The latter can cause CF activation and cardiac fibrosis. 2-Deoxy-D-glucose, a glycolysis inhibitor, can further rescue the TGFβ1-induced CF activation based on Mdivi-1 or Promotor M1-treated activated CF.

CONCLUSIONS Excessive Drp1-induced mitochondrial fission and impaired mitochondrial fusion can cause CF activation throughout enhancing glycolysis in TGFβ1-induced CF.

GW31-e0429

Neocryptotanshinone regulates energy metabolism in heart failure by targeting RXRα

Ma Lin, Wang Yong
Beijing University of Chinese Medicine

OBJECTIVES Neocryptotanshinone (NCTS) is a natural molecule identified from traditional Chinese herb Salvia miltiorrhiza Bunge, which is widely used in the treatment of cardiovascular diseases. RXRα is an attractive target due to its impressive effect on the heart energy metabolism. This study is to investigate whether the protective effect of NCTS on the heart failure (HF) was exerted via regulating RXRα-mediated energy metabolism pathway.

METHODS Microscale Thermophoresis (MST) were used to verify the binding force of NCTS to the target RXRα. The model of HF post-acute myocardial infarction (AMI) in mice was established by ligating the left anterior descending (LAD) coronary artery. Echocardiography was performed to evaluate mice cardiac function in different groups, including sham, model, NCTS low-dose, NCTS high-dose and Trimetazidine groups. In addition, an in vitro oxygen-glucose deprivation/recovery (OGD/R) injury model on H9C2 cells was established to clarify the effects and regulated energy metabolism mechanism of NCTS. H9C2 cells were divided into four groups, including control, model, NCTS treatment and NCTS+HX531 (RXRα inhibitor) treatment groups. Western Blot was used to detect the expression of RXRα, PPARα, CPT1a, CD36. Immunofluorescence detected the expression of RXRα in myocardial tissue. Adenosine Triphosphate (ATP) were examined by ATP Assay Kit.

RESULTS In this study, NCTS could dose-dependently bind to the RXRα protein with a KD value of 2.5×10^{-5} M, demonstrating that NCTS potentially bound with RXRα as a direct ligand. Echocardiography results indicated that NCTS could protect cardiac function. Compared with model group, NCTS could increases the expression of RXRα and the level of ATP in myocardial tissue ($P<0.05$). Positive drug Trimetazidine showed similar effects. Simultaneously, similar effects were revalidated in OGD/R-induced H9C2 injury model. NCTS in 2 μmol/L had protective effects. We discovered that compared with the model group, RXRα was significantly increased in the NCTS treatment group ($P<0.01$), and the co-treat with RXRα antagonist HX531 can eliminate the effect of NCTS. Interestingly, the expression of PPARα, CPT1a and CD36 decreased in model group ($P<0.01$). After treatment with NCTS, the expression of PPARα, CPT1a and CD36 was notably restored ($P<0.05$). In the NCTS+HX531 group, the effect of NCTS is also eliminated. These findings suggested that NCTS can effectively activate RXRα expression and protect cardiocytes by regulating RXRα-mediated energy metabolism pathway.

CONCLUSIONS This study demonstrates that NCTS can effectively improve the cardiac function of mice with HF post-AMI and has a protective effect on cardiomyocytes. The mechanism of NCTS is to improve energy metabolism disorders through targeting on RXRα. The present study provides a potential target-drug for clinical treatment of cardiovascular disease.

GW31-e0452

Nuclear receptor Rev-erbα improves cardiac dysfunction during sepsis through transcriptionally activating monocarboxylate transporter 8

Renyang Tong, Longwei Xu, Yichao Zhao, Jun Pu
Department of Cardiology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University

OBJECTIVES Sepsis and its resultant heart failure, characterized by the dysregulated inflammatory response, are among leading causes of death worldwide. However, no specific approaches have proven clinically effective and efficient in the treatment of septic cardiac dysfunction. Rev-erbα, a unique member of the nuclear receptors (NRs), was recently reported to pivotally participate in inflammation regulation. However, the role of Rev-erbα in sepsis-induced cardiac dysfunction remains unknown.

METHODS (1) Cardiomyocyte-specific Rev-erbα-knockout mice (KO) were established by Shanghai Model Organisms Center, Inc. (2) The mice septic model was established by a dose intraperitoneal injection (i.p.) of *Escherichia Coli O55:B5* LPS into 12- to 14-week-old male mice at ZT6 or ZT18 for 6 hours according to previous reports. (3) Polymicrobial sepsis was induced by Cecal ligation and puncture (CLP) in 12- to 14-week-od male mice as described previous. (4) 12 overnight-fasted Bama miniature pigs (30±2 kg) were utilized to establish sepsis pigs model. (5) *In vivo* cardiac function of each group mice was measured using echocardiography (Vevo 2100, VisualSonic, Toronto, Canada) and left ventricular hemodynamics (AD Instruments, Castle Hill, New South Wales, Australia) 6 hours after LPS injection, as previously described. (6) To assess the extent of myocardial interstitial edema of mice, *in vivo* CMR was conducted using a 7.0 T small animal MRI system (BioSpec70/20USR; Bruker BioSpin GmbH, Ettlingen, Germany; Software ParaVision 5.1). (7) The related mRNA and proteins expression were respectively determined by RT-PCR, Western blot and Enzyme-linked immunosorbent assay (ELISA). (8) Chromatin immunoprecipitation (ChIP) assays were performed by using SimpleChIP® Plus Enzymatic Chromatin IP Kit (#9005, CST, Beverly, MA) per manufacturer's protocol. (9) ChIP-seq library preparation and sequencing were performed by RiboBio.

RESULTS (1) Firstly, we found Rev-erbα owned the highest expression abundance among 49 NRs in the murine hearts, and once challenged with LPS, endogenous Rev-erbα level was significantly down-regulated in hearts from septic mice and LPS-treated mouse or human cardiomyocytes. (2) And we noticed that the diurnal oscillation of Rev-erbα expression was associated with the severity of cardiac injury in septic mice. (3) Furthermore, *in vivo* loss-of-function experiments indicated that Rev-erbα deficiency visibly exacerbated sepsis-induced cardiac dysfunction, inflammatory response and mortality. (4) Meanwhile, the protective role of Rev-erbα was confirmed in the *in vitro* loss-of- and gain-of-function experiments in the primary murine cardiomyocytes. (5) Additionally, pharmacological activation of Rev-erbα by SR9009 obviously ameliorated the LPS-induced adverse phenotype in both mice and bama miniature pigs. (6) Mechanistic studies revealed that monocarboxylate transporter 8 (MCT8, one of main thyroid hormone transporters) was a direct transcriptional activation target of Rev-erbα via binding with the its promoter region and mediated the Rev-erbα-elicited cardioprotection.

CONCLUSIONS In summary, the present study provides the first evidence that Rev-erbα acts as a novel protective receptor against septic cardiac injury via directly transactivating the TH transporter MCT8. Therefore, targeting the Rev-erbα-MCT8 signaling may represent a promising strategy to alleviate depressed hearts during sepsis.

GW31-e0476

FGF21 prevents diabetic cardiomyopathy via AMPK-mediated anti-oxidation and lipid-lowering effects

Chi Zhang
Wenzhou Medical University

OBJECTIVES Our previous studies showed that both exogenous and endogenous FGF21 inhibited cardiac apoptosis at the early-stage of type 1 diabetes. Whether FGF21 induces preventive effect on type 2 diabetes-induced cardiomyopathy was investigated in the present study.

METHODS High-fat-diet/streptozotocin-induced type 2 diabetes was established in both wild-type (WT) and FGF21-knockout (FGF21-KO) mice followed by treating with FGF21 for 4 months. Cardiac function, morphological changes, cardiac hypertrophy, fibrosis as well as apoptosis, oxidative stress and inflammation were diagnosed.

RESULTS Diabetic cardiomyopathy (DCM) was diagnosed by significant cardiac dysfunction, remodeling and cardiac lipid accumulation associated with increased apoptosis, inflammation and oxidative stress, which was aggravated in FGF21-KO mice. However, the cardiac damage above was prevented by administration of FGF21. Further studies demonstrated that the metabolic regulating effect of FGF21 is not enough contributing to FGF21-induced significant cardiac protection under diabetic condition. Therefore, other protective mechanisms must exist. The in vivo cardiac damage was mimicked in primary neonatal or adult mouse cardiomyocytes treated by HG/Pal, which was inhibited by FGF21 treatment. Knockdown of AMPKα1/2, AKT2 or NRF2 with their siRNAs revealed that FGF21 protected cardiomyocytes from HG/Pal partially via up-regulating AMPK-AKT2-NRF2-mediated anti-oxidative pathway. Additionally, knockdown of AMPK suppressed fatty acid β-oxidation via inhibition of ACC-CPT-1 pathway. And, inhibition of fatty acid β-oxidation partially blocked FGF21-induced protection in cardiomyocytes. Further in vitro and in vivo studies indicated that FGF21-induced cardiac protection against type 2 diabetes was mainly attributed to lipotoxicity rather than glucose toxicity.

CONCLUSIONS FGF21 functions physiologically and pharmacologically to prevents type 2 diabetic lipotoxicity-induced cardiomyopathy through activation of both AMPK-AKT2-NRF2-mediated anti-oxidative pathway and AMPK-ACC-CPT-1-mediated lipid-lowering effect in the heart.

GW31-e0485

N-acetylcysteine modifying mildly attenuate myocardial toxicity induced by magnetic iron oxide nanoparticles

Yunli Shen, Hao Zheng, Xiaobo Yao, Qizheng Lu
Department of Cardiology, Shanghai East Hospital, Tongji University School of Medicine

OBJECTIVES Magnetic iron oxide nanoparticles (MNP) as contrast agents or target carriers have been widely used in in the diagnosis and treatment for cardiovascular diseases. Correspondingly, the myocardial tissue safety of MNP is becoming the bottleneck to seriously restrict its clinical translation. We aimed to investigated whether MNP could aggravate oxidative stress injury in ischemic myocardium and further explored whether a potent antioxidant N-acetylcysteine (NAC) modifying could neutralize the toxicity of MNP.

METHODS NAC modified MNPs are prepared. We injected different nanoparticles in a rat model of ischemia/reperfusion, including MNP, mesoporous silica nanoparticles (MSN), magnetic mesoporous silica nanoparticles (M-MSN) and NAC loaded M-MSN (M-MSN@NAC). The myocardial ROS levels in the peri-infarct zone were detected by DHE 24 hours after the intramyocardial injection. At 2 weeks after intramyocardial injection, the MDA, GSH-Px and GSH were measured using colorimetric method or ELASA. The mitochondrial membrane potential (MMP) and ATP of myocardial cells were respectively detected by JC-1 kit and ATP Test Kit. Myocardial tissue non-heme iron levels were measured using the chromogen method. Myocardial mitochondria at injection sites were observed by transmission electron microscopy. At 4 weeks after injection, the cardiac function was measured by using echocardiography, and histologic analyses of infarct morphology was obtained.

RESULTS Both the MNP group and the M-MSN group showed higher levels of ROS in ischemic myocardium than that in the control group at 24 hours after injection (both $P<0.0001$). At 2 weeks after injection, compared with the control group, the MNP, M-MSN and M-MSN@NAC groups demonstrated significant increased content of non heme iron in cardiomyocytes (all $P<0.01$), especially dramatically increased of non heme iron content in mitochondria (all $P<0.01$). Compared to the control group, both MNP and M-MSN induced the significant increase of MDA (both $P<0.01$), the marked decrease of GSH (both $P<0.01$), the inactivation of GPx4 (both $P<0.01$), the loss of MMP and ATP depletion (all $P<0.0001$), suggesting that iron oxide nanoparticles could cause mitochondrial lipid peroxidation by inducing mitochondrial iron overload. The level of mitochondrial MDA in M-MSN@NAC group was lower than that in the MNP and M-MSN groups (both $P<0.01$), but it was still significantly higher than that in the control group ($P<0.01$). Moreover, the MMP and ATP levels in M-MSN@NAC group were similar to the MNP and M-MSN groups (all $P>0.05$), implying that NAC could only partly relieved mitochondrial lipid peroxidation induced by MNP or M-MSN. In addition, compared with the control group, the M-MSN with or without NAC modification also could cause serious destruction of mitochondrial structure. At 4 weeks after injection, MNP and M-MSN exaggerated the left ventricular negative remodeling and functional deterioration (all $P<0.0001$), and M-MSN@NAC exhibited NAC modification could only slightly mitigate the myocardial toxicity induced by iron oxide nanoparticles.

CONCLUSIONS The local application of magnetic iron oxide nanoparticles can aggravate the negative remodeling of ischemic myocardium by induction of mitochondria iron overload to lead to lipid peroxidation. Traditional antioxidant NAC can only mildly reduce the myocardial toxicity.

GW31-e0507

Klotho attenuated doxorubicin-induced cardiomyopathy by alleviating dynamin-related protein 1-mediated mitochondrial dysfunction

Xiuting Sun, Xiaodong Zhuang, Xinxue Liao
First Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES Doxorubicin (Dox)-induced cardiotoxicity could lead to dilated cardiomyopathy and heart failure, which limited its clinical application. Our previous study reported the protective effects of Klotho against hyperglycemia-induced cardiomyopathy. We investigated whether Klotho alleviated Dox-induced cardiotoxicity, and dissected the underlying mechanism.

METHODS Primary neonatal rat ventricular cardiomyocytes and H9c2 cells were incubated with 5 μM Dox for 24 h with or without Klotho (0.1 mg/mL). Dox-induced cardiotoxicity model was approached in C57BL/6 mice. Both *in vitro* and *in vivo* study were conducted in four groups (control, Dox, Klotho and Dox+Klotho group). Cardiac function and serum enzyme activity, apoptosis and mitochondrial dysfunction were measured.

RESULTS Pretreatment with Klotho significantly reduced Dox-induced apoptosis, mitochondrial fission and inflammation in cardiomyocytes. In Dox-treated mice, Klotho also suppressed cardiac cell death and inflammatory response, improved cardic function. The expression of Dynamin-related protein 1 (Drp1) was also increased after Dox-treatment. Furthermore, overexpression of Drp1 in cardiomyocytes increased Dox-induced heart injury which could also be attenuated by Klotho.

CONCLUSIONS This study demonstrated that Klotho alleviated Dox-induced cardiotoxicity by reducing apoptosis and mitochondrial fission though down-regulating Drp1 expression. Our findings highlight new targets for the therapy of Dox-induced cardiomyopathy.

GW31-e0509

Klotho prevents hyperglycemia-induced mitochondrial fission and cardiac dysfunction through SIRT1/PGC-1α/Drp1 pathway

Yue Guo[1,2], Xingfeng Xu[1,2], Huimin Zhou[1], Xiaodong Zhuang[1], Xinxue Liao[1,2]
[1]Department of Cardiology, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou 510080, P.R. China
[2]NHC Key Laboratory of Assisted Circulation (Sun Yat-sen University), Guangzhou, Guangdong 510080, P.R. China

OBJECTIVES Excessive mitochondrial fission plays a critical role in the pathogenesis of diabetic cardiomyopathy (DCM). Our previous study demonstrated

that anti-aging protein Klotho attenuated hyperglycemia-induced myocardial injury and cardiac dysfunction. Silent information regulator 1 (SIRT1) is an NAD+ dependent protein deacetylase involved in the cardioprotective effects of Klotho. However, whether SIRT1 signaling is involved in the regulatory effect of Klotho on mitochondrial fission has not been elucidated. Therefore, the purpose of this study were (i) to explore whether Klotho attenuates diabetes-induced cardiac dysfunction by inhibiting mitochondrial fission; (ii) if so, to determine whether Klotho prevents mitochondrial fission via activation of SIRT1 signaling.

METHODS Neonatal cardiomyocytes were exposed to 33 mM glucose in the presence or absence of Klotho (400 pM). Moreover, we established a diabetic mouse model to assess the protective effect of Klotho. Control and streptozotocin-induced diabetic mice were untreated or treated with Klotho (Intraperitoneal injection of Klotho at 0.01 mg/kg per 48 h) 1 weeks after diabetes induction and assessed 3 months afterward.

RESULTS Klotho prevented diabetes-induced myocardial dysfunction by inhibiting dynamin-related protein 1 (Drp1)-mediated mitochondrial fission. Klotho inhibited Drp1 expression, reduced oxidative stress, decreased cardiomyocyte apoptosis, improved mitochondrial function and cardiac function in diabetic mice, but not in SIRT1−/− diabetic mice. In addition, we found Klotho treatment increased the expression of SIRT1 and PGC-1α and inhibited Drp1-mediated mitochondrial fission and mitochondria-derived superoxide production in neonatal cardiomyocytes. Moreover, inhibition of SIRT1 or PGC-1α (by siRNA) canceled inhibitory effects of Klotho on Drp1 expression and mitochondrial fission. These data indicated that Klotho exerted its cardioprotective effects by reducing Drp1-mediated mitochondrial fission in a SIRT1/PGC-1α-dependent manner. Chromatin immunoprecipitation analysis further showed that PGC-1α negatively regulated Drp1 expression by binding to its promoter. Drp1 inhibitor mdivi-1 alleviated oxidative stress, mitochondrial dysfunction and myocardial dysfunction in diabetic mice.

CONCLUSIONS This work demonstrated that anti-aging protein Klotho prevented diabetes-induced cardiac dysfunction by inhibiting mitochondrial fission via SIRT1/PGC-1α/Drp1 pathway.

GW31-e0510

Endothelial microparticles derived from diabetic mice transferring microRNA-26a contributed to vascular endothelial cell damage via NLRP3 inflammasome-mediated pyroptosis

Xiuting Sun, Xiaofong Zhuang, Xinxue Liao
First Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES Pyroptosis played a crucial role in the development of diabetic endothelial injury. Endothelial microparticles (EMPs) served as potential drug delivery carriers that can carry non-coding RNAs which activated endothelial cells. Studying the function of miRNAs in EMPs will provide new perspectives for the clinical diagnosis and prognostic assessment of endothelial functional impairment.

METHODS Male db/db+ mice were randomly divided into: control, DM^{EMP}, Non-DM^{EMP}, DM^{EMP}+miR-26a, DM^{EMP}+miR-scr groups. EMP was administered intravenously 3 times a week for 4 weeks. EMP was administered by tail vein with an insulin needle three times a week for 4 weeks; 0.1 mL of 5 nmol miR-26a Agomir and miR-scr was administered by tail vein twice a week for 4 weeks. Three db/db+ and three db/m+ mice were selected, venous blood was collected, centrifuged to obtain EMP, high-throughput sequencing to screen for differential gene expression, and luciferase assay to verify miRNA target genes. Three db/db+ and three db/m+ mice were selected, high-throughput sequencing to screen for differential gene expressions in EMPs, luciferase assay to verify miRNA target genes. Thoracic aorta of mice was tested for vasodilatory function, and the aorta of each group of mice was stained with Hematoxylin and eosin (HE), and the aorta of mice was tested for unc-51-like kinase 1 (ULK1), NLRP3 inflammatory small body and cytokine-related protein expression by Western blot. Immunofluorescence detection of NLRP3 and Caspase 1 expression in the aorta of mice free of each group. Different EMPs were co-cultured with HUVEC, HUVEC migration and proliferation were observed. miR-26a was transfected with HUVEC to detect cell proliferation and migration function, Western blot to detect hydrolytic cleavage of NLRP3, Caspase-1, ULK1 expression, immunofluorescence to detect NLRP3 and Caspase 1 co-localization, and cell coke death assay kit to detect the number of cells with Active caspase-1+/7-AAD+; YVAD or MCC 950 pretreatment with HUVEC, pyroptosis assay kit was used to the number of cells with active Caspase-1+/7-AAD+; Western blotting was used to detect hydrolytic cleavage changes in Caspase-1 and GSDMD.

RESULTS Compared with the control group, DM^{EMP} damaged the repair function of aortic endothelium, but no significant reduction in endothelial repair function was seen in the Non-DM^{EMP} group. miR-26a expression was significantly increased in db/db+ mouse EMPs. The luciferase report validated ULK1 as a target gene for miR-26a. In $EMP^{miR\text{-}26a}$-treated mice, adhesion of aortic endothelial cells was further disrupted. DM^{EMP}-treated mice and HUVEC showed increased co-localization of Caspase 1 with NLRP3 and increased TUNEL co-localization with Caspase 1; Western blot detected hydrolytic cleavage of Caspase-1, GSDMD, IL-1β and IL-18. After transfection with HUVEC, miR-26a mimic suppressed ULK1 expression, inhibiting cell proliferation and migration. miR-26a mimic transfection of HUVEC revealed increased co-localization of Caspase 1 with NLRP3 and increased TUNEL co-transfection with Caspase 1. Protein expression of Caspase-1, GSDMD, IL-1β, and IL-18, flow cytometry detection of increased cell pyroptosis. Effects caused by DM^{EMP}-miR-26a were significantly inhibited by pretreatment with YVAD (Caspase-1 inhibitor), MCC950 (NLRP3 inflammatory small body inhibitor).

CONCLUSIONS Diabetic EMPs can lead to endothelial impairment by exerting endothelial damage by carrying miR-26a, which acts through the target protein ULK1. DM^{EMP}-carrying miR-26a promotes the onset of cell pyroptosis death by targeting downregulation of ULK1 expression, resulting in endothelial damage.

GW31-e0512

C1q/TNF-related protein 1 promotes arterial endothelial barrier dysfunction under disturbed flow

Chendie Yang, Xiaoqun Wang
Rui Jin Hospital, Shanghai Jiao-Tong University School of Medicine, Shanghai, P.R. China

OBJECTIVES Atherosclerotic lesions preferentially occur at branch points of arterial trees where the blood flow is disturbed. Disturbed flow increases endothelial permeability, vascular barrier dysfunction, and finally the development of atherosclerosis. CTRP1, a member of C1q/TNF related protein (CTRP) family, is a novel secreted glycoprotein and its biological functions are largely undefined.

METHODS Endothelial permeability was determined by Miles assay in vivo and F-actin staining in vitro. CTRP1 knockout mice were also established to further determine the effect of CTRP1 on vascular barrier function.

RESULTS We found CTRP1 expression was significantly increased by disturbed flow in endothelial cells, thereby promoting cytoskeleton assembly and the formation of paracellular holes. Inhibition of CTRP1 either by specific siRNA notably attenuated disturbed flow-dependent endothelial hyperpermeability. Next, CTRP1 knockout mice were established. Miles assay demonstrated impaired vascular barrier function in mice injected with recombinant CTRP1 proteins, but was greatly improved in CTRP1 knockout mice. Finally, we found leukocyte trans-endothelial migration and atherosclerotic progression was markedly attentuated either in CTRP1 knockout mice or by inhibition of CTRP1 with intravenous injection of specific neutralizing antibodies.

CONCLUSIONS CTRP1 is a mechano-sensitive proinflammatory factor that mediates disturbed flow-induced vascular barrier dysfunction. Inhibition of CTRP1 may inhibit the pathogenesis of atherosclerosis at early stage.

GW31-e0513

C1q/TNF-related protein 1 promotes vasodilatory dysfunctions by increasing arginase 1 activity and uncoupling of endothelial nitric oxide synthase

Chendie Yang, Xiaoqun Wang
Ruijin Hospital, Shanghai Jiaotong University School of Medicine

OBJECTIVES C1q/TNF-related protein (CTRP) 1 was initially identified as a paralog of adiponectin based on the similarity in C1q domain of these two proteins. Previously, we showed that CTRP1 promotes the development of atherosclerosis by increasing endothelial adhesiveness. Here, we sought to investigate whether CTRP1 also influences vascular dilatory functions.

METHODS Vascular dilatory responsiveness was compared by intravital microscopy of cremaster arterioles between CTRP1 transgenic (Tg-CTRP1), CTRP1 knockout (CTRP1 KO) and C57 wild type (WT) control mice. In situ production of reactive oxygen species (ROS) was determined by dihydroethidium (DHE) staining.

RESULTS We found a dramatic impairment of endothelium-dependent arteriolar dilation in Tg-CTRP1 mice, whereas vasodilation was markedly enhanced in CTRP1 KO mice as compared to WT controls. Meanwhile, elevated production of reactive oxygen species (ROS) was detected in the vascular wall of Tg-CTRP1 animals. In cultured endothelial cells, CTRP1 stimulation resulted in reduced nitric oxide (NO) bioavailability both in the cell lysates and conditioned media. Furthermore, we found that arginase 1 was significantly increased by CTRP1 in a dose-dependent fashion, thereby leading to endothelial nitric oxide synthase (eNOS)-uncoupling and reactive oxygen species generation. Inhibition of arginase activity by synthetic chemicals markedly improved CTRP1-dependent vasodilatory dysfunctions.

CONCLUSIONS These data define the essential role of CTRP1 in mediating vasodilatory dysfunctions, as well as propose a novel mechanism that increased arginase activity by CTRP1 leads to uncoupling of eNOS homodimers, thereby limiting NO biosynthesis and amplifying ROS production.

GW31-e0514

C1q/TNF-related protein 5 promotes atherogenesis by enhancing transcytosis and oxidative modification of low-density lipoprotein through increasing 12/15-lipoxygenase

Chendie Yang, Xiaoqun Wang
Ruijin Hospital, Shanghai Jiaotong University School of Medicine

OBJECTIVES Increased transcytosis of low-density lipoprotein (LDL) across the endothelium and oxidation of LDL deposited within the subendothelial space are crucial early events in atherogenesis. C1q/TNF-related protein (CTRP) 5 is a novel secreted glycoprotein and its biological functions are largely undefined.

METHODS In this study, we analyzed CTRP5 levels in sera of patients with coronary artery disease (CAD, n=288) and non-CAD controls (n=264). In this study, we analyzed CTRP5 levels in sera of patients with coronary artery disease (CAD, n=288) and non-CAD controls (n=264). The role of CTRP5 in LDL transcytosis and oxidative modification was investigated in vivo and in vitro.

RESULTS We found CTRP5 serum levels were higher in patients with than without CAD (247.26±61.71 vs. 167.81±68.08 ng/mL, P<0.001), and were positively correlated to the number of diseased vessels (Spearman's r=0.611, P<0.001). Increased expression of CTRP5 was detected in human coronary endarterectomy specimens as compared to non-atherosclerotic arteries. Immunofluorescence showed that CTRP5 was predominantly localized in endothelium and macrophages in human atherosclerotic lesions. *In vivo* and *in vitro* experiments demonstrated that CTRP5 promoted transcytosis of LDL across endothelial monolayers, as well as the oxidative modification of LDL in endothelial cells. Inhibition of CTRP5 with a neutralizing antibody dramatically attenuated the deposition of oxidized lipids in the aortic wall of ApoE$^{-/-}$ mice. Mechanistically, we found that CTRP5 up-regulated 12/15-lipoxygenase (LOX), a key enzyme in mediating LDL trafficking and oxidation, through STAT6 signaling. Genetic or pharmacological inhibition of 12/15-LOX dramatically attenuated the deposition of oxidized LDL in subendothelial space and the development of atherosclerosis.

CONCLUSIONS These data indicate that CTPR5 is a novel pro-atherogenic cytokine and promotes transcytosis and oxidation of LDL in endothelium through up-regulating 12/15-LOX.

GW31-e0521

Increased 12/15-lipoxygenase by disturbed flow promotes the oxidative modification of low-density lipoprotein in endothelial cells and the development of atherosclerosis

Xiaoqun Wang, Lin Lu
Rui Jin Hospital, Shanghai Jiao-Tong University School of Medicine, Shanghai, P.R. China

OBJECTIVES Atherosclerosis is predisposed at bifurcations, branch points and arterial curvatures where the blood flow is disturbed. Deposition and oxidative modification of low-density lipoprotein (LDL) in the subendothelial intima is an early event in the pathogenesis of atherosclerosis. However, the effect of disturbed flow (d-flow) on LDL oxidation and the underlying mechanisms remain unclear. In this study, we investigated the role of 12/15-lipoxygenase (LOX) in LDL oxidation in endothelial cells (EC) and the development of atherosclerosis at d-flow sites.

METHODS *En face* immunofluorescence was performed to analyze the expression of 12/15-LOX in EC under exposure to different flow patterns. Protein expression and LDL oxidation was studied *in vitro* by using 2 different flow apparatuses. Animal model of d-flow was established by partial ligation of the carotid artery.

RESULTS *En face* staining exhibited a significant increase in 12/15-LOX protein expression in EC in areas exposed to d-flow than those exposed to steady flow (s-flow). Carotid partial ligation in ApoE knockout mice led to substantially increased deposition of oxidized LDL in the subendothelial intima and formation of atherosclerotic plaques in the carotid artery, whereas these detrimental effects by d-flow were markedly attenuated in ApoE/12/15-LOX double knockout mice. In cultured EC, d-flow generated by a reversal flow pump markedly promoted the expression of 12/15-LOX and translocation of the protein onto the cell membrane. Inhibition of 12/15-LOX in EC, either by knockdown with its specific siRNA or a pharmacological inhibitor, evidently suppressed LDL oxidation in response to d-flow. Mechanically, we found d-flow induced the expression of 12/15-LOX by activating a specific responsive element in the 12/15-LOX promoter through recruiting a shear stress-sensitive transcriptional factor SREBP2. Chromatin immunoprecipitation further confirmed the interaction of SREBP2 with the promoter of 12/15-LOX upon d-flow exposure.

CONCLUSIONS These data define an essential role of 12/15-LOX in promoting the pathogenesis of atherosclerosis under d-flow by increasing LDL oxidation in EC through SREBP2 signaling.

GW31-e0523

Fibroblast growth factor 21 improves diabetic endothelial progenitor cells function and promotes diabetic ischemic angiogenesis

Xia Fan, Xiaoqing Yan, Yi Tan
Wenzhou Medical University

OBJECTIVES Diabetic vascular disease is one of most serious complications of diabetes mellitus. Promoting angiogenesis is an important strategy for the treatment of diabetic vascular disease. Endothelial progenitor cell (EPC) plays a key role in angiogenesis. The number of EPC is decreased and the function of EPC impaired in diabetic conditions. Increasing the number of EPC and/or improving EPC function can effectively promote diabetic ischemic angiogenesis. Fibroblast growth factor 21 (FGF21) is a member of the fibroblast growth factor family that plays a key role in regulating glucose and lipid metabolism and has the potential to treat diabetes mellitus and its complications. However, its role in diabetic vascular disease is largely unknown. This study explored the effect of FGF21 on diabetic ischemic angiogenesis and the underlying mechanism.

METHODS C57BL/6J mice received 5 doses STZ injection to induce type 1 diabetes mellitus. Hind limb ischemia (HLI) model was established by unilateral femoral aortic ligation, and 200 ng/mL FGF21 or equal volume of vehicle was administered by intraperitoneal injection every day. Laser Doppler assay was used to evaluate the blood perfusion of ischemic hind limb at day 0, 3, 7, 14, 21 and 28 days after surgery. After the last Laser Doppler assay, mice were sacrificed and the gastrocnemius muscle tissues of ischemic hind limb were collected. The expression of CD31 was detected by immunofluorescence staining to valuate the number of neovascularization in ischemic hind limbs. EPC was extracted from human umbilical cord blood and incubated in culture medium containing 33 mM glucose for 24 h to mimic in vivo diabetic condition, along with or without 200 ng/mL FGF21. The migration capability of EPC was investigated by scratch assay, and the angiogenic ability of EPC was investigated by matrix tube-like structure formation assay to evaluate the protective effect of FGF21 on the migration and tubing function of EPC treated with high glucose. The content of NAD+ in cell lysate was detected by the kit, and the expression of proteins of related pathways was detected by Western Blot.

RESULTS FGF21 could enhance blood perfusion in ischemic site of type 1 diabetic mice, but had no significant effect on blood sugar and body weight. The expression of CD31 in ischemic gastrocnemius muscle of mice treated with fibroblast growth factor 21 was up-regulated, indicating enhanced neovascularization. In vitro study also showed that both the receptor FGFR1 and co-receptor beta-klotho (KLB) were expressed on the cell surface of EPC. FGF21 can also stimulate AKT phosphorylation in EPC. Moreover, the migration and tubing ability of EPC were impaired by high glucose, while FGF21 can ameliorate this process. Meanwhile, the content of NAD+ in EPC treated with high glucose decreased, and it increased with the administration of fibroblast growth factor 21. Moreover, NAD+ supplementation can improve EPC migration and tubular damage caused by high glucose.

CONCLUSIONS FGF21 can effectively promote the recovery of blood flow in HLI tissue of type 1 mice. FGF21 may improve the angiogenesis ability of EPC treated with high glucose by increasing the content of NAD+ in EPC cells.

GW31-e0524

LncRNA H19-dependent mitophagy regulation is crucial in attenuating cardiac lipotoxicity protection

Shaohua Wang, Sixu Chen, Yangxin Chen
Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University

OBJECTIVES Cardiac mitophagy and mitochondrial respiratory function are altered during lipotoxicity but the underline mechanism are not largely unknown.

METHODS Palmitic acid and ob/ob mice were used to induce cardiac lipotoxicity *in vitro* and *in vivo*, respectively. Mitochondrial function was evaluated by measuring mitochondrial mass, respiratory complex expression and respiratory capacity. Mitochondrial biogenesis was determined by assessing related transcription factors (PPARγ coactivator 1α, PGC-1α and mitochondrial transcription factor A, TFAM). Mitophagy was determined by transmission electron microscopy (TEM) and fluorescence indicators (immunofluorescence co-staining of LC3 and Tomm20, mitoTimer and mtKemia). The crucial mitophagy pathways were identified and small molecule RNA interference against the target gene was used to assess the role of mitophagy in lipotoxic cardimomyocytes. Potentially critical involved long-coding RNAs were screened by analyzing high throughput data, function and mechanism of which on mitophagy were explored. The underlined mechanism regulating the expressions of the target lncRNA during lipotoxicity were also addressed.

RESULTS Lipotoxicity resulted in a substantial decrease of mitochondrial number and volume, along with a reduction of respiratory capacity. Lipotoxicity increased PGC-1α and TFAM protein levels and promoted mitophagy, as

indicated by TEM and fluorescence indicators. Fundc1 and Bnip/Nix were not changed significantly upon lipotoxicity while obvious up-regulation of Pink1 and Parkin were observed. Moreover, ubiquitination of mitochondrial membrane proteins were found. Knocking down of Parkin attenuated palmitic acid-induced mitophagy and increased respiratory capacity. Analysis of the lipid accumulation high throughput dataset (GEO Number: GSE27975) found that lncRNA H19 expression was mostly altered among the genes with human and rat homologous sequences. Forced expression of H19 dramatically reduced Pink1 expression, along with a decrease of mitophagy and a restoration of respiratory capacity. Pink1 mRNA was not changed by palmitic acid while RNA antisense purification (RAP, using H19 probe)-PCR revealed a combination of H19 and Pink1 mRNA. H19 was predicted to bind to eukaryotic translation initiation factor 4A3 (eIF4a3) but result from H19 RAP-mass spectrometry found eIFA2 rather than eIFA3 and RAP-Western blot showed much more eIF4a2 than eIF4A3 in abundance. RNA Immunoprecipitation using eIF4a2 antibody demonstrated the combination of eIF4a2 protein, H19 and Pink1 mRNA. Methylation levels of H19 promoter sequence were significantly increased by palmitic acid. Expression and activity of methylase Dnmt3b were up-regulated while those of Dnmt1 and Dnmt3a were suppressed. Chromatin-immunoprecipitation using Dnmt3b antibody yield a significantly enriched sequences around the putative methylation regions inside H19 promoter.

CONCLUSIONS Down-regulation of H19 played a crucial role in lipotoxicity-induced cardiac mitochondrial capacity impairment *via* promoting mitochondria mitophagy. H19, the expression of which was decreased by promoter methylation under lipotoxic circumstances, inhibited excessive mitophagy by imitating Pink1 mRNA translation.

GW31-e0531

The role of Wnt/β catenin signaling pathway in heart failure of rats with selenium deficiency

Yujie Xing, Ying Lv, Dong Liang, Xiaoxiang Liu, Junkui Wang
First Department of Cardiology, Shannxi Provincial People's Hospital, Xi'an, Shaanxi 710068, People's Republic of China

OBJECTIVES To investigate the role of Wnt/β-catenin signaling pathway in heart failure of rats with selenium deficiency.

METHODS Forty rats were randomly divided into the control group and the selenium deficiency group, with twenty rats in each group. Rats in the control group were fed with the standard feed, and rats in the selenium deficiency group were fed with selenium deficiency diet. All rats were fed for sixteen weeks. Then the blood selenium and BNP level of the rats were measured by the eyeball extraction, the cardiac function of the rats was detected by echocardiography, and the expression level of Wnt and β-catenin protein were detected by Western Blotting.

RESULTS The blood selenium level in selenium deficiency group was significantly lower than that in control group, while BNP level in selenium deficiency group was significantly higher than that in control group. Echocardiography showed that the heart function of the selenium deficiency group was lower than that of the control group. Western Blot showed that the expression level of Wnt and β-catenin in selenium deficiency group was higher than that in control group.

CONCLUSIONS Selenium deficiency can cause heart failure of rats, and its mechanism may be related to the activation of Wnt/β-catenin signaling pathway.

GW31-e0544

Effect of reinforcing Qi and activating blood recipe on regulation of myocardial mitochondrial function in rats with chronic heart failure and mechanisms involved

Yingyu Xie[1,2], Zihan Fang[3], Mingyang Wang[1], Yanan Wang[1], Junping Zhang[2]
[1]Tianjin University of Traditional Chinese Medicine
[2]First Teaching Hospital of Tianjin University of Traditional Chinese Medicine
[3]China National Center for Biotuchnology Development

OBJECTIVES To observe the intervention effect of Yiqi Huoxue recipe (YQHX) on rats with chronic heart failure, in order to explore mitochondrial function mechanism.

METHODS The left anterior descending coronary artery ligation was performed to construct the chronic heart failure (CHF) rat model. Among 64 male SD rats, 16 were randomly selected as the sham operation group. After modeling, they were randomly divided into model group, captopril group and YQHX group. After 8 weeks of intervention, cardiac tissues were collected, body mass and heart mass were weighed, and echocardiography were performed to detect the changes in cardiac structure, and detection of NT-probNP to determine the degree of heart failure in rats. Masson staining was performed to determine the myocardial interstitial collagen volume fraction. Transmission electron microscopy was used to observe the structure and morphology of mitochondria in myocardial tissue. Western blot was used to detect the expression levels of mitochondrial fusion protein optic atrophy 1 (Opa1) and cleavage protein dynamic-related protein 1 (Drpl). The quantitative Real-time PCR was applied to detect the expressions of PINK1/Parkin pathway-related factors.

RESULTS Compared with the sham group, the left ventricular wall of the model group was significantly thickened ($P<0.05$), the cardiac cavity was significantly enlarged, NT-proBNP was increased ($P<0.01$), and the content of collagen in the myocardial interstitium was increased ($P<0.01$). The expression level of Opal decreased, the expression level of Drp1 increased ($P<0.05$), the mRNA expression level of PINK1 and Parkin increased ($P<0.01$). Compared with the model group, YQHX group can reduce ventricular wall thickening, heart chamber enlargement, myocardial interstitial collagen content, up-regulate the low expression of Opa1, but down-regulate the high expressions of Drpl, PINK1, Parkin ($P<0.05$, $P<0.01$).

CONCLUSIONS YQHX can effectively improve mitochondrial function in rats with CHF. The mechanism may be related to the regulation of PINK1/Parkin and the maintenance of mitochondrial dynamic stability.

GW31-e0555

Short term vagus nerve stimulation targets to regulate Bcl-2 by upregulating miR-126, thereby improving cardiac function in rats with chronic heart failure

Yanhua Xuan[1], Shuangshuang Liu[2], Zhijun Sun[2]
[1]Department of Cardiology Medicine, Liaoning Provincial People's Hospital
[2]Department of Cardiology Medicine, Shengjing Hospital of China Medical University

OBJECTIVES Previous studies have reported that short-term vagus nerve stimulation (VNS) improves cardiac function in rats with chronic heart failure (CHF). The molecular mechanisms are unclear. The potential effect of microRNA (miR)-126 in apoptosis of short-term VNS was examined.

METHODS A total of 3 weeks after inducing CHF, the rats were divided into three groups: Sham stimulation in sham operated rats, sham stimulation in CHF rats (CHF-SS), and treated with VNS in CHF rats (CHF-VNS). The right vagus nerve of the neck was stimulated for 72 h in CHF rats with rectangular pulses of 40 ms duration at 1 Hz and 5 V. miR-126 was focused on, which exhibited differential expression in the miRNA microarray analysis of CHF rats, and the effects of VNS on apoptosis were examined.

RESULTS It was verified that the expression level of miR-126 in the CHF-VNS group was increased, and the expression was reduced in the CHF-SS group. Furthermore, mimics or inhibitor of miR-126 was transfected into H9c2 to investigate its function on apoptosis. B-cell lymphoma 2 (Bcl-2) was confirmed a target of miR-126 through a dual luciferase reporter assay and western blotting. It was demonstrated that upregulated miR-126 decreased apoptosis in H9c2 cells. The apoptosis-associated proteins were further detected in H9c2 cells and rat tissue. The mRNA and protein expression levels of caspase-3 and Bcl-2-associated X protein were decreased in the CHF-VNS group, the expression of Bcl-2 were increased. The results were consistent with the in vitro study in the miR-126 inhibitor group.

CONCLUSIONS The present study demonstrated that short-term VNS decreased apoptosis by upregulating miR-126 in rats with CHF. Therefore, the results of the present study provide basic evidence for short-term VNS in the clinical treatment of CHF.

GW31-e0561

Self-renewal of local macrophages attenuates doxorubicin-induced cardiomyopathy

Hanwen Zhang, Andi Xu, Qi Chen
Nanjing Medical University

OBJECTIVES Doxorubicin-induced cardiomyopathy (DiCM) is a primary cause of heart failure and mortality in cancer patients, in which macrophage-orchestrated inflammation serves as an essential pathological mechanism. However, the specific roles of tissue-resident and monocyte-derived macrophages in DiCM remain poorly understood. Our objective is to uncover the origins, phenotypes, and functions of proliferative cardiac resident macrophages and mechanistic insights into the self-maintenance of cardiac macrophage during DiCM progression.

METHODS Mice were administrated with doxorubicin to induce cardiomyopathy. Dynamic changes of resident and monocyte-derived macrophages were examined by lineage tracing, parabiosis, and bone marrow transplantation. We then conducted RNA-sequencing (RNA-seq) experiments to examine the global gene expression profile to dissect the regulatory mechanism of resident reparative macrophage proliferation in the DiCM heart. Both global or macrophage-specific SR-A1 knockout mice was used to confirm the role of SR-A1 in modulating resident reparative macrophage proliferation and DiCM progression. To further address the role of the SR-A1-c-Myc pathway in DiCM pathogenesis, the lentivirus to silence or overexpress macrophage c-Myc was produced using the SP-C1 promoter.

RESULTS We found that the monocyte-derived macrophages primarily exhibited a pro-inflammatory phenotype that dominated the whole DiCM pathological process and impaired cardiac function. In contrast, cardiac resident macrophages were vulnerable to doxorubicin insult. The survived resident macrophages exhibited enhanced proliferation and conferred a reparative role. Global or myeloid specifically ablation of class A1 scavenger receptor (SR-A1) inhibited proliferation of cardiac resident reparative macrophages and therefore exacerbated cardiomyopathy in DiCM mice. Importantly, the detrimental effect of macrophage SR-A1 deficiency was confirmed by the transplantation of bone marrow. At the mechanistic level, we show that c-Myc, a key transcriptional factor for the SR-A1-P38-SIRT1 pathway, mediated the effect of SR-A1 in reparative macrophage proliferation in DiCM.

CONCLUSIONS The SR-A1-c-Myc axis may represent a promising target to treat DiCM through augmentation of cardiac resident reparative macrophage proliferation.

GW31-e0562

CDK9-activated SGK3 promotes myocardial repair and regeneration after myocardial infarction via GSK-3β/β-catenin pathway

Yafei Li, Tianwen Wei, Yi Fan, Hao Wang, Liansheng Wang
Department of Cardiology, the First Affiliated Hospital of Nanjing Medical University

OBJECTIVES Neonatal heart maintains entire regeneration capacity in a transient regeneration window, but the adult heart loses this function. This process involves numerous core hubs dysregulation of expression and activity that adversely affect the myocardium regeneration ability. Present study screened a functional kinase of serine/threonine-protein kinase 3 (SGK3) in cardiac regeneration after neonatal myocardial infarction (MI) using quantitative phosphoproteomics.

METHODS We used quantitative phosphoproteomics data of infarct border zone in newborn heart after MI to identify regeneration related kinases. Gain- and loss-of-function experiments were performed to determine the effect of SGK3 in cardiomyocyte (CM) proliferation and cardiac repair after apical resection (AR) or MI. Pull-down assay and co-immunoprecipitation (Co-IP) experiments were conducted to investigate the direct binding target proteins of SGK3.

RESULTS SGK3 protein expression was highly expressed at postnatal day 1 (P1), reduced at postnatal day 7 (P7) until adult. *In vitro*, CM proliferation ratio was elevated by SGK3 overexpression, while it was decreased by knockdown of SGK3. *In vivo*, inhibition of SGK3 shortened the time window of cardiac regeneration after AR in neonatal mice, and overexpression of SGK3 significantly promoted CM proliferation and cardiac repair after MI. Mechanistically, SGK3 could be directly combined with and activated by cyclin dependent kinase 9 (CDK9). Inhibition of CDK9 partially abolished the effect of SGK3 on CM proliferation. Moreover, SGK3 could repress GSK-3β activity and increase β-catenin expression.

CONCLUSIONS Our study revealed a key role of SGK3 in cardiac regeneration following AR or MI injury, which may reopen a novel therapeutic avenue for MI.

GW31-e0568

Thyroid hormones inhibit apoptosis of macrophage induced by oxidized low density lipoprotein

Yu Ning[1,2], Wanwan Wen[2], Yunxiao Yang[2], Yifan Jia[2], Mengling Huang[2], Guihao Chen[1], Yuejin Yang[1], Ming Zhang[2]
[1]State Key Laboratory of Cardiovascular Diseases, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College
[2]Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University

OBJECTIVES Increasing evidence suggests that hypothyroidism aggravates atherosclerosis. Macrophages apoptosis plays a significant role in the formation and progression of atherosclerotic plaques. No known empirical research has focused on exploring the effect of thyroid hormones on macrophage apoptosis in atherosclerotic plaques.

METHODS Mouse RAW264.7 leukemic monocyte-macrophage cells were treated with 100 μg/mL oxidized low density lipoprotein (oxLDL) to elicit foam cell formation. Cells were also incubated with different concentrations of thyroid hormones (T3: 0.38, 0.75, 1.00 μg/L; T4: 25, 50, 100 nmol/L) to study their effects on functions of macrophage foam cells. Small interfering RNA (siRNA) was used to knock down the expression of thyroid hormone receptor alpha1 (TRα1) in RAW264.7. Then the cells survival, oxidative stress and apoptosis were tested.

RESULTS MTT assay revealed that T3 and T4 concentration-dependently decreased the cell proliferation inhibition rates of macrophage foam cells. Thyroid hormones protected RAW264.7 from reactive oxygen species generation induced by oxLDL in a concentration-dependent way, increasing expression of antioxidant enzymes (Sod1, Sod2, Catalase, Gpx1) and decreasing expression of NADPH oxidase subunits (gp91phox, p22phox, p47phox, p67phox). Thyroid hormones concentration-dependently attenuated apoptosis rates and expression of apoptosis-related proteins cleaved Caspase-3 and cleaved Caspase-9 of RAW264.7 induced by oxLDL. After knocking down the expression of thyroid hormone receptor alpha1 (TRα1), the antiapoptotic effects of T3 and T4 were markedly weakened.

CONCLUSIONS Thyroid hormones concentration-dependently promote macrophage foam cells survival and inhibit cell apoptosis. This may be ascribed to the antioxidant effect of thyroid hormones and the antiapoptotic effect of TRα1.

GW31-e0574

Recombinant fibroblast growth factor 21 blunts angiotensin II-induced pyroptosis and apoptosis in rat aortic adventitial fibroblasts by activating the APLN/APLNR and eNOS/ERK signaling

Jiuchang Zhong, Chen Fang, Ran Miao, Ying Liu, Juanjuan Song, Jiawei Song, Kun Zuo, Ying Dong, Xinchun Yang
Heart Center and Beijing Key Laboratory of Hypertension, Beijing Chaoyang Hospital Affiliated to Capital Medical University, Beijing 100020, China

OBJECTIVES Activation of the renin-angiotensin system (RAS) and increased angiotensin (Ang) II levels have been implicated in adverse vascular remodeling and progression to hypertension. APLN mediates important physiological effects in the vasculature and is an important pharmacological target while blockade of the RAS and Ang II signaling improves vascular dysfunction; reduce hypertension and cardiovascular events in patients. Adventitial fibroblasts (AFs) are the most abundant cell type in vascular adventitia and play a crucial role in the control of vascular function. Fibroblast growth factor 21 (FGF21) functions as a novel endocrine factor involved in the regulation of glucose, lipid and energy metabolism and has been shown to exert protective functions in hypertension and vascular dysfunction in Ang II-induced hypertensive mice by activation of the angiotensin-converting enzyme 2 (ACE2)/Ang-(1-7) axis. However, little was elucidated upon pathophysiology significance and underlying mechanisms of FGF21 in the AFs.

METHODS Here, we used APLN deficient ($APLN^{-/y}$) mice and cultured rat AFs to evaluate the influences of recombinant human FGF21 (rFGF21) and Pyr1-Apelin-13 on Ang II-mediated actions by real-time RT-PCR, Western blotting, TUNEL and dihydroethidium fluorescence staining, respectively.

RESULTS The 12-month aged $APLN^{-/y}$ mice developed vascular hypertrophy and dysfunction with reduced ACE2 and FGF21 levels. Ang II infusion potentiated oxidative stress, apoptosis, and pyroptosis in young $APLN^{-/y}$ aorta leading to exacerbation of vascular dysfunction. In cultured rat aortic AFs, stimulation of Ang II led to a marked decrease in FGF21 levels and increases in cellular proliferation, migration and transformation, which were improved by rFGF21 and Pyr1-apelin-13, respectively. Furthermore, pretreatement with rFGF21 strikingly prevented Ang II-induced promotion in ROS generation and levels of proinflammatory factor NF-κB and IL-1β. Notably, administration of rFGF21 and Pyr1-apelin-13 remarkably rescued Ang II-mediated pyroptosis and apoptosis in rat AFs by augmenting of the Bcl-2/Bax ratio and phosphorylated levels of eNOS and preventing expression of pyroptosis related protein caspase-1 and phosphorylated levels of ERK1/2.

CONCLUSIONS In summary, FGF21 and APLN-APLNR pathway are negative regulators of Ang II-mediated adverse vascular remodeling and adventitial dysfunction. We showed that loss of APLN leads to reduction of ACE2 and FGF21 and increased oxidative stress, apoptosis and vascular dysfunction in response to Ang II. Conversely, FGF21 and pyr1-apelin-13 play important roles in the Ang II-mediated oxidative stress, pyroptosis and apoptosis in rat aortic adventitial fibroblasts by modulating the eNOS/ERK signaling. Thus, targeting the FGF21 and APLN pathway represents a novel therapeutic approach against adventitial dysfunction and vascular disorders. This research was supported by the General Program and the National Major Research Plan Training Project of National Natural Science Foundation of China (81770253 and 91849111).

GW31-e0575

MiRNA-122-5p exacerbates angiotensin II-mediated promotion of apoptosis, oxidative stress and loss of autophagy in rat cardiofibroblasts by the modulation of APLN-AMPK-mTOR signaling

Jiuchang Zhong[1], Mei Yang[1], Juanjuan Song[1], Xiaoyan Liu[1], Jing Li[1], Juan Wang[1], Jun Cai[2], Xinchun Yang[1], Guangzhen Zhong[1]
[1]Heart Center and Beijing Key Laboratory of Hypertension, Beijing Chao-Yang Hospital, Capital Medical University, Beijing 100020, China

[2]Hypertension Center, Fuwai Hospital, National Center for Cardiovascular Diseases of China, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100037, China

OBJECTIVES Cardiac remodeling is characterized by ventricular hypertrophy and myocardial fibrosis, which are the main causes of heart failure. MicroRNAs (miRNAs) are a class of endogenous small non-coding RNA molecules and have emerged as crucial regulators of myocardial fibrosis, remodeling and cardiofibroblasts (CFs) dysfunction. We previously found that miRNA-122-5p is significantly upregulated in a rat model of cardiac hypertrophy and dysfunction induced by pressure overload in association with downregulated levels of APLN. However, the exact roles and underlying mechanisms of miRNA-122-5p in the Ang II-induced cardiac fibrosis and CFs dysfunction are still unclear.

METHODS Here, we evaluate roles of miRNA-122-5p in angiotensin (Ang) II-mediated hypertensive rats and rat CFs by real-time RT-PCR, Western blotting, TUNEL, Masson staining and dihydroethidium fluorescence staining, respectively. The Sprague-Dawley rats were randomized to Ang II infusion with an osmotic minipump and pretreated with recombinant adeno-associated viral vector (AAV)-miRNA-122-5p (rAAV-miRNA-122-5p) or rAAV-GFP for 4 weeks.

RESULTS Ang II infusion triggered promotion of myocardial fibrosis and apoptosis and reduction levels of apelin, p-AMPK and LCBII in hypertensive rats, which were exacerbated by rAAV-miRNA-122-5p treatment. In cultured rat CFs, stimulation of Ang II resulted in a marked decrease in autophagy and increases in apoptosis, proliferation and superoxide generation, which were prevented by pretreated with miRNA-122-5p inhibitor. Furthermore, Pyr1-apelin-13 abolished Ang II-induced loss of autophagy and promotion of apoptosis and oxidant injury in rat CFs linked with reduced levels of P62 and enhanced levels of beclin-1. Notably, miRNA-122-5p mimics significantly reversed Pyr1-apelin-13-mediated beneficial roles in apoptosis and autophagy in CFs associated with decreased AMPK phosphorylated levels and elevated mTOR phosphorylated levels.

CONCLUSIONS In summary, miRNA-122-5p plays an important role in myocardial fibrosis, apoptosis, autophagy and CFs dysfunction. Our data illustrated that miRNA-122-5p exacerbated Ang II-induced profibrotic, proapoptotic and anti-autophagic actions. Pyr1-apelin-13 activation and miRNA-122-5p inhibition appear to show counter regulation against Ang II-mediated loss of autophagy and promotion of apoptosis and oxidative injury in rat CFs by modulating the AMPK-mTOR phosphorylation signaling. Thus, the development of promising strategies to interfere with miRNA-122-5p might be a promising field for the therapeutic approach in myocardial fibrosis and related disorders. This research was supported by the General Program and the National Major Research Plan Training Project of National Natural Science Foundation of China (81770253 and 91849111).

GW31-e0576

HDAC6 mediates nicotine-induced macrophage pyroptosis in atherosclerosis via NF-κB/NLRP3 signaling pathway

Shuang Xu, Hangwei Chen, Huaner Ni, Qiuyan Dai
Department of Cardiology, Shanghai Genaral Hospital, Shanghai Jiao Tong University School of Medicine

OBJECTIVES In atherosclerotic development, nicotine activates inflammation and pyroptosis. Histone deacetylase 6 (HDAC6) is considered to participate in inflammation, however, whether HDAC6 mediates nicotine-induced pyroptosis is largely unknown. This study aims to investigate the role of HDAC6 in nicotine-induced pyroptosis in macrophages.

METHODS For *in vivo* study, macrophage pyroptosis in plaque was assessed by Tunel/CD68 and Caspase-1/CD68 staining. For *in vitro* study, pyroptosis and related signaling pathway in RAW264.7 cells were evaluated by western blotting, immunofluorescence, lactic dehydrogenase (LDH) activity, co-immunoprecipitation and chromatin immunoprecipitation.

RESULTS High fat diet and nicotine upregulates macrophage pyroptosis in atherosclerotic lesions. Nicotine promotes pyroptosis in RAW264.7 cells, as evidenced by Caspase-1 cleavege, IL-1β and IL-18 production, elevation of LDH activity and propidium iodide positive rate. In addition, nicotine stimulates the expression of HDAC6, and HDAC6 deficiency by siRNA and Tubastatin-A suppresses nicotine-induced pyroptosis. Moreover, HDAC6-mediated deacetylation of p65 enhances its nuclear translocation and binding to NLRP3 promoter regions. Silencing p65 or NLRP3 resulted in decreased pyroptosis.

CONCLUSIONS HDAC6 inhibition exhibited a protective role against nicotine-induced pyroptosis in macrophages, which is partly mediated by acetylation of p65.

GW31-e0607

β-Elemene activates PPARβ/δ to block lipid-induced inflammatory pathways in mouse HF heart

Mingyan Shao, Xue Tian, Pengrong Gao, Yong Wang
Beijing University of Chinese Medicine

OBJECTIVES β-Elemene has been widely used as a traditional medicine for its anti-tumor activity against a broad range of cancers. However, the effect of β-elemene on in heart failure mice has yet to be determined. This study aims to investigate the effects of β-elemene on heart failure and its underlying mechanism.

METHODS Left anterior descending (LAD)-induced HF mouse model *in vivo* and oxygen-glucose deprivation/recovery (OGD/R)-induced H9C2 model *in vitro* were established. HE staining was used to observe the morphology of heart; using oil red O staining to identify spatial distribution of lipids in mouse cardiac tissue; transcript levels of mitochondrial and peroxisomal FAO genes were assayed by real-time polymerase chain reaction (PCR) and the protein expression was measured by western blot and immunocytochemistry methods.

RESULTS β-Elemene improved heart function by up-regulating cardiac ejection fraction (EF) and fractional shortening (FS) values. Furthermore, β-elemene administration rescued ventricular dilation, lipid accumulation and inflammation infiltration in arginal areas of myocardial infarction. Moreover, β-elemene augmented the mRNA expression of fatty acid oxidation-associated genes, such as peroxisome proliferator-activated receptor β (PPARβ), carnitine palmitoyltransferase 1 (CPT1) and so on. Similar results were obtained *in vitro*, treatment with β-elemene increased the proteins expressions of PPARβ and CPT1 and suppressed inflammatory markers, such as nuclear factor κB (NF-κB) nuclear translocation, inhibitory κBα (IκBα) degradation, interleukin-6 (IL-6) expression, and pro-inflammatory cytokines (such as TNFα). siRNAs for PPARδ were reversed by β-elemene. Consistently, molecular docking estimate that β-elemene targeted on PPARβ.

CONCLUSIONS This study demonstrated that β-elemene as PPARβ agonist, protected the heart failure mice from lipid-induced inflammatory damage and widened new therapeutic effects for the treatment of heart disease in clinical.

GW31-e0632

Nano-simvastatin modulates macromphage polarization to influence healing of the infarcted myocardium

Xue Tian, Mingyan Shao, Yong Wang
Beijing University of Chinese Medicine

OBJECTIVES Macrophage polarization plays an essential role in the process of heart injury and repair, and is important for the regulation of inflammation after myocardial infarction (MI). This study aims to clarify whether nano-simvastatin can regulate macrophage polarization to exert anti-inflammatory effect and explore potential mechanism.

METHODS In our study, we constructed left anterior descending (LAD)-induced MI mice models and LPS (100 ng/mL) stimulated Raw264.7 cells for 24 h to induce M1 macrophage activation. *In vivo*, mice received either ddH_2O or nano-simvastatin (1 mg/kg) for 7 days. Echocardiography was used to evaluate cardiac function after MI. HE staining was used to observe the morphology of heart. MPI/MRI molecular imaging dynamically detected the distribution of drugs. *In vitro*, macrophage polarization pathway-related proteins (such as, CD206, STAT6, Arg-1, IRF4) were detected by Western blot and qPCR. Moreover, flow cytometry were applied *in vivo and vitro* to detect macrophage surface markers (Ly6Clow, Ly6Chigh/CD206, CD86) to measure the polarization state of macrophages.

RESULTS *In vivo*, nano-simvastatin is significantly condensed in the MI (area in risk) by MPI/MRI molecular imaging technology. Nano-simvastatin could improve cardiac function by up-regulating cardiac ejection fraction (EF) and fractional shortening (FS) values. The results of HE showed that nano-simvastatin could improve cardiac remodeling and inflammatory cell infiltration. The results of flow cytometry showed that the number of M1 macrophage surface markers were higher than that in the sham-operated mice. Treated by nano-simvastatin, M1 macrophages in the MI (area in risk) were inhibited and M2 macrophages were activated, suggesting that nano-simvastatin regulated cardiac macrophage polarization. *In vitro*, the results of western blot and qPCR showed that nano-simvastatin could up-regulated the markers of M2 macrophages (CD206, Arg-1), and down-regulated the markers of M1 macrophages (CD86), suggesting that nano-simvastatin could promote the conversion of M1 macrophages to M2 macrophages. Meanwhile, nano-simvastatin could increase the expressions of STAT6 and IRF4. Flow cytometry displayed that the number of M2 macrophages (CD206) in nano-simvastatin group was increased and M1 macrophage (CD86) was decreased compared with model group.

CONCLUSIONS This study identified that nano-simvastatin targeted macrophage polarization to reduce inflammation, alleviate myocardial fibrosis, and improve cardiac remodeling.

GW31-e0647

HPK1-interacting protein of 55 kD (HIP-55) recruits Smad7 to modulate/regulate TGF-β type I receptor (TβRI) degradation against Cardiac Fibrosis

Yang Sun, Zijian Li
Department of Cardiology and Institute of Vascular Medicine, Peking University Third Hospital; Key Laboratory of Cardiovascular Molecular

Biology and Regulatory Peptides, Ministry of Health; Key Laboratory of Molecular Cardiovascular Sciences, Ministry of Education; Beijing Key Laboratory of Cardiovascular Receptors Research, Beijing 100191, China

OBJECTIVES Pathological cardiac fibrosis is a common pathological feature of many cardiac diseases and an independent risk factor for cardiac morbidity and mortality. Dysfunction of TβRI receptors have been implicated in the pathogenesis of fibrotic diseases. Smad7 acts as scaffold to regulate TβRI degradation in plasma membrane and prevent the downstream of TGF-β, thus targets cardiac fibrosis. However, the mechanism how Smad7 is recruited to modulate receptors degradation is uncovered. Here, we explore whether HIP-55, HPK1-interacting protein of 55 kDa (HIP-55), its amplification confers poor prognosis in individuals with heart failure in our previous works, could regulates cardiac fibrosis by TβRI degradation and the molecular mechanisms underlying HIP-55 governs TβRI.

METHODS HIP-55 knockdown adenovirus and overexpression adenovirus were constructed to transfect primary mice cardiac fibroblasts (MCF). Biochemical experimental including western blot, real-time PCR were performed to test protein and gene expression. To explore degradation, ubiquitination assay and CHX half-time assay were performed. Immunofluorescence, Co-IP and GST pull down were used to dissect protein interaction. Transverse aorta constriction (TAC) were performed on wild type and HIP-55-deficient C57/BL6 mice to simulate TGF-β induced pathological process, control group were executed sham operation. Echocardiography were used to examine the ventricular contractibility and diastolic functions. Collagen fibers were stained with Picric acid-Sirius red to evaluate myocardial fibrosis.

RESULTS As an adaptor protein, HIP-55 conferred to resistant in cardiac fibrosis via recruiting Smad7 and this process is primarily attributable to promote Smad7/TβRI complex formation and accelerates TβRI receptor degradation. Besides that, HIP-55 could stabilize Smad7 by inhibiting ubiquitination-dependent degradation. These two regulation of HIP-55 impairs TβRI stability and dampens activated TGF-β signaling. These inhibitory effects were dependent on Smad7, as Smad7 ablation abolished them. The against cardiac fibrosis effects of HIP-55 were further confirmed in TAC induced cardiac fibrosis mice model. Cardiac fibrosis was highly exacerbated, cardiac functions whether in ventricular contractibility or diastolic function of HIP-55-decifient mice were worse than wild type mice including lower LVEF and LVFS and higher E/E′. And fibrosis area of HIP-55-decifient mice was remarkable more than wild type mice.

CONCLUSIONS The results presented here suggest that HIP-55 could recruit Smad7 to plasma membrane to accelerate TβRI receptors ubiquitin-dependent degradation. On the other hand, HIP-55 could also form complex with Smad7 to impede Axin/Smad7/Arkadia complex formation and consequently modulation of Smad7 protein stability. By harnessing the mechanism of HIP-55 regulating TβRI receptors could develop putative prophylactic and therapeutic strategies against cardiac fibrosis.

GW31-e0654

Effect of profilin-1 on the asymmetric dimethylarginine induced vascular lesion associated hypertension

Guohua Ni[1], Meifang Chen[2]
[1]Sohome Health Management Center, Sichuan Provincial People's Hospital
[2]Xiangya Hospital, Central South University

OBJECTIVES Asymmetric dimethylarginine (ADMA) is a naturally occurring substance, it inhibits the production of nitric oxide (NO) synthesis in vivo. Profilin-1, a small actin-binding protein, has been documented to be involved in endothelial injury and the proliferation of vascular smooth muscle cells (VSMCs) in hypertension. To investigate the relationship between ADMA and profilin-1 in hypertensive individuals and in cultured VSMCs.

METHODS Forty healthy subjects and 42 matched essential hypertensive patients took part in this study. Rat aortic smooth muscle cells (RASMCs) were treated with different concentrations of ADMA as indicated for 24 h or 30 μM ADMA for different periods of time. RASMCs were transfected with profilin-1 shRNA to interrupt protein expression of profilin-1. The expression of profilin-1 in RASMCs was tested via real time-PCR and western blot analysis. RASMCs were treated with ADMA after pretreated with AG490 (5×10^{-5} M) or rapamycin (10^{-8} M). The level and expression of profilin-1 in RASMCs were tested by real time-PCR and western blot analysis. Cell proliferation was measured via flow cytometry analysis and 3-(4,5-dim-ethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay.

RESULTS Compared with healthy subjects, the levels of ADMA, profilin-1, tumor necrosis factor (TNF-α), vWF and interleukin-8 (IL-8) were markedly elevated, and the levels of nitric oxide (NO) were significantly decreased in hypertensive individuals ($P<0.05$). In vitro, ADMA induced the expression of profilin-1 in concentration-dependent and time-dependent manners in RASMCs ($P<0.05$). ADMA-induced proliferation of RASMCs was significantly inhibited by knockdown of profilin-1 by short hairpin RNA. Furthermore, ADMA-mediated proliferation of RASMCs and expression of profilin-1 were inhibited by blockade of JAK2/STAT3 pathway.

CONCLUSIONS Profilin-1 may be involved in ADMA-mediated vascular lesion in hypertension.

GW31-e0681

Direct sGC stimulation ameliorated doxorubicin-cardiotoxicity mediated by PKG1 activation associated with mitochondrial ferritin

Xiaoxiao Zhao[1], Haneul Cho[2], Sora Lee[2], Weon Kim[2]
[1]Taizhou Hospital of Zhejiang Province, Taizhou, China
[2]Kyung Hee University Medical Center Hospital Center Cardiological Lab, Souel, Korea

OBJECTIVES Doxorubicin (DOX) administration decreases cardiac soluble guanylate cyclase (sGC) activity by reactive oxygen species (ROS) storm. We hypothesized direct sGC stimulation ameliorated doxorubicin-cardiotoxicity. The present study investigated the mechanism and therapeutic effect of sGC activation.

METHODS An activator of oxidized and deactivated sGC, BAY-602770, was used to direct stimulate sGC. H9c2 cardiomyoblasts were treated with DOX (0.5–10 μM), with or without pre-treated 10 μM BAY 60-2770. SD rats were orally administered with BAY60-2770 1 hour prior to every DOX treatment. Echocardiography and hemodynamic values were then analyzed. Proteins expression levels were examined by western blot analysis.

RESULTS BAY60-2770 improved cell viability and ROS in H9c2 cells expose to DOX, which was mediated by PKG1 activation. DOX-induced caspase-3 activation decreased after pretreatment with BAY60-2770 in vivo and in vitro. Mitochondrial ROS and TMRE fluorescence were attenuated by BAY60-2770 associated with high level mitochondrial ferritin (MtFt) expression. We constructed MtFt knock down (MtFt-KD) cells by using siRNA, subsequently did Cyto-ID autophagy detection. Autophagosome was decreased by MtFt-KD, however, BAY60-2770 offset disparate autophagy level between MtFt-KD cells and non-MtFt-KD cells exposed to DOX. As animal experiments, echocardiography showed that BAY60-2770 significantly improved DOX-induced myocardial dysfunction.

CONCLUSIONS PKG1 activation participated in myocardial protection against DOX cardiotoxicity, which associated with MtFt upregulation. MtFt could be one of the antioxidant mechanisms to prevent sGC and PKG1 from oxidative inactivation.

GW31-e0694

Angiotensin II-induced epigenetic regulation mediates cardiac hypertrophy in atrial cardiomyopathy

Liuying Zheng, Hongliang Cong
Tianjin Chest Hospital

OBJECTIVES In 2016, the European Heart Rhythm Association and four other associations established an expert consensus to define, characterise, and classify atrial cardiomyopathy into 4 subgroups based on their histopathological features. The predominant pathological feature of class I and III atrial cardiomyopathy is the hypertrophy of atrial cardiomyocytes. Angiotensin II (AngII) is a major effector peptide of the renin–angiotensin system (RAS) and it commonly stimulates hypertrophy. Emerging evidence suggests that epigenetic mechanisms are involved in RAS-induced cardiac remodelling. Epigenetic regulation such as histone (H3 and H4) lysine acetylation (H3Kac and H4Kac) plays a central role in gene transcription. Histone deacetylation by histone deacetylases (HDACs) promotes chromatin condensation, which causes transcriptional repression. We studied the epigenetic mechanisms by which AngII promotes atrial cardiomyopathy progression. We hypothesise that AngII induces the nuclear export of HDAC-4 and -5 and leads to the derepression of hypertrophy-related genes.

METHODS Atrial tissues were obtained from patients who underwent surgeries. Atrial cardiomyocytes were isolated from the hearts of neonatal rats. The effects and mechanisms of AngII-induced atrial cardiomyocyte hypertrophy were evaluated by enzyme-linked immunosorbent assay (ELISA), immunofluorescence, western blotting, RNA-seq, and chromatin immunoprecipitation (ChIP).

RESULTS Compared with that of sinus rhythm (SR) control individuals, the myocardium of patients with atrial fibrillation (AF) exhibited increased levels of AngII, chromatin-bound myocyte enhancer factor 2 (MEF2), H4ac, and H3K27ac; upregulation of hypertrophy-related genes; and decreased levels of HDAC-4 and -5 bound to the promoters of hypertrophy-related genes. Furthermore, incubation of atrial cardiomyoctytes with AngII increased their cross-sectional area and stimulated the expression of hypertrophy-related genes. AngII also promoted the phosphorylation of HDAC4 and HDAC5 and induced their nuclear export. RNA-seq analyses revealed that AngII significantly up-regulated genes associated with cardiac hypertrophy. ChIP revealed that AngII increased the levels of chromatin-bound MEF-2, H4ac, and H3K27ac and decreased HDAC-4 and -5 enrichment on the promoters of hypertrophy-related genes. All these AngII-induced pro-hypertrophic effects could be partially reverted by losartan (AngII receptor blocker).

CONCLUSIONS Patients with AF manifest an increased susceptibility to hypertrophy and exhibit epigenetic characteristics that are permissive for

the transcription of hypertrophy-related genes. MEF2 may act as platform to respond to positive or negative transcriptional signals by exchanging HATs and class II HDACs. AngII induces histone acetylation via the cytoplasmic-nuclear shuttling of HDACs, which is a novel mechanism of atrial hypertrophy regulation and might provide a promising therapeutic strategy for atrial cardiomyopathy.

GW31-e0705

Zfp36l1b protects angiogenesis through Notch1b/Dll4 and Vegfa regulation in zebrafish

Yangxi Hu[1,2], Rongfang Zhu[3], Yongwen Qin[1], Xianxian Zhao[1], Chun Liang[2], Qing Jing[1,3]
[1]Department of Cardiology, Shanghai Changhai Hospital, Naval Medical University
[2]Department of Cardiology, Shanghai Changzheng Hospital, Naval Medical University
[3]Shanghai Institutes for Biological Sciences, University of the Chinese Academy of Sciences

OBJECTIVES Angiogenesis is a key process for establishing functional vasculature during embryogenesis and involves different signaling mechanisms. The RNA binding protein Zfp36l1 was reported to be involved in various diseases in different species, including cardiovascular diseases. However, whether Zfp36l1b, one of the 2 paralogs of Zfp36l1 in zebrafish, works like mammalian Zfp36l1, and if their molecular mechanisms are different remain unclear. Here, we show that Zfp36l1b plays a crucial protective role in angiogenesis of zebrafish embryos.

METHODS We used transparent transgenic and wild-type zebrafish larvae to dynamically investigate the early stage of angiogenesis with confocal *in vivo*, after the knockdown of *Zfp36l1b* by morpholinos (MOs). *In situ* hybridization and fluorescence-activated cell sorting were performed to detect *Zfp36l1b* expression. mRNA rescue and CRISPR/Cas9 knockdown, and luciferase reporter experiments were performed to further explore the role of *Zfp36l1b* in angiogenesis.

RESULTS We found that knockdown of *Zfp36l1b* led to defected angiogenesis in intersomitic vessels and sub-intestinal veins (SIVs), which could be rescued by the supplement of *Zfp36l1b* mRNA. Moreover, knockdown of *Zfp36l1b* suppressed *Notch1b* expression, while knockdown of *Notch1b* resulted in partly relief of angiogenesis defects induced by *Zfp36l1b* down-regulation. Besides, *Zfp36l1b* knockdown alleviated the excessive branch of SIVs caused by *Vegfa* over-expression.

CONCLUSIONS Our results show that Zfp36l1b is responsible for establishing normal vessel circuits through affecting the extension of endothelial tip cells filopodia and the proliferation of endothelial cells partly through *Notch1b/Fll4* suppression and synergistic function with *Vegfa*.

GW31-e0706

Establishment of a lipid metabolism disorder model in ApoEb mutant zebrafish

Yangxi Hu[1,2], Changzhen Ren[2], Rongfang Zhu[3], Yanda Zhang[2], Zhiqing He[2], Yongwen Qin[1], Xianxian Zhao[1], Chun Liang[2], Qing Jing[1,3]
[1]Department of Cardiology, Shanghai Changhai Hospital, Naval Medical University
[2]Department of Cardiology, Shanghai Changzheng Hospital, Naval Medical University
[3]Shanghai Institutes for Biological Sciences, University of the Chinese Academy of Sciences

OBJECTIVES *ApoEb* is a characterized zebrafish gene homologous to mammalian *ApoE*. ApoE (Apolipoprotein E) is recognized as a ligand for the LDL receptor (LDLR), whose deficiency would largely lead to atherosclerosis and other cardiovascular diseases. Here, we attempted to knock out the zebrafish *ApoEb* gene using the CRISPR/Cas9 system and high-fat diet (HFD) feeding to construct a zebrafish model with a disorder of lipid metabolism.

METHODS The establishment of the model was confirmed by Oil Red O (ORO) staining and lipid measurement. We also detected whether ApoEb deficiency activated the sterol-regulatory element binding protein (SREBP) pathways or induced the malfunction of LDLR. At last, using dimethyl sulfoxide (DMSO) as a negative control and Simvastatin as a positive control, the model was treated with Xuezhikang (XZK), an extract derived from red yeast rice, which is commonly employed as a traditional Chinese medicine for treating coronary heart disease, decreasing blood lipids and preventing other cardiovascular events both within China and globally. ORO staining, lipid measurement of tissue homogenate, and fluorescence microscopy photography were used to obverse its effect on zebrafish larvae.

RESULTS The results demonstrated that in the mutant, significant lipid deposition in the blood vessels occurred, and lipid measurement of larvae's whole-body homogenate and adult plasma showed significant increase in total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels. Interestingly, these lipid metabolism disorders could be apparently relieved by Xuezhikang treatment, and the recruitment of neutrophils in the blood vessels was significantly inhibited.

CONCLUSIONS In conclusion, a lipid metabolism disorder model has been successfully constructed in zebrafish through *ApoEb* knockout. Using this novel model, we found that the preventive effect on atherosclerosis of XZK may be caused by lowering blood lipids and inhibiting the recruitment of neutrophils in blood vessels.

GW31-e0707

Homocysteine induces cell cycle arrest by the miR-21 mediated targeting of CDC25A in human umbilical vein endothelial cells

Yangxi Hu[1,2], Xia Zhu[1,3], Shaohua Dong[1], Jianliang Zhang[1], Xianxian Zhao[1], Chun Liang[2], Lujun Zhang[1]
[1]Department of Cardiology, Shanghai Changhai Hospital, Naval Medical University
[2]Department of Cardiology, Shanghai Changzheng Hospital, Naval Medical University
[3]Department of Cardiology, Urumqi Friendship Hospital

OBJECTIVES Hyperhomocysteinemia (HHcy) has emerged as an independent risk factor for vascular diseases. Previous observations demonstrated that homocysteine (Hcy) contributes to the arrest of endothelial cell (EC) growth, but the precise underlying mechanism is unclear. The present study focused on the role of miR-21 in Hcy-induced human umbilical vein ECs (HUVECs) and explored its underlying mechanisms.

METHODS HUVECs were treated with 0 mM, 3 mM or 5 mM Hcy, and then apoptosis and cell cycle were assessed through flow cytometry. Rt-qPCR was used to detect the expression levels of 15 miRNAs and 15 target genes of miR-21. Luciferase reporter assays and Western blot were used to confirm the down-regulation of miR-21 on *cell division cycle 25A* (*CDC25A*) expression. Flow cytometry revealed how lentivirus induced *CDC25A* overexpression and miR-21 mimics affected cell cycle progression.

RESULTS Treating HUVECs with Hcy caused cell cycle arrest and inhibited cell proliferation. Hcy treatment increased miR-21 levels, which repressed the expression of *CDC25A*. Overexpression of miR-21 downregulated *CDC25A* expression, whereas miR-21 inhibition up-regulated its expression. Luciferase assays showed that miR-21 regulated *CDC25A* level by binding to the 3′-UTR. MiR-21 overexpression induced cell cycle arrest and cell proliferation in Hcy-treated HUVECs. However, overexpressing *CDC25A* could promote cell proliferation and cell cycle, overcoming the effects of Hcy-induced miR-21 upregulation.

CONCLUSIONS This study demonstrated that miR-21 plays an important role in modulating cell cycle progression and cell proliferation by targeting *CDC25A* in an Hcy-induced cell and suggests new insights into the prevention of Hcy-associated cell dysfunction.

GW31-e0708

Renal natriuretic peptide receptor-C deficiency attenuates NaCl cotransporter activity in angiotensin II-induced hypertension

Shuai Shao, Jiguang Wang
Shanghai Key Laboratory of Hypertension, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

OBJECTIVES Hypertension is a leading risk factor for morbidity and mortality of cardiovascular disease. Genome-wide association studies have identified that natriuretic peptide receptor-C (NPR-C) variants are associated with elevation of blood pressure. However, whether NPR-C regulates blood pressure through sodium homeostasis is unknown. In this study, we tested the hypothesis that NPR-C signaling regulates the sodium retention-related hypertension.

METHODS AngII infusion hypertension mouse model was used in male and female wild type (WT) and NPR-C knockout (KO) mice. Systolic blood pressure was measured by tail cuff method. Acute saline expansion was performed in mice after AngII treatment. Renal sodium transporters expression and associated signaling pathway were evaluated by Western Blot. Renal Na^+ clearance was measured by NaCl cotransporter (NCC) blocker hydrochlorothiazide. Different dietary Na^+ intake include 4% high Na^+ and 0.02% low Na^+ were used to determine the role of NPR-C in the regulation of NCC activity. The effect of NPR-C on blood pressure was also evaluated in renal tubule-specific deletion of NPR-C mice were also infused with AngII. CoroNa Green, a sodium ion indicator, and flow cytometry was used to measure sodium uptake in distal convoluted tubule cells. In order to study the mechanism of NPR-C regulating water-salt metabolism, the changes of WNK4/SPAK/NCC expression in distal convoluted tubule cells were detected after giving the inhibitors of NPR-C upstream include natriuretic peptide system and downstream signal such as inhibitory G protein (Gi), phospholipase C (PLC), protein kinase C (PKC) respectively.

RESULTS (1) AngII infusion increased both blood pressure and sodium retention throughout two weeks infusion period both in male and female wild type mice. NPR-C gene knockout alleviates AngII-induced hypertension by inhibiting NCC activity and facilitating urinary sodium excretion. NPR-C deficiency led to natriuresis in response to acute saline expansion after treatment of AngII. Interestingly, AngII increased both total and phosphorylation of NCC abundance involving in activation of With-No-lysine Kinase 4 (WNK4)/Ste20 related proline/alanine rich kinase (SPAK) which was blunted by NPR-C deletion. NCC inhibitor, hydrochlorothiazide, failed to induced natriuresis in NPR-C knockout mice. Moreover, low salt and high salt diets-induced changes of total and phosphorylation of NCC expression were normalized by NPR-C deletion. Importantly, tubule-specific deletion of NPR-C also attenuated AngII-induced elevated blood pressure, total and phosphorylation of NCC expression. In primary cultured distal convoluted tubule cells, AngII upregulated NCC-mediated sodium uptake was suppressed by NPR-C knockdown. (2) Mechanistically, in distal convoluted tubule cells, AngII dose and time-dependently upregulated WNK4, p-SPAK, NCC and p-NCC expression. NPR-C signaling but not NPR-B signaling pathway mediated NCC activation. NPR-C regulates AngII-induced activation of WNK4/SPAK/NCC proteins expression via the Gi/PLC/PKC signal pathway.

CONCLUSIONS These results demonstrated a novel mechanism through which NPR-C deficiency decreases AngII-induced elevation of blood pressure by suppressing NCC-dependent sodium reabsorption in the kidney. These experiments further identify NPR-C as a potential strategy for the treatment of sodium retention-related hypertension.

GW31-e0723

Thymoquinone reduces hyperlipemia-induced cardiac damage in low-density lipoprotein receptor-deficient (LDL-R$^{-/-}$) mice

Zuowei Pei, Fang Wang
Department of Cardiology, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences

OBJECTIVES Hyperlipemia is a risk factor for cardiac damage and cardiovascular disease. Several studies have presented that thymoquinone (TQ) can protect cardiac damage. The aim of the study was to investigate the possible protective effects of TQ reduced hyperlipemia-induced cardiac damage in low-density lipoprotein receptor deficient (LDL-R$^{-/-}$) mice.

METHODS Eight-week-old male LDL-R$^{-/-}$ mice were randomly divided into the following three groups: the control group with a normal diet (ND group), the high fat diet (HFD) group, and the HFD mixed with TQ (HFD+TQ) group. All groups were used the different diets for 8 weeks. Blood samples were collected in serum tubes, and stored at 2280 °C until use. Cardiac tissues were stored in 10% formalin and then embedded in paraffin for histological evaluation. The remainder of the cardiac tissues was snap-frozen in liquid nitrogen for mRNA preparation or immunoblotting.

RESULTS The levels of metabolism-related factors, low-density lipoprotein-cholesterol, total cholesterol and high-sensitivity C-reactive protein, were decreased in the HFD+TQ group compared with that in the HFD group. Periodic acid-Schiff staining demonstrated that lipid deposition was lower in the HFD+TQ group than that in the HFD group. The expression of pyroptosis indicators (NLRP3, IL-1β, IL-18 and caspase-1), pro-inflammation factors (IL-6 and TNF-α), and macrophage markers (CD 68) was significantly downregulated in the HFD+TQ group compared with that in the HFD group.

CONCLUSIONS Our results indicate that TQ can serve as a potential therapeutic agent for hyperlipemia-induced cardiac damage.

GW31-e0726

Loss of long non-coding RNA DRR promotes heart regeneration through stabilizing sFPQ-NONO complex induced DNA repair

Wenbin Fu[1,2,3,4], Chunyu Zeng[1,2,3,4]
[1]Department of Cardiology, Daping Hospital, The Third Military Medical University, Chongqing 400042, China
[2]Department of Cardiology, Daping Hospital, Army Medical University, Chongqing 400042, China
[3]Chongqing Institute of Cardiology, Chongqing 400042, China
[4]Cardiovascular Research Center, Chongqing College, University of Chinese Academy of Sciences, Chongqing 400042, China

OBJECTIVES The mammalian cardiomyocyte is capable of regeneration for a brief window of time after birth, but the regenerative capacity is lost in adults, which is responsible for irreversible heart failure after myocardial infarction (MI). The molecular mechanisms controlling endogenous cardiac regeneration remain largely elusive. Multifaceted functions of long non-coding RNAs (lncRNAs) have been indicated in governing regulatory network of cardiac development and diseases, therefore we screened and verified novel lncRNAs in regulating cardiomyocyte proliferation and cardiac regeneration.

METHODS Using a neonatal cardiac regeneration model of apex resection (AR), we identified a lncRNA, named DRR (DNA repair regulator), that possessed a negative effect in regulating cardiomyocyte proliferation. Next, we generated lncRNA-DRR knockout mice through CRISPR system and performed mouse models of AR and MI. To explore the function and mechanisms of lncRNA-DRR in cardiomyocyte proliferation, various analyses were carried out including echocardiographic evaluation, histology immunofluorescence staining, quantitative real-time polymerase chain reaction, fluorescence in situ hybridization (FISH), western blot, immunoprecipitation and bioinformatics analysis.

RESULTS LncRNA-DRR was significantly reduced after AR in neonates, and overexpression of lncRNA-DRR decreased while silencing of lncRNA-DRR increased the proliferation of cultured cardiomyocytes. In addition, lncRNA-DRR deletion unaffected normal heart development but was sufficient to prolong postnatal window of regeneration capacity after AR injury. In adults, lncRNA-DRR deletion improved cardiac function and reduced infarct size in post-MI hearts, which was associated with significant improvement of cardiomyocyte proliferation mediated cardiac regeneration. Next, gene enrichment analysis revealed that cell cycle process and cellular response to DNA damage were up-regulated in hearts of lncRNA-DRR-/- mice. Further computational analysis and immunoprecipitation showed SFPQ, a DNA repair related molecule, was a target of lncRNA-DRR, and their binding site overlaps with the coiled coil domain of SFPQ which mediates interaction with NONO. LncRNA-DRR deletion could promote the binding of SFPQ-NONO heteromer, decrease DNA damage and activate cardiomyocyte cell-cycle re-entry.

CONCLUSIONS Collectively, our results identified that lncRNA-DRR was a negative regulator of cardiomyocyte proliferation, and loss of lncRNA-DRR promoted heart regeneration through stabilizing SFPQ-NONO heteromer induced DNA repair. LncRNA-DRR might be a novel target for stimulating cardiac regeneration and further MI treatment.

GW31-e0754

Decreased circulating miR-223 predicting major adverse cardiac events in patients with acute coronary syndrome

Yingying Zhang
Tianjin Chest Hospital

OBJECTIVES In previous studies, we found that decreased miR-223 level predicts high on-treatment platelet reactivity (HTPR) in patients with troponin-negative non-ST elevation ACS. But, some studies have shown that the level of miR-223 in the plasma are reduced following inhibition of platelet function. Accordingly, it is unclear decreased plasma or platelet miR-223 levels appear a marker of low or high responsiveness to DAPT. Furthermore, the relationship between the circulating miR-223 level and future clinical outcomes in ACS patients is obscure. Given the importance of the miRNA in platelet reactivity. The present study investigated whether the plasma miR-223 level can predict future MACE accure in ACS patients after PCI.

METHODS One hundred and eighty-eight consecutive NSTE-ACS patients undergoing PCI and on DATP were enrolled in this study and they were dichotomized according to the medians of their circulating miR-223 levels (group 1: miR-223 level >0.993, n=94; group 2: miR-223 level <0.993, n=94). The plasma miR-223 level was quantified by real-time PCR, and the platelet reactivity was determined by platelet reactivity index (PRI), measured by vasodilator-stimulated phosphoprotein (VASP) phosphorylation flow cytometry at least 2 hours after 600 mg clopidogrel plus aspirin treatment.

RESULTS Compared with group1, PRI level was significantly elevated in group 2 (45.0±19.3 vs. 54.6±18.5, P<0.01**). In addition, circulating miR-223 level was inversely correlated with PRI (Spearman r=−0.400, P<0.01). Cox regression analysis revealed that among factors that potentially influence Major Adverse Cardiac Events (MACE), decreased circulating miR-223 level (HR: 0.137, 95% CI: 0.040–0.462, P<0.05*) and PRI (HR: 1.038, 95% CI: 1.010–1.067, P<0.01**) were independent predictors for the presence of MACE during 24 months follow-up. ROC curve analysis also positive the ability of miR-223 (AUC: 0.804, 95% CI: 0.702–0.907, P<0.01) and PRI (AUC: 0.775, 95% CI: 0.680–0.870, P<0.01) in predicting MACE.

CONCLUSIONS Our data suggest that circulating miR-223 level may serve as novel biomarker for assessment of clopidogrel responsiveness and predicting the clinical ischemic outcomes for ACS patients with DAPT after PCI during 24 months follow up.

GW31-e0755

Relationship between hexosamine metabolic pathway and cardiac hypertrophy and bioinformatics analysis

Siang Wei[1], Zhiwen Ding[1], Ran Xu[1], Yuyao Ji[1], Yan Feng[2], Yunzeng Zou[1]
[1]Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital, Fudan University
[2]Shanxi Agricultural University

OBJECTIVES To study the relationship between hexosamine metabolic pathway and myocardial hypertrophy, and to provide new ideas and targets for the treatment of hypertrophic cardiomyopathy.

METHODS After 24 hours of primary culture of neonatal SD rat cardiomyopathy for 1–3 days, they were randomly divided into five groups, and 0.1% angiotensin II stimulated cardiomyopathy to construct a hypertrophy model. The acting time was 0, 6, 12, 24, and 48 hours, respectively. The mRNA expression levels of ANP, BNP, and GFPT2, the crucial factors of hexosamine metabolism and cardiac hypertrophy, were detected after 48 hours of culture. Then the physical and chemical properties, amino acid composition, GO, and KEGG of the GFPT2 gene were analyzed by bioinformatics software.

RESULTS ANP mRNA and BNP mRNA increased significantly with the prolongation of angiotensin II stimulation time, and reached the highest at 48 h. GFPT2 mRNA expression increased at 6, 12, 24, and 48 h after angiotensin II stimulation, and reached the highest at 48 h. Human GFPT2 protein contains 682 amino acids with a single-chain structure, also mainly including α and β structures. The isoelectric point/molecular weight was 7.03/76930.60. There are eight positive selection sites for GFPT2 amino acid codons. In addition, the phosphorylation sites, acetylation sites, and ubiquitination sites related to diseases are 10, 2, and 5. GO enrichment analysis of GFPT2 is mainly involved in the biological processes of GFPT enzyme activity, protein binding, carbohydrate derivative binding. KEGG analysis showed that the gene was fundamentally involved in amino sugar and nucleotide sugar metabolism, alanine, aspartic acid, and glutamic acid metabolism, and insulin resistance. According to the scores of edges' LLS, the top 10 genes were NNMT, ADAM12, BGN, COL5A1, MMP2, CRISOLD2, VCAN, MXKA5, PRRX1, COL5A2.

CONCLUSIONS high expression of hexosamine metabolism is induced by myocardial hypertrophy, which is aggravated with the prolongation of angiotensin II stimulation time, and the metabolic disorder may be the main cause of hypertrophic cardiomyopathy.

GW31-e0756

Effect of micro-scale stretch stimulus on hypertension-associated hypertrophied ventricular myocytes

Jiatong Wu[1], Zhuo Ao[2], Quanmei Sun[2], Maojing Shi[1], Cheng Cheng[1], Dong Han[2], Yuansheng Liu[1]
[1]Emergency Department, Peking University People's Hospital
[2]National Center for Nanoscience and Technology

OBJECTIVES To investigate the effect of micro-scale stretch stimulus on hypertension-associated hypertrophied ventricular myocytes.

METHODS Separating respectively ventricular myocytes from spontaneously hypertensive rats (SHRs) and homologous normotensive rats (Wistar-Kyoto, WKY) of 25-week-old, and dying intracellular calcium with fluo-4/AM, then, applying micro-scale stretch stimulus on single ventricular myocytes and observing the change of intracellular calcium average fluorescent intensity synchronously via an united imaging system of atomic force microscope and laser scanning confocal microscope (Bio-AC). On the other hand, adding streptomycin into ventricular myocytes loaded fluo-4/AM, obtaining the change of intracellular calcium average fluorescent intensity with laser scanning confocal microscope.

RESULTS After the same micro-scale stretch stimulus, both intracellular calcium average fluorescent intensity of ventricular myocytes from SHRs and WKY rats was increased significantly than before (3527.29±217.18 *vs.* 4891.79±648.65, 3447.02±151.58 *vs.* 4067.70±247.95, P<0.01). Whether before, during or after the application of micro-scale stretch stimulus, the intracellular calcium average fluorescent intensity of ventricular myocytes separated from SHRs was higher than that from WKY rats (3527.29±217.18 *vs.* 3447.02±151.58, 4322.20±265.01 *vs.* 3391.80±139.43, 4891.79±648.65 *vs.* 4067.70±247.95, P<0.01). Meanwhile, after stretch stimulus, comparing with WKY rats, the intracellular calcium average fluorescent intensity of ventricular myocytes from SHRs had a bigger elevation (39.49±4.90% *vs.* 18.19±8.21%, P<0.01). Besides, the response of ventricular myocytes from SHRs to stretch stimulus was more rapid than that from WKY rats. In the intervention of streptomycin, both of intracellular calcium average fluorescent intensity of ventricular myocytes from SHRs and WKY rats had significantly decreased (2512.81±320.81 *vs.* 1976.16±194.40, 2176.90±244.01 *vs.* 1910.92±38.01, P<0.01), however, the decreased degree of the former was notable than the latter (19.78±14.80% *vs.* 11.30±8.31%, P<0.01).

CONCLUSIONS Hypertrophied ventricular myocytes are more sensitive to stretch stimulus, and have a higher cellular calcium concentration more easily in the presence of mechanical stimulation, thus, the property can promote the occurrence of cardiac arrhythmias. Besides, the stretch-activated channels on hypertrophied ventricular myocytes have been increased or more powerful, and this change possibly takes an important part in the occurrence and maintenance of cardiac arrhythmias.

GW31-e0771

Inhibitory effect of D3 dopamine receptors on neuropeptide Y-induced migration in vascular smooth muscle cells

Xuewei Xia, Chunyu Zeng
Army Medical Center of PLA

OBJECTIVES Abnormal migration of vascular smooth muscle cells (VSMCs) serves an important role in hypertension, atherosclerosis and restenosis following angioplasty, which is regulated numerous hormonal and humoral factors, including neuropeptide Y (NPY) and dopamine. Dopamine and NPY are both sympathetic neurotransmitters, and a previous study reported that NPY increased VSMC proliferation, while dopamine receptor inhibited it. Therefore, the authors wondered whether or not there is an inhibitory effect of dopamine receptor on NPY-mediated VSMC migration.

METHODS The migration of VSMC was detected by transwell migration assay and wound healing assay.

RESULTS The present study demonstrated that stimulation with NPY dose-dependence (10-10-10-7 M, 24 h) increased VSMC migration, the stimulatory effect of NPY was via the Y1 receptor. This is because, in the presence of the Y1 receptor antagonist, BIBP3226 (10-7 M), the stimulatory effect of NPY on VSMC migration was blocked. Activation of the D3 receptor by PD128907 dose-dependence (10-11-10-8 M) reduced the stimulatory effect of NPY on VSMC migration. The effect of PD128907 was via the D3 receptor, because the inhibitory effect of PD128907 on NPY-mediated migration was blocked by the D3 receptor antagonist, U99194. The authors' further study suggested that the inhibitory effect of the D3 receptor was via the PKA signaling pathway, in the presence of the PKA inhibitor, 14–22 (10-6 M), the inhibitory effect of PD128907 on VSMC migration was blocked. Moreover, the inhibitory effect of PD128907 was imitated by PKA activator, Sp-cAMP [S], in the presence of Sp-cAMP [S], the NPY-mediated stimulatory effect on VSMC migration was abolished.

CONCLUSIONS The present study indicated that activation of the D3 receptor inhibits NPY Y1-mediated migration on VSMCs, PKA is involved in the signaling pathway.

GW31-e0772

MicroRNA-483 ameliorate hypercholesterolemia by inhibiting PCSK9 production

Jianjie Dong, Chen Wang, Zuyi Yuan
Department of Cardiology, First Affiliated Hospital, Xi'an Jiaotong University, Xi'an 710061, China

OBJECTIVES Proprotein convertase subtilisin/kexin type 9 (PCSK9) detriments cholesterol homeostasis by targeting hepatic low-density lipoprotein receptor (LDLR) for lysosomal degradation. Clinically, PCSK9 inhibitors effectively reduce LDL cholesterol (LDL-C) and the incidence of cardiovascular events. As microRNA (miR) are understood to be integral regulators of cholesterol homeostasis, we investigate the involvement of miR-483 in regulating LDL-C metabolism.

METHODS *In silico* methods and *in vitro* experiments were used to explore miR-483-5p inhibits PCSK9 production with ensuing increase in LDLR expression and LDL-C uptake in hepatocytes. AAV8-mediated hepatic overexpression of miR-483 together with various forms of PCSK9 were used to decipher the cholesterol-lowering effect of miR-483 in hypercholesterolemic mouse models.

RESULTS In HepG2 cells, miR-483-5p targets the PCSK9 3′UTR, which suppressed PCSK9 expression, increases LDLR level, and promotes LDL-C uptake. In hypercholesterolemic mouse models, hepatic miR-483 overexpression increased LDLR expression via PCSK9 targeting. Consequently, serum cholesterol and LDL-C levels drastically decreased. Mechanistically, the cholesterol-lowering effect of miR-483-5p was seen in mice receiving AAV8 PCSK9-3′UTR (WT), but was absent in mice administered AAV8 PCSK9-3′UTR (ΔBS) in which the miR-483-5p targeting site was deleted nor in LDLR knockout mice.

CONCLUSIONS MiR-483-5p targeting PCSK9 led to increased LDLR expression and LDL uptake in hepatocytes. Exogenously administered miR-483 could drastically ameliorate high-fat diet or PCSK9-induced hypercholesterolemia in mouse models.

GW31-e0773

MDM2-mediated ubiquitination of SARS-CoV-2 receptor ACE2 contributes to the development of pulmonary arterial hypertension

Jiao Zhang, Chen Wang, Zuyi Yuan
Department of Cardiology, First Affiliated Hospital of Xi'an Jiaotong University

OBJECTIVES Angiotensin-converting enzyme 2 (ACE2) converts angiotensin II (Ang-II), the most potent vasoconstrictor, to Ang 1-7 and is also a membrane protein that enables COVID-19 infectivity. AMP-activated protein kinase (AMPK) phosphorylation of ACE2 enhances ACE2 stability and this mode of post-translational modification (PTM) of ACE2 in vascular endothelial cells (ECs) is causative of a pulmonary hypertension (PH)-protective phenotype. The oncoprotein murine double minute 2 (MDM2) is an E3 ligase that ubiquitinates its substrates to cause their degradation. In this study, we investigate whether MDM2 is involved in the PTM of ACE2 via its ubiquitination of ACE2, and whether an AMPK and MDM2 crosstalk regulates the pathogenesis of PH.

METHODS Bioinformatic analyses were used to explore E3 ligase that ubiquitinates ACE2. Cultured ECs, mouse models, and specimens from patients with

idiopathic pulmonary arterial hypertension (IPAH) were used to investigate the crosstalk between AMPK and MDM2 in regulating ACE2 phosphorylation and ubiquitination in the context of PH.

RESULTS Levels of MDM2 were increased and those of ACE2 decreased in lung tissues and lung ECs isolated from IPAH patients and rodent models of experimental PH. MDM2 inhibition by JNJ-165 reverted the SU5416/Hypoxia-induced PH in C57BL/6 mice. ACE2 S680L (dephosphorylation at S680) mice showed PH susceptibility and ectopic expression of ACE2 S680L/K788R (dephosphorylation at S680; deubiquitination at K788) reduced experimental PH. Moreover, ACE2 K788R overexpression in mice with EC-specific AMPKα2 knockout mitigated PH.

CONCLUSIONS Maladapted PTM (phosphorylation and ubiquitination) of ACE2 at Ser-680 and Lys-788 is involved in the pathogenesis of PAH and experimental PH. Thus, a combined intervention of AMPK and MDM2 in the pulmonary endothelium might be therapeutically implicated in PH treatment.

GW31-e0777

New insights into apolipoprotein A5 and the modulation of human adipose-derived mesenchymal stem cells adipogenesis

Xin Su[1,2], Daoquan Peng[2]
[1]Xiamen Cardiovascular Hospital of Xiamen University
[2]Second Xiangya Hospital of Central South University

OBJECTIVES The hallmark of obesity is excessive accumulation of triglyceride (TG) in adipose tissue. Apolipoprotein A5 (ApoA5) has been shown to influence the prevalence and pathogenesis of obesity. However, the underlying mechanisms remain to be clarified.

METHODS Human adipose-derived mesenchymal stem cells (AMSCs) were treated with 600 ng/mL human recombinant ApoA5 protein. The effect of ApoA5 on intracellular TG content and adipogenic related factors expression were determined. Furthermore, the effect of ApoA5 on CIDE-C expression was also detected.

RESULTS During the process of adipogenesis, ApoA5 treatment reduced the intracellular accumulation of lipid droplets and the TG levels; meanwhile, ApoA5 down-regulated the expression levels of adipogenic related factors, including CCAAT enhancer binding proteins α/β (C/EBPα/β), fatty acid synthetase (FAS), and fatty acid-binding protein 4 (FABP4). Furthermore, the suppression of adipogenesis by ApoA5 was mediated through the inhibition of CIDE-C expression, an important factor which promotes the process of adipogenesis. However, over-expressing intracellular CIDE-C could lead to the loss-of-function of ApoA5 in inhibiting AMSCs adipogenesis.

CONCLUSIONS In conclusion, ApoA5 inhibits the adipogenic process of AMSCs through, at least partly, down-regulating CIDE-C expression. The present study provides novel mechanisms whereby ApoA5 prevents obesity via AMSCs in humans.

GW31-e0778

Apolipoprotein A1 inhibits adipogenesis of human adipose-derived mesenchymal stem cells through modulating sortilin expression

Xin Su[1,2], Daoquan Peng[2]
[1]Xiamen Cardiovascular Hospital of Xiamen University
[2]Second Xiangya Hospital of Central South University

OBJECTIVES Obesity is associated with a series of health problems which are always grouped together as metabolic syndromes. The hallmark of obesity is excessive accumulation of triglyceride (TG) in adipose tissue. Apolipoprotein A1 (apoA1) is a recently described protein that has been shown to influence obesity. However, the mechanism involved remains to be fully elucidated. The aim of this study was to examine the anti-obesity effect and the mechanism of apoA1 during the adipogenesis differentiation of human adipose-derived mesenchymal stem cells (AMSCs).

METHODS Human adipose-derived mesenchymal stem cells (AMSCs) were treated with 15 μg/mL wide-type human recombinant ApoA1 protein and 15 μg/mL loss-of-function mutation human recombinant ApoA1 protein. The effect of ApoA1 on intracellular TG content and adipogenic related factors expression were determined. Furthermore, the effect of ApoA5 on intracellular expression levels of sortilin was also detected.

RESULTS Both two type of apoA1 could significantly reduce the accumulation of intracellular lipid droplets, the concentration of TG and inhibited AMSCs differentiation by down-regulating the gene and protein expression of adipogenesis differentiation-related factors, including CCAAT enhancer binding proteins (C/EBPs), fatty acid synthetase (FAS) and fatty acid-binding protein 4 (FABP4), during the adipogenesis differentiation of AMSCs. In addition, both two type of apoA1 could significantly up-regulate the intracellular gene and protein expression level of sortilin.

CONCLUSIONS ApoA1 could inhibit adipogenesis differentiation of human AMSCs and prevents obesity, and the function did not depend on the property of apoA1 mediating cholesterol efflux. The present study also provides insight into the mechanisms underlying the anti-obesity activity of apoA1 and suggests that apoA1 has the potential to prevent obesity by acting on pre-adipocytes.

GW31-e0779

Omega-3 fatty acid protects cardiomyocytes against hypoxia-induced injury through targeting MiR-210-3p/CASP8AP2 axis

Xueju Yu[1,2], Fengyao Liu[1,2], Yuting Liu[1,2], Bingqing Bai[2], Han Yin[1,2], Haochen Wang[1,2], Yingqing Feng[1,2], Huan Ma[2], Qingshan Geng[1]
[1]Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, School of Medicine, South China University of Technology, Guangzhou, China
[2]Department of Cardiology, Guangdong Cardiovascular Institute, Guangdong Provincial People' s Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China

OBJECTIVES MicroRNAs (miRs) regulate diverse biological functions in both normal and pathological cellular conditions by post-transcriptional regulation of various genes expression. Nevertheless, the role of miRs in regulating the protective functions of omega-3 fatty acid in relation to hypoxia in cardiomyocytes, remains unknown. The aim of this study was to investigate the effects of omega-3 fatty acid supplementation on cardiomyocyte apoptosis and further, delineate the mechanisms underlying microRNA-210 (miRNA-210)-induced cardiomyocyte apoptosis *in vitro.*

METHODS H9C2 cultured cells were first subjected to hypoxia followed by a subsequent treatment with main component of the Omega-3 fatty acid, Docosahexaenoic Acid (DHA). Cell apoptosis were detected by flow cytometry and the expression of miR-210-3p were detected by RT-qPCR and caspase-8-associated protein 2 (CASP8AP2) at protein levels by immunoblotting. Dual luciferase assay was used to verify the mutual effect between miR-210-3p and the 3′-untranslated region (UTR) of CASP8AP2 gene.

RESULTS DHA was shown to reduce apoptosis in H9C2 cells subjected to hypoxia. Whilst DHA caused a significant increase in the expression of miR-210-3p, there was a marked reduction in the protein expression of CASP8AP2. MiR-210-3p and CASP8AP2 were significantly increased in H9C2 cardiomyocyte subjected to hypoxia. Overexpression of miR-210-3p could ameliorate hypoxia-induced apoptosis in H9C2 cells. MiR-210-3p negatively regulated CASP8AP2 expression at the transcriptional level. Both miR-210-3p mimic and CASP8AP2 siRNA could efficiently inhibit apoptosis in H9C2 cardiomyocyte subjected to hypoxia.

CONCLUSIONS We provide strong evidence showing that Omega-3 fatty acids can attenuate apoptosis in cardiomyocyte under hypoxic conditions via the up-regulation of miR-210-3p and targeting CASP8AP2 signalling pathway.

GW31-e0785

LncRNA MALAT1 enhances ox-LDL-induced autophagy through the SIRT1/MAPK/NF-κB pathway in macrophages

Jiaqi Yang, Yujie Zhou
Beijing Anzhen Hospital

OBJECTIVES Atherosclerosis is the main cause of cardiovascular and cerebrovascular diseases. In advanced atherosclerotic plaque, macrophage apoptosis coupled with inflammatory cytokine secretion promotes the formation of necrotic cores. Further study demonstrated that MALAT1 inhibited the expression of MAPK and NF-κB (p65) by upregulating SIRT1.

METHODS ox-LDL has been used to incubate human myeloid leukemia mononuclear cells (THP-1)-derived macrophages to establish an *in vitro* foam cell model. Quantitative reverse-transcription polymerase chain reaction and Western blot analyses confirmed the increased expression level of MALAT1 and the autophagy-related protein microtubule-associated protein light chain 3 (LC-3), beclin-1. The small interfering RNA study showed a significant decrease in autophagy activity and an increase in apoptotic rate when knocking down MALAT1.

RESULTS It has been demonstrated that the long-noncoding Ribo-nucleic Acid (lnc RNA) metastasis-associated lung adenocarcinoma transcript 1 (MALAT1), with its potent function on gene transcription modulation, maintains oxidized low-density lipoprotein (ox-LDL)-induced macrophage autophagy (i.e., helps with cholesterol efflux). It also showed that MALAT1 activated Sirtuin 1 (SIRT1), which subsequently inhibited the mitogen-activated protein kinase (MAPK) and nuclear factor kappa-B (NF-κB) signaling pathways.

CONCLUSIONS We conducted this in-vitro study to investigate the effect of MALAT1 on autophagy, apoptosis, and the formation of foam cells derived by macrophages. The primary finding indicated that knocking out MALAT1 suppressed autophagy, and thus aggravated apoptosis of macrophages through the SIRT1/MAPK/NF-κb pathway, which accelerated the progression of atherosclerosis.

GW31-e0797

A novel complement C3 inhibitor CP40-KK protects against experimental pulmonary arterial hypertension via an inflammasome NLRP3 associated pathway

Jinhua Wu, Hesong Zeng
Division of Cardiology, Department of Internal Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

OBJECTIVES Pulmonary arterial hypertension (PAH) is a progressive disorder in which endothelial dysfunction and vascular remodeling result in small pulmonary arteries occlusion, leading to right heart failure and death. Despite advances in our understanding of the pathophysiology and the management of PAH, effective treatment for this life-threatening disease is still lacking. In the current study, we aimed to explore how complement system gets involved in the pathophysiological process of PAH and test the effect of CP40-KK, a newly identified analog of selective complement C3 inhibitor CP40, on a monocrotaline (MCT) induced rat PAH model.

METHODS After MCT with or without CP40-KK treatment, right ventricle systolic pressure (RVSP) of the experimental rats was assessed by a pressure transducer system, then the animals were euthanized and lungs and hearts were dissected for further evaluation. The dry weights of the right ventricle (RV) and left ventricle (LV)+septum (S) were measured to calculate the RV/(LV+S) ratio and the RV/body weight ratio (RV/BW). The morphological indices were evaluated by hematoxylin and eosin (H&E) and immunohistochemical staining. The levels of NLRP3 inflammasome complexes and inflammatory cytokines were determined using western blotting, immunohistochemical staining and enzyme-linked immunosorbent assay (ELISA). Survival was evaluated by Kaplan–Meier analysis.

RESULTS Complement component C3 deposition increased significantly in the pulmonary small artery of the MCT group in compared with the control group, and it is associated with more perivascular monocyte/macrophage infiltration, elevated NLPR3 inflammasome activation and proinflammatory cytokines (IL-1β, IL-6 and IL-18) release, augmented vascular smooth cell proliferation and worsened hemodynamic and morphological indices, such as RVSP, RV/(LV+S) ratio, RV/BW ratio and pulmonary parietal wall thickness index, finally reduced survival rate, whereas CP40-KK treatment could significantly reverse these indices in an established rat PAH model.

CONCLUSIONS Our results indicated that complement component C3 could activate the NLRP3 inflammasome and promote subsequent release of the downstream proinflammatory cytokines, contributing to the pathophysiological process of PAH. Moreover, we found that CP40-KK treatment was protective in an established rat PAH model, which might serve as a therapeutic option for PAH.

GW31-e0798

Activated protein C ameliorates diabetic cardiomyopathy by restricting YB-1 ubiquitination via OTUB1

Xiaodan Zhong, Hongjie Wang, Hesong Zeng
Department of Cardiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology

OBJECTIVES This study intends to explore whether aPC plays a protective role in the occurrence and development of diabetic cardiomyopathy and whether YB-1 is involved in its molecular mechanism.

METHODS Mice diabetic cardiomyopathy was induced by continuous intraperitoneal administration of low-dose streptozotocin (STZ), following an exogenous PC intervention treatment. The cardiac function was measured by echocardiography and invasive hemodynamics. The expression level of YB-1 was determined by Western blot and immunohistochemistry (IHC) staining. Furthermore, mice with low expression level of YB-1 were obtained by administrating YB-1 shRNA adenoviruses *via* tail vein and the same PC intervention was performed. Next, CoIP was used to determine the ubiquitination modification of YB-1. Finally, the signal transduction pathway of aPC was identified by specific receptor agonists and blocking antibodies.

RESULTS In diabetic cardiomyopathy mice, endogenous aPC levels were reduced. After exogenous PC intervention, PC was activated and the plasma aPC levels were increased. Meanwhile, the cardiac function of diabetic mice was significantly improved with PC intervention. The expression level of YB-1 in diabetic cardiomyopathy mice was significantly decreased. Furthermore, it was observed that the therapeutic effect of aPC disappeared in diabetic mice with low YB-1 expression. The level of ubiquitination of YB-1 with high glucose treatment was increased and the interaction between YB-1 and deubiquitinating enzyme otubain-1 (OTUB1) decreased, which were both reversed by aPC. The ubiquitination of YB-1 induced by high glucose was reduced by the overexpression of OTUB1, while knocking down the expression level of OTUB1 via shRNA increasing it. Finally, PAR1 and EPCR receptors that aPC depended to transmit extracellular signals to the intracellular regulated the expression levels of OTUB1 and YB-1.

CONCLUSIONS In conclusion, aPC protects against diabetic cardiomyopathy *via* regulating the ubiquitination of YB-1. The underlying mechanism is that aPC acts through PAR1 and EPCR to restrict the ubiquitination and subsequent proteasomal degradation of YB-1 by maintaining the expression of OTUB1 in cardiomyocytes under diabetic state. This study identified the protective effect of aPC on diabetic cardiomyopathy, and discussed the role of YB-1 in the occurrence and development of it, which might provide a new therapeutic strategy for diabetic cardiomyopathy.

GW31-e0799

Meta-analysis of the association between single nucleotide polymorphisms on chromosome 9p21 and aortic aneurysm

Yuanchao Jin, Hesong Zeng, Ding Hu
Division of Cardiology, Tongji Hospital of HUST

OBJECTIVES Owing to explaining by a single race and prompting whether aneurysm is in common with the pathological changes of genetic characteristics, we conducted a meta-analysis to systematically summarize and clarify the association between single nucleotide polymorphisms (SNPs) on chromosome 9p21 and vascular aneurysm, meanwhile assessing the population attributable risk (PAR) of these variants.

METHODS A systematic search of studies on the association of the single nucleotide polymorphisms on chromosome 9p21 and vascular aneurysm was conducted in PubMed, EMBASE, China National Knowledge Infrastructure (CNKI), Chinese Biomedical (CBM) and Wan Fang (Chinese) database.

RESULTS The search yielded 14 studies including 62,805 participants. In 6 studies analyzing the association between SNPs on chromosome 9p21 and aortic aneurysm, the random effects summary estimate showed a positive relationships identified in allele model (OR: 1.36; 95% CI: 1.28–1.44; P<0.001). In 9 studies analyzing the relationships between Chr9p21 polymorphisms and intracranial aneurysm, the positive relationships were identified in allele model, with combined OR=1.28 (95% CI: 1.24–1.31; P<0.001). Similar results were found in subgroup analysis.

CONCLUSIONS SNPs with the 9p21 locus were strongly associated with the risk of vascular aneurysm.

GW31-e0823

Effects of regulation of mitochondrial autophagy and biogenesis on isoproterenol-induced cardiomyocyte injury

Zhuang Ma, Hao Zhang
State Key Laboratory of Organ Failure Research, Department of Cardiology, Nanfang Hospital, Southern Medical University, Guangzhou 510515, China

OBJECTIVES Mitochondrial quality control is critical for the development of myocardial hypertrophy, in which insufficient energy supply of mitochondria plays an important role. Studies have shown that PGC-1α is closely related to energy metabolism, but previous studies on PGC-1α have different conclusions on myocardial hypertrophy. Recent studies have proved that PINK1 degrades rapidly in normal mitochondria, but accumulates in damaged mitochondria and initiates mitochondrial autophagy to clear damaged mitochondria. However, it is not clear whether PINK1 can mediate isoproterenol (Iso)-induced mitochondrial autophagy and whether the comprehensive strategy of coordinating mitochondrial autophagy and biogenesis is useful for Iso-induced cardiomyocyte injury. The changes of PINK1 and autophagy activity were measured in the model of cardiomyocyte injury induced by Iso. The effects of regulation mitochondrial autophagy and biogenesis on myocardial mitochondrial structure and function and its mechanism were explored in a cardiac hypertrophy model.

METHODS Primary rat cardiomyocytes were extracted and stimulated with Iso (10 μM) for 48 hours to construct a model of cardiomyocytes injury. The role of PINK1 in cardiomyocyte injury model was studied by adenovirus-mediated PINK1 overexpression. Then PGC-1α was activated by Metformin, and the damage indexes of reactive oxygen species (ROS), mitochondrial membrane potential (MMP) and cardiomyocytes apoptosis were detected in each group. Protein levels of PINK1, PGC-1α, TFAM and NRF1 were detected by immunoblotting. Mitochondrial respiratory function was measured by oxygen consumption rate.

RESULTS (1) The effects of overexpression of PINK1 on cardiomyocyte function and expression of downstream gene: Compared with AD-Control+Iso group, the level of MMP increased, autophagy markers were up-regulated, ROS level and apoptosis rate decreased. Meanwhile, cell viability, ATP synthesis and mitochondrial respiratory function were improved. (2) Metformin can increase the expression of PGC-1α, which increased gradually with the stimulation concentration of Metformin to a certain extent. Compared with Iso+PINK1 group, although overexpression of PGC-1α, NRF1, TFAM and mitochondrial biogenesis, the synthesis of ATP and respiratory function of mitochondria were not significantly enhanced. (3) The effects of overexpression of MFN2 on cardiomyocyte function while overexpression the level of PINK1 and PGC-1α

protein: Overexpression of MFN2 could increased mitochondrial fusion while increasing mitochondrial autophagy and regeneration in the model of cardiomyocyte injury induced by Iso. Compared with Iso+PINK1 group, ROS level and apoptosis rate decreased, cell viability, ATP synthesis and mitochondrial respiratory function were further improved.

CONCLUSIONS Increasing mitochondrial autophagy and regeneration-promoting mitochondrial fusion and improving mitochondrial quality control can reduce cardiomyocyte injury and improve capacity supply. This findings may provide a novel therapeutic strategy into the prevention of cardiomyocytes injury.

GW31-e0824

miR-148a improved mitochondrial injury and apoptosis induced by high-glucose through inhibiting CRT expression

Jiayu Diao[1], Hongmou Zhao[2], Gong Cheng[1], Penghua You[1], Xiling Shou[1]
[1]Shaanxi Provincial People's Hospital
[2]Xi'an Honghui Hospital

OBJECTIVES To evaluate the effect of miR-148a on CRT expression and mitochondrial function in cardiomyocytes incubated with high-glucose.

METHODS miR-148a minic and inhibitor were used to intervene the H9c2 cardiomyocytes of rats. Western-blot was used to detect the expression of CRT protein. Then the cells were divided into control group, high-glucose group (HG), HG+miR-148a minic group, HG+miR-148a minic+TG (thapsigargin, CRT agonist) group, HG+miR-148a inhibitor group, and HG+miR-148a inhibitor+CRT- (CRT-siRNA) group. The content of adenosine triphosphate (ATP) and the level of reactive oxygen species (ROS) were detected by fluorescent enzyme labeling, the activity of mitochondrial respiratory chain complex enzyme was detected by spectrophotometry, and the apoptotic rate was detected by flow cytometry.

RESULTS miR-148a minic significantly inhibited the expression of CRT protein in cardiomyocytes, and miR-148a inhibitor increased the expression of CRT. miR-148a minic inhibited the decrease of ATP production, the increase of ROS production and cell apoptosis, and the inactivity of mitochondrial respiratory chain complex enzyme in cardiomyocytes induced by high-glucose, while TG weakened the above effects of miR-148a minic. miR-148a inhibitor aggravates the mitochondrial injury and apoptosis of cardiomyocytes induced by high-glucose, while the effects of miR-148a inhibitor were partially blocked by CRT-siRNA.

CONCLUSIONS miR-148a negatively regulated the expression of CRT in cardiomyocytes, and protected the mitochondrial injury and apoptosis induced by high-glucose through inhibiting CRT.

GW31-e0826

Resveratrol suppressed the high glucose-induced hypertrophy by ameliorating mitophagy in H9c2 cardiomyocyte

Jiayu Diao[1], Hongmou Zhao[2], Gang Fan[3], Xiling Shou[1]
[1]Shaanxi Provincial People's Hospital
[2]Xi'an Honghui hospital
[3]The Second Hospital Affiliated by Xi'an Jiaotong University

OBJECTIVES This study was to evaluate the role of mitophagy in the protective effect on high glucose-induced hypertrophy of RES in H9c2 cardiomyocyte.

METHODS The level of mitophagy in rats and H9c2 cells was detected. The reactive oxygen species (ROS) production, mitochondrial membrane potential (MMP), the activation of mitochondrial permeability transition pore (MPTP) and apoptosis rate, and indicators of cardiomyoctye hypertrophy were measured in each group.

RESULTS The expression of Parkin and LC3II/LC3I were significantly decreased in DCM rats and H9c2 cells incubated with high-glucose, and were both raised up by RES pretreatment. RES inhibited the production of ROS, dissolved MMP, activation of MPTP and excessive apoptosis. And the protective effects of RES were all reversed by Parkin-siRNA. RES alleviated HG-induced cardiomyocyte hypertrophy, the effect of RES was also blocked by Parkin-siRNA.

CONCLUSIONS Parkin-mediated mitophagy was involved in the protective effects of RES on the oxidative stress and cardiomyocyte hypertrophy.

GW31-e0832

Atorvastatin protects the proliferative ability of human umbilical vein endothelial cells inhibited by angiotensin II by changing mitochondrial energy metabolism

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES This study aimed to explore whether angiotensin II (Ang II) inhibits the proliferation of human umbilical vein endothelial cells (HUVECs) by changing mitochondrial energy metabolism, and whether atorvastatin has a protective role via restoration of endothelial function.

METHODS HUVECs were treated with 1 μM Ang II alone or with 10 μM atorvastatin for 24 h. Proliferation was detected by MTT assay, cell counting, 5-ethynyl-2′-deoxyuridine assay and real-time cell analyzer. Mitochondrial energy metabolism including oxygen consumption rate and extracellular acidification rate were measured using a Seahorse metabolic flux analyzer. Mitochondrial membrane potential was detected under fluorescence microscope following staining with tetramethylrhodamine. Respiratory chain complexes I–V were detected using western blotting.

RESULTS The current study showed that Ang II inhibits the proliferation of HUVECs. Results from the Seahorse metabolic flux analyzer indicated that Ang II decreased basal oxygen consumption, maximal respiration capacity, spare respiration capacity, adenosine triphosphate-linked respiration and non-mitochondrial respiration. By contrast, Ang II increased the proton leak. Additionally, Ang II increased glycolysis, glycolytic capacity and non-glycolytic acidification. Furthermore, these effects were all suppressed by atorvastatin.

CONCLUSIONS The results indicated that atorvastatin prevents cellular energy metabolism switching from oxidative phosphorylation to glycolysis induced by Ang II and protected the proliferative ability of HUVECs.

GW31-e0834

Atorvastatin inhibits the apoptosis of human umbilical vein endothelial cells induced by angiotensin II via the lysosomal-mitochondrial axis

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES This study was aimed to evaluate lysosomes-mitochondria cross-signaling in angiotensin II (Ang II)-induced apoptosis of human umbilical vein endothelial cells (HUVECs) and whether atorvastatin played a protective role via lysosomal-mitochondrial axis.

METHODS Apoptosis was detected by flow cytometry, Hoechst 33342 and AO/EB assay. The temporal relationship of lysosomal and mitochondrial permeabilization was established. Activity of Cathepsin D (CTSD) was suppressed by pharmacological and genetic approaches. Proteins production were measured by western blotting.

RESULTS Our study showed that Ang II could induce the apoptosis of HUVECs in a dose-depended and time-depended manner. Exposure to 1 μM Ang II for 24 h resulted in mitochondrial depolarization, cytochrome c release, and increased ROS production. Lysosomal permeabilization and CTSD redistribution into the cytoplasm occurred several hours prior to mitochondrial dysfunction. These effects were all suppressed by atorvastatin. Either pharmacological or genetic inhibition of CTSD preserved mitochondrial function and decreased apoptosis in HUVECs. Most importantly, we found that the protective effect of atorvastatin was significantly greater than pharmacological or genetic inhibition of CTSD. Finally, overexpression of CTSD without exposure to Ang II had no effect on mitochondrial function and apoptosis.

CONCLUSIONS Our data strongly suggested that Ang II induced apoptosis through the lysosomal-mitochondrial axis in HUVECs. Furthermore, atorvastatin played an important role in the regulation of lysosomes and mitochondria stability, resulting in an antagonistic role against Ang II on HUVECs.

GW31-e0859

Effect and mechanism of Si-Miao-Yong-An decoction on vasa vasorum remodeling in ApoE-/- mice with atherosclerosis vulnerable plague

Meng Li[1], Junping Zhang[1], Zhongwen Qi[2], Ke Zhu[2]
[1]First Teaching Hospital of Tianjin University of Traditional Chinese Medicine
[2]Tianjin University of Traditional Chinese Medicine

OBJECTIVES Observed the effect of Si-Miao-Yong-An decoction on AS vulnerable plaques, and the vasa vasorum (VV) angiogenesis and maturation were as the entry point to further discuss the mechanism of effect.

METHODS The male ApoE$^{-/-}$ mice were randomized into 3 groups: model group, simvastatin group and Si-Miao-Yong-An group, and C57BL/6 mice were used as the control group. The ApoE$^{-/-}$ mice were fed with high-fat diet added 1.1% L-methionine for 8 weeks to establish the AS vulnerable plaque model, and the C57BL/6 mice were as control group. After 8 weeks, the pathological morphology of plaque was observed by HE staining; the VV density in plaque and aortic adventitia were observed by immunohistochemistry; VV maturation was measured by double-labelling immunofluorescence; the critical proteins of HIF-1α-Apelin/APJ and Ang-1/Tie signal pathways were detected by western blotting.

RESULTS Si-Miao-Yong-An decreased the plaque area and the ratio of plaque area and lumen area, increased the minimum thickness of fibrous cap, which significantly improved the pathological feature of aortic plaque in mice; it

effectively suppressed the VV neovascularization; promoted smooth muscle cells recruitment; it regulated the HIF-1α-Apelin/APJ and Ang-1/Tie signal pathways.

CONCLUSIONS Si-Miao-Yong-An regulated the HIF-1α-Apelin/APJ signal pathway, suppressing VV neovascularization; it also regulated the Ang-1/Tie signal pathway, promoting VV maturation, which promoted the VV network reconstruction, improved VV function and finally stabilized AS vulnerable plaque.

GW31-e0860

Effect of Apelin on mitochondrial structure and energy metabolism in aged cardiomyocytes induced by D-galactose

Qjuyu Li[1], Pengli Zhu[1,2]
[1]Department of Geriatric Medicine, Fujian Provincial Hospital 350001
[2]Fujian Provincial Center of Geriatrics; Fujian Provincial Key Laboratory of Geriatric Disease 350001

OBJECTIVES To explore the effects of Apelin on D-galactose (D-Gal)-induced cardiomyocyte senescence and mitochondrial energy metabolism.

METHODS Through electroporation transfection technique, the Apelin receptor over and low expression (h-APJ and Si-APJ) H9c2 cells were established. To create the aging model, H9c2 cells were intervened with D-Gal in an optimum concentration of 20 g/L and tested by using cell counting kit-8, beta-galactosidase staining, RT-PCR detect P16 gene expression to confirm the aging myocardial model was established successfully. These cells were divided into six experimental groups: (1) Control Group: H9c2 cells were cultured without special treatment; (2) Aging Group: H9c2 cells were cultured with D-Gal; (3) Group Si-APJ D: Si-APJ H9c2 cells were cultured with D-Gal; (4) Group Si-APJ DA: Si-APJ H9c2 cells were cultured with D-Gal and Apelin; (5) Group h-APJ D: h-APJ H9c2 cells were cultured with D-Gal; (6) Group h-APJ DA: h-APJ H9c2 cells were cultured with D-Gal and Apelin. Using the high-content imaging analysis system to detect the fluorescence intensity, the mitochondrial morphology was analyzed including its density, size, and texture parameter. The citrate synthase detection kit detects cell citrate synthase activity. Western-Blotting detects protein expression of aging marker P16 and PGC-1α, fatty acid metabolism related marker CPT1A, glucose metabolism marker GLUT4. RT-PCR detects associated gene expression of P16, CPT1A, GLUT4, TFAM, NRF1.

RESULTS (1) H9c2 cells in the Aging Group compared with the Control Group, the relative expression levels of P16 increased; whereas in the h-APJ cells, with the intervention of Apelin, its expression decreased; besides it is no significant difference in Apelin receptor low expressing group, including Si-APJ D and Si-APJ DA. (2) The cell in the Aging Group showed significantly lower citrate synthase activity than the Control Group; the citrate synthase activity in the h-APJ DA Group was higher than that in the h-APJ D Group; while it was only slightly higher in Si-APJ DA Group than that of Si-APJ D Group. (3) Compared with the Control Group, the cell relative expression of PGC-1α, GLUT4 and CPT1A were reduced in the Aging Group; in h-APJ cells, the relative expression of these three markers consistently increased when they were in existence of Apelin; however there was no significant difference of them in between Si-APJ DA Group and Si-APJ D Group. 4. H9c2 cells in the Aging Group, compared with the Control Group, their mitochondrial biosynthesis decreased, but their size and texture parameters did not change significantly; in the h-APJ cells, with or without the intervention of Apelin, there was no obvious change in cell mitochondrial structure, membrane potential, and biosynthesis; furthermore it showed similar manifestation in Si-APJ cells.

CONCLUSIONS Apelin has a protective effect on D-Gal induced cardiomyocyte senescence. Apelin has a protective effect on mitochondrial energy metabolism in senescent cardiomyocytes induced by D-Gal, but it has no significant effect on mitochondrial structural damage and mitochondrial biosynthesis.

GW31-e0865

Serum inflammatory cytokines in non-human primate atherosclerotic models

Peining Liu, Wen Xi, Junhui Liu, Yuanyuan Wei, Zuyi Yuan, Yue Wu
The First Affiliated Hospital of Xi'an Jiaotong University

OBJECTIVES Recently the Canakinumab Anti-inflammatory Thrombosis Outcome Study (CANTOS) has confirmed the beneficial effect of inhibition of interleukin (IL)-1β on major cardiovascular events. However, there exists efficacy discrepancy depending on the reduction of serum high-sensitivity C-reactive protein (CRP). This study aimed to explore mechanisms underlying this discrepancy in a proper animal model for identification of individuals most likely to benefit from Canakinumab treatment.

METHODS Cynomolgus monkeys consumed a chow (n=20) or atherogenic diet (n=60) for over 3 years. Blood was collected after an overnight fasting. Serum levels of triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c) and glucose were measured in the central laboratory using an automatic biochemical analyzer. Serum levels of CRP, IL-6 and IL-1β were assayed by enzyme-linked immunosorbent assay (ELISA). Intima-media thickness (IMT) of common carotid arteries was measured by ultrasound. Monkeys were sedated by an intramuscular injection of 10% ketamine hydrochloride after fasting overnight and placed in a supine position with the neck fully exposed. Ultrasound examinations were performed with the use of a 15-MHz ultrasonic probe by a single trained sonographer who was kept blinded from the trial information. Whenever an atherosclerotic plaque was present, it was further confirmed by color Doppler ultrasonongraphy examination and included in the measurements of IMT.

RESULTS The atherogenic diet significantly raised the serum TC, LDL-c and carotid IMT both in male and female monkeys. Meanwhile, the serum levels of CRP and IL-1β were increased only in female atherogenic diet group compared with that of the female chow diet group. Correlation analysis showed that the levels of CRP and IL-1β were positively correlated with IMT in females. While in males, only IL-6 level was positively correlated with IMT. Association analysis between these circulating inflammatory cytokines and traditional risk factors of atherosclerosis depicted that IL-6 levels were positively correlated with fasting blood glucose, TC, LDL-c and TC/HDL-c ratio in males; IL-1β levels were positively correlated with fasting blood glucose in males. Whereas in females, only the significant associations between IL-6 and glucose were observed, indicating that glucose and lipid metabolism may have influences on systematic inflammatory status. When divided into two groups based on IMT median, IL-1β was showed to be an independent risk factor for higher IMT after adjusted for traditional risk factors including age, BMI, fasting blood glucose, TG and TC/HDL ratio in female monkeys (OR: 1.625, 95% CI: 1.049–2.516 for per 0.1 ng/mL rise). Additionally, in both sexes, IL-6 was positively and significantly correlated with IL-1β. Besides, IL-6 was also positively and significantly correlated with CRP in female monkeys. These results lent a support to the existence of CRP/IL-6/IL-1β axis and its possible roles in atherosclerosis, especially in females.

CONCLUSIONS Serum IL-1β elevation is independently associated with increased carotid IMT in female Cynomolgus monkeys, suggesting a promising animal model for further studies on the pathological roles of IL-1β/IL-6/CRP axis in atherosclerosis.

GW31-e0868

Glycoursodeoxycholic acid ameliorates metabolic disorders as a novel endoplasmic reticulum stress inhibitor

Lele Cheng, Zuyi Yuan
The First Affiliated Hospital of Xi'an Jiaotong University

OBJECTIVES Recent studies reveal that bile acid metabolite composition and their metabolism are changed in metabolic disorders, such as obesity, type 2 diabetes, and metabolic associated fatty liver disease (MAFLD). Glycoursodeoxycholic acid (GUDCA), glycine-conjugated bile acid produced from intestinal bacteria, may play a role in metabolic disorders, yet the mechanism remains largely unknown.

METHODS Metabolomic analysis of 163 serum and stool samples of our metabolic disease cohort was performed and comparative analysis was conducted between high and low glycated hemoglobin A1c (HbA1c) level groups. High-throughput RNA-sequencing analysis of liver transcriptome of high-fat diet (HFD)-fed mice was conducted. The effects of GUDCA on body weight, glucose homeostasis, insulin sensitivity, hepatic steatosis, lipid profiles, endoplasmic reticulum (ER) homeostasis and apoptosis were assessed.

RESULTS GUDCA levels were decreased in both serum and stool samples from patients with glucose metabolic disorders. RNA-sequencing results indicated that GUDCA alleviated ER stress in livers of HFD-fed mice without alteration of liver metabolism. *In vitro*, GUDCA reduced palmitic acid induced-ER stress and -apoptosis, as well as stabilized calcium homeostasis. *In vivo*, GUDCA exerted similar effects as tauroursodeoxycholic acid (TUDCA) on amelioration of HFD-induced insulin resistance and hepatic steatosis. In parallel, ER stress and apoptosis were decreased in GUDCA-treated mice as compared to vehicle-treated mice.

CONCLUSIONS Reduced GUDCA is an indicator of metabolic disorders. Supplementation of GUDCA could be an option for the treatment of metabolic disorders, including insulin resistance and hepatic steatosis.

GW31-e0881

Notch activation promotes endothelial quiescence by repressing MYC expression via miR-218

Xianchun Yan[1], Jiaxing Sun[1,2], Ziyan Yang[1], Peiran Zhang[1], Liang Liang[1], Hua Han[1]
[1]State Key Laboratory of Cancer Biology, Department of Biochemistry and Molecular Biology, Fourth Military Medical University
[2]Department of Ophthalmology, Eye Institute of Chinese PLA, Xijing Hospital, Fourth Military Medical University

OBJECTIVES After active embryonic and early postnatal vascularization mediated primarily by angiogenesis, endothelial cells (ECs) in most tissues

adopt a quiescent state, which is critical for tissue perfusion and EC functions. Notch signaling is essential in maintaining EC quiescence, but the downstream mechanisms have been elusive.

METHODS EdU or propidium iodide (PI) incorporation assay was used to determine EC proliferation ability. Lumen formation and fibrin beads sprouting assays were employed to evaluate EC angiogenic ability *in vitro*. Immunostaining of retinas was used to observe angiogenesis *in vivo*. RNA-seq was used to compare gene expression profiles. qRT-PCR and western blotting were used to determine gene expression level.

RESULTS miR-218 is a novel downstream Notch effector in quiescent ECs. Notch activation upregulated, while Notch blockade downregulated, miR-218 and its host gene Slit2, likely via transactivating the Slit2 promoter. miR-218 overexpression in human umbilical vein endothelial cells (HUVECs) significantly repressed cell proliferation and eroded sprouting *in vitro*. Transcriptional profiling showed that miR-218 overexpression attenuates MYC transcription program. MYC overexpression rescued miR-218-mediated repression of proliferation and sprouting of HUVECs. Furthermore, miR-218 downregulates MYC via multiple mechanisms including reducing MYC mRNA by unidentified target(s), repressing MYC translation by targeting hnRNPA1, and promoting MYC degradation by targeting EYA3. Inhibition of miR-218 partially reversed Notch activation-induced repression of HUVEC proliferation and sprouting. *In vivo*, intravitreal injection of miR-218 reduced retinal EC proliferation, and attenuated pathological angiogenesis in a choroidal neovascularization (CNV) model.

CONCLUSIONS miR-218 mediates the effect of Notch activation on promoting EC quiescence via MYC, and holds potentials in the treatment of angiogenesis-related diseases.

GW31-e0886

Regulation of angiotensin II-induced B-cell lymphoma-2-associated athanogene 3 expression in vascular smooth muscle cells

Shasha Yu, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Previous studies have demonstrated that angiotensin II (Ang II) is involved in the process of atherosclerosis and vascular restenosis through its proinflammatory effect. Bcl-2-associated athanogene 3 (BAG3) had been suggested to be associated with proliferation, migration and invasion in many types of tumor. However, the role of BAG3 among the proliferative process of vascular smooth muscle cells (VSMCs) induced by Ang II, to the best of our knowledge, remains to be investigated. The present study demonstrated that in growth-arrested VSMCs, Ang II-induced VSMC proliferation, accompanied by increased BAG3 mRNA and protein expression levels in a dose- and time-dependent manner. BAG3 expression levels were measured in VSMCs treated in the presence or absence of Ang II.

METHODS The proliferation of VSMCs was assessed using manual cell counting and Cell Counting kit-8 assays. mRNA and protein expression levels of BAG3, Toll-like receptor 4 (TLR4), proliferating cell nuclear antigen, nuclear factor (NF)-κB p65, smooth muscle protein 22α and phosphorylated NF-κB p65 were assessed by reverse transcription-quantitative polymerase chain reaction and western blotting, respectively.

RESULTS In non-transfected or scramble short hairpin RNA (shRNA)-transfected VSMCs cells, Ang II significantly induced VSMC proliferation. However, this Ang II-induce proliferation was attenuated when BAG3 was silenced, suggesting that inhibition of BAG3 may somehow reduce proliferation in Ang II-induced VSMCs. Furthermore, the TLR4/NF-κB p65 signaling pathway was involved in BAG3 gene upregulation.

CONCLUSIONS In conclusion, to the best of our knowledge, the present study demonstrated for the first time that inhibition of BAG3 attenuates cell proliferation. Furthermore, Ang II induced VSMCs proliferation through regulation of BAG3 expression via the TLR4/NF-κB p65 signaling pathway.

GW31-e0890

Klotho inhibits proliferation and migration of angiotensin II-induced vascular smooth muscle cells (VSMCs) by modulating NF-κB p65, Akt, and extracellular signal regulated kinase (ERK) signaling activities

Shasha Yu, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES It has been proven that phenotype shifting, from the contractile phenotype to the synthetic phenotype, of vascular smooth muscle cells (VSMCs), plays an important role in vascular diseases such as atherosclerosis, restenosis, and hypertension. Recently, accumulating evidence suggests that Klotho is associated with many cardiovascular diseases or damage. Through the estimation of the proliferation and migration of Ang II-induced VSMCs and the related intracellular signal transduction pathways, we researched the effects of Klotho on phenotype modulation in this study.

METHODS A rat vascular smooth muscle cell line was grown in vitro with or without Ang II or Klotho, and cell proliferation and migration were evaluated.

RESULTS The dose-dependent inhibition of Ang II-induced proliferation and migration by Klotho was shown in VSMCs. The phenotype modulation was inhibited by Klotho co-treatment; this co-treatment promoted the expression of contractile phenotype marker proteins, including SM22α, and also the proliferation phenotype marker protein PCNA compared with Ang II alone, which was suppressed, and activated VSMCs. Furthermore, by reducing the expression of Go/G1-specific regulatory proteins such as cyclin D1, cyclin-dependent kinase (CDK) 4, cyclin E, and CDK2, cell cycle arrest was induced by Klotho at Go/G1 phase. Although Ang II strongly stimulated NF-κB, p65, Akt, and ERK phosphorylation, these activation events were diminished by co-treatment with Ang II and Klotho.

CONCLUSIONS Phenotype modulation of Ang II-induced VSMCs and stimulation of the NF-κB, p65, Akt, and ERK signaling pathways were inhibited by Klotho, which suggests that Klotho may play an important role in the phenotype modulation of VSMCs.

GW31-e0892

Septin4 prevents PDGF-BB-induced HAVSMC phenotypic transformation, proliferation and migration by promoting SIRT1-STAT3 deacetylation and dephosphorylation

Naijin Zhang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES SIRT1 and STAT3 are key to human aortic vascular smooth muscle cells (HAVSMCs) proliferation, migration and phenotypic transformation, but the regulatory mechanism of SIRT1-STAT3 in this process is still unclear. Septin4 is a cytoskeleton-related protein that regulates oxidative stress-vascular endothelial injury. However, the role and underlying mechanism of Septin4 in atherosclerosis remains unknown. Here, we revealed the role and mechanism of Septin4 in regulating SIRT1-STAT3 in atherosclerosis. We determined that the expression of Septin4 were markedly increased in Apoe(-/-) atherosclerosis mice and PDGF-BB-induced HAVSMCs.

METHODS Knockdown of Septin4 significantly increased PDGF-BB-induced HAVSMCs proliferation, migration and phenotypic transformation, while overexpression of Septin4 had the opposite effects.

RESULTS Mechanically, co-immunoprecipitation results demonstrated that Septin4 was a novel interacting protein of STAT3 and SIRT1. Septin4 formed a complex with SIRT1-STAT3, enhancing the interaction between SIRT1 and STAT3, ensuing promoting SIRT1-regulated STAT3-K685 deacetylation and STAT3-Y705 dephosphorylation, which inhibited PDGF-BB-induced HAVSMCs proliferation, migration and phenotype transformation.

CONCLUSIONS Therefore, our findings provide novel insights into the prevention and treatment of atherosclerosis.

GW31-e0895

Septin4 as a novel binding partner of PARP1 contributes to oxidative stress induced human umbilical vein endothelial cells injure

Naijin Zhang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Oxidative stress induced vascular endothelial cell injure is one of the key and initial event in the development of atherosclerosis. Septin4, as a member of GTP binding protein family, is widely expressed in the eukaryotic cells and considered to be an essential component of the cytoskeleton which is involved in many important physiological processes. However, whether Septin4 is involved in cardiovascular diseases, such as oxidative stress inducted endothelial cell injury still unclear.

METHODS PARP1 as a DNA repair enzyme can be activated by identifying DNA damaged fragments, which consumes high levels of energy and leads to vascular endothelial cell apoptosis.

RESULTS Here, our results first found that Septin4 is involved in oxidative stress induced endothelial cell ROS production and apoptosis through knockdown and over-expression Septin4 approaches. Furthermore, to explore how Septin4 is involved in oxidative stress induced endothelial cells injure, we first identified that Septin4 is a novel PARP1 interacting protein and the interaction is enhanced under oxidative stress.

CONCLUSIONS In conclusions, our founding indicates that Septin4 is a novel essential factor involved in oxidative stress induced vascular endothelial cell injury by interacting with apoptosis-related protein PARP1.

GW31-e0896

Selective targeting of ubiquitination and degradation of PARP1 by E3 ubiquitin ligase WWP2 regulates isoproterenol-induced cardiac remodeling

Naijin Zhang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES The elevated expression of poly(ADP-ribose) polymerase-1 (PARP1) and increased PARP1 activity, namely, poly(ADP-ribosyl)ation (PARylation), have been observed in cardiac remodeling, leading to extreme energy consumption and myocardial damage. However, the mechanisms underlying the regulation of PARP1 require further study. WWP2, a HECT-type E3 ubiquitin ligase, is highly expressed in the heart, but its function there is largely unknown. Here, we clarified the role of WWP2 in the regulation of PARP1 and the impact of this regulatory process on cardiac remodeling.

METHODS We determined that the knockout of WWP2 specifically in myocardium decreased the level of PARP1 ubiquitination and increased the effects of isoproterenol (ISO)-induced PARP1 and PARylation, in turn aggravating ISO-induced myocardial hypertrophy, heart failure, and myocardial fibrosis. Similar findings were obtained in a model of ISO-induced H9c2 cells with WWP2 knockdown, while the reexpression of WWP2 significantly increased PARP1 ubiquitination and decreased PAPR1 and PARylation levels.

RESULTS Mechanistically, coimmunoprecipitation results identified that WWP2 is a novel interacting protein of PARP1 and mainly interacts with its BRCT domain, thus mediating the degradation of PARP1 through the ubiquitin-proteasome system. In addition, lysine 418 (K418) and lysine 249 (K249) were shown to be of critical importance in regulating PARP1 ubiquitination and degradation by WWP2.

CONCLUSIONS These findings reveal a novel WWP2-PARP1 signal transduction pathway involved in controlling cardiac remodeling and may provide a basis for exploring new strategies for treating heart disorders related to cardiac remodeling.

GW31-e0897

Role of WW domain E3 ubiquitin protein ligase 2 in modulating ubiquitination and degradation of septin4 in oxidative stress endothelial injury

Naijin Zhang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Oxidative stress-associated endothelial injury is the initial event and major cause of multiple cardiovascular diseases such as atherosclerosis and hypertensive angiopathy. A protein homeostasis imbalance is a critical cause of endothelial injury, and homologous to E6AP C-terminus (HECT)-type E3 ubiquitin ligases are the core factors controlling protein homeostasis. Although HECT-type E3 ubiquitin ligases are involved in the regulation of cardiac development and diseases, their roles in endothelial injury remain largely unknown. This study aimed to identify which HECT-type E3 ubiquitin ligase is involved in endothelial injury and clarify the mechanisms at molecular, cellular, and organism levels. We revealed a novel role of the HECT-type E3 ubiquitin ligase WWP2 in regulating endothelial injury and vascular remodeling after endothelial injury.

METHODS Endothelial/myeloid-specific WWP2 knockout in mice significantly aggravated angiotensin II/oxidative stress-induced endothelial injury and vascular remodeling after endothelial injury. The same results were obtained from in vitro experiments.

RESULTS Mechanistically, the endothelial injury factor Septin4 was identified as a novel physiological substrate of WWP2. In addition, WWP2 interacted with the GTPase domain of Septin4, ubiquitinating Septin4-K174 to degrade Septin4 through the ubiquitin-proteasome system, which inhibited the Septin4-PARP1 endothelial damage complex.

CONCLUSIONS These results identified the first endothelial injury-associated physiological pathway regulated by HECT-type E3 ubiquitin ligases in vivo as well as a unique proteolytic mechanism through which WWP2 controls endothelial injury and vascular remodeling after endothelial injury. These findings might provide a novel treatment strategy for oxidative stress-associated atherosclerosis and hypertensive vascular diseases.

GW31-e0903

TLR4/MyD88/NF-κB-mediated inflammation contributes to cardiac dysfunction in rats of PTSD

Moujie Liu, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Post-traumatic stress disorder (PTSD) is related with myocardial injury and cardiac dysfunction, while the molecular mechanism has not been clear. This study investigated whether TLR4/MyD88/NF-κB-mediated inflammation involved in myocardial injury of PTSD.

METHODS Adult male Wistar rats were exposed to single-prolonged stress (SPS), which was used broadly as a animal model of PTSD. Morris Water Maze (MWM) test and forced swimming test (FST) was carried out for behavioral testing. The protein expression of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) in the left ventricular of heart and TLR4/MyD88/NF-κB-mediated inflammation were examined.

RESULTS Our results showed that there were obvious increased in the protein expression of ANP and BNP in heart after exposure to SPS, SPS also significantly enhanced the serum level of IL-1β and TNF-α, and meanwhile, the TLR4/MyD88/NF-κB pathway were activated.

CONCLUSIONS These results demonstrated that the TLR4/MyD88/NF-κB pathway were involved in the myocardial injury of PTSD, which might be one of possible molecular mechanism contributed to the pathogenesis of cardiac dysfunction in PTSD.

GW31-e0907

Agomelatine protects against myocardial ischemia reperfusion injury by inhibiting mitochondrial permeability transition pore opening

Pengyu Jia, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Agomelatine is a melatonin (MT1/MT2) receptor agonist and serotonin (5-HT2C) receptor antagonist. To study the effects of agomelatine on myocardial ischemia reperfusion injury (MIRI), an isolated rat heart model was utilized. To induce MIRI, rat hearts were isolated and subjected to 30 min of ischemia followed by 120 min of reperfusion.

METHODS Rats were intraperitoneally injected with agomelatine (10, 20 or 40 mg/kg) 1 h before heart isolation.

RESULTS Agomelatine (20 mg/kg and 40 mg/kg) significantly improved cardiac function, alleviated pathological changes in the ischemic myocardium, reduced myocardial infarct size and decreased release of creatine kinase-MB and lactate dehydrogenase. Heart tissue from agomelatine-treated rats retained higher NAD(+) content and was more resistant to Ca(2+), indicating inhibition of mitochondrial permeability transition pore (MPTP) opening.

CONCLUSIONS Notably, agomelatine's protective effects were abrogated by atractyloside, a MPTP opener. We also found that agomelatine significantly enhanced GSK-3β phosphorylation and decreased expression of cytochrome C, cleaved caspase 9 and cleaved caspase 3, resulting in a decreased apoptosis rate. These findings demonstrate that agomelatine protects against MIRI by inhibiting MPTP opening.

GW31-e0908

Downregulation of MALAT1 alleviates saturated fatty acid-induced myocardial inflammatory injury via the miR-26a/HMGB1/TLR4/NF-κB axis

Pengyu Jia, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES The increased level of saturated fatty acids (SFAs) is found in patients with diabetes, obesity, and other metabolic disorders. SFAs can induce lipotoxic damage to cardiomyocytes, but the mechanism is unclear. The long noncoding RNA metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) acts as a key regulator in palmitic acid (PA)-induced hepatic steatosis, but its role in PA-induced myocardial lipotoxic injury is still unknown. The aim of this study was to explore the role and underlying mechanism of MALAT1 in PA-induced myocardial lipotoxic injury.

METHODS MALAT1 expression in PA-treated human cardiomyocytes (AC16 cells) was detected by RT-qPCR. The effect of MALAT1 on PA-induced myocardial injury was measured by Cell Counting Kit-8, lactate dehydrogenase (LDH), and creatine kinase-MB (CK-MB) assays. Apoptosis was detected by flow cytometry. The activities of cytokines and nuclear factor (NF)-κB were detected by enzyme-linked immunosorbent assay. The interaction between MALAT1 and miR-26a was evaluated by a luciferase reporter assay and RT-qPCR. The regulatory effects of MALAT1 on high mobility group box 1 (HMGB1) expression were evaluated by RT-qPCR and western blotting.

RESULTS MALAT1 was significantly upregulated in cardiomyocytes after PA treatment. Knockdown of MALAT1 increased the viability of PA-treated cardiomyocytes, decreased apoptosis, and reduced the levels of LDH, CK-MB, TNF-α, and IL-1β. Moreover, we found that MALAT1 specifically binds to miR-26a and observed a reciprocal negative regulatory relationship between these factors. We further found that the downregulation of MALAT1 represses HMGB1 expression, thereby inhibiting the activation of the Toll-like receptor 4

(TLR4)/NF-κB-mediated inflammatory response. These repressive effects were rescued by an miR-26a inhibitor.

CONCLUSIONS We demonstrate that MALAT1 is induced by SFAs and its downregulation alleviates SFA-induced myocardial inflammatory injury via the miR-26a/HMGB1/TLR4/NF-κB axis. Our findings provide new insight into the mechanism underlying myocardial lipotoxic injury.

GW31-e0909

E3 ligase Fbw7 participates in oxidative stress induced myocardial cell injury via interacting with Mcl 1

Xia Li, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Oxidative stress participates in several heart diseases and is an important mechanism contributing to the pathological alterations of myocardial cell injury. In recent years, ubiquitylation has been demonstrated to be an important biochemical reaction associated with apoptosis.

METHODS To investigate the effects and interactions of the E3 ligase F-box and WD repeat domain containing 7 (Fbw7) and MCL1 apoptosis regulator, BCL2 family member (Mcl-1) in myocardial cells during oxidative stress, Cell Counting Kit-8, flow cytometry, western blot, reactive oxygen species and co-immunoprecipitation assays were conducted.

RESULTS The current study revealed that Fbw7 may facilitate apoptosis via the Mcl-1-Bax pathway in oxidative stress-induced myocardial H9c2 cell injury. Mcl-1 inhibits the functions of Bcl-2 family members, including the mitochondrial apoptosis factor Bax, to maintain cell viability; however, the present study suggested that Fbw7 may degrade Mcl-1 and impaired this process.

CONCLUSIONS Therefore, it may be hypothesized that Fbw-7 promotes myocardial cell injury via interacting with Mcl-1.

GW31-e0927

Atorvastatin calcium inhibits PDGF-β β-induced proliferation and migration of VSMCs through the G0/G1 cell cycle arrest and suppression of activated PDGFRβ-PI3K-Akt signaling cascade

Shuang Chen, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Abnormal proliferation of vascular smooth muscle cells (VSMCs) is a hallmark of vascular lesions, such as atherosclerosis and restenosis. PDGF-β β, an isoform of PDGF (platelet-derived growth factor), has been demonstrated to induce proliferation and migration of VSMCs. Atorvastatin calcium, a selective inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, has favorable protective effects on VSMCs. This study examined the effects of atorvastatin calcium on the proliferation and migration of PDGF-β β-treated VSMCs, as well as its underlying mechanisms.

METHODS MTT assays, Edu imaging, cell cycle analysis, wound healing assays, transwell migration assays, and western blot analysis were performed.

RESULTS Atorvastatin calcium significantly inhibited cell proliferation, DNA synthesis and cell migration of PDGF-β β-treated VSMCs. We demonstrated that atorvastatin calcium induced cell cycle arrest in the Go/G1 phase in response to PDGF-β β stimulation and decreased the expression of Go/G1-specific regulatory proteins, including proliferating cell nuclear antigen (PCNA), CDK2, cyclin D1, cyclin E and CDK4 in PDGF-β β-treated VSMCs. Moreover, pretreatment with atorvastatin calcium inhibited the PDGF-β β-treated phosphorylation of PDGFRβ and Akt, whereas atorvastatin calcium did not affect the phosphorylation of PLC-γ1 or (ERK) 1/2.

CONCLUSIONS Our data suggested that atorvastatin calcium inhibited abnormal proliferation and migration of VSMCs through Go/G1 cell cycle arrest and suppression of the PDGFRβ-Akt signaling cascade.

GW31-e0928

Paired box 9 regulates VSMC phenotypic transformation, proliferation, and migration via sonic hedgehog

Jiaqi Xu, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Vascular smooth muscle cells (VSMCs) play a crucial role in the progression of atherosclerosis. Paired box 9 (Pax9) is a member of the Pax gene family which participates in the development of various tissues and organs. However, the effect of Pax9 on atherosclerosis and VSMCs and the underlying mechanisms remain unclear.

METHODS Western blotting was performed to assess Pax9 expression in atherosclerosis and VSMCs. Pax9 siRNA and overexpression plasmid were constructed to explore the biological function. Cell proliferation assay, phalloidin staining, and Transwell assay, accompanied by the sonic hedgehog (Shh) signaling pathway antagonist, cyclopamine (5 μM) and agonist, SAG (100 nM), were used to evaluate the VSMC phenotype, proliferation, and migration, as well as explore the associated mechanisms.

RESULTS We first discovered Pax9 to be significantly increased in atherosclerotic mice and platelet-derived growth factor-BB (PDGF-BB)-induced VSMCs. Pax9 knockdown inhibited the phenotypic transformation, proliferation, and migration of VSMCs, whereas the opposite effect was observed when Pax9 was overexpressed. Next, we established that Shh was activated in PDGF-BB-induced VSMCs. Moreover, Pax9 overexpression further activated Shh and exacerbated the phenotypic transformation, proliferation, and migration of PDGF-BB-induced VSMCs. These changes were effectively inhibited by treatment with the Shh signaling pathway antagonist. Consistently, Pax9 knockdown down-regulated Shh expression and inhibited the phenotypic transformation, proliferation, and migration of PDGF-BB-induced VSMCs. Treatment with the Shh signaling pathway agonist prevented these changes.

CONCLUSIONS Pax9 regulated VSMC phenotypic transformation, proliferation, and migration via Shh, which may represent a novel target for the treatment of atherosclerosis.

GW31-e0934

Single-nucleotide polymorphism rs17611 of complement component 5 shows association with ischemic stroke in northeast Chinese population

Liang Guo, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Complement component 5 (C5) has been described to play an important role in the development and progression of atherosclerosis and cardiovascular disease. Our aim was to determine whether genetic variation of C5 was associated with ischemic stroke (IS) in northeast Chinese population.

METHODS We used a case-control study involving 386 IS patients and 386 non-IS controls from a rural population and determined the genotypes of five polymorphisms (rs12237774, rs17611, rs4837805, rs7026551, and rs1017119) of C5 gene by Snapshot single-nucleotide polymorphism genotyping assays to assess any links with IS.

RESULTS In univariate analysis, rs17611 was significantly associated with IS in the additive model, the dominant model, and recessive model (additive P 0.031, dominant P 0.034, and recessive P 0.027). After adjustment for Binary Logistic Regression, rs17611 polymorphism was still significant in three models (adjusted odds ratio (OR)=1.306, 95% confidence interval (CI)=1.069–1.595, P-value=0.009 in an additive model; OR=1.378, 95% CI=1.024–1.856, P-value=0.035 in a dominant model; and OR=1.511, 95% CI=1.048–2.18, P-value=0.027 in a recessive model).

CONCLUSIONS In this sample of patients, genetic variation of rs17611 in C5 is associated with higher prevalence of IS.

GW31-e0940

Atorvastatin attenuates myocardial hypertrophy in spontaneously hypertensive rats via the C/EBPβ/PGC-1α/UCP3 pathway

Yintao Chen[1,2], Yingxian Sun[1]
[1]The First Hospital of China Medical University
[2]The First Affiliated Hospital of Chongqing Medical University

OBJECTIVES Many clinical and experimental studies have shown that treatment with statins could prevent myocardial hypertrophy and remodeling induced by hypertension and myocardial infarction. But the molecular mechanism was not clear. We aimed to investigate the beneficial effects of atorvastatin on hypertension-induced myocardial hypertrophy and remodeling in spontaneously hypertensive rats (SHR) with the hope of revealing other potential mechanisms or target pathways to interpret the pleiotropic effects of atorvastatin on myocardial hypertrophy.

METHODS The male and age-matched animals were randomly divided into three groups: control group (8 WKY), SHR (8 rats) and intervention group (8 SHR). The SHR in intervention group were administered by oral gavage with atorvastatin (suspension in distilled water, 10 mg/kg once a day) for 6 weeks, and the other two groups were administered by gavage with equal quantity distilled water. Blood pressure of rats was measured every weeks using a standard tail cuff sphygmomanometer. Left ventricular (LV) dimensions were measured from short-axis views of LV under M-mode tracings using Doppler echocardiograph. Cardiomyocyte apoptosis was assessed by the TUNEL assay. The protein expression of C/EBPβ, PGC-1α and UCP3 were detected by immunohistochemistry or Western blot analysis.

RESULTS At the age of 16 weeks, the mean arterial pressure of rats in three groups were 103.6±6.1, 151.8±12.5 and 159.1±6.2 mmHg respectively, and

there wasn't statistically significant difference between the SHR and intervention groups. Staining with Masson's trichrome demonstrated that the increased interstitial fibrosis of LV and ventricular remodeling in the SHR group were attenuated by atorvastatin treatment. Echocardiography examination exhibited that SHR with atorvastatin treatment showed an LV wall thickness that was obviously lower than that of water-treated SHR. In hypertrophic myocardium, accompanied by increasing C/EBPβ expression and the percentage of TUNEL-positive cells, the expression of Bcl-2/Bax ratio, PGC-1α and UCP3 were reduced, all of which could be abrogated by treatment with atorvastatin for 6 weeks.

CONCLUSIONS This study further confirmed that atorvastatin could attenuate myocardial hypertrophy and remodeling in SHR by inhibiting apoptosis and reversing changes in mitochondrial metabolism. The C/EBPβ/PGC-1α/UCP3 signaling pathway might also be important for elucidating the beneficial pleiotropic effects of atorvastatin on myocardial hypertrophy.

GW31-e0944

Genetic variants of the ATG16L1 gene promoter in acute myocardial infarction

Falan Han[1], Shuchao Pang[2], Yinghua Cui[3], Bo Yan[2,4,5]
[1]Cheeloo College of Medicine, Shandong University, Jinan 250012, China
[2]Shandong Provincial Key Laboratory of Cardiac Disease Diagnosis and Treatment, Affiliated Hospital of Jining Medical University, Jining Medical University, Jining 272029, China
[3]Division of Cardiology, Affiliated Hospital of Jining Medical University, Jining Medical University, Jining 272029, China
[4]The Center for Molecular Genetics of Cardiovascular Diseases, Affiliated Hospital of Jining Medical University, Jining Medical University, Jining 272029, China
[5]Shandong Provincial Sino-US Cooperation Research Center for Translational Medicine, Affiliated Hospital of Jining Medical University, Jining Medical University, Jining 272029, China

OBJECTIVES Acute myocardial infarction (AMI), a common complex disease caused by an interaction between genetic and environmental factors, is a serious type of coronary artery disease and is also a leading cause of death worldwide. Autophagy-related 16-like 1 (ATG16L1) is a key regulatory factor of autophagy and plays an important role in induced autophagy. In the cardiovascular system, autophagy is essential to preserve the homeostasis and function of the heart and blood vessels. Massive gene sequencing effort and function research promote a better understanding of causal risk factors. There are no studies on the association between ATG16L1 and AMI. To identify genetic risk loci for acute myocardial infarction and determine their functional role in disease development, we conducted a case-control study of ATG16L1 gene promoter versus acute myocardial infarction.

METHODS We conducted a case-control study, using polymerase chain reaction and sequencing techniques, dual-luciferase reporter assay, and electrophoretic mobility shift assay to analyze genetic and functional variation in the ATG16L1 gene promoter between AMI and controls. A variety of statistical analyses were used to analyze the allele and genotype frequencies and the relationship between DSVs and AMI. The TRANSFAC database was used to predict the relevant transcription factors for ATG16L1 gene promoter polymorphism. Values of $P<0.05$ were considered to indicate statistical significance.

RESULTS In all, ten SNPs and two DNA-sequence variants (DSVs) were identified in 688 subjects, and three ATG16L1 gene promoter mutations (g.233250693 T>C [rs185213911], g.233250946 G>A [rs568956599], g.233251133 C>G [rs1301744254]) that were identified in AMI patients significantly altered the transcriptional activity of ATG16L1 gene promoter in HEH2, HEK-293, and H9c2 cells ($P<0.05$). Further electrophoretic mobility shift assays indicated that the SNPs affected the binding of transcription factors. And by the TRANSFAC database, we found that the SNPs identified in AMI patients can create, modify, and eliminate putative binding sites for transcription factors.

CONCLUSIONS This was the first study to find that the ATG16L1 gene promoter polymorphism is associated with AMI. ATG16L1 gene promoter mutations in AMI patients may affect the binding of transcription factors and change the transcriptional activity of the ATG16L1 gene, changing the level of autophagy and contributing to the occurrence and development of AMI as rare and low-frequency risk factors. This research provides important evidence and insights for molecular studies of cardiovascular diseases. With the development of high-throughput sequencing technology, identifying individuals at presymptomatic genetic risk, evaluating and treating them hold the promise of preventing or improving cardiovascular disease morbidity and mortality. This will also drive the future development of genetic testing to identify subsets of patients at high risk of cardiovascular disease and to adopt the most effective treatment or preventive measures for them, thus achieving precision medicine.

GW31-e0990

C-X-C motif chemokine receptor 4 promotes the diastolic dysfunction in heart failure with preserved ejection fraction by enhancing macrophage recruitment and secretome

Ning Zhang, Xiaojie Xie
Second Affiliated Hospital Zhejiang University School of Medicine

OBJECTIVES Nearly half of all heart failure (HF) patients suffer from Heart failure with preserved ejection fraction (HFpEF), carrying a dismal prognosis without effective targeted therapies. However, the precise pathogenesis responsible for the HFpEF remains unknown. Studies have suggested that HFpEF correlates with macrophage activation and excessive secretion of pro-inflammatory cytokines, which drive left ventricular remodeling and diastolic dysfunction by stiffer cardiomyocytes and interstitial fibrosis. Furthermore, the chemokine CXCL12 and its receptor CXCR4 have been confirmed playing an important role in promoting the infiltration of macrophages into damaged tissues, and then activating the inflammatory cascade. However, whether CXCR4 in macrophages promotes fibrosis in HFpEF is uncleared.

METHODS SAUNA (unilateral nephrectomy and a continuous infusion of d-aldosterone (0.30 μg/h) via osmotic minipumps (Alzet) and salty (1% NaCl) drinking water) was administrated to wild-type (WT) mice and myeloid-specific CXCR4-deficient mice or bone marrow (BM) reconstituted chimeric mice for 30 days. In vitro, we first detected macrophage migration and cytokines secretion after HMGB1 treatment and explored the role of CXCR4 and Lyn interaction in macrophages. Then, we evaluated the paracrine effect from activated macrophages on fibroblasts through co-cultured with macrophage and fibroblasts.

RESULTS Loss of the myeloid cells-expressed CXCR4 in mice (MKO) markedly reduced cardiac inflammation, hypertrophy, fibrosis and diastolic dysfunction of HFpEF. These alterations were macrophage dependent because MKO compared with WT mice show decreased infiltration of macrophages but not neutrophils into the hearts at 30 days after SAUNA, whereas bone marrow transplantation from WT mice into MKO mice rescued the diastolic dysfunction and vice versa. Consistent results were seen in vivo, suppressed Lyn phosphorylation contributed to impaired migration and cytokine secretion in CXCR4 KO macrophages. Additionally, primary fibroblasts co-cultured with CXCR4 knockout macrophages showed repressed differentiation of cardiac fibroblasts into myofibroblasts and blocked the synthesis of extracellular matrix (ECM), confirming that macrophages influence cardiac fibrosis in a CXCR4-dependent paracrine manner through TGFβ-smad2/3 signal pathway.

CONCLUSIONS Our findings elucidate that CXCR4 in macrophages can affect left ventricular diastolic dysfunction by increasing macrophage infiltration and enhancing inflammatory secretion, and resulting in inflammation response and interstitial fibrosis.

GW31-e1033

Downregulation of cypher induces apoptosis in cardiomyocytes via Akt/p38 MAPK signaling pathway

Dongfei Wang, Xiaogang Guo
Department of Cardiology, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

OBJECTIVES Dilated cardiomyopathy (DCM) is considered as the most common form of non-ischemic cardiomyopathy with a high mortality worldwide. Cytoskeleton protein Cypher plays an important role in maintaining cardiac function. Genetic studies in human and animal models revealed that Cypher is involved in the development of DCM. However, the underlying molecular mechanism is not fully understood. Accumulating evidences suggest that apoptosis in myocytes may contribute to DCM. Thus, the purpose of this study is to define whether lack of Cypher in cardiomyocytes can elevate apoptosis signaling and lead to DCM eventually.

METHODS We used siRNA to downregulate the expression of Cypher in H9c2 cells and neonatal rat cardiomyocytes which was confirmed by RT-qPCR and western blot. Cell counting kit-8 assay was used to value cell viability. TUNEL and Flow cytometry were conducted to confirm the apoptosis of the cardiomyocytes. RT-qPCR and western blot were further used to detect the specific signal pathway contributed to the apoptosis of the cardiomyocytes.

RESULTS Cypher-siRNA sufficiently inhibited Cypher expression in cardiomyocytes. TUNEL-positive cardiomyocytes were increased in both Cypher knockdown neonatal rat cardiomyocytes and Cypher knockout mice hearts, which were rare in the control group. Flow cytometry further confirmed that downregulation of Cypher significantly increased myocytes apoptosis in vitro. Cell counting kit-8 assay revealed that Cypher knockdown in H9c2 cells significantly reduced cell viability. Cypher knockdown was found to increase cleaved caspase-3 expression and suppress p21, ratio of bcl-2 to Bax. Cypher-deficiency induced apoptosis was linked to downregulation of Akt activation and elevated p-p38 MAPK accumulation. Pharmacological activation of Akt

with SC79 attenuated apoptosis with enhanced phosphorylation of Akt and reduced p-p38 MAPK and Bax expression.

CONCLUSIONS Downregulation of Cypher participates in the promotion of cardiomyocytes apoptosis through inhibiting Akt dependent pathway and enhancing p38 MAPK phosphorylation. These findings may provide a new potential therapeutic strategy for the treatment of DCM.

GW31-e1035

TRPV1 activation attenuates endothelial cell inflammation: involvement of Ca^{2+}/PI3K/Akt/eNOS/NO pathway

Shiyu Zhang, Youping Wang
Central Laboratory and Division of Cardiology, First Affiliated Hospital, Henan University of Traditional Chinese Medicine

OBJECTIVES Our prior studies show that transient receptor potential vanilloid type 1 (TRPV1) exerts protective effects on renal inflammatory injury in salt-sensitive hypertension. However, the mechanisms are not determined. It is well accepted that endothelial dysfunction, especially a reduction of PI3K/Akt-dependent endothelial nitric oxide synthase (eNOS)-induced nitric oxide (NO) production, contributes to the development of inflammation. Recently, compelling evidence shows that TRPV1, originally cloned from primary sensory nerves, is also expressed in endothelial cells and is involved in regulating endothelial cell function. Thus, we aimed to test the hypothesis that NO derived from Ca^{2+}/PI3K/Akt-dependent eNOS contributes to TRPV1-induced anti-inflammatory effects *in vitro* in human umbilical vein endothelial cells (HUVECs).

METHODS Human umbilical vein endothelial cells (HUVECs) were cultured in the presence of capsaicin (CAP, a specific TRPV1 agonist) with or without the specific antagonist of TRPV1, NOS, or Ca^{2+}/PI3K/Akt pathway prior to lipopolysaccharide (LPS) stimulation. NO metabolites, protein expression, and inflammatory molecules were determined using a Griess assay, Western blot, and immune assay-based multiplex analysis, respectively. Monocyte adhesion was evaluated by assaying the fluorescently labeled human monocytes that adhered to LPS-stimulated endothelial cells.

RESULTS Treatment with CAP (3 or 10 μM) for 6 h dose-dependently increased NO production, and the NO production was time-dependently increased in response to CAP (10 μM) in HUVECs. The CAP-mediated NO production was associated with increased $eNOS^{ser1177}$ phosphorylation. The CAP-induced effects were abolished by pretreatment with capsazepine (CAPZ, a specific TRPV1 antagonist, 10 μM), LNMMA (a non-selective inhibitor of NOS, 1 mM), LY294002 (a specific inhibitor of PI3K/Akt pathway, 10 μM), or EGTA (500 nM) that removes extracellular Ca^{2+} from the medium for 1 h ($P<0.05$). In HUVECs, pretreatment with CAP (10 μM) for 1 h inhibited LPS (1 μg/mL)-induced increases in the production of proinflammatory cytokines/chemokines including TNF-α, IL-6 and MCP-1, the expression of adhesion molecules including ICAM-1 and VCAM-1, NF-κB activity, and the number of monocytes that adhered to HUVECs ($P<0.05$). Moreover, the inhibitory effects induced by CAP were completely abolished by concurrent treatment with CAPZ (10 μM), LNMMA (1 mM), or EGTA (500 nM) ($P<0.05$).

CONCLUSIONS Our study provides, for the first time, a direct link between TRPV1 and Ca^{2+}/PI3K/Akt/eNOS/NO pathway in TRPV1-mediated anti-inflammatory actions in endothelial cells. Our data indicate TRPV1 activation suppresses endothelial cell-associated inflammatory response via the activation of Ca^{2+}/PI3K/Akt/eNOS/NO pathway. (Corresponding author: Youping Wang. This work was supported by a grant from the National Natural Science Foundation of China (No. 81170243)).

GW31-e1058

Berberine alleviate pulmonary hypertension through Trx1 and β-catenin signaling pathways in pulmonary artery smooth muscle cells

Wande Yu, Hang Zhang
Nanjing First Hospital

OBJECTIVES The present study investigated whether berberine affected Trx1/β-catenin expression and/or activity and if it could reduce the development of pulmonary hypertension in the experimental rat model and the proliferation in human PASMCs (HPASMCs).

METHODS Immunofluorescence and Western blot used to detect Trx1 and β-catenin expression in human pulmonary tissues. All rats were randomized divided into four groups: the control group (n=6), the SU5416/hypoxia (Su/Hox) group (n=7), the Su/Hox+PX12 group (n=7) and the Su/Hox+berbrine group (n=7). In the latter three groups, these rats received injection of SU5416 under isoflurane anesthesia at day 1 and then were exposure to hypoxia started from day 2 to day 29, the third and fourth group also received PX-12 and berberine respectively for 4 weeks. Evaluation of cardiac function using echocardiography. The mean pulmonary artery pressure (mPAP) were measured by right heart catheterization according to Wanghong. Wall thickness and the percentage of medial wall thickness were used to assess the PA remodeling.

RESULTS The results showed that increased proliferation in hypoxia-induced healthy HPASMCs or PAH HPASMCs is associated with a significant increase in Trx1 and β-catenin expression. Treatment with Trx1 specific inhibitor PX-12 significantly reduced pulmonary arterial pressure and vascular remodeling, as well as improved in vivo cardiac function and right ventricular hypertrophy in Su/Hox-induced PAH rats. Berberine reversed right ventricular systolic pressure, right ventricular hypertrophy, and decreased pulmonary vascular remodeling in the rats. Furthermore, berberine has an antiproliferative effect on hypoxia-induced HPASMCs proliferation in a manner likely to be mediated by inhibiting of Trx1 and its target gene β-catenin expression.

CONCLUSIONS Our results illustrate that the expression of Trx1 and beta-catenin contribute to pathological PASMCs proliferation. BBR or PX-12 is a promising therapeutic utility and raise the possibility to alleviate hyperplastic proliferation of HPASMCs and improve cardiac function through manipulation of the expression of the Trx1 and β-catenin.

GW31-e1076

Branched-chain amino acids exacerbate obesity-related hepatic glucose and lipid metabolic disorders via attenuating Akt2 signaling

Huishou Zhao, Ling Tao
Department of Cardiology, Xijing Hospital, Air Force Medical University, Xi'an, Shaanxi, China

OBJECTIVES Branched chain amino acids (BCAAs) are associated with the progression of obesity-related metabolic disorders, including type 2 diabetes and nonalcoholic fatty liver disease. However, whether BCAAs disrupt the homeostasis of hepatic glucose and lipid metabolism and contribute to insulin resistance remains unknown.

METHODS we fed mice the ND diet, HF diet, or HF/BCAA diet for 16 weeks. Metabolic studies such as glucose tolerance testes, insulin tolerance tests, pyruvate tolerance tests were determined to examine the insulin resistance. Glucose and lipid metabolic related genes were tested to evaluated the hepatic metabolic homeostasis.

RESULTS In this study, we observed that BCAAs supplementation significantly reduced high-fat (HF) diet-induced hepatic lipid accumulation while increasing the plasma lipid levels and promoting muscular and renal lipid accumulation. Further studies demonstrated that BCAAs supplementation significantly increased hepatic gluconeogenesis and suppressed hepatic lipogenesis in HF-DIO mice. These phenotypes resulted from severe attenuation of Akt2 signaling via mTORC1- and mTORC2-dependent pathways. BCAAs/branched-chain a-keto acids (BCKAs) chronically suppressed Akt2 activation through mTORC1 and mTORC2 signaling and promoted Akt2 ubiquitin-proteasome-dependent degradation through the mTORC2 pathway. Moreover, the E3 ligase Mul1 played an essential role in BCAAs/BCKAs-mTORC2-induced Akt2 ubiquitin-dependent degradation. We also demonstrated that BCAAs inhibited hepatic lipogenesis by blocking Akt2/SREBP1/INSIG2a signaling and increased hepatic glycogenesis by regulating Akt2/Foxo1 signaling. Collectively, these data demonstrate that in DIO mice, BCAAs supplementation resulted in serious hepatic metabolic disorder and severe liver insulin resistance: insulin failed to not only suppress gluconeogenesis but also activate lipogenesis.

CONCLUSIONS Intervening BCAA metabolism is a potential therapeutic target for severe insulin-resistant disease.

GW31-e1077

BCAAs exacerbated diabetic glomerular injury through inducing podocytes metabolic remodeling via regulating PKM2

Huishou Zhao, Ling Tao
Department of Cardiology, Xijing Hospital, Air Force Medical University, Xi'an, Shaanxi, China

OBJECTIVES Diabetic nephropathy (DN) is a major cause of end-stage renal disease (ESRD) with few effective therapeutic strategies. There is an urgent need for new, curative treatments as well as for biomarkers to evaluate risk of DN. Podocyte dysfunction and loss is recognized to be a critical event associated with deterioration of renal function in DN. However, the underlying mechanisms remained elusive. Plasma branched chain amino acids (BCAAs) level is ascended in diabetic patients and is causatively correlated with the development of diabetes. Whether BCAAs accelerate the progression of DN remained unclear.

METHODS We fed mice the ND diet, HF diet, or HF/BCAA diet for 16 weeks. Four percent amino acids mixers (all 20 naturally occurring amino acids except Gln and Asn) were added into drinking water of HF and HF/Paired group. the blood urea nitrogen level, plasma creatinine levels and the ratio of urinary albumin/creatinine were determined to evaluate the renal function; Periodic acid Schiff (PAS) staining, Transmission electron microscope (TEM) analysis were utilized to analyze the glomerular abnormalities. Biochemical methods

such as Western blotting and real-time PCR were used to analyze the molecular mechanism.

RESULTS In this study, we observed that BCAAs supplementation exacerbated high fat diet (HF)-induced renal lipid accumulation, proteinuria, glomerulosclerosis, podocyte dedifferentiation, cellular skeletal disordered rearrangement and podocyte loss. Mechanistically, we demonstrated BCAA supplementation induced podocyte metabolic remodeling: enhanced glycolysis, inhibited sugar aerobic oxidation and accelerated serine-one carbon metabolism through depolymerization of pyruvate kinase type M2 (PKM2). BCAAs promoted a shift of PKM2 from tetramers to dimers and monomers and promoted protein and nucleotides synthesis, which elicited endoplasmic reticulum stress (ESR) and led to podocyte loss. PKM2 agonist TEPP46 reversed BCAAs-induced glucose and serine-one carbon metabolic disorders, improved ESR response in podocyte, and ameliorated BCAAs supplementation-induced renal lipid accumulation, proteinuria, and podocytes dysfunctioning and loss. In addition, we demonstrated BCAAs promoted PKM2 expression through activation of mTORC1 signaling, rapamycin treatment eliminated BCAAs supplementation induced up-regulation of PKM2 and produced renal protective effects upon BCAAs induced diabetic kidney injury.

CONCLUSIONS Collectively, we demonstrated BCAAs accumulation accelerated HF-induced renal injury through disrupting podocyte energetic and substance biosynthesis metabolisms, intervening BCAA metabolism or PKM2 may be effective for preventing obesity-associated DN progress.

GW31-e1101

Preliminary evaluation of a novel counterpoint overlapped double-layer retrievable stent in a canine peripheral artery model

Yujuan Jiang, Xiuyue Jia, Minghong Wang, Xu Han, Hongjuan Xia, Houliang Chen, Chong Li, Xue Zhao
Cardiovascular Department, Eastern Hepatobiliary Surgery Hospital, Shanghai, China

OBJECTIVES The stent therapy of peripheral artery stenosis remains challenging due to high incidence of restenosiscaused by permanent metallic implantation. Metallic stents may act as chronic stimulus for prolonged duration of proliferative response even when the stent surface is completely endothelialized. Besides drug coating balloon and bioresorbable stent, retrievable stent may be another strategy to achieve "nothing left" intervention. This study aimed to explore preliminary the feasibility and the controversial issues of retrievable stent in a canine intact iliac artery.

METHODS The stents were self-developed with counterpoint overlapped double-layer self-expandable drug-eluting scaffolds, which were composed of two-layer scaffolds, inner and outer. A small hook in the outer scaffold was used for retrieval by snare catheter. Four retrievable stents were implanted into the iliac arteries of four Labrador dogs at the same time and retrieved on day 21, 28, 35 and 42 after implantation respectively. The angiography and IVUS were performed before and after stent retrieval. The target vascular segments were harvested for staining of HE, Methyl violet, Masson trichrome and CD31. The dog with stent implanted for 28 days was followed for another 14 days after stent retrieval.

RESULTS The angiography showed all the stents were patency before retrieving. The stents implanted for 28 days (28-day-stent) and 42 days (42-day-stent) were successfully retrieved (Figure 1). IVUS showed a smooth vascular wall before and after stent retrieval. The inner surface of the retrieved 28-day-stent was covered with a white translucent thin layer substance, which was composed of more fibrin and scattered fibroblasts and smooth muscle cells (Figure 2). At the following up of 14 days after stent retrieval, angiography showed the vessel was patency. The artery diameter with 28-day-stent decreased by 10% before retrieval and 21% on day 14 after retrieval compared to baseline. The vascular inner surface was covered with an uneven neointima, which was thicker close to struts and thinner far to struts (Figure 3). The average neointima thickness was 36±2 μm when the gap distance between adjacent struts was ≥200 μm, and it turned to be 163±20 μm when this gap distance was <200 μm. The internal elastic lamina showed breaks in some areas. For the 42-day-stent, some petechiae were observed on the proximal and distal segments in the target artery. Under the stent struts, endothelial cells and smooth muscle cells decreased with local fibrosis, and also the internal elastic lamina was interrupted in partial area (Figure 4). The inner surface of the retrieved stent was covered with a white translucent layer substance, which contained more cell components than that in 28-day-stent, including endothelium and angiogenesis (Figure 2). The media and adventitia were intact. Unfortunately, stents after implantation of 21 days and 35 days failed to be retrieved because of catching failure due to stent displacement.

CONCLUSIONS The study demonstrated the feasibility of retrieving a stent from iliac artery as long as 42 days after implantation. Pulling slightly and slowly or even stopping temporarily was the critical skill to guarantee the higher safety and efficiency of the stent retrieval procedures. A modified stent without hook was under exploration for the further enhancement of retrieval safety. However, neointima formation would still be challenging in further study.

GW31-e1117

The novel nested intronic gene Laf4ir contributes to cardiovascular remodeling

Lei Huang[1], Yue Zhao[1], Lingfang Zeng[2], Tong Li[1]
[1]Tianjin Third Central Hospital
[2]School of Cardiovascular Medicine and Sciences, Faculty of Life Science and Medicine, King's College London

OBJECTIVES Recently, a novel nested intronic gene was discovered from the microarray profiling of the laminar flow-upregulated genes in mouse embryonic stem cells (ESCs). This gene is located in the intron 6 of the lymphoid transcription factor gene *Laf4/Aff3*. Therefore this novel gene is referred as *Laf4* intron resident (*Laf4ir*). *Laf4ir and Laf4* are transcribed using opposite strands of DNA. *Laf4ir* exhibits 7 exons and two transcript variants (Genbank accession: MH282850.1, GI: 1567433536 and MH282851.1, GI: 1567433538). *Laf4ir-tv2 a*ppears to be the dominant transcript variant. *Laf4ir* has been shown to be a polycistronic gene, encoding a 45-amino acid (aa) peptide from open reading frame 1 (ORF1) and a 109aa (*Laf4ir-tv1*) or 151aa (*Laf4ir-tv2*) protein from ORF2, respectively. ORF1 and ORF2 polypeptide expression was found in various adult organs, different stages of embryonic development, different cell types and different subcellular localisation. In this study, we aimed to investigated the potential function of *Laf4ir* in cardiovascular remodeling and utilized the global knockout mouse model to further understand the underlying mechanisms.

METHODS Mouse ESCs cultured in differentiation medium were subjected to laminar shear at 12 dynes/cm^2 for 24 h. The 3-day spontaneously differentiated ESCs were infected with *Ad-null* or *Ad-L151* (the adenovirus contains *the* cDNA sequence for the 151-aa of ORF2) at 10MOI for 16 h. The cells were then seeded and incubated for 24 h followed by the Br-dU incorporation assay with the cell proliferation. Mouse ECs C166 were seeded in complete growth medium for sixteen hours, then adenoviral particles were added at 10 MOI and incubated for 24 h. The cells were eventually incubated with serum free medium containing H_2O_2 at concentration indicated for 24 h. MTS assay and Annexin V/Dead Cell Apoptosis assay were performed accordingly to assess the cell survival. To investigate the potential contribution of *Laf4ir* in cardiovascular repair and pathology, transverse aortic constriction-mediated pressure overload in heart, aorta from *ApoE*$^{-/-}$ mice, femoral artery wall following vascular injury and ischemia were investigated. To explore the functionality of *Laf4ir* further, a Cre-*loxP in-vivo* global knockout model was developed and utilized.

RESULTS Overexpression of LAF4IR-ORF2 via adenoviral gene transfer could enhance laminar flow- and VEGF-induced endothelial cell (EC) differentiation and reduce cell proliferation. This could be due to cell cycle arrest via the retention of mini-chromosome maintenance protein 3 (MCM3) in the cytosol and as a consequence assist differentiation towards EC lineage. Overexpression of LAF4IR-ORF2 also promoted endothelial survival under oxidative stress induced by hydrogen peroxide. The upregulation of ORF2 polypeptide was detected in transverse aortic constriction-mediated pressure overload in heart, aorta from *ApoE*$^{-/-}$ mice, femoral artery wall following vascular injury and ischemia. Vascular ischemia in *Laf4ir* knockout mice confirmed the contribution of *Laf4ir* in vascular repair. Sca1$^+$ adventitia cells isolation from transgenic mice further validated functions of *Laf4ir* in proliferation.

CONCLUSIONS Overall, the novel nested *Laf4ir* gene may contribute to cardiovascular remodeling through spatiotemporal translation of different ORFs. Further detailed investigation on *Laf4ir* will undoubtedly yield new insights into cardiovascular physiology and pathology.

GW31-e1123

MAM-mediated mitochondrial calcium overload participate in ox-LDL-induced endothelial cell apoptosis

Sanjiu Yu, Jihang Zhang, Lan Huang
Institute of Cardiovascular Diseases, Xinqiao Hospital, Army Medical University

OBJECTIVES Oxidized low-density lipoprotein (ox-LDL)-induced endothelial cell (EC) apoptosis is the initial step of atherogenesis. Mitochondria-associated endoplasmic reticulum (ER) membrane (MAM), regulated by tethering proteins such as phosphofurin acidic cluster sorting protein 2 (PACS2), is essential for mitochondrial Ca^{2+} overload and subsequent cell apoptosis. Previously, we demonstrated that PACS2 played an important role in ox-LDL-induced EC apoptosis by regulating MAM formation, but the underlying mechanism was still unclear. In this study, we aimed to investigate the upstream of PACS2 in ox-LDL-induced apoptosis in human umbilical vein endothelial cells (HUVECs).

METHODS HUVECs were treated with ox-LDL at 0, 50, 100, 150, 200 or 250 μg/mL for 24 h or at 200 μg/mL for 0, 6, 12, 24, 48 or 72 h. Mitochondrial Ca^{2+} uniporter (MCU) and PACS2 were knocked down by using small interfering RNA. After treatments, cell viability and apoptosis were measured by cell counting kit-8 assay and Annexin V/propidium iodide staining, respectively. Mitochondrial membrane potential (MMP) was evaluated by JC-1. Reactive oxygen species (ROS) was examined by DCFH-DA. Mitochondrial Ca^{2+} level was assessed by fluorescent probe Rhod-2 AM. The mRNA or protein levels of

target genes were determined by quantitative real-time polymerase chain reaction or western blotting. MAM formation was detected by confocal microscopy and transmission electron microscopy.

RESULTS Ox-LDL dose- and time-dependently increased cell apoptosis concomitant with mitochondrial Ca^{2+} elevation, mitochondrial membrane potential (MMP) loss, reactive oxygen species (ROS) production. Besides, ox-LDL upregulated PACS2 expression and decreased miR499 level. Further, we found that over-expression of miR-499 could protect HUVECs against ox-LDL-induced apoptosis. Increased miR-499 level favored endothelial cell survival, while decreased miR-499 level favored apoptosis. In addition, over-expression of miR-499 could protect HUVECs against ox-LDL-induced mitochondrial Ca^{2+} elevation, MMP loss, ROS production. Further, we identified PACS2 as the target of miR-499. MiR-499 inhibited endothelial apoptosis through its suppressive effect on PACS2 expression, thereby blocking ox-LDL-induced MAM formation and ER-mitochondria Ca^{2+} transfer.

CONCLUSIONS Altogether, our findings suggest that miR-499 plays an inhibiting role in ox-LDL-induced EC apoptosis by regulating PACS2 expression, MAM formation and mitochondrial Ca^{2+} elevation, implicating that miR-499 may be a promising therapeutic target for atherosclerosis.

GW31-e1126

GRK4-mediated adiponectin receptor-1 phosphorylative desensitization as a novel mechanism of reduced renal sodium excretion in hypertension

Yan Zhang, Chunyu Zeng
Department of Cardiology, Daping Hospital, The Third Military Medical University

OBJECTIVES Patients with obesity-related hypertension have impaired sodium excretion. However, the mechanisms are incompletely understood. Adipocytes secrete numerous hormones, called adipokines, among which adiponectin is an important one. Whether and how adiponectin contributes to impaired sodium excretion in hypertension has not been previously investigated. The current study tested the hypothesis that adiponectin promotes natriuresis and diuresis and their impairment is involved in hypertension.

METHODS We used Wistar-Kyoto (WKY) rats, spontaneously hypertensive rats (SHRs), GRK4γ142A>V transgenic mice to test the natriuresis-effect of adiponectin through intrarenal arterial infusion. Renal proximal tubule (RPT) cells, adiponectin knock out ($Adipo^{-/-}$) mice, mutant plasmid were used.

RESULTS We demonstrate that sodium excretion was reduced in $Adipo^{-/-}$ mice. The intrarenal arterial infusion of adiponectin induced natriuresis and diuresis in WKY rats, which was impaired in SHRs. Adiponectin inhibited Na^+-K^+-ATPase activity in RPT cells from WKY rats but not from SHRs. Increased adiponectin receptor phosphorylation and subsequent uncoupling from Gαi, rather than altered adiponectin receptor expression, were responsible for the loss of adiponectin-mediated inhibition of RPT Na^+-K^+-ATPase activity, impaired natriuresis and diuresis in SHRs. Mutation of the AdipoR1 phosphorylation site restored its linkage to Gαi and the adiponectin-mediated inhibition of Na^+-K^+-ATPase activity in RPT cells from SHRs. Finally, we identified G protein-coupled receptor kinase 4 (GRK4) as the cause of adiponectin receptor hyper-phosphorylation. GRK4γ142A>V transgenic mice replicated the abnormal adiponectin function in SHRs, whereas down-regulation of GRK4 by renal-ultrasound directed siRNA restored the adiponectin-mediated sodium excretion and reduced the blood pressure in SHRs.

CONCLUSIONS Our present study indicates that the stimulatory effect of adiponectin on sodium excretion is impaired in hypertension, which is attributable to increased renal GRK4 expression and subsequent adiponectin receptor hyper-phosphorylation. Targeting GRK4/adiponectin receptor/Gαi may restore the impaired adiponectin-mediated sodium excretion in hypertension, thus representing a novel strategy against hypertension, particularly those patients with obesity-related hypertension.

GW31-e1143

NF-κB/NLRP3/GSDMD axis-mediated pyroptosis following myocardial ischemic/reperfusion injury in aged mice

Min Han, Yi Tong Ma
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, P. R. China

OBJECTIVES The rate of aging of the global population is growing, which contributes to increasing incidence and morbidity of acute myocardial infarction (AMI) in worldwide. Although the reperfusion therapy is currently regarded as the best strategy for AMI, the ischemic/reperfusion (I/R) injury leads to a poor prognosis, especially in the elderly patients. Pyroptosis is a pro-inflammatory programmed cell death that is related to myocardial I/R injury, but its effect has not been reported in aged heart. The present study is designed to investigate the underlying mechanism of pyroptosis in senile cardiomyocytes or heart.

METHODS First, we investigated the differences in the infarct size and left ventricular remodeling following I/R surgery between aged (18-mon) and young (3-mon) C57Bl/6 male mice and explored responsible mechanisms. Then, the AAV9 vector carrying mutant $IκBα^{Ser32A,Ser36A}$ gene were delivered to senile cardiomyocytes or 18-month-old C57BL/6 mice prior to hypoxia/reoxygenation (H/R) or I/R treatment. Cytosolic IκBα and p65/p50 nuclear translocation were identified by Western blot. The level of the pyroptosis was detected by Western blot and ELISA.

RESULTS The infarct size after I/R was significantly higher in aged than that in young mice (57.89±2.55% vs. 47.03±3.05%, P<0.05). Echocardiography revealed more profound LV chamber dilatation and dysfunction in aged mice. Subsequently, more dramatic IκBα degradation and nuclear translocation of NF-κB p65/p50 were found in aged than in young I/R hearts, in keeping with enhanced oxidative injury. Furthermore, we observed significantly higher contents of serum LDH and IL-1β, and markedly enhanced expression of gasdermin D-N (GSDMD-N) domains in the aged than in young mice. After transfection with the AAV9-IκBα into senescent cardiomyocyte or aged heart, the levels of NLRP3, Caspase-1 and GSDMD-N were downregulated during H/R or I/R treatment. Moreover, IκBα increased cell viability and decreased PI-positive cells *in vitro*, reduced the myocardial infarct size and the cardiac remodeling *in vivo* via suppressing NF-κB activation. Additionally, IκBα transfection significantly downregulated the oxidative injury as well as the levels of supernatant or serum LDH and IL-1β in senile cardiomyocyte or aged mice.

CONCLUSIONS This study confirms that aged mice had a worse outcome of I/R injury accompanied with a higher level of NF-κB activation and pyroptosis. Both *in vivo* and *in vitro*, IκBα transfection was able to alleviate myocardial I/R injury and inhibit pyroptosis in senile cardiomyocytes or aged heart inhibitory effect of IκBα on pyroptosis was mediated by suppressing the NF-κB/NLRP3/GSDMD axis. Therefore, targeted inhibition of NF-κB signaling may provide an alternative treatment for myocardial I/R injury in aged heart.

GW31-e1155

Genetic variation of RNF145 gene and blood lipid levels in Xinjiang population, China

Jing Ming, Yi Tong Ma
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, P. R. China

OBJECTIVES Dyslipidemia is one of the main risk factors for coronary heart disease (CHD). The E3 ubiquitin ligase which is encoded by the ring finger protein 145 (RNF145) gene is very important in the mediation of cholesterol synthesis and effectively treats hypercholesterolemia. Thus, the purpose of the present research is to investigate the connection between the polymorphism of the RNF145 gene and cholesterol levels in Xinjiang, China

METHODS A total of 1396 participants (male: 628, female: 768) were included in this study for genetic analysis of RNF145 gene, and we used the modified multiple connection detection response (iMLDR) technology to label two SNPs (rs17056583, rs12188266) of RNF145 genotyping. The relationship between the genotypes and the lipid profile was analyzed with general linear model analysis after adjusting confounding variables.

RESULTS Through the analysis of the two SNPs in RNF145 gene, we discovered that both rs17056583 and rs12188266 were related to total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) concentrations (All P<0.001). Compared to C, the G allele of rs17056583 has significantly lower plasma TC concentrations (2.76±0.70 mmol/L, 6.29±1.04 mmol/L, P<0.001) and LDL-C concentrations (1.27±0.29 mmol/L, 5.10±0.60 mmol/L, P<0.001). The G allele carrying rs12188266 had significantly higher TC concentrations (6.39±0.98 mmol/L (2.95±0.99 mmol/L, P<0.001) and LDL-C concentrations (5.15±0.55 mmol/L, 1.44±0.70 mmol/L, P<0.001) than those carrying the A allele. Meanwhile, we also found that rs17056583 was associated with high triglycerides concentrations (All P<0.001). In addition, the association of rs17056583 and rs12188266 with lipid profile concentrations is still statistically significant after multivariate adjustment of sex, age, smoking, obesity, alcohol consumption, diabetes, and hypertension.

CONCLUSIONS Our study shows that both rs17056583 and rs12188266 SNPs of RNP145 gene are related to TC and LDL-C concentrations in Xinjiang population.

GW31-e1160

Cartilage oligomeric matrix protein (COMP) controls blood pressure through regulating eNOS activation

Hui Wang, Yi Zhu
Tianjin Key Laboratory of Metabolic Diseases; Key Laboratory of Immune Microenvironment and Disease (Ministry of Education); Collaborative Innovation Center of Tianjin for Medical Epigenetics and Department of Physiology and Pathophysiology, Tianjin Medical University, Tianjin, China

OBJECTIVES Vascular endothelial cells (ECs) are of critical importance for maintaining blood pressure (BP). Although cartilage oligomeric matrix protein (COMP) plays a pivotal role in maintaining cardiovascular homeostasis, its

effect on endothelial function and blood pressure is largely unknown. In this study, we investigated the protective effect of COMP on blood pressure and its underlying mechanism.

METHODS Wild type (WT) mice and COMP$^{-/-}$ mice were infused with angiotensin II (450 ng/kg/min) for 3 days via an osmotic minipump, and BP was monitored by a tail-cuff system. Second-order mesenteric arteries were isolated from mice for microvascular tension measurement in an oxygenated organ chamber. Nitric oxide (NO) was detected by an electron paramagnetic resonance (EPR) technique using iron (II) diethyldithiocarbamate [Fe (DETC)$_2$] as the spin trap. To determine intracellular calcium influx, endothelial cells were loaded with a fluorescent probe fluo-4AM, and live cell images were acquired with a confocal microscope. Small interfering (si) RNA transfection, western blot, and co-immunoprecipitation were used for further detailed mechanism investigation.

RESULTS COMP deficiency showed higher blood pressure than WT mice in baseline or after angiotensin II infusion. Disruption of COMP impaired acetylcholine-evoked endothelium-dependent relaxation (EDR) in second-order mesenteric arteries as compared with WT mice. L-NG-nitroarginine methyl ester (L-NAME), an endothelial nitric oxide synthase (eNOS) inhibitor, abolished the difference in EDR between the two genotypes. Mechanistically, COMP increased intracellular calcium influx, which promoting the dissociation of eNOS and caveolin-1, augmenting the phosphorylation of Ca^{2+}/calmodulin-dependent protein kinases II (CaMKII) and eNOS. Furthermore, co-immunoprecipitation assays suggested that COMP bound directly to the endothelial mechanosensitive cation channel PIEZO1. SiRNA-mediated PIEZO1 deficiency blocked COMP-dependent eNOS activation. Meanwhile, PIEZO1 activator Yoda1 reduced the difference of EDR in WT and COMP$^{-/-}$ mice.

CONCLUSIONS Our study demonstrates that COMP plays a critical role in blood pressure homeostasis by interacting with PIEZO1, and increasing intracellular calcium influx, eNOS activity and NO formation.

GW31-e1165

The NAD+ precursor nicotinamide riboside alleviates alcoholic cardiomyopathy through FUNDC1-dependent mitophagy

Sai Ma[1,2], Ren Jun[2]
[1]Jinling Hospital, Medical School of Nanjing University
[2]University of Wyoming

OBJECTIVES Nicotinamide riboside (NR) is widely used as a NAD+ precursor vitamin. Supplementation with NR has been shown to protect against metabolic disease in mammals. However, the potential effect of NR in alcoholic cardiomyopathy (ACM) has not been well elucidated. This study was designed to examine the effect of NR supplementation on the progression of alcoholic cardiomyopathy.

METHODS Alcoholic cardiomyopathy was established using chronic alcoholic diet containing 36% kcal from ethanol. Echocardiography and IonOptixMyoCam were used to evaluate cardiac contractile function.

RESULTS Our data revealed that NR alleviated alcohol consumption-induced changes in myocardial and cardiomyocyte contractile function as well as cardiac remodeling. To examine the possible involvement of mitophagy in NR-induced beneficial effects, FUNDC1-/- mice with mitophagy deficiency were employed. Interestingly, NR-induced beneficial effect against alcoholic cardiomyopathy was partially attenuated in FUNDC1-/- mice, indicating a role for FUNDC1-mediated mitophagy in NR-offered cardioprotection. In vitro study using H9c2 myoblasts suggested that NR regulated mitochondrial homeostasis through induction of FUNDC1-dependent mitophagy, as suggested by mitophagy-related protein expressions and Mitotracker-LC3 dots overlay. NR treatment enhanced cellular NAD+ level, consequently elevated NAD+-dependent mitochondrial sirtuin SIRT3 activity. Using mass spectrum assay and Co-IP, PGAM5, which functions to phosphorylate FUNDC1 at serine 13 (Ser13), was found to interact with and deacetylated by SIRT3 following NR administration.

CONCLUSIONS Taken together, our results revealed a protective effect of NR supplementation against alcoholic cardiomyopathy possibly associated with a SIRT3-PGAM5-FUNDC1-dependent regulation of mitophagy. These findings suggested the therapeutic potential of the vitamin B3 precursor of NAD+ in the management of alcoholic cardiomyopathy.

GW31-e1173

Intervention PXDN plays an important role in the cardiac ferroptosis after myocardial infarction

Jing Cao[1], Zhaoya Liu[2], Qian Xu[3], Guogang Zhang[1], Ruizheng Shi[4]
[1]Department of Cardiovascular Medicine, The Third Xiangya Hospital, Central South University, 410013 Changsha, China
[2]Department of Geriatrics, The Third Xiangya Hospital, Central South University, 410013 Changsha, China
[3]Department of Cardiothoracic Surgery, Xiangya Hospital, Central South University, 410008 Changsha, China
[4]Department of Cardiovascular Medicine, Xiangya Hospital, Central South University, 410008 Changsha, China

OBJECTIVES It is well known that necrosis due to coronary artery occlusion is the main form of cardiomyocytes loss. Recently, there are a considerable number of studies focusing on non-necrotic cell death of cardiomyocytes stimulated by hypoxia and inflammatory factors in infarction border zone, which contributes a lot to the loss of interventional cells. Therefore, it is urgent to explore the regulatory mechanism of non-necrotizing myocardial cell death to reduce the loss of cardiomyocytes after myocardial infarction (MI). Ferroptosis that depends on iron and reactive oxygen species is a newly discovered way of programmed cell death. Myocardial iron level has been addressed as an important prognostic factor for heart failure after MI in numerous clinical studies. However, the mechanism of ferroptosis in cardiomyocytes after MI has not been fully elucidated. Peroxidasin (PXDN) is a member of the peroxidase family which contain heme groups in its structure domain and can generate hypochlorous acid (HOCl) by consuming hydrogen peroxide (H_2O_2). Previous studies have found that PXDN level is significantly increased in the plasma of patients with MI, but the specific mechanism of PXDN in MI remains unclear.

METHODS Eight-week-old systemic knockout of PXDN (PXDN$^{-/-}$) and homologous control mice (PXDN$^{+/+}$) were used to construct a model of myocardial infarction with left coronary artery ligation. Echocardiography and three-dimensional speckle tracking imaging were applied to assess left ventricular function and fibrosis. Effects of PXDN changes on infarction area, myocardial cell death and degree of myocardial fibrosis after MI were evaluated by Cardiac TTC, live/dead and masson staining. The expression and localization of non-heme, PXDN, heme oxygenase-1 (HO-1), 3-chlorot-yrosine (3-Cl-Tyr) in cells were detected by immunohistochemistry, iron staining, and immunofluorescence. Levels of PXDN, 3-Cl-Tyr, HO-1, ferroptosis-related marker and lipid peroxidation products were confirmed by Real-time PCR and western blot. *In vitro* experiments were performed in H9C2 cells. H9C2 cells with PXDN knockdown by siRNA were pretreated with 1% O_2 or ferric citrate. Cell death, expression of PXDN, 3-Cl-Tyr, HO-1, ferroptosis biomarker and lipid peroxidation products were detected by immunofluorescence, western blot and real-time PCR.

RESULTS Mice after MI had significantly weakened cardiac function, and severe myocardial fibrosis in the infarct area, accompanied with increased ferroptosis. Expression of PXDN, HO-1 and 3-Cl-Tyr were increased in mice myocardium after MI, whereas TfR were decreased. The cardiac iron levels, lipid peroxidation and ferroptosis of cardiomyocytes were decreased in Mice lacking PXDN, resulting in more mild cardiac function injury and fibrosis upon MI and increased survival rate. At the molecular level, mice with PXDN systemic knockout had lower level of non-hem, 3-Cl-Tyr and ferroptosis-related marker and higher expression of TfR. Expression of PXDN, HO-1 and 3-Cl-tyr in H9C2 cells were elevated during hypoxic conditions, as well as the biomarker of ferroptosis (ptgs2, NOX1 and COX2), lipid peroxidation level and cell death. Moreover, intracellular iron levels were increase together with expression of TfR in cell membrane decreased. These results had been found in cells treated with exogenous iron (ferric citrate) and could be reversed after PXDN silence.

CONCLUSIONS Lacking of PXDN in mice reduces the occurrence of myocardial ferroptosis after MI and improves the prognosis of MI.

GW31-e1206

Cofilin activation accelerated lamellipodia network debranching is critical for contractile machinery assembly and rigidity sensing during MSC engraftment after myocardial infarction

Dan Zhu, Wei Chen, Xinyang Hu, Jianan Wang
Second Affiliated Hospital of Zhejiang University School of Medicine

OBJECTIVES Mesenchymal stem cell (MSC) injection after myocardial infarction promotes recovery of heart function. But how matrix deposition and collagen crosslinking during the healing process affects cardiac stiffness and MSC engraftment are unknown. Cell probes rigidity by applying forces to the ECM through actomyosin-focal adhesions connections. However, whether rigidity influences contractile machinery assembly after initial contact with ECM during cell spreading is unknown. Focal adhesion forms under lamella network after lamellipodia retraction. Cofilin is an actin binding protein best known for its role in actin filament severing and lamellipodia network turnover. Here we investigate the role of cofilin in contractile machinery assembly, rigidity sensing and MSC engraftment.

METHODS Cardiac stiffness was measured by atom force microscopy. MSC engraftment was detected by immunofluorescence staining and PCR. Cell tractions exerted on substrate of different rigidity was detected by traction force microscopy. Actin retrograde flow (ARF) was measured by time-lapse microscopy. Cofilin activation after PIP2 hydrolysis was visualized by fluorescence resonance energy transfer (FRET) microscopy. Integrin–fibronectin interaction was measured by biomembrane force probe (BFP).

RESULTS Cardiac stiffness increased over time after myocardial infarction. MSC engraftment and adhesion increased with substrate stiffness. ARF, traction force and cofilin activity increased with substrate stiffness. PIP2 and

cofilin association decreased on stiffer substrate. Tropomyosin enriched in lamellipodia on stiffer substrate. Constitutive activated cofilin promotes ARF, tropmyosin enrichment and traction force on soft substrate, whereas branch dissociation defects decreased ARF, tropmyosin enrichment and traction force on stiffer substrate. Increasing force loading rate prolonged integrin and fibronectin bond lifetime.

CONCLUSIONS Our data demonstrate that increasing substrate rigidity depletes PIP2 level on cell membrane, which leads to cofilin translocation and activation. Cofilin activation induces lamellipodia actin debranching and contractile machinery assembly. Contractile machinery assembled on stiff substrate promotes ARF and force loading rate on integrin–ECM bond, which underlies enhanced MSC adhesion and engraftment after myocardial infarction.

GW31-e1209

Single cell engineering with surface-conjugated gelatin improves mechenchymal stem cell survival and therapeutic effects for heart repair

Ling Zhang, Kaiqi Lv, Xinyang Hu, Jianan Wang
Second Affiliated Hospital Zhejiang University School of Medicine

OBJECTIVES Cell therapy showed great potentials in the regenerative and related medicine in the past ten years, however, low survival rates and short residence time of transplanted cells staying at disease region after their implantation have hampered their functional outcomes. The purpose of the present study was to investigate whether single cell engineering with surface-conjugated gelatin could improve mechenchymal stem cell survival and therapeutic effects for myocardial infarction (MI).

METHODS Here, we artificially synthesize poly (sialic acid) based biocompatible anchor molecule that can self-assemble in the phospholipid bilayer of mesenchymal stem cell (MSC) membrane and which concatenates with microbial transglutaminase that can lead to catalytic formation of gelatin hydrogel on the surface of single MSCs. Then the cell survival after single cell engineering was detected in the hypoxia and ischemia environment *in vitro* and *in vivo*, and the cardiac function after cell transplantation was also investigated by echocardiography and Masson's trichrome staining. Furthermore, the underlying mechanism of cell protection against apoptosis by hydrogel encapsulation was detected by RNA-seq and western blot.

RESULTS In the present study, we report a novel approach to encapsulating a single MSC in a layer of gelatin by surface engineering with encapsulation efficiencies 94%. Our results show that in a single MSC modification significantly increase the ability to resistance to stress while the modification did not affect the paracrine effects of MSC *in vitro*. Bioluminescence images indicates that hydrogel engraftation improves MSC survival in vivo, moreover, the cell survival was further confirmed by GFP PCR and GFP immunostaining after transplanting GFP transfected MSCs in MI model. We also observed that hydrogel-engrafted MSCs protect cardiac cells against apoptosis and enhance angiogenesis in heart repair, and the MSCs-Gel transplantation results in better cardiac function recovery. Finally, Tnfrsf19/NFκB pathway was found to be involved in the cell protection against apoptosis by hydrogel encapsulation.

CONCLUSIONS The single cell-hydrogel engraftation provides a completely different vision of cell engineering and should find use in a variety of translational applications and hold great potentials for cell therapy of diseases.

GW31-e1211

The role of G protein coupled receptor kinase 4 in cardiomyocyte injury after myocardial infarction

Liangpeng Li, Chunyu Zeng
Deparment of Cardiology, Army Medical Center (Daping Hospital), Army Medical University, Chinese People's Liberation Army

OBJECTIVES G protein coupled receptor kinase 4 (GRK4) plays an important role in the development of hypertension, but its effect on cardiac ischemia injury is not clear. The aim of this study is to investigate the effect of GRK4 on myocardial infarction and its underlying mechanism.

METHODS In C57/BL6 mice, we assessed the expression and distribution of GRK4 in the basal state and at different time after MI. GRK4 A486V (GRK4 486 glycine mutation to valine) is a variant of GRK4 in human. Its distribution frequency in Asian people is about 66.4%, and its enzyme activity is higher than that of GRK4 wild type (GRK4 WT). We generated GRK4 WT and GRK4 A486V transgenic mice, as well as cardiac GRK4 knockout mice. We measured the cardiac function, infarct size, cardiomyocyte apoptosis and autophagy after MI, and examined the interaction between GRK4 and HDAC4 and its effect on Beclin1 expression. We also analyzed the correlation between cardiac function and GRK4 A486V variant in 550 patients with AMI.

RESULTS The mRNA and protein levels of GRK4 in the heart of C57/BL6 mice increased significantly 48 hours after MI, and were mainly distributed in the nucleus. Hypoxia induced the increase of GRK4 mRNA and protein levels and nuclear entry of primary cardiomyocytes. Compared with control group, the GRK4 WT transgenic mice exhibited impaired cardiac function of, enlarged infarct size and increased mortality, these were more significant in GRK4 A486V transgenic mice. On the contrary, cardiac GRK4 knockout mice had better cardiac function and smaller infarct size than the control group. TUNEL assays showed that overexpression of GRK4 WT and GRK4 A486V increased cardiomyocyte apoptosis. Overexpression of GRK4 decreased the LC3 II levels and the GFP puncta in primary cardiomyocyte transfected with GFP-LC3 adenovirus. Rapamycin, an autophagy agonist, partially rescued the autophagy inhibition and apoptosis induced by GRK4 overexpression in primary cardiomyocytes. Overexpression of GRK4 reduces the expression of Beclin1, which is positively regulated by histone deacetylase 4 (HDAC4) in the nucleus, while GRK4 reduces the nuclear entry of HDAC4 after hypoxia. HDAC4 S3A (HDAC4 246/467/632 serine to alanine mutation, which leads to phosphorylation resistance) ameliorated inhibition of autophagy and promotion of apoptosis induced by GRK4. The phosphorylation of HDAC4 632 serine was further confirmed by immunoprecipitation and Western blot after myocardial infarction. HDAC4 S632A (serine to alanine mutation at HDAC4 632, resistant to phosphorylation) decreased the inhibition of GRK4 on autophagy. Immunoprecipitation and proximal ligation assay indicated that GRK4 interacted with HDAC4 in mouse heart. Chip assay showed that HDAC4 bound to the promoter region of Beclin1, while GRK4 weakened this binding. The multiple regression analysis of 550 patients diagnosed with acute myocardial infarction showed that, the cardiac function of GRK4 A486V carriers were worse than that of GRK4 WT genotype carriers, GRK4 A486V genotype is an independent factor for predicting lower cardiac function after myocardial infarction.

CONCLUSIONS The expression of GRK4 increases in infarcted mice heart and it translocates into the cardiomyocyte nuclei. GRK4 inhibits autophagy and promotes apoptosis in cardiomyocyte after MI. This effect is depends on the phosphorylation of HDAC4 on 632 serine by GRK4 and the subsequent nuclear-export of HDAC4 which leads to down regulation of Beclin1.

GW31-e1213

Exosomal microRNA-486-5p promotes the angiogenic response to myocardial infarction by targeting matrix metalloproteinase 19 in fibroblasts

Qingju Li, Yinchuan Xu, Kaiqi Lv, Xinyang Hu, Jianan Wang
Second Affiliated Hospital Zhejiang University School of Medicine

OBJECTIVES The potency of mesenchymal stem cells (MSCs) for treatment of myocardial infarction (MI) in nonhuman primates (NHPs) can be significantly improved by culturing the cells under hypoxic conditions before administration, and most of the improvement is likely caused by increases in the cells' paracrine activity, which are often transported to their target cells by exosomes. Thus, exosomes have a key role in mechanisms that regulate apoptosis, inflammation, angiogenesis, and many other biological processes that protect and repair the heart after myocardial injury. We have shown that the potency of allogeneic MSCs for myocardial repair and angiogenesis in nonhuman primates (NHPs) can be significantly improved by culturing the cells under hypoxic conditions before administration. Our results also suggested that the improvement is likely mediated by increases in the paracrine activity of the hypoxia-preconditioned cells, but the molecular factors that contributed to this increase were not identified.

METHODS In a murine MI model, cardiac function, infarct size, vascular density were measured by echocardiography, Masson staining and immunofluorescence. Aortic ring and tube formation were performed to evaluate angiogenic activity. Microarray and RNA sequencing were applied to determine the difference between exosomes from hypoxia-preconditioned MSCs (hpEXOs) and normoxia-cultured MSCs (nEXOs) and with these treated heart tissue.

RESULTS Cardiac function, infarct size, and vascular density were significantly greater in mice treated with hypoxia-preconditioned MSCs (hpMSCs) than with normoxia-cultured MSCs (nMSCs) and with hpEXOs than with nEXOs. miR-486-5p levels were significantly greater in hpEXOs than in nEXOs, which also confirmed to play a central role in exosomal mediated cardiac repair. Matrix metalloproteinase 19 (MMP19) levels were significantly lower in tissues from hpEXO-treated than nEXO-treated hearts and significantly greater in cardiac fibroblasts (CFs). miR-486-5p interacted with the 3′ untranslated region of MMP19, and downregulated MMP19 expression in CFs, while both miR-486-5p upregulation and MMP19 silencing (MMP19 siRNA) in CFs increased the angiogenic activity of ECs cultured in the CF-conditioned medium. MMP19 silencing in CFs also reduced the cleavage of extracellular vascular endothelial growth factor (VEGF), and MMP19 cleaved VEGF in solution, while miR-486-5p upregulation significantly increased the potency of nEXOs for myocardial recovery and angiogenesis in an NHP MI model.

CONCLUSIONS In summary, the results presented in this report show that exosomal miR-486-5p is one of the primary pro-angiogenic paracrine factors produced by MSCs, and that it functions by downregulating MMP19 expression in fibroblasts and the cleavage of extracellular VEGFA. Furthermore, the exosomes produced by miR-486-5p – overexpressing MSCs significantly improved measures of cardiac function, infarct size, and angiogenesis when

delivered to the infarcted hearts of NHPs without increasing the occurrence of arrhythmic complications. Collectively, these observations support additional investigations of the role of miR-486-5p, as well as the exosomes produced by other stem-cell populations, in myocardial regeneration.

GW31-e1214

SRT1720 pretreatment improves survival of aged human mesenchymal stem cells in post-infarct non-human primate hearts by promoting mitochondrial biogenesis

Zhiru Zeng, Xianbao Liu, Jianan Wang
Second Affiliated Hospital, College of Medicine, Zhejiang University

OBJECTIVES Declined function of aged stem cells diminishes the benefits of autologous cell therapy for myocardial infarction. Mitochondrial dysfunction is associated with stem cell aging and it has received increasing attention as a target to restore aged stem cell function. Silent information regulator 1 (SIRT1) has a regulatory effect on mitochondrial dynamics. We have previously demonstrated SRT1720, a specific SIRT1 activator, protected aged human mesenchymal stem cells (hMSCs) against the extrinsic apoptotic pathway by upregulating FAIM1 and those cells pretreated with SRT1720 exhibited improved survival rate and achieved increased cardiac function in a rat model of myocardial infarction (MI). However, the role of mitochondria in SRT1720 mediated inhibition of apoptosis was not elucidated. The aim of the current study was to investigate the role of mitochondria in the anti-apoptotic effects of SRT1720 pretreatment of aged mesenchymal stem cells.

METHODS To study the effect of SRT1720 pretreatment on mitochondrial function, mitochondrial contents were evaluated by mitotracker staining, mtDNA measurements and expression of mitochondrial components and mitochondrial membrane potential was assessed by TMRM staining. Transmission electron microscopy was applied to assess mitochondrial morphology. As for in vivo studies, immunosuppressed Cynomolgus monkeys were subjected to myocardial infarction and treated with vehicle treated or SRT1720 pretreated aged hMSCs cells or DMEM. Cardiac function, cardiac cell apoptosis, angiogenesis and aged hMSCs engraftment were evaluated.

RESULTS Here we report that SRT1720 protects aged hMSCs against mitochondria apoptosis pathway by increasing mitochondrial biogenesis and function. We showed that SRT1720 pretreated aged hMSCs has reduced release of cytochrome C and caspase9 activation when subjected to H_2O_2 treatment and mitochondrial morphology was better preserved indicated by transmission electron microscopy. Mitochondria contents were compared between young and aged hMSCs by quantifying mtDNA level. Consistent with previous reports, aged hMSCs had decreased mitochondrial numbers and reduced expression of PGC1A and TFAM. We found that SRT1720 increased mitochondrial biogenesis of aged hMSCs, reflected by enhanced mtDNA levels, mitotracker staining, and expression of mitochondrial components. This resulted in higher mitochondrial respiratory capacity and oxidative phosphorylation (OXPHOS) efficiency. At 3 days after transplanted in the infarcted non-human primate hearts, SRT1720 pretreated aged hMSCs had more retention rate than vehicle treated controls. And histological analysis showed that cardiac cell apoptosis was attenuated in the SRT1720 group at 3 days post MI whereas no effect of the vascular density was observed at 3 months. Concomitantly, the recovery of cardiac contractile function at 3 months post MI in the SRT1720 group tended to be better than that in the vehicle group.

CONCLUSIONS SRT1720 promotes survival abilities of aged hMSCs in infarcted non-human primate hearts by increasing mitochondrial biogenesis and function. Although further research on the efficient strategies to rejuvenate aged hMSCs is required, the present study demonstrates that regulation of mitochondrial function through enhancing mitochondrial biogenesis is a potentially effective, low-cost, and stable treatment method to improve aged mesenchymal stem cell survival.

GW31-e1215

Cardiac fibroblastic LRP1-dependent endocytosis of hepatic angiotensinogen promotes sepsis-induced myocardial dysfunction

Jiabing Rong, Yinchuan Xu, Jianan Wang
Second Affiliated Hospital, Zhejiang University School of Medicine

OBJECTIVES Sepsis-induced myocardial dysfunction (SIMD) leads to severe mortality. The renin-angiotensin system (RAS) plays an important role in SIMD. Angiotensinogen (AGT) is the only known substrate of the RAS, and here we investigated the effects and mechanisms of AGT on the development of SIMD.

METHODS Male C57BL/6 mice were intraperitoneally injected with lipopolysaccharide (LPS) to induce sepsis and taken down 6 hours later. Cardiac function was evaluated by Vevo 2100 imaging system. Plasma levels of AGT, angiotensin II (AngII) and proinflammatory cytokines were detected by ELISA. Combination of AGT and its receptor, LDP receptor related protein1 (LRP1), was confirmed by ligand blotting in cardiac fibroblasts. Furthermore, RNA sequencing of cardiac tissue was performed to uncover the role of hepatic AGT on hearts after LPS challenge.

RESULTS Intraperitoneal injection of LPS significantly activated AGT expression both in liver and heart and elevated plasma AGT level. We further generated hepatocyte-specific AGT-deficient (hepAGT-/-) mice and cardiomyocyte-specific AGT-deficient (carAGT-/-) mice. Interestingly, we found that hepAGT-/- mice triggered resistance to SIMD. Contrarily, carAGT-/- mice had a similar phenotype with wild-type (WT) littermates. Depressed plasma AGT and AngII concentrations hinted hepatic deficiency of AGT may functioned via a circulatory AngII-dependent manner. However, WT mice infused with an AT1R antagonist, losartan, partially protected from cardiac dysfunction compared to hepatic AGT deficiency, which implied that liver-secreted AGT may have an another effect on heart via an AngII-independent pathway. Furthermore, we found cardiac AngII content of hepAGT-/- mice was comparable with WT littermates while IL-1β mRNA level in heart was lower, which proved there exited a pathway which IL-1β was involved in while AngII was not. Then, we discovered that hepAGT-/- heart showed a remarkably decreased AGT protein level. However, in carAGT-/- mice, cardiac AGT expression was restrained in mRNA level but had no change in protein level compared with their WT littermates. These facts implied that cardiac AGT was mainly derived from circulation rather than synthesized locally. Furthermore, we identified liver-derived AGT entered cardiac fibroblasts via LRP1-mediated endocytosis, which in turn activated NLRP3 inflammasome and improved IL-1β production.

CONCLUSIONS Hepatocyte-specific deficiency of AGT ameliorates SIMD via preventing cardiac fibroblastic LRP1-dependent endocytosis and then decreasing NLRP3 inflammasome expression, which alleviates IL-1β releasing. These findings provide potential therapeutic targets in liver to treat SIMD.

GW31-e1216

Long noncoding RNA Cfast regulates cardiac fibrosis

Feng Zhang[1], Xuyang Fu[1], Masaharu Kataoka[2], Tian Liang[1], Feng Gao[1], Ning Liu[1], Xiaoxuan Dong[1], Xiaoyun Hu[2], Wei Zhu[1], Hong Yu[1], Xingyang Hu[1], Jianan Wang[1], DaZhi Wang[2], Jinghai Chen[1]
[1]Second Affiliated Hospital Zhejiang University School of Medicine
[2]Boston Children's Hospital, Harvard Medical School

OBJECTIVES Cardiac fibrosis occurs in most cardiac disease, reduces cardiac muscle compliance, impairs both systolic and diastolic heart function and ultimately leads to heart failure. Long noncoding RNAs (lncRNAs) are recently emerging as important regulators of a variety of biological processes. However, little is known about the expression and function of lncRNAs in cardiac fibrosis. We aimed to identify cardiac fibroblasts (CFs)-enriched lncRNAs and investigate their role in regulation of cardiac fibrosis and heart function.

METHODS We performed microarray-based transcriptome profiling on mouse infarcted heart and from Microarray analysis we found a cardiac fibroblasts-enriched lncRNA, namely Cfast. We used lentivirus system to knockdown Cfast expression to investigate the functional regulation of Cfast in cardiac fibrosis in vivo and vitro. We further performed RNA pull down to find its downstream target protein for elucidating the molecular regulation of Cfast in cardiac fibrosis.

RESULTS Knockdown of *Cfast* in cardiac fibroblast, resulted in a significant down regulation in both mRNA and protein expression of fibrotic ECM-related gene. At the same time, we observed a significant decrease of α-SMA positive cells and a noticeable attenuation of the migratory ability of *Cfast*-silenced fibroblasts. After 28 days of MI, we found that mice with *Cfast* depletion exhibited significantly improved cardiac function. Immunohistochemical analysis showed that scars of *Cfast* knockdown mice contained more cardiomyocytes compared with control hearts. Histological analysis revealed that *Cfast* inhibition significantly reduced scar formation in infracted heart as well. We found that *Cfast* depletion significantly prevented isopropanol-induced cardiac pathological fibrosis in the heart. This protective evidence was also supported by the impact on expression of the molecular marker genes, as a significant reduction of *Nppa*, *Nppb*, and *Myh7* and of cardiac fibrosis associated genes, *Col1a1*, *Col3a1*, *Eln*, and *α-Sma* upon *Cfast* depletion. Finally, we performed RNA pull-down assay to elucidate the molecular mechanism. Among analyzed lncRNAs binding partners, five proteins were detected as specifically interacted with *Cfast*. Nevertheless, considering the subcellular localizations and documented reports, we speculated COTL1 can act as a functional binding protein because COTL1 involves in TGFβ signaling pathway. To confirm the mass spectrometry data, we performed independent batch of *Cfast* RNA pull-down assay, and then used western blotting experiment to detect COTL1 after the lncRNA pull-down. The binding of COTL1 was clearly observed in *Cfast* pull-down but not in the control samples. The association of COTL1 with *Cfast* was further confirmed by RNA immunoprecipitation. Co-immunoprecipitation assays indicated that COTL1 competitively binds with TRAP1, leads to abrogate the interaction of TRAP1 with SMAD4 and thus suppresses the formation of SMAD2/3/4 complex.

CONCLUSIONS We identified a novel cardiac fibroblast-enriched lncRNA, named *Cfast*, as an important regulator in the process of cardiac fibrosis. *Cfast*

depletion clearly exhibits protective effects from pathological fibrotic remodeling and improves cardiac function upon pathological stress. *Cfast* exerts its function via binding COTL1 and consequently affects TRAP1/SMAD mediated down cascades of fibrotic signal. Our study indicates that *Cfast* may represent a potential target in antifibrotic RNA therapy in heart diseases.

GW31-e1217

Long non-coding RNA LUCAT1 influences the survival ability and therapeutic effect of MSCs and related mechanisms exploration

Yue Tao, Rongrong Wu, Xinyang Hu, Jianan Wang
Second Affiliated Hospital of Zhejiang University School of Medicine

OBJECTIVES Bone marrow mesenchymal stem cells (MSCs) transplantation is a new hope for the treatment of myocardial infarction, but low survival rate of engrafted MSCs mainly limits the therapeutic effect of MSCs. Illustrating mechanism of stem cells survival and improving the therapeutic effect of engrafted cells are primary issues remained to be resolved. In this study, long non-coding RNA was used to improve the anti-apoptotic ability of MSCs and the mechanism involved was explored.

METHODS After 24 hours under normal culture of hypoxia treatment, MSCs were under the screening process of lncRNA sequencing, filtered for lncRNA LCUAT1. By lentivirus editing LUCAT1 level of MSCs and injecting the MSCs into the border zone of the infarcted heart, we aimed to find out whether LUCAT1 influences the apoptosis of MSCs and the therapeutic effect of MSCs for myocardial infarction. GFP staining 3 days after myocardial infarction, echo detection and Masson staining 28 days after myocardial infarction were conducted. Furthermore, through mass spectrometry analysis of proteins that were co-IP by LUCAT1 and RIP experiment, we screened regulatory proteins in the nucleus which LUCAT1 could bind to. Synthesis of the results from mass spectrometry and transcriptome sequencing of MSCs after LUCAT1 knocked down, we singled out the specific target gene regulated by LUCAT1. With CHIP assay and luciferase assay, we explored LUCAT1 may manipulate the apoptosis of MSCs by recruiting regulatory protein to target gene promoter.

RESULTS We found that LUCAT1 knock down decreased cell apoptosis resistance while LUCAT1 over expression showed opposite results. GFP staining showed that survival rate of the MSCs three days post injection was reduced, and the echo results 28 days after the myocardial infarction indicated that the cardiac function was worse than control group. In addition, the Masson staining results after 28 days showed that the scar area of heart was increased. Overexpression of LUCAT1 can enhance the anti-apoptotic ability of cells and the therapeutic effect after myocardial infarction. It was found that LUCAT1 could bind to a lot of regulatory proteins in the nucleus, RIP results showed LUCAT1 had strong binding ability with JMJD6. Through transcriptome sequencing of MSCs after LUCAT1 knock down, the expression of FOXQ1, an anti-apoptotic protein, was significantly decreased compared with control group. When LUCAT1 was overexpressed, FOXQ1 expression increased significantly. Lentivirus knockdown of JMJD6 in mesenchymal decreased FOXQ1 expression, but overexpression had no effect on FOXQ1 expression. Luciferase experiment verified that JMJD6 could bind to the promoter region of FOXQ1. CHIP detection detected that JMJD6 act in FOXQ1 promoter region on the methylation sites H3R2me2a and H4R3me2s reported. It was also found that the methylation level of these two sites increased when LUCAT1 was knocked down, while the methylation enrichment of H4R3me2s decreased when LUCAT1 was overexpressed and H3R2me2a showed no significant change.

CONCLUSIONS LUCAT1 can improve the viability of MSCs and enhance its therapeutic effect on myocardial infarction by recruiting JMJD6 to the anti-apoptotic protein FOXQ1 promoter, affecting the methylation enrichment level of H4R3me2s in the promoter region and thus changing FOXQ1 expression level.

GW31-e1220

Flavin containing monooxygenase 2 confers cardiac protection via unfolded protein response signaling modulated by disulfide bond catalysis

Qingnian Liu, Yue Tao, Hao Ding, Changchen Xiao, Yu Zhou, Cheng Ni, Changle Ke, Jingyi Wang, Rongrong Wu, Lin Fan, Xianpeng Wu, Jing Zhao, Yan Wu, Xinyang Hu, Jianan Wang
Second Affiliated Hospital, Zhejiang University School of Medicine

OBJECTIVES Myocardial infarction (MI) is characterized by cardiac dysfunction and increased cardiomyocyte death, induced mainly by apoptosis. Using an unbiased transcriptome analysis, we identified flavin containing monooxygenase 2 (FMO2) as one of the top-ranked genes involved in the process of MI. In this study, we investigate the roles of FMO2 in ischemic injury and its potential mechanisms. FMO2 exhibits the cardiac protection from MI injury.

METHODS Male SD rats receiving either adeno-associated virus serotype 9 containing FMO2 shRNA particles (AAV-shFMO2) or FMO2 (AAV-FMO2), and FMO2 knockout rats were subjected to myocardial infarction surgery. Cardiac function, fibrosis, and apoptosis were examined in these rats and related cellular and molecular mechanisms were investigated.

RESULTS Cardiac ischemia injury was associated with significant increases of FMO2 levels both in ex vivo and in vivo models. Loss of FMO2 significantly enhanced cardiomyocyte apoptosis and deteriorated cardiac function accompanied by augmented infarct size in infarcted rat hearts, while elevated expression of FMO2 exhibited the opposite results. Mechanically, located on the ER membrane, FMO2 inhibited activation of ER stress-initiated apoptotic proteins including caspase 12 and C/EBP homologous protein (CHOP), via down-regulating upstream unfolded protein response (UPR) pathway. Furthermore, we found that FMO2, as a novel chaperone in ER, directly catalyzed disulfide-bond synthesis to facilitate proteins folding. Finally, structure analysis of FMO2 revealed the active site GVSG for disulfide-bond catalysis, which was confirmed by the molecular docking experiment of GSH with FMO2. However, FMO2 with GVSG mutation failed to catalyze disulfide-bond formation and lost protection from ER stress or apoptosis in cardiomyocytes.

CONCLUSIONS FMO2 confers cardiac protection from ischemic damage due to improved cardiomyocyte apoptosis through UPR pathway, which is mediated by disulfide-bond catalysis at GVSG active site. Our findings uncover a novel FMO2-involved regulatory mechanism which could serves as a potential therapeutic target for ischemic cardiovascular diseases.

GW31-e1221

Knockdown of estrogen-related receptor α inhibits valve interstitial cells calcification in vitro via regulating heme oxygenase 1

Wangxing Hu, Rongrong Wu, Chenyang Gao, Xianbao Liu, Jianan Wang
Second Affiliated Hospital, Zhejiang University School of Medicine

OBJECTIVES Calcific aortic valve disease (CAVD) is the most common valvulopathy in developed countries and is characterized by inflammation, extracellular matrix (ECM) remodeling and calcification, leading a narrowing of the valve and the consequential obstruction of the cardiac outflow. A lot work has shown that valve interstitial cells within the aortic valve cusps when stimulated could differentiate toward an osteoblast-like cell and deposit bone-like matrix that leads to leaflet stiffening and calcific aortic valve stenosis. However, the mechanisms that promote pathological phenotypes in valve interstitial cells are still not clear. Nuclear receptors regulate the transcription of genes involved in mitochondrial biogenesis in a tissue-specific manner. Accumulating evidence has suggested that NRs make contributions to calcific vascular and valvular disease. Estrogen-related receptor α (ERRα) is an orphan nuclear hormone receptor capable of regulating transcription of genes involved in multiple cellular and physiological processes. However, the role of ERRα in valve calcification has not been investigated to date. The aim of the present study was to examine the role of ERRα in aortic valve calcification.

METHODS Aortic valve leaflets were collected from CAVD patients (N=10) undergoing aortic valve replacement, and Control samples (no calcified aortic valve tissue) were taken from age-matched patients who had severe insufficiency without calcification (n=7) and patients who underwent heart transplantation due to late stage of cardiomyopathy (n=3). We compared the protein level of ERRα by Western blot and immunohistochemistry between the non-calcific valve and the calcific ones. In vitro study, valve interstitial cells (VICs) were isolated from the control aortic valve cusps and cultured in calcifying medium to induce calcification. Treated with 10 μM XCT790 or ERRα small interfering RNA silencing to inhibit ERRα or overexpression of ERRα by lentivirus, the samples were assessed for calcium nodule formation, and calcific markers using alizarin red staining, ALP enzyme activity assay, Western blot and qPCR. The effect of ERRα on osteoblastic transdifferentiation and its downstream pathway were also studied.

RESULTS In this study, we have found that the protein level of ERRα is upregulated in CAVD samples versus the controls; moreover, during osteogenic differentiation of hVICs, the expression of ERRα is increased as the cultural time increased. Furthermore, we found that inhibition of ERRα prevented OM-induced upregulation of Runx2 and ALP. The ALP activity was markedly attenuated by ERRα silencing. Alizarin red staining revealed that shRNA-mediated ERRα knockdown markedly suppressed calcified nodules formation. Meanwhile, the content of calcium was significantly reduced. We also proved that ERRα overexpression enhances osteogenic potential of hVICs. In addition, RNA sequencing results suggested that heme oxygenase-1 (Hmox1) was a downstream target of ERRα and it was further confirmed by western blot. Additionally, we also found that downregulation of Hmox1 with shHmox1 efficiently reversed the inhibition of calcification induced by ERRα shRNA in hVICs. ChIP-qPCR and luciferase assay indicated that Hmox1 was negatively regulated by ERRα.

CONCLUSIONS The present results indicate that knockdown of ERRα could impair the osteoblastic transdifferentiation of VICs, suggesting that inhibition of ERRα is a potential therapeutic strategy for the prevention of aortic valve calcification.

GW31-e1244

Catabolic defect of BCAA promotes coronary microvascular dysfunction and diabetic cardiomyopathy via inhibition of STIM1-mTORC2-Akt1 passway in mouse coronary ECs during type 2 diabetes

Chong Huang[1], Xiong Guo[1,2], Ling Tao[1]
[1]Department of Cardiology, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, China
[2]Department of Cardiology, No. 952 Hospital of People's Liberation Army, Golmud, Qinghai, China

OBJECTIVES The study is designed to explore the role BCAA catabolic defect plays in the coronary microvascular dysfunction (CMD) and diabetic cardiomyopathy (DCM) in T2DM.

METHODS Genetically BCAA catabolism-defective mice ($PP2Cm^{-/-}$) and BCAA catabolism-enhanced mice ($PP2Cm^{OE/OE}$) were built and T2DM was induced in 3 groups of mice (WT, $PP2Cm^{-/-}$, $PP2Cm^{OE/OE}$) by high-fat diet feeding. In the diabetic duration, the cardiac function was monitored in each group of mice. After 12 weeks, the microvascular density (MVD) in heart tissue and leaky phenotype of the myocardial microvessel in each group of mice were detected with immunohistochemical staining. Also, cell survival, growth, migration and vascular permeability were tested in mouse coronary ECs (MCECs) isolated from each group of mice in vitro.

RESULTS $PP2Cm^{-/-}$ mice manifested deteriorated loss of cardiac function compared with WT mice. The MVD in heart tissue was significantly lower and myocardial microvessel leakage was markedly increased in $PP2Cm^{-/-}$. Meanwhile, In vitro, the MCECs isolated from $PP2Cm^{-/-}$ showed aggravated cell function loss of proliferation, migration and increased vascular permeability compared with WT. However, $PP2Cm^{OE/OE}$ mice manifested preserved cardiac function and MCECs function during T2DM. As to the mechanism, BCAA treatment markedly reduced expression of STIM1 and thereby inhibited mTORC2-Akt1 passway in MCECs. Restoration of STIM1 expression and mTORC2-Akt1 regain cell function of MCECs.

CONCLUSIONS BCAA catabolic defect promotes CMD and DCM in T2DM. Downregulation of STIM1 in MCECs induced by catabolic defect of BCAA and resulting inhibition of mTORC2-Akt1 were the potential mechanism.

GW31-e1248

CEMIP: a novel regulator in vascular smooth muscle cell proliferation and contraction

Qi Li, Bochuan Li, Yi Zhu
Tianjin Key Laboratory of Metabolic Diseases; Key Laboratory of Immune Microenvironment and Disease (Ministry of Education); Collaborative Innovation Center of Tianjin for Medical Epigenetics and Department of Physiology and Pathophysiology, Tianjin Medical University, Tianjin, China

OBJECTIVES CEMIP (cell-migration-inducing and hyaluronan-binding protein) is a newly discovered macromolecular protein. It plays an important role in the proliferation and migration of tumors. Bioinformatics analysis suggests that it is highly expressed in smooth muscle cells. Vascular smooth muscle cells are critical in maintaining vascular homeostasis. We aim to investigate the role of CEMIP in proliferation and contraction of vascular smooth muscle cells (VSMCs).

METHODS In vivo, we established tamoxifen-inducible smooth muscle specific CEMIP-deficient ($CEMIP\Delta^{smc}$) mice. Both $CEMIP^{fl/fl}$ mice and $CEMIP\Delta^{smc}$ mice were subjected to wire-guided common carotid injury to evaluate the neointima formation. Simultaneously, blood pressure was monitored by non-invasive tail-cuff system. Aortas and second-order mesenteric arteries were isolated from male mice and were used to evaluate the vascular tone by isometric force measurement in wire myograph. In vitro, flow cytometry, ki67 staining, cell count, cell scratch and transwell assay were used to detect elicited human aortic smooth muscle cells (HAoSMCs) proliferation and migration. Contractile gel assay was used to detect contraction. Small interfering RNA (siRNA) transfection, real-time PCR and western blot were utilized for further verifying the detailed effects of CEMIP on VSMCs phenotypes.

RESULTS CEMIP deficiency could significantly inhibit the platelet-derived growth factor-BB (PDGF-BB) induced VSMCs proliferation and migration. Compared with $CEMIP^{fl/fl}$ mice, the neointimal hyperplasia of $CEMIP^{\Delta smc}$ mice was dramatically reduced. Meanwhile, loss of CEMIP also reduced VSMCs contractile phenotype-dependent markers expression accompanied with less related contractile area. This phenomenon was also confirmed in CEMIPΔsmc mice aortas. In accordance, the blood pressure of CEMIPΔsmc mice was lower than littermate control mice under physiological state and angiotensin II-induced hypertension. The vascular ring experiments also confirmed that the CEMIP reduction could markedly inhibit phenylephrine-induced vasoconstriction, while not response to ET-1, PGF2α and 5-hydroxytryptamine.

CONCLUSIONS Our results demonstrate the significance of CEMIP in regulating vascular smooth muscle proliferation and vessel tension maintenance.

GW31-e1249

Activin A inhibits foam cell formation and up-regulates ABCA1 and ABCG1 through ALK-SMAD signaling pathway in RAW 264.7 macrophages

Hao Wang, Peng Zhang, Xiahuan Chen, Meilin Liu
Department of Geriatrics, Peking University First Hospital, Beijing 100034, People's Republic of China

OBJECTIVES Activin A, a member of the transforming growth factor-β superfamily, has been reported to play important roles in regulating macrophages foam cell formation. However, the underlying mechanisms remain to be elucidated. The purpose of this study is to investigate the effects of activin A on expressions of cholesterol influx/efflux transporters and underlying molecular mechanisms.

METHODS The effects of activin A on Dil-ox-LDL uptake by RAW 264.7 macrophages were analyzed by confocal microscopy and flow cytometry. The mRNA and protein levels of cholesterol influx/efflux transporters were examined by RT-qPCR and western blot analysis, respectively. To investigate whether ALKs are involved in the activin A-mediated inhibition of foam cell formation, macrophages were pretreated with selective ALKs inhibitor, SB431542, then co-treated with ox-LDL and activin A. The involvement of SMAD2, SMAD3 and SMAD4 were confirmed by transfection with specific siRNAs.

RESULTS The results showed that activin A decreased Dil-ox-LDL uptake in RAW 264.7 macrophages. The mRNA and protein levels of SR-A1 was significantly down-regulated in activin A treated macrophages, while the expression of ABCA1 and ABCG1 was up-regulated. Pre-treatment with SB431542 reversed the activin A-mediated inhibition of foam cell formation. Knockdown of SMAD2 reversed the activin A-mediated reduction of Dil-ox-LDL uptake and SR-A1 expression. However, knockdown of SMAD3 or SMAD4 did not have such effect. Meanwhile, knockdown of either SMAD2, SMAD3 or SMAD4 reversed the activin A-mediated upregulation of ABCA1 and ABCG1.

CONCLUSIONS Activin A inhibits ox-LDL-induced foam cell formation in RAW 264.7 macrophages. The molecular mechanism may be related to the down-regulation of SR-A1 and up-regulation of ABCA1 and ABCG1 through ALK-SMAD signaling pathway.

GW31-e1263

LCZ696 improved ethanol induced cellular apoptosis and cardiac inflammation in vitro

Ke Lin, Weijian Huang
The Key Laboratory of Cardiovascular Disease of Wenzhou, Department of Cardiology, The First Affiliated Hospital of WenZhou Medical University, WenZhou

OBJECTIVES LCZ696 was confirmed to be an effective mixture for numerous heart failure, whether it would be effective for alcoholic cardiomyopathy was still unknown. In this study, we aimed to elucidate the role of LCZ696 in ethanol induced cardiac injury and to explore possible mechanisms.

METHODS In vitro model of ethanol induced cardiac injury was established as previously reported. In our study, 10 μM and 20 μM LCZ696 was pretreated for 1 hour, and then 200 mM ethanol was added into the medium for 8 h. Cells were sacrificed for further study. Total protein was collected, and the expression of Bax, Bcl-2, caspase-3, p-p65, p-65 and GAPDH was detected using western blotting. And the expression of TNF-α, IL-1β and IL-6 was detected using qPCR.

RESULTS After the treatment of 200 mM ethanol for 8 h, expression of caspase-3 and Bax was elevated while the expression of Bcl-2 was decreased, indicating the cardiomyocytes apoptosis. However, treatment of LCZ696 could partially reverse the condition with declined expression of caspase-3, Bax and increased Bcl-2. Besides, NF-κB signaling was also detected. Two hundred millimolar ethanol for 6 h could significantly activate NF-κB with the increasing phosphorylation of p65. And the pretreatment of LCZ696 could effectively inhibit the activation, with the decrease of p-p65. Similarly, pretreatment of LCZ696 could also inhibit ethanol induced overexpression of TNF-α, IL-6 and IL-1β.

CONCLUSIONS In this study, we confirmed that LCZ696 could protect cardiomyocytes from ethanol induced cellular apoptosis and inflammation.

GW31-e1264

Pitavastatin activates mitophagy to protect EPC proliferation through a calcium-dependent CAMK1-PINK1 pathway in atherosclerotic mice

Jie Yang, Lan Huang
Department of Cardiology, the Second Affiliated Hospital, Third Military Medical University (Army Medical University), Chongqing, China

OBJECTIVES Statins play a major role in reducing circulating cholesterol levels and are widely used to prevent coronary artery disease and stroke. Although

they were recently confirmed to up-regulate mitophagy, little is known about the molecular mechanisms underlying statin-induced mitophagy. Whether mitophagy induction contributes to endothelial progenitor cell (EPC) proliferation also remains to be elucidated. Here, we explored the role and mechanism underlying statin (pitavastatin, PTV)-activated mitophagy in EPC proliferation using atherosclerotic mice.

METHODS ApoE-/- mice were fed a high-fat diet for 8–16 weeks to induce atherosclerosis. GFP-mRFP-LC3 and mt-Keima were used to evaluate autophagy and mitophagy flux, respectively. 3-MA and Atg7 silencing were used to inhibit autophagy. MMP assay kit, JC-1 and MitoSox red were employed to measure mitochondrial function. Calcium concentration was analyzed in cytoplasm and mitochondria in intact cells through Fluo-3-AM and Rhod2-AM, respectively. Cell proliferation was checked by the xCelligence Real-Time Cell Analyzer instrument. Mitochondrial morphology and autophagosomes were observed by transmission electron microscopy. Western blots were employed to detect the expression of protein in cytoplasm or mitochondria.

RESULTS EPC proliferation decreased in ApoE-/- mice, and was accompanied by mitochondrial dysfunction and mitophagy impairment via the PINK1-PARK2 pathway in comparison to those of normal diet mice. PTV reversed mitophagy and reduction in proliferation. Mitophagy inhibition by 3-MA treatment or by silencing Atg7 blocked PTV-induced proliferation improvement, suggesting that mitophagy contributed to the EPC proliferation increase. PTV elicited mitochondrial calcium release into the cytoplasm and further phosphorylated CAMK1. CAMK1 served as a PINK1 kinase to reverse the PINK1-PARK2 pathway of mitophagy and mitochondrial dysfunction in EPCs derived from atherosclerotic mice.

CONCLUSIONS Our findings describe a novel molecular mechanism of mitophagy activation, where mitochondrial calcium release promotes CAMK1 phosphorylation of threonine177 before phosphorylation of PINK1 at serine228, which recruits PARK2 and phosphorylates its serine65 to activate mitophagy. Our results further account for the pleiotropic effects of statins on the cardiovascular system and provide a promising and potential therapeutic target for atherosclerosis.

GW31-e1267

Harmine alleviates atherogenesis by inhibiting disturbed flow-mediated endothelial activation via PTPN14/YAP

Yujie Yang, Jinlong He
Tianjin Medical University

OBJECTIVES Disturbed flow induces endothelial dysfunction and contributes to uneven distribution of atherosclerotic plaque. Emerging evidence suggests that harmine, a natural small molecule in extracts of *Peganum harmala*, has potent beneficial activities. Here, we investigated whether harmine has an atheroprotective role under disturbed flow and the underlying mechanism.

METHODS Mice of ApoE$^{-/-}$, LDLR$^{-/-}$ and endothelial cell (EC)-specific overexpression of Yes-associated protein (YAP) in ApoE$^{-/-}$ background were fed with a western diet and given harmine for 4 weeks. Atherosclerotic lesion size, cellular composition and expression of inflammatory gene in the aortic roots were observed. Human umbilical vein ECs (HUVECs) were treated with oscillatory shear stress (OSS) and harmine, and also used for proteomic analysis.

RESULTS Harmine retarded atherogenesis in both ApoE$^{-/-}$ and LDLR$^{-/-}$ mice by inhibiting the endothelial inflammatory response. Mechanistically, harmine blocked OSS-induced YAP nuclear translocation and EC activation by reducing phosphorylation of YAP at Y357. Overexpression of endothelial YAP blunted the beneficial effects of harmine in mice. Proteomic study revealed that tyrosine-protein phosphatase non-receptor type 14 (PTPN14) could bind to YAP. Moreover, harmine increased PTPN14 expression by stabilizing its protein level and inhibiting its degradation in proteasome. PTPN14 knockdown blocked the effects of harmine on YAP^{Y357} and EC activation. Finally, overexpression of PTPN14 mimicked the effects of harmine and ameliorated atherosclerosis in a partial ligation mouse model.

CONCLUSIONS Harmine alleviated OSS-induced EC activation via a PTPN14/YAP^{Y357} pathway and had a potent atheroprotective role.

GW31-e1274

Role of thioredoxin-interacting protein in mediating endothelial dysfunction in hypertension

Ruiyu Wang, Jing Huang
Department of Cardiology, the Second Affiliated Hospital of Chongqing Medical University

OBJECTIVES Excessive oxidative stress is a major causative factor of endothelial dysfunction in hypertension. As an endogenous pro-oxidant, thioredoxin-interacting protein (TXNIP) contributes to oxidative damage in various tissues. The present study was aimed to investigate the role of thioredoxin-interacting protein (TXNIP) in mediating hypertension-induced endothelial dysfunction.

METHODS In vivo, 30 rats were divided into the control, sham, and hypertension groups (n=10 per group) randomly, and the experimental model of hypertension was conducted by two kidney one clip (2K1C) surgery. Blood pressure and heart rate were monitored regularly. At 4 weeks after the 2K1C surgery, multiple vascular tissues (carotid artery and aorta) and plasma were harvested for TXNIP and plasma angiotensin (Ang) II concentration detection, respectively. Subsequently, 32 rats were divided into the sham, sham+resveratrol (as a TXNIP inhibitor), hypertension and hypertension+resveratrol groups (n=8 per group). Endothelium-dependent vasodilation, DHE staining and Western blot were performed in the aorta of rats. In vitro, primary human aortic endothelial cells (HAECs) were stimulated with human Ang II to mimic endothelial injury in hypertension. Losartan (an Ang II type I receptor blocker) and PX-12 (an inhibitor of thioredoxin) were administered to HAEC in the presence of Ang II stimulation. In addition, TXNIP-specific siRNA and thioredoxin (TRX)-loaded GV230 plasmid were constructed and transfected into HAEC. The oxidative stress, cell apoptosis, eNOS activation and intracellular nitric oxide (NO) production were evaluated.

RESULTS In vivo, TXNIP was upregulated in vascular endothelial cell in parallel with elevated plasma Ang II in hypertensive rats. Inhibition of TXNIP by resveratrol improved the endothelium-dependent vasodilation, restored eNOS expression/activation and suppressed systemic and vascular oxidative stress in hypertension rats. In vitro, TXNIP was substantially increased in Ang II-stimulated HAECs in a time and concentration-dependent manner, and such increase could be partly reversed by Losartan. TXNIP knockdown by siRNA alleviated Ang II-induced oxidative stress and cell apoptosis as evidenced by a reduction of ROS generation and alterations in the protein levels of NOX2, NOX4, SOD2, ASK1, cleaved-Caspase 3 and the ratio of BCL2/BAX. In addition, inhibition of TXNIP effectively rescued the impaired NO production and maintained the ratios of p-eNOS (ser 1177)/eNOS and p-AKT (ser 473)/AKT in Ang II-treated HAECs. Importantly, TXNIP knockdown significantly upregulated TRX expression and promoted the nuclear translocation of TRX to activate the DNA repair related-transcription factors (AP-1 and REF-1). However, inhibiting TRX with PX-12 completely blunted the protective effect of silencing TXNIP on HAECs, and overexpression of TRX effectively upregulated p-eNOS (ser 1177)/eNOS ratio and improved NO production in HAECs under Ang II stimulation.

CONCLUSIONS Our study, for the first time, suggests that TXNIP contributes to oxidative stress and endothelial dysfunction in hypertension, and these effects are dependent on the antioxidant capacity of TRX. Maintaining vascular TXNIP/TRX homeostasis may be beneficial in the exploration of new treatments for hypertension and other cardiovascular diseases.

GW31-e1281

Therapeutic effect and prognosis of intraosseous norepinephrine infusion in a minipig model of septic shock

Yupeng Wang, Yanyan Liu, Lingyun Zu
Peking University Third Hospital

OBJECTIVES We compared the success rate on the first attempt, the procedure time, operator satisfactions with the instruments used, the pain score and complications between intraosseous (IO) access and central venous catheterization (CVC) in critically ill Chinese patients for whom two attempts to establish peripheral venous access had failed or for whom treatment was delayed.

METHODS Experimental minipigs were chosen for this study and were randomly divided into intraosseous access and central venous catheter groups (n=4 for each group). Cecal ligation and puncture was performed to establish the septic shock model. Immediately after the septic shock model was established, the intraosseous access group received norepinephrine via tibial intraosseous access infusion, whereas the central venous catheter group received norepinephrine via intravenous infusion of the internal jugular vein. The vital signs, blood pressure recovery time, post-septic shock survival time, and total survival time of the minipigs were recorded.

RESULTS There were no statistically significant differences between the two groups in terms of their vital signs (blood pressure, heart rate, temperature), blood routine, myocardial enzymes, kidney function, liver function, lactate, interleukin-6 and interleukin-8 at pre-Cecal ligation and puncture, 4 h post-Cecal ligation and puncture, 10 h post-Cecal ligation and puncture, and shock onset (P>0.05). There was no significant difference in the time needed to establish the septic shock model between the intraosseous access and central venous catheter groups [13.5 (10.5–25.5) vs. 14.5 (10.5–20.0) hours, P=0.886]. There was no significant difference in the mean arterial pressure at shock onset between the intraosseous access and central venous catheter groups [59.5 (57.0–62.0) vs. 61.0 (59.0–63.0) mmHg, P=0.343]. There was no significant difference in blood pressure recovery time between minipigs receiving intraosseous access and central venous catheter norepinephrine infusion [40 (20–60) vs. 30 (20–60) minutes, P=0.686]. The cumulative norepinephrine dose during the period of blood pressure recovery time did not differ significantly between the intraosseous access and central venous catheter groups [10.0 (3.0–21.0) vs. 6.5 (3.0–21.0) μg/kg, P=0.686]. There was no significant difference in the mean arterial pressure increase during the period of blood pressure recovery time

between the intraosseous access and central venous catheter groups [14.5(10.0–24.0) vs. 13.0 (10.0–17.0) mmHg, P=0.686]. The two groups did not show statistically significant differences at 6 h after norepinephrine infusion in terms of vital signs, blood routine, myocardial enzymes, kidney function, liver function, lactate, interleukin-6, and interleukin-8 (P>0.05). There were no significant differences in the post-septic shock survival time [7.75 (6.50–10.00) vs. 8.75 (6.50–14.00) hours, P=0.686] and total survival time [21.25 (16.50–35.50) vs. 25.75 (19.50–26.50) hours, P=0.686] of minipigs in the intraosseous access and central venous catheter groups.

CONCLUSIONS In the experimental minipig model of septic shock, tibial intraosseous access and central venous catheter infusion of norepinephrine achieved same therapeutic effect on hypotension and survival time. If peripheral vascular access cannot be established during septic shock, intraosseous access norepinephrine infusion can be used to correct the hypotensive state.

GW31-e1286

The role of transcriptional co-activator p300 in high hydrostatic pressure-induced atrial fibrosis

Shenghuan Yu[1,2,3], Long Zeng[1,2,3], Wei Wei[1,3]
[1]Department of Cardiology, Guangdong Cardiovascular Institute
[2]Guangdong Cardiovascular Institute, Key Laboratory of Clinical Pharmacology, Guangdong Provincial People's Hospital Medical Research Center, Guangdong Academy of Medical Sciences
[3]School of medical, South China University of Technology

OBJECTIVES To investigate the role of co-transcriptional activator p300 in atrial fibrosis caused by hydrostatic pressure.

METHODS Collect the left atrial appendage tissue of three groups of patients with sinus rhythm, simple atrial fibrillation, hypertension and atrial fibrillation, and detect the expression of p300 protein and fibrotic factors Collagen Type I Alpha 1 (Col1A1), Collagen Type III Alpha 1 Col3A1, matrix metalloproteinase 2 (MMP2), matrix metalloproteinase 9 (MMP9), Smad3, p-Smad3 and transforming growth factor-β (TGF-β) in the three groups of left atrial appendage tissue by western blot. Primary cultured atrial appendage fibroblasts of 8–12 weeks C57BL/6 mice, and cultured with 0 mmHg, 20 mmHg and 40 mmHg hydrostatic pressure; further, the fibroblasts cultured under 0 mmHg and 40 mmHg pressure were treated with p300 HAT specific inhibitor curcumin and p300 interfering RNA, respectively, and the changes in the expression of p300 protein and fibrosis indicators in the cells were detected.

RESULTS The expressions of p300 protein and fibrosis indicators in patients with hypertension with atrial fibrillation were significantly higher than those of patients with atrial fibrillation or sinus rhythm (P<0.05). Under high hydrostatic pressure, the expressions of p300 protein and fibrosis indicators of mouse atrial fibroblasts increased and were gradient-dependent (P<0.05). After addition of p300 HAT-specific inhibitor curcumin and p300 interfering RNA, the increase of p300 and fibrosis indicators protein expression was reversed (P<0.05).

CONCLUSIONS p300 is involved in atrial fibrosis induced by high hydrostatic pressure.

GW31-e1289

Sirt5 dependent succinylation of PDH induces atrial fibrillation by regulating the glycometabolism in atrial myocytes

Yue Yuan, Xuejie Han, Xinbo Zhao, Xin Bi, Yongtai Gong, Xiaoxu Duan, Yue Li
The First Affiliated Hospital of Harbin Medical University

OBJECTIVES Atrial glusose metabolism is dysregulated in atrial fibrillation (AF), but its precise molecular mechanism and its role in the progression of AF still remain unclear. Recent studies have reported that succinylation plays an important role to regulate cellular glucose metabolism. We hypothesize that downregulation of Sirt5 could induce PDH succinylation and suppress its activity, which promotes dysregulation of glucose metabolism resulting in atrial electrical and structural remodeling and the occurrence and persistence of AF.

METHODS We use the metabonomics, transgenic animal model, comprehensive techniques of bioinformational and functional biology to elucidate the role and mechanism of Sirt5 mediated succinylation in atrial abnormal glucose metabolism and progression of atrial fibrillation, by targeting regulation of PDH.

RESULTS We previously found that (1) The level of succinylated PDH, the essential enzyme to glucose metabolism, markedly increased in atrial tissues of AF patients accompanied with the downregulation of Sirt5, the key factor of succinylation. (2) Sirt5 knockout increased the level of PDH succinylation in atrial tissues, which resulted in the incidence and persistence of AF. (3) Overexpression of Sirt5 could prevent tachypacing-induced PDH succinylation, improve glucose metabolism and inhibit apoptosis and ion channel dysregulation in atrial myocytes.

CONCLUSIONS Sirt5 dependent succinylation of PDH drives the dysregulation of glucose metabolism resulting in atrial remodeling and the occurrence and persistence of AF.

GW31-e1291

Dapagliflozin rescues vasculogenic capacity of endothelial progenitor cells in diabetic limb ischemia via AMPK-mediated inhibition of inflammation and oxidative stress

Bing Dong, Wenhao Xia
The First Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES Previous clinical studies have suggested that beyond the on-target of lowering blood glucose, SGLT2 inhibitors offers a significant reduction in major cardiovascular events in type 2 diabetes mellitus (T2DM) patients. Endothelial progenitor cells (EPCs) has proven great potential for endothelial injury repairing in vascular complications. This study aimed to evaluate the effect of dapagliflozin (DAPA) on EPCs in diabetes and the underlying mechanism involved with a focus on inflammation and oxidative stress.

METHODS This study enrolled 62 T2DM patients (DM group) and 60 matched healthy control participants (Control group). The vasculogenic capacity of EPCs were compared *in vitro* (migration, adhesion, tube formation abilities) and *in vivo* (limb ischemia model). Inflammation marker genes (IL-1β, IL-8, TNF-α and MCP-1) and oxidative stress genes (SOD-2, HO-1, TXN and CAT) expression were determined by RT-PCR. The AMPK signaling were tested by Western blot.

RESULTS T2DM EPCs demonstrated a declined *in vitro* and *in vivo* vasculogenic capacity of EPCs Inflammation and oxidative stress maker genes expression were significantly elevated in T2DM, which was accompanied with decreased phosphorylation of AMPK. DAPA restored AMP/ATP ratio to trigger AMPK activation and decreased the level of inflammation and oxidative stress, which ultimately leads to restored vasculogenic capacity of EPC. Moreover, the enhanced functions of EPCs by DAPA were blocked by AMPK inhibitors.

CONCLUSIONS Dapagliflozin rescues vasculogenic capacity of endothelial progenitor cells in Diabetic Limb Ischemia via AMPK-mediated inhibition of inflammation and oxidative stress. Up-regulation of AMPK signaling by DAPA may be a novel therapeutic intervention for vasculogenic capacity of EPCs. Our findings provide at least a partial explanation for the mechanism underlying the DAPA off target effect of vascular protective.

GW31-e1294

Smooth muscle cells specific knockout of NDUFA13 ameliorates vascular injury

Hongye Chen, Zhenjie Liu, Yong Sun, XuanHao Wang, HaiQiong Zhen, LianLian Zhu, XiangMin Kong, Wei Zhu, Jianan Wang
The Second Affiliated Hospital, Zhejiang University School of Medicine

OBJECTIVES NADH dehydrogenase (ubiquinone) 1 alpha subcomplex subunit 13 is a subunit of Mitochondrial Respiratory Complexes I, namely NDUFA13. Our previous study shows that a moderate downregulation of NDUFA13 could protect against apoptosis and decrease cardiac ischemia reperfusion injury by generating a mild increase in ROS. This indicates that NDUFA13 might be a potential therapeutic target for treating cardiac injury. However, it remains unexplored regarding its role in vascular homeostasis. Therefore, our present study is designed to investigate the expression profile of NDUFA13 in an existing aortic aneurysm, and smooth muscle cell (SMC) specific NDUFA13 knock-out mice were established to study its function and mechanism in pathological process of vascular injury.

METHODS Immunohistochemistry staining of NDUFA13 was conducted in human and mouse aortic aneurysm tissues compared with normal aorta. Bioinformatic analyze was applied to find the expression profile of NDUFA13 in human vascular disease including aneurysm, dissection and hereditary vascular disease. NDUFA13$^{fl/fl}$ mice were crossed-bred with SM22-Cre^{ERT+} mice to generate SM22-Cre^{ERT+} NDUFA13$^{fl/fl}$ mice and SM22-Cre^{ERT-} NDUFA13$^{fl/fl}$ mice. By injecting tamoxifen at 75 mg/kg/d for 5 consecutive days, NDUFA13 was successfully knocked out. Twelve to fourteen weeks old male mice underwent abdominal aneurysm induction by elastase (>4.0 U/mg) perfusion for 10 minutes. After 14 days, aorta were gathered for general imaging, diameter measurement, hematoxylin-eosin (H&E), Verhoeff Van Gieson (EVG) staining and elastin integrity grading score. Another model was also established and utilized to induce thoracic aortic aneurysm and dissection in 3–4 weeks old mice by water intake of 3-Aminopropionitrile fumarate salt (BAPN) at 1 g/kg/Day for 4 weeks. Aneurysm size, formation and death rate, histomorphology data were analyzed. In vitro study was conducted in MOVAS and SMC to explore the underline mechanism in metabolism and programmed cell death.

RESULTS NDUFA13 expression is dramatically increased in aortic aneurysm (P<0.001), both in human and mouse aneurysm tissue. Bioinformatic scan reveals downregulation of NDUFA13 in human Marfan's syndrome. Aneurysm alleviation is significant in SM22Cre^{ERT+} NDUFA13$^{fl/fl}$ mice with

a mean diameter of 0.796 mm compared with 1.157 mm in SM22Cre^{ERT}-NDUFA13$^{flox/flox}$ mice (P<0.01). Better vascular integrity in H&E staining and less elastin fragmentation in EVG staining are observed after smooth muscle cells specific NDUFA13 knock out, and elastin integrity score is significantly decreased in knock-out mice (P<0.01). In BAPN induced aneurysm and dissection, aneurysm attenuation is observed at both aneurysm size (P<0.05), vascular integrity and aneurysm formation rate (P<0.05). After knockdown of NDUFA13 in MOVAS and SMC, the apoptosis and ferroptosis rates are significantly decreased in vitro (P<0.05).

CONCLUSIONS NDUFA13 is highly expressed in both human and mouse aortic aneurysm, and it has different expression profile in human hereditary vascular disease such as Marfan's syndrome. After NDUFA13 knock out in smooth muscle cells, mouse aortic aneurysm is dramatically attenuated in both elastase and BAPN induced model. The in-vitro study of MOVAS and SMC in programmed cell death has further elucidated its protection role for vascular injury after knockdown of NDUFA13. Our data indicates that NDUFA13 might be a promising therapeutic target for vascular injury.

GW31-e1298

Upregulation of Zip14 correlates with induction of ERS in hypertrophied hearts of Dahl salt sensitive rats

Jinyong Huang[1], Tianming Teng[1], Yuchen Xue[1], Longfei Huang[1], Zhelong Xu[2], Yuemin Sun[1]
[1]Tianjin Medical University General Hospital
[2]Tianjin Medical University

OBJECTIVES This study evaluated the correlation between Zip14 and expression of some proteins of endoplasmic reticulum stress (ERS) in hypertrophied hearts of rats.

METHODS Dahl salt-sensitive rats were fed a high salt diet to establish a left ventricular hypertrophy (LVH) rat model.

RESULTS Compared with the Control group, Zip14 mRNA and protein expression levels in the LVH rat heart were markedly increased (P<0.01). The zinc content in rat heart tissue was significantly increased in the LVH group compared with the Control group (P<0.05). Activating transcription factor (ATF)4, ATF6, and x box-binding protein 1 (xBP1) mRNA levels were increased in the LVH rat heart compared with Control hearts (P<0.001). Compared with the control group, C/EBP homologous protein (CHOP) and immunoglobulin-binding protein (BiP) mRNA and protein levels were markedly increased in the LVH rat heart (P<0.05, P<0.01). Linear regression models showed that Zip14 mRNA expression levels were positively correlated with zinc concentration, ATF4 and ATF6 mRNA expression levels in Control hearts (P=0.0005, P=0.0052 and P=0.0026, respectively) and LVH rat hearts (P<0.0001, P=0.0119 and P=0.0033, respectively).

CONCLUSIONS In summary, the upregulation of Zip14 in LVH rat hearts correlated with zinc accumulation and the induction of ERS.

GW31-e1326

Circular RNA Arhgap12 modulates doxorubicin induced cardiotoxicity by sponging miR-135a-5p

Xuejun Wang, Lingmei Qian
The First Affiliated Hospital of Nanjing Medical University

OBJECTIVES Doxorubicin is served as a common anti-tumor drugs, however the application is limited by its cardiotoxicity. Circular RNAs (circRNAs) have been proved to be associated with cardiovascular diseases in previous studies. However, the role of circRNAs on DOX-induced cardiotoxicity still needs to be clarified. This research is to investigate the differential expression mode of circular RNAs (circRNAs) in mice cardiomyocytes during doxorubicin induced cardiotoxicity.

METHODS Two groups of mice were injected with equal amount of normal saline and doxorubicin, the isolated mice heart tissues were submitted to next generation RNA-sequencing. Expression profiles of circRNAs and constructed circRNA-miRNA-mRNA networks were analyzed. Overall 48 upregulated circRNAs and 16 downregulated circRNAs in cardiotoxicity apoptosis were assessed. Bioinformatics analysis revealed several potential biological pathways might be related to cardiac toxicity induced by DOX. CircArhgap12 was up-regulated in the DOX treated group.

RESULTS The silencing of CircArhgap12 significantly attenuated DOX-induced apoptosis and oxidative stress. Overexpression of miR-135a-5p in rat primary cardiomyocytes reduced the anti-apoptotic effect of si-circArhgap12 and accelerated oxidative stress. With bioinformatic analysis of miR-135a-5p, it might have a potential target site for ADCY1 mRNA.

CONCLUSIONS Our research demonstrated that expression profiles of circRNAs were significantly modified and circArhgap12 might play a competitive function among endogenous RNAs in DOX-induced cardiotoxicity, which shed a new light on the mechanism of ceRNA network in DOX-induced cardiotoxicity.

GW31-e1330

Aerobic exercise promotes angiogenesis by increasing miR-122-5p

Jing Lou, Jie Wu, Xing Zhang, Feng Gao
Air Force Medical University

OBJECTIVES The significance of exercise in prevention and treatment of cardiovascular diseases is receiving increasing attention. Cardiovascular protective effects of exercise largely depend on its effect in improving blood perfusion and increasing vascular density of organs. miRNA has well-established functions in cancer, metabolic disorders, and cardiovascular diseases and it can travel around body contained within exosome, but the mechanism of exercise-induced angiogenesis by miRNA has not been fully elucidated. In this research, we are aim to identify the specific miRNA that cause angiogenesis during exercise and elucidate the mechanism underlying specific miRNA induced angiogenesis and explore the application potential of the selected miRNA as a pro-angiogenic drug.

METHODS We established aerobic exercise model with a combination of 3-day adaptive training and 9-day treadmill training. AgomiR was adopted to up-regulate the selected miRNA by skeletal muscle point injection, and the AntagomiR was injected through tail vein to interfere with the circulating miRNA level. To determine whether liver derived specific miRNA contributed to exercise-induced angiogenesis, mice were injected with AAV8 through tail vein 1 month before treadmill training, which carried specific antisense sequence. Wound scratch, tube formation and aortic ring assay were used to estimate angiogenesis effect in vitro. Wound healing and matrigel plug assays were used to detect angiogenesis in vivo.

RESULTS Nine days treadmill training significantly increased the expression of VEGF and CD31 in the quadriceps muscle of mice. According to cell proliferation assay, we screened miR-122-5p which was significantly promoted endothelial cell proliferation. Endothelial cell migration, tube formation and aortic ring assay confirmed that miR-122-5p had pro-angiogenic capacity. When we point injected AgomiR-122-5p in skeletal muscle, WB and IF results showed that the protein levels of VEGF and CD31 as well as the CD31 fluorescence density were increased, suggested that miR-122-5p can increase local vascular density in vivo. Then we injected AntagomiR-122-5p or AAV(8)-Anti-122-5p in tail vein to decrease circulatory or liver-derived miR-122-5p, the WB and IF results showed that the VEGF and CD31 expression increased in skeletal muscle of exercise group compared with the sedentary group, while it was not significantly different after AntagomiR-122-5p or AAV(8)-Anti-122-5p injection between the exercise group and the sedentary group, suggested that liver-derived miR-122-5p play a key role in exercise-induced angiogenesis. We used website to predicted and screened the downstream target and found Agpat1 (an enzyme participate triglyceride biosynthesis) is the key gene for this miRNA. CPT1A & CD36 were increased and Agpat1 was decrease when miR-122-5p was promoted in vitro or in vivo. We found that aerobic exercise can effectively increase lipid metabolism through miR-122-5p to promote angiogenesis.

CONCLUSIONS Our research found miR-122-5p as an angiogenic factor. miR-122-5p promoted angiogenesis by up-regulating the expression of CD36 & CPT1A and down-regulating the key target gene Agpat1, which in turn increases endothelial cell fatty acid utilization and VEGF expression. The exercised-induced angiogenesis partially depends on the elevation of circulating miR-122-5p, indicating that miR-122-5p may work as an exerkine and potentially help with the pro-angiogenesis and wound healing treatment.

GW31-e1331

Metformin alleviates hyperuricaemia-induced serum FFA elevation and insulin resistance by inhibiting adipocyte hypertrophy and reversing suppressed white adipose tissue Beiging

Mengqi Su, Yue Li
The First Affiliated Hospital, Harbin Medical University

OBJECTIVES we noticed that adipocytes from the white adipose tissue of patients with HUA were hypertrophied and had decreased UCP1 expression. To test the effects of UA on adipose tissue.

METHODS we built both in vitro and in vivo HUA models and elucidated that a high level of UA could induce hypertrophy of adipocytes, inhibit their hyperplasia and reduce their beige-like characteristics. According to mRNA-sequencing analysis, UA significantly decreased the expression of leptin in adipocytes, which was closely related to fatty acid metabolism and the AMPK signalling pathway, as indicated by KEGG pathway analysis.

RESULTS Our observations confirm that UA is involved in the aetiology of metabolic abnormalities in adipose tissue by regulating leptin-AMPK pathway, and metformin could lessen HUA-induced serum FFA elevation and insulin resistance by improving adipose tissue function via AMPK activation.

CONCLUSIONS metformin could represent a novel treatment strategy for HUA-related metabolic disorders.

GW31-e1339

The characteristics of mitral leaflet adaptive growth in a rhesus monkey model of ischemic mitral regurgitation

Yu Kang[1], Xiaojing Chen[1], Qiaowei Chen[1], Mian Wang[1], Mingqiang Rong[2], Qing Zhang[1]
[1]Department of Cardiology, West China Hospital, Sichuan University
[2]The National & Local Joint Engineering Laboratory of Animal Peptide Drug Development, College of Life Sciences, Hunan Normal University, Changsha, Hunan, China

OBJECTIVES To explore the phenomenon of mitral leaflet growth and its relationship to the dynamic change of ischemic mitral regurgitation (IMR) in rhesus monkey by using transthoracic echocardiography (TTE) and proteomic methods.

METHODS Rhesus monkeys who had completed left circumflex artery occlusion surgery received TTE at baseline, 1-, 2-, 3-, 4-, 8- and 16-week after surgery. Days within one week post-surgery was defined as the acute phase, and after that to the 16-week post-surgery was the chronic phase. The global remodeling parameters included left ventricular end-diastolic volume (LVEDV), end-systolic volume (LVESV) and ejection fraction (LVEF). The parameters to evaluate mitral annular remodeling [mitral annular diameter plus tenting height (MAD+TH)] and the length of anterior mitral leaflet (AML) and the posterior mitral leaflet (PML) were measured at the parasternal left ventricular long axis view. The IMR severity were measured as well. All monkeys who survived at 16-week post-surgery were sacrificed to obtain samples of mitral leaflets. The corresponding tissues of 2 normal monkeys were taken as the control. Differential protein analysis, gene enrichment analysis, functional annotation and pathway and network analysis were performed.

RESULTS A total of 13 monkey survived for 16 weeks after surgery. In the acute phase, 10 monkeys developed IMR (mild IMR, n=5; moderate IMR, n=5) which were defined as IMR (+) group. In IMR (+) group, LVESV (8.7±2.5 vs. 12.1±4.4 mL, P=0.006), (MAD+TH) (16.2±1.3 vs. 18.4±2.4 mm, P=0.003) and TA (0.22±0.04 vs. 0.38±0.09 cm^2, P=0.001) were significantly increased, but LVEF (59.1±4.9 vs. 48.4±11.5%, P=0.006) decreased when compared with baseline. PML slightly increased (6.3±0.8 vs. 6.9±0.6 mm, P=0.024), but the AML did not change (P=0.052) (Table 1). During the chronic phase, there were 8 monkeys in the IMR (+) group with stable/reduced IMR, but their LVEDV (P=0.064), LVESV (P=0.054) and LVEF (P=0.265) showed no statistically difference at each time point during the chronic period. However, (MAD+TH) increased further (1- vs. 4- vs. 16-week 16: 18.4±2.4 vs. 20.7±3.5 vs. 19.1±3.4, P=0.009). AML (1- vs. 4- vs. 16-week: 14.7±1.7 vs. 15.8±2.3 vs. 15.7±2.2, P=0.001) and PML (1- vs. 4- vs. 16-week: 6.9±0.6 vs. 7.9±1.0 vs. 8.0±1.3, P=0.013) increased correspondingly (Table 2). By protemetic analysis, 118 proteins were up-regulated and 52 proteins were down-regulated in AML, most of these differential expressed proteins riched in cellular mitochondrial components. The number of up-regulated proteins was 50, and the number of the down-regulated proteins was 10 in PML, most of these differential expressed proteins riched in extracellular matrix components.

CONCLUSIONS The growth of mitral leaflets failed to adapt to the structural and functional changes of LV and mitral apparatus in the acute phase might be one of the mechanisms of acute IMR. The further growth of mitral leaflets adapted to the degree of cardiac remodeling might be the reason for the IMR reduction in the chronic phase. This study further confirmed the existence of the differential expression of protein of the mitral leaflet in the rhesus monkey IMR model. Further study will be helpful to the explore the growth mechanism behind mitral leaflet growth and to develop new therapeutic targets.

GW31-e1341

Molecular mechanisms of cardiotoxicity induced by targeted drugs

Qinchao Wu, Baochen Bai, Xianming Chu
Department of Cardiology, The Affiliated hospital of Qingdao University

OBJECTIVES In recent years, there has been a revolutionary decrease in cancer-related mortality and prolonged survival due to the induction of novel targeted drugs. Nevertheless, targeted therapies also bring up inevitable adverse events and there is a lack of precise mechanisms and therapeutic measures about novel targeted agents. This review focuses on the molecular mechanisms of cardiotoxicity induced by some targeted agents. The purpose of this article is to stimulate awareness of the emerging cardiotoxicity of novel targeted anticancer drugs and provide novel insights into cardiovascular disease.

METHODS "Cardiotoxicity", "targeted drugs", "HER2", "trastuzumab", "angiogenesis inhibitor", "VEGF inhibitor" and "tyrosine kinase inhibitors" were used as keywords for article searches. We reviewed related articles and presented updated knowledge of the potential mechanisms of cardiotoxicity induced by targeted drugs.

RESULTS HER2-targeting drugs significantly increases the risk of heart failure. The mechanisms are involved in the inhibition of HER-2 and downstream signaling pathways including PI3K/Akt, MEK/Erk and Src/FAK pathways. Block of the downstream effectors result in mitochondrial dysfunction and cell injury, which predisposes to the development to heart failure. In addition, bevacizumab, an angiogenesis inhibitor, brings up inevitable adverse events, particularly hypertension. The potential mechanisms are related to the inhibition of the PI3K/Akt pathway and a decreased production of nitric oxide, prostacyclin, and increased level of endothelin-1, which promotes vasoconstriction, resulting in endothelium dysfunction. Besides, some tyrosine kinase inhibitors including sunitinib, sorafenib, and vandetanib are associated with higher incidence of QT interval prolongation. The inhibition of PI3K/Akt activity leads to disorders of related ion channels, which prolongs ventricular repolarization and gives rise to a prolonged QT interval.

CONCLUSIONS In this review, we concentrate on the molecular mechanisms of cardiotoxicity induced by certain targeted drugs and find several important signal pathways including PI3K-Akt and MEK-Erk signaling, as well as some potential mechanisms. Notably, the PI3K-Akt pathway exerts complicated biological effects by increasing NO production via activation of eNOS, inhibiting apoptosis, and modulating multiple ion channels. Currently, the management of cardiotoxicity induced by antitumor agents mainly depends on early detection, careful monitoring, and empirical treatment, there is still a lack of specific recommendations by guidelines. Future treatments for targeted drug-induced cardiotoxicity depend on a better understanding of mechanisms and further clinical evidence.

GW31-e1349

MiR-19b regulates mitochondrial oxidative stress in endothelial senescence via alterations sirtuin 5-mediated SOD1 desuccinylation

Jiang He, Yumin Qiu, Bin Dong, Bingbo Yu, Zhe Zhou, Zhichao Wang, Wenhao Xia
Department of Hypertension and Vascular Disease, The First Affiliated Hospital, Sun Yat-sen University

OBJECTIVES Decline in angiogenic capacity is the leading cause of age-related cardiovascular disease. Mitochondrial oxidative stress is implicated in the abnormalities of vascular formation. Sirtuin 5 (SIRT5) plays a critical role in maintenance of mitochondrial redox homeostasis through regulating the succinylome; however, the exact function of SIRT5 in angiogenesis and upstream regulated mechanisms remain largely unknown. The present study aim to investigate the role of microRNAs in SIRT5-mediated mitochondrial oxidative stress via desuccinylation of antioxidant enzymes.

METHODS Cellular signaling was analyzed in primary aortic endothelial cells (PAEC). miRNA array was used to identify differential expression of miRNAs. Electron spin resonance was used to detect mitochondrial superoxide anion ($O2^{-}$) generation. Proteomic analysis, luciferase assays, immunoprecipitation were performed.

RESULTS Duplicate senescence in PAEC was associated with decreased angiogenic capacity and excessive mitochondrial O_2^{-} production. miR-19b was highly enriched in senescent PAEC. Induction of miR-19b in PAEC impeded the formation of normal vascular structures along with downregulation of SIRT5 and global protein succinylation. Proteomic analysis of senescent PAEC revealed the specific lysine succinylation of a central mitochondrial antioxidant enzyme, SOD1. miR-19b downregulated SIRT5 expression through direct 3′-untranslated region targeting. SIRT5 provoked desuccinylation of SOD1 associated with enhanced enzymatic activity, leading to the elimination of O_2^{-}. Treatments with miR-19b mimics or SIRT5 silencing augmented mitochondrial oxidative damage with subsequent inhibition of angiogenesis. Suppression of miR-19b with antimiR oligonucleotides attenuated mitochondrial oxidative damage and rescued senescence-related abnormity in vascular formation via SIRT5-mediated SOD1 Desuccinylation.

CONCLUSIONS We demonstrated for the first time that miR-19b involves mitochondrial oxidative stress via direct suppression of sirt5 and enzymatic inhibition of SOD1. Blockage of MiR-19b may be a novel therapeutic target for age-related disorder of vascular formation.

GW31-e1352

The mechanism of ghrelin regulating Ang II/AT1R/Gal-3 axis inhibiting myocardial fibrosis in heart failure

Chunyan Yang, Ping Yang
China-Japan Union Hospital, Jilin University, Changchun, China

OBJECTIVES Ghrelin, a novel growth hormone-releasing peptide, potentially improves cardiac function, but the mechanisms remain unclear. Angiotensin II (Ang II), an important neurohormonal factor during heart failure, can induce myocardial fibrosis. However, the molecular mechanism of Ang II inducing myocardial fibrosis remains unclear, especially its role and mechanism in the progression of myocardial fibrosis in heart failure after myocardial infarction (MI). Galactosin-3 (Gal-3) is a member of the galactin family and is closely related to myocardial fibrosis. We hypothesized that Ang II may induce Gal-3 expression through its type 1 receptor (AT1R), thereby promoting myocardial fibrosis of heart failure after myocardial infarction, while Ghrelin can inhibit the above useful effect.

METHODS In the study, the left anterior descending coronary artery was ligated to establish a rat model of heart failure (HF), and then treated with ghrelin (100 μg/kg, subcutaneous injection, bid); the cardiac fibroblasts from neonatal rats were cultured and stimulated with Ang II (0.1 μM) and ghrelin (0.1 μM) to explore the role and mechanism of ghrelin in myocardial fibrosis. Hemodynamic and serum brain natriuretic peptide (BNP) concentrations were measured to assess cardiac function. Left ventricular mass index (LVMI), hematoxylin and eosin (H&E) staining, and Masson's trichrome staining were performed to evaluate myocardial fibrosis. To further explore whether ghrelin inhibits myocardial fibrosis by inhibiting Ang II/AT1R/Gal-3 axis, the levels of AT1R and Gal-3 were examined by immunohistochemistry, real-time quantitative PCR and ELISA in vivo and in vitro. Finally, to investigate the effect of Gal-3 on myocardial fibrosis, the primary rat cardiac fibroblasts (CFs) were cultured and treated with Gal-3, the proliferation of CFs was detected by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. Also, the expressions of type I and type III collagen (Col I and Col III) were measured by real-time quantitative PCR.

RESULTS The results showed that ghrelin significantly improved cardiac function and hemodynamics in HF rats after myocardial infarction (MI), and inhibited type I and type III collagen expression in vivo; inhibited the CFs proliferation and type I and type III collagen expression induced by Ang II in vitro. The results also showed that Gal-3 levels were significantly increased in the MI group, and ghrelin administered downregulated Gal-3 expression. Furthermore, ghrelin decreased Ang II-induced Gal-3 expression in primary rat cardiomyocytes in vitro by downregulating AT1R expression. In addition, Ang II upregulated gal-3 expression through AT1R, and Gal-3 treated cultured primary rat cardiac fibroblasts (CFs) showed increased proliferation and enhanced expressions of type I and type III collagen.

CONCLUSIONS These data suggest that Ang II can induce Gal-3 expression through AT1R, thereby promoting the proliferation of CFs and the expression of type I and III collagen to promote HF progression, while Ghrelin can inhibit myocardial fibrosis and protect heart failure by inhibiting Ang II/AT1R/Gal-3 axis.

GW31-e1366

Evidence of accelerated aging in genetic cardiomyopathy

Alex Chia Yu Chang
Department of Cardiology and Shanghai Institute of Precision Medicine, Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine

OBJECTIVES Dilated Cardiomyopathy (DCM) is a cardiac disease characterized by dilatation of the ventricular chamber resulting in decreased systolic function. DCM mostly occurs between the ages of 20–60 affecting approximately 1 in 2500. Between 30–50% of DCM cases are inherited with ~33 known DCM mutations classified as genetic DCM. DCM is the most common cause of heart failure after coronary artery disease and hypertension, as well as the leading indication for heart transplantations. Initially, therapy includes medications such as ACE inhibitors, angiotensin receptor antagonists, beta-blockers, aldosterone antagonists, digoxin, and diuretics. Some patients require surgery to have a pacemaker or defibrillator placed. For patients whose symptoms do not respond to these treatments, waiting for a heart transplant is the only option. We recently observed that telomeres, DNA-repeat sequences that protect the ends of chromosomes, are reduced in length by >40% in cardiomyocytes of genetic DCM patient hearts lacking dystrophin, Troponin t2, or Titin. We seek to test if telomere shortening is a hallmark of genetic cardiomyopathy.

METHODS Typically, telomeres shorten at every cell division due to replication insufficiency and are markers of cellular aging, but in healthy postnatal cardiomyocytes, telomere lengths are maintained throughout life, presumably because these cells do not proliferate. Here we used human induced pluripotent stem cell derived cardiomyocytes as model to study the mechanism of telomere shortening.

RESULTS This unexpected telomere shortening is recapitulated in cardiomyocytes differentiated from human induced pluripotent stem cells (hiPSC-CM) derived from DCM patients, enabling mechanistic studies. We observed aberrant calcium handling and decreased contractility using bioengineered micropatterned hydrogel traction force microscopy. Here we present new evidence where aberrant contraction results in telomere deprotection and resection in in non-dividing hiPSC-CMs. Induction of DNA damage response culminated in mitochondrial dysfunction and apoptosis.

CONCLUSIONS The proposed model enables the study of cause and effect and tests of interventions.

GW31-e1367

Accelerated circulatory aging in coronary heart disease patients

Honghui Wang[1], Dongjiu Li[2], Chia Yu Alex Chang[1,2]
[1]Department of Cardiology, Shanghai Institute of Precision Medicine, Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, China
[2]Department of Cardiology, Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, China

OBJECTIVES To study whether there is an accelerated aging (LTL shortening and increased inflammatory response) in the younger population that leads to higher incidence of CHD.

METHODS Blood samples and clinical data of more than 2000 patients with CHD undergoing coronary angiography or PCI in the department of cardiology of Shanghai ninth people's hospital from 2016 to 2019 were analyzed. Based on age inter quartile range (IQR) of all patients, CAG and PCI patients were divided into four age groups: <60 y, 60–65 y, 66–73 y and ≥73 y. LTL and clinical related factors in each group were measured and analyzed.

RESULTS Compared with CAG patients, PCI patients exhibited significantly shorter LTL. Interestingly, shorter LTL did not result in decrease in mitochondrial copy number. Importantly, <60 y PCI patients showed significant decrease in LTL similar to older PCI patients.

CONCLUSIONS These results suggest that LTL shortening is strongly associated with more severe CHD that required PCI treatment. Moreover, regardless of age, PCI patients overall exhibited shorter LTL compared to CAG cohort and provides the necessary samples to further characterize and define molecular aging in CHD.

GW31-e1372

Small extracellular vesicle-incorporated long noncoding RNA PUNISHER is increased in coronary artery disease and regulates endothelial cell function

Yangyang Liu[1,2], Felix Jansen[2]
[1]Department of Internal Medicine Cardiac Disease, Shanghai Ninth People's Hospital, Shanghai JiaoTong University School of Medicine
[2]Heart Center Bonn, Department of Internal Medicine II, University Hospital Bonn, University of Bonn Venusberg-Campus 1, 53127 Bonn, Germany

OBJECTIVES Extracellular vesicle (EV)-incorporated long noncoding RNAs (lncRNAs) have emerged as biomarkers and regulators of cardiovascular disease. Our aim was to study the expression pattern of circulating small EV (sEV)-incorporated lncRNAs in patients with and without coronary artery disease (CAD).

METHODS PCR-based human lncRNA array analysis revealed that certain sEV-lncRNAs are significantly different in patients with CAD compared to patients without CAD. Four atherosclerosis-related lncRNAs (PUNISHER, GAS5, MALAT1, and H19) were quantified in the circulating sEV by using real-time quantitative PCR (RT-qPCR) in 60 patients with (n=30) or without (n=30) CAD.

RESULTS Four atherosclerosis-related lncRNAs (PUNISHER, GAS5, MALAT1, and H19) were quantified in the circulating sEV by using real-time quantitative PCR (RT-qPCR) in 60 patients with (n=30) or without (n=30) CAD. Among these, PUNISHER (P=0.002) and GAS5 (0.02) were significantly increased in patients with CAD. In vitro, atherosclerotic stimuli upregulated PUNISHER levels in endothelial cells (EC) and in the corresponding sEV. Labeling of sEV and RT-qPCR demonstrated the transportation of PUNISHER into recipient ECs, which accelerated cell migration, proliferation, and tube formation. Mechanistically, the RNA-binding protein hnRNPK was identified to regulate PUNISHER loading into sEV. Knockdown of PUNISHER abrogated the sEV-mediated effects on EC migration, proliferation, and tube formation. PCR-based gene profiling showed that the expression of VEGFA RNA was increased in ECs by sEV treatments. Knockdown of PUNISHER in sEV abrogated the EV-mediated promotion of VEGFA gene- and protein expression.

CONCLUSIONS The circulating lncRNA PUNISHER is increased in CAD patients. Intercellular transfer of sEV-incorporated PUNISHER promotes a pro-angiogenic phenotype via a VEGFA-dependent mechanism.

GW31-e1377

Effect of inhalable porous microparticles containing H2S-releasing aspirin derivative on pulmonary arterial hypertension

Hui Zhang[1], Liuzhi Hao[2], JunFeng Zhang[1], Changqian Wang[1], Aizheng Chen[2], Huili Zhang[1]
[1]Department of Cardiology, Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 200011, PR China
[2]Fujian Provincial Key Laboratory of Biochemical Technology, Institute of Biomaterials and Tissue Engineering, Huaqiao University, Xiamen 361021, PR China

OBJECTIVES Pulmonary drug delivery offers tremendous opportunity, both systemically and locally, for treating pulmonary disorders. Hydrogen sulfide (H_2S) has recently emerged as a novel gaseous mediator with protective actions in treating pulmonary arterial hypertension (PAH). However, the therapeutic potential of H_2S has been substantially hampered due to the lack of appropriate donors that could mimic the tightly controlled endogenous production

in response to specific biological conditions. Therefore, an innovative formulation based on inhalable porous poly(lactic-co-glycolic acid) (PLGA) microspheres containing H2S-releasing aspirin derivative (ACS14) (ACS14 MSs) is fabricated using the microfluidic technology. In addition to physicochemical attributes, cytotoxicity, lung deposition characteristics, and H2S release profile, the protective effect of ACS14 MSs on PAH and the underlying mechanism concerning the process of endothelial-to-mesenchymal transition (EndMT) are evaluated both in vitro and in vivo.

METHODS ACS14 MSs were fabricated using microfluidic technology. The characterizations of ACS14 MSs including the surface morphology, the aerodynamic properties, the chemical functionalities, the crystal characteristics, the thermal properties were analyzed. Drug loading and encapsulation efficiencies were measured by HPLC. The cytotoxicity were analyzed by CCK-8 cell viability detection, TUNEL staining and Annexin V/PI flow cytometry. The lung deposition characteristics were detected using in vivo fluorescence imaging. Eight-week-old, male SD rats (200±20 g) were randomly given monocrotaline (60 mg/kg, i.p.) or saline. Seven days after the injection of MCT, rats were daily administered with sildenafil (25 mg/kg, i.g.), ACS14 MSs (46.5 mg/kg, i.t.), PLAG MSs (46.5 mg/kg, i.t.), or ACS14 (12 mg/kg, i.p.) daily for 14 days. Pulmonary artery pressure and the right-heart function were observed 21 days after MCT injection. Pulmonary arterial remodeling was examined by HE staining. EndMT was investigated by western blot immunoblotting and immunofluorescence. NFκB p65 DNA binding activity was also assayed. HPAECs were pre-incubated with PLGA MSs (50 μM, 2 h), sildenafil (1 μM, 30 min), ACS14 (25 μM or 50 μM, 2 h) or ACS14 MSs (25 μM or 50 μM, 2 h) and then stimulated with TGF-β1 (10 ng/mL, 1 h, 3 d or 10 d) to evaluate morphology changes, ultrastructural transformation in HPAECs, the process of EndMT and its underlying mechanism.

RESULTS These porous ACS14 MSs displayed excellent aerodynamic properties, high drug loading, and entrapment efficiency with slow drug release behavior and negligible cytotoxicity, indicating their suitability for delivering ACS14 via pulmonary administration. In human pulmonary artery endothelial cells (HPAECs), ACS14 MSs inhibited TGF-β1-induced EndMT, an important process in vascular remodeling of PAH and the activation of NF-κB-Snail pathway in a dose-dependent manner. Moreover, in a rat model of monocrotaline-induced PAH, daily inhalation of ACS14 MSs significantly inhibited the process of EndMT by suppressing the induction of NF-κB-Snail pathway and thus improved the severity of PAH with comparable efficacy to oral administration with sildenafil, a conventional PAH treatment.

CONCLUSIONS In conclusion, our findings demonstrated that the designed microfluidics-assisted porous ACS14 MSs have shown great potential for the inhalation treatment of PAH.

GW31-e1378

MiR-21-3p inhibits epicardial adipose tissue browning and promotes inflammation by targeting FGFR1 in diabetes

Jianan Pan, Hao Lin, Jianying Yu, Huili Zhang, Junfeng Zhang, Changqian Wang, Jun Gu
Department of Cardiology, Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, People's Republic of China

OBJECTIVES A relationship between the abundance of epicardial adipose tissue (EAT) and the risk of atrial fibrillation (AF) in diabetes mellitus (DM) has been reported. And browning of EAT might be a novel approach for prevention or treatment in AF by adjusting atrial fibrosis. MicroRNA-21 (miR-21) have shown been a regulatory factor in atrial fibrosis. The aim of this study was to examine the role of miR-21-3p in EAT browning in hyperglycemia conditions.

METHODS In vivo, Normal C57BL/6 wild type (WT) and miR-21 knockout (KO) mice were used to establish the diabetic model by intraperitoneal injection of streptozotocin (STZ). In vitro, The EAT adipocytes from miR-21 KO mice were cultured and transfected with miR-21-3p mimic or miR-21-5p mimic in both HG or LG conditions. The browning of EAT were assessed by western blotting and immunofluorescence, and the release of inflammatory factors were assessed by ELISA. The gain- and loss-of-function experiments were used to identified fibroblast growth factor receptor 1 (FGFR1) as the target gene of miR-21-3p, and the regulatory pathway of miR-21-3p FGFR1, fibroblast growth factor 21 (FGF21) and peroxisome proliferator-activated receptor gamma (PPARγ) that controlled EAT browning under hyperglycemia conditions.

RESULTS MiR-21 KO clearly ameliorated the atrial fibrosis in the diabetic mice. miR-21-3p as a key regulator that controls EAT browning and participates in atrial fibrosis under hyperglycemia conditions. Moreover, our gain- and loss-of-function experiments showed that FGFR1, as a direct target of miR-21-3p identified a regulatory pathway in EAT adipocytes consisting of miR-21-3p, FGFR1, FGF21 and PPARγ.

CONCLUSIONS MiR-21-3p regulated EAT browning and the inflammatory factors releasing i under hyperglycemia conditions by targeting FGFR1/FGF21/PPARγ pathway.

TRANSLATIONAL RESEARCH OF CARDIOVASCULAR DISEASE

GW31-e0030

Value of circulating microRNAs in the diagnosis of acute myocardial infarction: a systematic review and meta-analysis

Chuannan Zhai[1,2], Hongliang Cong[1,2]
[1]NanKai University, School of Medicine
[2]Tianjin Chest Hospital, Department of Cardiology

OBJECTIVES Recent studies have shown that blood-based miRNAs are dysregulated in patients with AMI and are therefore a potential tool for the diagnosis of AMI. However, the diagnostic value of miRNAs is still inconsistent due to differing results among previous studies. Therefore, this study summarized and evaluated studies focused on microRNAs as novel biomarkers for the diagnosis of AMI from the last ten years.

METHODS MEDLINE (including PubMed), the Cochrane Central database, and EMBASE were searched between January 2010 and December 2019. Studies that assessed the diagnosis accuracy of circulating microRNAs in AMI were chosen. The number of significantly dysregulated miRNAs identified, patients demographics, type of clinical sample, method of miRNA detection, and type of normalization were included. The pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio, and area under the curve were used to assess the overall test performance of miRNAs.

RESULTS A total of 58 studies that included 8206 participants assessed the diagnosis accuracy of circulating miRNAs in AMI. The main results of the meta-analyses are as follows: Total miRNAs: the overall pooled sensitivity and specificity were 0.82 (95% CI: 0.79–0.85) and 0.87 (95% CI: 0.84–0.90), respectively. The AUC value was 0.91 (95% CI: 0.88–0.93) in the overall summary receiver operator characteristic (SROC) curve. Results from the panel of two miRNAs: sensitivity: 0.88 (0.77–0.94), specificity: 0.84 (0.72–0.91), AUC: 0.92 (0.90–0.94); The panel of three miRNAs: sensitivity: 0.91 (0.85–0.94); specificity: 0.87 (0.77–0.92), AUC: 0.92 (0.89–0.94); miRNA-1: sensitivity: 0.78 (0.71–0.84), specificity: 0.86 (0.77–0.91), AUC: 0.88 (0.85–0.90); miRNA-133a: sensitivity: 0.85 (0.69–0.94), specificity: 0.92 (0.61–0.99), AUC: 0.93 (0.91–0.95); miRNA-208b: sensitivity: 0.80 (0.69–0.88), specificity: 0.96 (0.77–0.99), AUC: 0.91 (0.88–0.93); miRNA-499: sensitivity: 0.80 (0.69–0.88), specificity: 0.96 (0.77–0.99), AUC: 0.91 (0.88–0.93).

CONCLUSIONS MiRNAs may be used as potential biomarkers for the detection of AMI. For single, stand-alone miRNAs, miRNA-499 may have better diagnostic accuracy compared to other miRNAs. We propose that a panel of multiple miRNAs with high sensitivity and specificity should be tested.

GW31-e0041

Evolution of denervative effects over multiple time points after noninvasive stereotactic renal nerve radioablation in a hypertensive swine model

Xingxing Cai[1], Yuli Yang[1], Wei Wang[1], Yichen Shen[1], Li Qian[2], Zhixing Wei[1], Taizhong Chen[1], Jing Cai[1], Runmin Chi[1], Shunxuan Yu[1], Keke Li[1], Mawei Jiang[1], Yigang Li[1]
[1]Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine
[2]Affiliated Hospital of Nantong University

OBJECTIVES Noninvasive stereotactic body radiotherapy (SBRT) is a novel technique for renal denervation (RDN). The purpose of this study was to investigate the chronological evolution and mechanism of SBRT-induced renal nerve injury, as well as its antihypertensive effect and safety within 6 months in a hypertensive swine model.

METHODS Bama swine were randomly divided into 1-month group (n=4), 3-month group (n=4), 6-month group (n=5) according to the duration of follow-up post-RDN with a single dose of 25 Gy delivered by SBRT, and additional 5 swine served as control. Hypertension was induced by subcutaneous implantation of deoxycorticosterone acetate (DOCA) pellets in combination with a high-salt diet. Blood pressure and renal function were measured at baseline, 1 month, 3 months and 6 months after treatment. Abdominal contrast-enhanced CT scan was performed at the predetermined endpoint. The concentration of renal norepinephrine was measured by high performance liquid chromatography-mass spectrometry. The characteristics of injured nerves were analyzed by standard semi-quantitative scoring method. Nerve apoptosis was determined by TUNEL and immunofluorescence. Function of sympathetic nerves and nerve regeneration were evaluated with immunostains against tyrosine hydroxylase (TH) and growth-associated protein 43 (GAP43).

RESULTS All animals survived to the predetermined endpoint. Blood pressure at baseline, 1 month, 3 months and 6 months post-RDN were comparable to control, whereas renal norepinephrine was significantly lower at 6 months (384.2±103.6 ng/g vs. 700.9±121.8 ng/g, P<0.05). Compared with control

(1.4±0.4), nerve injury score was greatest at 6 months (3.2±0.8), followed by 3 months (2.5±0.4) and 1 month (2.3±0.3) (P<0.001). The proportion of TUNEL positive nerves at 3 months and 6 months were both significantly higher than control (14.2±3.3%, 23.0±7.3% vs. 1.3±2.5%, P<0.05). Compared with 1 month, arteriolar injury score was significantly greater at 3 and 6 months (2.5±0.4, 2.4±0.2 vs. 1.6±0.6, P<0.05), and arteriolar occlusion due to intimal hyperplasia and thrombosis was observed at 3 months and more common at 6 months. Although there seems to be a trend showing more severe soft tissue injury characterized by denatured collagen, fat necrosis and fibrosis at 3 and 6 months, no statistical difference was found between groups (3.0±0.8, 3.1±0.2 vs. 2.0±1.4, P>0.05). Compared with control, TH scores were significantly lower (1.6±0.5, 1.4±0.5, 1.6±0.5 vs. 2.6±0.5, P<0.05) and GAP43 scores were similar (1.8±0.4, 2.0±0.0, 1.6±0.5 vs. 1.6±0.5, P>0.05) after RDN. CT images and renal function remained normal, notwithstanding 1 apparent focal pathological renal injury at 6 months.

CONCLUSIONS SBRT delivering 25 Gy for RDN maintained a promising safety profile with sustainable reduction of sympathetic activity up to 6 months, despite failure to lower BP in the DOCA-salt hypertensive swine model. Radiation-induced renal nerve injury aggravated over time, resulting from direct effects of irradiation and secondary effects of regional fibrosis and damaged microvasculature which induced nerve apoptosis and necrosis, as well as inhibition of nerve regeneration.

GW31-e0141

Prognostic role of circulating microRNAs in human coronary artery disease: evidence from 4513 subjects

Chuannan Zhai[1,2], Hongliang Cong[1,2]
[1]School of Medicine, NanKai University, Tianjin, China
[2]Tianjin Chest Hospital, Tianjin, China

OBJECTIVES MicroRNAs (miRNAs) have been shown to play a critical role in the development of and morbidity from cardiovascular diseases. However, their value as novel prognostic biomarkers in coronary artery disease (CAD) remains unclear. The current study evaluated the value of circulating miRNAs in the prognosis of CAD over the past 10 years.

METHODS MEDLINE (including PubMed), Embase and the Cochrane Central database were searched from January 2010 to April 2020. Studies that assessed the prognosis values of circulating microRNAs in CAD were chosen. A meta-analysis was conducted to evaluate the correlation between circulating miRNAs expressions and mortality, major adverse cardiovascular events (MACEs), and left ventricular adverse remodeling (LVAR) among these studies.

RESULTS Twenty studies involving 4513 patients were included in this meta-analysis. Total miRNAs were associated with high mortality (combined HR: 1.77, 95% CI: 1.47–2.13), MACEs (combined HR: 1.22, 95% CI: 1.03–1.45; combined OR: 1.80, 95% CI: 1.47–2.20), and LVAR (combined OR: 1.18, 95% CI: 1.12–1.26) in patients with CAD. An elevated level of miRNA-208b was associated with high mortality (pooled HR: 2.55, 95% CI: 1.36–4.78) and MACEs (pooled OR: 1.80, 95% CI: 1.32–2.45). MiRNA-133a (pooled HR: 1.31, 95% CI: 0.93–1.83) might be related to the occurrence of MACEs. MiRNA-150 (pooled OR: 1.22, 95% CI: 1.12–1.34) was correlated with LVAR after acute myocardial infarction (AMI).

CONCLUSIONS The present study showed that circulating miRNAs may be valuable predictors of clinical outcomes in CAD. miRNA-133a, miRNA-208b, and miRNA-150 show potential as useful prognostic biomarkers in the follow-up of patients with CAD.

GW31-e0397

Checkpoint kinases important players in lung fibrogenesis and pulmonary vascular remodeling: a translational study

WenHui Wu[1,2], Geraldine Vitry[2], Valerie Nadeau[2], Junichi Omura[2], Mark Orcholski[2], David Marsolais[2], Eve Tremblay[2], Sandra Martineau[2], Sandra Breuils Bonnet[2], Roxane Paulin[2], Steeve Provencher[2], Olivier Boucherat[2], Sebastien Bonnet[2]
[1]Department of Cardio-Pulmonary Circulation, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai 200433, China
[2]Pulmonary Hypertension research Group, IUCPQ Research Centre, 2725, Chemin Sainte-Foy, QC, Canada G1V 4G5

OBJECTIVES Pulmonary fibrosis (PF) is an important commonality in pathogenesis of interstitial lung diseases, and pulmonary hypertension (PH) is a well-recognized severe complication of PF. Both significantly impact patients' survival and functional status, but without validated treatments. In the lung, parenchymal and vascular remodeling share pathomechanisms, mainly including excessive proliferation and resistance to apoptosis of fibroblasts (LFs) and pulmonary arterial smooth muscle cells (PASMCs). In cancer, sustained cell proliferation is ensured, in part, by a fine tuning of cell cycle and DNA repair machinery, of which checkpoint kinases (CHK1 and CHK2) are critical regulators. They are upregulated in cancer and their inhibition are currently tested in clinical trials. However, these pathways have never been explored in PF. We thus hypothesized that CHK1/2 are upregulated in PF-PH and contribute to both fibrotic and vascular lesions in PF-PH patients.

METHODS Lung tissues, LFs and PASMCs were obtained from PF patients and health control. CHK1/2 and other protein expression levels were monitored by western blotting, and their location were confirmed by immunofluorescence. To study the effect of CHKs on HLFs and PASMCs proliferation and apoptosis in vitro, cultured human cells were exposed to 10% FBS or 0.1% FBS in presence of MK-8776, LY2606368 or vehicle for 48 hours.

RESULTS Increased DNA damage (γH2Ax and p(S4/S8)-RPA32) as well as augmented expression and activity of CHK1/2 was observed by WB in lung and isolated LFs from PF patients compared to controls (P<0.05, n=8–15 per group) with marked expression in fibroblastic foci. Similarly, increased levels of CHK1/2 and DNA damage were detected by WB and IF in remodeled pulmonary arteries (PA) of PF patients with or without PH. Similar findings were noted in mice exposed to bleomycin. In isolated PF-LFs and PASMCs, dual inhibition of CHK1/2 using MK-8776 and LY2606368 significantly reduced expression of TCTP and RAD51 (two factors required for efficient DNA repair), leading to exacerbation of DNA damage and resulted in reduced cell proliferation (Ki67 labeling, WB PCNA) and resistance to apoptosis (Annexin V assay, WB Survivin). Furthermore, inhibition of CHK1/2 mitigated the hyper-activated state of PF-LFs, as illustrated by reduced expression of FN, CTGF, and pSTAT3 (WB). Similar results were observed in control LFs exposed to TGF-β1; all P<0.05.

CONCLUSIONS Our data provide compelling evidence that CHK1/2 are involved in lung fibrogenesis and PA remodeling in PF. Current experiments aim to determine whether CHK1/2 inhibitors elicit beneficial effects in animal models of PF-PH.

GW31-e0456

Injectable and antibacterial hydrogels based on hybrid crosslinking strategy prevents cardiovascular implantable electronic devices pocket infection

Quanbin Dong[1], Huihui Bao[1], Liang Liu[1], Lingyong Zhu[2], Xiaoshu Cheng[1]
[1]The Second Affiliated Hospital of Nanchang University
[2]East China University of Science and Technology

OBJECTIVES Cardiovascular implantable electronic device infections are associated with high hospitalization, mortality, increased costs, and adverse outcomes. However, many clinical studies have shown that neither pocket irrigation nor intravenous antibiotics can effectively prevent CIED infection. Moreover, the wide use of antibiotics to prevent CIED infection has led to escalating antibiotic-resistant associated with various pathogens.

METHODS Therefore, we first obtained cross-linked HA (**CHA**) with BDDE crosslinking agent, in which the degradation time in vivo could cover the acute infection period of 7–10 days after implantation. Then, we designed an injectable hydrogel via electrostatic interaction between carboxyl groups of **CHA** and amino groups of **CHX**, which can control the release of **CHX**.

RESULTS *In vitro* study with **CHA/CHX** hydrogel demonstrated **CHX** release effectively against (99.999% reduction) S. aureus and E. coli. Furthermore, pocket anti-infection was evaluated in vivo using a rabbit model and examined 1 week later. The results showed that **CHA/CHX** hydrogel group had no purulence and the S. aureus colonies were much lower than those in the bacterial only group (P<0.01). We have also shown that **CHX/CHA** hydrogel is relatively non-hemolytic and has excellent biocompatibility *in vivo*.

CONCLUSIONS In summary, **CHA/CHX** hydrogel may be excellent candidates as anti-infection materials for CIED pocket infection treatment.

GW31-e1115

Downregulating the P2X3 receptor in the carotid body to reduce blood pressure via acoustic gene delivery in canines

Qian Xue[1], Ruiyu Wang[1], Liang Wang[1], Bo Xiong[1], Lingjiao Li[1], Jun Qian[1], Lan Hao[2], Zhigang Wang[2], Dichuan Liu[1], Changming Deng[1], Shunkang Rong[1], Yuanqing Yao[1], Yonghong Jiang[1], Que Zhu[1], Jing Huang[1,3]
[1]Department of Cardiology, The Second Affiliated Hospital of Chongqing Medical University
[2]Chongqing Key Laboratory of Ultrasound Molecular Imaging, Chongqing Medical University
[3]Institute of Ultrasound Imaging, Department of Ultrasound, The Second Affiliated Hospital of Chongqing Medical University

OBJECTIVES The purinergic P2X3 receptor in the carotid body (CB) is considered a new target for treating hypertension, although approaches for targeted regulating P2X3 receptor expression are lacking. Here, we explored the feasibility of targeted P2X3 receptor down-regulation in CBs by localized low-intensity focused ultrasound (LIFU)-mediated gene delivery to reduce the blood pressure.

METHODS Thirty-two Kunming canines were randomly assigned to the treatment group (n=14), negative control group (n=10), LIFU+cationic microbubbles group (n=4), and LIFU-only group (n=4). Plasmid-loaded cationic microbubbles were injected and bilateral CBs were irradiated with a LIFU-based transducer.

RESULTS Flow cytometry showed that 33.15% of transfected cells expressed the green fluorescent protein reporter gene. T7 endonuclease I assays showed an insertion-deletion rate of 8.30%. The P2X3 receptor mRNA- and protein-expression levels in CBs decreased by 56.31% and 45.10%, respectively, in the treatment group. Mean systolic (152.5±3.0 versus 138.0±2.9 mmHg, P=0.003) and diastolic (97.8±1.5 versus 87.2±2.3 mmHg, P=0.002) blood pressures reduced on day 14 in the treatment group, compared with the baseline values, whereas no effects were observed with LIFU treatment or cationic microbubbles injection alone. Canines treated with this strategy exhibited no local or systemic adverse events.

CONCLUSIONS Thus, LIFU-mediated gene delivery to CBs successfully modulated CB function and reduced blood pressure in a canine model, suggesting a new possibility for treating hypertension and further clinical translation.

GW31-e1118

A tailorable hydrogel improves retention and cardioprotection of intramyocardial transplanted mesenchymal stem cells for the treatment of acute myocardial infarction in mice

Wenjun Yan[1], Youhu Chen[1], Yunlong Xia[1], Xinliang Ma[2], Ling Tao[1]
[1]Department of Cardiology, Xijing Hospital, Fourth Military Medical University
[2]Department of Emergency Medicine, Thomas Jefferson University

OBJECTIVES Poor engraftment of intramyocardial stem cells limits their therapeutic efficiency against myocardial infarction (MI)-induced cardiac injury. Transglutaminase cross-linked Gelatin (Col-Tgel) is a tailorable collagen-based hydrogel that is becoming an excellent biomaterial scaffold for cellular delivery in vivo. Here, we tested the hypothesis that Col-Tgel increases retention of intramyocardially-injected stem cells, and thereby reduces post-MI cardiac injury.

METHODS Adipose-derived mesenchymal stem cells (ADSCs) were co-cultured with Col-Tgel in a three-dimensional (3D) system in vitro, and Col-Tgel encapsulated ADSCs were observed using scanning electron microscopy and confocal microscopy. Vitality, proliferation, and migration of co-cultured ADSCs were evaluated. In addition, mice were subjected to MI and were intramyocardially injected with ADSCs, Col-Tgel, or a combination thereof. ADSCs engraftment, survival, cardiac function, and fibrosis were assessed.

RESULTS In vitro MTT and Cell Counting Kit-8 assays demonstrated that ADSCs survive and proliferate up to 4 weeks in the Col-Tgel. In addition, MTT and transwell assays showed that ADSCs migrate outside the edge of the Col-Tgel sphere. Furthermore, when compared with ADSCs alone, Col-Tgel-encapsulated ADSCs significantly enhanced the long-term retention and cardioprotective effect of ADSCs against MI-induced cardiac injury.

CONCLUSIONS In the current study, we successfully established a 3D co-culture system using ADSCs and Col-Tgel. The Col-Tgel creates a suitable microenvironment for long-term retention of ADSCs in an ischemic area, and thereby enhances their cardioprotective effects. Taken together, this study may provide an alternative biomaterial for stem cell-based therapy to treat ischemic heart diseases.

GW31-e1152

Numb gene methylation increases the susceptibility of coronary heart disease

Jialin Abuzhalihan, Yi Tong Ma
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, P.R. China

OBJECTIVES The aim of this study was to investigate whether DNA methylation of NPC1L1, LIMA1 and Numb genes were associated with CHD.

METHODS Patients with CHD were screened from The First Affiliated Hospital of Xinjiang Medical University between July 2012 and March 2016. DNA methylation levels of the candidate genes NPC1L1, LIMA1 and Numb were measured in peripheral blood leukocytes (PBLs) from 99 patients diagnosed with CHD and 89 control subjects. A total of 55 CPG sites around promoter regions of them were examined. The data were analyzed by IBM SPSS Statistics Version 23.0 (Armonk, NY: IBM Corp.). The measurement data are shown as the Means±SD, and the differences between CHD and control subjects were assessed using an independent-sample t-test. Differences in the enumeration data, such as the frequencies of smoking, drinking, hypertension and diabetes between CHD and control subjects were analyzed using the chi-square test. The methylation levels of LIMA1, NPC1L1, and NUMB did not meet the normality assumption, they were described as median (interquartile range) and compared with Mann–Whitney U test.

RESULTS The average age of the 188 analyzed patients was 59.46±10.61 years, and 127(67.6%) of them were male. There were 60(31.9%) patients with hypertension and 18(9.6%) with DM. Compared with patients without CHD, those with CHD had higher prevalence of HTN (40.4 vs. 22.5%, P=0.008) and T2DM (14.1 vs. 4.5%, P=0.025). Patients with CHD had higher TC (4.52 vs. 4.02 mmol/L, P=0.001), LDL (2.74 vs. 2.59 mmol/L, P=0.013), and TG (1.65 vs. 1.43 mmol/L, P=0.034) levels. The methylated levels of 4 sites in LIMA1, 1 site in NPC1L1, and 4 sites in Numb, respectively, were higher in CHD group than the control group. Compared with control subjects, patients with CHD had higher methylation levels of Numb (P=0.024). After adjustment of male, age, smoking, drinking, hypertension, diabetes, TG, TC, HDL-C and LDL-C, NUMB methylation levels were still associated with CHD (P=0.003, OR=0.260, 95% CI: 0.154–0.568).

CONCLUSIONS Our study showed that Numb methylation may be associated with the development of CHD, and high methylation of Numb gene may be a risk factor for CHD. Patients with higher methylation levels in Numb may have increased risks for CHD. Because our study was an observational study, further studies on the specific mechanisms of this relationship are needed.

GW31-e1154

Genetic polymorphism of IDOL gene was associated with the susceptibility of coronary artery disease in Han population in Xinjiang, China

Dilare Adi, Jialin Abuzhalihan, Yi Tong Ma
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, P.R. China

OBJECTIVES IDOL (inducible degrader of LDLR), also known as MYLIP, is an E3 ubiquitin ligase. It can stimulate the ubiquitination and degradation of the LDLR in the lysosome by interacting with its cytoplasmic domain. In this study, we aimed to explore whether some genetic variants of the IDOL gene were associated with CAD among Chinese population in Xinjiang.

METHODS We designed two independent case-control studies. The first one included in the Han population (448 CAD patients and 343 controls), and the second one is the Uygur population (304 CAD patients and 318 controls). SNP genotyping was performed based on the iMLDR (improved multiplex ligation detection reaction). We genotyped three SNPs (rs2072783, rs2205796, and rs909562) of the IDOL gene. Analyses were carried out using SPSS version 22.0 (SPSS, Chicago, IL). All data were assessed for normality (Kolmogorov-Smirnov test) and equal variance tests. A P value <0.05 was considered to be statistically significant.

RESULTS The genotype distributions of these SNPs met the Hardy-Weinberg equilibrium balance (all P>0.05). Our results showed that, in Han population, the differences in SNP rs2072783 between CAD patients and control subjects were not significant. However, there were significant differences in dominant model (TT vs. GG+GT) and overdominant model (GG+TT vs. GT) of SNP rs2205796 CAD between the two groups (P=0.048 and P=0.029; Table 2). Meanwhile, the dominant model (AA vs. GG+GA) of the rs909562 SNP was significantly different in two groups (P=0.032). Nevertheless, the three SNPs distribution did not show differences in Uygur population. According to the results of the multivariate adjustments for the confounders in Han population, the rs2205796 SNP is an independent risk factor for CAD [TT vs. GG/GT: odds ratio=0.834, 95% confidence interval=0.701–0.993, P=0.042]. Whereas after adjustment for other confounders, rs2072783 and rs909562 SNPs are not the independent risk factors for CAD (P=0.698 and P=0.098). The three SNPs do not represent the independent risk factors for CAD in Uygur population (all P>0.05).

CONCLUSIONS The rs2205796 polymorphism of the IDOL gene is associated with CAD in the Chinese Han population. Subjects with GG/GT genotype or G allele of rs2205796 were related to an increased risk of CAD.

GW31-e1157

Genetic polymorphisms of RNF145 gene are associated with the coronary artery disease in Han and Uygur population in Xinjiang, China

Jing Ming, Yi Tong Ma
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, P.R. China

OBJECTIVES Coronary artery disease (CAD) is a multifactorial disease. In this study, we used Xinjiang Han and Uygur populations as the research objects to screen and study the correlation between the genetic polymorphism of the RNF145 gene and CAD.

METHODS We designed two independent case-control studies. The first one included in the Han population (508 CAD patients and 512 controls), and the second one is the Uygur population (410 CAD patients and 330 controls). We used the modified multiple connection detection response (iMLDR) technology to label three SNPs (rs17056583, rs12188266, rs7732603) of RNF145 genotyping.

RESULTS In Uygur group and Han group, for three genotypes of three SNPs, we discovered that there was a difference between CAD and controls in the dominant model, recessive model, and additive model (All P<0.05). The recessive model (GC+GG vs. CC) of rs17056583 and rs7732603 CC genotype remain significantly associated with CAD after adjustment for confounders (OR=1.506, 95% CI=1.319–1.779, P=0.025; OR=1.782, 95% CI=1.636–2.027, P=0.032).

CONCLUSIONS The three SNPs of the RNF145 gene are associated with CAD in the Chinese Han and Uygur population.

GW31-e1194

Crocin, a novel broad-spectrum MMPs inhibitor screened by AI, attenuates thoracic aortic aneurysm/dissection in mice

Feiran Qi[1], Yanzhenzi Zhang[1], Ke Xu[1], Huinan Zhao[1], Yan Liu[1], Jianxin Chen[2], Yulin Li[1], Jie Du[1]
[1]Beijing Anzhen Hospital of Capital Medical University and Beijing Institute of Heart Lung and Blood Vessel Diseases
[2]Beijing University of Chinese Medicine

OBJECTIVES Thoracic aortic aneurysms and dissections (TAAD) are highly lethal diseases without effective drug therapeutic strategies. Multiple previous studies in animals and humans indicated a major role of matrix metalloproteinases (MMPs) in TAAD pathogenesis, but clinical trials of MMPs inhibitors for aneurysms all had negative results, which might result from the disadvantages of synthetic compounds. By using an artificial intelligence technology, we discovered that Crocin, a small molecule compound from herbal drug saffron crocus, is a novel MMPs inhibitor. And then we used a mouse model to investigate whether Crocin could attenuate TAAD progression.

METHODS We used surflex-Dock technology to select potential MMP inhibitors from natural products. The effect of crocin on MMPs activity was evaluated by generic MMPs activity kit, gelatin zymography and transwell tumour invasion assay. Biofilm interference technique (BLI) was used to indicate the possible way of interaction between crocin and MMPs. TAAD mouse model was established by 3-aminopropionitrile (BAPN) treatment (1 g/kg d) for 28 days in C57BL/6 mice. Crocin (50 mg/kg d, 80 mg/kg d) was given by intraperitoneal injection from the first day or the 14th day of BAPN treatment to the end of experiments. Aortic structure was evaluated by elastic tissue stain and situ MMPs activity on the aorta wall was detected by the Gelatinase/Collagenase Assay Kit.

RESULTS Crocin was estimated to have a high structural compatibility with MMP1, MMP2, MMP3, MMP10 and MMP14. Then we found crocin inhibited the activity of generic MMPs in Hep G2 cells and remarkably reduced the invasion amount of SL4 tumor cells. The result of BLI showed that crocin had a high affinity for MMP2 on the structure. It also inhibited the activity but not the mRNA or protein expression of MMP2 in HepG2 cells. Furthermore, we observed that either 28 days or 14 days of crocin treatment could suppress TAAD occurrence and rupture. Meanwhile, crocin significantly decreased aortic diameter, ameliorated integrity of vascular structure, inhibited elastin fragmentation and MMPs activity on the aorta wall.

CONCLUSIONS These results indicate that Crocin was a novel broad-spectrum MMPs inhibitor and attenuated TAAD progression in a mouse model, which demonstrated that Crocin was a promising agent for the pharmacological treatment of TAAD.

GW31-e1231

FNDC5/irisin attenuates diabetic cardiomyopathy in a type 2 diabetes mouse model by reducing oxidative/nitrosative stress

Chen Lin, Yongzhen Guo, Yunlong Xia, Wenjun Yan, Ling Tao
Department of Cardiology, Xijing Hospital, the Fourth Military Medical University, Xi'an, Shaanxi, China

OBJECTIVES Irisin, the cleaved protein of fibronectin type III domain containing 5 (FNDC5), plays a regulatory role in metabolism and inflammation. Recent findings indicate that irisin is involved in cardiovascular physiology and pathology. In the present study, we investigated the effect of FNDC5/irisin on diabetic cardiomyopathy (DCM) in type 2 diabetes mellitus (T2DM) model, db/db mice.

METHODS Myocardial FNDC5 overexpression in 16-week-old db/db mice was achieved by intramyocardial injection of adenovirus encoding FNDC5. Sixteen-week-old db/db mice received recombinant human irisin administration through peritoneal implant osmotic pumps for 4 weeks. Systemic insulin resistance was evaluated by glucose tolerance test. Cardiac diastolic function was evaluated by Doppler echocardiography. Systolic function was assessed by M-mode echocardiography. Left ventricular tissue was collected for histology and gene/protein expression analysis. Cardiac mitochondria and ultrastructure were evaluated by transmission electron microscope. Primary cardiomyocytes or H9C2 cells were treated with high glucose (25 mM)/high fat (palmitate, 300 μM) with or without irisin (1000 ng/mL) for 24 hours. DHE staining and DHR-123 staining were used to detect reactive oxygen species (ROS) and $ONOO^-$, respectively. JC-1 staining was applied to evaluate mitochondrial membrane potential. Expression of 3-nitrotyrosine was measured by western blot to evaluate nitrosative damage in different groups of cells.

RESULTS Compared with db/+ hearts, db/db hearts showed decreased FNDC5 level and exhibited normal cardiac systolic function but impaired diastolic function with adverse structural remodeling, including increased myocardial fibrosis, cardiac hypertrophy and myocardial apoptosis. As compared to db/+ hearts, db/db hearts showed excessive mitochondrial fission and abnormal mitochondrial morphology. Both myocardial FNDC5 overexpression or exogenous irisin administration markedly attenuated cardiac diastolic dysfunction and structural remodeling observed in db/db hearts. The mRNA and protein expression of FNDC5 were significantly decreased in high glucose/high fat treated primary cardiomyocytes and H9C2 cells as compared with control groups. Oxidative/nitrosative stress was evident in high glucose/high fat treated H9C2 cells, as evidenced by elevated iNOS, NOX2, 3-nitrotyrosine, ROS and $ONOO^-$ levels. Irisin alleviated oxidative/nitrosative stress induced by high glucose/high fat treatment. Moreover, mitochondria membrane potential ($\Delta\Psi m$) was decreased and cytochrome C was released from mitochondria with increased caspase-3 activities in high glucose/high fat treated H9C2 cells, indicating the presence of mitochondrial dependent apoptosis. Irisin treatment partly reversed the mitochondrial dependent apoptosis in high glucose/high fat treated H9C2 cells.

CONCLUSIONS Our data demonstrate that FNDC5/irisin exerts a cardioprotective role in diabetic cardiomyopathy in T2DM by alleviating insulin resistance, inhibiting myocardial apoptosis, myocardial fibrosis, and cardiac hypertrophy. FNDC5/irisin restored the diastolic function in T2DM. The attenuation of oxidative/nitrosative stress and apoptosis may be the possible mechanism involved in the process. These findings suggest that FNDC5/irisin may be a potential therapeutic intervention for DCM, especially in type 2 diabetes mellitus.

GW31-e1276

Association between thioredoxin and baroreflex sensitivity in hypertensive rats

Ruiyu Wang, Jing Huang
Department of Cardiology, The Second Affiliated Hospital of Chongqing Medical University

OBJECTIVES Baroreflex sensitivity (BRS) is impaired in patients with hypertension and is closely related to the increased oxidative stress that occurs in hypertension. As a major redox protein, thioredoxin (TRX) exerts regulatory effects on vascular biology by maintaining redox homeostasis in many cardiovascular diseases. However, the potential association between TRX and BRS under hypertension conditions is currently unknown.

METHODS We evaluated hemodynamic indexes, including pulse arterial pressure (PAP), mean blood pressure (MBP), heart rate (HR), heart rate variability (HRV), and cardiac BRS index in the two-kidney one-clip (2K1C) hypertensive rat model. Several representative biomarkers of oxidative stress and TRX system-related proteins were also evaluated. Additionally, the quantitative expression of TRX in carotid artery homogenates and plasma was detected, and the correlations among TRX, BRS and MBP were identified by regression analyses.

RESULTS BRS was considerably impaired in hypertensive rats, in association with a systemic and vascular oxidative imbalance. In addition, a dysfunctional vascular TRX redox system was observed in hypertensive rats. Additionally, the expression and distribution of TRX protein around the carotid sinus was significantly downregulated in hypertensive rats. The regression analysis showed that the protein level of TRX in the carotid artery homogenates was positively correlated with cardiac BRS index in all rats ($|r|=0.69$, $P<0.001$), and negatively correlated with MBP in hypertensive rats ($r=-0.43$, $P<0.05$).

CONCLUSIONS TRX is closely related to BRS, and TRX may serve as a potential regulatory protein in attempts to control blood pressure through baroreflex modulation.

CLINICAL RESEARCH ON CARDIOVASCULAR DISEASES

CORONARY HEART DISEASE

GW31-e0020

Does on-treatment platelet reactivity impact long-term prognosis in patients with acute coronary syndrome and thrombocytopenia who underwent percutaneous coronary intervention?

Ru Liu[1], Tianyu Li[1], Deshan Yuan[1], Yan Chen[1], Xiaofang Tang[1], Lijian Gao[1], Ce Zhang[1], Sida Jia[1], Pei Zhu[1], Ou Xu[2], Runlin Gao[1], Bo Xu[1], Jinqing Yuan[1]
[1]Fuwai Hospital, Chinese Academy of Medical Sciences
[2]Department of Pulmonary Vascular and General Medicine, Fuwai Yunnan Cardiovascular Hospital

OBJECTIVES This study analyzed the association between on-treatment platelet reactivity and long-term outcomes of patients with acute coronary syndrome (ACS) and thrombocytopenia (TP) in the real world.

METHODS A total of 10,724 consecutive cases with coronary artery disease who underwent percutaneous coronary intervention (PCI) were collected from January to December 2013. Cases with ACS and TP under dual anti-platelet therapy were enrolled from the total cohort. Five-year clinical outcomes were evaluated among cases with high on-treatment platelet reactivity (HTPR), low on-treatment platelet reactivity (LTPR) and normal on-treatment platelet reactivity (NTPR), tested by thromboelastogram (TEG).

RESULTS Cases with HTPR, LTPR and NTPR accounted for 26.2, 34.4 and 39.5%, respectively. Cases with HTPR were presented with the most male sex, lowest hemoglobin level, highest erythrocyte sedimentation rate and most LM or three-vessel disease, compared with the other two groups. The rates of 5-year all-cause death, major adverse cardiovascular and cerebrovascular events (MACCE), cardiac death, myocardial infarction (MI), revascularization, stroke and bleeding were all not significantly different among three groups. Multivariable Cox regression indicated that, compared with cases with NTPR, cases with HTPR were not independently associated with all endpoints, as well as cases with LTPR (all P>0.05).

CONCLUSIONS In patients with ACS and TP undergoing PCI, 5-year all-cause death, MACCE, MI, revascularization, stroke and bleeding risk were all similar between cases with HTPR and cases with NTPR, tested by TEG, in the real world. The comparison result was the same between cases with LTPR and cases with NTPR.

GW31-e0021

Effect of baseline thrombocytopenia on ischemic outcomes in patients with acute ST-segment elevated myocardial infarction: a large propensity score matching analysis from CAMI Registry

Ru Liu[1], Yang Hu[2], Jingang Yang[1], Qingsheng Wang[3], Hongmei Yang[3], Zhifang Wang[4], Shuhong Su[4], Jinqing Yuan[1], Yuejin Yang[1]
[1]Department of Cardiology, Fuwai Hospital, Chinese Academy of Medical Sciences
[2]Statistics Medical Research and Biometrics Center, Fuwai Hospital, Chinese Academy of Medical Sciences
[3]Department of Cardiology, The First Hospital of Qinhuangdao City
[4]Department of Cardiology, The Central Hospital of Xinxiang

OBJECTIVES This study analyzed the association of baseline thrombocytopenia (TP) with long-term outcomes of patients with acute ST-segment elevated myocardial infarction (STEMI).

METHODS A total of 16,957 consecutive cases with STEMI from multiple centers that participated in the China Acute Myocardial Infarction registry was included. Two-year clinical outcomes were evaluated between patients with TP and those with a normal platelet count. Possible confounders in baseline were adjusted in multivariable Cox regression. A propensity score matching (PSM) analysis was applied to control baseline differences.

RESULTS Cases coexisting with baseline TP accounted for 2.1%, and cases with moderate or severe TP accounted for 0.3%. The rates of 2-year all-cause death and major adverse cardiovascular and cerebrovascular events (MACCE) were significantly higher in cases with TP (21.4 and 11.4%, P<0.001; 23.6 and 13.9%, P<0.001), compared with those with a normal platelet count. After multivariate adjustment, compared with cases with a normal platelet count, cases with TP was independently associated with 2-year all-cause death (HR: 1.28; 95% CI: 1.02–1.60; P=0.037). After PSM, the rates of 2-year all-cause death and MACCE were significantly higher in cases with TP (20.5 and 14.0%, P=0.022; 22.8 and 16.0%, P=0.021), compared with those with a normal platelet count. Kaplan-Meier survival curves before and after PSM revealed the consistent results. Multivariable Cox regression after PSM showed baseline TP was an independent predictor of all-cause death (HR: 1.59; 95% CI: 1.11–2.29; P=0.013) and MACCE (HR: 1.51; 95% CI: 1.07–2.13; P=0.019).

CONCLUSIONS Baseline TP was an independent predictor of long-term ischemic outcomes in patients with STEMI.

GW31-e0035

Prognostic value of quantitative flow ratio measured immediately after drug-coated balloon angioplasty for in-stent restenosis

Xiaoqing Cai[1,2], Feng Tian[1], Jing Jing[1], Yundai Chen[1]
[1]Department of Cardiology, The First Medical Center of PLA General Hospital, Beijing, China
[2]Department of Cardiology, The 940th Hospital of Joint Logistics Support Force of PLA, Lanzhou, China

OBJECTIVES The study aimed to scientifically evaluate the risk factors of recurrent restenosis after drug-coated balloon (DCB) angioplasty for drug-eluting stent (DES) restenosis among patients enrolled in the RESTORE ISR China randomized trial.

METHODS Patients undergoing the RESTORE ISR China randomized trial with the follow-up angiography were enrolled and classified into the recurrent restenosis group and the non-recurrent restenosis group. The binary classifications followed the QCA standards of in-stent restenosis (ISR): diameter stenosis ≥50% in the in-segment area at follow-up angiography as recurrent restenosis. Clinical and angiographic characteristics of these two groups were analyzed, and the QFR value both before lesion preparation and after final DCB angioplasty were also measured and compared.

RESULTS Two hundred and twenty-six lesions in 208 patients with a follow-up angiography at 9 months were enrolled. Recurrent restenosis was detected in 43 patients (20.7%) and in 49 lesions (21.7%). QFR value after DCB angioplasty (odds ratio [OR] 0.88; 95% confidence interval [CI] 0.83–0.93; P<0.0001 for 0.01 increase), lesion length (OR: 1.08; 95% CI: 1.01–1.15; P=0.017 for 1 mm increase), and vessel diameter (OR: 0.35; 95% CI: 0.13–0.89; P=0.027 for 1 mm increase) were independently associated with recurrent restenosis after DCB angioplasty.

CONCLUSIONS QFR value after DCB angioplasty, lesion length and vessel caliber were independent risk factors of recurrent restenosis after DCB angioplasty. Furthermore, QFR value after DCB angioplasty was a novel and promising predictor in evaluating prognosis after DCB angioplasty of DES ISR.

GW31-e0037

The association of lipoprotein (a) and coronary atherosclerotic burden and all-cause mortality in STEMI patients treated with primary PCI

Yuzhou Xue, Jian Shen, Zhou Wei, Xiang Li, Jing Xiang, Zhenxian Xiang, Yuansong Zhu, Haonan Yang, Suxin Luo
The First Affiliated Hospital of Chongqing Medical University

OBJECTIVES Coronary atherosclerotic burden in patients with ST-segment elevation myocardial infarction (STEMI) is recognized as the main predictor of prognosis. However, the association of lipoprotein (a) [Lp(a)] with atherosclerotic burden is uncertain for patients with STEMI.

METHODS Patients with STEMI were continuously enrolled in our study. Multivariate logistic regression analysis was used to assess the relationship between Lp(a) and atherosclerotic burden after adjusted for traditional cardiovascular risk factors. Generalized additive model and restricted cubic spline analyses were employed to visualize the association of Lp(a) with Gensini score and no-reflow phenomena respectively. Kaplan-Meier curve was conducted to explore whether Lp(a) is a predictor of long-term follow up.

RESULTS One thousand and three hundred and fifty-nine patients underwent PCI for STEMI were ultimately included in our study. Patients in the highest tertile of Lp(a) group had increased incidence of acute kidney injury and heart failure during hospitalization. Furthermore, patients with high levels of Lp(a) (>19.1 mg/dL) had sharply increased risk for higher Gensini score ($P_{for\ trend}$=0.03) and no-reflow phenomena ($P_{for\ trend}$=0.002) after adjusted. During a median follow up of 930 (interquartile range: 579–1243) days, 132 deaths (9.95%) were registered. Patients with high values of Lp(a) (>19.1 mg/dL) had the worst long-term prognosis ($P_{for\ trend}$<0.0001). In the subgroup analysis, the patients with high Lp(a) still had the highest all-cause mortality.

CONCLUSIONS This was a new finding that Lp(a) was independently associated with coronary atherosclerotic lesions and prognosis in STEMI patients treated with PCI.

Clinical Trial Registration: identifier ChiCTR1900028516 (http://www.chictr.org.cn/index.aspx).

GW31-e0038

The association of thyroid hormones with cardiogenic shock and prognosis in ST segment elevation myocardial infarction (STEMI) patients treated with primary PCI

Yuzhou Xue, Yuansong Zhu, Jian Shen, Wei Zhou, Jing Xiang, Zhenxian Xiang, Linbang Wang, Suxin Luo
The First Affiliated Hospital of Chongqing Medical University

OBJECTIVES Cardiogenic shock (CS) is the leading cause of the death in patients with ST elevation myocardial infarction (STEMI). Thyroid dysfunction is related to prognosis of patients with myocardial infarction. Hence, the aim of this study is to explore the relationship between thyroid hormones (free triiodothyronine [FT3] and free thyroxine [FT4]) and CS.

METHODS One thousand two hundred and seventy STEMI patients treated with percutaneous coronary intervention (PCI) were consecutively enrolled in our study. Patients were classified into two groups depend on with or without CS during hospitalization. Stepwise multivariate logistic analysis was conducted to investigate the association of thyroid hormones with CS. Restricted cubic spline method was employed to further explore relationship between CS and thyroid hormones.

RESULTS Patients who developed CS (n=103) had lower FT3 and higher FT4 on admission. The stepwise logistic analysis showed both FT3 (P=0.038) and FT4 (P=0.024) were independently related to CS. Restricted cubic splines indicated that lower FT3 (<2.25 pg/mL) or higher FT4 (>1.25 ng/dL) was correlated with higher prevalence of CS. Over 2.5 years follow-up, patients (n=294) with low FT3 (<2.85 pg/mL) and high FT4 (>=0.88 ng/dL) had the highest all-cause mortality (18.2%), whereas patients (n=293) with high FT3 and low FT4 had the lowest all-cause mortality (3.8%) ($P_{for\ trend}$<0.0001).

CONCLUSIONS Both FT3 and FT4 are independently associated with in-hospital CS development in STEMI patients treated with PCI. Patients with lower range of FT3 and upper range of FT4 had the worst outcomes in a long-term follow-up.

Clinical Trial Registration: identifier: ChiCTR1900028516 (http://www.chictr.org.cn).

GW31-e0046

Establishment and validation of a prognostic nomogram for critically ill myocardial infarction patients

Qi Guo[1,2], Maoxiong Wu[1,2], Hongwei Li[1,2], Huijun Ouyang[1,2], Runlu Sun[1,2], Junjie Wang[1,2], Zhijian He[1,2], Yuling Zhang[1,2], Jingfeng Wang[1,2]
[1]Department of Cardiology, Sun Yat-sen Memorial Hospital of Sun Yat-sen University, Guangzhou, China
[2]Guangdong Province Key Laboratory of Arrhythmia and Electrophysiology, Guangzhou, China

OBJECTIVES Myocardial infarction (MI) is a leading cause of mortality worldwide, and prognostic prediction is critical for identifying high-risk patients and making decisions regarding treatment. We aimed to develop and validate a prognostic nomogram in order to improve the prediction of survival of critically ill MI patients.

METHODS Critically ill patients with MI were identified from the Medical Information Mart for Intensive Care (MIMIC)-III database. Factors included in the nomogram were determined by univariate and multiple Cox proportional hazard analyses based on the primary cohort. The receiver operating characteristic (ROC) and calibration curves were used to assess the predictive accuracy and discriminative ability of the nomogram. The clinical utility of the nomogram was evaluated using decision curve analysis (DCA) and survival curve analysis in an independent validation cohort.

RESULTS Independent prognostic factors, including age, heart rate, white blood cell count (WBC), blood urea nitrogen (BUN) level, and bicarbonate level, were identified and used in the nomogram. Good agreement between the prediction by the nomogram and the actual observation was indicated by the calibration curve for 30-day survival. In the primary cohort, the area under the ROC curve [AUC, 95% confidence interval (CI)] and the C-index (95% CI) were 0.803 (0.771–0.835) and 0.787 (0.757–0.817), respectively. In the validation cohort, the nomogram still exhibited excellent discrimination [AUC (95% CI), 0.765 (0.716–0.814)] and good calibration [C-index (95% CI), 0.758 (0.712–0.804)]. DCA demonstrated that the nomogram was clinically beneficial. Additionally, participants could be classified into two risk groups (low and high) by the nomogram, and the 30-day survival probability was significantly different between these groups (P<0.001).

CONCLUSIONS This 5-factor nomogram can accurately predict 30-day survival in critically ill MI patients and might be helpful for risk stratification and decision making for MI patients undergoing clinical treatment.

GW31-e0047

The association between heart rate fluctuation and mortality in critically ill myocardial infarction patients: a retrospective cohort study

Qi Guo[1,2], Hongwei Li[1,2], Huijun Ouyang[1,2], Runlu Sun[1,2], Junjie Wang[1,2], Maoxiong Wu[1,2], Yue Pan[1,2], Jingfeng Wang[1,2], Yuling Zhang[1,2]
[1]Department of Cardiology, Sun Yat-sen Memorial Hospital of Sun Yat-sen University
[2]Guangdong Province Key Laboratory of Arrhythmia and Electrophysiology, Guangzhou, China

OBJECTIVES Whether heart rate (HR) fluctuation after admission has an impact on the outcomes of critically ill myocardial infarction (MI) patients remains unknown.

METHODS A total of 2031 MI patients were enrolled from the Medical Information Mart for Intensive Care (MIMIC-III) database. HR fluctuation was calculated as the maximum HR minus the minimum HR in the initial 24 hours after admission. Participants were divided into 3 groups, namely, low HR fluctuation (<30 beats per minute (bpm)), medium HR fluctuation (30–49 bpm), and high HR fluctuation (≥50 bpm). The main outcomes were 30-day and 1-year mortality. Cox regression and restricted cubic spline model were used.

RESULTS Each 10-bpm increase in HR fluctuation was associated with a higher risk of 30-day mortality and 1-year mortality, with hazard ratios of 1.214 (95% CI, 1.179–1.250) and 1.193 (95% CI, 1.164–1.222), respectively. Compared with the low HR fluctuation group, the high HR fluctuation group suffered a significantly higher risk of mortality after adjustment, with hazard ratios of 1.858 (95% CI, 1.277–2.701) for 30-day mortality and 1.620 (95% CI, 1.221–2.151) for 1-year mortality. A typical J-type curve was observed in restricted cubic splines for the association between HR fluctuation and 30-day or 1-year mortality of MI patients, with the lowest risk on the HR fluctuation of 30 bpm. Sensitivity analyses emphasized the robustness of our results.

CONCLUSIONS This retrospective cohort study revealed an independent positive association between HR fluctuation and 30-day and 1-year mortality in critically ill MI patients, which warrants further investigation.

GW31-e0051

Association of thrombocytopenia and infection in patients with acute myocardial infarction undergoing percutaneous coronary intervention

Litao Wang[1,2], Yining Dai[2], Jiyan Chen[2], Ling Xue[2], Pengcheng He[1,2], Yuanhui Liu[2], Ning Tan[1,2]
[1]Guangdong Provincial People's Hospital, School of Medicine, South China University of Technology, Guangzhou, China
[2]Department of Cardiology, Guangdong Cardiovascular Institute, Guangdong Provincial Key Laboratory of Coronary Heart Disease Prevention, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China

OBJECTIVES Thrombocytopenia has been reported to be associated with several adverse events, however, there is little data on the prognostic value of thrombocytopenia for infection in patients with acute myocardial infarction (AMI) undergoing percutaneous coronary intervention (PCI). We evaluated the association between thrombocytopenia and infection in such patients.

METHODS A total of 1401 consecutively admitted AMI patients treated with PCI were enrolled between January 2010 and June 2016, with a median follow-up of 2.85 years. All patients were divided into two groups according to the presence (n=186) or absence (n=1215) of thrombocytopenia based on the platelet counts at admission. The primary endpoint was the development of infection during hospitalization, and the major adverse clinical events (MACE) and all-cause death were considered as secondary endpoints.

RESULTS During hospitalization, 186 (13.3%) patients with AMI following PCI were diagnosed with thrombocytopenia (platelet count <150×10^9/L) in our study. The prevalence of in-hospital infection was significantly higher in the thrombocytopenic group (30.6 versus 16.2%, P<0.001) compared to non-thrombocytopenia group. Similarly, the incidences of in-hospital MACE (30.1 versus 16.4%, P<0.001) and in-hospital death (8.1 versus 3.8%, P=0.008) revealed an increased trend among thrombocytopenia patients. The multivariate analysis indicated that thrombocytopenia was independently associated with in-hospital infection (odds ratio (OR), 2.09; 95% confidence interval (CI), 1.32–3.27; P=0.001). Similar consequences were detected in MACE (OR, 1.92; 95% CI, 1.27–2.87; P=0.002) but not all cause death (OR, 1.87; 95% CI, 0.88–3.78; P=0.091). After follow up with a median time of 2.85 years, patients with thrombocytopenia were not associated with all-cause death (adjusted hazard ratio (HR)=1.19, 95% CI, 0.80–1.77, P=0.383).

CONCLUSIONS Thrombocytopenia, as a common symptom in patients with AMI undergoing PCI, is significantly correlated with infection and in-hospital MACE, and may be used as a prognostic tool in these patients.

GW31-e0053

Management strategies and long-term clinical outcomes of patients with coronary chronic total occlusions

Lei Guo, Lei Zhong, Jian Wu, Haichen Lv, Huaiyu Ding, Jiaying Xu, Rongchong Huang
First Affiliated Hospital of Dalian Medical University

OBJECTIVES Limited data exist regarding the clinical outcomes of the three potential therapeutic strategies of percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), and medical therapy (MT). The aim of this study was to compare the clinical outcomes of coronary chronic total occlusion (CTO) patients according to the initial treatment strategy.

METHODS Consecutive patients with at least one coronary CTO were included and categorized as managed either by PCI, CABG, or MT. Propensity-score matching was also performed to adjust for baseline characteristics. The primary outcome was a major adverse cardiac event (MACE), including cardiac death, myocardial infarction, and target vessel revascularization.

RESULTS A total of 1655 patients with 1944 CTOs were enrolled in this study. A CTO was treated by MT in 800 (48.3%) patients and PCI in 734 (44.4%), while 121 (7.3%) underwent CABG. The median overall follow-up duration was 3.6 years. Patients referred for MT had a higher incidence of MACE (28.0 vs. 17.3 and 12.4%, respectively; all P<0.001) than those managed by PCI and CABG. After propensity-score matching analysis, the rate of PCI was lower than that of MACE (19.2 vs. 28.9%, HR=0.62, 95% CI=0.45–0.85, P=0.003) when compared with MT. 286 matched pairs of patients were created for patients undergoing successful PCI or MT. There was no significant difference in the prevalence of MACE (HR 0.76, 95% CI=0.53–1.09, P=0.130) or cardiac death (HR 0.51, 95% CI=0.23–1.15, P=0.104) between the successful PCI and MT groups.

CONCLUSIONS As an initial management strategy for patients with CTOs, PCI or CABG reduced the risk of MACE, as compared with MT alone on follow-up.

GW31-e0062

Validation of DAPT score for dual antiplatelet therapy in patients with coronary chronic total occlusion

Yuhong Peng, Leisheng Ru, Haoliang Li, YuYing Zhao, XiaoYing Guo, Yanzhuo Ma
The 980th Hospital of the PLA Joint Logistics Support Force

OBJECTIVES To validate the use of DAPT score for dual antiplatelet therapy in patients with chronic total occlusion (CTO) after percutaneous coronary intervention.

METHODS Patients with CTO who underwent PCI with stent placement and were treated with DAPT for 12 months or prolonged to 12–58 months. The incidence of major cardiovascular and cerebrovascular events (MACCE) and bleeding were valued.

RESULTS A total of 504 patients with CTO who underwent PCI with stent placement were included in the final analysis, median follow-up 34 (28, 44) months. In patients with a DAPT score ≥2, the incidence of MACCE was significantly lower in prolonged group compared with standard group (5.5 vs. 14%, P=0.040). Kaplan-Meier analysis showed that the prolonged group had lower MACCE-free survival rate compared with the standard group (P=0.046). The incidences of cardiac death and target vessel revascularization were significantly lower than standard treatment group (1.8 vs. 8.6%, P=0.046; 1.8 vs. 8.6%, P=0.046, respectively). In patients with a DAPT score <2 points, there was no significant difference in the incidence of MACCE between the two groups. But bleeding events were significantly lower in the standard treatment group than in the prolonged DAPT group (3.4 vs. 12.8%, P=0.018). Kaplan-Meier analysis showed that there was a lower bleeding survival rate in the standard treatment group according to BARC criteria (type 2, 3 or 5) (P=0.034).

CONCLUSIONS DAPT score can be used for dual antiplatelet therapy in patients with CTO after percutaneous coronary intervention. CTO patients with DAPT ≥2 points after intervention with a higher risk of ischemic events, might benefit from prolonged DAPT, while patients with DAPT <2 points might benefit from standard treatment, with a lower risk of bleeding events.

GW31-e0064

Alkaline phosphatase to albumin ratio as a novel predictor of long-term adverse outcomes in patients with coronary artery disease after undergoing percutaneous coronary intervention: a retrospective cohort study

Xinya Dai[1,2], Yingying Zheng[1,2], Jinying Zhang[1,2]
[1]Department of Cardiology, First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, P.R. China
[2]Key Laboratory of Cardiac Injury and Repair of Henan Province, Zhengzhou, China

OBJECTIVES Alkaline phosphatase (ALP) and albumin (ALB) have been shown to be associated with coronary artery disease (CAD), and it has been reported that alkaline phosphatase to albumin ratio (AAR) is a novel independent predictor for the prognosis of pancreatic ductal adenocarcinoma. However, to our knowledge, the relationship between AAR and long-term adverse outcomes in CAD patients after undergoing percutaneous coronary intervention (PCI) has not been investigated. Therefore, we aim to access the relation between AAR and long-term adverse outcomes in post-PCI patients with CAD.

METHODS Three thousand three hundred and seventy eight post-PCI patients with CAD were enrolled in the retrospective CORFCHD-ZZ study from January 2013 to December 2017. The median duration of follow-up was 37.59 months. The primary endpoint was long-term mortality including all-cause mortality (ACM) and cardiac mortality (CM). The secondary endpoints were major adverse cardiac events (MACEs) and major adverse cardiac and cerebrovascular events (MACCEs).

RESULTS Kaplan-Meier analyses showed that an increased AAR was positively correlated with incidences of long-term ACM (log-rank, P=0.014), CM (log-rank, P=0.011), MACEs (log-rank, P=0.013) and MACCEs (log-rank, P=0.006). Multivariate Cox regression analyses showed that the elevated AAR was an independent predictor of long-term ACM (adjusted HR=1.488 [1.031–2.149], P=0.034), CM (adjusted HR=1.837 [1.141–2.959], P=0.012), MACEs (adjusted HR=1.257 [1.018–1.551], P=0.033) and MACCEs (adjusted HR=1.237 [1.029–1.486], P=0.024).

CONCLUSIONS An elevated AAR is a novel independent predictor of long-term adverse outcomes in CAD patients following PCI.

GW31-e0076

Active retrograde extra backup with a mother-and-child catheter to facilitate retrograde microcatheter collateral channel tracking in recanalization of coronary chronic total occlusion

Yong Wang, Aijie Hou, Bo Luan
The People's Hospital of Liaoning Province

OBJECTIVES Guiding support plays an important role in guidewire and microcatheter coronary channel (CC) tracking in retrograde percutaneous coronary intervention (PCI) therapy for chronic total occlusion (CTO) patients. However, the feasibility and safety of retrograde active use of a mother-and-child catheter are still unclear.

METHODS A total of 271 consecutive CTO patients undergoing retrograde PCI between January 2015 and January 2020 were prospectively analyzed. Clinical data of two groups were compared to explore their feasibility and safety.

RESULTS A total of 271 CTO patients underwent retrograde interventional therapy; 69.0% (187/271) underwent therapy through the septal branch, 31.0% (84/271) through the epicardial collateral channel, and 47.6% (129/271) underwent active retrograde extra backup with a mother-and-child catheter to facilitate retrograde microcatheter collateral channel tracking. The time of wire CC tracking was shorter in the **a**ctive **r**etrograde **b**ackup (ARB) group than in the non-ARB group (25.4±8.5 vs. 26.4±9.7, P=0.348), but there was no significant difference. The time of retrograde microcatheter tracking (10.2±3.8 vs. 15.5±6.8, P=0.012) and time of retrograde approach (62.8±20.3 vs. 70.4±24.3, P=0.026) in the ARB group were significantly shorter than those in the non-ARB group. The radiation dose (223.6±112.7 vs. 295.2±129.3, P=0.028), fluoroscopy time (50.6±21.3 vs. 62.3±32.1, P=0.030), and contrast volume (301.8±146.7 vs. 352.2±179.5, P=0.032) in the ARB group were significantly lower than those in the non-ARB group. There were no serious life-threatening procedural complications in either group. Complications unrelated to ARB included 2 cases of donor vessel dissection, 1 case of CC perforation, and 2 cases of target vessel perforation. There was no statistically significant difference in major adverse cardiac and cerebrovascular events (MACCE) between the groups during hospitalization (P>0.05).

CONCLUSIONS ARB is feasible, safe, and conducive to guidewire and microcatheter coronary channel tracking in recanalization of coronary CTO. It improves the procedural efficiency and is worthy of further promotion.

GW31-e0077

Incidence, predictors, and strategies for failure of retrograde microcatheter tracking after successful wiring of septal collateral channels in chronic total occlusions

Yong Wang, Aijie Hou, Bo Luan
The People's Hospital of Liaoning Province

OBJECTIVES Retrograde microcatheter collateral channel (CC) tracking after successful wiring of septal CC is crucial for retrograde revascularization of coronary chronic total occlusion (CTO). However, the incidence, predictors, and strategies for failure of retrograde microcatheter CC tracking after successful wiring of septal CC remain unclear.

METHODS In total, 298 CTO patients who underwent retrograde septal CC PCI between January 2015 and May 2019 were retrospectively analyzed. Clinical data were compared to investigate predictors for initial microcatheter tracking failure.

RESULTS The initial and final microcatheter tracking success rates were 79.2% (236/298) and 96.6% (288/298), respectively. The procedural success rate was 94.0% (280/298). The RCA to LAD septal ratio (48.4 vs. 33.1%, P=0.037) and CC tortuosity (34.6 vs. 20.8%, P=0.045) were significantly higher in the initial microcatheter CC tracking failure group than in the success group. Multivariate logistic regression analysis revealed that severe collateral tortuosity (OR: 13.241, 95% CI: 3.429–27.057, P=0.038), CC entry angle <90° (OR: 4.921, 95% CI: 1.128–9.997, P=0.002), CC exit angle <90° (OR: 5.037, 95% CI: 2.237–11.182, P=0.004), Finecross MG as initial microcatheter (OR: 1.826, 95% CI: 1.127–3.067, P=0.035), and initial retrograde application of guidezilla (OR: 0.321, 95% CI: 0.267–0.915, P=0.024) were independent predictors of initial microcatheter CC tracking failure in patients with CTO undergoing retrograde septal CC PCI.

CONCLUSIONS The initial microcatheter CC tracking failure was 20.8% in total. Severe collateral tortuosity, CC entry and exit angle <90°, Finecross MG as initial microcatheter, and initial retrograde application of guidezilla were independent predictors of initial microcatheter CC tracking failure in patients with CTO undergoing retrograde septal PCI.

GW31-e0078

Efficacy and safety of standard and low dose ticagrelor versus clopidogrel in east Asian Patients with chronic total occlusion undergoing percutaneous coronary intervention: a single center retrospective study

Yong Wang, Aijie Hou, Bo Luan
The People's Hospital of Liaoning Province

OBJECTIVES Patients with coronary chronic total occlusion (CTO) require effective antiplatelet therapy after percutaneous coronary intervention (PCI). Ticagrelor has more pronounced platelet inhibition than clopidogrel. However, the most appropriate dose of ticagrelor in East Asian populations remains unclear.

METHODS We compared ticagrelor (180 mg loading dose, 90 mg twice daily thereafter and 120 mg loading dose, 60 mg twice daily thereafter) and clopidogrel (300 mg loading dose, 75 mg daily thereafter) for prevention of cardiovascular events in 525 patients with CTO undergoing PCI.

RESULTS The rate of in-hospital major adverse cardiac and cerebral events (MACCE) was not different between the groups. At 1-year follow-up, target vessel revascularization (TVR) in both ticagrelor groups were significantly lower than that in the clopidogrel group (P=0.047); TVR was significantly decreased in 60 mg ticagrelor compared to standard dose clopidogrel (P=0.046). At 1-year follow-up, overall MACCE in both ticagrelor groups were significantly lower than that in the clopidogrel group (P=0.023). Kaplan–Meier analysis showed MACCE-free survival was significantly higher in both ticagrelor groups than in the clopidogrel group (P=0.024). During hospitalization, minor bleeding was significant increased in the 90 mg ticagrelor group (P=0.021). At 1-year follow-up, risk of major and minor bleeding were significantly increased in the 90 mg ticagrelor group.

CONCLUSIONS In East Asian patients with CTO undergoing PCI, 60 mg ticagrelor was as effective as 90 mg, at the same time significantly reduced risk of bleeding.

GW31-e0079

Incidence, predictors, and prognosis of coronary slow flow and no reflow phenomenon in patients with chronic total occlusion who underwent percutaneous coronary intervention

Yong Wang, Aijie Hou, Bo Luan
The People's Hospital of Liaoning Province

OBJECTIVES The incidence and prognosis of coronary slow flow (CSF) and no reflow phenomenon (NRP) in patients with coronary chronic total occlusion (CTO) who underwent percutaneous coronary intervention (PCI) remains unclear.

METHODS We conducted a single-center prospective study to investigate the incidence of CSF/NRP during CTO interventional therapy, determine predictors of CSF/NRP, and evaluate the effect on patient outcomes.

RESULTS In this study, 552 patients with CTO who underwent PCI were included. CSF/NRP occurred in 16.1% of the patients. They had higher incidence rates of diabetes mellitus (53.9 vs. 36.3%, P=0.002) and hypertension (50.6 vs. 37.1%, P=0.018), and a lower incidence rate of retrograde filling of grade >2 (34.8 vs. 47.1%, P=0.036). Patients with CSF/NRP had a higher neutrophil ratio (55.6±19.4 vs. 52.4±18.3, P=0.038) and levels of low-density lipoprotein (LDL; 3.0±0.8 vs. 2.8±0.6, P=0.029), fasting glucose (8.3±1.3 vs. 6.8±1.1, P=0.005), uric acid (332.6±82.9 vs. 308.2±62.8, P=0.045), and high-sensitivity C-reactive protein (Hs-CRP; 9.8±4.8 vs. 7.3±3.9, P=0.036). A multivariate logistic regression analysis revealed that diabetes mellitus (odds ratio [OR], 95% confidence interval [CI]: 1.962, 1.198–2.721, P=0.042), mean platelet volume (MPV; OR: 1.284; 95% CI: 1.108–1.895, P=0.046), LDL cholesterol (LDL-C; OR: 1.383, 95% CI: 1.105–2.491, P=0.036), fasting glucose (FG; OR: 2.095, 95% CI: 1.495–2.899, P=0.018), Hs-CRP (OR: 2.218, 95% CI: 1.556–3.519, P=0.029), and retrograde filling of grade >2 (OR: 0.822, 95% CI: 0.622–0.907, P=0.037) were independent predictors of CSF/NRP in the CTO patients who underwent PCI. Kaplan-Meier analysis revealed that the patients in the CSF/NRP group had a significantly lower cumulative major cardiac and cerebrovascular events (MACCEs)-free survival than those in the non-CSF/NRP group (P<0.0001).

CONCLUSIONS Of the patients with CTO who underwent PCI, 16.1% developed CSF/NRP and they had a significantly lower cumulative MACCE-free survival rate. Diabetes mellitus; higher levels of MPV, LDL-C, FG, and Hs-CRP; and lower incidence of retrograde filling grade >2 were independent predictors of CSF/NRP in CTO patients who underwent PCI and can therefore be used for risk stratification.

GW31-e0097

Cardiopulmonary exercise test in patients with increasing atherosclerotic burden: specific to non-obstructive coronary artery disease

Siyuan Li[1,2], Yifang Yuan[1,2], Ping Zhang[2]
[1]Tsinghua University, School of Clinical Medicine
[2]Beijing Tsinghua Changgung Hospital

OBJECTIVES To compare the differences in cardiopulmonary exercise test (CPET) key variables in healthy participants and patients with increasing atherosclerotic burden, especially non-obstructive coronary artery disease (NOCAD).

METHODS Six-hundred and fourteen symptomatic patients (mean age 60 years old, 42% female) and one-hundred and one healthy volunteers (mean age 37 years old, 58% female) were included and all conducted CPET. Symptomatic patients were divided into NOCAD, obstructive coronary artery disease (OCAD) and acute myocardial infarction (AMI) according to the degree of coronary stenosis on coronary angiography. We compared the differences in CPET key variables among NOCAD, OCAD, AMI and healthy participants.

RESULTS Significant associations were observed between increasing atherosclerotic burden and unfavorable CPET variables, including those related to ischemia (O_2 pulse trajectory), cardiac function (CO, HR, HR/WR, HR exercise/rest ratio), prognosis (VO_2, predicted% VO_2 peak, OUES, VE/VCO_2 slope). NOCAD patients had significantly lower VO_2 AT (β for NOCAD where the healthy as reference, −1.35; 95% CI −2.16 to −0.54), VO_2 peak (β for NOCAD where the healthy as reference, −2.05; 95% CI −3.18 to −0.93), OUES (β for NOCAD where the healthy as reference, −0.24; 95% CI −0.36 to −0.11) in pairwise comparison after adjustment for confounders. NOCAD patients might be associated with higher odds for flattening/downward O_2 pulse trajectory pattern (OR, 3.62; 95% CI, 1.08, 12.17). The association between increasing atherosclerotic burden and unfavorable CPET variables might be stronger in male NOCAD.

CONCLUSIONS Unfavorable CPET variables were associated with increasing atherosclerotic burden. There were associations between NOCAD patients and myocardial ischemia as well as malignant prognosis in CPET. CPET can be a potential tool for early identification and assessment of NOCAD.

GW31-e0102

Predictors and long-term prognosis of left ventricular aneurysm in patients with acute anterior myocardial infarction treated with primary percutaneous coronary intervention in contemporary era

Jieyun You, Liming Gao, Yunli Shen, Xingxu Wang, Qing Wan, Wei Guo, Qi Zhang
Department of Cardiovascular Medicine, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China

OBJECTIVES Left ventricular aneurysm (LVA), as a common complication of acute myocardial infarction (AMI), relates to worse prognosis in patients with AMI. Although primary percutaneous coronary intervention (PCI) has been adopted as the first-line treatment for AMI patients in contemporary era, the predictor and prognosis of LVA in AMI patients treated with primary PCI were still limited, especially in those involved with anterior wall infarction. We aimed to investigate the predictors and prognosis of LVA in patients with acute anterior myocardial infarction treated with primary PCI in contemporary era.

METHODS Altogether 942 consecutive patients with acute anterior myocardial infarction undergoing primary PCI were prospectively enrolled, among which 15.92% were in the LVA group and the rest were in the non-LVA group. The primary endpoint of major adverse cardio-cerebral events (MACCEs) was defined as a composite of cardiac death, cardiogenic shock, target vessel revascularization, and ischemic stroke. Baseline characteristics and 1-year clinical outcomes were compared by Chi-square test, t-test, or Kaplan-Meier survival analysis as appropriate. Multiple logistic regression was applied to predict LVA formation. Receiver operating characteristic (ROC) curves were plotted for the accuracy of the multivariate analysis model.

RESULTS At 1-year clinical follow-up, the primary endpoint of MACCEs was significantly increased in the LVA group than in the non-LVA group (23.33 vs. 7.45%, P<0.01), which was mainly driven by higher incidence of cardiac death (8.00 vs. 2.78%, P<0.01), cardiogenic shock (16.00 vs. 3.03%, P<0.01), target vessel revascularization (5.33 vs. 2.27%, P=0.04), and ischemic stroke (4.00 vs. 1.39%, P=0.03). Longer symptom-to-balloon time [odds ratio (OR): 1.15, 95% confidence interval (CI): 1.10–1.21, P<0.01], increased baseline SYNTAX Score (OR: 1.20, 95% CI: 1.16–1.25, P<0.01) and residual SYNTAX Score (OR: 1.54, 95% CI: 1.37–1.74, P<0.01), impaired left ventricular ejection fraction (OR: 0.89, 95% CI: 0.86–0.93, P<0.01), and persistent ST segment elevation (OR: 1.92, 95% CI: 1.03–3.56, P=0.04) were independent predictors of LVA formation in patients with acute anterior myocardial infarction undergoing primary PCI by multivariate analysis.

CONCLUSIONS In contemporary era, patients with LVA still had worse clinical outcomes. Promote reperfusion response with reduction of symptom-to-balloon time, and achieve complete revascularization may help to prevent LVA and improve the prognosis of patients with acute anterior myocardial infarction treated by primary PCI.

GW31-e0123

Difference in inflammation, atherosclerosis, and platelet activation between coronary artery aneurysm and coronary artery ectasia

Wei Wei, Wang Xingxu, Huang Zhenghao, Luo Yu
Department of Cardiovascular Medicine, East Hospital, Tongji University School of Medicine, Shanghai, China

OBJECTIVES Coronary artery aneurysm (CAA) and coronary artery ectasia (CAE) may be two different types of coronary artery dilatation with unknown etiology. This study aimed to compare the differences between CAA and CAE and to investigate their pathogenesis and the necessity of antiplatelet therapy.

METHODS It was a case-control study. One hundred patients each with confirmed CAA, CAE, and normal coronary artery (NCA) from September 2017 to July 2019 were included. All patients completed examinations of the ankle-brachial index (ABI), pulse wave rate, and carotid ultrasonography; were tested for routine blood, lipid, and immune parameters; and given a routine oral loading dose of antiplatelet drugs before coronary angiography. Blood samples were collected 1 week after the withdrawal of antiplatelet drugs, and vascular inflammatory indexes, platelet activation indexes, thromboelastography, and the platelet aggregation rate were measured. Analysis of variance and the chi-square or Fisher exact test was used in statistical analysis.

RESULTS The mean age and prevalence rate of hypertension were significantly higher in CAA and CAE than in NCA (P<0.05). The perinuclear antineutrophil cytoplasmic antibody (ANCA), endothelial-1, matrix metallopeptidase-9, and tumor necrosis factor-α were significantly higher in CAE than in NCA, while cytoplasmic ANCA was appreciably higher in CAE than in CAA (P<0.05). Myeloperoxidase and growth/differentiation factor-15 were significantly higher in CAE than in CAA and NCA (P<0.05). ABI was significantly lower in CAA and CAE than in NCA (P<0.05), low-density lipoprotein/high-density lipoprotein was significantly higher in CAA than in NCA (P<0.05), and the detection rate of carotid artery thickening was significantly higher in CAA than in CAE and NCA (P<0.05). The Gensini and SYNTAX scores were significantly higher in CAA than in CAE (P<0.05). The percentages of CD62P and PAC-1 were significantly higher in CAA and CAE than in NCA (P<0.05). The arachidonic acid aggregation rate in CAA and adenosine 5′-diphosphate aggregation rate in CAE were significantly higher than in NCA (P<0.05). The values of K and R were significantly lower in CAE than in NCA (P<0.05), and α angle was significantly higher in CAE than in NCA. There were no significant differences in the values of K, α angle, and R between CAA and NCA (P<0.05).

CONCLUSIONS CAE was closely related to inflammation, whereas CAA was closely related to atherosclerosis. Platelet activation was present in both diseases; therefore, antiplatelet therapy is recommended.

GW31-e0125

Plasma branched-chain amino acids level is increased in patients with heart failure with reduced ejection fraction and not associated with long-term survival

Shuai Zhao[2], Qin Wang[1], Chenxiang Li[2], Kun Lian[2]
[1]Department of Pharmacogenomics, Fourth Military Medical University
[2]Department of Cardiology, Xijing Hospital, Fourth Military Medical University

OBJECTIVES Branched-chain amino acids (BCAA) is an important nutrient which can preserve heart function. Previous study reported that BCAA catabolic defect can promote the development of heart failure. However, the role of plasma BCAA in patients with heart failure with reduced ejection fraction (HFrEF) remains largely unknown. The aim of our study is to evaluate the relationship between plasma BCAA level with Chinese HFrEF patients and whether plasma BCAA level is associated with long-term all-cause mortality.

METHODS We conducted a prospective study on a cohort of HFrEF patients (n=168) who was admitted to our hospital and assessed survival at 5 years. Another 107 healthy people who underwent routine physiological examination were selected as control subjects. Plasma BCAA level and other biochemical and clinical parameters were assayed in the studied population. The end-points were adverse cardiac events, including all-cause mortality and re-hospitalization.

RESULTS Plasma BCAA level was significantly increased as well as total adiponectin (total APN) and higher molecular weight adiponectin (HMW APN) (P<0.01) in HFrEF patients. HFrEF patients with myocardial infarction (MI) indicated a significant elevation of plasma BCAA level when compared with HFrEF but not accompanied with MI patients (r=0.164, P=0.033). In all-population, plasma BCAA level correlated with Total APN (r=0.187, P<0.01), HMW APN (r=0.129, P<0.05), left ventricular ejection fractions (LVEF) (r=0.272, P<0.01), N-terminal pro brain natriuretic peptide (NT-proBNP) (r=0.269, P<0.01) and blood uric acid (BUN) (r=0.269, P<0.01). After a follow-up of 5 years, 125 (74.4%) adverse cardiac events occurred, including 84 (50.0%) all-cause mortality and 41 (24.4%) re-hospitalization. Additionally, we observed that plasma BCAA level was not associated with all-cause mortality or adverse cardiac events in HFrEF patients.

CONCLUSIONS Our study finds that plasma BCAA level is increased in HFrEF patients. However, plasma BCAA level is not an independent predictor of long-term all-cause mortality or adverse cardiac events in HFrEF patients.

GW31-e0133

The clinic outcomes of ECMO combined with IABP assisted selective PCI in extremely complex and high-risk coronary heart diseases

Kun Lian, Chenxiang Li
Department of Cardiology, Xijing Hospital, The Forth Military Medical University

OBJECTIVES To evaluate the safety and efficiency of extracorporeal membrane oxygenation (ECMO) combined with intra-aortic balloon counter pulsation (IABP) assisted selective percutaneous coronary intervention (PCI) in extremely complex and high-risk coronary heart diseases.

METHODS Fourty three consecutive patients who underwent ECMO combined with IABP assisted selective PCI were reviewed from May 2018 to February 2020. Detailed baseline clinical, angiography, revascularization and follow-up data were collected.

RESULTS A total of 43 patients including 36 (83.7%) male, with the mean age of (66.89±11.47) years and ejection fraction (EF) of (40.23±12.10)%. Previous myocardial infarction was 19 cases (44.19%), previous PCI was 10 cases (23.26%), previous CABG (Coronary Artery Bypass Grafting) was 2 cases (4.65%). There were 26 patients with left main severe lesions (60.47%), 32 patients with chronic total occlusion lesions (74.42%), 16 patients with severe 3-vessel lesions (37.21%). Coronary perforation and death occurred in 1 cases (2.33%). Overall procedural success was 97.67% and 4 cases performed complete revascularization (9.30%). The average procedure time was (346.8±77.03) min, ECMO assisted time was (7.60±3.91) h and IABP assisted time was (71.2±86.9) h. Additionally, postoperative complications was 5 cases (11.63%) and in-hospital major adverse cardiovascular events (MACE) occurred in 2 cases (4.65%). During a median follow-up of (6.55±5.22) months, 30 d MACE rate was 16.28%; EF was markedly improved (40.50 vs. 48.94%, P=0.031) and NYHA was decreased significantly (P=0.008), 2–13 m MACE-free was 100%.

CONCLUSIONS In highly selected patients ineligible for CABG, ECMO and IABP supported selective PCI can be performed with a promising clinical outcome.

GW31-e0137

Long-term out-come of successful percutaneous coronary intervention in Chinese CTO patients with low LVEF: a single-center-operator analysis

Kun Lian[1], Wei Wang[2], Qin Wang[2], Shuai Zhao[1], Genrui Chen[1], Chengxiang Li[1]
[1]Department of Cardiology, Xijing Hospital, Fourth Military Medical University
[2]Department of Pharmacogenomics, Fourth Military Medical University

OBJECTIVES This study set out to assess the long-term outcome of chronic total occlusion treated with percutaneous coronary intervention (CTO-PCI) in Chinese patients with low left ventricular ejection fraction (LVEF) (<40%).

METHODS Consecutive patients undergoing elective PCI of CTO were included at Xijing Hospital from Jan 2012 to Feb 2018. Patients with acute ST-segment elevation myocardial infarction were excluded. Patients were subdivided into 3 groups: group A (LVEF≥50%), group B (LVEF 40–50%), and group C (LVEF<40%). Detailed baseline clinical, angiography, revascularization and long-term follow-up data were collected. Accordingly, data were analyzed

for long-term outcome and predictors of successful CTO-PCI in patients with low LVEF.

RESULTS A total of 1197 patients (mean 61.92±10.71 years of age, 83.88% men) underwent CTO PCI attempts. Baseline group C was present in 247 (20.63%) patients. The angiographic success was high (overall 91.9%), but lower in group C (93.84 vs. 94.03 vs. 84.21%, respectively; all P<0.0125). Mean clinical follow-up of 42.25±28.96 months duration was available in 1029 (85.96%) patients including those with group C. The major cardiac events (MACE) was higher in group C when compared with group A (16.41 vs. 30.83%; P<0.001), and all-cause mortality was also higher in group C (11.04 vs. 28.57%; P<0.001). In patients with LVEF<40%, cardiac function improved significantly (P<0.001) after a successful PCI. Further, the independent risk factors of MACE in successful revascularization patients with LVEF <40 patients were history of diabetes (OR=3.813, 95% CI 1.212–11.993, P=0.022) and using long stent (OR=13.633, 95% CI 2.597–71.565, P=0.002).

CONCLUSIONS PCI could represent an effective revascularization strategy achieving good long-term outcome in CTO patients with low LVEF.

GW31-e0143

Comparison of J-CTO and other competing scores in assessing chronic total occlusion difficulty for recanalization: a systematic review and meta-analysis

Wenjie Zuo, Genshan Ma
Department of Cardiology, Zhongda Hospital, School of Medicine, Southeast University

OBJECTIVES Although the J-CTO score is widely used in grading the complexity of chronic total occlusions (CTOs), there remains uncertainty regarding its comparative performance with other predictive scores.

METHODS We searched PubMed, EMBASE, and Cochrane Library systematically for relevant studies reporting diagnostic accuracy of J-CTO from the year 2011 onwards. Estimates of discrimination and calibration would be pooled with a random-effects model if possible. The methodological quality of included studies was assessed using the PROBAST system. When analyzing the relative performance of models, we examined the potential for optimism bias in studies favoring new models and models developed by the same authors.

RESULTS Twenty-one eligible studies (31,410 lesions) and 11 scoring systems were included. The J-CTO score exhibited a strong discriminatory capacity for 30-min wire crossing (pooled C-statistic: 0.76, 95% CI 0.68–0.84) while performing moderately for technical success (0.68, 95% CI 0.61–0.74). Forty-three pairwise comparisons were based on discrimination but only 18 of them (42%) reported a statistical result. Of 23 independent comparisons, the J-CTO score performed better (relative difference >5%) in 10 cases and worse in another 7. However, calibration was inappropriately assessed in most studies, leading to potential risk of bias.

CONCLUSIONS The J-CTO score have useful discrimination in both time-efficient wire crossing and final angiographic success but its validation on calibration needs to be strengthened. To date, there is insufficient evidence supporting the superiority of newly introduced models over the J-CTO score.

GW31-e0166

Prevalence and features of clopidogrel resistance in patients with coronary artery disease after PCI

Baxrom Alyavi, Jamol Uzokov, Akbar Abdullaev
Republican Specialized Scientific and Practical Medical Center of Therapy and Medical Rehabilitation

OBJECTIVES To determine the frequency of development of clopidogrel resistance in patients with coronary heart disease and to identify risk factors for the development of resistance to clopidogrel in patients with coronary heart disease.

METHODS One hundred and twenty patients were enrolled in this study with stable forms of ischemic heart disease who received a standard dose of clopidogrel 75 mg/day for at least a year after PCI. Patients were divided into 3 groups according to the prescription of clopidogrel. Group 1 consisted of patients who did not receive clopidogrel, the second group consisted of patients taking clopidogrel up to 1 year, and the third group consisted of patients taking clopidogrel more than 1 year. An addition, according to the results of determining clopidogrel resistance, patients were divided into 2 groups. Platelet aggregation was measured using a laser analyzer: adenosine diphosphate (ADP) with 1.0 and 5.0 µmol was used. Resistance criterion: ADP ≥72% at 5.0 µmol.

RESULTS 19.0% of patients who took clopidogrel in a standard dose of 75 mg/day were resistant to clopidogrel, and a third of them took clopidogrel for more than a year. According to the results of a study of platelet aggregation activity, the average degree of platelet aggregation with 5.0 µmol of ADP was 81.0% in patients with no reaction to clopidogrel. An inadequate response to clopidogrel was observed more in women and the elderly (55.0 and 68.0%). When analyzing the results of routine laboratory studies in patients with clopidogrel resistance, there was a tendency to higher levels of cholesterol and glucose (P<0.05). Possible risk factors for the development of clopidogrel resistance are hypercholesterolemia and hyperglycemia, since clopidogrel resistance was more common in patients with diabetes (12 out of 18) and obesity (10 out of 19).

CONCLUSIONS Clopidogrel resistant is high in patients with coronary artery disease after PCI, especially on those who suffer from hypercholesterolemia and hyperglycemia with type 2 diabetes mellitus and obesity.

GW31-e0173

Studying the characteristics of CVD risk factors among military personnel

Masimova Aysel[1], Mekhman Mamedov[2]
[1]Central Clinical Hospital of the Armed Forces of Azerbaijan, Baku, Azerbaijan
[2]National Medical Research Center for Therapy and Preventive Medicine of the Ministry of Health, Moscow, Russia

OBJECTIVES To study the behavioral and biological risk factors for CHD among male military personnel.

METHODS The study included 100 men with CHD. Patients were divided into 2 groups according to their social status. Of these, 60 patients were civilians (group I), and the remaining 56 patients (group II) were military personnel. All patients were treated in the cardiovascular department of the Main Hospital of the Armed Forces (Baku, Azerbaijan). The age range was 30–82 years (average age 56±4 years). The following risk factors were studied: smoking, obesity, arterial hypertension, hypercholesterolemia, stress and anxiety/depression.

RESULTS In the study group, the most common risk factor was hypercholesterolemia – 80% (n=93): 46 were military personnel and 47 civilians. AH was detected in 78% of military personnel and 68% among civilians. Smoking was reliably often detected among military personnel – 68% compared with the control group – 50%. Abdominal obesity and diabetes mellitus were statistically significantly detected among civilians with coronary artery disease (57 and 36% versus 38 and 20%). Psychosomatic disorders (chronic stress, anxiety and depression) were 50% or more pronounced among military personnel compared with civilians.

CONCLUSIONS Thus, in both groups of men with CHD, the most common risk factors are hypertension and hypercholesterolemia. Moreover, between the groups there are some differences in a number of risk factors. Among the military, smoking, chronic stress, anxiety/depression predominated, while among civilians, diabetes and abdominal obesity were more often detected. The data obtained can be used to determine the treatment tactics and secondary prevention of CVD among military personnel.

GW31-e0185

Elevated high-mobility group box 1 level is associated with in-hospital cardiac function and new-onset atrial fibrillation in patients with acute myocardial infarction

Lingyun Gu[1,2], Ruolong Zheng[1], Wenlong Jiang[1]
[1]Department of Cardiology, Jiangyin People's Hospital
[2]Department of Cardiology, Zhongda Hospital, Medical School of Southeast University

OBJECTIVES Patients with acute myocardial infarction (AMI) often result in adverse ventricular remodeling and cardiac arrhythmia. The innate immune system is an important mechanism involved in this process. In this study, we tried to investigate the predictive value of high-mobility group box 1 (HMGB1), a protein involved in the innate immune system, on cardiac dysfunction and new-onset atrial fibrillation in patients with AMI.

METHODS Three hundred and forty eight AMI patients underwent primary percutaneous coronary intervention and 312 control subjects without apparent coronary artery disease were enrolled between January 2016 and December 2018. Serum HMGB-1 level was determined by Enzyme-linked immunosorbent assay (ELISA). Echocardiography, N-terminal prohormone of brain natriuretic peptide and continuous electrocardiographic monitoring were recorded for evaluation of in-hospital cardiac function and new-onset atrial fibrillation (NOAF).

RESULTS During hospitalization, elevated serum HMGB1 expression was associated with increased myocardial necrosis and reduced cardiac function in AMI patients. AMI patients with NOAF presented higher serum HMGB1 levels than AMI patients without NOAF. Patients with higher serum levels of HMGB1 were at increased risk of suffering from NOAF.

CONCLUSIONS In our study, we demonstrated that serum level of HMGB1 is positively related to the levels of LDL, cardiac troponin I, NT-proBNP, LVEF and time of symptom onset to balloon dilatation in AMI patients. We also

found that an increased prevalence of post-MI NOAF was observed in patients with higher serum HMGB1 levels, serum HMGB1 level could predict post-MI NOAF. Higher levels of serum HMGB1 may be a new predictive factor for in-hospital cardiac dysfunction and NOAF in AMI patients.

GW31-e0189

Study on the risk factors of hospital complications in young patients with acute myocardial infarction

Sulan Huang, Guo Ning, Ge Liangqing
The First People's Hospital of Changde

OBJECTIVES To investigate the risk factors of nosocomial complications in young patients with acute myocardial infarction.

METHODS In this study, 122 young patients with acute myocardial infarction from January 2018 to December 2019 were included according to the study's inclusion criteria. There were 30 cases with complications and 92 cases without complications. The medical history, test index and coronary angiography were compared between the two groups. Multivariate Logistic regression was used to analyze the risk factors of nosocomial complications in young patients with acute myocardial infarction, and the regression equation of nosocomial complications was established. ROC curve was drawn to evaluate the efficacy of regression equation in evaluating the nosocomial complications in young patients with acute myocardial infarction.

RESULTS Young patients with complications of acute myocardial infarction compared with patients without complications, between the two groups of history of high blood pressure, creatinine, fibrinogen, b-type brain natriuretic peptide precursor, heart ejection fraction and coronary artery lesion number type and scope of coronary lesions and acute myocardial infarction, the difference was statistically significant (P<0.05). Logistic regression analysis showed that creatinine (OR=1.01, 95% CI: 1.001–1.019, P=0.036), number of coronary artery lesions (OR=2.519, 95% CI: 1.185–5.357, P=0.016) and fibrinogen (OR=14.984, 95% CI: 3.863–58.113, P<0.001) were risk factors for nosocomial complications in young patients with AMI. ROC curve analysis results showed that the maximum value of Youden index, AUC, sensitivity and specificity of the regression equation for the assessment of nosocomial complications in young patients with AMI were 0.644, 0.873 (95% CI: 794–0.952, P<0.001), 0.769 and 0.875 respectively.

CONCLUSIONS Creatinine, coronary lesion number and fibrinogen were risk factors for nosocomial complications in young patients with acute myocardial infarction. The established regression equation has a high predictive value for the occurrence of nosocomial complications in young patients with acute myocardial infarction.

GW31-e0190

In-hospital management and outcomes of acute myocardial infarction before and during the coronavirus disease 2019 epidemic

Bing Huang, Hong Jiang
Department of Cardiology, Renmin Hospital of Wuhan University

OBJECTIVES The outbreak of coronavirus disease 2019 (COVID-19) has rapidly spread worldwide. This study sought to share our experiences with in-hospital management and outcomes of acute myocardial infarction (AMI) before and during the COVID-19 epidemic.

METHODS We retrospectively analyzed consecutive AMI patients, including those with ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI), from February 1, 2020, to April 15, 2020 (case group), and from January 1, 2019 to December 31, 2019 (control group) and conducted a 1:1 ratio-matched case-control study.

RESULTS Fifty-three AMI (31 STEMI, 22 NSTEMI) patients during the COVID-19 epidemic were matched to 53 AMI patients before the epidemic. Baseline characteristics were comparable between the groups. STEMI patients in the case group had a longer delay time, less primary or remedial PCI and more emergency thrombolysis than those in the control group. Less coronary angiography and stenting were performed in AMI patients in the case group than in the control group. Although there were no statistically significant differences in clinical outcomes between the two groups, STEMI patients in the case group had more than a three-fold increase in mortality rates. AMI combined with COVID-19 infection was associated with higher rates of mortality than AMI alone.

CONCLUSIONS The COVID-19 epidemic has resulted in significant reperfusion delays in STEMI patients and has a marked impact on the treatment options selection in AMI patients. This epidemic also results in more than a three-fold increase in mortality rates in STEMI patients, although the differences were not statistically significant.

GW31-e0195

A novel risk score for predicting post-acute myocardial infarction infection among patients with ST-segment elevation myocardial infarction: an observational cohort study

Yuanhui Liu[1], Litao Wang[2], Ji Yan Chen[1], Peng Cheng He[1], Chong Yang Duan[3], Ning Tan[1]
[1]Department of Cardiology, Guangdong Cardiovascular Institute, Guangdong Provincial Key Laboratory of Coronary Heart Disease Prevention, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China
[2]Guangdong Provincial People's Hospital, School of Medicine, South China University of Technology, Guangzhou, China
[3]Department of Biostatistics, School of Public Health, Southern Medical University, Guangzhou, China

OBJECTIVES Post-acute myocardial infarction (P-AMI) infection is a serious complication in patients with ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI). We aimed to develop and validate a new risk score for early prediction of P-AMI infection in such patients.

METHODS A total of 1842 STEMI patients undergoing PCI enrolled between January 2010 and May 2016 served as a derivation cohort, and 1270 STEMI patients enrolled between June 2016 and May 2018 served as external validation cohort. We conducted multivariable logistic regression treating a novel risk score as an independent variable predictive for the primary outcome of interest, P-AMI infection during hospitalization.

RESULTS The incidence of P-AMI infection was 11.8% in development cohort. Seven clinical variables were included to establish the risk score: Age, Killip classification, WBC count, serum albumin, insulin use, diuretic use, and transfemoral approach. The risk score demonstrated high discrimination, with a C-statistic of 0.851 (95% CI, 0.824–0.877) in the development cohort and 0.851 (95% CI, 0.818–0.884) in validation cohort, and showed adequate calibration in both cohorts. The incidence of P-AMI infection increased steadily across risk score groups in both development and validation groups. The risk score also performed well in subgroup analysis for infection and in the outcomes of in-hospital all-cause death and major adverse cardiovascular events.

CONCLUSIONS The present risk score is easily applicable in clinical practice for identifying patients at high risk of infection and in-hospital outcomes in patients with STEMI undergoing PCI and may help clinical decision-making allowing for timely measures to improve clinical outcomes.

GW31-e0196

Is TMAO related to in-stent restenosis in patients with acute coronary syndrome?

Boda Zhou, Ping Zhang
Beijing Tsinghua Changgung Hospital

OBJECTIVES Trimethylamine N-oxide (TMAO), a metabolite of gut microbes, has been reported to participate in the development of atherosclerosis and CVD. The purpose of our study was to assess whether the occurrence of in-stent restenosis (ISR) is associated with plasma TMAO level in acute coronary syndrome patients after drug eluting stent (DES) implantation.

METHODS This was a single retrospective case-control study performed in 1371 acute coronary syndrome (ACS) patients underwent percutaneous coronary intervention (PCI) and DES implantation. Of them, 15 symptomatic patients were found to suffer from ISR and included in this study (ISR group), 16 gender and age matched patients without ISR were included in this study (non-ISR group). High-performance liquid chromatography with tandem mass spectrometry was used to measure plasma TMAO levels.

RESULTS This study found no significant difference in plasma TMAO (247.40±181.30 ng/mL vs. 204.86±172.39 ng/mL, P=0.04) between ISR and non-ISR groups. Plasma TMAO level showed no significant correlation with ISR, but was significantly positively correlated with diabetes mellitus (r=0.45, P=0.01), serum HbA1c level (r=0.39, P=0.03) and serum creatinine level (r=0.47, P=0.007); significantly negatively correlated with female gender (r=−0.39, P=0.03). ISR was significantly positively correlated with diabetes mellitus (r=0.43, P=0.02), fasting blood glucose level (r=0.45, P=0.01), neutrophil to lymphocyte ratio (r=0.39, P=0.03) and syntax score (r=0.37, P=0.04); significantly negatively correlated with platelet (r=−0.39, P=0.03). Logistic regression analysis indicated that fasting blood glucose was the only independent predictors for ISR (B=0.669, 95% CI: 1.065–3.579, P=0.030).

CONCLUSIONS This study provides an information that plasma TMAO may not be related to ISR and plaque burden in ACS patients after DES implantation, while FBG may predict the development of ISR in these patients.

GW31-e0212

Clinical characteristics and outcomes for STEMI patients treated with primary PCI in low risk area during the pandemic of COVID-19: a retrospective cohort study

Ou Zhang, Yajun Xue, Ping Zhang
Beijing Tsinghua Changgung Hospital

OBJECTIVES To determine whether the pandemic of coronavirus disease 2019 (COVID-19) may affect clinical outcome of ST segment elevation myocardial infarction (STEMI) patients in North of Beijing, China, the epidemiological low risk area.

METHODS It was a single center retrospective observational study. Clinical characteristics and outcomes of all STEMI patients treated with primary percutaneous coronary intervention (PPCI) from January 24, 2020 to April 24, 2020 (group 2020) and in the same period in 2019 (group 2019) were compared.

RESULTS Totally 90 STEMI patients were included in our study (group 2020, n=51 vs. group 2019, n=39). No confirmed COVID-19 case in group 2020 tended to have longer door-to-balloon (DTB) time (135 (90, 184) *vs.* 76 (59, 102), P<0.0001), system delay time (from first medical contact to wire crossing time (206.5 (118, 313) *vs.* 92 (73, 114), P=0.003) and total delay time (from symptoms to wire crossing time) (333 (204, 581) *vs.* 173 (150, 362), P<0.0001)). There was no significant difference in the incidence of composite outcome of in-hospital death, cardiogenic shock, heart failure and use of mechanical circulatory support between group 2020 and 2019 (17 (33.33%) *vs.* 11 (28.21%), P=0.60). However, the rate of left ventricular aneurysm was significantly increased in group 2020 (27.45 *vs.* 5.13%, P=0.006) compared with 2019.

CONCLUSIONS COVID-19 may delay the treatment time of PPCI for STEMI patients, but no significant difference was observed on clinical outcome.

GW31-e0215

Derivation and validation of the score system for predicting all-cause death and myocardial infarction in coronary artery ectasia

Yintang Wang[1,2], Weihua Song[1]
[1]Chinese Academy of Medical Sciences and Peking Union Medical College, National Center for Cardiovascular Diseases, Fuwai Hospital
[2]Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University

OBJECTIVES Coronary artery ectasia (CAE) bears high risk of death and myocardial infarction. Risk stratification in CAE patients is crucial for their management, but there are no risk score systems intended for risk evaluation of CAE patients so far. This study is designed to investigate a user-friendly tool for risk evaluation, in order to help the clinical decision of the patients with CAE.

METHODS In a retrospective cohort of 595 hospitalized CAE patients from January 2009 and December 2013, the baseline characteristics (clinical history, biomarkers and quantitative coronary angiography variables) were collected. Follow-up via telephone interview were conducted by investigators blind for patients' baseline characteristics and the endpoint event was the composite of all-cause death and non-fatal myocardial infarction. The candidate predictors of end-point event were analyzed using Cox proportional hazards regression models to derive a risk score in the form of nomogram. The predictive performance and discriminative ability of the novel nomogram were determined by concordance index (C-index) and calibration curve, that were validated internally with bootstraps resampling and leave-one-out cross-validation. According to the 60^{th}P and 90^{th}P pencentiles of the nomogram-derived score, the CAE patients were divided into three risk groups and risk stratification was further evaluated. The decision curve analysis (DCA) was conducted to evaluate clinical usefulness of the nomogram-assisted decisions to help improve CAE patients' outcomes.

RESULTS During a median follow-up time of 62.3 (interquartile range 46.9–79.3) months, 26 all-cause deaths and 37 non-fatal myocardial infarctions were identified. In univariable analysis, age, BNP (Brain natriuretic peptide), hs-CRP (high sensitivity C-reactive protein), maximum dilated area of ectatic lesions, erythrocyte sedimentation rate, lymphocyte count, red blood cell count and hemoglobin were associated with the composite endpoint events. The final risk-prediction model named ABCD-CAE score included four items: age (A), BNP (B), hs-CRP (C) and maximum Dilated area of ectatic lesions (D). The nomogram yielded a C-index for end-point event of 0.72 (95% confidence interval, 0.64–0.79). The calibration curve demonstrated that there was good agreement between risk prediction by nomogram and actual observation of endpoint events. Compared with the low-risk group (score ≤100), the risk of composite events was significantly increased in the intermediate-risk group (score: 100–130) and high-risk group (score >130) [hazard ratio (95% confidence interval): 2.23 (1.23–4.06), P=0.008 and 7.02 (3.81–12.97), P<0.001 respectively]. Consistently, Kaplan-Meier curves were separated very well by the three groups both for composite events and all-cause death (log-rank test, both P<0.001). Compared with a model including clinical variables (age, sex, smoker, diabetes, hypertension, body mass index, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol ratio) alone, the ABCD-CAE model yielded a substantial net benefit when the decision thresholds approximately ranged from 25 to 65% in the DCA.

CONCLUSIONS The ABCD-CAE score is a simple four-item risk score, that provides a clinically useful tool for the risk prediction of all-cause death and myocardial infarction in patients with CAE. This user-friendly tool might support clinical decision making for the management of CAE.

GW31-e0217

Clinical features of coronary heart disease in patients with diabetes mellitus

Kokozheva Madina, Mekhman Mamedov
National Medical Research Center for Preventive Medicine, Moscow, Russia

OBJECTIVES Determination of the clinical course of CHD and risk factors in patients with diabetes mellitus.

METHODS A comparative clinical study included 200 patients with CHD (men and women aged 35–70 years). Depending on the glycemic status, patients were divided into two groups: with (n=100) and without (n=100) T2DM. All patients were questioned, conducted a clinical examination, instrumental studies, including ECG alone, ECHO KG, treadmill test and coronary angiography. The presence of concomitant diseases was also analyzed.

RESULTS In the group of people with diabetes, 40% smokes, and in the control group, the percentage of smokers was 60%. Alcohol abuse in the group of people with CHD and diabetes was 7%, and in the control group 10%. All patients in both groups had hypertension. In the group with diabetes, concomitant diseases were recorded 30% more compared to the group of people with coronary heart disease without diabetes and obesity, nephropathy, COPD and cerebrovascular diseases dominated. According to resting ECG and ECG, in both groups, most patients had left ventricular hypertrophy. The frequency of systolic dysfunction in patients with diabetes is detected by 50% more compared to the group without diabetes, and diastolic dysfunction is comparable and averages 80%. Among people with diabetes, stenosis of the LAD and proximal interventricular branch LCA are detected more often in comparison with patients without diabetes, while the frequency of stenosis up to 50 and 70% in both groups is comparable.

CONCLUSIONS Thus, a high frequency of risk factors is detected in both groups. In people with CHD and diabetes, the comorbidity of somatic diseases is detected more often due to nephropathy, cerebrovascular disease, COPD and obesity. Despite the comparable frequency of coronary artery stenosis in patients with diabetes mellitus, damage to some coronary arteries was more pronounced, which is associated with systolic dysfunction of the left ventricle.

GW31-e0218

Low expression of EGR1 gene in peripheral blood leukocytes may cause acute myocardial infarction

Xue Wang, Jianjun Ruan, Heyu Meng, Lihong Li, Fanbo Meng
Department of Cardiology, The Third Hospital of Jilin University

OBJECTIVES To evaluate the correlation between the expression level of EGR1 gene in peripheral blood leukocytes and the risk of acute myocardial infarction (AMI); combined with the baseline data analysis of the study subjects, to explore the role of EGR1 gene in AMI.

METHODS In this study, we selected 86 patients with AMI as the case group and 77 patients with coronary heart disease as the control group. Both patients were diagnosed by coronary angiography. The clinical data of the two groups were analyzed and compared. In the peripheral venous blood, real-time fluorescence quantitative PCR was used to detect the mRNA expression of EGR1 gene in peripheral blood.

RESULTS The relative expression of EGR1 gene mRNA level in the group of patients with AMI and coronary heart disease showed that the relative expression of EGR1 gene mRNA in peripheral blood leukocytes of AMI group was significantly lower than that of control group, and its relative expression level was control group 0.49 times. The clinical data analysis results of the study objects indicated that there was no significant difference between the two groups in terms of age, smoking history, triglyceride level, total cholesterol level, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, hypertension diagnosis, type-II diabetes diagnosis. Further analysis of the relationship between clinical data and EGR1 gene expression results: the relative expression level of EGR1 gene mRNA level was independent of age (P=0.207), triglyceride levels (P=0.470), high density lipoprotein levels (P=0.949), low density lipoprotein levels (P=0.138); related to total cholesterol levels (P=0.017). Binary Logistic regression analysis showed that the low expression of mRNA in peripheral blood leukocytes of EGR1 gene is an independent risk factor for the development of coronary heart disease to AMI. Compared with the high expression of EGR1 gene, the risk of AMI with low expression of EGR1 gene is increased by 2.389 times.

CONCLUSIONS EGR1 gene is significantly under-expressed in peripheral blood of patients with AMI. Low expression of EGR1 gene is an independent risk factor for the occurrence of AMI. EGR1 gene may be used as a genetic marker to assess the risk of AMI.

GW31-e0238

Indobufen versus aspirin combined with clopidogrel used for dual antiplatelet therapy after drug-eluting stent implantation: randomized controlled study

Yuexi Wang, A. Rong
Department of Cardiology, 1st Hospital Affiliated to Inner Mongolian Medical University, Huhhot 010050, China

OBJECTIVES Indobufen as a new antiplatelet drug has been considered for antiplatelet replacement therapy before thrombolysis in patients with ST-segment elevation myocardial infarction who are intolerant of aspirin in the gastrointestinal tract. The aim of this trial was to investigate the efficacy and safety of antiplatelet therapy with indobufen in patients with troponin negative coronary artery stent implantation within one year compared with aspirin.

METHODS This trial is a prospective, open, non-inferiority, 1:1 randomized controlled exploratory study. We selected some patients with coronary artery disease (CAD) who underwent percutaneous coronary intervention (PCI) from June 2018 to February 2019 in the Department of Cardiovascular Medicine of our hospital. 60 patients who met the inclusion and exclusion criteria were selected and randomly assigned to the experimental group and the control group with 30 patients each. Within 24 hours after stent implantation, the experimental group received indobufen (100 mg bid) plus clopidogrel (75 mg qd), and the control group received aspirin (100 mg qd) plus clopidogrel (75 mg qd) dual antiplatelet therapy regularly for 12 months. The primary end point of net adverse clinical and cerebral events (NACCE)

RESULTS (1) The demographic data and baseline condition of the experimental group and the control group were balanced. There was no significant difference in the incidence of the end point events between the experimental group and the control group during the 12 month follow-up period. (2) The primary endpoint was analyzed by Kaplan-Meier method. The incidence of NACCE was 6.7% in the experimental group and 16.7% in the control group (HR, 0.238 [95% CI, 0.041–1.375]; Log-rank P=0.16). The choice of two dual antiplatelet regimens was not statistically associated with the occurrence of NACCE. (3) The incidence of major bleeding (BARC type 2, 3 and 5) at 12 months was 3.33% and 13.33% (HR, 0.238 [95% CI, 0.041–1.375]; Log-rank P=0.16) in the experimental group and the control group, and there was no statistical correlation between the two treatment regimens and the occurrence of major bleeding.

CONCLUSIONS Indobufen combined with clopidogrel as dual antiplatelet therapy did not significantly reduce the incidence of death, non-fatal myocardial infarction, ischemic stroke and major bleeding in troponin negative patients with CAD who received percutaneous coronary intervention and implanted at least one drug-eluting stent, but could play a stable antiplatelet role without increasing stent thrombosis Risk and occurrence of upper gastrointestinal adverse events.

GW31-e0239

To investigate the significance of heat shock protein 70 (HSP70) detection in the diagnosis and treatment of acute myocardial infarction

Yuexi Wang, Nari Han
Department of Cardiology, Affiliated Hospital of Inner Mongolian Medical University, Huhhot 010050, China

OBJECTIVES Acute myocardial infarction (AMI) is one of the main causes of morbidity and mortality worldwide. The myocardial cells in patients with AMI are hypoxic and ischemic, and the structure and function of myocardium are changed. Some patients even eventually develop heart failure. Early diagnosis of AMI Treatment and prognosis play an important role. At present, clinical detection of troponin T (cTnT), creatine phosphokinase (CK), creatine phosphokinase isoenzyme (CK-MB) and myoglobin (MYO), the degree of increase is similar to the development and prognosis of the disease Related. Existing studies have confirmed that peripheral blood heat shock protein 70 (HSp70) is significantly abnormal in patients with acute myocardial infarction. Whether heat shock protein 70 can be used as a new diagnostic indicator for acute myocardial infarction needs further confirmation. Therefore, this study will explore the diagnostic significance of HSP70 in AMI.

METHODS This study selected 160 patients with acute myocardial infarction (male 112, female 48) in the Department of Cardiology, Inner Mongolia Medical University Affiliated Hospital from December 2017 to December 2018 and 40 healthy controls who were examined at the hospital's physical examination center during the same period. Cases were divided into two groups: the Acute and convalescent phase. Serum heat shock protein 70 was detected by enzyme-linked immunosorbent assay (double antibody sandwich method) for statistical analysis.

RESULTS The serum HSP70 in the acute phase of the test group was significantly higher than that in the recovery period of the same group [25.37 (10.32, 50.08) μg/L vs. 0.088 (0.215, 0.557) μg/L and 0.092 (0.027, 0.976) μg/L, P<0.01]. The area under the ROC curve of the test group HSP70 was 0.722 (95% CI: 0.982–0.999), CK 0.883 (95% CI: 0.837–0.929), CK-MB 0.929 (95% CI: 0.894–0.964), cTNT 0.949 (95% CI: 0.918–0.980), BNP 0.853 (95% CI: 0.923–0.982), MY 0.775 (95% CI: 0.705–0.845). Serum HSP70 was positively correlated with CK, CK-MB, cTNT, MYO (P=0.0000). Logistic regression analysis showed that HSP70 was independently associated with the incidence of AMI (OR=3.201, 95% CI: 0.248–0.414).

CONCLUSIONS This study found that the serum HSP70 level of patients in the acute phase of the experimental group was significantly higher than that of the control group. Moreover, HSP70 levels were positively correlated with myocardial necrosis markers CK-MB and cTnT.

GW31-e0252

Elevated level of plasma big endothelin-1 associated with in-stent restenosis: a retrospective study in patients undergoing percutaneous coronary intervention

Yue Ma, Zhuoxuan Yang, Yue Zhou, Shubin Qiao
Department of Coronary Heart Disease, National Center for Cardiovascular Diseases, Fuwai Hospitai, CAMS & PUMC

OBJECTIVES Percutaneous coronary intervention (PCI) is the treatment of myocardial ischemia perfusion by using cardiac catheter technique to dredge the stenosis or occlusion of the coronary artery. There is a certain proportion of in-stent restenosis (ISR) after stent implantation that causes problems clinically. ISR involves many pathologic mechanisms, including intraplaque inflammation, lipid deposition, proliferation of vascular smooth muscle cells, endoluminal thrombus formation, and intraplaqu angiogenesis. Endothelins are 21-amino acid vasoconstricting peptides produced primarily in the endothelium having a key role in vascular homeostasis. Endothelin 1 (ET-1) is a potent vasoconstrictor that in patients with coronary artery disease is related with the occurrence of cardiovascular events. However, the low circulating concentration and the short half-life of ET-1 make it difficult to measure, big endothelin-1 (Big ET-1) is the precursor of ET-1 and has the same measurement value. The aim of this study is to investigate the relationship between big endothelin-1 and the risk of in-stent restenosis in patients with coronary artery disease undergoing PCI.

METHODS After retrieving the patient database, 3098 patients who diagnosed with coronary artery disease and underwent percutaneous coronary intervention (PCI) at Fuwai hospital from October 2014 to March 2015 were enrolled. All patients received standard dual therapy with aspirin 100 mg/day and clopidogrel 75 mg/day for 12 months following PCI. The patient's level of plasma big endothelin-1 (Big ET-1), general condition, related risk factors of admission, other laboratory examination, coronary lesion characteristics, interventional therapy and other baseline data was recorded. All patients were followed up for the occurrence of in-stent restenosis (ISR) and other cardiovascular events. ISR was defined as the presence of >50% diameter stenosis in the stented segment. Statistical software SPSS22.0 was used for data analysis of the clinical epidemiological characteristics and prognosis. The study followed the principles outlined in the Declaration of Helsinki and it was approved by the ethics committee.

RESULTS In all participants, the level of plasma big endothelin-1 (Big ET-1) is associated with the risk of in-stent restenosis (ISR). Patients with a higher level of plasma Big ET-1 (>0.25 pmol/L) had a significantly higher incidence of ISR (2.89 vs. 0.44%, P=0.011) and incidence of angina after stent implantation (13.2 vs. 2.8%, P=0.007) during the follow-up. In logistic multivariable analysis, high level of plasma Big ET-1 (HR 1.968, 95% CI 1.083–5.022, P=0.031) was significantly associated with incidence of ISR.

CONCLUSIONS Elevated level of plasma big endothelin-1 is associated with the risk of in-stent restenosis in patients undergoing percutaneous coronary intervention.

GW31-e0253

Low expression of ZCCHC9 in peripheral blood may become a genetic molecular marker to predict the occurrence of acute myocardial infarction

Lihong Li, Xue Wang, Fanbo Meng
The Third Hospital of Jilin University

OBJECTIVES ZCCHC9 gene is a CCHC-type zinc-containing finger protein that has the function of binding DNA and RNA, and sometimes mediates protein interactions, and participates in various cellular processes in physiological conditions and diseases. This study aimed to assess whether the expression of ZCCHC9 gene can be used as a biomarker to predict the occurrence of acute myocardial infarction.

METHODS In this study, we selected 126 patients with acute myocardial infarction (AMI) as the experimental group, 117 patients with stable coronary artery disease (CAD) as the control group, collected peripheral venous blood, after total RNA extraction, cDNA synthesis, Real-time fluorescence quantitative PCR test to measure the expression level of ZCCHC9 gene at the mRNA level in peripheral blood.

RESULTS (1) The relative expression level of ZCCHC9 gene mRNA level in the objects showed that ZCCHC9 gene was differentially expressed between the experimental group and the control group. The relative expression level of ZCCHC9 gene mRNA level in the peripheral blood of AMI patients was significantly lower than that of the control group, and its relative expression was 0.753 times of the CAD group. (2) The analysis of the clinical date of the objects showed that there were no significant differences in age, gender, smoking history, serum lipid levels, previous history of hypertension, and diabetes between the AMI group and the stable CAD group. However, there was a significant difference in the fasting blood glucose levels between the two groups (Z=−3.168, P=0.002). (3) The analysis of whether there was correlation between clinical date and the relative expression level of ZCCHC9 gene mRNA level showed that the relative expression level of ZCCHC9 gene mRNA level was no related to age, serum triglyceride, total cholesterol, high density lipoprotein, low density lipoprotein and the fasting blood glucose. (4) Binary Logistic regression analysis showed that the low expression of ZCCHC9 gene is an independent risk factor of AMI. Compared with the high expression of ZCCHC9 gene, the risk of AMI in the low expression of ZCCHC9 gene group was increased by 2.597 times. The low expression of ZCCHC9 gene in peripheral blood can be a standard to diagnose AMI. And its sensitivity was 27.4%, its specificity was 88.9%. (5) The relationship between the relative expression level of ZCCHC9 gene mRNA level and concentration of serum troponin I showed that the relative expression level of ZCCHC9 gene mRNA level had no correlation with serum troponin I concentration (P>0.05), that is, the relative expression level of ZCCHC9 gene may not predict the size of AMI.

CONCLUSIONS The expression of ZCCHC9 gene in peripheral blood of patients with AMI was significantly lower than that of patients with stable CAD. The low expression of ZCCHC9 gene is an independent risk factor for AMI. The low expression of ZCCHC9 gene in peripheral blood may used as a genetic marker to predict the occurrence of AMI.

GW31-e0254

Low expression of NUMB gene in peripheral blood may become a molecular marker for early diagnosis of acute myocardial infarction

Lihong Li, Xue Wang, Fanbo Meng
The Third Hospital of Jilin University

OBJECTIVES NUMB is an endocytic adaptor protein that has the function of controlling the physiological development process and plays a key role in the occurrence of diseases. To evaluate whether the low expression of NUMB gene in peripheral blood can be used as a molecular marker to predict the early diagnosis of acute myocardial infarction.

METHODS In our study, we selected 124 patients with acute myocardial infarction (AMI) as the experimental group, and 115 patients with stable coronary artery disease (CAD) as the control group, collected their peripheral venous blood, after total RNA extraction, cDNA synthesis, real-time fluorescence quantitative PCR test was used to measure the expression level of NUMB gene at mRNA level in peripheral blood.

RESULTS (1) The relative expression level of NUMB gene mRNA level of objects indicated that NUMB gene was differentially expressed between the experimental group and the control group, the relative expression level of NUMB gene in peripheral blood of AMI patients was significantly lower than that of the control group, and its relative expression quantity was 0.932 times of that in the control group. (2) The analysis of the clinical date of objects showed that there were no significant statistical differences between the two groups in terms of gender, history of hypertension, smoking history, diabetes, serum triglycerides, total cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol. patients in the AMI group were significantly older than the control group (t=−2.318, P=0.020), and there was a significantly difference in the fasting blood glucose between the two groups (z=−2.505, P=0.012). (3) The analysis of whether there was correlation between clinical data and the relative expression level of NUMB gene mRMA level showed that the expression level of NUMB gene mRNA level was no related to the fasting blood glucose (P=0.551), and it was no related to age (P=0.645). There was no correlation between the expression of NUMB gene and fasting blood glucose and age. (4) Binary Logistic regression analysis indicated that low expression of NUMB gene is an independent risk factor of AMI. Compared with the high expression of NUMB gene group, the risk of AMI in the low expression of NUMB gene group was increased by 3.287 times. Advanced age was also an independent risk factor of AMI, which can increase the risk of AMI by 1.853 times. Fasting blood glucose was not an independent risk factor of AMI. (5) The relationship between the relative expression of NUMB gene and serum concentration of troponin I showed that there was no correlation between the expression of NUMB gene in peripheral blood and serum troponin I concentration (r=−0.027, P=0.797), that is, the expression level of NUMB gene in peripheral blood may not predict the size of AMI.

CONCLUSIONS The expression of NUMB gene in peripheral blood of patients with AMI was significantly lower than that of patients with stable CAD. Patients with low expression of NUMB gene in peripheral blood are more likely to develop AMI. The low expression of NUMB gene is an independent risk factor of AMI. The low expression of NUMB gene in peripheral blood may become a molecular marker for early diagnosis of AMI.

GW31-e0256

Comparison of the preventive efficacy of rosuvastatin versus atorvastatin in post-contrast acute kidney injury in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention

Yining Dai, PengCheng He, Ning Tan, YuanHui Liu
Department of Cardiology, Guangdong Cardiovascular Institute, Guangdong Provincial Key Laboratory of Coronary Heart Disease Prevention, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences

OBJECTIVES Post-contrast acute kidney injury (PC-AKI) is associated with a prolonged hospital stay and increased mortality. PC-AKI cannot be treated effectively after it occurs; thus, avoiding this condition is particularly important. Statins have been shown to reduce the risk of PC-AKI in patients undergoing percutaneous coronary intervention (PCI). However, the preventive effect of rosuvastatin versus atorvastatin on PC-AKI in patients with ST-segment elevation myocardial infarction (STEMI) undergoing PCI remains unclear.

METHODS Patients with STEMI undergoing PCI between January 2010 and May 2016 were consecutively enrolled. Finally, 1300 patients were included and divided into two groups according to the statin type (atorvastatin: n=1040; rosuvastatin: n=260). All patients were administrated with statins at admission. Patients in the two groups received statin therapy (rosuvastatin: 10 mg daily; atorvastatin: 20 mg daily) before contrast agent exposure. The primary endpoint was PC-AKI defined as an absolute increase of ≥0.5 mg/dL in the level of serum creatinine or an increase of ≥25% over baseline within 48–72 hours after contrast media exposure.

RESULTS In total, 245 (18.8%) patients developed PC-AKI. The atorvastatin and rosuvastatin groups had similar rates of PC-AKI (19.1 vs. 17.7%, P=0.595), in-hospital mortality (4.1 vs. 3.8%, P=0.833), and major adverse clinical events (MACE). Multivariate logistic regression analysis revealed that rosuvastatin treatment had an effect similar to atorvastatin regarding PC-AKI (odds ratio [OR]=0.97, 95% confidence interval [CI], 0.66–1.43, P=0.874). Propensity score analyses and subgroup analysis demonstrated similar results for PC-AKI. Kaplan-Meier survival curves and Cox proportional regression showed that the atorvastatin and rosuvastatin groups had no differences regarding follow-up mortality.

CONCLUSIONS Rosuvastatin exerted a similar preventive effect against PC-AKI and showed similar levels of in-hospital and follow-up all-cause mortality and in-hospital MACE compared with atorvastatin in patients with STEMI undergoing PCI.

GW31-e0259

Feasibility of distal radial access for coronary angiography and percutaneous coronary intervention – a single center experience

Lianna Xie, Xianjing Wei, Zezhou Xie, Shengying Jia, Siwei Xu, Chunlin Jiang, Xingping Xiao, Botao Luan, Kaijun Wang, Xue Yang
Affiliate Zhongshan Hospital of Dalian University

OBJECTIVES Asymptomatic radial artery occlusion remains the most common complication in transradial coronary interventional procedure. To prevent radial artery occlusion, distal radial access site has been suggested recently. We aimed to describe our experience and to assess feasibility and safety of this new access site for coronary angiography (CAG) and percutaneous coronary intervention (PCI).

METHODS One thousand and sixty three patients were assigned to undergo CAG or procedural PCI through distal radial access between 1 January 2018 and 31 December 2019. The size of radial sheath used was 5 or 6 French (F). The sheath was removed at procedure termination, and hemostasis was obtained by compression bandage with gauze.

RESULTS The successful rate of radial artery cannulation via distal radial access was 89.7%. Mean age of successful cases is 64.6±11.2 years (26–94 years) with 35.6% women. 38.1% of procedures were PCI. 28.2% of procedures were via left distal radial access. 6F sheath was used in 63.2% of cases. Hemostasis was obtained within 2 hours in 89.5% patients. There were 110 procedural failures: artery puncture failed in 59 cases, wire failed in 49 cases, and sheath failed in 2 cases. Complications potentially related to distal radial access were as follows: radial artery occlusion at the access site 1.4%, forearm radial artery

occlusion 0.4%, hematoma of forearm 0.5%, and transient thumb numbness 0.2%.

CONCLUSIONS Distal radial access is a feasible and safe access and can be used as a rational alternative to traditional radial access for coronary interventional procedure.

GW31-e0279

Efficiency of Liraglutide application in patients with CHD and DM type 2

N. F. Tashkenbayeva, D. A. Alimova, R. K. Trigulova, F. M. Bekmetova, L. T. Ilkhamova
Republican specialized scientific Practical Medical Center of Cardiology of the Uzbekistan Public Health Ministry

OBJECTIVES To assess glucagon-like peptide-1 Liraglutide (LG) efficacy on glycemia control, losing weight, lipid profile, and EchoCG parameters in patients with CHD and diabetes mellitus type 2 (DM 2).

METHODS The study included 15 patients (LG) unstable angina UA (ESC) and diabetes mellitus 2 (DM-2) (WHO, 1999) in the age 56.4±2.7 years old. Patients BMI was 30.7±0.6 kg/m^2; duration of DM 2 was 8.1±2.1 years. Using standard methods we determined complete lipid spectrum, fasting glycemia (FG), postprandial glycemia (PG), HbA1c, body weight, and EchoCG parameters. All Echocardiograms were performed by one cardiologist using ultra sound «En VisorC» system («PHILIPS», Holland) with 3.5 MHz sensor with a patient in lying position on the left flank with 45° angle in compliance with standard methods. Therapy mode: anticoagulants, antiplatelet agents, nitrates, beta-blockers, RAAS blockers, statins, Liraglutide. Liraglutide's efficacy was assessed according to the decrease of HbA1c level compared to original HbA1c ≥0.5%. A group of patients with CHD with DM 2, who administered Gliclazide (GL) with parameters corresponding to the studied parameters of the basic group was considered to be a control group (n–10). Follow-up period was 3 months.

RESULTS Within the follow-up period there was a notable improvement of HbA1c compared to original level in both groups: LG from 9.2±1.6 to 7.3±1.1, P=0.004; and GL 8.9±1.5, P=0.04. However, in relation to fasting glycemia significant improvement of glycemic control was observed in the 8th group with LG: LG from 10.5±3.1 to 8.1±2.4 mmol/L, P=0.07; and GL 10.9±4.3 to 8.9±3.8 mmol/L, P=0.22. It was probably linked with different number of patients in two groups. Alterations of BMI from the original level till the 12th week was equal to –1.2 kg (P=0.007) in LG group and –0.2 kg (P=0.9). In relation to dynamic lipid profile parameters with background 3-months therapy there was insignificant tendency for decrease, and particularly dynamic LDL: LG group to (–) 4.1±3.6 mg/dL (P=0.6) versus GL group (–) 0.7±1.5 mg/dL (P=0.9); HDL (–) 0.3±2.1 versus 0.6±1.9 mg/dL (P=0.8) respectively; fasting triglycerides (–) 11.6±3.7 (P=0.19) versus (–) 8.1±4.7 (P=0.8) mg/dL. In LG group basic level ten patients had diastolic dysfunction (DD) I stage, while 5 patients (33.3%) had DD II stage. By the 3rd month of therapy in LG group there was observable improvement of diastolic function and transfer of all patients from DD II stage to the group of patients with DD I stage. None of the patients stopped Liraglutide therapy and informed of hypoglycemia. Clinical tolerance of the agent was good.

CONCLUSIONS In clinical practice addition of Liraglutide to the therapy of patients with CHD and DM type 2 with insufficient control of carbohydrate profile improves glycemic control, diminishes body weight, does not affect lipid exchange parameters with background basic therapy. In this preliminary research Liraglutide had a favorable effect on DD in patients with DM type 2. It is an important conclusion, as DD is a known additive risk of unfavorable events development.

GW31-e0280

Sitagliptin and diastolic dysfunction of the left ventricle in patients with comorbidity of CHD and DM 2

D. A. Alimova, N. F. Tashkenbayeva, R. Kh. Trigulova, F. M. Bekmetova, M. A. Musayeva
Republican Specialized Scientific Practical Medical Center of Cardiology of the Uzbekistan Public Health Ministry

OBJECTIVES To assess DDLV status dependent on the markers determining cardiovascular events development risks.

METHODS We studied forty patients with IHD, who applied to the 2nd and 6th units of the RSSPMC of Cardiology of the MH of the RUz in destabilization period of angina combined with DM type 2 and hypertonic disease (HD) aged 59.2±9.5 years old. Using standard methods we determined complete lipid spectrum (TC, CL LDL, VLDL, HDL, TG), fasting glycemia (FG), postprandial glycemia (PG), HbA1c, and C-reactive protein (CRP). Therapy mode: anticoagulants, antiplatelet agents, nitrates, RAAS blockers, beta-blockers, and statins. Patients with DM type 2 administered metformin, and sulphonyl urea agents. Exclusion criteria were heart failure (HF) II B, chronic kidney disease (CKD) 4, any incretin therapy, and insulin therapy. At the 3–5th day after status stabilization with basic therapy 30 patients were randomly selected for administration of sitagliptin/metformin (SG/M) with a day dose 50/500–50/1000 mg/day, with monitoring of glycemia, heartbeat rate, SAP, DAP, lipid profile, and CRP level. The rest 10 patients continued taking gliclazide (GL). Primary results were changes in ratio of e′ speed and E/e′ from the original level within 24 weeks (6 months) follow-up. Secondary results included: HbA1c, lipid profile. CRP level. Follow-up duration was 6 months.

RESULTS Decrease of HbA1c and body weight was significantly higher in SG/M group, than in GL group (–0.8±0.5% versus –0.4±0.5, P<0.005; –1.7±3.9 kg versus 0.5±3.1 kg, P<0.05 respectively). In the lipid profile and CRP level of the compared groups there were no changes. We did not reveal any significant alterations in the speed (e′) and E/e′ of the original level within the whole follow-up period in any of the groups.

CONCLUSIONS Sitagliptin efficacy in relation to glycemic status was more expressed compared to Gliclazide (decrease of HbA1c level). In echocardiographic parameters of diastolic function of the left ventricle in patients with CHD and DM 2 there were yet no observable differences.

GW31-e0286

Relationship between serum sulfatide concentration, estimated glomerular filtration rate and left cardiac structure and function in elderly patients with coronary heart disease

Li Gang, Guo Yifang, Zuo Qingjuan, He Lili, Wang Yan, Zhang Lu, Zhang Tingting, Wang Qiuyan, Liang Yi
Hebei General Hospital

OBJECTIVES Chronic renal dysfunction and coronary heart disease are the major diseases that affect the health of the elderly. The change of left ventricular structure and function is one of the most prominent features of heart damage in chronic kidney disease patients. Serum sulfatide, a very sensitive indicator of atherosclerosis and changes in renal function, may be important in monitoring the occurrence and progression of cardiac and renal insufficiency. This study aimed to investigate the relationship between serum sulfatide and glomerular filtration rate in patients with coronary heart disease and left ventricular structural and functional changes in order to further understand the inherent relationship between renal dysfunction and cardiovascular events.

METHODS Sixty hospitalized patients diagnosed with coronary heart disease were enrolled in this research. All of them were assigned to 3 groups according to the tertiles of the estimated glomerular filtration rate (eGFR): A group contain 19 patients (eGFR<57.28 mL min^{-1} 1.73 m^{-1}), B group contain 21 patients (57.28<eGFR<74.86 mL min^{-1} 1.73 m^{-1}), C group contain 20 patients (eGFR>74.86 mL min^{-1} 1.73 m^{-1}). Venous blood was collected early in the morning and sent to the laboratory for detection of serum creatinine. The eGFR was calculated according to the simplified MDRD formula. Another 3 mL of venous blood was collected and the serum was separated. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry was used to detect the level of serum sulfatide. Left ventricular structure and function were measured by echocardiography. Relevant test indicators were compared between different renal function patients. Then, the correlation between serum sulfatide concentration, eGFR and left ventride structure and function were analyzed.

RESULTS (1) With the decline of eGFR, serum sulfatide levels gradually decrease (A<B<C, P<0.05), and serum creatinine levels gradually increased (A>B>C, P<0.05). When the eGFR is significantly decreased, the left atrial diameter increases (A>C, P<0.05), the ejection fraction decreases (A<B, P<0.05), and the left ventricular end-systolic diameter increases (A>C, P<0.05). (2) Serum sulfatide concentration was negatively related to left atrial diameter (r=–0.635, P<0.05), or E peak (r=–0.577, P<0.05), but was significantly positively related to eGFR (r=0.817, P<0.01). (3) eGFR was significantly negatively correlated with left atrial diameter and E peak (r=–0.716, P<0.05; r=–0.699, P<0.05, respectively). After multivariable adjustments, serum sulfatide is still significantly correlated with eGFR (P<0.05), and eGFR is significantly negatively correlated with E peak (P<0.05).

CONCLUSIONS Serum sulfatide and eGFR levels were negatively correlated with left atrium diameter. Compared with group C, group A had a gradually increased left atrial diameter as the level of serum sulfatide and eGFR decreased. B group compared with A group, serum sulfatide and glomerular filtration rate decreased significantly, can cause the ejection fraction decreased. Due to the enlargement of left atrium and the decline of the ejection fraction, it is an important predictor of the prognosis of atrial fibrillation, cardiac insufficiency and cardiovascular disease, suggesting that the joint monitoring of serum levels of sulfatide and eGFR may open up a new idea for delaying the progression of cardiac insufficiency.

GW31-e0362

The efficacy and safety of dual antithrombotic therapy with rivaroxaban and ticagrelor in elderly post-PCI patients with atrial fibrillation

Dili Xie[1], Yong Chen[2]
[1]Geriatric Cardiovascular Department, Sichuan Academy of Medical Science & Sichuan Provincial People's Hospital
[2]Cardiovascular Departmen, Sichuan Academy of Medical Science & Sichuan Provincial People's Hospital

OBJECTIVES This study was to compare the efficacy and safet among three different antithrombotic therapies in elderly post-PCI patients with atrial fibrillation (AF).

METHODS One hundred and forty Chinese cases with chronic coronary syndromes (CCS), permanent non-valvular AF, and diabetes mellitus (DM), were included in this study. The age of patients ranged from 70 to 78 years old. All of them received PCI therapy. After PCI, three different antithrombotic therapies were adopted in the patients. Ticagrelor dual therapy group first received one-year treatment with rivaroxaban (15 mg o.d.) and ticagrelor (90 mg bid). Rivaroxaban triple therapy group first received three-month triple therapy with rivaroxaban (15 mg o.d.), clopidogrel (75 mg o.d.) and aspirin (100 mg o.d.), then received nine-month dual therapy with rivaroxaban (15 mg o.d.) and clopidogre (75 mg o.d.). Warfarin triple therapy group first received three-month therapy with warfarin (INR 2.0–2.5, TTR>70%), clopidogrel (75 mg o.d.) and aspirin (100 mg o.d.), then received nine-month dual therapy with warfarin (INR 2.0–3.0, TTR>70%) and clopidogrel (75 mg o.d.). All the patients received rabeprazole (10 mg o.d.) during antithrombotic therapies after PCI. The incidences of cardiovascular events and hemorrhagic events were analyzed among the three groups.

RESULTS There were no differences of age, gender, BMI and CHA2DS2-VASC score among the three groups, but HAS-BLED score, proportion of high bleeding risk cases, proportion of frail patients in the warfarin triple therapy group was lower than in the other two groups (P<0.05). The incidences of stroke/TIA, non-central nervous system (CNS) embolism, myocardial infarction (MI) and unstable angina in the ticagrelor dual therapy group and in the rivaroxaban triple therapy group were lower than in the warfarin triple therapy group (P<0.05), however, there was no statistical difference of the cardiovascular events between the two groups. The incidences of gastrointestinal, intracranial, urinary tract bleeding in the ticagrelor dual therapy group were lower than in the other two groups (P<0.05). Each group had no hemoptysis case. There was no case with severe bleeding in the ticagrelor dual therapy group.

CONCLUSIONS Dual antithrombotic therapy with ticagrelor and rivaroxaban was not inferior to triple antithrombotic therapy with rivaroxaban, clopidogrel and aspirin, and was superior to triple antithrombotic therapy with warfarin, clopidogrel and aspirin, to prevent cardiovascular events. Besides the dual therapy can also reduce the bleeding risk significantly. Therefore, this dual antithrombotic therapy maybe a good choice in elderly post-PCI patients with CCS and AF.

GW31-e0369

Clinical characteristics between early and late drug-eluting stent in-stent restenosis (DES-ISR) and mid-term prognosis after repeated percutaneous coronary intervention

Jianfeng Zheng[1], TingTing Guo[1], Yuan Tian[2], Yong Wang[1], XiaoYing Hu[1], Yue Chang[1], Hong Qiu[1], KeFei Dou[1], YiDa Tang[1], JinQing Yuan[1], YongJian Wu[1], HongBing Yan[1], ShuBin Qiao[1], Bo Xu[1], YueJin Yang[1], RunLin Gao[1]
[1]Fu Wai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
[2]Urumqi Friendship Hospital, Urumqi, Xinjiang Uygur Autonomous Region, China

OBJECTIVES The mechanism and characteristics between early and late drug-eluting stent in-stent restenosis (DES-ISR) have not been fully clarified. Whether there are different outcomes among those patients being irrespective of their repeated treatments remain a knowledge gap.

METHODS A total of 250 patients who underwent initial stent implantation in our hospital, and then were readmitted to receive treatment for the reason of recurrent significant DES-ISR in 2016 were involved. The patients were categorized as early ISR (<12 months; E-ISR; n=32) and late ISR (≥12 months; L-ISR; n=218). Associations between patient characteristics and clinical performance, as well as clinical outcomes after repeated percutaneous coronary intervention (PCI) were evaluated. Primary composite endpoint of major adverse cardiac events (MACE) included cardiac death, non-fatal myocardial infarction, or target lesion revascularization (TLR).

RESULTS Most baseline characteristics are similar in both groups, except for the period of ISR, initial pre-procedure TIMI, and some serum biochemical indicators. The incidence of MACE (37.5 vs. 5.5%; P<0.001) and TLR (37.5 vs. 5.0%; P<0.001) is higher in the E-ISR group. After multivariate analysis, E-ISR (odds ratio [OR], 13.267; [95% CI 4.984–35.311]; P<0.001) and left ventricular systolic dysfunction (odds ratio [OR], 6.317; [95% CI 1.145–34.843]; P=0.034) are the independent predictors for MACE among DES-ISR patients in the mid-term follow up of 12 months.

CONCLUSIONS Early ISR and left ventricular systolic dysfunction are associated with MACE during the mid-term follow-up period for DES-ISR patients. The results may benefit the risk stratification and secondary prevention for DES-ISR patients in clinical practice.

GW31-e0387

CD14 C-260T gene polymorphism and ischemic heart disease susceptibility: a huge review and meta-analysis

Haifeng Zhang[1,2], Qingyuan Gao[1,2], Chengzhang Xu[1,2], Yangxin Chen[1,2], Shaohua Wang[1,2], Zhiteng Chen[1,2], Jingfeng Wang[1,2]
[1]Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong 510120, PRC
[2]Laboratory of Cardiac Electrophysiology and Arrhythmia in Guangdong Province, Guangdong 5101120, PRC

OBJECTIVES The *CD14* gene C-260T polymorphism has been reported to be associated with ischemic heart disease, but results were conflicting. To evaluate the role of the *CD14* C-260T polymorphism in ischemic heart disease, we performed meta-analyses of all available data.

METHODS Comprehensive searches for studies on the association between the genotypes (CC, CT, TT) distributions and ischemic heart disease risk were performed. Patients with acute coronary syndrome, prior myocardial infarction, stable angina pectoris, or angiographic coronary artery stenosis were included. Potential sources of heterogeneity were explored by meta-regression. Analyses were performed under European, East Asian, and Indian studies, respectively.

RESULTS Data were available for 19 studies involving 11,813 cases and 6196 controls. The summary odds ratio under the recessive model was 1.53 (95% confidence interval: 1.20–1.96) for East Asian studies published in English language journals on overall ischemic heart disease. Pooled odds ratios under the codominant model were about 1.81 (95% confidence interval: 1.36–2.40) and 1.70 (95% confidence interval: 1.26–2.29) for Chinese studies on overall ischemic heart disease and other ischemic heart diseases (angina pectoris and angiographic coronary artery stenosis), respectively. No significant association was found in a European population, an Indian population, or the vulnerable plaque ischemic heart disease (acute coronary syndrome and prior myocardial infarction) subgroup of an East Asian population.

CONCLUSIONS It is probable that T allele and TT genotype are associated with ischemic heart disease in the East Asian population but not in the European or Indian populations. Further studies are warranted to assess these associations in greater detail, especially in East Asian and Indian populations.

GW31-e0393

Low expression of Sub1 gene in peripheral blood leukocytes of patients with acute myocardial infarction

Xiaomin Tian, Heyu Meng, Fanbo Meng
China-Japan Union Hospital of Jilin University

OBJECTIVES Sub1, also known as p15, PC4, P14 (hereinafter referred to as PC4), is commonly found in 27 tissues of the human body, and most expressed in brain and fat tissue. Sub1 can rapidly collect DNA damage sites, combine with DNA damage sites early and briefly, play a role in detecting and/or exposing DNA damage, specifically protect DNA from oxidative damage, and reduce chronic inflammation. Inflammation plays an important role in the development of myocardial infarction. The purpose of this study is to evaluate whether the expression level of sub1 gene in peripheral blood can be used as a biomarker to predict the risk of acute myocardial infarction (AMI).

METHODS The peripheral blood of 75 patients with stable coronary heart disease and 113 patients with acute myocardial infarction were collected. The expression of sub1 gene was detected by real-time fluorescence quantitative polymerase chain reaction (PCR) and Western blot analysis.

RESULTS The results showed that the expression level of sub1 gene in the peripheral blood of patients with AMI was significantly lower than that of patients with stable coronary heart disease (z=−2.095, P 0.036). The low expression of sub1 gene had no correlation with blood lipid, blood glucose, smoking history, age and blood pressure.

CONCLUSIONS The expression of sub1 gene in the peripheral blood of patients with acute myocardial infarction was significantly lower than that of patients with stable coronary heart disease. Its low expression was an independent risk factor and could be used as a biomarker to predict acute myocardial infarction.

GW31-e0400

The prognostic value of mean platelet volume-to-lymphocyte ratio for long-term mortality in patients with coronary artery disease and diabetes mellitus who underwent primary percutaneous coronary intervention: a retrospective cohort study

Fenghua Song[1,2], Chaojian Zhang[1,2]
[1]Department of Cardiology, First Affiliated Hospital of Zhengzhou University
[2]Key Laboratory of Cardiac Injury and Repair of Henan Province, Zhengzhou, China

OBJECTIVES In present study, we aimed to explore the association of MPVLR with long-term mortality in CAD patients with diabetes mellitus (DM) who underwent percutaneous coronary intervention (PCI).

METHODS A total of 838 patients with CAD and DM who underwent PCI in the department of cardiology, the First Affiliated Hospital of Zhengzhou University from January 2013 to December 2017 were followed up. According to the cutoff value of MPVLR, all of the patients were divided into two groups: the low-MPVLR group (<5.69, n=583) and the high-MPVLR group (≥5.69, n=240). Multivariate Cox proportional hazards regression model was used to detect the predictors of endpoint events.

RESULTS In univariate analysis, there was significant difference in cardiovascular mortality (CM) (P<0.001) and all-cause mortality (ACM) (P<0.001) between the two groups. Multivariate Cox regression analysis showed that the MPVLR was an independent risk factor for long-term CM (hazard risk [HR]=3.579, 95% confidence interval [CI]: 1.602–8.078, P=0.002) and ACM (HR=2.390, 95% CI: 1.278–4.469, P=0.006) in patients with CAD and DM who underwent PCI.

CONCLUSIONS Elevated MPVLR was an independent and reliable predictor of long-term mortality patients with DM who underwent PCI.

GW31-e0402

Low expression of ADIPOR1 in peripheral white blood cells may be a genetic marker for early diagnosis of acute myocardial infarction

Xue Wang, Lihong Li, Fanbo Meng
The Third Hospital of Jilin University

OBJECTIVES To evaluate the correlation between the expression level of ADIPOR1 gene in peripheral blood leukocytes and the risk of acute myocardial infarction (AMI); combined with the baseline data analysis of the study subjects, to explore the role of ADIPOR1 gene in AMI.

METHODS In this study, we selected 69 patients with AMI as the case group and 63 patients with non-coronary heart disease as the control group. Both patients were diagnosed by coronary angiography. The clinical data of the two groups were analyzed and compared. In the peripheral venous blood, real-time fluorescence quantitative PCR was used to detect the mRNA expression of ADIPOR1 gene in peripheral blood.

RESULTS The relative expression of ADIPOR1 gene mRNA level in the group of patients with AMI and non-coronary heart disease showed that the relative expression of ADIPOR1 gene mRNA in peripheral blood leukocytes of AMI group was significantly lower than that of control group, and its relative expression level was control group 0.49 times. The clinical data analysis results of the study objects indicated that there was no significant difference between the two groups in terms of smoking history, total cholesterol level, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, hypertension diagnosis. However, there were significant differences in age, history of type 2 diabetes, smoking history, and triglyceride levels, and the differences were statistically significant (P<0.05). Further analysis of the relationship between clinical data and ADIPOR1 gene expression results: the relative expression level of ADIPOR1 gene mRNA level was independent of age (P=0.76), triglyceride levels (P=0.77), high density lipoprotein levels (P=0.99), low density lipoprotein levels (P=0.73), history of type 2 diabetes (P=0.80), and total cholesterol levels (P=0.42). Binary Logistic regression analysis showed that the low expression of mRNA in peripheral blood leukocytes of ADIPOR1 gene is an independent risk factor for the development of AMI. Compared with the high expression of ADIPOR1 gene, the risk of AMI with low expression of ADIPOR1 gene is increased by 3.01 times.

CONCLUSIONS ADIPOR1 gene is significantly under-expressed in peripheral blood of patients with AMI. Low expression of ADIPOR1 gene is an independent risk factor for the occurrence of AMI. ADIPOR1 gene may be used as a genetic marker to assess the risk of AMI.

GW31-e0406

Lipoprotein(a) level in early adulthood and subclinical atherosclerosis in middle age

Zhenyu Xiong, Xiangbin Zhong, Xiaodong Zhuang, Shaozhao Zhang, Xinxue Liao
Department of Cardiology, the First Affiliated Hospital, Sun Yat-Sen University

OBJECTIVES To measure the association between LP(a) and coronary artery calcification (CAC) during young to middle adulthood.

METHODS The Coronary Artery Risk Development in Young Adults study enrolled 5115 healthy black and white American aged 18–30 years at baseline. LP(a) was measured by a double monoclonal antibody enzyme-linked immunosorbent assay method at year 5. CAC was identified by computed tomography at years 15, 20 and 25.

RESULTS Of 3146 participants, the average (SD) level of LP (a) was 20.6 (21.5). About 28.2% participants developed CAC during 25 years. After multivariable adjustment, the hazard ratio for CAC associated with LP (a) was 1.11 (95% CI 1.01, 1.23) per 5 years increment. Results were similar when categorized individuals by clinical practice: compared with LP (a) ≤30 mg/dL, the hazard ratio of LP (a) >50 mg/dL was 1.26 (1.03, 1.56).

CONCLUSIONS Severe LP (a) level during young adulthood is independently associated with CAC at midlife, suggesting its potential use in predicting cardiovascular disease in an early stage.

GW31-e0409

Predictive efficacy of neutrophil-to-lymphocyte ratio for long-term prognosis in new onset acute coronary syndrome: a retrospective cohort study

Wang Jun[1], Yang Yi[2], Haibing Jiang[2]
[1]The People's Hospital of Xuancheng City
[2]The Xinjiang Medical University Affiliated Hospital of Traditional Chinese Medicine

OBJECTIVES Inflammation is involved in the pathogenesis and progression of coronary artery diseases (CADs), including acute coronary syndrome. The neutrophil-to-lymphocyte ratio (NLR) has been identified as a novel marker of the pro-inflammatory state. We aimed to evaluate the predictive efficacy of the NLR for the prognosis of patients with new-onset ACS.

METHODS We retrospectively included consecutive patients with new-onset ACS treated with emergency coronary angiography. NLR was measured at baseline and analyzed by tertiles. The severity of coronary lesions was evaluated by the Gensini score. Correlations of NLR with the severity of CAD and the incidence of major adverse cardiovascular diseases (MACEs) during follow-up were determined.

RESULTS Overall, 737 patients were included. The NLR was positively correlated with the severity of coronary lesions as assessed by Gensini score (P<0.05). During the follow-up period (mean, 43.49±23.97 months), 65 MACEs occurred. No significant association was detected between baseline NLR and the risk of MACEs during follow-up by either Kaplan–Meier or Cox regression analysis. The results of multivariable logistic regression analysis showed that a higher NLR was independently associated with coronary lesion severity as measured by the GS (1st tertile vs. 3rd tertile hazard ratio [HR]: 0.527, P<0.001, and 2nd tertile vs. 3rd tertile HR: 0.474, P=0.025).

CONCLUSIONS The NLR may be associated with coronary disease severity at baseline but is not associated with adverse outcomes for patients with new-onset ACS.

GW31-e0410

Clinical characteristics and the severity of coronary artery diseases of bundle-branch block

Jun Wang[1], Yang Yi[2], Benfang Wang[3]
[1]The People's Hospital of Xuancheng City, Anhui 242000, China
[2]Department of Cardiology fourth ward, The Xinjiang Medical University Affiliated Hospital of Traditional Chinese Medicine, Urumqi 830011, China
[3]Department of Coronary Heart Disease, The First Affiliated Hospital of Bengbu Medical College; Anhui 233000, China

OBJECTIVES Right bundle-branch block (RBBB) and left bundle-branch block (LBBB) plays a role in the pathogenesis and progression of coronary artery disease (CAD); however, the effect of RBBB and LBBB on the severity of coronary artery is not well characterized.

METHODS We retrospectively analyzed data pertaining to consecutive patients with RBBB or LBBB who underwent coronary angiography at two centers. The severity of coronary lesions was evaluated using the SYNTAX score. The differential effect of new-onset RBBB, old RBBB, new-onset LBBB, and old LBBB on the severity of CAD and its association with clinical characteristics was quantified. Multivariate logistic regression analysis was performed to evaluate the effect of RBBB and LBBB on the degree of coronary atherosclerosis.

RESULTS Out of the 243 patients, 72 patients had old LBBB, 37 had new-onset LBBB, 93 patients had old RBBB, and 41 patients had new-onset RBBB. On univariate analysis, age, systolic blood pressure, diastolic blood pressure, creatinine, serum glucose, and glycosylated hemoglobin level were associated with high SYNTAX score (P<0.05 for all). Patients in the new-onset RBBB, old RBBB, new-onset LBBB, and old LBBB groups showed significant differences in baseline characteristics and coronary atherosclerosis (P<0.05 for all). However, there were no significant between-group differences with respect to the degree of coronary atherosclerosis as assessed by SYNTAX score. On multivariate logistic analysis, age, systolic pressure, diastolic blood pressure, creatinine, serum glucose, lipoprotein(a), and previous myocardial infarction were associated with high SYNTAX score (P<0.05).

CONCLUSIONS New-onset RBBB, old RBBB, new-onset LBBB, and old LBBB were not associated with the severity of coronary lesions as assessed by SYNTAX score. Our findings suggest the clinical significance of RBBB in patients with chest pain due to suspected CAD.

GW31-e0419

Effects of statins and treatment duration on cardiovascular disease risk in patients with nephrotic syndrome: a nested case-control study

Xinliang Zou[1], Li Nie[2], Yi Liao[3], Zhihui Liu[1], Xiang Xu[1], Haoran Qin[1], Haidong Wang[3], Jianping Liu[1], Guoxiang He[1], Tao Jing[1]
[1]Department of Cardiology, The First Hospital Affiliated to Army Medical University (Southwest Hospital)
[2]Department of Internal Medicine, Central Hospital of Wandong
[3]Department of Thoracic Surgery, The First Hospital Affiliated to Army Medical University (Southwest Hospital)

OBJECTIVES Patients with nephrotic syndrome often have disorders of lipid metabolism. Elevated circulating low-density lipoprotein cholesterol (LDL-C) increases the risk of Atherosclerosis and is a risk factor for nephrotic syndrome complicated with cardiovascular events. Statins are the cornerstone of lipid management, but it is unclear whether statins can effectively reduce the occurrence of cardiovascular disease and improve the prognosis of patients with nephrotic syndrome who do not meet the criteria for chronic kidney disease. We designed a retrospective nested case-control study to observe whether the treatment of statins can reduce cardiovascular risk in patients with nephrotic syndrome. It provides new and strong evidence for the primary prevention of cardiovascular disease and the treatment of lipid metabolism disorders in patients with nephrotic syndrome.

METHODS In a single-center, retrospective nested case-control study, 350 patients with nephrotic syndrome at the First Affiliated Hospital of the Army Military Medical University between January 1, 1991, and November 30, 2019, were included in the study cohort. Of these, patients diagnosed with coronary artery disease (CAD) at the end of the observation period formed the case groups (n=115), or vice versa, the control groups (n=235). Obtain baseline information, duration of nephrotic syndrome, history of previous system diseases, HDL-C, LDL-C, eGFR, Alb, Fbg, and other biological test results. And also, statins using in treatment records as well as the accumulated medication duration. Use propensity score matching (ratio=1) to process the research cohort, construct contingency tables based on outcome events and statin usage, perform chi-square tests, and perform subgroup analysis based on different variables to draw forest maps. Perform binary logistic analysis to stratify by statins medication duration.

RESULTS Kept all the case group with propensity score matching (n=115), as well as the control group. Confounding of partly factors can be adjusted well. Chi-square test results shows that statin can reduce the risk of cardiovascular disease in patients with nephrotic syndrome (χ^2=9.939, OR=0.355 (0.183–0.685), P=0.002). Subgroup analysis suggests that females, age over 60 years, no smoking, no alcohol consumption, course of NS over ten years, BMI>25 kg/m^2, diabetes, eGFR≥90 and <60 mL/(min 1.73 m^2), ALB<30 g/L, Fbg≤3.8 g/L, the effect on the outcome was not significantly different. Compared with patients without statin, treatment followed by between 2–6 months and 7–12 months is statistically significant (0.36 (0.18–0.71), P=0.003) and (0.24 (0.10–0.61), P=0.002) in binary logistic regression analysis, with no significant difference by more than 12 months (P=0.863).

CONCLUSIONS In patients with nephrotic syndrome who have dyslipidemia, statin therapy can decrease their CAD risk in the future. In a cumulative treatment duration of 2–12 months, with a risk reduction of CAD as the treatment term extension.

GW31-e0444

Impact of macrophage infiltration on morphology of eroded plaque in patients with ST-segment elevation myocardial infarction assessed by optical coherence tomography

Chen Zhao[1,2], Sining Hu[1,2], Lulu Li[1,2], Wei Meng[1,2], Xi Chen[1,2], Ming Zeng[1,2], Bo Yu[1,2], Haibo Jia[1,2]
[1]Department of Cardiology, The 2nd Affiliated Hospital of Harbin Medical University
[2]The Key Laboratory of Myocardial Ischemia, Chinese Ministry of Education, Harbin, China

OBJECTIVES Autopsy series showed that plaques underlying coronary thrombi in acute coronary syndromes (ACS) may have different features, and the most common phenotypes are plaque rupture and plaque erosion, which was affirmed by the optical coherence tomography (OCT) studies. Different plaque morphologies might be potentially amenable to different treatments, and identification of patients with of ACS resulting from erosion may permit a less invasive approach to management than the current standard of care. Recent studies have revealed that 30% of ST-segment elevation myocardial infarctions (STEMI) are caused by plaque erosion. Chronic inflammatory infiltration is a common process for atherosclerosis development. However, autopsy studies reveal that incidence rate of inflammatory infiltrates are less abundant in erosion compared with rupture. Studies performed by OCT have allowed to establish the severity of plaque inflammation by assessing macrophage infiltration. In this study, we aimed to assess the impact of macrophage infiltration on morphology of eroded plaque in patients with STEMI by OCT.

METHODS Consecutive patients with STEMI undergoing OCT imaging during primary percutaneous coronary intervention (PPCI) between October 2014 and December 2017 were included in this study. Among them, only patients with plaque erosion at the site of the culprit lesion were included for analysis. Plaque morphology were compared between the plaques with and those without macrophage.

RESULTS Three hundred and eight patients with plaque erosion were enrolled in this study finally. Macrophage infiltration was detected in 162 (52.6%) patients with plaque erosion at the site of culprit lesion, whereas 146 (47.4%) patients had no evidence of macrophage infiltration. Patients with macrophage infiltration were significantly younger (P=0.014) than those without macrophage. Patients presenting macrophage infiltration in the culprit plaques had a smaller minimal lumen area (MLA) (P<0.001) as compared with those without macrophage. Culprit segments exhibiting macrophage infiltration had thinner minimum fibrous cap thickness (FCT) (P<0.001). Of note, the maximal lipid arc and lipid core length were significant larger in culprit plaque with macrophage infiltration despite no difference was found in the latter. The subgroup analysis was performed to estimate the impaction of macrophage infiltration in culprit lesions progress by OCT from baseline to 1-year follow-up. The severity of culprit lesions was well decreased and stability of culprit plaques was well improved in both of two groups at 1-years follow-up. Moreover, the minimal FCT was significantly increased in patients with macrophage infiltration (P=0.046).

CONCLUSIONS Macrophage infiltration increased culprit lesion severity and plaque vulnerability in patients with STEMI caused by plaque erosion. These results may help to further understand the pathophysiology of plaque erosion and potentially tailored treatment strategies.

GW31-e0446

Significance of low expression of AGPAT1 gene in peripheral blood leukocytes of patients with acute myocardial infarction

Xiaomin Tian, Heyu Meng, Fanbo Meng
China-Japan Union Hospital of Jilin University

OBJECTIVES AGPAT1 gene encodes 1-acyl-sn-glycerin-3-phosphate acyltransferase α, also known as LPA acyltransferase (LPAAT), is a key enzyme in the biosynthesis of phospholipids and triglycerides. It catalyzes the conversion of lysophosphatidic acid to phosphatidylcholine, and participates in cell signal transduction, inflammation, blood clot formation and other important biological processes. Inflammatory reaction and thrombosis are important pathological processes in the occurrence and development of coronary heart disease and myocardial infarction. The aim of this study was to evaluate whether the low expression of agpat1 gene in peripheral blood is associated with the risk of acute myocardial infarction (AMI), and whether it can be used as a biomarker to predict the risk of AMI.

METHODS Peripheral blood was collected from 91 patients with stable coronary heart disease and 95 patients with acute myocardial infarction. The mRNA expression of AGPAT1 gene was detected by real-time fluorescent quantitative polymerase chain reaction (PCR), and the expression level of AGPAT1 gene was detected by Western blot analysis at protein level.

RESULTS The results showed that the expression level of AGPAT1 gene in peripheral blood of AMI patients was significantly lower than that in stable CAD patients at RNA and protein levels (z=–2.358, P=0.018). There was no

correlation between agpat1 gene expression and age, blood pressure, blood glucose, blood lipid level, smoking history and drinking history. The expression level of AGPAT1 gene in peripheral blood of patients with acute myocardial infarction is 0.28 times higher than that of patients with stable coronary heart disease.

CONCLUSIONS AGPAT1 gene expression in peripheral blood of patients with acute myocardial infarction was significantly lower than that in patients with stable coronary heart disease. Its low expression is an independent risk factor and related to the occurrence of acute myocardial infarction, which can be used as a biomarker to predict acute myocardial infarction.

GW31-e0448

Comparison of kissing balloon dilation versus snuggling balloon dilation on stent deformation in bifurcations

Yifan Chen[1,2], Genshan Ma[1,2]
[1]Cardiology Department of Nanjing Zhongda Hospital
[2]School of Medicine, Southeast University

OBJECTIVES This study was sought to compare of kissing balloon dilation (KBD) versus snuggling balloon dilation (SBD) on stent deformation in bifurcations.

METHODS Three stenting techniques of DK-Crush, DK-Culotte and T-stent were simulated on a bifurcation model, each stenting technique repeated 3 times, resulting in 18 stented phantoms, and then each phantom received either KBD or SBD, finally yielding 9 KBD and 9 SBD treatment. Micro-CT was performed on the stented phantoms to qualitatively grade stent deformation as mild, moderate and severe, to quantitatively measure the lumen over-expansion index (LOEI) and lumen asymmetric index (LASI) in the bifurcation core and its adjacent regions.

RESULTS The baseline features between KBD and SBD were similar in stent diameter and balloon diameter for main- and side-branch, KBD and SBD inflation pressure and distal bifurcation angle. Whatever stenting techniques being used, KBD produced severe stent deformation in and near the bifurcation core in all phantoms while SBD induced only mild stent deformation in one phantom in DK-Culotte, with severe stent deformation rate of 100% (9/9) for KBD vs. 0% (0/9) for SBD (P<0.001). Compared to KBD, LOEI or LASI was much lower in SBD (LOEI: 1.05±0.06 vs. 1.36±0.15, P<0.01; LASI: 1.03±0.04 vs. 1.26±0.10, P<0.01).

CONCLUSIONS SBD doesn't cause and KBD frequently causes severe bifurcated stent deformation, indicating SBD is superior to KBD in optimization of bifurcated configuration in 2-stent techniques.

GW31-e0450

Incidence, management, and in-hospital mortality of cardiogenic shock complicating ST-elevation myocardial infarction in China: insights from the China acute myocardial infarction registry

Yu Ning, Guihao Chen, Jingang Yang, Chunyan Tian, Yanyan Zhao, Xiaoyu Zhang, Yang Wang, Haiyan Xu, Yuejin Yang
State Key Laboratory of Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES Compared with America or Europe, the situation of cardiogenic shock (CS) complicating ST-elevation myocardial infarction (STEMI) in Asia is less known. The present study aimed to reveal the incidence rate, management, and in-hospital mortality of patients with CS complicating STEMI (STEMICS) in the whole China and at different-level (provincial, prefectural and county-level) hospitals.

METHODS We queried the 2013–2016 China Acute Myocardial Infarction (CAMI) registry databases to identify all patients with STEMI and/or CS (developing before or during hospitalization). We analyzed the incidence, management, and in-hospital mortality of patients with STEMICS in the whole China and at provincial, prefectural, and county-level and hospitals. Multivariable logistic regression models were used to identify predictors of CS and in-hospital death.

RESULTS The CAMI Registry enrolled 40,200 patients with acute myocardial infarction from 2013 to 2016. We finally included 28,054 STEMI patients in the study cohort. Of 2273 patients (8.1%) had CS, including 1132 (4.0%) with prehospital CS (developing before hospitalization) and 1141 (4.1%) with in-hospital CS (developing during hospitalization). Twenty-five thousand seven hundred eighty-one patients had no CS. 29.7% of the patients with overall STEMICS underwent primary percutaneous coronary intervention (PPCI). Rates of PPCI were 33.9 and 25.5% in patients with prehospital and in-hospital STEMICS respectively. In-hospital mortality were 49.8% in overall STEMICS, 33.7% in prehospital STEMICS, and 65.6% in in-hospital STEMICS. PPCI was an independent predictor of in-hospital STEMICS (odds ratio, 0.72; 95% CI, 0.59–0.88; P=0.0015) and in-hospital death in patients with prehospital STEMICS (odds ratio, 0.53; 95% CI, 0.33–0.83; P=0.0062). In terms of hospital level, the incidence rates of STEMICS (overall, prehospital, and in-hospital STEMICS) and in-hospital mortality of patients with prehospital STEMICS from county-level hospitals were dramatically higher than those from provincial or prefectural hospitals, which might be associated with the much lower PPCI rates in the patients from county-level hospitals.

CONCLUSIONS Rates of STEMICS in China between 2013 and 2016 were consistent with those in western countries. However, the PPCI rates of STEMICS in China were relatively low and in-hospital mortality were dramatically high. In China, STEMICS patients from county-level hospitals had higher rates of CS and in-hospital mortality but lower PPCI rate than those from provincial or prefectural hospitals. PPCI was an independent protective factor against CS developing during hospitalization and in-hospital death in patients with prehospital STEMICS.

GW31-e0451

Traits of coronary angiography in renal transplant recipients with coronary artery disease

Xunxun Feng, Qianyun Guo, Guangyao Zhai, Yujie Zhou
Capital Medical University, Beijing Anzhen Hospital

OBJECTIVES Patients that undergo renal transplantation (RT) often suffer from high rates of cardiovascular disease-related mortality, yet there have not been sufficient angiographic studies of coronary artery disease (CAD) findings in RT patients conducted to date.

METHODS This study examined coronary angiography findings from 45 patients with functional renal grafts for over 6 months that were analyzed in Anzhen Hospital (Beijing, China) from 2014 to 2019. For comparison purposes, we additionally examined coronary angiography findings from 45 age- and sex-matched patients undergoing chronic dialysis due to end-stage renal disease (ESRD). We used the SYNTAX score to gauge CAD severity.

RESULTS The duration of ESRD in patients in the RT group was significantly longer than for that of patients in the dialysis comparison group (19.31±7.83 vs. 11.43±8.04 years, P<0.001). The SYNTAX scores for patients in the dialysis and RT groups were 17.76±7.35 and 12.57±5.61, respectively (P<0.01). We found that 64.4 and 28.9% of dialysis and RT patients, respectively, exhibited the presence of moderate or severe calcified lesions upon examination. In addition, the SYNTAX scores of RT patients were correlated with ESRD duration (P<0.001).

CONCLUSIONS We observed less serious CAD in RT patients relative to long-term dialysis patients even though the former group exhibited a longer mean ESRD duration. Both groups exhibited high rates of calcification of the coronary artery, even following RT.

GW31-e0453

The left distal transradial artery (LDTRA) access for coronary angiography and intervention: a single center experience

Xianjing Wei, Lianna Xie
The Affiliated Zhongshan Hospital of Dalian University, Dalian

OBJECTIVES Although the right radial artery access is considered as the default technique for Percutaneous Coronary Intervention access, the incidence of radial artery occlusion is still relatively high, discomfort from perioperative patients is common and Inconveniences are overflowed for operators whose patient's right radial occlusion, underdeveloped right radial artery, extreme right radial tortuosity, sclerosis or calcifications, arteria lusoria, previous right radial failure, presence of an arteriovenous shunt in the right arm, post-CABG patients requiring LIMA angiography. The aim of this report is to evaluate the feasibility of the left distal transradial (lDTRA namely, anatomical snuffbox) assess.

METHODS Of 550 consecutive patients needed coronary angiography or intervention therapy in the Affiliated Zhongshan Hospital of Dalian University, from January 2019 to January 2020, no forearm artery ultrasound before operation, were stratified into two groups: group A: the patients underwent right radial artery puncture; group B: underwent LDTRA puncture. We analyze the safety and Feasibility between 2 groups. Feasibility was the success rate of cannulate the distal left radial artery and completing Coronary Intervention detail: X-ray exposure time, the number of angiographic catheters to per patient, the number of completed target revascularization, complexity of coronary intervention. The safety point included hematoma, bleeding or neuropathy.

RESULTS Of 260 consecutive patients assigned to group A, 248 cases underwent (Success rate of 95.38%) right radial puncture, 106 cases were cannulated 6F radial artery sheaths and 142 cases were cannulated 5F radial artery sheaths; Group B was attempted in 290 patients, 277 cases (95.52%) had successful completion of the procedure, 96 cases were cannulated 6F radial artery sheaths and 181 cases were cannulated 5F radial artery sheath. The success rate between the two group is no statistical significance, P<0.05. There was no significant difference between the two groups in the details of coronary intervention (the

number of angiographic catheters to per patient, the number of completed target revascularization, complexity of coronary intervention) P<0.05. However, the rate of forearm hemorrhage and radial artery occlusion during hospital to LDTRA is lower than that of right radial artery approach.

CONCLUSIONS LDTRA is a safe and feasible arterial access. LDTRA provides improved operator ergonomics and patient's comfort.

GW31-e0455

Serum uric acid and hyperuricemia as risk factors in postmenopausal women with coronary artery disease

Xunxun Feng, Qianyun Guo, Guangyao Zhai, Yujie Zhou
Capital Medical University, Beijing Anzhen Hospital

OBJECTIVES Serum uric acid (SUA) levels has been considered a possible risk factor for coronary artery disease (CAD) for many years. Since SUA levels is greatly affected by the body's medication therapies, dietetic status, and metabolism, the interactions between SUA and CAD have been controversial for centuries. However, the state of hyperuricemia (HUA) has been proven to have a negative impact on CAD in previous studies, but there is still few clinical and epidemiological evidence of HUA in CAD. In view of the fact that there are few studies on postmenopausal women, this study explored the influence of SUA levels and HUA on CAD in this demographic group.

METHODS In total, 5435 postmenopausal women were allocated to either a non-CAD group (n=2021) or a CAD group (n=3414). Regression analysis, correlation analysis, comparison between stratified groups, and statistical analysis of diuretics were carried out on data obtained in this study.

RESULTS In the multivariate analysis, we found that SUA and HUA were independent risk factors for CAD (SUA OR model 1 to model 4: 1.004, 1.004, 1.004 and 1.003; HUA OR model 1 to model 4: 1.844, 1.837, 1.731 and 1.486). Correlation analysis showed that SUA and HUA positively correlated with CAD (P<0.001). By comparing the stratified age groups, we found that the differences between the groups were significant (P<0.05).

CONCLUSIONS SUA levels might be greatly affected by age while HUA could be influenced by diuretic use, so the effects of both age and diuretic use on SUA levels and HUA should not be ignored. To some extent, SUA and HUA could be independent risk factors for postmenopausal women with CAD.

GW31-e0457

Myocardial work echocardiography is a new method to predict major adverse cardiac events in patients with acute myocardial infarction

Zhiqing Qiao, Xuedong Shen, Ying Zheng, Wei Wang, Hang Zhao, Jun Pu
Renji Hospital, Shanghai Jiao Tong University School of Medicine

OBJECTIVES Myocardial work echocardiography (MWE) is a new method to evaluate myocardial contraction, which is based on the left ventricular pressure and speckle tracking echocardiography. This study was aimed to analyze the relationship between the measurements of MWE and outcome in patients with acute ST-elevated myocardial infarction (STEMI) after primary percutaneous cardiac intervention (PCI) during hospitalization.

METHODS The study included 42 patients with acute STEMI who successfully underwent primary PCI (37 men, age 61.9±9.5 years). The 42 patients underwent MWE within 24 hours after PCI, and 25 of them underwent MWE again within 2–9 days after PCI (mean 4.36±2.02 days). The measurements included global myocardial work index (GWI), global myocardial constructive work (GCW), global myocardial wasted work (GWW), global myocardial work efficiency (GWE). Each segment of left ventricle was further analyzed for pressure-strain loop to evaluate its shape, orientation and size. Other parameters included brain natriuretic peptide (BNP) and left ventricular ejection fraction (LVEF).

RESULTS Five patients had major adverse cardiac events (MACE) after PCI, including 1 death and 4 acute heart failures during hospitalization. There were significant improved in LVEF, GWI, GCW, GWW and GWE (P=0.002–0.04) at second follow up after PCI, but not in BNP (P=0.06). The sensitivity and specificity of GWE predicting MACE were 83 and 81%, respectively (cutoff point<75.7%, AUC=0.86, P=0.0001). Multivariate regression analysis showed that GWE independently predicted MACE (OR=0.89, 95% CI=0.81–0.98, P=0.02). Further analysis showed that the shape, orientation and size of left ventricular pressure-strain loop in ischemic segment had no significantly improved in 8 of 25 patients at follow up. The shape of the loop was narrow and it shifted to right in those patients. The incidence of MACE in patients who had unimproved loops in ischemic segments was significantly higher than that in patients who had improved loops (50.0 vs. 5.9%, P=0.01).

CONCLUSIONS MWE provides us a new sight to evaluate the outcome after PCI. It is of vital importance to explore the regression of ischemic segments after PCI.

GW31-e0463

In patients with acute coronary syndrome, the STOP LINE is the location of vulnerable plaques caused by violent collision between antegrade and retrograde coronary flow in patients

Thach Nguyen[1,2], Nguyen Thanh Luan[2], Vy Le[2], Duy Chung[1], Tra Ngo[1], Luan Ngo[1], Phuong M. Nguyen[1], Phuoc T. Nguyen[1], Thai Truong[1], An T. Ngo[1], Hoang C. Nguyen[1], Quang N.N. Do[2], Hien D.N. Duong[2], Vu Tri Loc[2], Tran P.H. Nhan[3], Cao Van Thinh[4], Ho Thuong Dung[5], Gianluca Rigatelli[6], Aravinda Nanjundappa[7]
[1]Methodist Hospital, Merrillville IN
[2]Tan Tao University School of Medicine
[3]Tam Duc Hospital, Hochiminh City, VN
[4]Pham Ngoc Thach School of Medicine, Hochiminh City, VN
[5]Thong Nhat Hospital, Hochiminh City, VN
[6]Cardiovascular Diagnosis and Endoluminal Interventions, Section of Adult Congenital Interventions, Rovigo General Hospital, Rovigo, Italy
[7]The University of West Virginia Medical Center, Charleston, WV

OBJECTIVES Coronary injuries are hypothesized to be caused by the cavitation phenomenon (explosion of air bubbles) which is seen frequently in domestic or industrial pipes. Following hydraulics principle, with distal negative suctioning in diastole, if the coronary dynamic pressure decreases below the vapor pressure (VP) most likely of nitrogen in the blood, bubbles would form. They explode when the coronary dynamic pressure recovers>the VP during systole. These explosions create jet waves weakening and rupturing the cap of the plaque, triggering acute coronary syndrome (ACS). How could these events be located, recorded and tabulated?

METHODS Angiograms with ACS culprit lesions were selected. The left coronary arteries were recorded in the right anterior oblique caudal view and the right coronary artery in the left anterior oblique view (at 15 frames per second). Then the angiograms were viewed off line frame by frame. The first frame was the angiogram of an artery completely filled with contrast. The following frames showed the blood moving in, seen in white. The flow could be LAMINAR (Figure 1A and B). TURBULENT (mixing of blood in white and contrast in black) (Figure 2) or RETROGRADE (black column traveling backward). The turbulent flow reflects the collision between antegrade and retrograde flow. The LOCATION and the length in TIME of laminar, retrograde and mainly turbulent flow were recorded. The intensity of turbulent flow was measured by (1) the length of coronary segment with mixing contrast and blood (2) the length of the stagnant retrograde flow.

RESULTS The results of 50 angiograms with ACS showed that after being laminar (85%) at the beginning of diastole, the flow became turbulent with diffuse mixing of black (contrast) and white (blood) at the MID SEGMENT of the LAD, LCX or RCA. This observation matched with the location of 82% of ruptured plaques. The length of the time of retrograde flow lasted more than 30 frames encompassing 2 systoles.

CONCLUSIONS This is the first time, the matching of location of ruptured plaques and turbulent flow representing the collision between antegrade flow in diastole and retrograde flow in systole was confirmed. These results may help to find the precise measures preventing ACS.

GW31-e0490

Mediation differences of gender on coronary heart disease risk by modifiable traditional cardiovascular factors in youth stage: a cohort study

Xiangbin Zhong, Yifen Lin, Shaozhao Zhang, Xiaodong Zhuang, Xinxue Liao
First Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES Cardiovascular disease remains the leading cause of mortality world wild. Coronary heart disease (CHD) accounts for the greatest proportion of CVDs. Coronary heart disease was thought to be an infirmity of age, but the proportion of AMI hospitalizations attributable to young patients increased and was most pronounced among women, which indicates the risk factors has already accumulated among sex even in the youth. Risk assessment with long-term prediction algorithms can help to identify individuals who would benefit most from risk-factor interventions [1], but failed in suggesting the difference proportion among sex in youth. To further optimize preventive strategies for coronary heart disease among sex, it is essential to understand and appropriately quantify the mediation differences of gender on CHD by traditional cardiovascular factors [2].

METHODS This investigation included Framingham Heart Study offspring cohort participants attending their first examination cycle (1971–1975), when traditional risk factors data were first reliably collected. During the following, newly onset coronary heart disease before 2010 was recorded. Written informed consent was obtained from participants for all study procedures. Mediation analysis was used to compare the mediation proportion of sex on Coronary Heart Disease by traditional cardiovascular factors mentioned in Framingham risk score. Each study was approved by relevant local or national ethics committees and all procedures performed in these studies were in

accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Statistical analysis was performed by R version 3.5.2, while mediation analysis was achieved by package "Mediation".

RESULTS Of 5013 offspring cohort participants, consists of 2427 males and 2586 females were enrolled. 615 male (25.3%) and 287 (11.1%) female adjudicated to have a CHD during the study period. All of the traditional risk factors showed statistically different distribution between males and females (Table 1).

CONCLUSIONS The different mediation of sex on CHD was mostly contributed by blood pressure (DBP 31% or SBP 26%). High-density cholesterol and low-density cholesterol (or total cholesterol) provided 23 and 19% (or 13%) difference. Age, smoking status, and diabetes provided less than 10% contribution to CHD risk. The imbalanced distribution of traditional risk factors made up to 88% differences in CHD risk among males and females.

GW31-e0496

Visit-to-visit glycemic variability is associated with in-stent restenosis in patients with type 2 diabetes after percutaneous coronary intervention

Chendie Yang, Xiaoqun Wang
Department of Cardiology, Ruijin Hospital, Shanghai Jiao-Tong University School of Medicine, Shanghai, P.R. China

OBJECTIVES Patients with type 2 diabetes are under substantially higher risk of in-stent restenosis (ISR) after coronary stent implantation. We sought to investigate whether visit-to-visit glycemic variability is a potential predictor of ISR in diabetic patients after stent implantation.

METHODS Type 2 diabetic patients underwent elective percutaneous coronary intervention were consecutively enrolled and 1-year follow-up coronary angiography was performed. The incidence of ISR and its relationship with visit-to-visit HbA_{1c} variability, expressed as coefficient of variation (CV), standard deviation (SD) and variability independent of the mean (VIM), were studied. Multivariable Cox proportional hazards models were constructed to analyze the predictive value of glycemic variability for ISR.

RESULTS From September 2014 to July 2018 in Ruijin Hospital, a total of 420 diabetic patients (688 lesions) after stent implantation were included in the final analysis. During a mean follow-up of 12.8±1.3 months, the incidence of ISR was 8.6%, which was significantly increased in patients with higher CV of HbA_{1c} (P=0.001) The mean diameter stenosis (DS), net luminal loss and net luminal gain were 22.9±16.8%, 0.42±0.88 mm and 1.66±0.83 mm, respectively. Greater DS was observed in subjects with higher tertiles of CV of HbA_{1c} (P<0.001), and this trend was more prominent in patients with optimal glycemic control (HbA_{1c}≤7%). In multivariate analysis, HbA_{1c} variability was independently associated with incidence of ISR after adjustment for traditional risk factors and mean HbA_{1c} (HR: 3.00 [95% CI: 1.14~7.92] for highest vs. lowest tertile). Inclusion of CV of HbA_{1c} led to a better risk stratification accuracy. Assessing glycemic variability by SD or VIM yielded similar findings.

CONCLUSIONS This study suggests that visit-to-visit HbA_{1c} variability is an independent predictor of incidence of ISR in patients with type 2 diabetes after stent implantation.

GW31-e0516

Increased serum TREM-1 level is associated with in-stent restenosis, and activation of TREM-1 promotes inflammation, proliferation and migration in vascular smooth muscle cells

Chendie Yang, Xiaoqun Wang
Rui Jin Hospital, Shanghai Jiao-Tong University School of Medicine, Shanghai, P.R. China

OBJECTIVES In-stent restenosis (ISR) remains a major limitation of percutaneous coronary intervention despite improvements in stent design and pharmacological agents, whereas the mechanism of ISR has not been fully clarified. In the present study, we sought to investigate the potential association of serum soluble TREM-1 (sTREM-1) levels with the incidence of ISR. The role of TREM-1 was evaluated in cultured vascular smooth muscle cells (VSMCs).

METHODS In 1683 patients undergoing coronary intervention and follow-up coronary angiography after approximately one year, 130 patients were diagnosed with ISR, and 150 gender- and age-matched patients with no ISR were randomly included as controls. Levels of sTREM-1 were determined by ELISA. The role of TREM-1 signaling in the activation of VSMCs was tested.

RESULTS Serum sTREM-1 concentrations were significantly elevated in patients with than without ISR. Multivariable logistic regression analysis showed that sTREM-1, besides conventional factors, was independently associated with the incidence of ISR. Evident expression of TREM-1 in VSMCs was detected both in the neointimal and medial layers of stenotic lesions of mouse carotid ligation models. In cultured VSMCs, expression of TREM-1 was significantly induced upon exposure to lipopolysaccharide. Blocking of TREM-1 with a synthetic inhibitory peptide LP17 dramatically inhibited, whereas TREM-1-activating antibody promoted cellular inflammation, proliferation and migration in VSMCs.

CONCLUSIONS These data suggest that TREM-1 is a predictive biomarker of ISR and an important mediator of cellular inflammation, migration, and proliferation in VSMCs. Pharmacological inhibition of TREM-1 may serve as a promising approach to attenuate the progression of ISR.

GW31-e0519

Association of cholesterol efflux capacity of high-density lipoprotein with coronary collateralization in patients with stable angina and chronic total occlusion

Xiaoqun Wang
Rui Jin Hospital, Shanghai Jiao-Tong University School of Medicine, Shanghai, P.R. China

OBJECTIVES High-density lipoprotein (HDL) is a pluripotent atheroprotective factor with reverse cholesterol transport, anti-inflammatory, and pro-angiogenic activities. Increasing evidence suggests that HDL function rather than concentration would be a more relevant measure to predict cardiovascular risk. In this study, we sought to investigate whether cholesterol efflux capacity (CEC) of HDL is related to coronary collateralization in patients with stable angina and chronic total occlusion.

METHODS CEC was determined *in vitro* in 115 patients with stable angina and angiographic total occlusion of at least one major coronary artery. The degree of coronary collaterals supplying the distal aspect of a total occlusion from the contralateral vessel was graded according to Rentrop classification.

RESULTS CEC of HDL was significantly elevated in good collateralization (Rentrop score of 2–3) than poor collateralization (Rentrop score of 0–1) group (15.39±10.17% vs. 10.18±5.41%, P=0.004). While CEC was positively correlated to Rentrop score (Spearman's r=0.275, P=0.005), no correlation was observed between Rentrop score and serum levels of HDL-cholesterol or apolipoprotein A. Receiver operating characteristic curve yielded an AUC of 0.662 (95% confidence interval: 0.558–0.767, P=0.006) in discriminating good or poor collateralization. After adjusting for age, gender, body mass index and conventional risk factors for coronary artery disease in multivariate logistic regression analysis, CEC persisted to be an independent determinant for good collateralization (odds ratio: 1.11 per 1% increase, P=0.006).

CONCLUSIONS Increased CEC of HDL is associated with good coronary collateralization in patients with stable angina and chronic total occlusion.

GW31-e0522

Revascularization of coronary artery chronic total occlusion by active antegrade reverse wire technique

Xiaojiao Zhang, Aijie Hou, Bo Luan
Department of Cardiology, The People's Hospital of China Medical University, The People's Hospital of Liaoning Province

OBJECTIVES To assess the effectiveness and safety of ARW for vascular recanalization in CTO patients.

METHODS A total of 301 consecutive CTO patients who received the antegrade percutaneous coronary intervention (PCI) between December 2015 and December 2019 at our institution were included, of whom 11 were treated with ARW (10 successfully) for vascular recanalization. The applicability and safety of ARW were assessed.

RESULTS Among the 301 CTO patients who received antegrade vascular recanalization, 11 were treated with ARW. The following treatment approach was successful in 10 patients as follows: from the diagonal branch (D) to anterior descending branch (LAD) in 4 patients; from the septal branch (S) to LAD in 1 patient; from D to S and LAD in 1 patient; from the circumflex branch (LCX) to obtuse marginal branch (OM) in 1 patient; from OM to LCX in 1 patient; from a posterior descending artery (PDA) to the posterior lateral vein (PLV) in 2 patients. Yet, the treatment in the other patient with RCAm CTO failed, while the consequent reverse vascular recanalization succeeded. The mean J-CTO score of the 11 patients was 2.7±0.65, among whom eight were accompanied with calcifications. Sion Black and Fielder XT-R reverse wires were used in 9 and 2 patients, respectively. No loss of side branches or severe surgery-related complications occurred in 11 patients.

CONCLUSIONS Therefore, WRW can improve surgical efficiency and should be popularized for further application.

GW31-e0588

An evaluation for the expanding needs on lipid-lowering treatment strategies in patients with acute coronary syndrome by applying newly issued definition of extreme high-risk by Chinese Society of Cardiology: findings from CCC-ACS project

Yuhong Zeng, Dong Zhao
Department of Epidemiology, Beijing Anzhen Hospital, Capital Medical University, Beijing Institute of Heart, Lung and Blood Vessel Diseases

OBJECTIVES Recently, Chinese Society of Cardiology (CSC) expert consensus on lipid management of extreme high-risk atherosclerotic cardiovascular disease (ASCVD) patients recommended further risk stratification among patients with ASCVD. A new definition of category of "extreme high-risk" has been proposed by this expert consensus, along with, the new and lower treatment target of low-density lipoprotein cholesterol (LDL-C) was recommended for the patients. This study aimed to assess the expanding needs on lipid-lowering treatment by applying the new risk category among patients with acute coronary syndrome (ACS).

METHODS The study was based on the Improving Care for Cardiovascular Disease in China (CCC) project, which was launched in 2014 as a collaborative initiative of the American Heart Association and the CSC. This study enrolled ACS inpatients in CCC from 240 hospitals nationwide from November 2014 to July 2019. The proportion of patients at extreme high-risk, mean LDL-C levels at admission and the median distance between LDL-C level and the new target were assessed.

RESULTS Among 104,516 ACS inpatients enrolled in this study, 75.1% (78,521) met the criteria of extreme high-risk and were expected to achieve the new LDL-C goal. Among patients at extreme high-risk, 21.2% (16,651) had multiple severe ASCVD events and 78.8% (61,870) had 1 severe ASCVD event and at least two high-risk factors. For the extreme high-risk patients, the mean level of LDL-C was 106.5±39.3 mg/dL, 92.8% of them had LDL-C≥55 mg/dL at admission and the median distance between LDL-C level and the target of 55 mg/dL was 51.3 (30.1, 76.1) mg/dL.

CONCLUSIONS About three fourth of inpatients with ACS were categorized as extreme high-risk based on the definition of CSC expert consensuses, nine out of ten patients at extreme high-risk didn't achieve the new LDL-C target at admission. There are substantially expanding needs for more effective lipid-lowering strategies.

GW31-e0596

Value of platelet-to-lymphocyte ratio on prediction of left ventricular thrombus in anterior ST-elevation myocardial infarction with left ventricular dysfunction

Qian Zhang, Daoyuan Si, Zhongfan Zhang, Haikuo Zheng, Wenqi Zhang
China-Japan Union Hospital of Jilin University

OBJECTIVES The predictors of left ventricular thrombus (LVT) formation are not well-defined in the contemporary era, especially in those patients at high risk. We aimed to evaluate whether platelet-to-lymphocyte ratio (PLR) be valuable in determining LVT formation in patients with anterior ST-Elevation Myocardial Infarction (STEMI) and left ventricular (LV) dysfunction.

METHODS LVT group (n=46) were identified from the anterior STEMI patients with LV dysfunction, who were treated with the primary percutaneous coronary intervention (PCI) from January 2017 to December 2019 in China-Japan Union Hospital of Jilin University. The controls (n=92) were also selected from the same batch patients, with age and gender matched and without LVT. PLR were determined at admission, which was calculated as the ratio of the platelet count to the lymphocyte count using complete blood count. LVT was defined by echocardiography.

RESULTS The PLR levels were significantly higher in patients with LVT than those in controls (P=0.001). In a receiver operator characteristic curve (ROC) analysis, using a cut-off value of 118.07 (AUC 0.673, 95% CI: 0.574–0.771, P=0.001) could independently predict the occurrence of LVT. Multivariate analysis showed that increased PLR (OR=1.011, 95% CI: 1.004–1.018, P=0.002), left ventricular aneurysm (OR=46.350, 95% CI: 5.659–379.615, P<0.001) and DTBT (OR=1.005, 95% CI: 1.001–1.009, P=0.012) were independent predictors in predicting LVT formation.

CONCLUSIONS In acute anterior STEMI patients with LV dysfunction, PLR is an independent predictor of LVT formation. A larger prospective study is warranted to evaluate this result.

GW31-e0598

In-hospital outcomes of ticagrelor versus clopidogrel in combination with aspirin in patients 75 years and older with acute coronary syndrome: findings from CCC-ACS project

Na Yang[1], Jing Liu[1], Jun Liu[1], Yongchen Hao[1], Yuhong Zeng[1], Sidney C. Smith Jr[2], Yong Huo[3], Gregg C. Fonarow[4], Junbo Ge[5], Kathryn A. Taubert[6], Louise Morgan[7], Changsheng Ma[8], Yaling Han[9], Dong Zhao[1]
[1]Department of Epidemiology, Beijing An Zhen Hospital, Capital Medical University, Beijing Institute of Heart, Lung and Blood Vessel Diseases, Beijing, China
[2]Division of Cardiology, University of North Carolina, Chapel Hill, NC
[3]Department of Cardiology, Peking University First Hospital, Beijing, China
[4]Division of Cardiology, Geffen School of Medicine at University of California, Los Angeles, CA
[5]Department of Cardiology, Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital, Fudan University, Shanghai, China
[6]Department of International Science, American Heart Association, Basel, Switzerland
[7]International Quality Improvement Department, American Heart Association, Dallas, TX
[8]Department of Cardiology, Beijing An Zhen Hospital, Capital Medical University, Beijing, China
[9]Cardiovascular Research Institute and Department of Cardiology, General Hospital of Shenyang Military Region, Shenyang, Liaoning, China

OBJECTIVES To evaluate the effect of ticagrelor plus aspirin in in-hospital outcomes compared with clopidogrel plus aspirin in patients 75 years and older with acute coronary syndrome (ACS) in a real-world population.

METHODS The Improving Care for Cardiovascular Disease in China-ACS project is an ongoing quality improvement project of the American Heart Association and Chinese Society of Cardiology. The primary effectiveness outcome was in-hospital major adverse cardiovascular event (MACE) including cardiac death, myocardial infarction (MI), stent thrombosis, and ischemic stroke during hospitalization. The major safety outcome was major bleeding. Cox proportional hazard models adjusting for confounders were used to evaluate the effect of ticagrelor plus aspirin in in-hospital outcomes compared with clopidogrel plus aspirin. A propensity score-matched analysis was also conducted.

RESULTS From November 2014 to December 2019, 18,244 ACS patients aged 75 years and older receiving dual antiplatelet therapy (3566 received ticagrelor plus aspirin and 14,678 received clopidogrel plus aspirin) were included. Patients receiving ticagrelor plus aspirin were more likely to be ST-segment-elevation myocardial infarction and male, and had less comorbidities. The MACE had occurred in 4.57% of the patients receiving ticagrelor plus aspirin as compared with 4.28% of those receiving clopidogrel plus aspirin (hazard ratio (HR): 1.14; 95% confidence interval (95% CI): 0.93–1.39; P=0.20). The major bleeding had occurred in 3.31% of the patients receiving ticagrelor plus aspirin as compared with 2.64% of those receiving clopidogrel plus aspirin (HR: 1.00; 95% CI: 0.74–1.35; P=0.99). Among 6396 propensity score-matched patients, 4.47% of the patients receiving ticagrelor plus aspirin had MACE, while 4.00% of the patients receiving clopidogrel plus aspirin had MACE (HR: 1.18; 95% CI: 0.90–1.55; P=0.24). A total of 3.00% of the patients receiving ticagrelor plus aspirin had major bleeding, while 2.41% of the patients receiving clopidogrel plus aspirin had major bleeding (HR: 1.08; 95% CI: 0.69–1.69; P=0.73).

CONCLUSIONS In patients with ACS and aged 75 years and older, ticagrelor had comparable effects with clopidogrel in reducing the occurrence of in-hospital MACE and major bleeding.

GW31-e0601

Rebound of acute myocardial infarction admission after COVID-19 pandemic

Yong Liu[1], Yibo He[1], Liwei Liu[1], Guoli Sun[1], Shiqun Chen[1], Jin Liu[1], Wenhua Liang[2], Chunquan Ou[3], Kaihong Chen[4], Liling Chen[4], Jianfeng Ye[5], Yan Liang[6], Yunzhao Hu[7], Jie Li[1], Xin Li[1], Ning Tan[1], Jiyan Chen[1]
[1]Department of Cardiology, Guangdong Cardiovascular Institute, Guangdong Provincial Key Laboratory of Coronary Disease, Guangdong Provincial People's Hospital, South China University of Technology, Guangzhou 510100, China
[2]Department of Pneumology, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China
[3]Department of Statistics, Southern Medical University, Guangzhou, China
[4]Longyan First Affiliated Hospital of Fujian Medical University, Longyan, China
[5]Dongguan TCM Hospital, Dongguan, China
[6]Maoming People's Hospital, Maoming, China
[7]Shunde Hospital of Southern Medical University, Shunde, China

OBJECTIVES To assess the tendency of acute myocardial infarction (AMI) patients admission during and after the COVID-19 outbreak.

METHODS This study is a cross-sectional study. Admission data of acute myocardial infarction patients were enrolled in five PCI centers, which were also the designated hospital for COVID-19 patients of the 5 cities in southern China. The section of pandemic period of COVID-19 was defined as January 23, 2020 to February 24, 2020, when public health First Level Emergency Response were carried out by provincial health commission. AMI admission of pandemic period were compared with pre-pandemic period (January 1–22, 2020), recovery period following pandemic (February 25 till April 30, 2020). Considering the influence of China Spring Festival, the adjusted section of the former

corresponding period of pandemic period in 2019 was defined as January 12 till May 10, 2019. The cross-sectional number of AMI patients admission were compared to assess the difference with the use of Poisson regression. Weekly admission was drawn to understand the tendency of how it changed along the pandemic period to the recovery period.

RESULTS During the COVID-19 pandemic period, the average admission rate of AMI patients was 5.45 per day, which was significant lower than that of pre-pandemic period and the former corresponding period in 2019 (8.32 and 10.38 patients per day respectively, P<0.001). As the pandemic period ended up, the AMI patients admission rate was 6.89 per day, significantly higher than the pandemic period, however, lower than the pre-pandemic period and the former corresponding period. Weekly admissions were drawn from January 1 to April 28, the number of AMI admission was on the rise, returning to the same level of the corresponding period in 2019 at the eighth week following the end of pandemic period.

CONCLUSIONS When the COVID-19 pandemic period end up, the number of AMI patients admission which have fallen since the outbreak would rebound gradually.

GW31-e0604

The independent and incremental value of ultrasound carotid plaque length to predict the presence and severity of coronary artery disease: analysis from the carotid plaque length prospective registry

Pan Li, Wendong Tang, Xiaxian Shen, Pan Hou, Hailing Li, Xian Guo, Xianxian Zhao
Changhai Hospital, Shanghai

OBJECTIVES Early detection and prevention of high-risk coronary artery disease (CAD), especially in atypical patients, is clinically crucial to reduce cardiovascular death. Computed tomography angiography (CTA) or coronary angiography (CAG) have limited application as screening tools, due to invasiveness, costliness, radiation risk and potential renal injury. Carotid ultrasound is a noninvasive and sensitive screening method for detecting subclinical atherosclerosis and identifying CAD. The commonly used prediction index, the intima-media thickness (IMT) and carotid plaque score (PS) have been shown to be associated with CAD. However, recent evidence has proven that IMT has a weak predictive value of CAD. Moreover, the variation range in plaque thickness is small (approximately 0.01–0.1 mm), and the measurement process of PS is complicated and time-consuming; hence, following individual changes in atherosclerosis progression is difficult. In contrast, plaque length grows faster than its thickness and has a large dynamic range, which makes it convenient for clinical observation. Nevertheless, the relationship between ultrasound-based carotid plaque length (CPL) and CAD has not been fully explored. This study therefore compares CPL with coronary findings in patients with suspected CAD undergoing CAG.

METHODS We prospectively enrolled 2149 consecutive patients who underwent both first coronary angiography and carotid ultrasonography with measurements of IMT, PS and CPL (Figure 1).

RESULTS We prospectively enrolled 2149 consecutive patients who underwent both first coronary angiography and carotid ultrasonography with measurements of IMT, PS and CPL (Figure 1). In total, 1408 (65.5%) patients had CAD (defined as stenosis ≥50%), and 741 (34.5%) patients had no CAD. Patients with CAD had longer maximal CPL than those without CAD (P<0.001). The severity of CAD, measured by the Gensini score (GS), was closely correlated with max-CPL (r_s=0.560), followed by PS (r_s=0.486) and mean-IMT (r_s=0.292) (Figure 2). Multivariate analysis revealed that max-CPL remained independently associated with CAD and high-GS after adjustment for traditional risk factors (TRF). Max-CPL, compared with PS or mean-IMT, had significantly higher discrimination value for predicting high-GS (area under the curve [AUC] 0.819 vs. 0.769 vs. 0.634, P<0.001) (Figure 3). At a cut-off value for the max-CPL of 6.3 mm, the sensitivity and negative predictive value for high-GS were 84.6 and 89.1%, respectively. Furthermore, the addition of max-CPL significantly improved the discrimination (AUC 0.832 vs. 0.720, P<0.001) and reclassification (net reclassification improvement [NRI]=0.431, P<0.001) over TRF for high-GS.

CONCLUSIONS Our study demonstrates that ultrasound max-CPL showed better independent and incremental value in predicting the presence and severity of CAD than PS or mean-IMT, thus suggesting that it may help identify high-risk CAD patients for widening the window for earlier prevention (Figure 4). However, further studies are required to confirm our findings and establish the link between max-CPL and prognosis of patients with CAD.

GW31-e0610

Questionnaire survey evaluating knowledge for non-vitamin K antagonist oral anticoagulants in Chinese doctors

Zhicheng Hu, Yan Yao
Department of Cardiology, Fuwai Hospital, National Center for Cardiovascular Diseases, CAMS & PUMC

OBJECTIVES To investigate knowledge for non-vitamin K antagonist oral anticoagulants (NOACs) in Chinese doctors and identify the target doctors for continuing medical education.

METHODS Clinical doctors attending 2019 the 30th Great Wall International Congress of Cardiology were interviewed with modified Anticoagulation Knowledge Tool (AKT) including 10 questions regarding demographic data, clinical practice characteristics and 20 questions about knowledge of NOACs. Correction rate of knowledge questions over 80% is regarded as well-known for NOACs.

RESULTS A total of 578 valid questionnaires were collected from 597 ones. Among all investigated doctors, 39.4% were from north China. Males accounted for 50.9%. The average number of correctly-answered questions about knowledge of NOACs was 14.8±1.9. The overall well-known rate was 39.1%. The knowledge poorly-handled was how to treat overdose use (10.0%), the hazard of one does missing (31.1%) and how to reduce adverse side effects when taking NOACs (38.1%). The multivariate logistic analysis revealed that doctor degree acquired [odds ratio (OR)=3.70, 95% Confidential interval (CI)=1.49–9.17, P<0.01], practiced in Class A tertiary hospital (OR=1.51, 95% CI=1.07–2.13, P<0.05) predicted doctors had good knowledge of NOACs and worked in hospital in west China (OR=0.42, 95% CI=0.27–0.66, P<0.01) predicted doctors had poor knowledge.

CONCLUSIONS The majority of Chinese doctors had poor knowledge of NOACs, particularly in how to treat overdose use, the understanding of the hazard of one does missing and how to reduce adverse side effects of NOACs. Continuing medical education should be performed intensively to improve the quality of knowledge, especially for doctors who worked in non-Class A tertiary hospital and west China.

GW31-e0612

In-hospital outcomes of triglyceride level among inpatients with acute coronary syndrome in China: findings from the improving care for cardiovascular disease in China-acute coronary syndrome project

Haowei Li, Yue Qi
Department of Epidemiology, Beijing Anzhen Hospital, Capital Medical University, Beijing Institute of Heart, Lung and Blood Vessel Diseases, Beijing 100029, China

OBJECTIVES Blood concentrations of triglycerides (TG) are generally considered to reflect atherogenic lipoproteins. Treatment strategies to improve TG clearance or reduce TG production have become a central topic in the debate over residual risk of ASCVD. Guidelines have recommended patients with high TG and high cardiovascular risk or ASCVD should lowering TG. However, there are significant differences in the recommendations of guidelines for the management of patients with high TG levels, especially in those with acute coronary syndrome (ACS), considering their extremely high risk. It remains unclear whether triglyceride lowering is effective in preventing ASCVD in patients with residual risk. This study aims to evaluate whether triglyceride level is associated with the risks of in-hospital major adverse cardiovascular and cerebrovascular events (MACCE) for ACS inpatients in China.

METHODS The Improving Care for Cardiovascular Disease in China-ACS Project is ongoing nationwide registry of the American Heart Association and the Chinese Society of Cardiology. A total of 104,513 inpatients with a definitive diagnosis of ACS were included. TG levels measured at admission were divided into lower (<200 mg/dL) and higher (≥200 mg/dL) groups. Multivariate logistic regression was performed to examine the association between triglyceride level and in-hospital MACCE outcomes, and a propensity-score-matched analysis was further conducted.

RESULTS Among these ACS patients, 23,685 (22.6%) patients had TG ≥200 mg/dL, and even 39.0% patients had TG ≥150 mg/dL. Patients with high TG were younger, with high proportion of cardiovascular risk factors such as smoking, hypertension and diabetes, but had lower comorbidities and less severe clinical conditions. Multivariate logistic analysis identified TG level as a negative predictor for in-hospital MACCE. TG ≥200 mg/dL was significantly

associated with 27% lowering risk of MACCE (OR 0.73, 95% CI 0.62–0.82, P<0.001). The results were similar among STEMI and NSTE-ACS patients and even after propensity score-matched analysis.

CONCLUSIONS High level of triglyceride was highly prevalent in ACS inpatients in China. On-admission TG levels was inversely related with MACCE. TG level may be regarded as an indicator of good nutritional status that protects such patients from short cardiovascular events rather than a hazard factor, and therefore does not warrant aggressive treatment to lowering it to the so-called normal level.

GW31-e0630

Protective effect of Shexiang Baoxin Pill on myocardial ischemia reperfusion injury in patients with STEMI

Haixia Qin, Zhenbing Liu
Ordos Central Hospital

OBJECTIVES To evaluate the protective effect of Shexiang Baoxin Pill (SBP) on MI/RI and myocardial infarction area in STEMI patients.

METHODS One hundred and three STEMI patients were randomly divided into PPCI group (patients only receiving PPCI) (n=52) and PPCI+SBP group (patients receiving SBP and PPCI) (n=51). The area at risk of infarction (AAR) and final infarct size (FIS) were examined by gated single photon emission CT (SPECT). MI/RI was assessed using myocardial salvage (MS) and salvage index (SI) calculated from AAR and FIS.

RESULTS The STR in PPCI+SBP group was significantly higher than that in PPCI group (73.04±24.25 vs. 63.30±22.14, P=0.036), the peak value of hsTNT was lower than that of the PPCI group (5.54±3.23 vs. 7.09±4.51, P=0.048), and FIS was smaller than that of the PPCI group [6.50 (3.00–15.00) vs. 15.00 (4.00–29.50), P=0.047]. MS [2.50 (0.125–9.750) vs. 1.00 (–1.30 to 3.50), P=0.023] and SI [27.95 (0.00–45.00) vs. 4.30 (–18.35 to 20.55), P=0.006] were larger than those in the PPCI group. The LVEF was higher than that of the PPCI group (56.53±7.42% vs. 53.27±9.09%, P=0.049) and the NT-proBNP level was lower than that of the PPCI group (567.02±988.82 vs. 1014.86±1259.38, P=0.048).

CONCLUSIONS SBP can alleviate MI/RI (MS and SI), decrease in myocardial infarction area (peak value of hsTNT and FIS), and improve myocardial reperfusion (MBG and STR) and cardiac function (LVEF and NT-proBNP), so it protects myocardium in patients with STEMI.

GW31-e0643

A simple prediction model of postoperative acute heart failure undergoing percutaneous coronary intervention: a cohort study

Liwei Liu[1,2], Jiyan Chen[1,2]
[1]The Second School of Clinical Medicine, Southern Medical University, Guangzhou, 510515 Guangdong, China
[2]Department of Cardiology, Guangdong Provincial Key Laboratory of Coronary Heart Disease Prevention, Guangdong Cardiovascular Institute, Guangdong

OBJECTIVES The emergence of AHF after percutaneous coronary intervention (PCI) would lead to a seriously worse prognosis. However, there is few models of predicting post-PCI AHF for patients undergoing PCI. Therefore, we aim to establish a simple prediction model of postoperative AHF among patients following PCI.

METHODS Among 2091 patients undergoing PCI in a prospective observational cohort (PRECOMIN, ClinicalTrials.gov NCT01400295) were enrolled from January 2010 and October 2012. The primary endpoint was post-PCI AHF, which was defined according to a detailed history of symptoms, previous cardiovascular events, the evaluation of signs/symptoms of congestion and/or low perfusion by the physical test with further confirmation by specific investigations such as ECG, chest X-ray, laboratory test (with cardiac biomarkers), and echocardiography. Based on the univariate logistic regression and stepwise logistic regression, we developed a clinical prediction model for post-PCI AHF by successively removing nonsignificant covariates. The discrimination of the nomogram was assessed by the area under the receiver operating characteristic (AUROC) curve and calibration was assessed using the Hosmer-Lemeshow statistic. We internally validated the model by using 1000 bootstrap samples to assess the stability of the model and translated this model into a nomogram. To evaluate the clinical implication of nomogram, we also presented by the classification of the model predictions into low-risk, middle-risk, and high-risk categories.

RESULTS Overall, the prevalence of post-PCI AHF was 1.91% (n=40). 402 (19.2%) of all enrolled patients are females and median age is 63 years (IQR 55–72) years. The final prediction model included heart rate (HR), acute myocardial infarction (AMI), age and left ventricular ejection fraction (LVEF). This model had a high discriminatory ability for post-PCI AHF (AUC=0.845), with calibration (Hosmer-Lemeshow statistic 6.063 P=0.640). For the internal validation using 1000 bootstrap samples, the bootstrap-corrected C-statistic based on data from the development cohort was 0.831. And the incidence of post-PCI AHF in the cohort based on the nomogram showed the good consistency in all three risk classification groups.

CONCLUSIONS The simple model of post-PCI AHF performed stable performance and improved clinical implication in risk stratification for high-risk individuals. Using a nomogram, the risk of each patient developing post-PCI AHF can be estimated, which is beneficial for clinicians in making early clinical decisions and prompt intervention.

GW31-e0645

A comparison between two different definitions of contrast-induced acute kidney injury for long-term mortality in patients with chronic kidney disease

Liwei Liu[1,2], Jiyan Chen[1,2]
[1]The Second School of Clinical Medicine, Southern Medical University, Guangzhou 510515 Guangdong, China
[2]Guangdong Provincial People's Hospital affiliated with South China University of Technology, Guangzhou 510000, Guangdong, China

OBJECTIVES Contrast-induced acute kidney injury (CI-AKI) was the major complication in patients with chronic kidney disease (CKD) undergoing angiography and usually led to poorer prognosis. Previous studies have shown that different definitions of CI-AKI have different effects on the long-term prognosis of patients. It is unknown which definition of CI-AKI accounts for most long-term mortality among patients with CKD. The population-attributable risk (PAR) represents the proportion of cases in a population that would not have occurred in the absence of a risk factor. To the best of our knowledge, no studies have quantified the contributions of different definitions of CIAKI to long-term mortality in patients with CKD. Therefore, we aimed to evaluate this association and compared the PARs of two major CI-AKI definitions.

METHODS This is a single-center, prospective observational study (PRECOMIN, NCT01400295) in Guangdong Provincial People's Hospital, China. From January 2010 to December 2013, we enrolled patients aged ≥18 years who continued to be hospitalized for 2–3 days after angiography. And 610 consecutive coronary artery disease (CAD) patients with CKD undergoing angiography were included in the final analysis. The endpoint was all-cause mortality. CI-AKI was evaluated according to two major definitions: (1) CI-AKIA, with a serum creatinine elevation ≥50% or ≥0.3 mg/dL from baseline in the 72 h after the contrast procedure; (2) CI-AKIB ≥0.5 mg/dL or ≥25% in 72 h after the contrast procedure. Kaplan-Meier analysis was used to count the cumulative mortality, and the log-rank test was used to assess the differences between curves. Multivariable Cox analysis was conducted to evaluate the association between CI-AKI and long-term mortality and expressed as the hazard ratio (HR). The adjusted risk factors were selected through univariable Cox regression or based on previous studies and clinical importance. Population attributable risks (PAR) was used to evaluate the impact of two different definitions of CI-AKI and was calculated using the equation PAR=P (HR–1)/[1+P (HR–1)], where P is the prevalence of CI-AKI under different definitions in our database.

RESULTS Among 610 CAD patients with CKD, 113 patients developed CI-AKIA, and 95 patients developed CI-AKIB after contrast exposure. About 27% (165/610) of patients were female, the mean age was 70.01±9.55 years, and the mean eGFR was 45.66±11.43 mL/min/1.73 mm^2. During the median follow-up period of 6.3 (5.8; 7.6) years, the mortality rate of patients was 25.57% (156/610). Kaplan-Meier curves revealed that patients with CIAKI demonstrated poorer long-term prognosis than those without CI-AKI (log-rank test, P<0.001). After adjusting for heart rate, eGFR, acute myocardial infarction, age, left ventricular ejection fraction <40%, blood urea nitrogen, and the use of intra-aortic balloon pump, both two definitions of CI-AKI was independently associated with the poorer outcome. Among the two definitions of CI-AKI, the adjusted HR of CI-AKIB was higher than CI-AKIA (1.862 vs. 1.817). And the prevalence of CI-AKIA was higher (18.5 vs. 15.6%), with the higher PAR (13.1%, 95% CI: 3.7–24.2).

CONCLUSIONS Our results suggested that CI-AKI is associated with long-term mortality in CAD patients with CKD irrespective of its definitions. Cardiologists and studies regarding long-term prognosis should pay more attention to the presence of CI-AKI, especially CI-AKIA with the higher PAR.

GW31-e0646

Predictive value of hypoalbuminemia for contrast-induced acute kidney injury: a systematic review and meta-analysis

Liwei Liu[1,2], Jiyan Chen[1,2]
[1]The Second School of Clinical Medicine, Southern Medical University, Guangzhou 510515 Guangdong, China
[2]Guangdong Provincial People's Hospital affiliated with South China University of Technology, Guangzhou 510000, Guangdong, China

OBJECTIVES Contrast-induced acute kidney injury (CI-AKI) is a major adverse effect caused by intravascular administration of contrast medium.

Current studies showed that hypoalbuminemia might be a novel risk factor for predicting CI-AKI. This study performed a systematic review and meta-analysis to investigate whether hypoalbuminemia is an independent risk factor for CI-AKI.

METHODS Relevant studies were searched in Ovid Medline, Embase, Cochrane Library until December 31, 2019. The inclusion and exclusion criteria were clearly addressed. Two authors independently screened studies for inclusion, consulting with a third author where necessary to resolve discrepancies. The pooled odds ratio was calculated to assess the association between hypoalbuminemia and risk of CI-AKI using a random-effects model or fix-effects model. Publication bias was tested using funnel plots and the Egger test.

RESULTS Eight relevant studies involving a total of 18,687 patients met our inclusion criteria. The presence of hypoalbuminemia was associated with an increased risk of CI-AKI development (pooled OR: 2.59, 95% CI: 1.80–3.73). It suggests that hypoalbuminemia should be evaluated to reduce the incidence of CI-AKI in patients undergoing contrast exposure.

CONCLUSIONS Hypoalbuminemia is independently associated with the occurrence of CI-AKI and may be a potentially modifiable risk factor for clinical intervention. However, more studies are needed to validate these findings.

GW31-e0652

Nomogram for the prediction of contrast-associated acute kidney injury in patients with hypoalbuminemia undergoing coronary angiography

Liwei Liu[1,2], Jingjing Liang[1,2,3], Jiyan Chen[1,2]
[1]The Second School of Clinical Medicine, Southern Medical University, Guangzhou 510515 Guangdong, China
[2]Department of Cardiology, Guangdong Provincial Key Laboratory of Coronary Heart Disease Prevention, Guangdong Cardiovascular Institute, Guangdong
[3]Department of Cardiology, Shunde Hospital of Southern Medical University, Shunde, China

OBJECTIVES Contrast-associated acute kidney injury (CA-AKI) is one of the major complications that occurs after contrast exposure and patients complicated with hypoalbuminemia are at high risk of CA-AKI. Patients with hypoalbuminemia are prone to CA-AKI and do not have their own risk stratification tool. Therefore, we developed and validated a nomogram for predicting CA-AKI in patients with hypoalbuminemia undergoing CAG/PCI.

METHODS A total of 1272 consecutive patients with hypoalbuminemia undergoing CAG/PCI were enrolled and randomly assigned (2:1 ratio) to a development cohort (n=848) and a validation cohort (n=424). CA-AKI was defined as a serum creatinine (SCr) increase of ≥0.3 mg/dL or 50% from baseline within the first 48–72 hours following CAG/PCI. A nomogram was established with independent predictors according to multivariate logistic regression and a stepwise approach. The discrimination of the nomogram was assessed by the area under the receiver operating characteristic (ROC) curve and was compared to the classic Mehran CA-AKI score. Calibration was assessed using the Hosmer–Lemeshow test.

RESULTS Overall, 8.4% (71/848) of patients in the development cohort and 11.2% (48/424) of patients in the validation cohort experienced CA-AKI. The simple nomogram included estimated glomerular filtration rate (eGFR), serum albumin (ALB), age and the use of intra-aortic balloon pump (IABP); showed better predictive ability than the Mehran score (C-index 75.6 vs. 69.3%, P=0.02); and had good calibration (Hosmer–Lemeshow test P=0.887). According to the log-rank analysis, patients with CA-AKI presented a worse long-term outcome.

CONCLUSIONS Our data suggested that the simple nomogram might be a good tool for predicting CA-AKI in high-risk patients with hypoalbuminemia undergoing CAG/PCI, but our findings require further external validation.

GW31-e0658

Relation of fibrinogen-to-albumin ratio to severity of coronary artery disease and long-term prognosis in patients with non-ST elevation acute coronary syndrome

Mingkang Li[1], Chengchun Tang[2]
[1]School of Medicine, Southeast University
[2]Department of Cardiology, Zhongda Hospital, Southeast University

OBJECTIVES Previous studies showed that fibrinogen-to-albumin ratio (FAR) regarding as a novel inflammatory and thrombotic biomarker was the risk factor for coronary artery disease (CAD). In this study, we sought to evaluate the relationship between FAR and severity of CAD, long-term prognosis in non-ST elevation acute coronary syndrome (NSTE-ACS) patients firstly implanted with drug-eluting stent (DES).

METHODS A total of 1138 consecutive NSTE-ACS patients firstly implanted with DES from January 2017 to December 2018 were recruited in this study. Patients were divided into tertiles according to FAR levels (Group 1: ≤8.715%; Group 2: 8.715–10.481%; Group 3: >10.481%). The severity of CAD was evaluated using the Gensini Score (GS). The endpoints were major adverse cardiovascular events (MACE), including all-cause mortality, myocardial reinfarction and target vessel revascularization (TVR).

RESULTS Positive correlation was detected by Spearman's rank correlation coefficient analysis between FAR and GS (r=0.17, P<0.001). On multivariate logistic analysis, FAR was an independent predictor of severe CAD (OR=1.060, 95% CI 1.005~1.118, P<0.05). Multivariate Cox regression analysis indicated that FAR was an independent prognostic factor for MACE at 30 days, 6 months, and 1 year after DES implantation (HR 1.095, 95% CI 1.011~1.186, P=0.025; HR 1.076, 95% CI 1.009~1.147, P=0.026; HR 1.080, 95% CI 1.022~1.141, P=0.006, respectively). Furthermore, adding FAR to the model of established risk factors, the C-statistic increased from 0.706 to 0.720, 0.650 to 0.668, 0.611 to 0.632, respectively. And the models had incremental prognostic value for MACE, especially for 1-year MACE (NRI: 13.6% improvement, P=0.044; IDI: 0.6% improvement, P=0.042).

CONCLUSIONS In conclusion, FAR was associated independently with the severity of CAD and prognosis, helping to improve risk stratification in NSTE-ACS patients firstly implanted with DES.

GW31-e0667

Impact of serum albumin levels on contrast-induced acute kidney injury in patients undergoing coronary angiography and percutaneous coronary intervention

Ming Ying[1], Liwei Liu[1,3], Jin Liu[1], Yong Liu[1,2,3], Haozhang Huang[1,3], Zhujun Chen[1]
[1]Department of Cardiology, Provincial Key Laboratory of Coronary Heart Disease, Guangdong Cardiovascular Institute, Guangdong Provincial People's Hospital, Affiliated Guangdong Provincial People's Hospital of South China University of Technology, Guangzhou 510100, China
[2]Guangdong Provincial People's Hospital, School of Medicine, South China University of Technology, Guangzhou 510000, China
[3]The Second School of Clinical Medicine, Southern Medical University, Guangzhou 510515, China

OBJECTIVES Contrast-induced acute kidney injury (CI-AKI) is one of the major complications after coronary angiography (CAG) or percutaneous coronary intervention (PCI). Nowadays, most of the risk factors predicting CI-AKI are irreversible and complicated, such as diabetes, congress heart failure and chronic kidney disease. Albumin is the most abundant circulating protein that plays an important role in anti-inflammatory and antioxidant activities. Serum albumin levels are strongly associated with cardiovascular morbidity and mortality. Serum albumin levels are strongly associated with cardiovascular morbidity and mortality. We investigated the relationship between Serum albumin and accidence of CI-AKI in patients after coronary angiography.

METHODS Two hundred eighty-nine consecutive patients aged ≧18 years who agreed to stay in the Guangdong Province's Peoples Hospital 2–3 days after coronary angiography were consecutively enrolled from January 2010 till October 2012. According to whether patients developed contrast induced acute kidney injury or not, they were assigned to either a contrast-induced acute kidney injury group (80 cases, 2.69%) or a non-contrast-induced acute kidney injury group (2899 cases; control).

RESULTS On multivariate logistic regression analysis, adjusted with Chronic heart failure (OR 1.947, 1.103–3.407), Age (OR 1.268, 1.009–1.104) and IABP (OR 4.238, 2.007–8.750), Serum album (OR 0.860, 0.806–0.917) were independent predictors for CI-AKI in patients after coronary angiography. Levels of serum albumin ≤32.15 pg/mL (0.772, 0.72–0.83) were the optimal cutoff value. Serum Album is more effective in predicting CI-AKI in CKD patients (OR 0.809, 0.752–0.870) than in Non-CKD patients (OR 0.848, 0.786–0.914).

CONCLUSIONS Serum albumin was an independent risk factor of contrast-induced acute kidney injury among patients that received percutaneous coronary intervention. Album is more effective in predicting CI-AKI in CKD patients than in Non-CKD patients.

GW31-e0685

Complex PCI and risk of adverse events in relation to high bleeding risk among patients receiving drug-eluting stents

Haoyu Wang, Kefei Dou, Bo Xu, Yuejin Yang
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES The relation between complex percutaneous coronary intervention (PCI), high bleeding risk (HBR), and adverse events after coronary artery implantation of drug-eluting stents has been incompletely characterized. This study sought to investigate the ischemic and bleeding events after complex PCI including stratification according to HBR estimated by PARIS bleeding risk score.

METHODS Between January 2013 and December 2013, 10,167 consecutive patients undergoing PCI were prospectively enrolled in Fuwai PCI Registry. Complex PCI was defined when having at least one of the following characteristics: 3 vessels treated, ≥3 stents implanted, ≥3 lesions treated, bifurcation with 2 stents implanted, total stent length >60 mm, treatment of chronic total occlusion, unprotected left main PCI, in-stent restenosis target lesion, and severely calcified lesion. The primary ischemic endpoint was major adverse cardiovascular events (MACE) (composite of cardiac death, myocardial infarction, definite/probable stent thrombosis, and target lesion revascularization), and primary bleeding endpoint was Bleeding Academic Research Consortium (BARC) type 2, 3, or 5 bleeding.

RESULTS The median duration of follow-up was 29 months. In adjusted Cox regression analysis, patients having complex PCI procedures experienced higher risks of MACE (hazard ratio (HR): 1.63, 95% confidence interval (CI): 1.38–1.92; P<0.001), compared with noncomplex PCI. In contrast, the risk of clinically relevant bleeding was statistically similar between the 2 groups (HR: 0.86 [0.66–1.11]; P=0.238). There was no statistical interaction between HBR (PARIS bleeding score ≥8 or <8) and complex PCI in regard to MACE (adjusted P interaction=0.388) and clinically relevant bleeding (adjusted P interaction=0.279).

CONCLUSIONS Patients who had undergone complex PCI resulted in substantially more ischemic events, without an increase in clinically relevant bleeding risk, and these associations did not seem to be modified by HBR status. More intensified antiplatelet therapy may be beneficial for patients with complex percutaneous coronary revascularization procedures.

GW31-e0686

Contribution of ESC DAPT guideline-endorsed high thrombotic risk features to long-term clinical outcomes among patients with and without high bleeding risk after PCI

Haoyu Wang, Kefei Dou, Bo Xu, Runlin Gao
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES Whether the underlying risk of high bleeding risk (HBR) influences the relationship of high thrombotic risk (HTR) features with adverse events after drug-eluting stent implantation remains unclear. The purpose of this study was to evaluate (1) the prognostic effect of ESC guideline-endorsed HTR features on long-term clinical outcomes and (2) whether the outcomes of HTR versus non-HTR features vary by HBR status.

METHODS Of 10,167 consecutive patients who underwent percutaneous coronary intervention between January 2013 and December 2013 were prospectively enrolled in Fuwai PCI Registry. Patients who are at HTR were defined as: diffuse multivessel disease in diabetic patients, chronic kidney disease, at least three stents implanted, at least three stents lesions treated, bifurcation with two stents implanted, total stent length >60 mm, or treatment of chronic total occlusion. The definition of HBR was based on the Academic Research Consortium for HBR criteria. The primary ischemic outcome was major adverse cardiac event (MACE), a composite of cardiac death, myocardial infarction, target vessel revascularization and stent thrombosis. The primary bleeding outcome was clinically relevant bleeding, defined according to Bleeding Academic Research Consortium (BARC) type 2, 3 or 5 bleeding.

RESULTS With a 2.4-year median follow-up, 4430 patients (43.6%) having HTR experienced a significantly higher risk of MACE (hazard ratio $[HR]_{adjust}$: 1.56, 95% confidence interval [CI]: 1.34–1.82; P<0.001) and device-oriented composite endpoint (composite of cardiac death, target-vessel MI, and target lesion revascularization) (HR_{adjust}: 1.52 [1.27–1.83]; P<0.001), compared to those having non-HTR. The risk of clinically relevant bleeding did not differ between groups (HR_{adjust}: 0.85 [0.66–1.08]; P=0.174). Associations between HTR and adverse events were similar in HBR and non-HBR groups, without evidence of interaction (all $P_{interaction}$>0.05); however, adverse event rates were highest among subjects with both HTR and HBR.

CONCLUSIONS ESC guideline-endorsed HTR was associated with significantly increased risk of MACE without any significant differences in clinically relevant bleeding. The presence of HBR does not emerge as a modifier of cardiovascular risk for patients at HTR, suggesting more potent and longer antiplatelet therapy may be beneficial for this patient population.

GW31-e0687

Benefit-risk profile of extended dual antiplatelet therapy beyond 1 year in patients with high risk of ischemic or bleeding events after PCI

Haoyu Wang, Bo Xu, Kefei Dou, Runlin Gao
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES The benefits and harms of dual antiplatelet therapy (DAPT) continuation with aspirin and clopidogrel beyond 1 year after percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation for high ischemic or bleeding risk patients remain unclear.

METHODS All consecutive patients undergoing PCI were prospectively included in the Fuwai PCI Registry from January 2013 to December 2013. We evaluated 7521 patients who were at high risk for thrombotic or hemorrhagic complications and were events free at 1 year after the index procedure. "TWILIGHT-like" patients with high risk of bleeding or ischemic events were defined by clinical and angiographic criteria. The primary ischemic outcome was major adverse cardiac and cerebrovascular events [MACCE] (a composite of all-cause death, myocardial infarction, or stroke). Median follow-up duration was 2.4 years.

RESULTS The risk of MACCE was significantly lower in DAPT>1-year group (n=5252) than DAPT≤1-year group (n=2269) (1.5 vs. 3.8%; hazard ratio [HR]: 0.37; 95% confidence interval [CI]: 0.27–0.50; P<0.001). This difference was largely driven by a lower risk of all-cause death. In contrast, the risk of Bleeding Academic Research Consortium (BARC) type 2, 3 or 5 bleeding was statistically similar between the 2 groups (1.0 vs. 1.1%; HR: 0.80; 95% CI: 0.50–1.28; P=0.346). Results were consistent after multivariable regression and propensity-score matching.

CONCLUSIONS Prolonged DAPT beyond 1 year after DES implantation resulted in a significantly lower rate of atherothrombotic events, including a mortality benefit, with no higher risk of clinically relevant bleeding in "TWILIGHT-like" patients who were at high-risk for ischemic or bleeding events.

GW31-e0688

Benefit-risk profile of DAPT continuation beyond 1 year after PCI in patients with high thrombotic risk features as endorsed by 2018 ESC/EACTS myocardial revascularization guideline

Haoyu Wang, Kefei Dou, Bo Xu, Runlin Gao
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES The ischemic/bleeding trade-off of continuing dual antiplatelet therapy (DAPT) beyond 1 year after PCI for patients with high thrombotic risk (HTR) as endorsed by 2018 ESC/EACTS myocardial revascularization guidelines remain unknown.

METHODS Patients undergoing coronary stenting between January 2013 and December 2013 from the prospective Fuwai registry were defined as HTR if they met at least 1 ESC/EACTS guideline-endorsed HTR criteria. 4578 patients who were at HTR and were events free at 1 year after the index procedure were evaluated. The primary efficacy outcome was major adverse cardiac and cerebrovascular events [MACCE] (composite of all-cause death, myocardial infarction, or stroke).

RESULTS Median follow-up period was 2.4 years. >1-year DAPT with clopidogrel and aspirin significantly reduced the risk of MACCE compared with ≤1-year DAPT (1.9 vs. 4.6%; hazard ratio [HR]: 0.38; 95% confidence interval [CI]: 0.27–0.54; P<0.001), driven by a reduction in all-cause death (0.2 vs. 3.0%; HR: 0.07; 95% CI: 0.03–0.15). Cardiac death and definite/probable stent thrombosis also occurred less frequently in prolonged DAPT group. Bleeding Academic Research Consortium (BARC) type 2, 3 or 5 bleeding occurred similarly between both groups (1.1 vs. 0.9%; HR: 1.11; 95% CI: 0.58–2.13; P=0.763). Similar results were found using multivariable Cox model, propensity score-matched, and inverse probability of treatment weighting analysis.

CONCLUSIONS Among patients with ESC-endorsed HTR who were free from major ischemic or bleeding events 1 year after coronary stenting, continued DAPT beyond 1 year might offer better effectiveness in terms of atherothrombotic events and comparable safety in terms of clinically relevant bleeding compared with ≤1-year DAPT. ESC-HTR criteria is an important parameter to take into account in tailoring DAPT prolongation.

GW31-e0690

The predictive value of three scoring systems on the risk of in-hospital hemorrhage after PCI for ACS and discussion on influencing factors of potential hemorrhage

Chuyi Han[1,2], Hongliang Cong[1]
[1]Tianjin Chest Hospital
[2]Tianjin Medical University

OBJECTIVES To evaluate the value of three systems, namely CRUSADE, PARIS, and PRECISE-DAPT, in predicting the risk of in-hospital hemorrhage in ACS patients receiving PCI.

METHODS We retrospectively analyzed 1384 consecutive patients with ACS received PCI attending. In this study, End point of bleeding event was defined as BARC non-CABG-related bleeding ≥type 2 (except type 4). The predictive value of three scoring systems for nosocomial bleeding events after intervention was evaluated by drawing a ROC curves.

RESULTS (1) In the selected 2 278 patients diagnosed with ACS, 1384 were treated with PCI and finally enrolled after applying the exclusions. 252 patients of the 1384 patients had non-CABG-related bleeding events of type BARC ≥2 (except type 4). There were 128 cases of type 2, 114 cases of type 3 and 10 cases of type 5. (2) Comparison of bleeding scores among three series in bleeding group When BARC ≥type 2 (except type 4) was used as the end point of hemorrhage, CRUSADE score (32.78±13.89), PARIS score (5.02±2.26), and PRECISE-DAPT score (18.88±10.86) of patients with hemorrhage were significantly higher than those without hemorrhage (22.36±12.45), (3.82±1.72), and (12.69±7.51) (all P<0.001), respectively. (3) Logistic regression analysis of the bleeding event as the dependent variable. According to the CRUSADE score, the patients were divided into five groups. Logistic regression analysis showed that the risk of bleeding increased along with the increase of the CRUSADE score. The risk of bleeding in group B was 2.031 times higher than in group A. Group C was 2.047 times higher than in group A. Group D was 2.441 times higher than in group A, and group E was 4.885 times higher than in group A. According to the PARIS score, the patients were divided into three groups. Logistic regression analysis showed that the risk of bleeding increased with the increase of PRECISE-DAPT score. The risk of bleeding in group B was 1.801 times higher than in group A, and the risk of bleeding in group C was 5.053 times higher than in group A. According to the PRECISE-DAPT score, the enrolled patients were divided into four groups. Logistic regression analysis showed that the risk of bleeding increased with the increase of PRECISE-DAPT score. The risk of bleeding in group B was 1.434 times higher than in group A. The risk of bleeding in group C was 2.452 times higher than in group A, and the risk of bleeding in group D was 4.267 times higher than in group A. (4) ROC curve analysis on predictive ability for bleeding events. Using BARC ≥type 2 (except type 4) as the bleeding criteria, the area under the curve of the CRUSADE, PARIS and PRECISE DAPT score was 0.694 (95% CI: 0.669–0.718), 0.660 (95% CI: 0.634–0.685), 0.679 (95% CI: 0.654–0.704). The results showed that all three scores are valuable on the assessment of in-hospital hemorrhage in patients with ACS after PCI. No differences were observed in the ability of the three scores to predict nosocomial bleeding events in patients with ACS.

CONCLUSIONS All three scores have predictive value for nosocomial bleeding events in the patients of our study. They can be used for hazard layering. No differences were observed in the ability of the three scores to predict nosocomial bleeding events in patients with ACS.

GW31-e0697

Differential diagnosis of idiopathic right ventricular PVC or VT with arrhythmogenic right ventricular cardiomyopathy concomitant PVC or VT by Hoffmayer ECG integral

Donglei Luo, Jingtao Guo
Chengde Central Hospital/Second Clinical College of Chengde Medical University

OBJECTIVES To explore the clinical significance of Hoffmayer ECG integral method in differential idiopathic right ventricular ventricular premature beat (PVC) or ventricular tachycardia (VT) with arrhythmogenic right ventricular cardiomyopathy (ARVC) PVC or VT in early stage

METHODS Forty cases with heart disease patients were collected, who were from the Chengde Central Hospital from Sep. 2016 to Sep. 2019. In all of them, 30 cases with right ventricular outflow tract PVC or VT, 10 cases with ARVC sinus rhythm concomitant PVC or VT. And then the ECG integrals of 40 patients were analysed through the calculating of the total and single integral of the patients with ARVC concomitant PVC or VT, in the meanwhile, the clinical diagnosis was compared. The susceptibility, specificity, positive and negative predictive value and diagnosis coincidence rate of the patients were observed.

RESULTS The susceptibility, specificity, positive and negative predictive value and diagnosis coincidence rate of the patients was 80, 90, 80, 81.3 and 90% respectively through the Hoffmayer ECG integral for the patients with ARVC concomitant PVC or VT was more than 5 points or less than 5 points.

CONCLUSIONS It's effective to differential diagnose idiopathic right ventricular ventricular premature beat or ventricular–tachycardia with arrhythmogenic right ventricular cardiomyopathy concomitant PVC or VT. It's worth applying in clinical for the higher sentivity and speciality, fastly and simply.

GW31-e0727

The effect of metabolic syndrome on the onset age and long-term outcomes in patients with acute coronary syndrome

Jingjing Xu, Jinqing Yuan
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Science and Peking Union Medical College

OBJECTIVES The definite effect of metabolic syndrome on the onset age and long-term outcome in acute coronary syndrome (ACS) patients remains unclear. The aim of this study is to investigate the effect of metabolic syndrome on onset age and long-term outcome of ACS patients.

METHODS Of 6431 ACS patients undergoing PCI from January to December 2013 were enrolled. After the exclusion of previous coronary artery disease history, 1558 patients accorded with early-onset ACS (man ≤50 and woman ≤60 years old), and 3044 patients with late-onset ACS. The baseline characteristics and 5 years clinical outcomes were collected.

RESULTS Compared with late-onset ACS group, BMI, levels of TG, LDL-C, and uric acid were significantly higher, while HDL-C was lower in early-onset ACS group (all P<0.001). Multivariable logistic analysis showed metabolic syndrome components including obesity (odd ratio: 1.590, P<0.001), hypertriglyceridemia (odd ratio: 1.403, P<0.001) and low HDL-C (odd ratio: 1.464, P<0.001) were independent risk factors of early-onset ACS. Five years follow-up showed that, the incidence of all cause death (1.5 vs. 3.8%, P<0.001), cardiac death (1.1 vs. 2.0%, P=0.023) and recurrent stroke (2.2 vs. 4.2%, P<0.001) were lower, while the bleeding events were higher (16.4 vs. 12.4%, P<0.001) in early-onset ACS group. However, subgroup analysis showed a higher incidence of recurrent MI and revascularization in early-onset ACS patients combined with metabolic syndrome.

CONCLUSIONS Metabolic syndrome components including obesity, hypertriglyceridemia and low HDL-C are independent risk factors of early-onset ACS and relate to the increase of recurrent MI and revascularization. Effective control of metabolic syndrome may reduce the incidence of early-onset ACS and improve long-term prognosis.

GW31-e0740

Long-term prognosis of moderate to severe coronary artery calcification in patients undergoing percutaneous coronary intervention

Sida Jia, Jianxin Li, Ce Zhang, Yue Liu, Deshan Yuan, Na Xu, Xueyan Zhao, Runlin Gao, Yuejin Yang, Bo Xu, Zhan Gao, Jinqing Yuan, Yin Zhang
Fuwai Hospital, Chinese Academy of Medical Science

OBJECTIVES Moderate/severe coronary calcification predicts worse clinical outcomes in patients undergoing percutaneous coronary intervention (PCI). However, to date most studies were modest in size and with limited follow-up. We aim to assess the association between calcification severity and long-term clinical outcomes in a large patient cohort undergoing PCI.

METHODS Totally 10,068 consecutive patients who underwent PCI at Fuwai Hospital were enrolled in this prospective observational study. Patients were categorized as none/mild calcification or moderate/severe calcification according to the severity of target lesion by visual assessment of coronary angiography. Major adverse cardiovascular events (MACE), a composite event of death, myocardial infarction and revascularization, at 5 years were assessed.

RESULTS None/mild calcification was observed in 8229 (81.7%) patients, while moderate/severe calcification was observed in 1839 (18.3%) patients. Patients with moderate/severe calcification had significantly higher rate of 5-year unplanned revascularization (15.2 vs. 13.2%, P=0.022) and MACE (20.7 vs. 17.9%, P=0.005). After propensity score match, moderate/severe CAC group still had higher rate of 5-year unplanned revascularization (15.2 vs. 12.6%, P=0.019). Multivariable Cox regression analysis found that moderate/severe calcification was independently associated with higher risk of 2-year unplanned TVR (HR=1.287, 95% CI: 1.036–1.600, P=0.023) and MACE (HR=1.242, 95% CI: 1.039–1.484, P=0.017), but not 5-year unplanned revascularization and MACE.

CONCLUSIONS In patients undergoing PCI, moderate/severe coronary calcifications increases the risk of long-term MACE.

GW31-e0770

Effects of mental stress on heart rate variability, salivary cortisol and salivary α-amylase in patients with coronary heart disease comorbid depression and anxiety disorders

Yuting Liu, Qingshan Geng
Guangdong Cardiovascular Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, Guangdong, China

OBJECTIVES The aim of this study was to explore the changes of heart rate variability, salivary cortisol and salivary α-amylase in CDA disease group during mental stress comparing with healthy control group and CHD group.

METHODS The Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) were used to evaluate anxiety and depression disorders in patients with CHD (*N*=81) and healthy individuals (*N*=10). According to the scale score, the subjects were divided into 3 groups: the healthy control group, the CHD group and the CDA group (CHD comorbid mild and above anxiety and/or depression), and all subjects were evaluated for changes in hemodynamics, heart rate variability, salivary cortisol and salivary α-amylase during the mental stress test, followed by subjective psychological evaluation. Statistical comparison analysis was performed between different time points and between groups. correlation factor analysis was performed. Correlation analysis was carried out on the factors that may affect the mental stress responses.

RESULTS The autonomic nerve response to mental stress in CDA patients was characterized by low reactivity and slow recovery, with no significant changes in rMSSD and HF during mental stress, less increase in LFnu than that of the healthy and CHD groups (31.5 *vs.* 68.5 *vs.* 33.9%) and with delayed recovery to baseline. The responses of hypothalamic-pituitary-adrenal axis and the sympathetic-adrenal medulla system under mental stress have similar trends to those in healthy individuals and CHD groups, showing a peak at 10 minutes after mental stress and a return to baseline 30 minutes after. After adjusting for other factors, the correlation between high levels of GAD-7 in CDA patients and low response in sympathetic nerve activity was still significant (F=6.528, P=0.014), showing a progressive low response to stressful events. Besides, the subjective stress score was found to be significantly positively correlated with changes of most indicators in the response to mental stress.

CONCLUSIONS The physiological flexibility of patients with CDA is diminished under mental stress, which is manifested by a significant reduction in the amplitude of autonomic nerve responses, which is also closely related to the degree of anxiety and subjective stress feeling.

GW31-e0775

Long-term antiplatelet therapy in medically managed non ST segment elevation acute coronary syndromes: The EPICOR Asia study

Juan Zhou, Zuyi Yuan
Department of Cardiology, First Affiliated Hospital, Xi'an Jiaotong University

OBJECTIVES To describe long-term antithrombotic management patterns (AMPs) in medically managed Asian patients with non-ST-segment myocardial infarction (NSTEMI) or unstable angina (UA).

METHODS Data were analyzed from medically managed NSTEMI and UA patients included in the prospective, observational EPICOR Asia study (NCT01361386). Survivors to hospital discharge were enrolled (June 2011 to May 2012) from 8 countries/regions across Asia. Baseline characteristics and AMP use up to 2 years post-discharge were collected. Outcomes were major adverse cardiovascular events (MACE: myocardial infarction, ischemic stroke, and death) and bleeding.

RESULTS Among 2289 medically managed patients, dual antiplatelet therapy (DAPT) use at discharge was greater in NSTEMI than in UA patients (81.8 vs. 65.3%), and was significantly associated with male sex, positive cardiac markers, and prior cardiovascular medications (P<0.0001). By 2 years, 57.9 and 42.6% of NSTEMI and UA patients, respectively, were on DAPT. On multivariable Cox regression analysis, risk of MACE at 2 years was most significantly associated with older age (HR [95% CI] 1.85 [1.36, 2.50]), diagnosis of NSTEMI vs. UA (1.96 [1.47, 2.61]), and chronic renal failure (2.14 [1.34, 3.41]), all P≤0.001. Risk of bleeding was most significantly associated with region (East Asia vs. Southeast/South Asia) and diabetes.

CONCLUSIONS Approximately half of all patients were on DAPT at 2 years. MACE were more frequent in NSTEMI patients during follow-up.

GW31-e0776

Goals of non-high density lipoprotein cholesterol need to be adjusted in Chinese acute coronary syndrome patients: findings from the CCC-ACS project

Xin Su[1,2], Daoquan Peng[2]
[1]Xiamen Cardiovascular Hospital of Xiamen University
[2]Second Xiangya Hospital of Central South University

OBJECTIVES Guidelines recommended non-high density lipoprotein cholesterol (non-HDL-C) as a co-primary target, and set non-HDL-C goals as 30 mg/dL higher than low density lipoprotein cholesterol (LDL-C) goals. However, the value is largely uncertain in Chinese patients.

METHODS We assigned non-HDL-C values at the same percentiles correspondent to LDL-C goals for patients from the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome (CCC-ACS) Project. We calculated the differences between non-HDL-C and LDL-C and proposed appropriate adding values according to LDL-C and TG levels.

RESULTS Among 73,495 patients, 17.7% used lipid-lowering agents before admission. Of these, 27.2% achieved LDL-C<70 mg/dL while 39.4% achieved non-HDL-C<100 mg/dL. The mean difference between non-HDL-C and LDL-C was 23.2 mg/dL, which could be affected by LDL-C and TG levels. Importantly, of patients with LDL-C levels ≤100 mg/dL, the mean differences were 19.1 mg/dL in patients with TG ≤150 mg/dL and 24.6 mg/dL in patients with TG >150 mg/dL.

CONCLUSIONS There are significant differences between LDL-C and non-HDL-C in Chinese ACS patients. For secondary prevention, on average, the adding values should be 20 mg/dL for patients with TG ≤150 mg/dL and 25 mg/dL for patients with TG >150 mg/dL when LDL-C goals of 70 mg/dL is achieved.

GW31-e0782

Contrast-induced encephalopathy of patients with atherosclerotic cardiovascular disease: a retrospective analysis of cases about this field

Dongxia Jin[1,2], Hongliang Cong[1,2], Tingting Li[1,2], Ximing Li[1,2]
[1]Tianjin Chest Hospital
[2]Institute of Cardiovascular Disease of Tianjin in China

OBJECTIVES Studying the current states of contrast-induced encephalopathy (CIE) of atherosclerotic cardiovascular disease (ASCVD) in documents, including the clinical epidemiological characteristics, pathogenic mechanism and clinical symptoms, and analyzing the patients' gender, age, preexisted hypertension, diabetes mellitus, old cerebral infarction (OCI) or transient ischemic attack (TIA), renal impairment or renal dysfunction, the category and doses of contrast, manifestation and prognosis, so as to promote the diagnosis and treatment of CIE of ASCVD.

METHODS Search the paper with Chinese and English in database. The retrieval words are "atherosclerotic cardiovascular disease, contrast-induced encephalopathy, neurotoxicity, encephalopathy, brain injury, cortical blindness, cerebral/carotid arteriography, cardiac catheterization, coronary angiography, percutaneous coronary intervention, peripheral arteriography". Consult the documents and the references from the primary articles. And then bring in the cases of CIE of ASCVD, referred to the diagnostic criteria of NLA in 2014, and then collect the basic information and use the SPSS 20.0 and Excel statistic software to conduct the retrospective analysis.

RESULTS In the total 90 cases including 88 patients, male patient is 58, occupying 65.91%, while female is 30, accounting for 34.09%. It seems that there is a higher incidence of CIE in male patient. Age conforms to normal distribution, and the minimal age is 39, the maximal is 89, the average is (66.88±10.51) years old, which indicates that possibly the elder suffers more from CIE. And the number of hypertension is 63 (71.59%), and non-hypertension is 25 (28.41%). The mean and median volumes of iodinated contrast media administered were 228.41 and 190 mL, respectively (range: 25–1500 mL). High-, low-, isosomolar contrast media were used in 8.89% (8/90), 74/90 (82.22%) and 1/90 (1.11)% of patients, respectively. Symptoms of patients: cortical blindness, delirium, hemiplegia, seizure, ophthalmoplegia accounted for 25.56, 13.33, 10.00, 8.89 and 5.56% respectively. Symptoms typically appear within minutes to hours of contrast administration and resolve entirely within 24–72 hours. And most of the patients (86/90, about 95.56%) had completely recovered, and only 4 patients suffered irreversible damage: 1 suffered of right-hand muscle strength decline, 1 suffered of blepharoptosis, diplopia, and 1 with persistent forgetting and vision loss, unfortunately 1 patient died from CIE after 56-days treatment. Risk factors may include hypertension, renal impairment, transient ischemic attack, the administration of large volumes of iodinated contrast, percutaneous coronary intervention or selective angiography of internal mammary grafts.

CONCLUSIONS Though CIE is a very rare complication during the intervention procedure and the presentation of CIE is variable, ranging from cortical blindness to encephalopathy, seizures, and hemiparesis, which often pose a difficult differential diagnosis. In any acutely confused patient, it is important, however, to carry out the relevant investigations, as CIE is often a diagnosis of exclusion. Usually its prognosis is excellent, rarely can it bring some clinical troubles with the neurological sequelae, even to death. Physicians should be aware of it in time and take some measures to treat it.

GW31-e0817

Serum homocysteine is an independent risk factor for coronary heart disease in northern China

Haoyu Wu
Department of Cardiology, Shaanxi Provincial People's Hospital, Shaanxi, Xi'an, China

OBJECTIVES Although there have been many studies on circulating homocysteine and the incidence of coronary heart disease (CHD). However, the result on homocysteine (Hcy) in CHD has been conflicting as several studies have failed to demonstrate an association between Hcy and CHD, especially in Asian population. These studies include a small population. Therefore, this study aims to assess the relationship between Hcy level and CHD in the northern communities of China. We compared the adjusted conventional risk factors with Hcy in CHD patients to determine the predictive rate of CHD.

METHODS A total of 1987 patients in northern China who had undergone coronary angiographies were enrolled in the study, of which 672 with normal coronary arteries (control group) and 1315 proven CHD. Hcy levels were measured by enzyme-linked immunosorbent assay. Hyperhomocysteinemia (HHcy) was defined as Hcy ≥15 μmol/L.

RESULTS There were significant differences between the CHD and control groups with regard to male sex (P<0.05), diabetes (P<0.001), hypertension (P<0.001) and smokers (P<0.001), but no remarkable difference in family history of premature CHD (P>0.05). Hcy levels were significantly higher in the

CHD group than those in the control group (P<0.001). Multivariate logistic regression showed that HHcy were both independently correlated with CHD in young patients (aged ≤55 years, OR, 3.03; 95% CI, 2.10–5.76) and old patients (aged >55 years, OR, 2.56; 95% CI, 1.21–4.25). Male, diabetes, hypertension, and smoking were also independently correlated with CHD in young and old patients. HHcy showed the highest sensitivity (93.05%), specificity (86.12%), positive prediction value (89.94%), negative prediction value (90.56%) and accuracy (90.01%) when compared to other risk factors (area under curve: 0.904, 95% CI: 0.865–0.924, P<0.001). Cut-off values of 15.13 μmol/L for Hcy (Youden's index=0.815) gave the highest index.

CONCLUSIONS HHcy is an important independent risk factor for CHD in northern China after adjusting for other risk factors.

GW31-e0818

Effect of Gelan Xinning soft capsule on insulin-like growth factor-1 in patients with unstable angina pectoris

Haoyu Wu
Department of Cardiology, Shaanxi Provincial People's Hospital, Xi'an 710068

OBJECTIVES To investigate the effect of Gelan Xinning soft capsule on the expression of insulin-like growth factor-1 (IGF-1) in patients with unstable angina pectoris.

METHODS Ninety-two patients with unstable angina pectoris were randomly divided into control group and observation group. The control group was given conventional drug treatment, and the observation group was given Gelan Xinning soft capsule based on conventional drug treatment, 2 capsules/time, 3 times/day. The course of treatment was 8 weeks. The clinical efficacy and serum IGF-1 level were observed.

RESULTS The frequency and duration of angina pectoris in the observation group and the control group after treatment were decreased compared with those before treatment (P<0.05). The frequency and duration of angina pectoris in the observation group were lower than those in the control group after treatment (P<0.05). The serum IGF-1 level in the observation group and the control group after treatment was higher than that before treatment (P<0.05). The serum IGF-1 level in the observation group was significantly higher than that in the control group after treatment (P<0.05).

CONCLUSIONS Gelan Xinning soft capsule has good therapeutic effect on unstable angina pectoris, which may be related to the increase of IGF-1 level.

GW31-e0819

Related factors of coronary artery in-stent restenosis in patients with mild to moderate chronic kidney disease

Haoyu Wu
Shaanxi Provincial People's Hospital, Xi'an 710068, Shaanxi, China

OBJECTIVES To investigate the relative factors of in-stent restenosis (ISR) in patients with mild to moderate chronic kidney disease after coronary drug-eluting stent implantation.

METHODS One hundred and eighty-nine cases of patients with mild to moderate chronic kidney disease were performed coronary drug-eluting stent from November 2015 to September 2018. According to the second angiography results performed 9~15 months after stent implantation, patients were divided into ISR group and non-ISR group. Clinical data and biochemical indicators were analyzed.

RESULTS The mean follow-up time was (12.6±2.1) months, and the incidence of ISR was 20.1%. Compared with the non-ISR group, active smoking, family history of myocardial infarction, diabetes mellitus, glycosylated hemoglobin, low density lipoprotein, eGFR and uric acid were statistically significant in ISR group (P<0.05). Multivariate logistic proportional hazards regression model showed that diabetes mellitus, glycosylated hemoglobin, uric acid and family history of myocardial infarction were independent risk factors for ISR.

CONCLUSIONS Diabetes mellitus, family history of myocardial infarction, glycosylated hemoglobin and uric acid are independent risk factors of ISR in patients with mild to moderate chronic kidney disease after coronary drug-eluting stent implantation.

GW31-e0850

Impact of multiple objective factors on diagnostic interpretability of coronary computed tomographic angiography using a 256-detector row CT scanner

Lixue Xu, Yi He
Capital Medical University Affiliated Beijing Friendship Hospital

OBJECTIVES To explore impact of patient related, vessel related, image quality related and cardiovascular risk factors on CCTA interpretability by using a 256-detector row CT.

METHODS One hundred and ten patients who underwent CCTA and invasive coronary angiography (ICA) were consecutively retrospectively enrolled from January, 2018 to October, 2018. Using ICA as the reference standard, ≥50% diameter stenosis was defined as the cutoff criterion to detect diagnostic capacity of CCTA. Diagnostic consistency was investigated by calculating interrater reproducibility of CCTA. Multiple logistic regression models were performed to evaluate impact of 14 objective factors.

RESULTS A total of 1019 segments were evaluated. Per-segment sensitivity, specificity, accuracy, positive predictive value, negative predictive value of CCTA was 76.8, 93.7, 91.2, 67.8 and 95.9%, respectively. Per-segment diagnostic consistency was 0.44 for CCTA. Discrimination and calibration of regression models were satisfied. For accuracy, negative association was found in stenosis severity, calcium load and hyperlipidemia. For sensitivity, calcium load and diabetes mellitus (DM) was positively correlated. For specificity, negative correlation was observed in stenosis severity and calcium load. For interrater reproducibility, stenosis severity and calcium load were negatively associated while male sex and signal to noise ratio (SNR) were positively related (all P<0.05).

CONCLUSIONS Per-segment 256-detector row CCTA capacity was best in no stenosis or occluded segments. Heavier calcium load was correlated to poorer CCTA interpretability. Our findings, on one hand, confirmed the rule-out value of CCTA, on the other hand, suggested improvements in calcium subtractions and deep learning-based tools to improve CCTA diagnostic interpretability.

GW31-e0851

A comparison of diagnostic performance between 64- and 256-detector row coronary CT angiography in patient with different risk stratification of coronary artery disease

Lixue Xu, Yi He
Capital Medical University Affiliated Beijing Friendship Hospital

OBJECTIVES Although 256-detector coronary CT angiography (CCTA) performed better in patients with higher heart rate, direct comparison of diagnostic performance between 64- and 256-detector row CCTA in patients with different pretest probability (PTP) of coronary artery disease (CAD) and in clinical important subgroups remained unknown.

METHODS One hundred and ten patients (76 males, 63.8 years±9.3 years) who underwent 256-detector row CCTA and 120 patients (68 males, 65.7±8.8 years) who underwent 64-detector row CCTA were retrospectively enrolled from January, 2017 to October, 2018. Multiple clinical information was recorded and applied to construct a risk model of CAD by conducting a multivariable regression model. The PTP of CAD was calculated for every patient, then used to stratify patients into PTP<15% and ≥15% risk subgroups. Using invasive angiography as reference standard and ≥50% stenosis as cutoff, group comparison of diagnostic performance was calculated between 64- and 256-detector row CCTA in risk-based, sex and age-based subgroups and in patients with and without chest pain.

RESULTS Sixty-four and 166 patients were with risk<15% and ≥15%, respectively. Group comparison showed that per-segment diagnostic performance of 256-detector row CCTA was significantly better than 64-detector row CCTA, especially in patients with risk of ≥15%, with age<65 years, with chest pain and in males.

CONCLUSIONS Our findings confirmed >64 detector row CCTA was more appropriate diagnostic test in chest pain center and for patients with PTP≥15%.

GW31-e0855

Association of red cell distribution width and in-hospital mortality among critically ill patients with acute myocardial infarction

Sulan Huang, Ning Guo
The First People's Hospital of Changde

OBJECTIVES Some studies have showed that there was an independent association between increased red cell distribution width (RDW) and mortality after acute myocardial infarction (AMI). However, evidence regarding the predictive significance of repeated-measure of RDW in patients with AMI remains scarce. We investigated the association of dynamic profile of RDW and in-hospital mortality in a large population with AMI.

METHODS We extracted clinical data from the MIMIC-III V1.4 database. Then, we collected demographics, vital signs, laboratory tests, other clinical data and comorbidities from the database. The clinical endpoint was in-hospital mortality among critically ill patients with AMI. Cox proportional hazards models were used to evaluate the prognostic values of basic RDW, and the Kaplan-Meier method was used to plot survival curves. Subgroup analyses were performed to measure mortality across various subgroups. The repeated-measure data be compared by using generalized additive mixed model.

RESULTS A total of 3101 eligible patients were studied. In multivariate analysis, adjusted for age, ethnicity and gender, RDW were significant predictors

of risk of in-hospital mortality. Furthermore, after adjusting for more confounding factors, RDW remained a significant predictor of in-hospital mortality (tertlile 3 versus tertile 1: adjusted HR, 95% CI: 2.36, 1.39–4.01; P for trend<0.05). A similar trend was observed in the RDW group division by quartiles. The Kaplan-Meier curve for tertile of RDW indicated that survival rates were the highest when RDW ≤13.2% and the lowest when RDW≥14.2% after adjustment for age, gender, and ethnicity. Subgroup analysis revealed no significant interactions in most strata. During staying in ICU, the RDW of most patients had raised up over time. The levels RDW of survivors changed smoothly and lower than those in non-survivors. Similarly, the levels RDW of non-survivors progressively increased after 3 days in ICU.

CONCLUSIONS Our findings showed that higher RDW was associated with risk of in-hospital mortality in critically ill patients with AMI.

GW31-e0915

Five-year outcomes after left atrial appendage closure using LAmbre: from a premarket registered case-series study

Shuang Li[1], Jingying Zhang[1], Xiang Li[2], Qiang Ming[1], Xianlin Zhang[3], Wei Chen[1], Mengyun Zhu[1], Yatyin Lam[4], Yawei Xu[1]
[1]Cardiology, Shanghai Tenth People's Hospital, Tongji University School of Medicine
[2]Nursing, Shanghai Tenth People's Hospital, Tongji University School of Medicine
[3]Cardiology, The First Affiliated Hospital of Bengbu Medical College
[4]Division of Cardiology Department of Medicine and Therapeutics, Clinical Sciences Building Prince of Wales Hospital, Hong Kong SAR

OBJECTIVES Percutaneous left atrial appendage (LAA) closure has been demonstrated to be an alternative to oral anticoagulation for the prevention of ischemic stroke in non-valvular atrial fibrillation (AF) patients using Watchman. However, few data are available for the novel LAmbre occluder, especially with long-term data. This study was to evaluate the feasibility of LAmbre LAA occluder followed for more than 5 years.

METHODS This study included consecutively 66 consecutive AF patients implanted with the LAmbre from April 2014 to October 2015 in our center. Patients received 3-month, double anti-platelet therapies and single alone thereafter. Patients were followed for up to July 7, 2020.

RESULTS The mean CHA2DS2-VASc and HAS-BLED score were 6.0±1.6 and 3.0±0.8, respectively. The implantation success rate was 98.5%. No death, stroke, major bleedings or device-related severe events were observed within 7 days after the procedure. Adequate LAA sealing was observed in 98.3 and 98.2% patients at respectively 3- and 12-month follow-up echocardiographic examinations. After a mean follow-up of 67±12.1 months, all-cause death was observed as 2.5 per 100 patient-years (n=9). Ischemic stroke and major bleeding were 1.9 per 100 patient-years (n=7) and 0.8 per 100 patient-years (n=3), respectively, both significantly lower than the cumulative expected rates according to risk factors.

CONCLUSIONS In patients with AF, the protocol of LAA closure with the LAmbre plus anti-platelet therapy was feasible and associated with low ischemic and bleeding events in the periprocedural period and in a long-term follow-ups of more than 5-years.

GW31-e0945

Effect of new atrial fibrillation after acute myocardial infarction on prognostic patients

Jie Zhang, Likun Ma
Department of Cardiology, the First Affiliated Hospital of USTC, Division of Life Science and Medicine, University of Science and Technology of China, Hefei, Anhui, P.R. China

OBJECTIVES To evaluate the effect of NOAF after AMI on prognostic patients.

METHODS In this study, we evaluated 335 patients with AMI admitted to our department of cardiology with emergency coronary intervention during from January 2017 to December 2018. According to whether atrial fibrillation (AF) occurred during hospitalization, patients were classified as NOAF (n=32) group and no-NOAF (n=299) group. Baseline clinical characteristics (general clinical conditions, anamnesis, biochemical indexes, myocardial injure markers, NT-proBNP, cardiac color ultrasound, coronary angiography) of the two groups were counted and analyzed.

RESULTS We compared outcomes between these groups and adjusting for differences in baseline characteristics. After multivariate adjustment, NOAF was an independent predictor of death in-hospital (odds ratio (OR=4.259, P=0.024) rather than in 2-year (OR=3.061, P=0.124). In addition, NOAF was an independent predictor of adverse prognostic events like pump failure (OR=6.770, P=0.000), cardiogenic shock (OR=8.321, P=0.000), malignant arrhythmia (OR=2.877, P=0.027) in-hospital and heart failure (OR=9.892, P=0.004) in 2-year.

CONCLUSIONS These suggest that although NOAF was an independent predictor of all-cause death in-hospital but not in 2-year, it was associated with worse prognosis closely.

GW31-e0984

Free-breathing coronary CT angiography using a novel dedicated cardiovascular CT system for patients with atrial fibrillation

Jiaxin Cao, Yi He
Beijing Friendship Hospital, Capital Medical University

OBJECTIVES Image quality and diagnostic accuracy of coronary CT angiography (CCTA) could be impaired with inability of breath holding, high heart rate and heart rate variability. A novel dedicated cardiovascular CT system (CardioGraphe™) combining stereo dual source with 14 cm z-coverage and new iterative reconstruction algorithm (ASiR-CV) has come into clinical service recently. We aim to evaluate the feasibility of CCTA in patients with atrial fibrillation (AF) and free-breathing using the new dedicated cardiac CT scanner.

METHODS Thirty patients with AF (persistent AF without antiarrhythmic medication, 21 men and 9 women; mean age 70.3±9.4 years, ranged 40–82 years; mean BMI 26.8±3.4 kg/m², ranged from 21.48 to 35.82 kg/m²) underwent clinically indicated CCTA on a 560-slice scanner (120 kV, 50-600 Smart mA, 0.24 s/rot, 560×0.25 mm collimation). Twelve patients were holding breath during acquisition time (group A) and in the remaining 18 with free-breathing (group B). A motion correction algorithm (SnapShot Freeze) was used to further minimize motion artifacts. A total of 316 in 538 coronary artery segments were rated as interpretable. Two experienced radiologists blinded to the electrocardiograph, independently graded the CT images in terms of visibility and artifacts with a 4-grade Likert rating scale. SNR and CNR were calculated by mean CT attenuation values and standard deviations within 3 regions of interest placed in the proximal left main (LM) and proximal right coronary artery (RCA). The CNR and SNR of two groups were compared using independent-sample T-test. The image quality of two groups were compared using Wilcoxon rank-sum test.

RESULTS Mean heart rate during scanning was 101.4±43.4 bpm in group A and 90.5±11.2 bpm in group B (P>0.05). The CNR and SNR of LM and RCA showed no significant difference between the two groups. There was no significant difference in image quality score between group A and group B on per-vessel level (3.7±0.4 vs. 3.6±0.5, P>0.05) and per-patient level (3.7±0.5 vs. 3.6±0.5, P>0.05).

CONCLUSIONS Free-breathing CCTA using the new dedicated cardiac CT scanner in patients with AF is equally effective with free-holding.

GW31-e1000

Periostin, a new predictor of diabetic coronary artery calcification

Yi Zhu, Naifeng Liu
Department of Cardiology, Zhongda Hospital, School of Medicine, Southeast University, Nanjing

OBJECTIVES Periostin (PN) is important for bone and tooth maintenance. CML (basis of advanced glycation end products) accelerates diabetic vascular calcification. This study aims to investigate the association between serum PN levels, CML levels and coronary artery Agatston score, and the effects of PN on vascular smooth muscle cell (VSMC) osteogenic differentiation in vitro.

METHODS We recruited 147 patients with suspected angina pectoris. Subjects were divided into 3 groups based on coronary Agatston score: score=0 (n=51), score=1–300 (n=39), score >300 (n=57). Serum PN and CML levels were measured using ELISA. VSMC calcification was induced with β-glycerophosphate (β-GP).

RESULTS Patients with coronary artery calcification (Agatston score >0) exhibited significantly higher serum PN and higher CML levels than those of control patients (Agatston score=0). Cardiovascular risk factors, including older age, male gender, lower creatinine clearance, diabetes mellitus and hypertension were more prevalent in patients with coronary calcification. High PN levels were associated with high CML levels. However, multivariate logistic analysis showed that high PN and CML levels could not predict the occurrence of coronary calcification. In vitro, PN elevated VSMC osteogenic differentiation marker (RUNX2 and BMP2) protein levels in a dose-dependent manner and that maximal stimulation was attained at 24 h.

CONCLUSIONS These findings suggest that diabetic vascular calcification is an important determinant of the induced circulating PN levels.

GW31-e1048

The association of TM6SF2 rs58542926 with acute myocardial infarction in Han population of north China

Xuelian Song, Yi Dang, Xiaoyong Qi
Hebei General Hospital

OBJECTIVES Acute myocardial infarction (AMI) is the most serious type of coronary heart disease that can be influenced by multiple environmental and inherited factors. It is well known that dyslipidemia is a definitely predisposing factor of acute myocardial infarction, further more, previous studies have found many single nucleotide polymorphisms (SNPs) of lipid metabolism

associated with AMI occurrence. However, the results are inconsistent. So we designed this study to investigate four genes of lipid metabolism pathways by analysis of 4 SNPs that have not been reported the association with AMI in Han population of north China.

METHODS Three hundred and thirty-six patients with AMI confirmed by coronary angiography and 270 normal healthy controls are included. Four single nucleotide polymorphisms (SNPs): rs58542926 (E167K) in TM6SF2, rs505151 in PCSK9, rs320 in LPL and rs688 in LDLR were selected and genotyped via real time polymerase chain reaction followed by NGS (next-generation sequencing). The χ^2 test and haplotype analysis were performed to analyse the associations between the four SNPs and AMI by comparing the different distribution using the SPSS V.22.0 software package.

RESULTS Obvious differences of alleles distribution in AMI cases and controls were observed in TM6SF2 rs58542926, LPL rs320 and LDLR rs688, as well as genotype distribution of rs320 and rs688 in recessive model from analysis of single gene locus. It was also found significant difference of triglyceride (TG) of LPL rs320 and APOB/APOA1 in TM6SF2 rs58542926 of total study population. In binary logistic regression analysis, TM6SF2 rs58542926 was associated with reducing acute myocardial infarction risk (TT/CC, OR=0.098, 95% CI=0.024–0.392). Stratified association analysis revealed PCSK9 rs505151 was associated with acute myocardial infarction in male group (GA/AA, OR=2.445, 95% CI=1.094–5.465) and in non-hypertension group (GA/AA, OR=2.368, 95% CI=1.013–5.533).

CONCLUSIONS The genotype TT of TM6SF2 rs58542926 was associated with reducing acute myocardial infarction risk.

GW31-e1054

Predictive value of severity scoring systems in patients with acute myocardial infarction

Chao Sun, Baojian Zhang, Na Liu, Biao Li, Qiming Liu
Department of Cardiovascular Medicine, The Second Xiangya Hospital, Central South University

OBJECTIVES To explore the predictive values of simplified acute physiology score II (SAPS II) and Oxford acute severity of illness score (OASIS) for prognosis in patients with acute myocardial infarction (AMI).

METHODS Data including baseline information, vital signs, and some laboratory test results of adult AMI patients was extracted from medical information mart for intensive care III (MIMIC-III). SAPS II and OASIS of each patient were calculated according to the requirements of each scoring system. The patients were divided into two groups according to the occurrence of in-hospital mortality. We compared the difference of baseline information between two groups. Logistic regression analysis and receiver operating characteristic (ROC) analysis was performed to analyze the association between scoring systems and in-hospital mortality. The discharged patients were divided into four groups according to the quartile values of the score, respectively. The association between scoring systems and 1-year mortality after discharge were evaluated by Cox proportional hazards model.

RESULTS A total of 5031 adult AMI patients with in-hospital mortality rate of 14.5% (728/5031) were included finally, of which female patients accounted for 38.9% (1959/5031). When compared with the survivors, non-survivors had higher SAPS II and OASIS scores and the differences were statistically significant (P<0.001, P<0.001). Logistic regression analysis showed that both SAPS II (OR=1.043, 95% CI 1.033–1.054, P<0.001) and OASIS (OR=1.046, 95% CI 1.030–1.063, P<0.001) were independent predictors of in-hospital mortality in AMI. ROC analysis showed that the area under curve (AUC) of SAPS II and OASIS was 0.803 (95% CI 0.786–0.820, P<0.001) and 0.770 (95% CI 0.750–0.789, P<0.001), respectively. The optimal SAPS II threshold was 42 and yielded a 72.9% sensitivity and 74.4% specificity. The optimal OASIS threshold was 36 and yielded a 67.5% sensitivity and 75.1% specificity. The Hanley-McNeil test showed a significant difference of AUC between the two scoring systems (Z=4.393, P<0.001). Cox proportional hazards model showed that increased SAPS II was the independent risk factor of 1-year mortality after discharge in AMI (HR=1.017, 95% CI 1.006–1.027, P=0.002) and OASIS was not the independent predictor (HR=1.007, 95% CI 0.993–1.022, P=0.337).

CONCLUSIONS Both SAPS II and OASIS are independent predictors of in-hospital mortality in AMI. They can predict in-hospital mortality of AMI effectively, and the predictive value of SAPS II is superior to OASIS. SAPS II is also the independent predictor of 1-year mortality after discharge in AMI.

GW31-e1072

Evaluation of neutrophil-to-lymphocyte ratio as a predictor of drug eluting stent restenosis in patients with type 2 diabetes mellitus

Zhichao Wang, Jun Tao
Department of Hypertension and Vascular Disease, The First Affiliated Hospital, Sun Yat-Sen University

OBJECTIVES It is well known that there is a clear correlation between neutrophil-to-lymphocyte ratio (NLR) and the occurrence of in-stent restenosis (ISR). However, few studies focused on patients with type 2 diabetes mellitus (T2DM) and evaluated the dynamic changes of NLR value to predict ISR. We aimed to assessed the predictive value of two pre-procedural NLR on ISR in patients with T2DM.

METHODS This retrospective study consecutively enrolled 96 patients with T2DM who underwent Drug-eluting stents (DES) implantation and follow-up coronary angiography (CAG). Pre-procedural blood cell parameters were analyzed in the first percutaneous coronary intervention (PCI) and the second CAG. Multivariate logistic regression analysis to determine the predictors of ISR. Receiver operating characteristic (ROC) curves assessed predictive value of NLR in ISR patients with T2DM.

RESULTS Patients were divided into 2 groups at mean follow-up of 11.0±2.2 months: Non-ISR group (n=64), ISR group (n=32). The two pre-procedural NLR levels in the ISR group were significantly higher than that in the Non-ISR group (P≤0.001), respectively. Multivariate logistic regression analysis indicated that pre-procedural NLR was an independent risk predictor for ISR in patients with T2DM (NLR1, odds ratio [OR]=1.94, 95% confidence interval [CI]: 1.08–3.50, P=0.03; NLR2, OR=3.90, 95% CI: 1.78–8.55, P=0.001). Receiver operating characteristic (ROC) curves showed that the first pre-procedural NLR (NLR1) cutoff value for predicting ISR rate was 2.86 with a sensitivity of 59% and a specificity of 73%. The second pre-procedural NLR (NLR2) cutoff value for predicting ISR rate was 2.51 with 75% sensitivity and 70% specificity.

CONCLUSIONS NLR was an independent risk factor for DES-ISR in patients with T2DM, and NLR before second CAG may have a better predictive value in identifying ISR.

GW31-e1088

The effects of gender and severity of anatomical stenoses on fractional flow reserve measurements

Xiuxiu Xu[1,2,3], Junmei Zhang[2,3], Ru San Tan[2,3], Ping Chai[4], Qinghua Wu[1], Huan Han[2], Lynette L.S. Teo[4], Ris Low[2], Jiang Ming Fam[2], Chee Yang Chin[2], Mark Chan[4], Adrian F. Low[4], Swee Yaw Tan[2,3], Terrance Chua[2,3], Soo Teik Lim[2,3], Liang Zhong[2,3]
[1]Department of Cardiovascular Medicine, the Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi 330006, China
[2]National Heart Centre Singapore, 5 Hospital Drive, 169609 Singapore
[3]Duke-NUS Medical School, 8 College Rd, 169857 Singapore
[4]National University Hospital Singapore, 1E Kent Ridge Road, 119228 Singapore

OBJECTIVES Fractional flow reserve (FFR), the ratio of mean blood pressure distal to the coronary artery (CA) stenoses to mean aortic blood pressure measured under drug-induced hyperemia during invasive coronary angiography (ICA), is the gold standard for diagnosing CA ischemia. We studied the effects of gender and CA severity on FFR measurements.

METHODS Subjects underwent computed tomographic coronary angiographic (CTCA) and clinically indicated ICA with FFR measurements. CA lesions were stratified according to ICA-assessed diameter stenosis (DS) using quantitative coronary analysis: <50% (mild), 50–69% (moderate), 70–99% (severe).

RESULTS One hundred and nine subjects (mean age 59.9±9.2 years, 32 females) from multi-centers were enrolled and FFR measurements were performed in 169 CA stenoses. FFR was similar between females and males in mild stenosis (0.90±0.04 vs. 0.90±0.06, P=0.70) and moderate stenoses (0.83±0.09 vs. 0.85±0.06, P=0.40), but were significantly different in severe stenoses (0.77±0.09 vs. 0.69±0.16, P=0.02). FFR was not influenced by the location of the stenoses (left artery descending, circumflex, and right coronary artery) (all P>0.05) between genders.

CONCLUSIONS There were significant gender differences in FFR measured in severe but not mild and moderate CA stenoses. The mechanism of this observation is unclear and how this will affect the physiological assessment of CA stenosis warrants further studies.

GW31-e1131

Heart-type fatty acid binding protein predicts cardiovascular outcomes in patients with premature coronary artery disease

Huiwen Zhang, Yuanlin Guo, Naqiong Wu, Ying Gao, Ruixia Xu, Qian Dong, Jing Sun, Jianjun Li
Fu Wai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College

OBJECTIVES Heart-type fatty acid binding protein (H-FABP), a cardiac biomarker, which has been used as a diagnostic marker of myocardial injury and a predictive indicator for clinical outcomes in patients with acute coronary syndrome. However, its prognostic utility in patients with premature coronary artery disease (PCAD) has been less investigated. The aim of this study was to assess the relationship between H-FABP and cardiovascular events (CVE) in patients with PCAD.

METHODS A total of 2828 consecutive patients with PCAD (defined as male <55 years, female <65 years) were enrolled and followed-up for CVEs. The CVEs were defined as cardiovascular death, myocardial infarction, stroke and coronary revascularization. Plasma H-FABP levels were measured using the Latex immunoturbidimetric method. The association between H-FABP with CVEs was analyzed by Cox regression analysis and Kaplan-Meier analysis.

RESULTS There were 205 CVEs occurred duringa median of 49 months follow-up. H-FABP levels were significantly higher in patients with CVEs compared with those without CVEs (mean: 2.71 ng/mL vs. 2.15 ng/mL, P<0.001). In addition, patients with the highest level of H-FABP had increased rate of CVE compared with ones in the lowest groups (P<0.05). Moreover, in Cox regression analysis, data indicated that elevated H-FABP levels were independently correlated with a higher risk of CVEs (P<0.05) after adjusted for confounders.

CONCLUSIONS Elevated levels of H-FABP were independently associated with increased risk of CVEs in patients with PCAD. These data might provide novel information of H-FABP in predicting adverse outcomes in patients with PCAD.

GW31-e1140

ABIC score, a novel predictive model for long term prognosis of CAD patients after PCI

Ting Ting Wu, Xiang Xie, Yi Tong Ma
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi, 830054, P.R. China

OBJECTIVES Prognostic stratification of patients with coronary artery disease (CAD) may improve the clinical management and facilitate clinical trials. We aimed at developing a scoring system capable of providing prognostic stratification of patients with CAD.

METHODS A retrospective study (identifier: ChiCTR-INR-16010153) contains 6046 CAD patients were evaluated finally. Using the Kaplan-Meier analysis with the cut off value of 7.985, patients were divided into two groups (ABIC score ≥7.985, n=2808; <7.985, n=3238). The primary outcome long-term mortality and secondary endpoints mainly major adverse cardiovascular and cerebrovascular events (MACCEs) were recorded. Multivariate Cox regression models were used to determine risk factors for mortality and MACCEs.

RESULTS A total of 309 patients died during the following up time. There were significantly higher adverse events in the high group compared to that in the low group with 192 (6.8%) vs. 117 (3.6%), cardiac death 148 (5.3%) vs. 103 (3.2%) and MACCE 422 (15.0%) vs. 440 (13.6%) respectively. However, the frequency of MACCE did not differ significantly between the two groups. After adjusting for eight confounders, the multivariate Cox proportional hazards model showed that when ABIC score ≥7.985, the incidence of all cause mortality would be increased 1.7 times (adjusted HR=1.729 (1.347–2.218), P<0.001), and 1.5 times in cardiac death (adjusted HR=1.482 (1.126–1.951), P=0.005).

CONCLUSIONS The present study indicated that ABIC score predicts high long-term mortality risk for PCI patients, ABIC score might be a potential prognostic model for patients with CAD.

GW31-e1142

A novel long-term prognostic markers average platelet volume to platelet count ratio in ACS patients after PCI

Ting Ting Wu, Xiang Xie, Yi Tong Ma
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, P.R. China

OBJECTIVES To investigate the long-term prognosis of average platelet volume (MPV) to platelet count (PC) ratio in acute coronary syndrome (ACS) patients underwent percutaneous coronary intervention (PCI).

METHODS A retrospective cohort study including 2751 ACS patients after PCI in the First Affiliated Hospital of Xinjiang Medical University from January 2008 to December 2016 was conducted. All laboratory data including platelet parameters, biochemical data, and cardiovascular disease-related risk factors were collected from the medical records. Follow-up endpoints were all-cause mortality, cardiac deaths, major cardiovascular adverse events (MACE), stroke, and bleeding events. Follow-up data was obtained from telephone interview with the patients or family members.

RESULTS The optimal clinical cut off point of MPV/PC value of patients was 0.043 selected by ROC curve. Baseline data analysis showed that compared with the low MPV/PC group (MPV/PC ≤0.043), cardiac deaths 54 (3.1%) vs. 62 (6.3%), all-cause mortality 73 (4.1%) vs. 71 (7.2%), and MACE events 424 (24.0%) vs. 274 (27.9%) were significantly higher in the high-value MPV/PC group. Multivariate Cox regression analysis showed that all cause mortality increased by 1.7 times in the MPV/PC high-value group (OR 1.713, 95% CI 1.225–2.397, P=0.002); the cardiac deaths will increased by 2 times (OR 2.037, 95% CI 1.400–12.963 P<0.001).

CONCLUSIONS High MPV/PC ratio is associated with poor prognosis after PCI and it could be an independent risk factor for all-cause mortality and cardiac deaths.

Keywords: Acute coronary syndrome, MPV, PLT, prognosis

GW31-e1167

Identification and function analysis of differentially expressed miRNAs in rat myocardial infarction model

Jing Liu[1,2], Daomin Yao[2], liang Xie[1], Yanming Liu[1], Jianbin Gong[1]
[1]Nanjing General Hospital of Nanjing Military Command
[2]Nanjing University Of Chinese Medicine

OBJECTIVES To identify differentially expressed microRNAs (miRNAs) in rat myocardial infarcted tissues and predict their interaction with lncRNAs and target genes, as well as explore potential pathophysiology mechanisms in myocardial infarction.

METHODS A rat model of myocardial infarction was established by ligating the left anterior descending coronary artery. Trizol was used to extract total RNA from infarcted myocardial area for Microarray detection. Bioinformatics methods were used to predict interaction lncRNAs, target genes prediction, and functional enrichment of miRNAs that were significantly differently expressed. Find possible lncRNA-miRNA-mRNA regulatory networks finally.

RESULTS The elevation of ST segment of ECG showed that the rat model of myocardial infarction was successfully prepared. Microarray results showed that there were 19 significantly differently expressed miRNAs. Eight of these miRNAs (miR-21, miR-132, miR-222, miR-223-3p, miR-146a/b, miR-181b, miR-449a-5p, miR-122) have been proven to be myocardial infarction treatment Candidates. Whether seven miRNAs (miR-365-5p, miR-490-5p, miR-6333, miR-30c-1-3p, miR-3591, miR-3596c, miR-877) are related to myocardial infarction has not been confirmed. There may be several new lncRNA-miRNA-mRNA mechanisms in the development of myocardial infarction. ENSRNOT00000076620-miR-146b-5p-STAT3/Rnf7/Qrsl1 may be involved in the process of cardiomyocyte apoptosis and mitochondrial damage during myocardial infarction. ENSRNOT00000071991-miR-122-Deptor may inhibit the autophagy of cardiomyocytes and exacerbate myocardial infarction

CONCLUSIONS The ternary relationship of lncRNA-miRNA-mRNA obtained in this study may provide possible research directions and a certain theoretical basis for further exploration of the molecular level pathological mechanism of myocardial infarction, as well as finding new therapeutic targets for myocardial infarction.

GW31-e1168

A novel Japanese nutritional index serve as a useful prognostic indicator in Chinese patients with coronary heart disease

Qiuzhen Lin[1,2,3,4], Qiming Liu[1,2,3,4]
[1]Department of Cardiovascular Medicine, The Second Xiangya Hospital, Central South University
[2]Modern Cardiovascular Disease Clinical Technology Research Center of Hunan Province
[3]Cardiovascular Disease Research Center of Hunan Province
[4]Research Institute of Blood Lipid and Atherosclerosis, Central South University

OBJECTIVES It was recognized that malnutrition and an increased risk of adverse outcomes in patients with different cardiovascular diseases had a close relationship. The aim of this study was to use a novel Japanese calculated nutritional index in Chinese patients with coronary heart disease (CHD).

METHODS This study was a retrospective observational analysis. There was 11,935 patients with CHD at department of cardiovascular medicine, the Second Xiangya Hospital, Central South University from 2011 to 2019 were recruited in this study. The novel Japanese nutritional index was calculated by the formula: Triglycerides (TG)×Total Cholesterol (TC) ×Body Weight (BW) Index (TCBI)=TG×TC×BW/1000 (TG and TC: mg/dL, and BW: kg). The most often used conventional nutritional index, Geriatric Nutritional Risk Index (GNRI)=14.89×serum Alb (g/dL)+41.7×(measured BW (kg)/ideal BW (kg)). Ideal BW was calculated using Lorentz-formula. Ideal BW=(height (cm)–100)–(height (cm)–150)/4 for men and (height (cm)–100)–(height (cm)–150)/2 for women. Then, we calculated the values of TCBI and GRNI of the included patients. Because the normality test indicated that both of them were non-naormal distribution, we used the Spearman non-parametric correlation coefficient between TCBI and GNRI to evaluate the predictive ability of the novel nutritional index of Chinese patients with CHD.

RESULTS All subjects were 22~94 years old, including 3406 (28.5%) women and 8529 (71.5%) men. The BMI ranged from 15.06 kg/m^2 to 40.09 kg/m^2. The means of TG and TC were 153.17 mg/dL and 150.31 mg/dL, respectively. The Spearmen non-parametric correlation coefficient between TCBI and GNRI was 0.397, which was similar to the result of the study committed in Japan, indicating modest correlation.

CONCLUSIONS This study indicated that TCBI may be a useful prognostic indicator in Chinese patients with CHD.

GW31-e1174

Protective features of gut microbiota in high altitude Tibetan patients with coronary artery disease

Yulan Ma, Youlu Shen, Lin Li, Shiming Fan, Xiuying Chai, Huizhen Tian, Yue Lin, Zhongshan Gao, Ming Ren
Department of cardiology Afflicted hospital of Qinghai University

OBJECTIVES This study was designed to demonstrate the structural characteristics of gut microbiota of Tibetan patients with coronary artery disease in the Qinghai-Tibet Plateau, and to preliminarily determine the relationship between it and the pathophysiology of coronary artery disease in the Tibetan population of the Qinghai-Tibet Plateau.

METHODS The fecal tissues of patients with coronary artery disease and healthy Tibetans living on the Qinghai-Tibet Plateau, and those Han people with coronary artery disease living in Xining and Wuhan were collected. The 16S rRNA of the gut microbiota of the above specimens was sequenced and analyzed by bioinformatics.

RESULTS (1) There are certain differences in the α diversity and β diversity of the gut microbiota between high-altitude Tibetan patients with coronary artery disease and healthy individuals, and high-altitude Tibetan patients with coronary artery disease showed higher proportion of the beneficial bacteria Verrucomicrobia and its main member Akkermansia. (2) Compared with Xining and Wuhan Han patients with coronary artery disease, the α diversity of the gut microbiota in high-altitude Tibetan patients with coronary heart disease was significantly increased, and the β diversity also formed different cluster. The proportion of pathogenic bacteria Streptococcus, Escherichia/Shigella, and Klebsiella decreased. While the proportion of beneficial bacteria Faecalibacterium, Prevotella, Catenibacterium, and Lactobacillus increased.

CONCLUSIONS These results indicated that the gut microbiota of high-altitude Tibetan patients with coronary artery disease presented protective features, which might inhibit the progression of coronary artery disease.

GW31-e1177

Intermediate HDL-C fractions were identified to be an independent protect factor for CAD

Ting Ting Wu, Wan Rong Wang, Xiang Xie, Yi Tong Ma
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, P. R. China

OBJECTIVES Previous studies have linked HDL cholesterol (HDL-C) to cardiovascular protection, and the general public refers to it colloquially as good protein. In order to achieve therapeutic and health benefits, some drugs are used to specifically increase HDL-C levels. However, some recent studies have suggested that higher HDL-C is not better, and that there is a u-shaped curve between HDL-C levels and coronary artery disease (CAD). Therefore, the purpose of this study is to further clarify the role of HDL-C by analyzing the fractions of HDL-C.

METHODS We adopted the extreme study strategy to conduct subgroup analysis of HDL-C fractions in 17 patients with CAD whose HDL-C content were >50 mg/dL and 14 healthy controls whose HDL-C content were <30 mg/dL, so as to clarify the correlation between HDL-C fractions and CAD. From January to March 2019, 144 subjects in the case group and control group with HDL-C content of 40–60 mg/dL were admitted in the first affiliated hospital of Xinjiang medical university to further verify the results of the extreme value strategy study.

RESULTS The patients fasting serum lipid parameters (total cholesterol, triglycerides, low-density lipoprotein cholesterol, HDL-C, and cholesterol in 10 lipoprotein fractions were determined. For the comparison of the extreme set, there were no significant differences in small HDL-C fractions between groups. Decreases in large and intermediate HDL-C fractions 1–7 were observed in CAD group. In the verified group, intermediate HDL-C fractions of 4 and 7 were decreased significantly. In CAD group, decreases of intermediate and large HDL-C fractions were noticed, and the reverse in health group. After adjusted for other CAD risk factors, large and intermediate HDL-C fractions were identified to be independent protect factors for CAD by multivariate logistic analysis. When large and intermediate HDL-C fractions increase 1 unit, the incidence of CAD would be decreased 0.891 times (adjusted OR=0.891 (0.823–0.966), P=0.005), and 0.808 times (adjusted OR=(0.726–0.898), P<0.001) respectively. When intermediate HDL-C fractions ≥27.5 mg/dL, the risk will decrease to 0.205 (adjusted OR=0.205 (0.070–0.604).

CONCLUSIONS The results show that large and intermediate HDL-C fractions were identified to be an independent protect factor for CAD, and that the intermediate HDL-C fractions is a more accurate indicator of HDL-C function than existing indices.

GW31-e1198

Prognostic significance of inflammatory biomarkers (high-sensitivity C-reaction protein-to-albumin and fibrinogen-to-albumin ratios) in patients undergoing percutaneous coronary intervention

Yue Liu, Sida Jia, Deshan Yuan, Na Xu, Lin Jiang, Lianjun Xu, Ying Song, Zhan Gao, Jue Chen, Yuejin Yang, Runlin Gao, Bo Xu, Jinqing Yuan
Fuwai Hospital, Chinese Academy of Medical Sciences

OBJECTIVES The relationship between inflammatory markers, high-sensitivity C-reactive protein-to-albumin ratio (CAR) and fibrinogen-to-albumin ratio (FAR), and coronary artery disease has not been fully evaluated. This study aimed to investigate the predictive value of admission CAR and FAR for 5-year outcomes in patients undergoing percutaneous coronary intervention.

METHODS Data came from a large prospective cohort study with 10,724 patients consecutively enrolled between January 2013 and December 2013. The primary endpoint was all-cause death. And the secondary endpoints were cardiac death and major cardiovascular and cerebrovascular events (MACCEs). The optimal cutoff value of each ratio for all-cause mortality was determined according to the receiver operating curve.

RESULTS A total of 6617 patients were eligible for analysis. Patients with high CAR (>0.035) or FAR (>0.075) presented a high-risk profile for complications. During 5-year follow-up, significantly more all-cause death [CAR: 2.7 versus (vs) 4.9%; FAR: 2.6 vs. 5.0%, both P<0.001) and cardiac death (CAR/FAR: 1.4 vs. 3.1%, P<0.001) occurred in both high ratio groups, while MACCEs were only different between low and high FAR groups (21.8 vs. 24.9%, P=0.006). After adjusting confounders, both ratios remained independently predictive of all-cause death [CAR: hazard ratio (HR) 1.65 (1.16–2.35), P=0.005; FAR: HR 1.44 (1.01–2.05), P=0.046] and cardiac death [CAR: hazard ratio (HR) 2.20 (1.35–3.57), P=0.001; FAR: HR 2.04 (1.23–3.36), P=0.005]. The associations were also relatively consistent in subgroups with no significant interactions. Additionally, incorporating CAR or FAR further improved the reclassification ability of SYNTAX score II for mortality prediction.

CONCLUSIONS CAR and FAR were independent predictors for long-term prognoses after percutaneous coronary intervention. The inflammatory biomarkers could enhance the predictivity of SYNTAX score II for mortality.

GW31-e1210

Effect of enhanced external counterpulsation on left ventricular strains: a three-dimensional speckle tracking echocardiograpgic study

Ling Xu, Wei Zhao, Cui Ming
Department of Cardiology, Peking University Third Hospital, NHC Key Laboratory of Cardiovascular Molecular Biology and Regulatory Peptides. Beijing 100191, China

OBJECTIVES To prove the clinical efficacy of enhanced external counterpulsation (EECP) in patients with coronary heart disease after incomplete revascularization.

METHODS Forty subjects with coronary heart disease after incomplete revascularization were assigned to EECP group (standard course of EECP combined with drug therapy) and control group (drug therapy) according to their treatment intention, with 20 patients in each group. All subjects underwent three-dimension speckle tracking endocardiography (3D-STE), transthoracic echocardiography (TTE) examinations at baseline, 18 hours of treatment (control group for 3–4 weeks of follow-up), 35 hours of treatment (control group for 7 weeks of follow-up).

RESULTS After 35 hours of EECP treatment, the myocardial strain parameters Twist (7.4±4.9° vs. 2.8±3.5°, P=0.016) and Torsion (1.5±0.7°/cm vs. 0.8±0.6°/cm, P=0.006) improved significantly, while the 3D-STE and TTE related parameters in the control group did not change significantly during the follow-up period. Correlation analysis found that in the control group the improvement of Twist was negatively correlated with the baseline coronary Gensini score (r=–0.597, P=0.015), which was not observed in the EECP group. In the subgroup analysis, it was found that in the patients without diabetes mellitus (DM), EECP had a more significant effect on the improvement of myocardial strain parameters than the patients with DM.

CONCLUSIONS For patients with coronary heart disease after incomplete revascularization, the standard course of EECP treatment can increase myocardial strain parameters Twist and Torsion, suggesting that EECP can effectively improve cardiac systolic function in such patients.

GW31-e1225

Relationship of urine output and in-hospital and 90-day all-cause mortality in patients with acute myocardial infarction

Zhijie Mao[1], Ya Lin[1], KangWei Wang[1], JianJian Huang[2], LuYa Wang[1], YiHe Chen[1], WeiJian Huang[1], Zhouqing Huang[1]
[1]The Key Laboratory of Cardiovascular Disease of Wenzhou, Department of Cardiology, The First Affiliated Hospital of WenZhou Medical University, WenZhou, ZheJiang, China
[2]Department of Anaesthesiology, Wenzhou Medical University, Wenzhou, Zhejiang, China

OBJECTIVES Acute kidney injury (AKI) is a serious and common complication of acute myocardial infarction (AMI), which significantly increases mortality. However, the definition of acute kidney injury (AKI) based on urine output is usually neglected in the prognosis of patients with Acute Myocardial Infarction. This study is to access the influence of three AKI definitions, especially based on urine output, on the accuracy of mortality prediction in patients with AMI.

METHODS This study was a retrospective study based on the open MIMIC-III database. We enrolled 1953 patients with AMI. Exposure is based on the maximum AKI stage after admission to the ICU. Multiple Cox proportional hazards models were used to test the association between different definitions of acute kidney injury and all-cause mortality. The discriminant degree of the model was compared using the area under the ROC curve (AUC) and integrated discrimination improvement (IDI). In addition, we do a nomogram according to AKI-UO to predict in-hospital mortality of patients with AMI. The predictive accuracy of the nomogram was according to the c-index and calibration using Hosmer-Lemeshow (H-L) chi-square statistics.

RESULTS Of the 1953 participants, the mean (SD) age was 67.4 (14.1) years; the mean weight was 81.2 (9.7) kg; and the serum creatinine (scr) initial was 1.2±0.8 mg/dL. Overall, 1264 (64.7%) study participants were male and 118 (6.0%) have old myocardial infarction (OMI), 1548 (79.3%) have coronary diseases, 944 (48.3%) had hypertension, 518 (26.5%) had diabetes mellitus. 191 (9.8%) patients appear in-hospital death. After a total of 90 days of follow-up, 293 (15.0%) participants death. AKI as defined by AKI-uo, AKI-scr, AKI-kdigo occurred in 54, 38, 65.6% of the study patients during hospitalization, respectively. And AKI-UO, AKI-Scr, and AKI-KDIGO were independent predictors of in-hospital mortality (with adjusted OR of 3.4 (95% CI, 2.1–5.7), 2.4 (95% CI, 1.7–3.5) and 3.7 (95% CI, 1.9–7.2), respectively). AUC was 0.8238 for the clinical model containing age (per 10 years increase), heart rate, surgery, PT, haemoglobin-min and glucose-max. Meanwhile, the addition of AKI-UO, AKI-Scr, AKI-KDIGO to the clinical model improved the in-hospital mortality models. (AUC plus AKI-UO: 0.8625, plus AKI-Scr: 0.8537, and plus AKI-KDIGO: 0.8612; integrated discrimination improvement (IDI) was 5.9% (P<0.0001), 1.6% (P=0.0038), and 1.3% (P=0.0002), respectively). With regard to 90-day mortality, the IDI of AKI-UO, AKI-Scr, and AKI-KDIGO was 6.2% (P<0.0001), 2.3% (P<0.0001), and 2.1% (P<0.0001), respectively. Finally, in our study, we performed a nomogram to predict in-hospital mortality of patients with AMI based on AKI-UO. The nomogram had a c-index of 0.8625 (95% CI 0.8386–0.8864) and a cut-off value of −2.4735, with a sensitivity of 87% and a specificity of 70%. The Hosmer-Lemeshow chi-square test indicated that the nomogram was well-calibrated (chi-square: 9.182, P=0.327).

CONCLUSIONS AKI-UO is an independent predictor of all-cause mortality in AMI patients. The addition of AKI-UO to the traditional clinical model significantly improved its predictive accuracy for in-hospital and 90-day all-cause mortality.

GW31-e1238

MicroRNA-21 promotes the expansion of myeloid-derived suppressor cells via targeting STAT-3 pathway in patients with acute coronary syndrome

Wencai Zhang, Zhanying Han
The First Affiliated Hospital of Zhengzhou University

OBJECTIVES The aim of this study was to explore the mechanisms accounting for the expansion of myeloid-derived suppressor cells (MDSCs) in patients with acute coronary syndrome (ACS).

METHODS The frequencies of circulating $CD14^{+}HLA\text{-}DR^{-/low}$ MDSCs were detected by flow cytometry, and *miR-21-5p* expression was analyzed by real-time reverse transcription polymerase chain reaction (RT-PCR). Correlation analyses between MDSC frequencies and *miR-21* levels were also performed. Then, to determine the role of *miR-21* in the expansion of MDSCs, cells were transfected with *miR-21-m*, *miR*-NS-m or control. In addition, levels of phosphatase and tensin homolog (PTEN) and phospho-signal transducer and activator of transcription-3 (p-STAT-3) were detected by western blotting.

RESULTS The frequencies of circulating $CD14^{+}HLA\text{-}DR^{-/low}$ MDSCs and the levels of *miR-21-5p* were both obviously increased in patients with ACS, and there was a positive correlation between these parameters. Furthermore, treatment with *miR-21-m* markedly increased *miR-21* expression and thus promoted the expansion of MDSCs. Meanwhile, treatment with *miR-21-m* markedly decreased PTEN expression and increased STAT-3 activity. In addition, disruption of STAT-3 activity with the specific inhibitor S3I201 nearly abolished *miR-21*-induced MDSC expansion.

CONCLUSIONS Our results demonstrated that *miR-21* contributed to the expansion of MDSCs through reduction of PTEN expression, thereby leading to STAT-3 activity, in patients with ACS.

GW31-e1252

Impact of shock index before IABP insertion on recent prognosis of patients with cardiogenic shock complicating acute myocardial infarction

Haobo Teng, Chao Guo, Shubin Qiao
Center of Coronary Heart Disease, Fuwai Hospital, National Center for Cardiovascular Diseases

OBJECTIVES To investigate the impact of shock index before IABP insertion on recent prognosis of patients with cardiogenic shock complicated by acute myocardial infarction supported by intra-aortic balloon pump.

METHODS A total of 103 patients diagnosed as cardiogenic shock complicated by acute myocardial infarction admitted in our hospital from 2014.6 to 2018.5 were enrolled in our study. We collected the data from medical records and investigated their clinical manifestation and laboratory examination, as well as 28-day mortality retrospectively, we calculated the shock index (ratio of heart rate to systolic blood pressure) before IABP insertion.

RESULTS Compared with lower SI before IABP insertion, patients with higher SI had higher proportion of anterior infarction (81.5 vs. 61.2%, P=0.022), history of PCI (24.1 vs. 8.16%, P=0.030), left main as culprit vessel (31.5 vs. 12.2%, P=0.019), and final TIMI flow ≤2 (55.5 vs. 26.5%, P=0.003), invasive ventilation (40.7 vs. 20.4%, P=0.026) as well as 28-day-mortality (81.5 vs. 61.2%, P=0.022). SI could predict the recent prognosis, with a cut-off of 1.625, a sensitivity of 0.655 and a specificity of 0.708, AUC of ROC was 0.713; On multiple analysis, SI, together with final TIMI flow, arterial pH and creatinine were independent predictive factors of recent prognosis in this population.

CONCLUSIONS Among patients with cardiogenic shock complicated by acute myocardial infarction, higher SI before IABP insertion was associated with poorer prognosis, SI was an independent risk factor of recent mortality, and could predict the recent prognosis well.

GW31-e1304

Monocyte to high-density lipoprotein ratio was associated with the severity of coronary artery disease

Haoyu Wu, Lijun Wang, Chen Wang, Shanshan Gao, Zuyi Yuan
Department of Cardiovascular Medicine, First Affiliated Hospital of Xi'an Jiaotong University

OBJECTIVES Atherosclerosis (AS) is the pathophysiological basis of coronary artery disease (CAD) with inflammation and cholesterol metabolism disorder as its two basic hallmarks. Monocytes in the circulation are the main cells secreting various pro-inflammatory factors, and play an extremely important role in the initiation of coronary AS, plaque formation and stability. Studies have shown that vulnerable plaques exhibit significant monocyte infiltration, and monocytes in the peripheral blood of patients are mostly activated. High-density lipoprotein cholesterol (HDL-C) is a lipid component that exerts anti-AS effects, by promoting cholesterol efflux and preventing monocyte activation, proliferation and adhesion to endothelium. Increased monocyte counts and decreased HDL-C levels have been reported to be associated with inflammatory disorders. Recently, monocyte to HDL-C ratio (MHR) has emerged as a novel and useful marker in different disease models, such as CAD, diabetes mellitus (DM), saphenous vein graft disease (SVGD) and acute ischemic stroke (AIS). In a cross-sectional study on 1229 CAD patients, Akboga et al. found that MHR is significantly correlated with the burden of AS. Another study also found that MHR was obviously higher in 428 stable CAD patients with SYNTAX score of ≥23 than those with SYNTAX score of <23. However, the abovementioned studies usually had relatively small sample size, and few study has ever investigated the association of MHR with the severity of CAD assessed by Gensini score in a large scale population. Therefore, in this study, we evaluated the association of MHR with the severity and complexity of CAD using the Genisi score and determined the ability of MHR in predicting severe CAD and acute atherothrombosis events.

METHODS A total of 4950 patients who presented to the Department of Cardiovascular Medicine of the First Affiliated Hospital of Xi'an Jiao University for angiography between 2017 January and 2018 July were recruited. The total population included 3930 CAD patients and 1020 non-CAD patients. The CAD patients were classified into four groups according to the quartile of the MHR

(≤0.28, N=1218; 0.28–0.39, N=1262; 0.39–0.53, N=1209; >0.53, N=1261). CAD severity was quantified according to the Gensini score. A receiver operating characteristic (ROC) curve analysis was also performed to predict severe CAD and acute coronary thrombotic events.

RESULTS MHR was significantly higher in the CAD group than in the non-CAD group (0.45±0.22 vs. 0.35±0.17, P<0.001) and had a significant positive correlation with Gensini score. Compared with lower MHR value, a MHR in the fourth quartile was strongly associated with severe CAD and acute coronary thrombotic event after adjusting for baseline factors. Receiver-operating characteristic (ROC) curve analysis showed that combination of MHR and traditional risk predictors could better predict severe CAD especially acute coronary thrombosis events such as non-ST-elevation myocardial infarction (NSTEMI) and acute ST-elevation myocardial infarction (ASTEMI).

CONCLUSIONS We demonstrated in this study that MHR is positively associated with the severity of CAD and MHR is an independent indicator to predict severe CAD and acute coronary thrombosis events.

GW31-e1333

Effect of nicorandil on the index of microcirculatory resistance in IHD patients with intervention therapy: a meta-analysis

Xuyang Wang, Xiaogang Guo
Department of Cardiology, The First Affiliated Hospital, Zhejiang University School of Medicine, 79 Qingchun Road

OBJECTIVES The aim of this study is to evaluate the effect of nicorandil on IMR in IHD patients with PCI and other intervention therapy by means of a meta-analysis.

METHODS CENTRAL, PUBMED, EMBASE, CNKI, and Wanfang electronic databases were searched for randomized controlled trials and non-randomized controlled trials published until October 2018. We included clinical controlled trials comparing the effect of nicorandil on IMR versus placebo or other pharmacological interventions in IHD patients with PCI and other intervention therapy.

RESULTS Four trials including a total number of 232 participants were identified. The baseline IMR between the nicorandil group and the control group showed no statistically difference; the posttreatment IMR between the nicorandil group and the control group showed significant statistically difference; the change of IMR in the nicorandil group was significant larger than that in the control group.

CONCLUSIONS Nicorandil could reduce the value of index of microcirculatory resistance (IMR) in the IHD patients who has received interventional treatment, sequentially improve coronary microcirculation function of patients.

GW31-e1335

Long non-coding RNA SOX2-OT exacerbates hypoxia-induced cardiomyocytes injury by regulating miR-27a-3p/TGFβR1 axis

Guang Yang, Chunsheng Lin
Shaanxi Provincial People's Hospital, Department Cardiology

OBJECTIVES Myocardial infarction (MI) was a severe cardiovascular disease resulted from acute, persistent hypoxia or ischemia condition. Additionally, MI generally led to heart failure, even sudden death. A multitude of researches proposed that long non-coding RNAs (lncRNAs) frequently participated in the regulation of heart diseases. The specific function and molecular mechanism of SOX2-OT in MI remained unclear. The current research was aimed to explore the role of SOX2-OT in MI.

METHODS Bioinformatics analysis (DIANA tools and Targetscan) and a wide range of experiments (CCK-8, flow cytometry, RT-qPCR, luciferase reporter, RIP, caspase-3 activity, trans-well and western blot assays) were adopted investigate the function and mechanism of SOX2-OT.

RESULTS We discovered that hypoxia treatment decreased cell viability but increases cell apoptosis. Besides, lncRNA SOX2-OT expression was up-regulated in hypoxic HCMs. Hereafter, we confirmed that SOX2-OT could negatively regulate miR-27a-3p levels by directly binding with miR-27a-3p, and miR-27a-3p also could negatively regulate SOX2-OT levels. Furthermore, knock-down of SOX2-OT promoted cell proliferation, migration and invasion, but limited cell apoptosis. However, these effects were reversed by anti-miR-27a-5p. Besides, we verified that miR-27a-3p binding with the 3′UTR of TGFBR1 and SOX2-OT regulated TGFβR1 level by collaborating with miR-27a-3p in HCMs. Eventually, rescue assays validated that the influence of SOX2-OT silence or miR-27a-3p overexpression on cellular processes in cardiomyocytes injury was counteracted by TGFBR1 overexpression.

CONCLUSIONS Long non-coding RNA SOX2-OT exacerbated hypoxia-induced cardiomyocytes injury by regulating miR-27a-3p/TGFβR1 axis, which may provide a novel insight for heart failure treatment.

GW31-e1362

Berberine inhibits P2X7 purinergic receptor to regulate EMMPRIN and MMP9 expression by AMPK through MAPK signaling in oxLDL-stimulated macrophages

Lu Lin[1], Jianjian Huang[2], Xue Xia[1], Zhongqiu Lu[1], Bozhi Ye[1], Zhouqing Huang[1]
[1]The Key Laboratory of Cardiovascular Disease of Wenzhou, Department of Cardiology, The First Affiliated Hospital of WenZhou Medical University, WenZhou, ZheJiang, China
[2]Department of Anesthesiology, Wenzhou Medical University

OBJECTIVES At present the pathogenesis of atherosclerosis has not been fully elucidated which including the lipid infiltration oxidative stress Ca^{2+} overload abnormal immune function and so on While as a theory of relatively new inflammatory mechanism attracts much attention in recent years Studies have shown that the inflammatory response mediated by mononuclear macrophage and foam cells plays a key role in the pathogenesis of atherosclerosis MMPs and EMMPRIN overproduced and released by mononuclear macrophage and foam cells result in the rupture of atherosclerotic plaque through degrading the extracellular Moreover as another receptor protein high expressed in mononuclear macrophage and foam cells P2X7R also regulate the progress of atherosclerosis Recent studies show that berberine as a traditional Chinese medicine could reduce the risk factors of atherosclerosis such as blood glucose and blood fat which add a new entry point to treat the inflammation mediated by mononuclear macrophage and foam cells. We aimed to study whether P2X7R regulate the expression of MMP9 and EMMPRIN in oxLDL stimulated macrophages Moreover the study is to investigate whether berberine could inhibit the expression of P2X7R in mononuclear macrophage and foam cells and its potential mechanisms.

METHODS PMA differentiated macrophages were stimulated with ox-LDL for different time to detect the protein expression of P2X7R by Western blot analysis Then PMA-differentiated macrophages were pretreated with A-438079 or berberine for 1 hour before induced by ox-LDL 50 μg/mL for 48 hours Protein and total RNA were collected for Real-time PCR and Western blot analysis respectively Zymography was used to determine the MMP-9 activity through the culture supernatants.

RESULTS P2X7R was highly expressed in oxLDL stimulated macrophages in a time dependent manner The inhibition of P2X7R led to the suppression of EMMPRIN and MMP9 both at the protein and mRNA levels and that also reduced MMP9 activity Moreover P2X7R is necessary for the phosphorylation of AMPKα and MAPK pathway (ERK1/2 p38 JNK) which further regulated the expression of EMMPRIN and MMP9 We also observed that berberine suppressed the expression of P2X7R EMMPRIN and MMP9 through AMPKα and MAPK pathway in a dose dependent manner.

CONCLUSIONS In oxLDL stimulated macrophages berberine could suppress the expression of P2X7R in a dose dependent manner which further reduce the expression of EMMPRIN and MMP 9 with the participation of AMPK α and MAPK pathway.

GW31-e1368

Serum levels of ANGPTL3 and ANGPTL4 and coronary artery disease severity

Ting Sun, Wanlin Zhan, Lijiang Wei, Zuojun Xu, Zhaofang Yin, Li Fan, Yang Zhuo, Jingchao Hu, Changqian Wang
Department of Cardiology, Shanghai Ninth People's Hospital, Shanghai JiaoTong University School of Medicine

OBJECTIVES ANGPTL3 and ANGPTL4 are regulators of lipid metabolism and confirmed to associate with coronary artery disease (CAD). However, whether serums of ANGPTL3 and ANGPTL4 can predict the degree of coronary stenosis is still uncertain. In this study we investigate the role of ANGPTL3 and ANGPTL4 in atherosclerosis development via a mechanism independent of its effect on plasma lipid levels.

METHODS Three hundred and five consecutive patients with coronary heart diseases referring to Departments of Cardiology of Shanghai Ninth People's Hospital between August 2016 and December 2017 were enrolled in this retrospective study. Coronary angiography was performed by two expert cardiologists who were blinded in the blood test results. Competitive ELISA Kits for human ANGPTL3 and ANGPTL4 were used. Univariate and Multivariate logistic regression models were performed to discriminate the risk factors of atherosclerosis.

RESULTS The serum A3 levels were higher in the atherosclerosis group (coronary stenosis ≥30%) (51.71±52.67 ng/mL) than those in the coronary without obvious stenosis group (coronary stenosis <30%) (24.65±10.32 ng/mL) and ANGPTL4 levels were lower in the atherosclerosis group (561.86±716.07 ng/mL) compared with the coronary with no obvious stenosis group (626.94±729.88 ng/mL). There was a positive association between the serum

levels of ANGPTL3 and the severity of coronary atherosclerosis and no significant association between ANGPTL4 levels and atherosclerosis development. In addition, the ROC curve analyses indicated that ANGPTL3 concentrations of equal to or more than 29.1 ng/mL can predict atherosclerosis (sensitivity=72.9%, specificity=73.5%) and ANGPTL4 levels of lower than 313 ng/mL was a predictor of atherosclerosis (sensitivity=71%, specificity=60%). However, in the present study, we failed to find correlations of ANGPTL3 and ANGPTL4 with clinical and biochemical parameters.

CONCLUSIONS ANGPTL3 may promote the development of atherosclerosis and increase the risk of atherosclerosis while ANGPTL4 may protect against atherosclerosis and its levels did not differ in various degree of coronary stenosis. ANGPTL3 and ANGPTL4 independently exerted an essential influence on atherosclerosis and may be better predictors of atherosclerosis than lipids.

HYPERTENSION

GW31-e0033

Analysis of heart rate characteristics in patients with primary aldosteronism and its correlation with renin and aldosterone

Sulan Huang
The First People's Hospital of Changde

OBJECTIVES To explore the heart rate characteristics of patients with primary aldosteronism (PA) and its relationship with renin and aldosterone.

METHODS This study is a retrospective case-control study. A total of 195 cases of patients with PA diagnosed for the first time in our hospital from January 2015 to December 2019 were included in this study. Meanwhile, 195 cases of patients with primary hypertension (PH) were selected as the control group. The resting heart rate, 24 h average heart rate, day average heart rate, night average heart rate and serum potassium were observed and compared between the two groups. The relationship between renin, aldosterone and aldosterone/renin activity rates [plasma aldosterone concentration (PAC)/plasma renin activity (PRA) rate, ARR] and heart rate was studied by correlational analysis. Then the effects of renin, aldosterone and ARR on heart rate were analyzed by multiple linear regression.

RESULTS (1) The resting heart rate, 24 h average heart rate, day average heart rate and night average heart rate of PA patients were all slower than those of PH patients ($P<0.05$). Compared the heart rate of PA patients with different serum potassium levels, the resting heart rate, 24 h average heart rate and day average heart rate of PA patients in the hypokalemia group were slower than those in the normal potassium group ($P<0.05$). The resting heart rate, 24 h average heart rate, day average heart rate and night average heart rate of the adenoma group were all faster than those of the hyperplasia group, but the difference was not statistically significant ($P>0.05$). (2) Correlation analysis showed that renin was positively correlated with resting heart rate, 24 h average heart rate, day average heart rate and night average heart rate ($P<0.05$). The aldosterone/renin ratio (lnARR) was negatively correlated with resting heart rate, 24 h average heart rate, day average heart rate and night average heart rate ($P<0.05$). (3) Multiple linear regression analysis showed that after adjusting for age, gender and serum potassium levels, lnARR level had independent predictive value for resting heart rate, 24 h average heart rate, day average heart rate and night average heart rate ($P<0.05$).

CONCLUSIONS The resting heart rate, 24 h average heart rate, day average heart rate and night average heart rate of PA patients were all slower than those of PH patients. LnARR was an independent predictor of resting heart rate, 24 h average heart rate, day average heart rate and night average heart rate.

GW31-e0086

Polymorphisms of microRNAs are associated with salt sensitivity of blood pressure in a Han Chinese population

Yunyi Xie, Zheng Liu, Ling Zhang
Capital Medical University

OBJECTIVES Salt sensitivity of blood pressure (SSBP) increases the morbidity and mortality of cardiovascular disease and is an independent risk factor for cardiovascular events. SSBP is a complex health issue associated with genetic factors. At present, there is still a lack of research reports on the relationship between SSBP and genetic polymorphisms in non-coding region, especially micro-RNA (miRNA). This study aimed to identify the association between candidate single-nucleotide polymorphisms in miRNAs and SSBP in a Han Chinese population.

METHODS The study was based on a Cohort Study of Systems Epidemiology on Salt-Sensitivity of Blood Pressure (EpiSS) in two cities of north China. We conducted a population-based case-control study, 219 salt sensitivity and 543 salt resistant were recruited in the study. A modified Sullivan's acute oral saline load and diuresis shrinkage test (MSAOSL-DST) was used to distinguish the person of salt-sensitive and salt-resistant. Medical history, lifestyle risk factors are obtained by questionnaire, while blood pressure and weight were measured by physical examination, and blood and urine specimens are collected. Candidate single nucleotide polymorphisms (SNPs) were summarized from two approaches: literature retrieval of association studies in candidate miRNAs related SNPs and miRNAs related SNPs in previous our study results. We used the Sequenom Mass ARRAY Platform to genotype the 24 single-nucleotide polymorphisms, and the genetic risk score (GRS) was used to evaluate the joint genetic effect.

RESULTS According to screening principles, we selected 30 coding miRNAs related SNPs (miRNAs-SNPs) for validation. Multiple logistic regression analysis showed that 6 miRNAs-SNPs (miR-1307-5p/rs11191676, miR-1307-5p/rs2292807, miR-145/rs41291957, miR-19a-3p/rs4284505, miR-382-5p/rs4906032 and miR-4638-3p/rs6601178) were associated with SSBP in general population. After adjusting for potential confounders, the six SNPs (miR-1307-5p/rs11191676, miR-1307-5p/rs2292807, miR-145/rs41291957, miR-4638-3p/rs6601178, miR-382-5p/rs4906032 and miR-15b-5/rs10936201) showed significant correlation. In acute salt loading process, after adjusting for the confounding factors of waist-to-hip ratio, hypertension, total cholesterol, baseline urinary sodium concentration and smoking, miR-15b-5p/rs10936201, miR-145/rs41291957, miR-4638-3p/rs6601178 were significantly associated with DBP elevation ($P\leq0.05$); miR-145/rs41291957 and miR-382-5p/rs4906032 were significantly associated with the increase of MAP ($P\leq0.05$); In the process of diuresis shrinkage, miR-15b-5p/rs10936201 was significantly correlated with the decrease of SBP ($P\leq0.05$); rs11191676/miR-1307-5p, rs11191676/miR-1307-5p and miR-145/rs41291957 were significantly associated with DBP decrease ($P\leq0.05$); rs10936201/miR-15b-5p, rs11191676/miR-1307-5p, rs2292807/miR-1307-5p, rs41291957/miR-145 were significantly associated with MAP decrease ($P\leq0.05$). A weighted GRS was composed of 6 coding miRNAs-SNPs. In a multiple logistic regression analysis adjusted by sex, age and hypertension demonstrate that with rising 1 score for weighted GRS, the risk of SSBP increased to 2.663-fold (95% CI: 1.869–3.795).

CONCLUSIONS Seven SNPs in miRNAs are associated with salt sensitivity of blood pressure. GRS was performed to evaluate the joint genetic effect. With increasing of GRS, the risk of SSBP in different populations were increased. It played a certain role to systematically screening SNPs.

GW31-e0093

Association of thyroid function with hypertension subtypes such as white coat hypertension and sustained hypertension

Peng Cai, Yan Peng, Xukai Wang
Daping Hospital, Army Medical University

OBJECTIVES This study aimed to explore the relationship of thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) levels with hypertension subtypes.

METHODS One thousand fifty six euthyroid adults were included as research samples. They underwent measurement of clinic blood pressure and 24-h ambulatory blood pressure monitoring. Then, they were divided into normotension (NT), white coat hypertension (WCH), masked hypertension (MHT), and sustained hypertension (SHT) groups. The 24-h dynamic electrocardiogram was performed to analyze the heart rate variability (HRV), so as to reflect the cardiac autonomic function. The relationship between hypertension subtypes, thyroid function, and HRV was analyzed.

RESULTS The TSH concentration was significantly higher in the SHT group than in the NT group ($P=0.001$). The FT3 concentration was higher in the SHT group than in the NT and MHT groups ($P=0.013$, $P=0.008$), while the FT4 concentration was significantly higher in the WCH group than in the NT group ($P=0.002$). The changes in HRV were observed between the SHT, WCH, and MHT groups and the NT groups, as well as between the SHT and the MHT groups. The multiple linear regression analysis also showed that FT3, HRV (RMSSD and PNN50), and blood pressure levels linearly correlated with one another ($P<0.05$). Meanwhile, the linear regression analysis showed a linear negative correlation between FT4 and HRV (SDANN) in the WCH+NT group ($P=0.001$).

CONCLUSIONS Thyroid function was closely related to hypertension subtypes such as WCH probably due to the changes in the cardiac autonomic function.

GW31-e0094

Effects of white-coat, masked and sustained hypertension on coronary artery stenosis and cardiac arrhythmia

Peng Cai, Xukai Wang
Department of Cardiology, Institute of Field Surgery, Daping Hospital, Army Medical University

OBJECTIVES This study aimed to investigate whether hypertension subtypes such as white-coat hypertension (WCHT), diagnosed with the addition of nighttime blood pressure (BP) criteria, were related to coronary artery stenosis (CAS) and cardiac arrhythmia.

METHODS In this cross-sectional observational study, 2106 adult participants were recruited in Daping Hospital between December 2017 and April 2019. After rigorous screening, 844 participants were selected who did not use antihypertensive, lipid-lowering and anti-platelet drugs. They were divided into normotensive (NT), WCHT, masked hypertension (MHT) and sustained hypertension (SHT) groups based on the results of clinic BP measurement and ambulatory BP monitoring. Coronary angiography and ambulatory electrocardiography were performed to determine the participants' CAS and cardiac arrhythmia status.

RESULTS Coronary angiography revealed 555 patients with CAS and 288 patients with normal coronary arteries. Logistic regression analysis showed that the incidence of CAS was higher in the MHT and SHT groups than in the NT group, while no significant change was found in the WCHT group. The logarithm of Gensini score was used to compare the degree of CAS between the groups. Multiple linear regression analysis showed that the degree of CAS was higher in the WCHT, MHT and SHT groups than in the NT group. The incidence of frequent atrial premature beat, atrial tachycardia and ventricular cardiac arrhythmia were significantly higher in the WCHT and SHT groups than in the NT group, while only ventricular cardiac arrhythmia change was found in the MHT group. There was no difference in ventricular arrhythmias between the groups in participants with normal coronary arteries, while there was difference in atrial arrhythmias in the WCHT and SHT groups as compared to the NT group.

CONCLUSIONS This study found that hypertension subtypes such as WCHT were closely associated with CAS and cardiac arrhythmia.

GW31-e0172

The relationship between hypertension and glycemic control in patients with type 2 diabetes

Mekhman Mamedov[1], Samir Mehdiyev[2], Isakh Mustafayev[2]
[1]National Medical Research Center for Preventive Medicine, Moscow, Russia
[2]Azerbaijan State Advanced Training Institute for Doctors Named After A. Aliyev, Baku, Azerbaijan

OBJECTIVES To study the clinical features of hypertension in patients with DM2, depending on the level of glycemic control.

METHODS A cohort study included 528 patients aged 30–69 years (30.5% men, 69.5% women). Patients answered the questions of the ARIC questionnaire which include the duration, severity of hypertension, tactics and the form of antihypertensive therapy taken. The level of blood pressure (BP) was measured twice, in the sitting position with a 5-minute interval, and the average values were taken. Electrocardiographic (ECG) signs of left ventricular hypertrophy (LVH) were taken using the Sokolow-Lyon criteria and the Cornell voltage index, and echocardiographic (EchoCG) signs of LVH were determined in the presence of a left ventricular mass index in men >115 g/m^2, and in women >95 g/m^2. Glycohemoglobin values (HbA1c) ≥7% were regarded as inadequate control of glycemic status. Statistical analysis of the data was carried out using the discriminant method.

RESULTS The HbA1c level in the inadequate control stage was 50.3% higher than in the compensation stage (9.42 vs. 6.27%, respectively, P.

CONCLUSIONS Most of patients with poor glycemic control did not reach target BP. Treatment with blockers of the renin-angiotensin-aldosterone system was received by 24.0% of the respondents, and combination and long-term antihypertensive therapy was administered to only half of the subjects. It is necessary to strengthen the patients' adherence to treatment, as well as measures aimed at improving the knowledge and skills of endocrinologists and cardiologists.

GW31-e0205

Synergistic interaction of hyperuricemia and hypertension on reduced eGFR: insights from a general Chinese population

Haoyu Wang
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES Hyperuricemia and Hypertension are two independent risk factors of renal function damage. Our research aimed to investigate the synergistic interaction between hyperuricemia and hypertension toward reduced eGFR.

METHODS Our analyses included 11,694 participants from a cross-sectional population-based Northeast China Rural Cardiovascular Health Study. Interaction was assessed on both multiplicative and additive scales.

RESULTS The prevalence of reduced estimated glomerular infiltration rate (eGFR) was 2.11% in our population. After adjustment of age, sex, race, education level, family income, current smoking and drinking status, body mass index, total cholesterol, high-density lipoprotein cholesterol, and diabetes, subjects with both hyperuricemia and hypertension suffered from a 11.004 (95% CI: 7.080–17.102) times risk of reduced eGFR than the healthy reference group, greater than that in participants with only hyperuricemia (5.741, 95% CI: 3.045–10.825) or hypertension (1.145, 95% CI: 0.764–1.715). Furthermore, additive interaction between hyperuricemia and hypertension was statistically significant and synergistic (relative excess risk due to interaction: 5.118, 95% CI: 0.611–9.624; the attributable proportion due to interaction: 0.465, 95% CI: 0.151–0.779; Synergy index: 2.047, 95% CI: 1.017–4.120). However, our results revealed no significant interaction on the multiplicative scale.

CONCLUSIONS Hyperuricemia and hypertension may have a synergistic interaction toward renal function loss in addition to their independent impacts. Our findings may provide a straightforward illustration which is easy for the public to realize the hazard of coexistent hypertension and hyperuricemia on renal injury.

GW31-e0246

Does hyperhomocysteinemia aggravate the cognitive decline in patients with hypertension

Huan Sun[1], Xiaoping Li[2], Yuhua Zhang[2], Shengnan Liu[2], Xiaochun Chen[2]
[1]Inner Mongolia Medical University
[2]Inner Mongolia Autonomous Region International Mongolian Medical Hospital

OBJECTIVES To investigate the effect of hyperhomocysteinemia on cognitive function in patients with hypertension

METHODS One hundred and eight primary hypertensive patients were selected from October 2018 to October 2019 in the outpatient clinic of Cardiovascular Medicine Department of International Mongolian Hospital of Inner Mongolia Autonomous Region. History of hypertension and related risk factors were collected and fasting plasma homocysteine, liver function, renal function, blood lipids and blood glucose were detected. The patients were divided into two groups according to the level of plasma Hcy. Those with Hcy ≥10 μmol/L were the experimental group (Hypertension combined with hyperhomocysteinemia group), and those with Hcy <10 μmol/L were the control group (Simple Hypertension Group). The cognitive function of patients was measured by mini-mental state examination (MMSE) and Montreal cognitive assessment (MoCA), and the differences in cognitive function and related influencing factors between the two groups were analyzed.

RESULTS There were no significant differences in hypertension grade, course of hypertension, smoking and drinking history between the two groups (P>0.05), and there were no significant differences in serum total cholesterol, low density lipoprotein, blood glucose, office systolic blood pressure and diastolic blood pressure between the two groups (P>0.05). The plasma Hcy level in the experimental group was significantly higher than that in the control group (17.02±13.13 μmol/L vs. 8.92±1.70 μmol/L, P<0.05), and the difference was statistically significant. The plasma triglycerides, creatinine and uric acid were higher than those in the control group (2.011±25 mmol/L vs. 1.66±0.91 mmol/L; 67.66±17.12 μmol/L vs. 60.22±13.08 μmol/L; 331.00±90.42 μmol/L vs. 281.14±59.28 μmol/L, all P<0.05); plasma high density lipoprotein was lower than control group (1.35±0.29 mmol/L vs. 1.53±0.42 mmol/L, P<0.05). The total score of MMSE in the experimental group was lower than that in the control group (25.94±3.88 vs. 27.57±1.81, P>0.05), and there was no statistical difference between the two groups. In the MMSE score, the language ability of the experimental group was lower than that of the control group (8.47±1.06 vs. 8.90±0.30, P<0.05), and the difference was statistically significant. The total score of cognitive function test group by MoCA was lower than that of control group (21.61±4.87 vs. 24.24±3.17, P<0.05), the difference was statistically significant, and the visuospatial and executive functions, attention and orientation were significantly lower than that of control group (2.94±1.37 vs. 4.05±1.01, 4.95±1.31 vs. 5.52±0.97, 5.64±0.69 vs. 5.90±0.30, all P<0.05). The correlation analysis showed that the total score of MoCA was negatively correlated with plasma Hcy level (r=–0.311 P=0.001), negatively correlated with age (r=–0.413 P=0.000), and positively correlated with years of education (r=0.617 P=0.000). The partial correlation controlled for years of education and age respectively, and plasma Hcy was negatively correlated with total score of MOCA (P<0.05). Multiple linear regression analysis of Hcy, years of education and age showed that Hcy was an independent risk factor for MoCA (B=–0.061 P=0.036).

CONCLUSIONS Hyperhomocysteinemia aggravates the decline of cognitive function in hypertensive patients; plasma Hcy is negatively correlated with total MoCA score and is an important risk factor affecting cognitive level; MoCA is more sensitive than MMSE in evaluating cognitive function.

GW31-e0380

Association analysis of CACNA1D c.A920G gene exon site mutation with hypertension

Huan Wang[1,2], Jingkang Zhu[1,2], Huiwu Hong[1,2], Canwang Wang[1,2], Hui Chen[1,2]
[1]Hypertension Laboratory, Fujian Provincial Cardiovascular Disease, Fujian Provincial Hospital
[2]The Shengli Clinical Medical College of Fujian Medical University

OBJECTIVES *CACNA1D* encodes the pore-forming α1-subunit of Cav1.3, an L-type voltage-gated Ca^{2+}-channel. The CACNA1D rs9810888 polymorphism was significantly associated with DBP and MAP. Therefore, the relationship between CACNA1D c.A920G gene mutant with hypertension was researched.

METHODS Human CACNA1D c.A920G gene mutant families were investigated. Immunofluorescence was used to detect the expression of CACNA1D in human endothelial cells (HUVECs) and human umbilical vein. HUVECs were transfected with liposome carrying CACNA1D wild-type gene and CACNA1D c.A920G, respectively. Cav1.3 and ET-1 protein expression were observed by Western blot. The contents of intracellular calcium were measured by Flou-4, and the effect of expression of ET-1 mRNA by RT-qPCR and Western blot. The CACNA1D c.A920G mutant rats were edited using genetic engineering.

RESULTS Human CACNA1D c.A920G germline mutant families were prone to hypertension. Cav1.3 l-type calcium channels were found in HUVECs and human umbilical vein. Compared with wildtype HUVECs, the intracellular Ca^{2+} (0.05364±0.00252 vs. 0.07105±0.00236, n=3 P<0.01), the protein of CAV1.3 (1.04±0.25 vs. 1.44±0.32, n=6, P<0.05) and ET-1 (1.32±0.54 vs. 2.43±0.98, n=8, P<0.01), and the mRNA expression of ET-1 (1.00±0.00 vs. 1.49±0.19, n=3, P<0.05) in HUVECs with CACNA1D c.A920G mutant were increased significantly. We first found that twelve human CACNA1D c.A920G mutant 28-week rats that had significant elevated blood pressure than ten wildtype 28-week rats (146.80±1.91 vs. 134.20±2.67, P<0.05).

CONCLUSIONS The CACNA1D c.A920G mutant was related with hypertension. This work was supported by the National Youth Science Foundation Project of China (81800363), the Provincial Natural Science Foundation of Fujian (2018J01240), Youth Innovation Project of Science and Technology Department of Fujian Province (20GJ05136), the Fujian Provincial Medical Innovation Project (2018CX4), the Funding Scheme for Young and Middle-aged Talents Development Projects (2018XQN24) in Fujian Provincial Health Family Planning Commission, and the Joint Fund for Research and Construction of High-Level Hospitals in Fujian Provincial Hospital (2017LHJJ03).

GW31-e0447

Serum sulfatide and carotid IMT may be biomarkers for atherosclerosis in elderly patients with hypertension

Gang Li, Yifang Guo, Qingjuan Zuo, Lili He, Yan Wang, Lu Zhang, Tingting Zhang, Qiuyan Wang, Yi Liang
Hebei General Hospital

OBJECTIVES Hypertension is closely related to atherosclerosis. Atherosclerosis is considered to be a chronic inflammatory condition. Carotid intima-media thickness (IMT) reflects the degree of apparent changes in atherosclerosis. Some studies have shown that sulfatide is closely related to inflammatory response and atherosclerotic lesions. In this study, we observed whether there was a correlation between serum sulfatide and carotid IMT in elderly patients with hypertension, and which index could more accurately reflect the progression of atherosclerotic lesions.

METHODS One hundred and fifteen elderly patients with hypertension admitted to our hospital from July 2018 to July 2019 were selected as the experimental group. According to blood pressure level, they were divided into mild hypertension group (n=35), moderate hypertension group (n=40) and severe hypertension group (n=40). In addition, 110 old people of the same age who underwent physical examination in the physical examination center of our hospital were selected as the control group. Firstly, the difference of serum sulfatide level and carotid IMT level between the experimental group and the control group was observed, and then the difference of serum sulfatide level and carotid IMT level between different hypertension groups was compared in the experimental group.

RESULTS Serum sulfatide level and carotid IMT in the experimental group were higher than that in the control group, and the difference was statistically significant (P<0.05). Moreover, with the increase of blood pressure, serum sulfatide level and carotid IMT in elderly patients with hypertension showed an increasing trend (r=0.389, P=0.021).

CONCLUSIONS Serum sulfatide level and carotid IMT in the experimental group were higher than that in the control group, and the difference was statistically significant (P<0.05). Moreover, with the increase of blood pressure, serum sulfatide level and carotid IMT in elderly patients with hypertension showed an increasing trend (r=0.389, P=0.021).

GW31-e0571

Effects of catheter-based renal denervation on glycemic control and lipid levels: a systematic review and meta-analysis

Zhipeng Zhang, Xiaoping Chen
West China Hospital, Sichuan University

OBJECTIVES As an emerging interventional technique to treat resistant hypertension, renal denervation (RDN) has also attracted considerable attention due to its potential beneficial effects on glucose and lipid metabolism. Given that inconsistent results documented among studies, we aimed to perform a systematic review and meta-analysis to further elaborate this issue.

METHODS The PubMed, EMBASE, Web of Science (SCI) and ClinicalTrials.gov databases were comprehensively searched from their inception date to June 18, 2020 for relevant clinical studies evaluating the efficacy of RDN on glucose and lipid levels. The outcomes of interest were changes in fasting glucose, insulin, C-peptide, hemoglobin A1C (HbA1C), homeostatic model assessment-insulin resistance (HOMA-IR), cholesterol and triglyceride (TG) levels before versus after RDN and also RDN versus control group. The mean differences (MD) of the outcomes measured before versus after RDN and RDN versus control group were pooled by a fixed or randomized effects model. Heterogeneity was quantified with chi-square (χ^2) and inconsistency index (I^2). Assessment of publication bias was performed by funnel plot and Egger's test.

RESULTS A total of 1600 studies were initially identified and 20 of them (randomized controlled studies: 6; non-randomized controlled studies: 1; observational cohort studies: 13) involving 2277 subjects were included in the final analysis. No significant changes were observed after RDN in fasting glucose (weighted mean difference [WMD] −0.16 mmol/L; 95% CI −0.34, 0.02 mmol/L), insulin (standardized mean difference [SMD] 0.06; 95% CI −0.13, 0.26), C-peptide (SMD −0.06; 95% CI −0.25, 0.14), HbA1C (SMD −0.04; 95% CI −0.14, 0.06), HOMA-IR (SMD −0.12; 95% CI −0.35, 0.11), total cholesterol (TC) (WMD −0.11 mmol/L; 95% CI −0.37, 0.15 mmol/L), low-density lipoprotein cholesterol (LDL-C) levels (WMD −0.18 mmol/L; 95% CI −0.59, 0.24 mmol/L) during the follow-up. Changes of fasting glucose, insulin, HbA1C and TC levels in RDN groups were not significantly different from that in control group. High-density lipoprotein cholesterol (HDL-C) and TG were slightly but significantly improved after RDN (WMD 0.07 mmol/L, 95% CI 0.01, 0.14 mmol/L; WMD −0.26 mmol/L, 95% CI −0.51, −0.01 mmol/L, respectively). Funnel plot and Egger's test demonstrated the absence of potential publication bias.

CONCLUSIONS Catheter-based RDN appeared to have no impact on glucose metabolism. There was a statistically significant but clinically negligible improvement in HDL-C and TG levels on the basis of the current whole body of evidences. Future researches with more rigorous designs are warranted to draw definitive conclusions.

GW31-e0594

Preliminary experience of bilateral adrenal venous sampling via femoral vein using single 5F Tig catheter

Jindong Wan[1,2], Peijian Wang[1,2]
[1]Department of Cardiology, The First Affiliated Hospital, Chengdu Medical College, Chengdu, Sichuan 610500, PR China
[2]Key Laboratory of Aging and Vascular Homeostasis of Sichuan Higher Education Institutes, Chengdu, Sichuan 610500, PR China

OBJECTIVES To evaluate the safety and feasibility of bilateral adrenal venous sampling (AVS) via femoral vein using single 5F Tig catheter with preliminary experience.

METHODS One hundred and six consecutive patients diagnosed with primary aldosteronism underwent AVS via femoral vein using single 5F Tig catheter. 5F Tig catheters were properly used catheter molding technology during AVS. The result of success rate of bilateral AVS, operate time, and operative complications were analyzed. Based on operation time versus sequence of cases, the learning curve was plotted.

RESULTS All patients were sequentially cannulated into bilateral adrenal veins with a single 5F Tig catheter. The success rate of bilateral AVS was 90.6% (96/106). The mean operation time was (33±8) min, mean fluoroscopy time was (5.8±1.7) min, average X-ray dose was (117.3±25.5) mGy, and dosage of contrast media was (17.3±5.5) mL. One patient (0.9%) experienced a hematoma at the femoral vein puncture, while other patients were not occurred any complications. The learning curve showed that the operation time shortened as the number of cases increased, and about 33 cases could cross the learning curve.

CONCLUSIONS AVS via femoral vein using single shaped 5F Tig catheter is safe and technically feasible, with a high success rate of bilateral AVS. The required number of operating procedures to the technique was approximate 33, and single 5F Tig catheter can be a preferred method of saving consumables when bilateral AVS via femoral vein.

GW31-e0635

The fluctuations of home blood pressure monitored by a smartphone-based application among elderly hypertensive patients during the COVID-19 outbreak: an observational study in China

Shuyuan Zhang, Jun Cai, Weili Zhang
State Key Laboratory of Cardiovascular Disease, Hypertension Center, FuWai Hospital, National Center for Cardiovascular Diseases, Peking Union Medical College & Chinese Academy of Medical Sciences, Beilishi Road 167, Xicheng District, Beijing 100037, China

OBJECTIVES A novel coronavirus disease 2019 (COVID-19) is currently breaking out around the world and greatly threatening the people's health. Along with the appearance of psychological stress such as anxiety, depression and other negative emotions caused by this special circumstance, hypertensive patients may experience large fluctuations in blood pressure, especially for the elderly. However, it is uncertain that whether the home BP monitored by smartphone-based application (app) can be controlled well during the epidemic.

METHODS The home BP data were longitudinally collected via the app from October 21st, 2019 to March 21st, 2020 (before and during the COVID-19 outbreak in China) of 7394 hypertensive patients aged 60–80 years who were enrolled from 42 hospitals at 23 provinces/municipalities in the strategy of blood pressure intervention in the elderly hypertensive patients (STEP) study (ClinicalTrials.gov, NCT03015311). The fluctuation of home morning BP was compared in Wuhan, the epidemic center, and in other areas of China. The mental disorder-anxiety was assessed by the Generalized Anxiety Disorder Scale.

RESULTS The variation of average morning systolic BP (SBP) of patients in Wuhan was significantly higher than in other areas of China by 1.8–3.9 mmHg (all P<0.05). In Wuhan, the morning SBP, compared with 132 (9.4) mmHg before the epidemic (Oct 21st–Nov 20th, 2019), increased by an average of 3 mmHg during the outbreak, while reduced to 131.9 (10.3) mmHg again during the epidemic control period (Feb 21st–Mar 21st, 2020). In other areas of China, the morning SBP of patients fluctuated less than 1 mmHg, with an average of 131 mmHg. The logs of doctors or patients accessing the BP module in the app were analyzed, and the results showed that the frequency of app visits by doctors during the epidemic period was consistent with the fluctuation of patient's morning SBP. During Nov 21st, 2019–Feb 20th, 2020, since doctors were engaged in control of the COVID-19 epidemics, the frequency of checking the patients' BP by doctors dramatically fell to 34% per month and then nearly to zero in the most serious days in Wuhan, and consequentially, during the epidemic control period (Feb 21st–Mar 21st, 2020), the numbers of BP visits grew back to 16% per month. In addition, the frequency of checking BP by patients through the app continuously increased when compared with the non-epidemic period, while it was in particular higher in Wuhan than in other areas of China. Compared with those without anxiety, the morning SBP of patients with mild anxiety increased by about 6–7 mmHg in Wuhan and 2 mmHg on average in other areas of China, respectively (P<0.05).

CONCLUSIONS Our findings showed that the epidemic of COVID-19 could cause a short-term remarkably increase of morning SBP among elderly hypertensive patients in Wuhan. Using smartphone-based apps for managing home BP is feasible for BP control during the special epidemic period.

GW31-e0669

New risk factors and prediction model of uncontrolled hypertension among patients with antihypertensive treatment in community

Shiqun Chen, Zhiping Gao, Jin Liu, Zhidong Huang, Yong Liu
Guangdong Provincial People's Hospital

OBJECTIVES The risk assessment of blood pressure failure in community hypertension patients can help identify high-risk patients and carry out active blood pressure Control measures, the current lack of uncontrolled hypertension rate study and its predictive factors of hypertension patients receiving anti-hypertensive treatment in community clinics. Therefore, the study exploring the risk predictors of controlled hypertension among patients in the community receiving anti-hypertensive therapy and build a risk prediction model for it.

METHODS We were consecutively selected in February 2018 and March 2018 in Guangdong Province, and received 1089 patients ≥18 years old, and finally included 1039 patients in the analysis and collected the socio-demographic information of hypertension patients, disease awareness, hypertension management, and the use and demand of mobile health tools in patients with hypertension in the community. The controlled blood pressure of patients is the main end point, which is defined as patients self-reporting most families/offices. Blood pressure is measured below 140/90 mmHg. This study compared the socio-demographic information, disease awareness, and the use of mobile health tools among hypertensive patients in the community between the blood pressure compliance and non-compliance groups. The variables with P<0.05 in Logistic regression multivariate analysis are independent risk factors that affect the blood pressure of hypertension patients. The risk factors that are important in univariate analysis can be used to select the final prediction model for blood pressure failure. The modeling data set of 906 community hypertension patients was used, and the internal verification was performed by bootstrap method for 100 times.

RESULTS The average age was 61±13 years old, there were 549 (53.9%) males, the average body mass index was 24.3±3.2 kg/m². Multivariable analysis showed that: full-time work (Ratio, OR: 1.98, 95% confidence interval, CI: 1.46—2.69), self-financed medical care (OR: 3.47, 95% CI: 2.08–5.80), non-marital status (OR: 2.01, 95% CI: 1.35–3.27), poor knowledge of hypertension diagnosis (OR: 3.28, 95% CI: 2.42–4.45), poor drug compliance (OR: 1.51, 95% CI: 1.08–2.11), poor knowledge of hypertension treatment (OR: 2.94, 95% CI: 2.16–3.99) and reluctance to remind blood pressure measurement information (OR: 1.64, 95% CI: 1.08–2.50) were identified independent predictors of uncontrolled hypertension among patients in the community who received anti-hypertensive treatment, the risk model includes the following seven factors: full-time work (4 points), self-pay medical care (7 points), non-marital status (4 points), poor cognitive diagnosis of hypertension (6 points), poor drug compliance (3 points), poor cognition of hypertension treatment (6 points) and unwilling reminder of blood pressure measurement (3 points), Hosmer Lemeshow statistics of multivariate models do not suggest lack of appropriateness (χ^2=6.5649, P=0.5842). In the verification data set, the risk score showed good discriminating ability and predicting ability for the incidence of uncontrolled hypertension (C-static: 0.771) by bootstrap method.

CONCLUSIONS We have established 7 key predictors based prediction model with good predictability and high discriminatory ability. Our prediction model provide an good evaluation tool for community hypertension prevention and treatment to identify high-risk populations of uncontrolled hypertension.

GW31-e0671

Association of medication nonadherence with mobile health intervention needs: a cross-sectional study

Shiqun Chen, Xiaoling Cen, Zhidong Huang, Yong Liu
Guangdong Provincial People's Hospital

OBJECTIVES Investigate the status of nonadherence in patients with hypertension and their requirements for the function of mobile health tools.

METHODS A total of 1089 patients with hypertension in the community were investigated by questionnaire. Nonadherence was defined as the monthly proportion of days covered <90%.

RESULTS Patients with poor adherence accounted for 26.4%. Significantly related factors were less than 65 years old (OR: 0.549, 95% CI: 0.313–0.963), single (OR: 0.599, 95% CI: 0.361–0.993), inaccurate recognition of the diagnostic value of hypertension (OR: 0.657, 95% CI: 0.439–0.983), failure to purchase antihypertensive drugs at community health stations (OR: 0.642, 95% CI: 0.424–0.972), poor blood pressure control (OR: 0.391, 95% CI: 0.254–0.602), irregularity of blood pressure measuring (OR: 0.523, 95% CI: 0.351–0.780) and smoking (OR: 1.586, 95% CI: 1.018–2.469). The patients had a large demand for functions such as doctor-patient communication, hypertension knowledge, and changes in blood pressure over a week.

CONCLUSIONS Enhancing the patient's medication habits may improve the patient's drug nonadherence. Mobile health tools can help patients strengthen their medication habits, but the exploration of their functions needs more verification.

GW31-e0701

A speckle tracking echocardiographic study on right ventricular function in primary aldosteronism

Yilin Chen, Tingyan Xu, Jiguang Wang
The Shanghai Institute of Hypertension, Department of Hypertension, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

OBJECTIVES We investigated right ventricular (RV) function using speckle tracking echocardiography (STE) in patients with primary aldosteronism (PA).

METHODS Our study included 51 PA patients and 50 age- and gender-matched primary hypertensive patients. We performed 2-dimensional echocardiography to measure cardiac structure and function. We performed STE offline analysis on RV four-chamber (RV4CLS) and free wall longitudinal strains (RVFWLS).

RESULTS PA patients, compared with primary hypertensive patients, had a significantly (P≤0.045) larger left ventricular (LV) mass index (112.0±22.6 g/m² *vs.* 95.8±18.5 g/m²) and left atrial volume index (26.9±6.0 mL/m² *vs.* 24.7±5.6 mL/m²) and higher prevalence of LV concentric hypertrophy (35.3 *vs.* 12.0%), although they had similarly normal LV ejection fraction (55–77%). PA patients also had a significantly (P≤0.047) larger right atrium and ventricle, lower tricuspid annular plane systolic excursion, and higher E/E′$_t$ (the peak early filling

velocity of trans-tricuspid flow to the peak early filling velocity of lateral tricuspid annulus ratio), estimated pulmonary arterial systolic pressure and RV index of myocardial performance. On RV strain analysis, PA patients had a significantly (P<0.001) lower RV4CLS (–18.1±2.5% *vs.* –23.3±3.4%) and RVFWLS (–21.7±3.7% *vs.* –27.9±4.5%) than primary hypertensive patients. Overall, RV4CLS and RVFWLS were significantly (r=–0.58 to –0.41, P<0.001) correlated with plasma aldosterone concentration and 24-h urinary aldosterone excretion. After adjustment for confounding factors, the associations for RV4CLS and RVFWLS with 24-h urinary aldosterone excretion remained significant, with a standardized coefficient of –0.48 and –0.55, respectively (P<0.001).

CONCLUSIONS In addition to LV abnormalities, PA patients also show impaired RV function, probably because of adrenal aldosterone hypersecretion.

GW31-e0702

Ambulatory blood pressure in relation to interaction between dietary sodium intake and serum uric acid in the young

Wei Zhang, Jiguang Wang
Department of Cardiovascular Medicine, Centre for Epidemiological Studies and Clinical Trials, Shanghai Key Laboratory of Hypertension, The Shanghai Institute of Hypertension, Department of Hypertension, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

OBJECTIVES We investigated ambulatory blood pressure (BP) in relation to hyperuricemia, dietary sodium intake and their interaction in children and adolescents with hypertension.

METHODS The 616 study participants were 10–24 years old and had primary hypertension diagnosed after admission in a specialized inpatient ward. Ambulatory BP monitoring was performed during hospitalization. 24-hour urine was collected for measurements of electrolytes. Hyperuricemia was defined as a serum uric acid of ≥327.25 μmol/L in patients <18 years old and of ≥420 μmol/L and ≥360 μmol/L, respectively, in male and female patients ≥18 years old.

RESULTS In adjusted analyses, patients with hyperuricemia (n=283), compared with those with normal serum uric acid, had similar 24-h systolic BP (131.7 mmHg, P=0.54) and a significantly (P≤0.005) lower 24-h diastolic BP (77.5 *vs.* 80.9 mmHg) and higher 24-h pulse pressure (54.2 *vs.* 51.7 mmHg). In similar adjusted analyses, 24-h ambulatory pulse pressure, but not systolic/diastolic BP (P≥0.12), significantly differed across the quartile distributions of urinary sodium excretion (P for trend ≤0.04). Further adjusted analyses showed significant (P≤0.04) interaction between serum uric acid and urinary sodium excretion in relation to 24-h systolic BP. In patients with hyperuricemia (P=0.04), but not those with normal serum uric acid (P=0.13), 24-h systolic BP was significantly associated with urinary sodium excretion, with a 6.5±2.1 mmHg difference between quartiles 4 and 1. Similar results were observed for daytime and nighttime BP and pulse pressure.

CONCLUSIONS Both hyperuricemia and higher dietary sodium intake were associated with higher pulse pressure, and their interaction further heightened systolic BP.

GW31-e0703

Age-dependent association between blood pressure and albuminuria but not left ventricular hypertrophy in patients with hypertension and/or diabetes mellitus

Wei Zhang, Jiguang Wang
Centre for Epidemiological Studies and Clinical Trials, Shanghai Key Laboratory of Hypertension, The Shanghai Institute of Hypertension, Department of Hypertension, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

OBJECTIVES We investigated associations of blood pressure (BP) with albuminuria and left ventricular hypertrophy (LVH) in young, middle and older aged patients with hypertension and/or diabetes mellitus.

METHODS Study participants were treated patients with hypertension or diabetes, enrolled in a China nationwide registry. The 2510 patients were classified into young (<45 years, n=345), middle (45–64 years, n=1383) and older (≥65 years, n=782) age groups. Clinic BP was measured three times consecutively on each of the two clinic visits. These six readings were averaged for analyses. Albuminuria was defined as a urinary albumin-to-creatinine ratio of ≥30 mg/g. LVH was assessed by the electrocardiogram (ECG) Cornell product and voltage methods.

RESULTS The prevalence of albuminuria and ECG-LVH was 17.8 and 6.5%, respectively. Mean (±SD) systolic/diastolic BP was 132.0±16.5/85.2±11.9 mmHg, 136.8±17.9/81.7±11.2 mmHg, and 139.8±16.7/75.8±10.4 mmHg in the young, middle and older age groups. In the young age group, the prevalence of albuminuria increased from 8.8% in systolic/diastolic BP <120/80 mmHg to 14.6, 16.0 and 16.5% in 120–129/80–84, 130–139/85–89 and ≥140/90 mmHg, respectively. The corresponding values were 8.9, 7.0, 18.1 and 22.2%, respectively, in the middle age group, and 21.2, 15.5, 16.4 and 24.4%, respectively, in the older age group. Analyses adjusted confirmed the J-shaped relation between BP and albuminuria in the older but not young age group. The prevalence of ECG-LVH was significantly (P for trend ≤0.04) higher with increasing BP similarly in all age groups.

CONCLUSIONS The relationship between BP and organ damage seems to be age-dependent for albuminuria but not ECG-LVH.

GW31-e0724

A randomized controlled trial on home blood pressure monitoring and quality of care in stage 2 and 3 hypertension

Di Zhang, Yan Li, Qifang Huang, Jiguang Wang
Centre for Epidemiological Studies and Clinical Trials, The Shanghai Institute of Hypertension, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

OBJECTIVES In a 12-week, randomized, controlled trial, we investigated whether home blood pressure monitoring (HBPM) would improve treatment adherence and blood pressure control in stage 2–3 hypertension.

METHODS Eligible patients (18–75 years old and a systolic/diastolic blood pressure of 160–199/100–119 mmHg after 1-week wash-out) were randomized in a 1:4 ratio to HBPM and a control group without HBPM. All patients started antihypertensive treatment with the irbesartan 150 mg/hydrochlorothiazide 12.5 mg/day combination, with the possible addition of irbesartan 150 mg/day and up-titration to irbesartan 300 mg/hydrochlorothiazide 25 mg/day at 4 and 8 weeks of follow-up, respectively. The primary endpoint was the clinic blood pressure control (systolic/diastolic, non-diabetes <140/90 mmHg and diabetes <130/80 mmHg) rate at 12 weeks of follow-up.

RESULTS The randomized patients in the HBPM (n=96) and control groups (n=405) had similar characteristics at baseline, and similar use of higher dosages of irbesartan/hydrochlorothiazide (300 mg/12.5–25 mg) at 4 (9.4 *vs.* 12.2%, P=0.45) and 8 weeks of follow-up (27.1 *vs.* 35.5%, P=0.13). During follow-up, both the treatment discontinuation rate (1.0 *vs.* 12.6%, P=0.0008) and less optimal compliance rate (<90% of prescribed medication, 1.0 *vs.* 9.9%, P=0.005) were significantly lower in the HBPM than control group. The proportion of patients who achieved the goal of clinic blood pressure control at 12 weeks of follow-up was significantly higher in the HBPM than control group (66.7 *vs.* 55.1%, P=0.04).

CONCLUSIONS In conclusion, HBPM improved treatment adherence and blood pressure control in patients with hypertension, in spite of similar antihypertensive treatment intensity.

GW31-e0911

Sex differences in impact of long-term burden and trends of body mass index and blood pressure from childhood to adulthood on arterial stiffness in adults: a 30-year cohort study

Yueyuan Liao, Jianjun Mu
First Affiliated Hospital of Medical College, Xi'an Jiaotong University, Xi'an 710000, China

OBJECTIVES Arterial stiffening is an important independent risk factor for cardiovascular disease and events. Obesity and hypertension are closely related to arterial stiffness and play an important role in the development of arterial stiffness. The impact of the long-term burden of BMI and BP from childhood to adulthood on arterial stiffness in adults, especially between sexes, still need to be explored. We aimed to examine the impact of the cumulative long-term burden and trends of BMI and BP from childhood on adult arterial stiffness and explore sex differences in this association.

METHODS This study is based on the Hanzhong Adolescent Hypertension Cohort, an ongoing prospective study. This longitudinal study consisted of 1553 individuals aged 6–15 years who were examined 4 or more times for BMI and BP since childhood, with a follow-up period of 30 years. Growth curves of BMI and BP, measured repeatedly at multiple time points from childhood, were constructed using a random-effects model. The area under the curve (AUC) was calculated as a measure of the long-term burden (total AUC) and trends (incremental AUC) of BMI and BP from childhood. Brachial–ankle pulse wave velocity (baPWV) was recorded by a non-invasive automatic waveform analyser in adulthood. Statistical significance was set as a two-tailed P value of less than 0.05.

RESULTS An analysis of the subjects' general characteristics found that males had higher height, weight, BMI, SBP, DBP, waist circumference, hip circumference, total cholesterol, low-density lipoprotein cholesterol, triglycerides, fasting glucose, serum uric acid, urine albumin and baPWV than females. The results from the simple correlation analysis showed that baPWV in adults was significantly correlated with BMI total AUC (r=0.12), BMI incremental AUC (r=0.05), SBP total AUC (r=0.45), SBP incremental AUC (r=0.26), DBP total AUC (r=0.38), DBP incremental AUC (r=0.19). The total effect of the total AUC and incremental AUC of BMI and BP on adult baPWV were analyzed by linear regression models. Adult baPWV was associated with SBP total AUC (standardized regression coefficient, β=6.45, P<0.001), SBP incremental AUC (β=2.60,

P<0.001), DBP total AUC (β=7.60, P<0.001) and DBP incremental AUC (β=1.57, P<0.001). And there were no gender differences in the effect of total AUC and incremental AUC of BP on adult baPWV. There was no association between the total AUC of BMI and arterial stiffness regardless of sex. However, there were sex differences in the association between the incremental AUC of BMI and arterial stiffness (P=0.019 for interaction). The incremental AUC of BMI indicated an increased risk of arterial stiffening during adulthood in males, but this association was not found in females.

CONCLUSIONS In summary, we demonstrated that the cumulative long-term burden and incremental trends of BP are all significantly associated with adult arterial stiffness measured as baPWV. In addition, there were differences in the impact of long-term trends of BMI from childhood to adulthood on the development of arterial stiffness between males and females. The long-term growth trends of BMI can increase the risk of arterial stiffness in males, independent of BP trends, but not in females. These results emphasize the importance of developing prevention and intervention strategies for hypertension and obese men (especially those who are gradually gaining weight) to reduce the risk of arterial stiffening and cardiovascular disease in adulthood.

GW31-e0996

The ankle-brachial index (ABI) and risk of incident stroke in Chinese hypertensive population without atrial fibrillation: a cross-sectional study

Yumeng Shi, Lihua Hu, Minghui Li, Congcong Ding, Wei Zhou, Tao Wang, Lingjuan Zhu, Huihui Bao, Xiaoshu Cheng
The Second Affiliated Hospital of Nanchang University

OBJECTIVES We aimed to evaluate the relation of the ankle-brachial index (ABI) with the risk of stroke and to examine any possible effect modifiers among hypertensive patients without atrial fibrillation.

METHODS A total of 10,750 subjects with hypertension aged 27–96 years was included in the current study. The outcome was a stroke. Odds ratios of stroke concerning ABI were calculated using multivariate logistic regression models.

RESULTS Among 10,750 hypertensive participants, 690 (6.42%) had a stroke. Multivariate logistic analyses showed that ABI was negatively correlated with ABI was negatively correlated with the risk of stroke (Per SD increment; adjusted OR, 0.88; 95% CI, 0.82–0.94). Compared with participants in Q 1, the odds ratios (95% CI) for those in the Q2 (1.05–1.10), Q3 (1.10–1.15) and Q4 (≥1.15) were 0.71 (0.56, 0.90), 0.87 (0.70, 1.08) and 0.81 (0.65, 1.01), respectively. However, compared with higher ABI value, lower ABI value (<1.05) would significantly increase the risk of stroke [OR: 1.26, 95% CI (1.05–1.50)], especially in the elderly over 65 years old. A generalized additive model and a smooth curve fitting showed that there existed an L-shaped association between ABI and the risk of stroke.

CONCLUSIONS Our results suggest that an L-shaped association between ABI and risk of stroke was found in general hypertensive patients, with a turning point at about 1.05. Compared with higher ABI value, lower ABI value (<1.05) would significantly increase the risk of stroke [OR: 1.26, 95% CI (1.05–1.50)], especially in the elderly over 65 years old.

GW31-e1180

Blood pressure management in rural China: evidence from a randomized trial

Qiong Ma, Yu Yan, Jianjun Mu
The First Affiliated Hospital of Xi'an Jiaotong University

OBJECTIVES Hypertension is the most common preventable risk factor for cardiovascular disease and is associated with an increased risk of all-cause morbidity. Elevated blood pressure (BP) affects approximately 270 million people in China and represents a public health crisis nationwide. Although considerable progress has been made on effective antihypertensive medications, current control rates for hypertension remain low in China, especially in rural areas. Controlling blood pressure and therefore reducing the risk of cardiovascular events remains a serious challenge. In this study, we aim to provide an evidence-based approach to the management of hypertension in rural China.

METHODS A parallel cluster randomized controlled trial was undertaken in 24 rural villages in Hanzhong, Shaanxi, China. Eligible villages were randomized using a computer-generated randomization method. After baseline evaluation, we enrolled 2116 hypertensive participants over 40 years of age who met inclusion criteria in this study. Participants of intervention villages (9 clusters) were offered intensive anti-hypertensive treatment, including the use of antihypertensive medication, healthy lifestyle guidance, and intensive BP monitoring by the village doctors. All major classes of antihypertensive agents were provided at low cost to the participants. BP measurements data were recorded by a mobile device and uploaded to the monitoring center, and medications were adjusted on a monthly basis to target a BP of less than 130/80 mmHg. Participants in the control villages (11 clusters) were advised to continue with their regular treatment. Participants were seen monthly for the first 3 months and every 6 months thereafter. Hypertension control was defined as SBP <140 mmHg and DBP <90 mmHg, and an intensive control rate (SBP <130 and DBP <80 mmHg) of hypertension were also estimated according to the 2017 American College of Cardiology/American Heart Association High Blood Pressure Guideline.

RESULTS At baseline, the mean age was 65.6±9.5 years and there was no significant difference in mean BP between the intervention and control groups (SBP, 153.7±16.3 *vs.* 154.9±16.1 mmHg; DBP, 86.7±11.1 *vs.* 85.2±10.7 mmHg; all P>0.05). After 18 months, there was a significant higher rate of the antihypertensive treatment in the intervention group compared with the control group (94.0 vs. 73.62%, P<0.05). Importantly, the mean SBP was 126.5±11.6 mmHg and DBP was 71.0±9.1 mmHg in the intervention group, which was significantly lower than that in the control group (145.3±19.0 and 78.6±11.2 mmHg; all P<0.05). The intervention group also presented a higher control rate of hypertension, both at 140/90 mmHg (86.1%) and 130/80 mmHg (68.6%) standard, compared with the control group (38.3 and 17.4%, respectively; all P<0.05).

CONCLUSIONS The internet-based integrated management approach can significantly reduce blood pressure and improve the control rate of hypertension and is expected to provide an effective approach for BP controlling in rural China.

GW31-e1201

Metabolic syndrome is more frequent in patients with bilateral primary aldosteronism than unilateral primary aldosteronism

Zhihua Zhang, Qin Luo, Nanfang Li
Hypertension Center of People's Hospital Of Xinjiang Uygur Autonomous Region, Xinjiang Hypertension Institute, National Health Committee Key Laboratory of Hypertension Clinical Research

OBJECTIVES Metabolic syndrome (MetS) is a complex disorder comprising obesity, hyperglycemia, dyslipidemia, and hypertension, which is associated with a greater risk of cardiovascular disease. In a recent meta-analysis of 31 studies, comprising 3838 patients with primary aldosteronism (PA) and 9284 patients with essential hypertension, PA had increased risk of (OR 1.53, 95% CI 1.22–1.91) than patients with essential hypertension. PA has two main subtypes: unilateral, largely represented by aldosterone producing adenoma (APA), and bilateral, usually idiopathic hyperaldosteronism (IHA). We aimed to compare the prevalence of MetS in patients with the two subtypes of PA, diagnosed using adrenal venous sampling (AVS), and to determine the factors associated with the presence of MetS in PA patients.

METHODS This was a retrospective cross-section study in a single center. We included one hundred and sixty-nine hypertensive patients who had been diagnosed with PA in hypertension center of People's Hospital of Xinjiang Autonomous Region between January and December 2017. We analyzed metabolic parameters from 169 PA patients subtyped by AVS, including 85 unilateral PA patients and 84 bilateral PA patients, and we also included 169 non-PA patients matched for age and sex.

RESULTS The prevalence of MetS in patients with PA was higher than in patients without PA, but this difference was not statistically significant ((72.2 *vs.* 65.7%, P>0.05). Patients with unilateral PA had higher concentrations of aldosterone and lower serum potassium than patients with bilateral PA. However, patients with bilateral PA had higher prevalence of MetS (79.8 *vs.* 64.7%, P=0.029), obesity (40.5 *vs.* 24.7%, P=0.029), dyslipidemia (72.6 *vs.* 55.3%, P=0.019) and hyperglycemia (29.8 *vs.* 16.5%, P=0.040) than those with unilateral PA. Meanwhile, compared to unilateral PA, patients with bilateral PA had higher BMI (27.6±4.6 *vs.* 25.6±3.3 kg/m² P=0.001), waist circumference (98.5±11.4 *vs.* 93.3±10.6 cm, P=0.003) and fasting plasma glucose (4.98±1.16 vs. 4.64±0.93 mmol/L, P=0.034). We conducted logistic regression analysis to clarify the association between bilateral PA and MetS/obesity. Bilateral PA was significantly associated with MetS (OR, 2.150; 95% CI, 1.074–4.302; P=0.031) and obesity (OR, 2.072; 95% CI, 1.073–4.001; P=0.030). The associations remained statistically significant after adjustment for age, sex and duration of hypertension.

CONCLUSIONS Patients with bilateral PA have a higher prevalence of MetS than those with unilateral PA, despite unilateral PA patients exhibiting higher concentrations of aldosterone and lower serum potassium, suggesting that unilateral PA and bilateral PA may have differing mechanisms of MetS.

GW31-e1207

Higher prevalence of abdominal aortic calcification in patients with unilateral primary aldosteronism than bilateral primary aldosteronism

Tilakezi Tuersun, Qin Luo, Nanfang Li
Hypertension Center of People's Hospital Of Xinjiang Uygur Autonomous Region, Xinjiang Hypertension Institute, National Health Committee Key Laboratory of Hypertension Clinical Research, Urumqi 830001, Xinjiang, China

OBJECTIVES Patients with primary aldosteronism (PA) have increased risk of target-organ damage, among which vascular calcification is an important

indicator of cardiovascular mortality. A recent study indicated that the abdominal aorta calcification (AAC) prevalence was almost 1-fold higher in patients with PA than controls with essential hypertension, matched for age, sex, and blood pressure. Unilateral and bilateral PA are the most common subtypes of PA. However, no studies have addressed the difference in the prevalence of AAC between the two subtypes. In addition to aldosterone, parathyroid hormone (PTH), an important regulator of calcium metabolism, was also reported to be elevated in individuals with unilateral PA. Therefore, we hypothesized that the prevalence of AAC may be higher in individuals with unilateral PA, which may be related to the plasma aldosterone concentration (PAC) and PTH levels.

METHODS This was a single-center, cross-sectional study conducted in the Hypertension Center of People's Hospital of Xinjiang Uygur Autonomous Region. From January 2017 to January 2018. A total of 156 patients diagnosed with PA who underwent AVS were included in our study, among whom, 76 were diagnosed with unilateral PA and 80 were diagnosed with bilateral PA. We also included 156 with essential hypertension (EH) matched by age and sex. The aortic calcification index (ACI) presented the severity of AAC and was measured by adrenal computed tomography scan and measured in all subjects.

RESULTS Patients with PA had higher PAC, PTH, and 24 h urinary calcium levels than EH patients, whereas serum potassium and TC levels were lower than those in the EH group (P<0.05). The prevalence of AAC was significantly higher in patients with PA than those with EH (32.7 vs. 19.6%; P=0.013). Moreover, the degree of ACI was more severe in PA patients than in EH patients (4.32±3.61% vs. 2.53±2.42%, P=0.028). In the PA subgroup analysis, unilateral PA was associated with a higher prevalence and more severe AAC than bilateral PA (40.7 vs. 25.0%; 5.12±4.07% vs. 3.08±2.34%, respectively). Moreover, PAC and PTH levels were higher in individuals with unilateral PA than in those with bilateral PA (P<0.05). After adjusted for age, age, duration of hypertension, abdominal circumference, phosphorus, etc., multivariate regression analysis revealed that PAC and PTH were positively-associated with AAC in patients with PA (OR 1.235, 95% CI 1.100–1.373, P<0.001; OR 1.038, 95% CI 1.013–1.064, P=0.002, respectively).

CONCLUSIONS Unilateral PA patients exhibited a higher prevalence of AAC and more severe AAC due to elevated PAC and PTH levels.

GW31-e1222

Comparative efficacy of six antihypertensive drugs in reversing left ventricular hypertrophy in hypertensive patients: a network meta-analysis of randomized controlled trials

Jianshu Chen, Jing Yu
Lanzhou University Second College of Clinical Medicine

OBJECTIVES Reversing left ventricular hypertrophy (LVH) can reduce the incidence of adverse cardiovascular events. However, there is no clear superiority-inferiority differentiation between angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), angiotensin receptor neprilysin inhibitors (ARNI), beta-blockers (BB), calcium channel blockers (CCB), and diuretics in reversing LVH in hypertensive patients.

METHODS To provide further evidence for choosing the optimal antihypertensive drug for improving LVH, we performed a network meta-analysis of randomized controlled trials (RCTs) based on the Cochrane library database, Embase, and PubMed, and identified 49 studies involving 5402 patients that were eligible for inclusion.

RESULTS It was found that ARB could improve LVH in hypertensive patients more effectively than CCB (MD −4.05, 95% CI −7.81 to −0.34) and BB (MD −4.52, 95% CI −7.80 to −1.13). Matched comparison of renin-angiotensin system inhibitors (RASi) showed that the effect of ACEI in reducing left ventricular mass index (LVMi) was not effective as that of ARB (MD −3.68, 95% CI −7.30 to −0.15). The surface under the cumulative ranking for each intervention indicated that the use of ARB was more effective among the six types of antihypertensive drugs (98%). This network meta-analysis revealed that the use of ARB in antihypertensive therapy could achieve better efficacy in reversing LVH in hypertensive patients.

CONCLUSIONS This network meta-analysis revealed that the use of ARB in antihypertensive therapy could achieve better efficacy in reversing LVH in hypertensive patients.

GW31-e1269

Study on serum pentraxin-3 levels in vasculitis with hypertension

Ting Wu[1,2,3], Qing Zhu[1,2,3], Bin Zhu[1,2,3], Shasha Liu[1,2,3], Shanshan Liu[1,2,3], Nanfang Li[1,2,3]
[1]Hypertension Center of People's Hospital of Xinjiang Uygur Autonomous Region
[2]Xinjiang Hypertension Institute
[3]National Health Committee Key Laboratory of Hypertension Clinical Research

OBJECTIVES Hypertension induced with vasculitis leads to more serious damage to the target organs. Pentraxin-3 (PTX-3) derived from the secretion of macrophages, neutrophils, endothelial cells, epithelial cells and vascular smooth muscle cells, which expressed locally at the sites of inflammatory processes and regulate the immune activity of macrophages. The objectives of our study were to investigate the serum PTX-3 levels in vasculitis (Vas) and analyze this correlation with hypertension.

METHODS A total of 155 cases consisting 51 patients with Vas [including 7 cases of takayasu arteritis (TA), 24 cases of polyarteritis nodosa (PAN), and 20 cases of antineutrophil cytoplasmic antibody-associated Vas (AAV)] were screened by angiography and/or biopsy; 46 patients with essential hypertensions (EH) and 58 healthy controls (HC) were enrolled in this study. Serum PTX-3 levels were determined by enzyme-linked immunosorbent assay.

RESULTS Compared with the HC and EH, the serum PTX-3 levels in systemic Vas were significantly higher (both P<0.001, 4.42±0.95 vs. 2.67±0.92, 4.42±0.95 vs. 2.95±0.60), and there was no significant difference between HC and EH (P=0.886, 2.67±0.92 vs. 2.95±0.60). There was no significant difference of PTX-3 levels among TA, PAN, and AAV, as well as active and inactive groups, and renal and nonrenal groups, respectively. There was no significant correlation between PTX-3 levels and blood pressure, erythrocyte sedimentation rate, or Birmingham Vasculitis Activity Score. Receiver operating characteristic analysis has shown that the best cutoff point was at 3.618 ng/mL; the sensitivity and specificity were calculated as 84.3 and 93.5% for the diagnosis of Vas from heath control, and the best cutoff point was at 3.425 ng/mL, The sensitivity and specificity were calculated as 88.2 and 82.6% for the diagnosis of Vas from essential hypertension.

CONCLUSIONS Serum PTX-3 levels were significantly higher in patients with Vas than essential hypertension or health control, and elevated PTX-3 levels can help identify Vas patients from healthy or essential hypertensive populations.

GW31-e1280

Long-term Impact of spironolactone compliance on microalbuminuria in patients with primary aldosteronism

Xiaotong Wang, Nanfang Li
Hypertension Center of People's Hospital of Xinjiang Uygur Autonomous Region; Xinjiang Hypertension Institute, National Health Committee Key Laboratory of Hypertension Clinical Research, Urumqi 830001 Xinjiang, China

OBJECTIVES Our study aimed to analyze the effect of SPL compliance on endothelial dysfunction by assessing MAU in patients with PA.

METHODS The study included 145 confirmed PA patients who received long-term medical treatment (mean, 5 years). We assigned patients who took SPL continuously as the compliant group (N=102) and those who withdrew from SPL treatment for at least 6 months as the noncompliant group (N=43). The primary outcome was the prevalence of MAU and secondary were clinical outcomes include serum potassium, blood pressure and the defined daily doses of antihypertensive agents.

RESULTS Expectedly, compliance with SPL treatment better improved patients' blood pressure and serum potassium levels. Patients with PA who complied fully with SPL treatment had a lower rate of MAU than did the noncompliant patients (13.7 vs. 34.9%, respectively; P=0.004). Multivariate logistic regression analyses adjusted for age and sex showed that continuous SPL treatment was associated with a lower presence of MAU (odds ratio,0.319; 95% confidence interval, 0.135–0.750; P=0.009). This association remained significant after further adjusting for other major risk factors. However, in the subgroup analysis, the protective effect against MAU was limited in compliant patients treated with ≥40 mg/day SPL compared with that of the noncompliant patients (9.6 vs. 34.9%, P<0.05).

CONCLUSIONS Our findings demonstrated that in addition to improving high blood pressure and hypokalemia, full compliance with the appropriate dose of SPL may benefit endothelial function as reflected by a lower prevalence of MAU in patients with PA.

GW31-e1306

Serum MCP-1 levels are increased in systemic vasculitis of patients with hypertension with renal involvement

Shasha Liu, Qing Zhu, Ting Wu, Guoliang Wang, Xintian Cai, Ayiguzaili Aihemaiti, Xiayire Aierken, Nanfang Li
Hypertension Center of People's Hospital of Xinjiang Uygur Autonomous Region

OBJECTIVES Systemic vasculitis is a group of unexplained connective tissue diseases with non infectious inflammation and necrotizing vasculitis as the basic pathological changes. Its clinical manifestations are nonspecific and often lead to multiple system invasion and multiple organ failure. It can also lead to hypertension or malignant hypertension. But it is difficult to diagnose. In recent years, related studies have found that MCP-1 is related to inflammation and immune response. Monocyte chemotactic protein 1 (MCP-1), which is able to adjust the migration of monocytes/macrophages, osmosis and raise

monocytes and T lymphocyte cells to participate in a variety of inflammation, are closely linked to various types of systematic vasculitis. However, serum MCP-1 levels have not been evaluated in patients with systemic vasculitis, who also have moderate hypertension. The study was performed to investigate the level of serum MCP-1 in determining the patients.

METHODS We reviewed all patients admitted to our center for the etiology screening of hypertension between January 2013 and December 2016. All vasculitis are diagnosed by a rheumatologist and fulfilled the American College of Rheumatology (ACR) 1990 criteria. Serum samples were collected in 43 patients with systemic vasculitis with hypertension, 46 patients with essential hypertension (EH) and 43 healthy controls (HC). Serums MCP-1 were measured using commercially available ELISA kits.

RESULTS The serum MCP-1 levels were significantly higher in patients with systemic vasculitis, compared with EH (134.65 (73.74, 262.75) pg/mL, 68.43 (65.42, 104.84) pg/mL, P<0.008) and HC (134.65 (73.74, 262.75) pg/mL, 59.1 (37.41, 90.18) pg/mL, P=0.001), and no difference regarding serum MCP-1 levels could be found between EH and HC (P=0.197). Furthermore, it was significantly increasing in patients with renal than non-renal involvement (196.16 (104.41, 310.35) pg/mL, 73.74 (41.24, 145.95) pg/mL, P=0.001) and HC (P<0.001). However, there was no significant statistical differences between active and inactive phase. Serum MCP-1 levels with patients in systemic vasculitis were positive correlation with serum creatinine levels (r=0.387, P<0.010), 24-hour proteinuria (r=0.3627, P<0.0297) and. white blood cell counts (r=0.365, P<0.016).

CONCLUSIONS Serums MCP-1 were significantly higher in patients with systemic vasculitis compared with EH and HC, especially in patients with renal involvement. Serum MCP-1 might be as a potential biomarker tools in the systemic vasculitis with renal involvement.

GW31-e1359

Prospective study of serum uric acid level and first stroke events in Chinese adults with hypertension

Fengyu Han, Feng Hu, Xiaoshu Cheng
Department of Cardiovascular Medicine, the Second Affiliated Hospital of Nanchang University, Nanchang of Jiangxi, China

OBJECTIVES Serum uric acid (SUA) is a product of human purine metabolism. Most studies revealed that high level of SUA was associated with stroke risk and indicated that the influence of SUA on stroke is due to the secondary association of SUA with other established etiological risk factors, including hypertension, arterial stiffness, obesity, hyperinsulinemia. We propose that hypertension may be an intermediate in the pathway between hyperuricemia and stroke. However, the previous results concerning the role of SUA as an independent risk factor for stroke in hypertensive patients were still controversial. Our aim was to investigate the association between SUA level and the risk of first stroke in Chinese adults with hypertension.

METHODS This prospective study enrolled 14, 268 participants and was conducted from July 2018 to July 2023 in Wuyuan, Jiangxi province of China. After excluding 34 individuals without hypertension at baseline, 7 cases lost to follow-up, 7 cases without serum uric acid data, 191 cases with atrial fibrillation, 1371 cases with eGFR ≤60 mL/min/1.73 m², and 817 cases with prior stroke at baseline, finally 11, 841 Chinese adult hypertensive individuals (median follow-up time: 614 days) were included in our analysis. Computed tomography or magnetic resonance imaging as well as medical records were conducted to confirm first stroke events (ischemic stroke, hemorrhagic stroke or unspecified stroke). Multivariate linear regression models and Kaplan-Meier curves were used to examine the associations between SUA level or HUA (hyperuricemia) and first stroke events.

RESULTS The clinical baseline characteristics of this cohort (age: 62.95±9.14 years, range 27–93 years; male, 45.67%) were presented by the quartiles of baseline SUA level, and the prevalence of HUA was 52.23%. A total of 99 (0.84%) first stroke events (51 ischemic events, 15 hemorrhagic events and 33 unspecified stroke events) occurred. There were no statistically significant differences in various stroke events between groups by the quartiles of baseline SUA level (P>0.05). The risk of first stroke was not significantly associated with the increased SUA levels or HUA. This unrelated association was also found after adjustment for gender and age. Subgroup analyses found that this association between SUA level and total first stroke events was modified by aging (age ≥60 years): in group with age less than 60 years, subjects with HUA had an statistically significant higher risk of total first stroke events compared to population without HUA (adjusted-HR: 4.89, 95% CI 1.36–17.63, P=0.015). However, this positive association was disappeared in aging population (adjusted-HR: 0.97, 95% CI 0.60–1.56, P=0.886; P-value for interaction=0.043). Survival analysis further confirmed this discrepancy (Kaplan–Meier, log-rank P=0.013 for non-aging group, P=0.899 for aging group, respectively). There were not statistically significant interactions in any of the subgroups, including gender, mean arterial pressure tertiles, systolic blood pressure tertiles, diastolic blood pressure tertiles, antihypertensive drugs usage, body mass index tertiles and central obesity.

CONCLUSIONS No significant evidence in present study indicates that increased SUA levels or HUA are predictive of first stroke in Chinese adults with hypertension. Nonetheless, subgroup analyses found that this correlation was modified by aging.

GW31-e1380

Life's simple 7 cardiovascular health metrics versus Fuster-BEWAT score to predict the new 4-tiered left ventricular hypertrophy classification: insight from a large Asian-population

Haoyu Wang
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES AHA's Life's Simple 7 cardiovascular health score is recommended for use in primary prevention. Simpler tools not requiring laboratory tests, such as the Fuster-BEWAT score (FBS) (blood pressure [B], exercise [E], weight [W], alimentation [A], and tobacco [T]), are also available. This study sought to compare the effectiveness of Life's Simple 7 and FBS in predicting the newly proposed 4-tiered LVH classification based on LV dilatation (high LV end-diastolic volume [EDV] index) and concentricity (mass/end-diastolic volume $[M/EDV]^{0.67}$) in the general Chinese population.

METHODS Participants from Northeast China Rural Cardiovascular Health study who underwent cardiac echocardiography (n=11,261) were enrolled. Patients with LVH were divided into 4 groups – eccentric nondilated (normal M/EDV and EDV), eccentric dilated (increased EDV, normal M/EDV), concentric nondilated (increased M/EDV, normal EDV), and concentric dilated (increased M/EDV and EDV) – and compared with patients with normal LVM.

RESULTS With poor Life's Simple 7 and FBS as references, individuals with ideal Life's Simple 7 and FBS showed lower adjusted odds of having eccentric nondilated (Life's Simple 7, odds ratio [OR]: 0.26; 95% confidence interval [CI]: 0.20–0.34 vs. FBS, OR: 0.28; 95% CI: 0.20–0.38), eccentric dilated (OR: 0.73 [0.57–0.94] vs. OR: 0.57 [0.43–0.76]), concentric nondilated (OR: 0.12 [0.04–0.38] vs. OR: 0.19 [0.07–0.52]), and concentric dilated LVH (OR: 0.12 [0.03–0.37] vs. OR: 0.26 [0.10–0.72]). Similar levels of significantly discriminating accuracy were found for Life's Simple 7 and FBS with respect to the eccentric nondilated (C-statistic: 0.737; 95% CI: 0.725–0.750 vs. 0.731; 95% CI: 0.718–0.744, respectively), eccentric dilated (0.684 [0.670–0.699] vs. 0.686 [0.671–0.701]), concentric nondilated (0.658 [0.624–0.692] vs. 0.650 [0.615–0.684]), and concentric dilated LVH (0.711 [0.678–0.744] vs. 0.698 [0.663–0.733]).

CONCLUSIONS Our findings demonstrate that the FBS appears capable of performing just as well as does the Life's Simple 7 in predicting the novel 4-group classification of LVH, making the FBS particularly suited as a reliable low-cost indicator of CV health in settings where access to laboratory analysis is limited and health care resources are constrained.

ARRHYTHMIAS

GW31-e0068

Lead I R-wave amplitude to distinguish ventricular arrhythmias with lead V3 transition originating from the left versus right ventricular outflow tract

Jue Wang, Suyun Liu
Second Hospital of Hebei Medical University

OBJECTIVES Although several electrocardiography (ECG) criteria have been purposed to distinguish left and right origins of outflow tract ventricular arrhythmias (OT-VAs) with lead V3 transition, they remain limited in clinical practice. The purpose of this study was to determine if lead I R-wave amplitude is effective to distinguish left and right origin.

METHODS We measured lead I R-wave amplitude in a retrospective cohort of 82 OT-VAs patients with lead V3 transition and positive complex in lead I who underwent successful catheter ablation from right ventricular outflow tract (RVOT) and left ventricular outflow tract (LVOT). The optimal R-wave threshold was identified and diagnostic indices were compared with V2S/V3R, transitional zone (TZ) index, and the V2 transition ratio.

RESULTS Lead I R-wave amplitude for LVOT origins was significantly higher than that of RVOT origins (0.55±0.13 vs. 0.32±0.15 mV; P<0.001). The area under the curve (AUC) for the lead I R-wave amplitude by receiver operating characteristic (ROC) analysis was 0.926, with a cut-off value of ≥0.45 predicting an LVOT origin with a 92.9% sensitivity and 88.2% specificity. In accuracy, lead I R-wave amplitude was superior to V2S/V3R, TZ index, and the V2 transition ratio. 92.3% LVOT cases exhibiting lead I R-wave amplitude ≥0.45 mV originated from the right coronary cusp (RCC) and the left and right coronary cusp junction (L-RCC).

CONCLUSIONS The R-wave amplitude in lead I provides a useful and simple criterion to identify RCC or L-RCC origin in OT-VAs with lead V3 transition.

GW31-e0070

Application of wearable full-lead ambulatory electrocardiogram monitoring devices in physical training

Yuhong Peng, Yanzhuo Ma, Dongmei Wang
The 980st Hospital of the PLA Joint Logistics Support Force (Bethune International Peace Hospital of PLA)

OBJECTIVES To observe the feasibility of applying a new full-lead wearable ambulatory ECG based on fabric electrodes for non-invasive long-range batch ECG monitoring in physical training.

METHODS Fifty-four subjects were selected, wearing a new ambulatory ECG monitoring suit for 48 hours and performing physical training, observing their tolerance and equipment reliability, and comparing the information (heart rate, arrhythmia and ST segment changes) obtained by ambulatory ECG monitoring before and after the training.

RESULTS Forty-four subjects completed the whole process of ambulatory ECG monitoring. The average record time is 43.44±3.56 h. All subjects indicated that the suit is comfortable or bearable. The real-time monitoring signal has clear graphics and reliable quality. The incidence of arrhythmia was compared before and after the training. The incidence of atrial arrhythmia on the day of the training was significantly lower than before the training (P=0.001). The average heart rate, total heart rate, and maximum heart rate on the day of the training are higher than before. The standard deviation of NN intervals (SDNN), SD of 5 min N–N intervals (SDANN), and SDNN index are also higher than the normal working state (P<0.05). The slowest heart rate, root mean square of successive RR interval differences (RMSSD), percentage of successive RR intervals that differ by more than 50 ms (PNN50), and frequency domain indicators did not differ between groups (P>0.05).

CONCLUSIONS The new wearable full-lead ambulatory electrocardiogram monitoring devices can be used for long-term batch ECG monitoring in physical training. Appropriate intensity training can reduce the occurrence of arrhythmia and improve heart rate variability. e, total heart rate, and maximum heart rate on the day of the training are higher than before. The standard deviation of NN intervals (SDNN), SD of 5 min N-N intervals (SDANN), and SDNN index are also higher than the normal working state (P<0.05). The slowest heart rate, root mean square of successive RR interval differences (RMSSD), percentage of successive RR intervals that differ by more than 50 ms (PNN50), and frequency domain indicators did not differ between groups (P>0.05).

GW31-e0071

Effects of long-term high intensity training on cardiovascular of military personnel

Yuhong Peng, Yanzhuo Ma, Dongmei Wang
The 980st Hospital of the PLA Joint Logistics Support Force (Bethune International Peace Hospital of PLA)

OBJECTIVES To investigate the effects of long-term high intensity training on cardiovascular in military personnel.

METHODS High-intensity training soldiers were divided into long-term high-intensity group (127 cases) and short-term control group (87 cases) according to the training time. The data of blood pressure and electrocardiogram and the incidence of arrhythmia were compared in 5 km weight-bearing training. Phosphocreatine kinase isoenzyme (CKMB), troponin T (TnT), adrenocorticotropic hormone (ACTH), adrenaline (ADR), norepinephrine (NADR) and angiotensin II (ANG2) were collected from 45 individuals.

RESULTS The diastolic blood pressure measured immediately after exercise in both groups is lower than before training (P<0.01). The P-wave width in II, RV5 amplitude (mv), and RV5+SV1 (mv) voltage of the long-term high-intensity training group were higher than those of the short-term control group no matter before or after training (P<0.01). There was no statistically significant difference in the incidence of atrial premature beats, short PR interval, first-degree AVB, complete right bundle branching and ST-T changes (P>0.05). The elevated levels of TnT, ACTH, ADR and ANG2 after training in the long-term high-intensity training group were lower than that in the short-term high-intensity training group (P<0.01).

CONCLUSIONS High-intensity military training leads to the potential risk to the heart of soldiers. The body's heart structure undergoes adaptive changes after long-term training, and the stress response can be adjusted adaptively.

GW31-e0072

Study on the application of heparin during radiofrequency ablation of atrial fibrillation in patients undergoing continuous new oral anticoagulants therapy

Na Wang, Lianjun Gao, Yunlong Xia, Xiaomeng Yin, Xianjie Xiao, Zhengyan Wang, Rongfeng Zhang
The First Affiliated Hospital of Dalian Medical University

OBJECTIVES By comparing the different initial heparin doses in patients with atrial fibrillation (AF) ablation who continuously took new oral anticoagulants (NOACs) and warfarin, the appropriate initial heparin dose in radiofrequency ablation for patients with NOACs was obtained.

METHODS This study was a single-center, randomized, double-blind, prospective clinical trial, which was selected from 2018.06 to 2019.05 in 187 patients with AF who underwent the first catheter radiofrequency ablation at the First Affiliated Hospital of Dalian Medical University and met the inclusion criteria. Patients were divided into warfarin (WG) group (38 cases) and new oral anticoagulants (NG110, NG120, NG130) group (149 cases) according to different anticoagulation schemes before surgery. The warfarin group was given an initial heparin dose of 100 U/kg as a control group, while the NOACs group was randomly divided into three groups using an SPSS random number generator and, respectively given an initial heparin dose of 110, 120, and 130 U/kg. Monitor the ACT every 15 minutes during the operation and achieve the target ACT value of 250–350 s. To observe the baseline ACT, average ACT compliance rate, and ACT at each time period in the Chinese Farin group and the new oral anticoagulant group, and the incidence of bleeding and thromboembolic complications during ablation, postoperative hospitalization, and 1 month after discharge, Statistical analysis was performed on the four groups of observation indicators.

RESULTS There was no difference in baseline ACT between warfarin group and NOACs (NG110, NG120, NG130) group; at 15 minutes, the average ACT (324±65 s) of warfarin group was significantly longer than that of NG110 group (289±51 s) and NG120 group (285±49 s) (P values were 0.015 and 0.006); at 30 minutes, the ACT (320±61 s) of warfarin group was significantly longer than that of NG110 group (279±41 s) and NG120 group (286±26 s) (P values were 0.001, 0.003); at 45 min, the ACT (302±58 s) of the warfarin group was significantly longer than that of the NG110 group (270±39 s) and the NG120 group (277±32 s) (P values were 0.01 and 0.037); at 60 min and 75 min, There was no statistical difference in ACT between warfarin group and NOACs (NG110, NG120, NG130) group. The average ACT compliance rate of NG120 (82.2±23.6%) and NG130 (84.8±23.7%) was significantly higher than that of warfarin group (63.4±36.2%) (P values were 0.007 and 0.003, respectively). In the subgroup analysis, the average ACT compliance rate of NG120 in the dabigatran group (84.3±20.6%) and NG130 in the dabigatran group (87.8±22.2%) was significantly higher than that of the warfarin group (63.4±36.2%). The results are statistical (P values were 0.008 and 0.004, respectively); the average ACT compliance rate of Ng120 (81.1±25.4%) of rivaroxaban group and NG130 (83.2±24.6%) of rivaroxaban group was significantly higher than that of warfarin group (63.4±36.2%), the results were statistically different (P values were 0.02 and 0.008, respectively). There was no statistical difference in perioperative bleeding and thromboembolic complications between the four groups.

CONCLUSIONS For patients with AF ablation who continuously take NOACs (dabigatran, rivaroxaban), the appropriate initial heparin dose during surgery is 120 U/Kg or 130 U/kg.

GW31-e0099

Ablation strategies for arrhythmogenic right ventricular cardiomyopathy: a systematic review and meta-analysis

Lishui Shen, Limin Liu, Yan Yao
Fuwai Hospital, Chinese Academy of Medical Science, Peking Union Medical College

OBJECTIVES Catheter ablation for ventricular tachycardia (VT) in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) has significantly evolved over the past decade. However, different ablation strategies showed inconsistency in acute and long-term outcomes.

METHODS We searched the databases of Medline, Embase and Cochrane Library through October 17, 2019 for studies describing the clinical outcomes of VT ablation in ARVC. Data including VT recurrence, all-cause mortality, acute procedural efficacy and major procedural complications were extracted. A meta-analysis with trial sequential analysis was further performed in comparative studies of endo-epicardial versus endocardial-only ablation.

RESULTS A total of 24 studies with 717 participants were enrolled. The literatures of epicardial ablation were mainly published after 2010 with total ICD implantation of 73.7%, acute efficacy of 89.8%, major complication of 5.2%, follow-up of 28.9 months, VT freedom of 75.3%, all-cause mortality of 1.1% and heart transplantation of 0.6%. Meta-analysis of 10 comparative studies revealed that compared with endocardial-only approach, epicardial ablation significantly decreased VT recurrence (OR: 0.50; 95% CI: 0.30–0.85; P=0.010), but somehow increased major procedural complications (OR: 4.64; 95% CI: 1.28–16.92; P=0.02), with not evident improvement of acute efficacy (OR: 2.74; 95% CI: 0.98–7.65; P=0.051) or all-cause mortality (OR: 0.87; 95% CI: 0.09–8.31; P=0.90).

CONCLUSIONS Catheter ablation for VT in ARVC is feasible and effective. Epicardial ablation is associated with better long-term VT freedom, but with more major complications and unremarkable survival or acute efficacy benefit.

GW31-e0164

Efficacy and safety of the rivaroxaban in patients with nonvalvular atrial fibrillation and metabolic syndrome

Baxrom Alyavi[1,2], Jamol Uzokov[1], Akbar Abdullaev[1]
[1]Republican Specialized Scientific and Practical Medical Center of Therapy and Medical Rehabilitation
[2]Tashkent Pediatric Medical Institute

OBJECTIVES Atrial fibrillation (AF) is common in general population and is known to have a high risk of bleeding and stroke. Metabolic syndrome (MetS) is a cluster of several risk factors such as hypertension, dyslipidemia, abdominal obesity (AO), insulin resistance (IR) and impaired glucose tolerance (IGT), and patients with MetS are increased risk for the development of cardio and cerebrovascular diseases. Prevalence of AF and MetS are rising and co-existence of these two conditions will increase related complications. Aim of the study was to estimate the efficacy and safety of – rivaroxaban in patients with MetS and nonvalvular atrial fibrillation (NVAF).

METHODS We compared the efficacy and safety – rivaroxaban versus warfarin in patients with NVAF and MetS. One hundred sixty-eight patients (aged 42–67 years; mean age 51.2 years; 46% male) were enrolled in this study dividing into two groups by 84. First group was provided with rivaroxaban 20 mg/day and the second group with warfarin 1–3 mg/day (under the control of the INR between 2.0 and 3.0). Mean follow-up period was 1.9 years. The primary safety and efficacy outcomes were major and non-major bleeding, stroke and embolism in both groups.

RESULTS The primary endpoints were similar in both groups during the follow-up period (1 stroke in rivaroxaban vs. 1 stroke in warfarin). There was no embolism in both groups. However, major and non-major clinically relevant bleeding were observed more in warfarin group when compared to rivaroxaban group (HR 1.3; 95% CI 1.06–1.38; P=0.01). Among components of the MetS, hypertension and dyslipidemia were correlated with major and non-major bleeding (HR 1.25; 95% CI 1.07–1.36; P<0.05 and HR 1.10; 95% CI 1.06–1.17; P<0.05). There were no correlations between AO, IR and IGT with major and non-major bleeding.

CONCLUSIONS Rivaroxaban was superior to warfarin in NVAF patients with MetS. Among MetS, components, hypertension and dyslipidemia are the risk factors for major and non-major bleeding. Further studies are needed with large amount of patients.

GW31-e0169

Characteristics of atrial fibrillation after percutaneous coronary interventions

Baxrom Alyavi[1,2], Jamol Uzokov[1], Djamshid Payziev[1], Shukhratjon Azizov[2]
[1]Republican Specialized Scientific and Practical Medical Center of Therapy and Medical Rehabilitation
[2]Tashkent Pediatric Medical Institute

OBJECTIVES Atrial fibrillation is common type of heart rhythm disorders occurring after percutaneous coronary interventions (PCI). Aim of the study was to estimate prevalence and characteristics of new onset atrial fibrillation after PCI.

METHODS This retrospective study was carried out at our Interventional Cardiology department from 2014 to 2019 August. Two hundred eighty-five consecutive patients with stable coronary artery disease were enrolled in the retrospective study among 9125 patients who underwent PCI in whom new onset AF were developed during the procedure. All laboratory, anthropometric data, CHA2DS2-VASC scores, AF risk factors were assessed.

RESULTS Among 285 patients 65% of them were men (n=171) and mean age was 58±12.6 years. An average AF was occurred after the 2–24 hours of the PCI (mean time 4±16.4). Sixty-second percent of patients had hypertension, 43% type 2 diabetes mellitus (T2DM), 25% metabolic syndrome (MS), 24% anemia. Among them in 21% of patients were found single-vessel lesion, 45% two-vessel lesion, 34% three-vessel lesion. Mean CHA2DS2-VASC scores was high in patients with T2DM vs. non-diabetes patients (3.2; 2.9; 3.1). High sensitive CRP (hsCRP) was higher in patients with three-vessel lesion (7.2 mg/L) than two-vessel lesion (6.1 mg/L) and/or single-vessel lesion (5.9 mg/L). Among risk factors hsCRP was higher in T2DM (7.1 mg/L), MS (5.9 mg/L) than hypertension (5.2 mg/L) and anemia (5.4 mg/L).

CONCLUSIONS Hypertension and T2DM are the common risk factors for the new onset AF after PCI. Deeply monitoring of high-risk patients after PCI might be useful to detect new onset AF in the earliest period.

GW31-e0183

A case of exercise induced chest distress followed by syncope

Yajun Xue, Jie Zhou, Ping Zhang
Beijing Tsinghua Changgung Hospital

OBJECTIVES Chest distress happened during exercised are always associated with coronary heart disease, especially among aged male and female. However, as a nonspecific symptom, lots of patients complained of chest distress can have other underline problems. Here we reported a aged female who experienced recurrent exercise related chest-distress, and suffered from syncope during exercise test.

METHODS A 62 year female aggravated chest distress, during the treadmill exercise test, when Bruce Stage 4 was achieved, the patient complaint of palpitation and chest distress, and the synchronous ECG showed a slight horizontal depression of ST segment in leads V3–V6, then a new onset complete left bundle branch block (CLBBB) took place. One milligram nitroglycerin were given to the patient. The feeling of chest distress got worsen, with decreasing of heart rate to 39 bpm, and blood pressure to 80/50 mmHg, followed by transient loss of consciousness, the ECG showed junctional escape rhythm.

RESULTS CLBBB due to asynchronous contraction of left ventricular wall and increased mitral regurgitation, LVEF decreased, which led to the decrease of oxygen supply. The imbalance of oxygen demand-supply will eventually led to the symptom of chest distress which mimicked angina.

CONCLUSIONS *1. Chest distress during exercise.* As early as 1983, Dean A. Bramlet and his colleagues had studied the effect of Rate-dependent left bundle branch block (RDLBBB) on global and regional left ventricular function. In the subjects with RDLBBB, the LVEF increased before the development of LBBB. However, after LBBB developed, the LVEF decreased abruptly (From 68±7% to 62±7%), however the control patients demonstrated a progressive increase in LVEF with increasing exercise (From 62±8% to 78±7%). All RDLBBB patients had asynchronous contraction, and four had hypokinesis, mainly located at lower septum or inferior apical segments. As for our patient, we first exclude coronary heart disease by Coronary Angiography, and confirmed the Rate-dependent left bundle branch block by using stress test. As her heart rate going up during exercise, the demand of oxygen also increased. However, CLBBB took place, and then due to asynchronous contraction of left ventricular wall and increased mitral regurgitation, LVEF decreased, which led to the decrease of oxygen supply. The imbalance of oxygen demand-supply will eventually led to the symptom of chest distress which mimicked angina. *2. Syncope which happened while 2 pills of Nitroglycerine (0.5 mg each) were taken.* NTG is commonly administered to relief the symptom of angina pectoris, and it is also widely used in Head-up tilt test (HUTT) to increase its diagnostic yield. After taken sublingually, NTG is rapidly converted to nitric oxide (NO) by mitochondrial aldehyde dehydrogenase in smooth muscle cells. NO is a potent natural vasodilator, which causes venous dilation and decreasing of cardiac preload. Nitroglycerin is lipid-soluble and readily crosses cell membranes. It will also act centrally on circulatory control and inhibiting the baroreflex control of heart rate (HR) and arterial peripheral resistance, thus leading to syncope by dual pathways.

GW31-e0220

Ventricular fusion with intrinsic atrioventricular conduction in biventricular pacing: a retrospective study of 31 patients with congestive heart failure

Zhuxinyue Xie[1,2], Tao Guo[2], Ke Liu[2], Jinrui Guo[2], Yulong Guo[2], Qiuzhe Guo[3]
[1]Kunming Medical University
[2]Department of Cardiology, Fuwai Yunnan Cardiovascular Disease Hospital
[3]Department of Cardiac Surgery, Fuwai Yunnan Cardiovascular Disease Hospital

OBJECTIVES Cardiac resynchronization therapy (CRT) reduces morbidity and mortality in patients with congestive heart failure, while one-third of recipients remains non-responsive. Optimization of atrioventricular (AV) and interventricular (VV) delays may improve CRT efficacy. But the conventional echocardiographic optimization (echo optimization) method is complex and time-consuming. Fusion with intrinsic conduction might increase the benefit of CRT. The study aimed to describe ventricular fusion with AV node intrinsic conduction in biventricular pacing (BiV+intrinsic), a method of optimizing CRT based on electrocardiography (ECG), and to assess its impact on the clinical efficacy in a long-term.

METHODS Thirty-one consecutive patients in sinus rhythm with preserved AV conduction were included and performed with both echo optimization and the BiV+intrinsic method after CRT implantation. The BiV+intrinsic method included increasing the AV delay progressively to obtain the narrowest QRS fusion band on ECG, and adjusting the VV delay in different pacing configurations until achieving the shortest QRS width. The AV and VV delays set by the BiV+intrinsic method were considered as optimal values. The acute changes of ECG and echocardiographic parameters in these two methods were collected. NYHA functional class, pro-NT BNP, ECG, and echocardiographic parameters were recorded before CRT implantation and at 3-, 6- and 12-month follow-up.

RESULTS Both methods improved LVEF and decreased QRS duration immediately, while the BiV+intrinsic method achieved a further reduction of QRS width after optimization, compared with echo optimization (123.94±12.21 ms vs. 142.32±20.13, P<0.001). The BiV+intrinsic method narrowed the QRS duration and improved NYHA classification during follow-up (P<0.05). Additionally, the Pearson correlation showed that a significantly correlation between the variation of QRS width and LVEF (r=0.572, P=0.004) at 6-month

follow-up, which meant that the patient with evident QRS narrowing was likely to have a better LVEF.

CONCLUSIONS BiV+intrinsic method is a feasible and practical method to optimize the CRT device, which narrows QRS width and is likely to improve LVEF and CRT non-response in the long-term. But a well-designed study is needed to demonstrate its impact on reversing LV remodeling and improving mechanical synchrony.

GW31-e0225

Cumulative pulse pressure in midlife and incident atrial fibrillation: the atherosclerosis risk in communities study

Yi quan Huang, Xinxue Liao
Cardiology Department, First Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES The influence of cumulative blood pressure (BP) in midlife on incident atrial fibrillation (AF) is not well studied.

METHODS The analysis included 9150 adults without prior AF at visit 4 (1996–1998) from the ARIC (Atherosclerosis Risk in Communities) cohort. Cumulative BP was calculated as the area under the curve (mmHg×years) from visit 1 (1987–1989) to visit 4.

RESULTS For the study population, mean (standard deviation) age at visit 4 was 62.9 (5.7) years of which 4045 (44.2%) were male. After a median follow up of 16 years, 1455 persons (15.9%) had incident atrial fibrillation. In adjusted Cox models (per 1-SD increment), cumulative pulse pressure was the strongest cumulative BP predictor of incident AF (hazard ratio [HR], 1.20; 95% confidence interval [CI], 1.13–1.26; P<0.001). In contrast, cumulative mean arterial pressure was unrelated to incident AF (HR, 1.03; 95% CI, 0.97–1.10; P=0.36). Cumulative systolic BP was associated with incident AF (HR, 1.14; 95% CI, 1.07–1.22; P<0.001). When evaluated in the same model with cumulative systolic BP, the diastolic relation was significant but opposite (HR, 0.84; 95% CI, 0.78–0.90; P<0.001), consistent with a cumulative pulse pressure effect. The predictive effect of cumulative systolic and diastolic BP together was similar to that of cumulative pulse pressure.

CONCLUSIONS Exposure to higher cumulative pulse pressure in midlife independently predicts incident AF in a community-based sample.

GW31-e0281

Serum sST2 combined with LAD is related to the low voltage of left atrium in patients with atrial fibrillation and can predict the recurrence of AF after radiofrequency ablation

Jiali Fan, Yuan Li, Wenhuan Wu, Jiahong Xue
The Second Affiliated Hospital of Xi'an Jiaotong University

OBJECTIVES The present study was aimed to determine whether serum sST2, a kind of mechanical stress-induced protein, could be used as a marker of left atrial low voltage areas (LVAs) and it could be predicted the recurrence of AF in patients undergoing radiofrequency catheter ablation.

METHODS Eighty-four cases (average age 64.24±10.17, including 57 paroxysmal AF and 27 persistent AF) undergoing radiofrequency ablation were finally included in the study. Electroanatomical voltage mapping was employed to determine the extent of left atrial low-voltage. LVAs were defined as bipolar electrogram amplitudes ≤0.5 mV during sinus rhythm. The general clinical data and hematological indexes of all patients were collected before ablation. The concentration of serum sST2 was determined by ELESA. All patients were followed up at 3, 6 and 12 months after RF procedure.

RESULTS The results showed that sST2 could be used as a marker for left atrial low voltage area by single factor screening and binary logistic regression analysis (OR 1.054, P<0.05); by single factor cox regression model and multi factor cox regression model, we found that the serum level of sST2 could be the predictive factor for the recurrence of AF after RFA (HR 1.014, 95% CI 0.986–1.035, P=0.035). Furthermore, it was showed that there was 95% AF-free survival after ablation in the lower levels of serum sST2 whereas there was only 59.6% AF-free survival in the higher levels of serum sST2 according to the subgroup analysis.

CONCLUSIONS Serum sST2 may a new biomarker in the assessment of atrial fibrosis and is associated with the recurrence of atrial fibrillation after radiofrequency ablation.

GW31-e0354

Effects of ultrasound parameters in predicting left atrial pressure and atrial fibrillation recurrence after ablation

Jinqiu Wei, Yinglong Hou
The First Affiliated Hospital of Shandong First Medical University

OBJECTIVES Atrial fibrillation (AF) recurrence after ablation has been reported to be associated with many factors, including type of AF, duration of AF, ablation technique, left atrium (LA) function and structure. AF recurrence has a well-known relation with LA diameter, LA volume, LA stiffness, LA compliance, LA systole and diastolic function. Prior studies have also concluded that LA pressure (LAP) in an independent predictor of AF recurrence. However, LAP measurements were performed during ablation after the transseptal puncture. As LAP is an important indictor of LA diastolic function which can be reflected using cardiac ultrasound, we hypothesize that ultrasound parameters are the surrogate markers of LAP in patients without ablation. The aim of this meta-analysis was to investigate the potential role of cardiac ultrasound parameters in predicting LAP.

METHODS MEDLINE (up to March 31, 2020), EMBASE (up to up to March 31, 2020), and Cochrane Controlled Trials Register (up to up to March 31, 2020) databases were searched for all published trials written in English and related to LAP and AF recurrence. The search terms were as follows: "atrial fibrillation" AND "ablation" AND "recurrence" AND "atrial pressure" AND "ultrasound". The recurrence rate is expressed as odds ratio with 95% confidence interval (CI). The values measured during ablation were expressed as weighted mean differences (WMD) and 95% CI. Heterogeneity was assessed using the Q statistic, which is the result of a statistical test based on Q statistic (p) and I^2 statistic. Considering that many aspects, such as age, gender composition and history of AF can differ among studies, we selected a random effect model for the analysis.

RESULTS A total of 574 relevant papers were retrieved and 54 articles were scrutinized after removing duplicates and irrelevant studies. After the papers were rigorously selected, 5 trials focusing on LAP, AF recurrence and ultrasound parameters were included in this meta-analysis. The pooled data showed that left atrial volume index (LAVi) is significantly correlated with AF recurrence (MD 5.34, 95% CI 2.16–8.52, P=0.001), I^2=64% (Figure 1a). After excluding one study, the heterogeneity among studies was eliminated (Figure 1b). Besides, the recurrence group had a higher E/E′ ratio than the SR maintained group (MD 1.03, 95% CI 0.31–1.75, P=0.005), I^2=41% (Figure 2a). We further revealed that heterogeneity was from the same study (Figure 2b). The study was investigated, and we found that several factors can account for the heterogeneity. Firstly, all the patients included were paAF, while the other studies contained peAF and paAF patients. Secondly, the ablation procedure was second-generation cryoballoon in all patients, while other studies were conducted through RF or either RF or cryoballoon ablation. Thirdly, the standard deviation (SD) is not reported in this article, so we calculated SD according to given values. The data conversion may lead to the heterogeneity.

CONCLUSIONS LAVi and E/E′ are important parameters for predicting LAP in patients without ablation. In addition, they are related to AF recurrence after successful ablation.

GW31-e0357

Whether sodium-glucose co-transporter 2 inhibitors reduce the incidence of atrial fibrillation: a meta-analysis of randomized controlled trials

Yue Ma, Dongxia Jin, Hongliang Cong
TianJin Chest Hospital

OBJECTIVES The association between sodium-glucose co-transporter 2 (SGLT2) inhibitors and atrial fibrillation remains controversial because of the conflicting data. We searched all available data and conducted a meta analysis to examine the relationship between them in patients with type 2 diabetes.

METHODS We have searched electronic database, include Medline, Embase and Cochrane library to find researches and trials comparing the effect of SGLT2 inhibitors and placebo to the morbidity of atrial fibrillation in patients with type 2 diabetes. We queried database for relevant studies up to April 2020. Only randomized controlled trials were included. Results from trials were described by odds ratios and 95% confidence intervals.

RESULTS Eight studies were included in this meta-analysis. The investigation carried out by us has revealed that there are significant differences on the incidence of atrial fibrillation between the SGLT2 inhibitors group and placebo group (OR 0.83, 95% CI 0.72–0.96). In subgroup analysis, the group of dapagliflozin has significant differences on the incidence between experimental group and control group (OR 0.82, 95% CI 0.70–0.96).

CONCLUSIONS SGLT2 inhibitors may reduce the incidence of atrial fibrillation, especially dapagliflozin.

GW31-e0360

Elevated homocysteine levels associated with atrial fibrillation and recurrent atrial fibrillation

Lei Huang
Ningbo Hangzhou Bay Hospital

OBJECTIVES There is increasing evidence linking plasma homocysteine levels and atrial fibrillation (AF). The association between the elevated level of plasma homocysteine and AF was examined by meta-analysis in this study.

METHODS The PubMed and ScienceDirect databases until August 2019 were utilized to collect previous literature on homocysteine and the potential relation to AF. The pooled effects were evaluated depending on standardized mean differences (SMDs) or odds ratios (ORs) with 95% confidence intervals (CIs), and the calculation was performed using Stata 12 software.

RESULTS A total of 11 validated articles was included in the meta-analysis. For pooled effect, the results confirmed that AF patients had higher homocysteine levels than control subjects (SMD: 0.58, 95% CI: 0.09–1.06). Compared with control subjects, homocysteine levels were higher in paroxysmal AF (SMD: 0.45, 95% CI: 0.18–0.72) and persistent AF patients (SMD: 1.21, 95% CI: 0.50–1.92). The pooled analysis suggested that patients with elevated homocysteine levels had markedly higher risk of AF compared with lower homocysteine levels in the categorical variable (OR: 2.21, 95% CI: 1.16–4.21) and continuous variable analysis (OR: 1.13, 95% CI: 1.00–1.27), respectively. In addition, the pooled analysis indicated that recurrent AF patients had significantly higher homocysteine levels than those without recurrence (SMD: 0.65, 95% CI: 0.42–0.88). The pooled analysis of the categorical variables indicated that elevated homocysteine levels were associated with increased risk of AF recurrence (OR: 3.81, 95% CI: 3.11–4.68). However, the association is weak in the pooled analysis of continuous variables (OR: 1.88, 95%: 0.74–4.81).

CONCLUSIONS Our meta-analysis identified that plasma homocysteine levels were significantly elevated in AF and recurrent AF patients. Elevated homocysteine is associated with increased risk of AF and AF recurrence.

GW31-e0366

Long-term lead performance and feasibility of left bundle branch pacing

Yiwen Pan, Guosheng Fu
Department of Cardiology, Key Laboratory of Cardiovascular Intervention and Regenerative Medicine of Zhejiang Province, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, China

OBJECTIVES The aim of the study was to evaluate the long-term lead performance and clinical outcomes of LBBP.

METHODS We retrospectively enrolled 123 consecutive pacemaker-indicated patients scheduled to have LBBP implantation from January 2018 to December 2018. The pacing parameters, electrocardiograms, echocardiographic measurements, and complications associated with LBBP were tracked at implant and follow-up.

RESULTS LBBP was successfully performed in 110 of 123 (89.4%) patients. The primary indication for pacing was atrioventricular (AV) conduction disease in 38.2%, sinus node dysfunction in 26.8%, AV node ablation in 3.2%, CRT in 12.2%, and pulse generator change in 15.4%. Compared to baseline, LBBP capture thresholds (0.7±0.3 V vs. 0.8±0.3 V, P=0.007) and pacing impedance (525.8±92.7 Ohms vs. 785.7±226.9 Ohms, P<0.001) decreased significantly at 1-month, respectively, while there was no statistically significant change in sensed R-wave amplitude (11.1±6.2 mV vs. 9.9±6.1 mV, P=0.38). LBBP lead parameters remained stable during follow-up period. Purkinje (P) potentials could be recorded in 81 patients with a mean P potential-ventricle (PV) interval of 27.5±6.1 ms. The LV activation time (LVAT) was 68.8±14.4 ms. There was no difference in QRS duration between baseline rhythm and post-implantation of LBBP (125.0±38.6 ms vs. 118.3±27.1 ms, P=0.17). In 43 patients of baseline QRS duration >120 ms, LBBP could slightly narrow the QRS complex (126.0±24.1 ms vs. 167.0±26.2 ms, P<0.001). Both LVEDd and LVEF improved from baseline in patients with reduced LVEF (n=29) while no significant change was found in patients with preserved LVEF (n=81). In 7 patients, LBBP lead protuberance into the LV cavity was observed, with mean distance between the screw tip and the LV septum of 3.0 mm (range from 1.8 to 3.9 mm). The rehospitalization rate for heart failure was 3.6% (n=4).

CONCLUSIONS LBBP is a novel physiological, safe and effective pacing technique for patients with a standard pacemaker indication, particularly for patients with systolic heart failure.

GW31-e0383

Comparative effectiveness and safety of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation: a meta-analysis of propensity score-matching studies

Wengen Zhu, Yuzhong Wu, Yugang Dong
The First Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES Several observational studies have compared the effect of the non-vitamin K antagonist oral anticoagulants (NOACs) to each other in patients with atrial fibrillation (AF). However, confounding by indication is a major problem when comparing NOAC treatments in some of these studies. This meta-analysis was conducted to compare the effectiveness and safety between NOAC and NOAC by only including propensity score-matching studies.

METHODS We systematically searched the PubMed and Ovid databases until May 2020 to identify relevant observational studies. Hazard ratios (HRs) and 95% confidence intervals (CIs) of the reported outcomes were collected and then pooled by a random-effects (RE) model complemented with an inverse variance heterogeneity (IVhet) or quality effects (QE) model.

RESULTS A total of 17 cohorts were included in this meta-analysis. Compared with dabigatran use, the use of rivaroxaban was significantly associated with increased risks of stroke or systemic embolism (SSE) (HR=1.16, 95% CI 1.05–1.29) and major bleeding (HR=1.32, 95% CI 1.24–1.41), whereas the use of apixaban was associated with a reduced risk of major bleeding (HR=0.78, 95% CI 0.67–0.90), but not SSE (HR=0.84, 95% CI 0.56–1.28). Compared with rivaroxaban use, the use of apixaban was associated with a decreased risk of major bleeding (HR=0.63, 95% CI 0.54–0.73), but not SSE (HR=0.83, 95% CI 0.67–1.04). Re-analyses with the IVhet or QE models produced similar results as the RE model.

CONCLUSIONS Current observational comparisons with propensity score-matching methods suggest that apixaban might be a better choice compared to dabigatran or rivaroxaban for stroke prevention in AF patients.

GW31-e0385

Usefulness of CHADS2, R2CHADS2, and CHA2DS2-VASc scores for predicting incident atrial fibrillation in HFpEF patients: an ancillary analysis of the TOPCAT trial

Yuzhong Wu, Wengen Zhu, Yugang Dong
The First Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES Coexisting of atrial fibrillation (AF) in patients with heart failure with preserved ejection fraction (HFpEF) could increase the risk of mortality. In this study, we aimed to assess the values of the CHADS2, R2CHADS2, and CHA2DS2-VASc scores for AF prediction in HFpEF patients.

METHODS We performed a retrospective analysis on symptomatic HFpEF patients in the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist) trial. Associations of the CHADS2, R2CHADS2, and CHA2DS2-VASc scores with the risk of incident AF in HFpEF patients without baseline AF (n=2202) were assessed using the multivariable competing risk regression models. The discriminatory performances of these scores were calculated using the C-index.

RESULTS During a median follow-up of 3.3 years, the average incidence of AF was 1.80 per 100 patient-years in HFpEF patients. When score was analyzed as a continuous variable, per 1-point increase in the CHADS2 (hazard ratio [HR]=1.42, 95% confidence interval [CI]: 1.20–1.68, C-index: 0.71), R2CHADS2 (HR=1.25, 95% CI: 1.10–1.42, C-index: 0.69), or CHA2DS2-VASc (HR=1.30, 95% CI: 1.16–1.46, C-index: 0.70) scores was associated with an increased risk of incident AF. When score was analyzed as a categorical variable, patients with CHADS2≥3 (HR=2.62, 95% CI: 1.70–4.04), R2CHADS2≥3 (HR=2.55, 95% CI: 1.56–4.17), or CHA2DS2-VASc≥4 (HR=2.54, 95% CI: 1.59–4.07) had a higher risk of incident AF compared with the corresponding controls.

CONCLUSIONS Our data first suggest that the CHADS2, R2CHADS2 and CHA2DS2-VASc scores could predict the risk of incident AF in HFpEF patients with modest predictive abilities.

GW31-e0439

Identification of differentially expressed genes and signaling pathways in left atrial appendage of patients with atrial fibrillation by integrated bioinformatics analysis

Liu Peng[1,2], Ping Zhang[2]
[1]School of Clinical Medicine, Tsinghua University, Beijing, China
[2]Cardiology, Beijing Tsinghua Changgung Hospital, Beijing

OBJECTIVES Atrial fibrillation (AF) is the most common tachycardia in clinic with high mortality and morbidity. By 2010, there were more than 33 million people diagnosed with AF worldwide. A recent study has confirmed that lifetime risk for developing AF was quantified to be more than 30% in Europe. Patients with AF are at high risk for stroke, heart failure and hospitalizations, and exhibit variable comorbidities that largely increase economic burden on society. AF is an independent risk factor for thromboembolic events, including stroke and systemic thromboembolism. It has been reported that 57% of thrombi in valvular AF and 91% in nonvalvular AF (NVAF) originate in the left atrial appendage (LAA). However, the underlying molecular mechanism of AF and its associated thrombus formation is not clear. In this study, we applied integrated bioinformatics analysis to compare the gene expression differences in LAA between patients with AF and sinus rhythm (SR).

METHODS The expression profiles of GSE115574, GSE79768 were downloaded from the Gene Expression Omnibus (GEO) database, which contained 43 LAA samples in total, including 20 cases of AF samples and 23 cases of SR samples. The two microarray datasets were integrated to obtain differentially expressed genes (DEGs) and were deeply analyzed by bioinformatics methods. These DEGs were performed through gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichments by DAVID and KOBAS online analyses.

RESULTS Two expression microarray datasets, including microarray datasets GSE115574 and GSE79768 were standardized by the limma package. When the GSE115574 dataset was screened by the limma package, 574 DEGs were obtained. Among them, 212 downregulated genes and 362 upregulated genes were identified. Additionally, 4087 DEGs were screened from the GSE79768 dataset. Among them, 1740 down-regulated genes and 2347 upregulated genes were identified. A total of 96 DEGs which were the same expression changes were identified in the two GEO datasets. GO analysis of DEGs was consisted by three functional groups. In the biological process group, the DEGs were mainly enriched in cellular responses to cytokine, antigen processing and presentation and basement membrane disassembly. In the molecular function group, these DEGs were mainly concentrated on IgG binding. In the cell composition group, the DEGs were mainly enriched in cell surface, junctional sarcoplasmic reticulum membrane, plasma membrane and junctional membrane complex. KEGG pathway analysis suggested the signaling pathways of DEGs were mainly enriched in phagosome pathways, and the results indicated these DEGs were involves in signaling pathways as staphylococcus aureus infection, tuberculosis and asthma. PPI network of DEGs was confirmed including 46 nodes and 84 edges.

CONCLUSIONS In conclusion, our study provides an integrated bioinformatics analysis of DEGs in LAA of patients with AF. We have identified 96 GEGs in total. Among them, 69 genes were upregulated and 27 genes were downregulated. By analyzing the GO and KEGG pathways, we found that numbers of DEGs involved in inflammation and immune response.

GW31-e0441

Effects of different ablation methods on coagulation parameters, myocardial injury and quality of life in patients with atrial fibrillation

Yaqiong Jin, Jingchao Lu
The second Hospital of Hebei medical University

OBJECTIVES To investigate the effects of different ablation methods on coagulation parameters, myocardial injury and quality of life in patients with atrial fibrillation.

METHODS The clinical data of 200 patients with atrial fibrillation who were hospitalized in cardiology department of our hospital from January 2018 to July 2019 were analyzed retrospectively. According to the treatment methods, they were divided into radiofrequency ablation (RFCA) group (n=99, RFCA treatment) and cryoablation (CBA) group (n=101, CBA treatment). The perioperative indexes, coagulation parameters, myocardial injury and quality of life of the two groups were compared. The postoperative complications of the two groups were recorded.

RESULTS The operation time and ablation time of CBA group were shorter than those of RFCA group, and the lowest freezing temperature was lower than that of RFCA group (P<0.05). The activated partial thromboplastin time (aPTT) decreased at 24 hours after operation in both groups, but CBA group was higher than RFCA group (P<0.05). The von Willebrand factor (vWF), D-Dimer (D-D) increased at 24 hours after operation in both groups, but CBA group was lower than RFCA group (P<0.05). The creatine kinase (CK), creatine kinase isoenzyme (CK-MB), troponin I (TNI) at 24 hours after operation in both groups were higher than those before operation, and CBA group was higher than RFCA group (P<0.05). The scores of emotional function, physical pain, physiological enginery, mental health, vitality, physiological function, health status and social function in both groups were higher than those before operation, and CBA group was higher than RFCA group (P<0.05). There was no significant difference in the incidence of complications between the two groups (P>0.05).

CONCLUSIONS Compared with RFCA, CBA is used to treat atrial fibrillation, can shorten the operation time and ablation time, reduce the influence on coagulation parameters, improve the quality of life of patients, and do not increase the incidence of complications, but CBA has a greater impact on the body myocardial injury, so we should choose the appropriate operation method according to the specific situation of patients.

GW31-e0464

Effects of left bundle branch area pacing and his bundle pacing versus right ventricular pacing on safety and efficacy: a systematic review and meta-analysis

Xinyi Peng, Yu Chen, Lijun Zeng, Yunqiu Jiang, Xingpeng Liu
Heart Center, Beijing Chao-Yang Hospital, Capital Medical University

OBJECTIVES Recent studies have demonstrated that right ventricular pacing (RVP) has deleterious effects and was not synchronized to atrial and ventricular contraction, while His-bundle pacing (HBP) or left bundle branch area pacing (LBBaP) contribute to improvements in mid- and long-term outcomes. This meta-analysis was conducted to compare the safety and efficacy of HBP and LBBaP versus RVP.

METHODS Eligible studies were included by systematically searching the electronic literature databases PubMed, Cochrane Library, and Embase, and selected based on specific inclusion and exclusion criteria. Standard data extraction, quality assessment and publication bias were also performed before statistical analyses.

RESULTS Fifteen articles (n=2127 patients) were included in this meta-analysis. Instant Implantation outcomes, surgical complications, cardiac function and long-term clinical outcomes were analyzed between physiologic pacing (HBP and LBBaP) and RVP. HBP and LBBaP had shorter QRS duration (WMD −41.84, 95% CI −50.74, −32.94), better cardiac function, less mitral regurgitation (WMD −1.53, 95% CI −4.50, 1.45), less rate of pacing induced cardiomyopathy (OR 0.14, 95% CI 0.05, 0.40) and less incidence rate of mortality, HFH and AF. However, physiological pacing also had some disadvantages. RVP had apparently higher successful rate than HBP and LBBaP (OR 0.05, 95% CI 0.02, 0.11), shorter fluoroscopic time and mean procedure duration (MD 6.21, 95% CI, 2.00, 10.42; MD 20.75, 95% CI 13.78, 27.72), lower pacing threshold (WMD 0.48, 95% CI 0.24, 0.72), and less surgical complications (OR 1.80, 95% CI 1.06, 3.06).

CONCLUSIONS HBP and LBBaP were more physiological pacing site and could produce better primary and long-term clinical outcomes, compared with traditional RVP. HBP and LBBaP engaged better electrical conduction, provided more synchronizing cardiac contraction, and avoided markable dyssynchrony, which were the better pacing site for patients and clinicians.

GW31-e0535

Anatomical superiority of modified versus conventional posterior line in patient with atrial fibrillation: implications for left atrial posterior wall isolation

Xiaofeng Lu, Songwen Chen, Shaowen Liu
Department of Cardiology, Shanghai General Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

OBJECTIVES Left atrial posterior wall (LAPW) isolation was performed as an additional strategy for atrial fibrillation (AF) ablation based on pulmonary vein (PV) isolation. A modified posterior line (MPL) was proposed for reducing the potential risk of esophageal injury. The purpose of this study was to compare the anatomical features of MPL with conventional posterior line (PL).

METHODS Multidetector computed tomography (MDCT) was performed in 102 consecutive patients (male 60) with paroxysmal and persistent AF before the ablation procedure. The distance from MPL and PL to esophagus, the presence and thickness of fat pad on the course of MPL and PL, the esophageal route below PL were evaluated.

RESULTS The average distance from MPL to esophagus was farther than that from PL to esophagus (3.7±1.5 mm vs. 1.7±0.4 mm, P<0.001). The thickness of fat pad on the course of MPL was thicker than that on the course of PL (1.4±0.6 mm vs. 0.9±0.2 mm, P<0.001). Moreover, the average thickness of LAPW muscle under MPL was greater than that under PL (2.9±1.1 mm vs. 1.6±0.3 mm, P<0.001). These characteristics were identified in all 3 types of esophageal route. The average distance from MPL to esophagus in not esophagus compressed group was longer than that in esophagus compressed group (3.9±1.6 mm vs. 3.3±1.0 mm, P=0.026).

CONCLUSIONS A longer distance from MPL to esophagus, thicker LAPW muscle and higher presence of fat pad on MPL course may protect esophagus from ablation injury. This line may be a selective approach for LAPW isolation.

GW31-e0537

Radiofrequency catheter ablation of supraventricular tachycardia in patients with pulmonary hypertension: feasibility, safety and long-term outcome

Bin Zhou[1], Zhengqin Zhai[1], Zhicheng Jing[2], Min Tang[1]
[1]State Key Lab of Cardiovascular Disease, Fu Wai Hospital, National Center for Cardiovascular Disease, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
[2]Department of Cardiology, Key Laboratory of Pulmonary Vascular Medicine, Peking Union Medical College Hospital, Chinese Academy Medical Sciences, Beijing, China

OBJECTIVES This study aimed to investigate the feasibility, safety and long-term outcome of radiofrequency catheter ablation (RFCA) of SVT in PH patients.

METHODS Consecutive PH patients who underwent Electrophysiological study (EP) study or/and RFCA of SVT between September 2010 and July 2019 were enrolled. Acute and long-term outcome of RFCA was recorded.

RESULTS Seventy-one confirmed PH patients with SVT were enrolled of which 76 tachycardias were recorded. Sixty patients underwent RFCA with 90% acute success rate and 6.7% complication rate. Cavotricuspid isthmus (CTI)-dependent atrial flutter (AFL) was more common in the failed RFCA group

compared with the successful RFCA group (66.6 vs. 6.8%, P<0.01). Pulmonary artery diameter (PAD) in the failed group was wider than the successful group (38.7±8.9 mm vs. 31.9±5.2 mm, P=0.006). Univariate logistic regression analysis showed that wider PAD was a predictor of RFCA failure (odds ratio (OR) 1.192, 95% confidence interval (CI) 1.03–1.38; P=0.016). During the follow-up (40.3±26.6 months), the long-term successful rate of RFCA was 81.7%. In the Kaplan–Meier survival, successful RFCA was associated with increased survival compared with failed and non RFCA (log-rank P=0.025). In univariate Cox model, successful RFCA was protective against mortality (hazard ratio (HR) 0.32, 95% CI 0.11–0.92; P=0.034).

CONCLUSIONS RFCA of SVT in PH patients is feasible and safe. Successful RFCA may decrease the risk of death. Wider PAD may be a predictor of RFCA failure.

GW31-e0597

Contemporary outcomes in patients with long QT syndrome in China

Kun Li, Jing Yang, Yuanwei Liu, Fei She, Rong He, Yajun Xue, Boda Zhou, Tingting Lv, Bihe Xu, Siyuan Li, Shenjie Sun, Fulan Liu, Fang Liu, Ping Zhang
Cardiology Department, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University

OBJECTIVES The clinical characteristics of congenital long QT syndrome (LQTS) may be variable among different population groups and they have not yet been well studied in Chinese population. The aim of the study is to investigate the contemporary outcomes in patients with long QT syndrome in China.

METHODS Clinical characteristics were retrospectively reviewed from patients with congenital long QT syndrome whose blood samples were sent for whole exon genotyping during 2006–2019.

RESULTS Of the 112 gene-positive subjects (63 families), 64% were female, median QTc was 512.0 (471.0, 570.0) ms and total Schwartz's score was 4.5 (4.0, 5.5). Only 46% of the probands were correctly diagnosed after the first onset. Cardiac events occurred in 70 (64%) patients under specific circumstances in a gene-specific manner. Most of the families carried mutations from canonical LQTS-susceptibility genes: KCNH2 (49%), KCNQ1 (28%) and SCN5A (5%). Patients with LQT3 had a significantly longer median QTc interval. Compared with LQT2 patients, the onset age of LQT1 (19[15, 26] vs. 6[1, 8], P<0.05) and LQT3 (19[15, 26] vs. 5[2, 15], P<0.05) was earlier. Treatment strategies involved no active therapy in 57 (51%) patients and beta-blockers combined of mexiletine, LCSD or ICD in 55 (51%) patients. Mexiletine shortened the QT interval in 8 patients with potassium channel-mediated LQTS (531 [499, 598]ms vs. 473 [456, 503]ms, P<0.05). LCSD shortened the QT interval (528[497, 582] vs. 513[482, 521], P=0.16) and reduced the event burden (0.36[0.14, 2.14] vs. 0[0, 0.28], P=0.03) in 9 patients. Eighteen patients were operated on ICD implantation because of persistent symptoms.

CONCLUSIONS This study sheds light on number of important facets of genetic and clinical characteristics in patients with LQTS in China.

GW31-e0599

Analyses of risk factors for cardiac events recurrence in 38 patients with symptomatic long QT syndrome

Kun Li, Ping Zhang
Cardiology Department, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University

OBJECTIVES To evaluate the main causes of cardiac event recurrence in symptomatic long QT syndrome (LQTS) patients during follow-up.

METHODS As a retrospective cohort study, clinical characteristics were reviewed from 38 symptomatic LQTS with recurrent cardiac events during 2006–2020. Patients were included if they met the following diagnostic criteria for LQTS using the 2015 European Society of Cardiology guidelines and only gene positive patients were finally included in the study. LQTS-related cardiac events were defined as arrhythmogenic syncope, ICD shock, aborted cardiac arrest (ACA), sudden cardiac death (SCD) or TdP.

RESULTS Main recurrent cardiac events included syncope (27), ICD shock (5), ACA (2), SCD (4) and ventricular tachycardia during exercise test (1). During the follow-up, the main causes for the recurrence of cardiac events were drug withdrawal or drug leakage (18/38), followed by some patients who still suffered from specific inducements (13/38) under the condition of taking medicine regularly, 1 female patient suffered from syncope during pregnancy, and 2 patients suffered from inappropriate ICD shock. Totally, 34 patients were treated with β-blocker, and some patients were not effective with metoprolol. Two children with Jervell and Lange Nielson syndrome (JLNS) had recurrent syncope after regular administration of β-blocker, while left cardiac sympathetic denervation (LCSD) could significantly alleviate the symptoms of patients.

CONCLUSIONS Medication withdrawal is an important cause of the recurrence of cardiac events. Close follow-up and timely adjustment of drug treatment will help patients to reduce the recurrence of cardiac events. Patients with poor drug effect can consider LCSD, or even ICD. Regular drug administration and avoiding specific incentives are of vital importance for reducing the recurrence of cardiac events.

GW31-e0600

Mexiletine in the treatment of patients with potassium channel-mediated long QT syndrome

Kun Li, Ping Zhang
Cardiology Department, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University

OBJECTIVES Long QT syndrome (LQTS) is a genetically transmitted cardiac channelopathy that can lead to lethal arrhythmia and sudden cardiac death (SCD). Considerable proportion of the SCD and aborted cardiac arrest (ACA) cases associated with beta blocker intolerance or ineffectiveness. Mexiletine is often utilized for sodium channel-mediated type 3 long QT syndrome (LQT3) patients. The aim of the study is to investigate the potential role of mexiletine in patients with potassium channel-mediated long QT syndrome.

METHODS We performed a retrospective chart review on 8 genetically established potassium channel-mediated LQTS patients, who received mexiletine. Data were collected on symptomatic status, treatments, and breakthrough cardiac events before and after initiation of treatment. Additionally, 12-lead ECGs and 24-hour holter were collected before and after initiation of mexiletine to evaluate the drug's effect on QTc.

RESULTS Before initiation of mexiletine, all patients were symptomatic, including 4 patients experienced ≥1 breakthrough cardiac event on beta-blocker and 4 patients for failure to tolerate beta-blocker. Age at first syncope was 13.25±9.39 years, while the mean age at first mexiletine dose was 24.0±10.07 years. After mexiletine, the median QTc decreased from 552.4±20.05 ms premexiletine to 476.7±8.91 postmexiletine (P<0.01) for all patients. Clinical symptoms and quality of life were improved in 5 (62.5%) patients. And mexiletine didn't reduce the annual event burden of 3 (37.5%) patients (1, 2 and 5). Seven (88%) patients experienced recurrent cardiac events and ICD were implanted in 6 of them for preventing SCD.

CONCLUSIONS Our research showed mexiletine is a promising concomitant or alternative choice for managing patients with potassium channel-mediated LQTS. And although mexiletine was highly effective in shortening QTc interval and reducing event burden, close follow-up is essential because of the high recurrence rate of cardiac events. ICD is recommended for patients with high SCD risk.

GW31-e0639

Age and gender-related differences in PR interval: results from China national survey of ECG parameters

Yifang Yuan[1], Tingting Lv[1], Yangfeng Wu[2], Huijuan Li[2], Jihong Guo[3], Jing Ynag[1], Xingjie Li[4], Yingxian Sun[5], Xuewen Li[6], Zheng Zhang[7], Xiaoshu Cheng[8], Lirong Wu[9], Xuerui Tan[10], Bing Han[11], Zhaoguo Zhang[12], Hua Li[1], LingYun Kong[1], Yanfang Wang[2], Jiayu Wang[2], Ping Zhang[1]
[1]Cardiology of Department, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University
[2]Peking University Clinical Research Institute
[3]Department of Cardiology, Peking University People's Hospital
[4]Jining NO. 1 People's Hospital
[5]The First Hospital of China Medical University
[6]Shanxi Academy of medical Sciences, Shanxi Dayi Hospital
[7]The First hospital of Lanzhou University
[8]The Second Affiliated Hospital of Nanchang University
[9]The Affiliated Hospital of Guiyang Medical College
[10]Department of Cardiology, the First Affiliated Hospital of Shantou University Medical College
[11]Xuzhou Central Hospital
[12]Beijing Sijiqing Hospital

OBJECTIVES PR interval carried important prognostic information for prediction of cardiovascular disease. Prolonged PR interval was shown to be strong predictors for atrial fibrillation, stroke and all-cause mortality. However, few studies reported age- and gender-related differences of PR interval. We examined age-gender interaction for PR interval in general Chinese population enrolled in a China National Survey of ECG Parameters.

METHODS A multi-stage, stratified cluster sampling across China was performed to select the representative Chinese adults aged 18–85 years old. PR interval were measured using Marquette 12SL algorithm in MUSE Cardiology Information System (GE Healthcare, USA). Demographic variables, including age and gender was confirmed by information on ID card. Age was treated as both continuous variable and categorical variable. Age group was defined as below: <35, 35–45, 45–55, 55–65, ≥65. Distribution of short (PR<120 ms) and prolonged (PR>200 ms) PR interval was reported by age and gender groups.

Spline curve for the association between age and PR interval was plotted by gender to explore non-linear relationship. General linear regression model was constructed to assess the association between age and PR interval for each gender. If non-linear relationship was detected, piecewise linear model was applied for easier interpretation in clinical practice. Knots were identified according to the univariate exploratory curve. All models were adjusted for heart rate, blood pressure, body mass index (BMI), history of cardiovascular disease and clinical center.

RESULTS After an exclusion of missing value, 10,466 participants with 54% women and a mean age of 48±15 years old were finally included from the nationwide study. PR interval was normally distributed with a mean of 150±20 ms. Prevalence of prolonged PR ranged from 1.5 to 3.3% for men (overall 1.8%) and 0.4–1.8% for women (overall 0.9%) across age groups (P<0.05). Prevalence of short PR interval ranged from 2.5 to 4.8% for men (overall 3.6%) and 4.3–9.5% for women (overall 6.1%) across age groups (P<0.05). Men had longer PR interval, compared with women (153±20 ms versus 147±20 ms, P<0.0001). In multivariate model, PR interval increased with age in men (β=0.19, 95% CI 0.15–0.24, P<0.0001). Women had similar pattern before 55-year-old (β=0.20, 95% CI 0.14–0.26, P<0.0001). A flattening pattern was observed in women after 55, with an increment of 0.001 ms per year. When age was analyzed as categorical variable, men showed smaller differences for adjusted mean in PR interval between 55–65 and ≥65 years of age group (men vs. women: –2.85 (95% CI –5.88–0.19) versus –0.64 (95% CI –3.30, 2.00).

CONCLUSIONS Men had longer PR interval than women. PR interval increased with aging in men. For women, this increasing pattern became flat from middle age. Future study is warranted for the pathophysiological mechanism of this non-linear pattern in women.

GW31-e0641

The impact of atrial fibrillation types on the risk of stroke in patients hospitalized with non-valvular atrial fibrillation: findings from CCC-AF project

Yongchen Hao[1], Jing Liu[1], Jun Liu[1], Na Yang[1], Yuhong Zeng[1], Sidney C. Smith Jr.[2], Yong Huo[3], Gregg C. Fonarow[4], Junbo Ge[5], Kathryn A. Taubert[6], Louise Morgan[7], Changsheng Ma[8], Yaling Han[9], Dong Zhao[1]
[1]Department of Epidemiology, Beijing An Zhen Hospital, Capital Medical University, Beijing Institute of Heart, Lung and Blood Vessel Diseases, Beijing, China
[2]Division of Cardiology, University of North Carolina, Chapel Hill, NC, USA
[3]Department of Cardiology, Peking University First Hospital, Beijing, China
[4]Division of Cardiology, Geffen School of Medicine at University of California, Los Angeles, CA, USA
[5]Department of Cardiology, Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital, Fudan University, Shanghai, China
[6]Department of International Science, American Heart Association, Basel, Switzerland
[7]International Quality Improvement Department, American Heart Association, Dallas, TX, USA
[8]Department of Cardiology, Beijing An Zhen Hospital, Capital Medical University, Beijing, China
[9]Cardiovascular Research Institute and Department of Cardiology, General Hospital of Northern Theater Command, Shenyang, Liaoning, China

OBJECTIVES There is controversy on the relationship between types of non-valvular atrial fibrillation (NVAF) and risk of stroke. This study aims to investigate whether types of NVAF is associated with stroke risk during hospitalization.

METHODS The Improving Care for Cardiovascular Disease in China (CCC) – AF project is an ongoing nationwide registry of the American Heart Association and Chinese Society of Cardiology, with 240 participating hospitals reporting clinical information on management and in-hospital outcomes of patients hospitalized with NVAF. We compared in-hospital stroke event rates between paroxysmal NVAF (n=21,289) and sustained (persistent or permanent) NVAF (n=20,059) enrolled from February 2015 to December 2019.

RESULTS Patients with sustained NVAF were older, more likely to have hypertension, diabetes mellitus, valvular disease, previous stroke, and heart failure than patients with paroxysmal NVAF. There were 350 stroke events during the hospitalization. The crude event rate was higher among the patients with sustained NVAF (1.07%) than among those with paroxysmal NVAF (0.63%, P<0.01). After adjusting for CHA_2DS_2-VASc score components, the association between types of NVAF (sustained vs. paroxysmal NVAF) and stroke risk during hospitalization was no longer observed (adjusted odds ratio, 1.23; 95% confidence intervals: 0.98–1.54, P=0.074).

CONCLUSIONS The observed stroke event rate was higher in sustained NVAF than in paroxysmal NVAF. However, after adjusting for CHA_2DS_2-VASc score components, sustained and permanent NVAF patients had similar risk of stroke. The observed higher in-hospital stroke event rate in sustained NVAF was mainly attributable to worse clinical profiles of these patients.

GW31-e0644

Efficacy of upgrading to left bundle branch pacing in patients with heart failure after right ventricular pacing

Zhiyong Qian, Jiangang Zou
Jiangsu Province Hospital

OBJECTIVES Chronic right ventricular (RV) pacing is associated with an increased incidence of heart failure and mortality. Left bundle branch (LBB) pacing could produce near-physiological electrical activation and mechanical synchrony. We aimed to report the effects of upgrading to LBB pacing in heart failure patients after chronic RV pacing.

METHODS The indications included pacing-induced cardiomyopathy (PICM) in Group 1 and heart failure after RV pacing with left ventricular ejection fraction (LVEF) ≥50% in Group 2. LBB pacing was achieved by penetrating the pacing lead to the sub-endocardium of left-side interventricular septum through the venous access. Left ventricular activation time (LVAT) was measured from the pacing stimulus to the ascending peak of lead V5 or V6. All patients underwent clinical and echocardiographic evaluations before and after upgrading.

RESULTS Totally 27 patients (13 in Group 1 and 14 in Group 2) were consecutively enrolled. The mean follow-up time after upgrade was 10.4±6.1 months. Paced QRS duration was significantly shortened from 174.1±15.8 ms to 116.6±11.7 ms (P<0.0001). The mean LVAT was 83.2±11.7 ms. LVEF increased from 40.3±5.2% before upgrading to 48.1±9.5% at follow-up in patients with PICM. Serum N-terminal pro-brain natriuretic peptide levels decreased and New York Heart Association classification improved in both groups. No upgrade-related complications were observed.

CONCLUSIONS Upgrading to LBB pacing was feasible and effective with improved cardiac function in heart failure patients with both reduced and preserved LVEF after RV pacing.

GW31-e0656

Clinical characteristics and drug selection strategy of arrhythmia in neonates with mothers with autoimmune diseases

Xi Yang, Jia Li, Ying Su, Jiqiu Wang, Guiying Liu
Department of Pediatrics, Beijing Anzhen Hospital, Capital Medical University

OBJECTIVES To investigate the clinical characteristics and drug selection strategies of arrhythmia in neonates with mothers with autoimmune diseases.

METHODS The clinical manifestations, laboratory tests and treatment of arrhythmia in newborns with mothers with autoimmune diseases who were hospitalized in Anzhen Hospital affiliated to Capital Medical University from January 2016 to January 2019 were analyzed.

RESULTS Between January 2016 and January 2019 treated 135 cases of neonatal arrhythmia except premature infants and children with structural heart disease, 33 cases (24.4%) of the newborn mothers were complicated with autoimmune diseases, including 7 cases of mixed connective tissue disease, 6 cases of systemic lupus erythematosus (SLE), 5 cases of Sjgren's syndrome, 3 cases of undifferentiated connective tissue disease, 10 cases of Hashimone's thyroiditis and 2 cases of Grave's disease. All children with cardiac arrhythmia within 72 hours after birth, compared with the newborns with mother without autoimmune disease, neonatal group of children with autoimmune mother ominous higher incidence of arrhythmia (23/33 vs. 13/102), since paroxysmal supraventricular tachycardia is most commen in the children with autoimmune mothers (19/23), followed by atrioventricular block (12/23), atrial flutter (3/23), sinoatrial block (3/23), atrial tachycardia (2/23), ventricular tachycardia (2/23), atrial fibrillation (1/23), frequent ventricular bigeminy (1/23). There were 9 cases (12/23) with alternating tachyarrhythmia, and there was no statistical difference in MMB, TnI and BNP between the two groups. All children with treatment for the primary disease, the mother is not associated with autoimmune diseases group of neonatal arrhythmia disappeared, and mother neonatal autoimmune disease group of benign arrhythmia disappeared, with ominous arrhythmia of 23 cases were treated with hormone, of which 8 cases of children with rapid arrhythmia were eased, 15 cases with rapid arrhythmia after hormone still exists, to the beta blockers (metoprolol) treatment, 9 cases of children with rapid arrhythmia were eased, 6 cases of children with ease is not ideal, to switch to propranolol treatment, 1 case still had intermittent supraventricular tachycardia and was treated with propafenone 5 days later. During betaloc administration, 1 case developed intermittent torsion ventricular velocity and was changed to slow static propafenone (1 mg/kg times) transposion, followed by oral propafenone to prevent seizures.

CONCLUSIONS The rate of non-benign arrhythmia is higher in the newborns with mothers with autoimmune diseases, and the arrhythmia type is mostly bradyarrhythmia simultaneously or alternately, or multiple arrhythmias successively. When tachyarrhythmia appears at the same time or alternately, it is mainly to treat the primary disease. Since the newborns with mothers with autoimmune diseases have non-benign arrhythmia, hormone therapy should

be added. Anti – arrhythmia drugs should be carefully selected, in the presence of rapid arrhythmia, should be careful with digitalis drugs, the first choice of beta blockers.

GW31-e0734

Comparison of cardiac function between left bundle branch pacing and right ventricular outflow tract septal pacing in the short-term: a registered controlled clinical trial

Qian Liu, Ruiqin Xie
The Second Hospital of Hebei Medical University

OBJECTIVES The purpose of this study was to compare the changes in cardiac function (especially in brain natriuretic peptide (BNP) levels, left atrial function, and left ventricular diastolic function) within 7 days between LBBP and RVOP.

METHODS A single-centre prospective controlled registered clinical study was conducted with 84 patients with bradycardia indications. Forty-two patients underwent RVOP, and 42 patients underwent LBBP. The pacemaker parameters were adjusted so that the ventricular ratio was over 90% and rate was 60–70 bpm. The changes in BNP levels and echocardiogram and speckle-tracking echocardiography findings were compared between the two groups before and within 7 days after implantation.

RESULTS (1) BNP: there was no significant difference in BNP level between the two groups before and 1 day after implantation, while the LBBP group had significantly lower levels than the RVOP group on day 7 [(65.15±56.96) pg/mL vs. (129.82±101.92) pg/mL, P<0.001]. (2) Cardiac echocardiography: the e′ value of the LBBP group was higher than that of the RVOP group 7 days after implantation [(6.39±2.65) cm/s vs. (5.45±1.35) cm/s, P=0.049]. The E/e′ and peak E-wave velocity in the LBBP group decreased significantly after 7 days [16.57±6.55 vs. 12.75±5.16 P=0.043, (88.6±24.37) cm/s vs. (75.68±28.10) cm/s P=0.030]; in contrast, there were no significant changes in the RVOP group [14.13±3.85 vs. 14.10±4.85 P=0.50, (77.33±21.14) cm/s vs. (74.45±23.03) cm/s P=0.56). (3) Speckle-tracking echocardiography: there was no significant difference in left atrial strain or the strain rate between the LBBP and RVOP groups, but the absolute values of left atrial strain and strain rate in the LBBP group increased, while those in the RVOP group decreased.

CONCLUSIONS This study demonstrates that compared to RVOP, LBBP can increase left ventricular early diastolic function, improve BNP levels, and has a tendency to increase left atrial myocardial elasticity and left atrial strain capacity in the short term in pacemaker-dependent patients.

GW31-e0741

Left ventricular non-compaction is a potential cardiac events predictive factor of long QT syndrome and catecholaminergic polymorphic ventricular tachycardia

Jing Yang, Ping Zhang
Beijing Tsinghua Changgung Hospital

OBJECTIVES This study sought to determine the prevalence of co-phenotype of LVNC in geneticallypositive LQTS and CPVT patients, and evaluated its association with cardiac events.

METHODS Patients genetically established LQTS/CPVT enrolled in our study performed echocardiography or/and CMR examinations and were defined as LCNV co-phenotype patients based the diagnosis criteria of LVNC. A retrospective chart review of clinic, electrocardiograms (ECG), echocardiography, treatment and genetic assessment of the co-phenotype patients were performed.

RESULTS Seven patients (7/128, 5.5%) corresponded to diagnosis criteria of LVNC, including 2 LQT2 (KCNH2 T273M), 1 LQT7 (KCNJ2 V93I), 1 had both LQT2 and LQT3 (KCNH2 G626S; SCN5A A1428S), 1 JLNS (KCNQ1 R174C), and 2 with CPVT1 (RyR2 R2401H, RyR2 E4005V). Sinus bradycardia, frQRS and malignant ventricular tachycardia were recorded in series of electrocardiograms or electrophysiological examinations. Echocardiography revealed a normal EF% estimated at 64.2±8.3%, and maximum ratio of non-compacted and compacted myocardium thicknesses (NC: C ratio) in the end of diastole was 2.34±0.3/1. Medication was received in all patients with beta-blocker (n=6) and/or mexiletine (n=3)/flecainide (n=1). Only two patients received ICD implantation and one received dual chamber pacemaker because of unacceptable ICD. The median time of clinical follow-up was 25 months, 6 proband patients (85.7%) experienced symptomatic cardiac events, which including 2 patients experienced one syncope with appropriate ICD discharge after sustained ventricular arrhythmia and 4 patients (57.1%) died from a cardiovascular cause after medication leakage.

CONCLUSIONS Low incidence of co-phenotype LVNC showed in LQTS and CPVT patients and LVNC can potentially provide important prognostic information for the risk stratification of patients with LQTS/CPVT patients.

GW31-e0805

The effect of left atrial remodeling after cryoballoon ablation and radiofrequency ablation for paroxysmal atrial fibrillation

Wang Xule, Song Beibei, Qiu Chunguang, Han Zhanying, Wang Xi, Lu Wenjie, Chen Xiaojie, Chen Yingwei, Pan Liang, Sun Guoju, Qin Xiaofei, Liran
The First Affiliated Hospital of Zhengzhou University

OBJECTIVES Atrial remodeling is considered pivotal to the occurrence and development of AF, therefore we sought to assess the influence of atrial remodeling in patients with paroxysmal AF after CBA and RFA in this study.

METHODS In this nonrandomized retrospective observational study, we enrolled 328 consecutive patients who underwent CBA or RFA for refractory paroxysmal AF in May 2014-May 2017 in our hospital. After propensity score matching, 96 patients were included in the CBA group, and 96 were included in the RFA group. Patients were asked to undergo a 12-lead electrocardiogram, a 24-h Holter monitor, and an echocardiogram and to provide their clinical history and symptoms at 6 months and 1, 2, and 3 years postprocedurally. Electrical remodeling of the left atrium was assessed by P wave dispersion (Pdis); structural remodeling was assessed by the left atrium diameter (LAD) during scheduled visits.

RESULTS As of January 2020, compared with baseline, at 1 year, 2 years and 3 years after ablation, the average changes in Pdis (ΔPdis) and LAD (ΔLAD) were significant in both the CBA and RFA groups. Six months after ablation, ΔPdis and ΔLAD were greater in the CBA group than in the RFA group. There was no significant difference between the two groups in ATa recurrence, but the survival time of CBA group may be longer than RFA group after 2 years after ablation. A higher ΔPdis and a higher ΔLAD at 1 year after ablation increased ATa-free survival.

CONCLUSIONS Although CBA and RFA are both effective in left atrial electrical and structural reverse-remodeling in paroxysmal AF, CBA may outperform RFA for both purposes six months after ablation. However, during long-term follow-up, there was no significant intergroup difference.

GW31-e0866

The influence of plasma BNP and atrial structure and function after radiofrequency ablation of idiopathic frequency premature contractions in different origins

Liheng Ma, Miaomiao Pei, Wenwen Cui, Ruiqin Xie
The Second Hospital of Hebei Medical University

OBJECTIVES To evaluate the changes of function of left and right atrium and BNP level after radiofrequency catheter ablation (RFCA) and the influence of different original frequent premature ventricular contractions (PVC) on left and right atrial function before and after RFCA.

METHODS A total of 62 inpatients with frequent PVC observed on 24 h Holter monitoring (>10%) and successful RFCA were included in this study in the Second Hospital of Hebei Medical University from Mar. 2018 to Nov. 2019. Among them 23 patients with frequent PVC originated from the left ventricle and 39 originated from the right ventricle. Function of Left and right atrial and BNP level were measured by echocagdiography and BNP quantitative detector before RFCA and after RFCA at 1 day, 1 month, 3 month and 9 month (±3 month), collecting 32 healthy people in the same time, to investigate whether there was a difference between groups.

RESULTS 1. Left atrial diameter (LAD) in right ventricle group and left ventricle group before RFCA were significantly higher than those in control group, while LAD in right ventricle group and left ventricle group were decreasing in 9 month (±3 month) after RFCA. 2. Right atrial ejection fraction (RAEF) in right ventricle group and left ventricle group before RFCA were significantly lower than those in control group. Meanwhile, RAEF in right ventricle group after RFCA was gradually improved. 3. With the significant reduction in PVC load after surgery in both treatment groups, the left atrial strain in the groups was significantly higher than before surgery, and S, SRe, and SRa in the right ventricular source group were significantly higher than those in the left ventricular source group. 4. BNP in right ventricle group and left ventricle group before RFCA were significantly higher than those in control group, while BNP in right ventricle group and left ventricle group were decreasing in 9 month (±3 month) after RFCA.

CONCLUSIONS 1. Simple frequent PVC beats can increase the diameter of the left atrium, significantly reduce the strain of the left and right atria, the diameter and strain could gradually improve after RFCA. Besides the right ventricle-derived ventricle has a significant effect on the left atrium, and left ventricle-derived ventricle has a significant effect on the right atrium. 2. Frequent ventricular premature beats potentially increase plasma BNP levels in patients with normal cardiac function, and reduce plasma BNP after effective catheter ablation treatment. Plasma BNP maybe used to evaluate the severity, development and prognosis of patients with ventricular premature contraction.

GW31-e0873

The relationship between mean ventricular heart rate of dynamic electrocardiogram and all-cause mortality among patients with non-valvular atrial fibrillation and without coronary artery disease

Zefeng Chen, Lin Chen
Department of Cardiovascular Medicine, The Third Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES To investigate the relationship between mean ventricular heart rate of dynamic electrocardiogram and all-cause mortality among patients with non-valvular atrial fibrillation and without coronary artery disease.

METHODS One hundred sixty-eight patients with non-valvular atrial fibrillation and without coronary artery disease at the Third Affiliated Hospital of Sun Yat-sen University between October 2012 and July 2016 who underwent dynamic electrocardiogram were enrolled. Patients were divided into 2 groups based on mean heart rate of dynamic electrocardiogram (Group A: mean heart rate no higher than 80 b.p.m. and Group B: mean heart rate higher than 80 b.p.m.). The median following up time was 28 months and all-cause mortality was recorded. Propensity score matching was used to control confounding factors and then the relationship between mean heart rate and all-cause mortality was investigated.

RESULTS In this atrial fibrillation population, all-cause mortality is statistically lower in group A (mean heart rate no higher than 80 b.p.m.) then group B (mean heart rate higher than 80 b.p.m.) (OR=0.282, 95% CI: 0.082–0.974, P=0.043).

CONCLUSIONS Mean heart rate of dynamic electrocardiogram no higher than 80 b.p.m. predict a lower all-cause mortality in patients with non-valvular atrial fibrillation and without coronary artery disease.

GW31-e0910

Inflammatory response after different ablation strategies for paroxysmal atrial fibrillation

Guangli Yin[1,2], Bofei Ma[1], Ruiqin Xie[1]
[1]Department of Cardiology, The Second Hospital of Hebei Medical University, Shijiazhuang 050000, China
[2]Department of Cardiology, Cangzhou Hospital of Integrated TCM-WM Hebei, Cangzhou 061000, China

OBJECTIVES Atrial fibrillation (AF) has increasingly aroused the concern of the world. The biggest harm of AF is cerebral apoplexy, thus impairing quality of life. Current therapy of catheter ablation of AF as an effective means of converting and maintaining sinus rhythm of AF is playing an important role. Catheter ablation for AF include Radiofrequency catheter ablation (RFCA); Cryoballoon catheter ablation (CBCA), etc. Catheter ablation for AF, an important therapeutic modality for patients with AF, is known to cause an increase in several inflammation markers.1,2 Inflammation is increasingly recognized to play a significant role in the genesis and perpetuation of AF.3 however, the changes in the trends of inflammatory response markers and their ability to predict AF recurrence in patients treated with different catheter ablation strategies over time remain unknown.

METHODS A total of 210 patients with AF were enrolled and grouped according to the ablation modality as follows: freeze group, radiofrequency group (RF group), and freeze3D group. White blood cells (WCC) and high-sensitivity C-reactive protein (hs-CRP) were measured. The inflammation indices were measured before ablation and at 1, 2, 3 days and 1, 2, 3, and 4 weeks and 2 and 3 months after ablation. To determine AF recurrence during follow up, 24-h ambulatory electrocardiography was performed at 2, 3, 6, and 12 months after ablation.

RESULTS The inflammation indices of the three groups including WCC, percentage of neutrophils (NE%), neutrophil absolute value (NE num), neutrophil-to-lymphocyte ratio (NLR) and hs-CRP peaked between 1 and 3 days after ablation but decreased at different time points (P<0.05). The recurrence rate of paroxysmal atrial fibrillation (PAF) was positively correlated with the increase in NE% and white blood cells after ablation (P<0.05).

CONCLUSIONS Recently, the emerging cryo-3D ablation technique combines the advantages of both RFCA and CBCA and can isolate the circumferential pulmonary vein and perform complementary ablation against the hypertrophic site of the myocardium simultaneously, thereby reducing the recurrence rate of AF.4 The postoperative inflammation indices peaked and decreased at different time points after different ablation strategies. Additionally, the recurrence rate of AF after ablation in patients treated with freeze3D was lower.

GW31-e0950

Different effect of plasma homocysteine levels on one-year atrial fibrillation recurrence after radiofrequency catheter ablation

Jianqiang Zhao, Liangrong Zheng
Department of Cardiology and Atrial Fibrillation Center, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China

OBJECTIVES Circumferential pulmonary vein isolation (CPVI) has emerged as a cornerstone in the treatment of drug-resistant AF. However, patients remain at high risk for AF recurrence after catheter ablation. The relationship between homocysteine (Hcy) levels and AF recurrence has yet to be determined. Therefore, the aim of the study is to assess the association and the predictive value of plasma Hcy with the one-year AF recurrence rate in patients after radiofrequency catheter ablation (RFCA).

METHODS This study included 499 consecutive patients with AF who underwent RFCA. Plasma Hcy levels were quantitatively determined before catheter ablation. The one-year AF recurrence rate was documented. Cox regression analysis was used to evaluate the association of Hcy levels with the one-year AF recurrence rate.

RESULTS During one-year follow-up, 119 (23.8%) patients experienced AF recurrence. Patients with AF recurrence were more likely to be persistent AF (P=0.003) and larger LAD (3.94±0.60 vs. 4.05±0.76 cm, P=0.038) and have different levels of plasma Hs-CRP (P=0.036). The Hcy levels values were categorized into 2 μmol/L increments in the following manner: <10, 10–12, 12–14, 14–16, >16 μmol/L and there were significant differences in recurrence rate among different groups (P=0.044). The unadjusted HR for AF recurrence compared group (Hcy level 10–12 μmol/L) were 0.55 (95% CI: 0.32–0.94), 0.60 (95% CI: 0.36–1.00), 0.53 (95% CI: 0.29–1.95) and 0.51 (95% CI: 0.30–0.87), for each group. The adjusted HRs were 0.54 (95% CI: 0.31–0.93), 0.59 (95% CI: 0.36–0.99), 0.47 (95% CI: 0.26–0.86) and 0.51 (95% CI: 0.30–0.87), for each group. In younger patients (≤60 years), Hcy had better predictive effect (P=0.015), and had no significant difference (P=0.887) in older patients (>60 years).

CONCLUSIONS Patients with 10–12 μmol/L Hcy had the highest AF recurrence and AF recurrence was reduced with<10 μmol/L or ≥12 μmol/L Hcy. In younger patients (≤60 years), Hcy had better predictive effect on AF recurrence.

GW31-e0951

Feasibility of the coronary computed tomography angiography examinations in patients with atrial fibrillation using a novel dedicated cardiovascular CT system: initial clinical experience with CardioGraphe

Jiaxin Cao, Yi He
Beijing Friendship Hospital, Capital Medical University

OBJECTIVES Patients with atrial fibrillation (AF) were regarded as a challenge for coronary computed tomography angiography (CCTA). We aimed to evaluate the clinical performance of a novel dedicated cardiovascular CT system in patients with AF.

METHODS A total of 52 patients with suspected coronary artery disease, including 30 patients with persistent AF (Group A) and 22 patients with sinus rhythm (Group B), underwent CCTA on a 560-slice Stereo CT (CardioGraphe™, GE healthcare). Image data was transferred to a advanced workstation (AW4.6) for post-reconstruction. Image quality was assessed subjectively by Likert scale and objectively by SNR, CNR. Two experienced radiologists who were blinded to the electrocardiograph, independently graded the CT images in terms of visibility and artifacts with a 4-grade rating scale (4, excellent; 3, good; 2, poor; 1, insufficient) on per-segment, per-vessel and per-patient level. SNR and CNR were calculated based on the mean CT attenuation values and standard deviation within 3 regions of interest placed in the proximal left main and proximal right coronary artery. THE CNR and SNR of two groups were compared using independent-sample T-test. The image quality of two groups were compared using Wilcoxon rank-sum test.

RESULTS The two groups are matched in BMI (P>0.05). Mean HR and HR variability during acquisition were 94.87±45.414 and 89.03±51.49 bmp in Group A, which were significantly higher than 64.36±8.856 and 8.73±14.907 bmp in Group B (P<0.05). No significant differences were observed in CNR, SNR (P>0.05). Subjective image quality score was not significantly different between group A and group B in vessel-based (3.6±0.5 vs. 3.5±0.7, P>0.05) or patient-based analysis (3.7±0.5 vs. 3.6±0.5, P>0.05).

CONCLUSIONS CCTA examinations using the novel dedicated cardiovascular CT system yielded high image quality equally for AF and sinus rhythm patients.

GW31-e1071

Comparison of left bundle branch block correction versus narrow QRS morphology in patients undergoing atrioventricular junction ablation for atrial fibrillation

Shengjie Wu, Mengxing Cai, Weijian Huang
Department of Cardiology, the First Affiliated Hospital of Wenzhou Medical University

OBJECTIVES His-Purkinje Conduction System pacing (HPSP) utilizing His (HBP) or left bundle branch pacing (LBBP) in patients with atrial fibrillation (AF) and wide QRS duration has not been well studied. We aimed to assess the benefit of left bundle branch block (LBBB) correction during HPSP in AF patients undergoing AVJ ablation with left bundle branch block, compared to those with narrow QRS duration.

METHODS This is an observational study in consecutive patients with typical LBBB or narrow QRS duration (≤120 ms) who had HPSP after AVJ ablation for AF and heart failure with a left ventricular eject fraction (LVEF) ≤50%. Echocardiographic responses and clinical outcomes were assessed at baseline and during 1-year follow-up.

RESULTS A total of 170 patients were enrolled (age 69.3±10.1 years; LVEF 34.3±7.7%), 133 (78.2%) patients had a normal QRS duration and 37 (21.2%) had a LBBB. The QRS duration changed from baseline of 159.7±16.6 ms to paced QRS duration of 103.1±13.6 ms in the LBBB cohort and from 95.6±10.4 ms to 100.8±14.5 ms in the narrow QRS cohort after AVJ ablation and pacing. Compared to the narrow QRS cohort, the LBBB cohort show greater absolute increases in LVEF (+22.3 vs. +14.2%, P<0.001), higher super LVEF responder rate (75 vs. 49.2%, P=0.006) and greater NYHA improvement (−1.9 vs. −1.4, P<0.001) at 1-year.

CONCLUSIONS Patients with LBBB have greater improvement in LVEF and NYHA Class than patients with narrow QRS from HPSP after AVJ ablation.

GW31-e1074

Safety and effectiveness of left bundle branch pacing and right ventricular outflow tract septum pacing

Weilin Jing, Ruiqin Xie
The Second Hospital of Hebei Medical University

OBJECTIVES To evaluate the safety and effectiveness of left bundle branch regional pacing within one year by comparing the pacing parameters, electrocardiogram, cardiac function and surgical related complications between left bundle branch regional pacing and right ventricular outflow tract septum pacing.

METHODS From August 1, 2018 to August 1, 2019, 50 patients who met the indications of artificial permanent pacemaker implantation were selected and divided into two groups. The matching indications were as follows: the operation indications of the two groups were the same before the operation, the cardiac function classification of the New York Heart Association was the same, and the pacing dependence ratio was not different (left bundle branch group, 18/25; right ventricular outflow group, 19/25), There was no significant difference in baseline data between the two groups (P>0.05). The pacing lead parameters, cardiac function indexes, ECG parameters and adverse events were compared between the two groups 6–12 months after operation.

RESULTS Fifty patients were followed up for an average of 9±3 months, including 25 left bundle branch pacing group and 25 right ventricular pacing group. Compared with the right ventricular pacing group, QRS duration of left bundle branch pacing group was significantly shorter immediately and 6–12 months after operation [(104.2±20.3) ms vs. (122.6±23.7) ms, P<0.05] and [(113.5±15.2) ms vs. (119.8±17.3) ms, P<0.05]. In terms of pacing parameters, there was no significant difference in pacing threshold and impedance between the two groups during and 6–12 months after operation. Compared with right ventricular pacing group, BNP in left bundle branch pacing group was significantly lower than that in right ventricular pacing Group [(103.2±114.3) pg/mL vs. (159.7±112.9) pg/mL, P<0.05] and [(81.3±110.1) pg/mL vs. (121.9±104.4) PG/mL, P<0.05]. There were no obvious complications such as pacemaker electrode dislocation and ventricular septal perforation in both groups.

CONCLUSIONS Compared with right ventricular septum pacing, left bundle branch regional pacing is effective and safe within one year, and pacing parameters are stable.

GW31-e1171

The relationship between mean ventricular heart rate of dynamic electrocardiogram and all-cause mortality and all-cause re-hospitalization among patients with non-paroxysmal atrial fibrillation

Zefeng Chen, Lin Chen
Department of Cardiovascular Medicine, The Third Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES To investigate the relationship between mean ventricular heart rate of dynamic electrocardiogram and all-cause mortality and all-cause re-hospitalization among patients with non-paroxysmal atrial fibrillation.

METHODS Three hundred forty patients with non-paroxysmal atrial fibrillation at the Third Affiliated Hospital of Sun Yat-sen University between October 2012 and July 2016 who underwent dynamic electrocardiogram were enrolled. Patients were divided into 2 groups based on mean heart rate of dynamic electrocardiogram (Group A: mean heart rate no higher than 80 b.p.m. and Group B: mean heart rate higher than 80 b.p.m.). The median following up time was 28 months and all-cause mortality and all-cause re-hospitalization was recorded. Propensity score matching was used to control confounding factors (244 patients were matched) and then the relationship between mean heart rate and all-cause mortality/re-hospitalization was investigated.

RESULTS In this atrial fibrillation population, all-cause mortality is statistically lower in group A (mean heart rate no higher than 80 b.p.m.) then group B (mean heart rate higher than 80 b.p.m.) (OR=0.440, 95% CI: 0.227–0.933, P=0.031) while all-cause re-hospitalization is not statistically different between group A (mean heart rate no higher than 80 b.p.m.) and group B (mean heart rate higher than 80 b.p.m.) (OR=0.791, 95% CI: 0.446–1.401, P=0.421).

CONCLUSIONS Mean heart rate of dynamic electrocardiogram no higher than 80 b.p.m. predicts a lower all-cause mortality in non-paroxysmal atrial fibrillation patients.

GW31-e1185

Significant benefit of ablation versus pacing in patients with tachycardia bradycardia syndrome

Rongfeng Zhang, Yunlong Xia
First Affiliated Hospital of Dalian Medical University

OBJECTIVES There remains unclear that whether catheter ablation should be the first-line therapy for tachycardia bradycardia syndrome (TBS). To compare the long-term outcomes between ablation treatment and pacing treatment in TBS patients.

METHODS This study was a retrospective study comparing ablation vs. pacing in patients meeting TBS diagnostic criteria. The primary endpoint was cardiovascular-related hospitalization, stroke or peripheral thrombosis.

RESULTS Among 306 patients enrolled, 141 received ablation and 165 received pacemaker implement. After a median follow-up of 75.4 months, the primary endpoint occurred significantly more frequently in patients in the pacing group than in those in the ablation group (67.2 vs. 15.6%, OR 6.05, 95% CI: 3.73–9.80, P<0.001). Cardiovascular-related hospitalization occurred in 50.9% of the pacing group and 14.2% of the ablation group (OR: 4.87, 95% CI: 2.99–7.95, P<0.001). More thrombosis events occurred in the pacing group than in the ablation group (16.4 vs. 2.1%, OR 6.06, 95% CI: 1.81–20.35, P=0.004). Significantly more patients progressed to persistent atrial fibrillation in the pacing group than in the ablation group (23.6 vs. 2.1%, P<0.001). The NYHA classification of the pacing group was significantly higher than that of the ablation group (2.11±0.83 vs. 1.50±0.74, P<0.001). Significantly more antiarrhythmic drugs used in the pacing group than that in the ablation group (P<0.001).

CONCLUSIONS Ablation for patients with TBS was associated with a significantly lower rate of a composite endpoint of hospitalization for cardiovascular reasons and thromboembolic events than was pacing therapy.

GW31-e1226

Serum human epididymis protein 4 levels in the prediction of the recurrence of atrial fibrillation after catheter ablation

Zhijie Mao, Ya Lin, XiaoKang Hu, YiHe Chen, Weijian Huang, Zhouqing Huang
The Key Laboratory of Cardiovascular Disease of Wenzhou, Department of Cardiology, The First Affiliated Hospital of WenZhou Medical University, WenZhou, ZheJiang, China

OBJECTIVES The aim of this study is to assess serum human epididymis protein 4 (HE-4) levels as a biomarker for predicting the recurrence of atrial fibrillation (AF) after catheter ablation in a prospective cohort of AF patients.

METHODS One hundred eighty-four consecutive nonvalvular AF patients (65 persistent, 119 paroxysmal) who were eligible for their first ablation were enrolled. Multiple Cox proportional hazards models and Kaplan-Meier curve analyses were used to test the association between serum HE-4 levels and AF recurrence after catheter ablation.

RESULTS During the maximum 36-month follow-up, we observed that 56 patients (30.4%) experienced AF recurrence. The patients with AF recurrence had higher serum HE-4 levels than those without recurrence (73.9±39.4 pmol/L vs. 58.3±30.4 pmol/L, P=0.002). The recurrence rate of persistent atrial fibrillation was significantly higher (49.2 vs. 20.2%, P<0.001). Generalized additive models were used to visually assess functional relationships between the serum HE-4 levels and the risk of AF recurrence. When stratified with serum levels as the cut-off value, Kaplan-Meier analysis showed that patients with serum HE-4 levels (>69.5 pmol/L) had a significantly increased risk of AF recurrence. In addition, multivariate Cox proportional hazard modelling revealed that HE-4 (≥69.5 pmol/L) (HR: 1.795; 95% CI: 1.012, 3.187, P=0.046) were independent predictors of AF recurrence.

CONCLUSIONS Serum HE-4 levels in patients with AF are associated with postoperative recurrence of AF, and high HE-4 levels are an independent predictor of AF recurrence after ablation.

GW31-e1230

His bundle pacing upgrades improve the heart performances in patients suffering from pacing-induced cardiomyopathy with or without atrial fibrillation

Kexin Wang, Yiheng Yang, Yingxue Dong
The First Affiliated Hospital of Dalian Medical University

OBJECTIVES The efficacy and safety of His bundle pacing (HBP) and left bundle branch pacing (LBBP) upgrades in patients with pacing-induced cardiomyopathy (PICM) and atrial fibrillation (AF) are still unknown.

METHODS Patients with PICM were continuous enrolled from January 2018 to March 2020 in the first affiliated hospital of Dalian Medical University. The clinical data, including echocardiographic examination parameters, ECG measurements, and New York Heart Association (NYHA) classification, were assessed before and after an HBP upgrade. PICM was defined as RVP dependence (RVP>40%) and new onset left ventricular ejection fraction (LVEF) decreases >10% from baseline resulting in an LVEF of ≤50% without other identifiable causes. Patients with other identifiable causes of heart failure, including myocardial infarction, severe valvular heart disease, arrhythmia-related cardiomyopathy, and long-term uncontrolled hypertension, were excluded. The 4.1F 3830 (SelectSecure, Medtronic, Minneapolis, MN) pacing lead was delivered using the C315HIS (Medtronic, Minneapolis, MN) sheath. His bundle electrograms were mapped in a unipolar configuration and recorded on the recording system (Prucka Cardiolab, GE Healthcare, Waukesha, WI). To locate the optimal site for the His bundle lead, the shethes and leads were delivered to the ventricular end for the distal HBP/LBBP, and the pacing rate was decreased to 30 bpm for an escape rhythm. If no His electrogram was observed, pace mapping was conducted to identify a site with evidence for His bundle capture. His bundle pacing was acceptable when capture threshold was lower than 2.0 V/1.0 ms. For the patients with third-degree atrioventricular block (III° AVB) and the threshold of his bundle pacing is more than 2.0 V/0.5 ms, the right ventricular backup pacing was retained. If HBP failed or the ventricular escape rhythm was found, we would try LBBP. Patients were followed up in the cardiology and device clinic and at 1, 3, and 6 months and at 1 year. Clinical data, including the LVEF, QRS duration, device programming information and echocardiography parameters, were recorded at each visit. The New York Heart Association (NYHA) class was assessed at baseline during follow-up.

RESULTS After HBP implantation (during a median follow-up of 115 (1–484) days), 2 patients died from acute exacerbation of heart failure. The LVEF significantly increased from baseline 34.6±8.56% to 44.80±7.63% (P<0.001, Figure 3A). The LVEDD was reduced to 52.89±5.8 mm (P<0.01, Figure 3C). The NYHA functional class improved to 1.96 from 2.56 at baseline during follow-up (P<0.001). Furthermore, the paced QRSd markedly decreased from 184.2±23.76 ms at baseline to 120.5±16.67 ms with HBP (P<0.001, Figure 3B). Further, these improvements also observed in AF and non-AF subgroup. Over a median follow-up period of 115 (1–484) days, the threshold of the His bundle lead increased from baseline 0.94±0.44 mv@0.4 ms to 1.11±0.83 mv@0.4 ms (P=0.89, Figure 3D) but not significantly. However, there was no significant difference in the improvement of the LVEF between the patients with or without AF (11.5±7.67% vs. 13.67±6.07%, P=0.434). The improvements of LVEDD, QRS duration also had no significant difference between the AF and non-AF subgroup (Figure 4).

CONCLUSIONS HBP and LBBP upgrades improved the heart performance and reversed the left ventricular remodeling in patients suffering from PICM with or without AF significantly, and it should be actively consideration in patients with PICM.

GW31-e1239

The relation between serum homocysteine and uric acid and the risk of device detected subclinical atrial fibrillation in patients with cardiac implantable electronic devices

Shihao Wang, Yunsong Wang, Yunlong Xia
The First Affiliated Hospital of Dalian Medical University

OBJECTIVES Increased serum homocysteine (Hcy) and uric acid (UA) are both considered risk factors for cardiovascular diseases. The presence of Cardiac Implantable Electronic Devices (CIEDs) detected Subclinical Atrial Fibrillation (SCAF) has been related to increased risk of stroke, systemic embolism and cardiovascular mortality. However, their clinical relevance and their predictive role in SCAF has not yet been thoroughly investigated. The objective of this study is to assess their clinical relevance and role in SCAF.

METHODS Patients with CIEDs implanted from 2013 to 2019 from our hospital were collected continuously. Individuals without atrial lead, with prior diagnosis (ECG or Holter monitoring) of atrial fibrillation, atrial flutter and atrial tachycardia, or after replacement of elective unit were excluded. SCAF was defined as episodes lasting >6 min in duration with an atrial rate >190 beats/min detected by CIEDs. The multivariate Cox regression analysis model were used for survival analysis. P<0.05 was considered statistically significant.

RESULTS A total of 1230 patients were included in the study. Considering the gender differential among patients on the metabolism of Hcy and UA, data were analyzed separately for women and men. Over a median follow up of 462 days, 228 (18.5%) presented SCAF episodes ≥6 min. The results showed that serum Hcy and UA levels were significantly elevated in patients with SCAF than those without SCAF, and these associations did not differ by gender (P<0.001). A positive association was significantly found between Hcy and UA levels in males (r=0.11, P<0.001) and females (r=0.11, P=0.006). In in multivariable analyses, a higher level of serum Hcy and UA at baseline were the independent predictors of SCAF in both genders (P<0.001). When we regard Hcy as a continuous variable and UA as a dichotomous variable, (above/below the median), all adjusted Cox interaction model showed that with an increase in 1 SD of Hcy, patients in the higher uric acid group had an elevated risk for SCAF compared the lower group of all genders (in males, P interaction=0.017, in females, P interaction=0.003). These results indicated that their combination might prove reinforcing the risk of SCAF occurrence. Compare with the lower group, participants with both serum Hcy and UA above the median had the highest risk of SCAF (hazard ratio [95% CI] 2.39 [1.35, 4.22], P=0.003 in males and 5.15 [2.53, 10.49], P<0.001 in females).

CONCLUSIONS Elevated serum Hcy and UA increase the risk of device detected SCAF in Patients with CIEDs. Their combination might prove additional increased risk for SCAF. Patients with higher Hcy and uric acid levels should be followed carefully due to more susceptible to SCAF. The underlying mechanisms of this phenomenon remain to be further elucidated.

GW31-e1240

An observational study of long-term outcomes in cancer survivors after permanent pacemaker implantation

Ruiyuan Gao[1], Minghui Yang[1], Yunlong Xia[2]
[1]First Affiliated Hospital of Dalian Medical University
[2]Dalian Medical University

OBJECTIVES Bradyarrhythmia is a significant cardiotoxic side effect of radiotherapy and chemotherapy treatments for cancer patients. Permanent pacemaker implantation (PPI) can improve the clinical outcomes of bradyarrhythmia patients who are not affffected by cancer. However, it is unclear whether cancer survivors benefit from PPI.

METHODS We selected 269 cancer survivors with bradyarrhythmia who were treated with radiotherapy or chemotherapy and were eligible for pacemaker implantation for our study. The patients were screened and a total of 165 survivors (61.3%) were enrolled. Those with sick sinus syndrome (SSS) and atrioventricular blocks accounted for 123 and 42 of the patients, respectively. One hundred fifteen survivors received permanent pacemaker implantation (PPI group) and 50 did not (medical group).

RESULTS Patients with bradycardia had an average survival time of 9.9 months after radiotherapy or chemotherapy. The patients enrolled in our study had the following cancers: digestive system cancer (49.7%), lung cancer (28.5%), and urinary system cancer (14.5%). We compared the all-cause mortality, unplanned hospitalization for any cause, death from cardiovascular disease, and unplanned hospitalization related to cardiovascular disease between the 2 groups. The all-cause mortality was significantly lower in the PPI group than the medical group (17 patients [14.8%] vs. 22 patients [44.0%]; hazard ratio: 0.14; 95% confidence interval [CI]: 0.06–0.30; P<0.001). The number of patients that died from cardiovascular disease was lower in the PPI group (2 [1.7%] vs. 6 [12.0%]; hazard ratio: 0.00; 95% CI: 0.00–0.13; P=0.002), unplanned hospitalization for any cause (61 [53.0%] vs. 34 [68.0%]; hazard ratio: 0.43; 95% CI: 0.26–0.70; P=0.001), or unplanned hospitalization related to cardiovascular disease (24 [20.9%] vs. 19 [38.0%]; hazard ratio: 0.28; 95% CI: 0.13–0.59; P=0.001). The PPI group also had a significantly longer survival time than the medical group (56.5 months vs. 44.4 months, P<0.001). The benefits to the PPI group were significant in the sick sinus syndrome subgroup of patients.

CONCLUSIONS Cancer survivors with bradyarrhythmia and a permanent pacemaker implanted had a significantly lower rate of death from all cause than patients who did not receive a pacemaker.

GW31-e1250

Feasibility and effectiveness of permanent left bundle branch pacing combined with atrioventricular junction ablation in atrial fibrillation patients with heart failure with both preserved and reduced left ventricular ejection fraction

Mengxing Cai[1,2], Weijian Huang[1,2]
[1]Department of Cardiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China
[2]The Key Lab of Cardiovascular Disease of Wenzhou, Wenzhou, China

OBJECTIVES Left bundle branch pacing (LBP) has been demonstrated to result in effective left ventricular synchronization. We aimed to evaluate the long-term performance of LBP combined with atrioventricular junction (AVJ) ablation in patients with AF and symptomatic heart failure.

METHODS From June 2017 to June 2019, consecutive patients with AF and HF who underwent AVJ ablation and LBP were enrolled. Left ventricular ejection fraction (LVEF), New York Heart Association Classification (NYHA), and pacing parameters were assessed at implant and during follow-up.

RESULTS Of 84 patients enrolled (age 69.3±10 yrs; Male 47.6%; Diabetes 29.8%; LVEF 39.2±14.6%), permanent LBP and AVN ablation was successful in 84 (100%) pts. Median follow-up was 15.6 (11.4–20.1) months. LBP as a bailout technique successfully implanted in 39 patients with HBP implantation failure due to high capture threshold (n=19, 48.7%), increased threshold caused by AVJ ablation (n=13, 33.3%), high correct threshold (n=2, 5.1%), high threshold remain failed to correct LBBB or RBBB (n=2, 5.1%), and no recording His potential (n=2, 5.1%), fail to fix the lead in His region (n=1, 2.6%). In the subgroup of pts with reduced LVEF who implanted more than 1-year, the EF improved from 30.9±5.2% at baseline to 47.7±14 at 1-year follow-up (n=54/56, P<0.001). The NYHA class reduced from 3.0±0.5 to 1.5±0.6 (P<0.001). None patient who underwent LBP has increased threshold after ablation (>0.5 V). The implant pacing threshold was 0.48±0.16 V@ 0.5 ms and increased to 0.61±0.17 V@0.5 ms at 1-year follow-up.

CONCLUSIONS LBP combined AVJ ablation is emerging as a necessary bailout technique for difficult HBP following AVJ ablation and have well-pacing parameter at implant and during follow-up. LBP combined AVJ ablation provides a significant improvement in echocardiographic data and clinical outcomes in patients with AF and HF both in HFrEF and HFpEF.

GW31-e1265

Association of plasma C1q/TNF-related protein-3 (CTRP3) in patients with atrial fibrillation

Liwen Chen, Lijie Sun, Ming Cui
Peking University Third Hospital

OBJECTIVES Atrial fibrillation (AF) is a highly prevalent cardiac arrhythmia characterized by atrial remodeling. Complement C1q tumor necrosis factor-related protein 3 (CTRP3) is one of the adipokines associated with obesity, diabetes, and coronary heart disease. The association between plasma CTRP3 levels and AF is uncertain. The aim of this study was to investigate whether plasma CTRP3 concentrations were correlated with AF.

METHODS Our study included 75 AF patients who underwent catheter ablation at our hospital and 47 sinus rhythm patients to determine the difference in plasma CTRP3 concentrations. Blood samples before the ablation were collected and ELISA was used to measure the concentrations of CTRP3.

RESULTS Plasma CTRP3 concentrations were significantly lower in AF patients compared with control group (366.9±105.2 ng/mL vs. 429.1±100.1 ng/mL, P=0.002). In subgroup studies, patients with persistent AF had lower plasma CTRP3 concentrations than those with paroxysmal AF (328.3±83.3 ng/mL vs. 380.0±109.2 ng/mL, P=0.037). The concentrations of plasma CTRP3 in the recurrence group after radiofrequency ablation of AF were lower than those in the non-recurrence group (337.9±77.3 ng/mL vs. 386.6±108.1 ng/mL, P=0.045). Multivariate regression analysis revealed the independent correlation between plasma CTRP3 level and NT-proBNP.

CONCLUSIONS Plasma CTRP3 concentrations were correlated with the presence of AF and AF recurrence.

GW31-e1314

Adherence with cardiovascular medications and the outcomes in patients with coronary arterial disease: 'real-world' evidence

Chen Chen, Wen Zhuo, Kui Hong
Department of Cardiovascular Medicine, The Second Affiliated Hospital of Nanchang University

OBJECTIVES Cardiovascular medications are vital for the secondary prevention of coronary arterial disease (CAD). However, the effect of cardiovascular medication may depend on the optimal adherence of the patients. This meta-analysis aims to determine the magnitude of adherence to vascular medications influences the absolute and relative risks (RRs) of mortality in patient with CAD in real-world settings.

METHODS The Cochrane Library, PubMed, and EMBASE databases were searched through October 1, 2019. Prospective studies reporting association as RR and 95% CI between cardiovascular medication adherence and any cardiovascular events and/or all-cause mortality in patients with CAD were included. A one-stage robust error meta-regression method was used to summarize the dose-specific relationships.

RESULTS A total of 18 studies with 382,350 participants were included. There is a significant inverse linear association between cardiovascular medication adherence and cardiovascular events ($P_{non\text{-}linearity}$=0.68) or mortality ($P_{non\text{-}linearity}$=0.82). The exposure-effect analysis showed that an improvement of 20% cardiovascular medication adherence was associated with 8 or 12% lower risk of any cardiovascular events or mortality, respectively. In subgroup analysis, the benefit was observed in adherence of stain (RR: 0.85 for cardiovascular events, RR: 0.84 for mortality), ACEI/ARB (RR: 0.85 for mortality), and anti-platelet agent (RR: 0.88 for mortality) but not in beta-blocker (RR: 0.91, P=0.14 for cardiovascular events, RR: 0.98, P=0.32 for mortality). Estimated absolute differences per 1 million individuals per year for mortality associated with 20% improvement were 175 cases for statin, 129 cases for anti-platelet, 117 cases for ACEI/ARB.

CONCLUSIONS Evidence from real-word showed poor adherence to vascular medications contributes to a considerable proportion of all CVD events and mortality in patients with CAD.

GW31-e1315

Is atrial fibrillation noninducibility by burst pacing after catheter ablation associated with reduced clinical recurrence? A systematic review and meta-analysis

Hualong Liu, Ping Yuan, Xin Zhu, Linghua Fu, Kui Hong, Jinzhu Hu
Department of Cardiovascular Medicine, the Second Affiliated Hospital of Nanchang University

OBJECTIVES To date, there is no cumulative evidence supporting the association of atrial fibrillation (AF) noninducibility after ablation and freedom from AF. We performed a systematic review and meta-analysis to determine whether AF noninducibility by burst pacing after catheter ablation is associated with reduced AF recurrence.

METHODS We searched PubMed, Embase, Web of Science, and Cochrane Library databases through July 2019 to identify studies that evaluated AF noninducibility versus inducibility by burst pacing after catheter ablation for freedom from AF. A fixed effects model was used to estimate relative risk (RR) with 95% CIs.

RESULTS Twelve prospective cohort studies with AF noninducibility (n=1612) and inducibility (n=1160) were included. Compared with AF inducibility, AF noninducibility by burst pacing after ablation was associated with a reduced risk of AF recurrence (RR, 0.68; 95% CI, 0.60–0.77). Subgroup analysis showed that different AF types (paroxysmal AF and nonparoxysmal AF), different follow-up times (≤6, 6–12, and >12 months), and different degrees of burst pacing (mild, moderate, severe) had no significant impact on the RRs. However, different cut-off times for AF inducibility had a significant impact on the RR (Pinteraction=0.009), and only the cut-off time of 1 minute showed a significant correlation (RR, 0.54; 95% CI, 0.45–0.66).

CONCLUSIONS AF noninducibility by burst pacing after catheter ablation is associated with reduced clinical recurrence of AF. Induction protocols with a different cut-off time for AF inducibility have a significant impact on the correlation, and the AF ≥1 minute for AF inducibility is recommended.

GW31-e1328

A clinical checking to the formula for estimating the true QT interval in the presence of left bundle branch block

Yue Wang, Yunlong Xia
First Affiliated Hospital of Dalian Medical University

OBJECTIVES The presence of left bundle branch block (LBBB) with a false QT prolongation produced by the widen QRS duration. Ignoring the true QT prolongation in LBBB could cause the development of malignant ventricular arrhythmia like torsade de pointes. Since Dr. Wang and his team provided a formula to recover the true QT interval, this study is ready to check the formula out in the clinical setting.

METHODS A total of 36 consecutive patients with LBBB who received His bundle pacing were enrolled in this study. The narrow and widen QRS, QT, and JT interval appeared before and after the operation were measured by two investigators independently. The QTc interval was calculated with the Bazett formula. Compare the post-operative QTc with the QTc calculated by Wang's formula.

RESULTS There are no significant differences between the QTc calculated by Wang's formula and QTc with narrow QRS duration (P=0.859).

CONCLUSIONS In this study, we confirmed that Wang's formula has better applicability and the ability to correct the QT interval of LBBB than other published formulas.

GW31-e1373

Feasibility and efficacy of a new left atrial appendage occluder in patients with non-valvular atrial fibrillation

Guiyang Li, Weimei Ou, Qiang Li, Faguang Zhou, Linlin Li, Jianghai Liu, Xingcai Wan, Dong Chang
Xiamen Cardiovascular Hospital, Xiamen University

OBJECTIVES Most thrombi associated with atrial fibrillation (AF) were found in left atrial appendage. This study reported the initial safety, feasibility,

3-month, 6-month and 12-month clinical data following Leftear implantation in patients with non-valvular atrial fibrillation.

METHODS From October 2018 to September 2019, thirty-three patients with NVAF were enrolled in this prospective study in Xiamen Cardiovascular Hospital Xiamen University. All of them accepted LAAO using LAAO protocol and were followed at 3-month, 6-month and 12-month after surgery, respectively.

RESULTS The implant success rate was 100%. In the 12th month after surgery there were no postoperative complications, no incidence of ischemic events, no incidence of bleeding and no deaths.

CONCLUSIONS Left atrial appendage closure with Leftear appears to be safe, feasible with encouraging 1-yr clinical outcomes.

GW31-e1374

Remarkable response to cardiac resynchronization therapy via left bundle branch pacing in patients with true left bundle branch block

Jincun Guo, Linlin Li, Xinyi Huang, Dong Chang, Qiang Li, Binni Cai
Xiamen Cardiovascular Hospital, Xiamen University

OBJECTIVES Left bundle branch pacing (LBBP) has been suggested as an alternative means to deliver cardiac resynchronization therapy (CRT). LBBP may deliver resynchronization therapy along with an advantage over traditional biventricular pacing (BiV) in clinical outcomes.

METHODS Heart failure patients who presented LBBB morphology according to Strauss's criteria and received successful CRT procedure were enrolled in the present study. Propensity score matching was applied to match patients into LBBP-CRT group and BiV-CRT group. Then, the electrographic data, the echocardiographic data and New York heart association (NYHA) class were compared between the groups.

RESULTS Twenty-one patients with successful LBBP procedure and another 21 matched patients with successful BiV-CRT procedure were finally enrolled in the study. The QRS duration (QRSd) was narrowed from 167.7±14.9 ms to 111.7±12.3 ms (P<0.0001) in the LBBP-CRT group and from 163.6±13.8 ms to 130.1±14.0 ms (P<0.0001) in the BiV-CRT group. A trend toward better left ventricular ejection fraction (LVEF) was recorded in the LBBP-CRT group (50.9±10.7% vs. 44.4±13.3%, P=0.12) compared to that in the BiV-CRT group at the 6-month follow-up. A trend toward better echocardiographic response was documented in patients receiving LBBP-CRT procedure (90.5% vs. 80.9%, P=0.43) and more super CRT response was documented in the LBBP-CRT group (80.9% vs. 57.1%, P=0.09) compared to that in the BiV-CRT group.

CONCLUSIONS LBBP-CRT can dramatically improve the electrical synchrony in heart failure patients with LBBB. Meanwhile, compared with the traditional BiV-CRT, it has a tendency to significantly improve LVEF and enhance the NYHA cardiac function scores.

HEART FAILURE

GW31-e0089

Age, creatinine, and ejection fraction (ACEF) score continues to predictive prognosis in patients with ischemic cardiomyopathy

WenZhong Chen, Peng Ran, Liwen Li
Guangdong General Hospital

OBJECTIVES ACEF (Age, Creatinine, and Ejection Fraction) and ACEFMDRD (Age, Creatinine, and Ejection Fraction, the Modification of Diet in Renal Disease) score have been validated as effective predictors for prognosis in patients undergoing elective cardiac surgery or PCI. However, the predictive value for ICM (Ischemic Cardiomyopathy) was not clear. This study sought to investigate their predictive value of ICM patients.

METHODS ICM patients hospitalized in the Department of Cardiology were prospectively enrolled between November 2014 and December 2017. Inclusion criteria: previous definite diagnosis of myocardial infarction, previous PCI, CABG, or coronary angiographic findings of one or more vessel stenosis >70%; Simpson echocardiography showed LVEF <45%. Exclusion criteria: chronic hepatic insufficiency while ALT more than three times the normal upper limit; malignant tumors history; and other serious diseases with estimated survival time less than one year. The ACEF score=age/ejection fraction+1 (if creatinine >176 μmol/L). As for ACEFMDRD score, eGFR was calculated using the MDRD formula. Then using the formula: age/EF +1 point for every 10 mL/min reduction in eGFRMDRD below 60 mL/min per 1.73 m^2 (up to a maximum of 6 points). Patients were divided into three groups according to original ACEF and ACEFMDRD score by tertile: for original ACEF score: low (<1.66), middle (1.66~2.09) and high (>2.09); for ACEFMDRD: low (<1.72), middle (1.72~2.59) and high (>2.59). The clinical endpoints were all-cause mortality, cardiac mortality, major adverse cardiovascular and cerebrovascular events (MACCEs) and re-hospitalization for heart failure (HF).

RESULTS 45.5, 38.4 and 1.5% had history of myocardial infarction, PCI and CABG, respectively. Patients in the high ACEF score group were more frequently undergoing PCI, and usage of spironolactone and diuretics. Median follow-up was 13 months (IQR: 7–23 months). Thirty-nine (4.5%) patients died. Cardiac death, MACCEs and re-hospitalization occurred in 38, 56 and 34 patients, respectively. The cumulative rate of all-cause death, cardiac death, MACCEs and re-hospitalization for HF were higher in high tertile of both scores. Compared with ACEFMDRD score, original ACEF exhibited similar discrimination and predictive ability on all clinical endpoints. In multivariate Cox analysis, the original ACEF or ACEFMDRD score were related with increasing risks of all-cause mortality (HR: 2.00 vs. 1.32, 95% CI: 1.46~2.73 vs. 1.13~1.53, P<0.001), cardiac mortality (HR: 1.97 vs. 1.28, 95% CI: 1.43~2.70 vs. 1.10~1.50, P<0.001 vs. P=0.002), MACCEs and re-hospitalization for HF, respectively.

CONCLUSIONS In ICM patients, the original ACEF and ACEFMDRD score were independent and potentially useful predictors of all-cause and cardiac mortality, MACCEs and re-hospitalization for HF during 13-month follow-up.

GW31-e0176

A study on the association between ventricular repolarization stability and age-related cardiac diastolic subclinical state in healthy population

Zhidan Li, Xiaojuan Bai
Shengjing Hospital of China Medical University

OBJECTIVES The purpose of this study is to assess the correlation between ventricular repolarization stability and cardiac diastolic function in healthy population from both cross-sectional and longitudinal perspectives, to explore the predictive value of ventricular repolarization variables in the changes of cardiac diastolic function, and to provide a theory for improving ventricular repolarization stability as a potential treatment for heart failure in the future.

METHODS This was a community-based cross-sectional study in which all subjects were randomly selected from 15 different Shenyang communities between September 2007 and June 2008. After excluding persons with abnormal physical examination or laboratory results, 414 healthy subjects (186 men and 228 women) were included in the study. In 2011, 414 healthy subjects who were selected in 2008 made an appointment for a longitudinal follow-up visit. Following a three-year follow-up, 270 subjects were confirmed as participants. All subjects underwent a 12-lead ECG, which was recorded at a paper speed of 25 mm/sec and a voltage of 10 mm/mV by a standard ECG system. For ECG analysis, we performed manual measurements of the values with a digital caliper using a computer program. All subjects underwent a complete M-mode, two-dimensional and pulsed-wave (PW) Doppler echocardiographic examination.

RESULTS In this cross-sectional study, we found electromechanical coupling variables were significantly different among the three age groups, and they also were significantly different between the sexes. Ventricular repolarizations variables were associated with cardiac diastolic function parameters in healthy people. The binary logistic regression analyses performed using reduced diastolic function as the dependent variable and the longer QTc interval as the independent variables shows that, in men, compared to the subjects with normal QTc interval, the odds ratios in subjects with longer QTc interval was 2.567 (95% CI, 1.227–5.370, P=0.012) after adjustment for all other variables. In the longitudinal study, we found that baseline ventricular repolarizations variables were significantly different among the four groups based on cardiac diastolic function. Baseline levels of QTc interval was significantly correlated with cardiac diastolic function. The multiple logistic regression analysis shows that, compared to the individuals with normal baseline QTc interval, the individuals with longer baseline QTc interval seemed to have higher risk of deteriorate and impaired diastolic function with the odds of 1.946 (95% CI 0.921–4.098, P=0.081) and 1.919 (95% CI 0.935–3.953, P=0.076) separately.

CONCLUSIONS This cross-sectional study reveals that even in healthy people, ventricular repolarization variables are linearly associated with cardiac diastolic function parameters and the associations are different between the sexes. A prolonged QTc interval is associated with a decline in cardiac diastolic function. We also note an independent linear association between the QTc interval and echocardiographic diastolic function parameters in males. Furthermore, longer QTc interval tend to have increased risk of diastolic dysfunction in men. In this longitudinal study, our results confirm that there is interaction of ventricular repolarization variables and various cardiac diastolic function. Baseline levels of QTc interval was significantly correlated with cardiac diastolic function.

GW31-e0209

Analysis of influencing factors of COVID-19 outbreak in elderly patients with heart failure

Hu Rui[1], Li Gang[2], Chen Hua[2], Li Li[2], Hu Xiao[3], Guo Ran[1], Ji Xin[1], Geng Yanping[2]
[1]The Second Hospital of Hebei Medical University
[2]Hebei General Hospital
[3]Hebei Medical University

OBJECTIVES To understand the clinical characteristics and psychological status of elderly patients with heart failure during COVID-19 epidemic, and analyze relevant influencing factors.

METHODS The elderly patients with heart failure who were hospitalized in the cardiovascular department of Hebei general hospital on January 20, 2020 and March 19, 2020 were selected as the observation group, and the elderly patients with heart failure in the same period last year were selected as the control group. The differences of gender, age, severity of disease, combined disease, treatment and length of hospital stay were compared between the two groups.

RESULTS A total of 52 patients were collected in the observation group, including 29 males and 23 females, with an average age of (81.5±8.3) years. The control group included 71 patients, including 43 males and 28 females, with an average age of (80.7±8.5) years. There were no differences in age or sex between the two groups. The number of patients with NYHA class III or IV heart failure (40 cases, 76.9%) in the observation group was significantly higher than that in the control group (39 cases, 54.9%, P<0.05). The number of patients with depression and anxiety in the observation group (26 cases, 50.0%) was higher than that in the control group (24 cases, 33.8%, P<0.05). The number of patients with pulmonary infection in the observation group (16 cases, 30.7%) was higher than that in the control group (12 cases, 16.9%, P<0.05), and the length of hospital stay in the observation group [16 (13, 19) d] was longer than that in the control group [12 (8, 15) d, P<0.05].

CONCLUSIONS During the COVID-19 epidemic, the number of heart failure patients admitted to our department decreased significantly compared with that in the same period last year. However, the patients admitted to the hospital were in a serious condition, with significantly increased rates of anxiety, depression and pulmonary infection. This study suggested that comprehensive treatment of the cardiac function status and anxiety and depression in elderly patients with heart failure during the epidemic period was conducive to the control of the disease and the reduction of hospital stay. At the same time, due to the fear of COVID-19 and other reasons to delay the time of hospitalization and stay in bed for a long time and other factors, leading to the increased risk of complicated pulmonary infection; As for the cases of fever and respiratory symptoms in patients during hospitalization, we should actively screen COVID-19, exclude relevant virus infection and actively control pulmonary infection, so as to reduce the rehospitalization rate and fatality rate of elderly patients with heart failure.

GW31-e0258

Comparison of echocardiography and cardiac magnetic resonance imaging for the assessment of left ventricular ejection fraction in heart failure patients

Qing Li, Yao Chen, Jinrui Guo
Fuwai Yunnan Cardiovascular Hospital

OBJECTIVES To examine the accuracy and agreement in quantification of left ventricular ejection fraction (LVEF) by use of echocardiography versus cardiac MRI in heart failure (HF) patients.

METHODS A total of 352 HF patients were retrospectively enrolled from 2017 to 2019 in the Fuwai Yunnan Cardiovascular Hospital. Left ventricular volume and function parameters including LAD, LVD, LVEDV, LVESV and LVEF measured by echocardiography were compared with those calculated by cardiac MRI. Paired t-test and Bland-Altman method was used for analysis.

RESULTS The echocardiographic values of LAD, LVD, LVEDV, LVESV and LVEF were significantly overestimated than those of cardiac MRI (P<0.05). The LVEF measured by M-mode Teichholz method were correlated with cardiac MRI in ischemic HF patients r=0.596 vs. non-Ischemic HF patients r=0.692; of 79 patients LVEF measured by echocardiographic Simpson's method were better correlated with cardiac MRI r=0.816, consistency between them was strong ICC=0.810 (95% CI: 0.718–0.874, P<0.05), Bland-Altman analysis of LVEF measurement showed best agreement between echocardiographic Simpson's method and cardiac MRI.

CONCLUSIONS Echocardiography Simpson's method was more accurate than M-mode Teichholz in the evaluation of LVEF in HF patients and there was a better correlation and consistency in non-Ischemic HF when compared with cardiac MRI measurement.

GW31-e0361

Elevated homocysteine levels in patients with heart failure: a systematic review and meta-analysis

Lei Huang
Department of Cardiology, Ningbo Hangzhou Bay Hospital

OBJECTIVES Elevated homocysteine levels showed increasing significance as the predisposing factor for the pathogenesis of atherosclerotic sequelae, including cardiovascular mortality, coronary artery disease and stroke. There is increasing evidence linking plasma homocysteine levels and heart failure (HF). The association between the elevated level of plasma homocysteine and HF was examined by meta-analysis and systematic review in this study.

METHODS The PubMed and ScienceDirect databases until December 2019 were utilized to collect previous literature on plasma homocysteine levels and the potential relation to HF. The pooled effects were evaluated depending on standardized mean differences (SMDs) with 95% confidence intervals (CIs), and the calculation was performed using Stata 12 software. Potential sources of heterogeneity were assessed with subgroup analysis and sensitivity analysis.

RESULTS A total of 12 research projects including 5506 subjects were selected. For pooled effect, the results confirmed that patients with HF had higher homocysteine levels than the control subjects [SMD, 1.148 and 95% CI, (0.715, 1.581)]. Based on the classification of New York Heart Association (NYHA), the homocysteine levels for the group of NYHA I or II [SMD, 1.484 and 95% CI, (0.442, 2.527)] and the group of NYHA III or IV [SMD, 3.361 and 95% CI, (1.902, 4.820)] were significantly increased compared to controls, while the increase was more intensive for the group of NYHA III or IV. Subgroup analyses revealed similar results.

CONCLUSIONS Our meta-analysis identified that plasma homocysteine levels were significantly elevated in HF patients compared to control subjects, which is positively related to the advancement of NYHA class.

GW31-e0386

Living alone and clinical outcomes in patients with heart failure with preserved ejection fraction: from the TOPCAT trial

Yuzhong Wu, Wengen Zhu, Yugang Dong
The First Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES In patients with heart failure with preserved ejection fraction (HFpEF), whether living alone could contribute to a poor prognosis remains unknown. We sought to investigate the association of living alone with clinical outcomes in HFpEF patients.

METHODS Symptomatic HFpEF patients with a follow-up of 3.3 years in the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist) trial were classified as patients living alone and those living with others. The primary outcome was defined as a composite of cardiovascular death, aborted cardiac arrest, or HF hospitalization.

RESULTS A total of 3445 HFpEF patients were included; 25.2% of them were living alone and were older, predominantly female, and more likely to be white and have more comorbidities than the other patients. After multivariate adjustment for confounders, living alone was associated with increased risks of HF hospitalization (hazard ratio [HR] 1.29, 95% confidence interval [CI] 1.03–1.61) and any hospitalization (HR 1.26, 95% CI 1.12–1.42). A significantly increased risk of any hospitalization (HR 1.16, 95% CI 1.01–1.34) was also observed in the Americas-based population. In addition, each year increase in age, female sex, white race, New York Heart Association functional classes III and IV, dyslipidemia, and chronic obstructive pulmonary disease were independently associated with living alone.

CONCLUSIONS This study was the first to assess the effect of living arrangement status on clinical outcomes in patients with HFpEF and suggested that living alone was associated with an independent increase in any hospitalization.

GW31-e0389

Diagnostic value of combining serum soluble ST2 and interleukin-33 for heart failure patients with preserved left ventricular ejection fraction

Haifeng Zhang[1,2], Zhiteng Chen[1,2], Qingyuan Gao[1,2], Shaohua Wang[1,2], Chang Guan[1,2], Yangxin Chen[1,2], Jingfeng Wang[1]
[1]Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong 510120, PRC
[2]Laboratory of Cardiac Electrophysiology and Arrhythmia in Guangdong Province, Guangdong 5101120, PRC

OBJECTIVES Diagnostic efficacy of serum markers is low for heart failure patients with preserved left ventricular ejection fraction (HF-pEF) as compared to heart failure patients with reduced left ventricular ejection fraction. We sought to explore the diagnostic value of serum levels of soluble ST2 (sST2) combined with interleukin-33 (IL-33) for the diagnosis of HF-pEF in this study.

METHODS A total of 376 patients with HF-pEF (HF group), 376 matched-control patients without heart failure who shared similar clinical characteristics (non-HF group) were included in the study. Another 500 healthy individuals were recruited for assessing the normal ranges of IL-33 and sST2. Serum levels of NT-proBNP were measured by chemiluminescence assay, while IL-33 and sST2 were measured by enzyme-linked immunosorbent assay.

RESULTS Serum levels of IL-33 and sST2 were not normally distributed in healthy population. Serum concentrations of IL-33 and sST2 were significantly higher in HF-pEF patients than in patients in non-HF group (median, IL-33: 0.437 μg/L vs. 0.127 μg/L, P<0.01; sST: 0.118 μg/L vs. 0.067 μg/L, P<0.01). The area under receiver operating characteristic curve (AUC) of sST2 for detecting HF-pEF was 0.763 (95% CI 0.729–0.795, P<0.01), with 71.01% sensitivity and 66.75% specificity, the AUC was 0.884 (95% CI 0.859–0.908, P<0.01), with 80.05% sensitivity and 81.91% specificity in patients with serum IL-33 higher

than 0.117 μg/L (median level of serum IL-33 in healthy individuals, n=306). The AUC of NT-proBNP for detecting HF-pEF was 0.83, with 74.73% sensitivity and 84.57% specificity. The AUC of sST2 for detecting HF-pEF was significantly higher than NT-proBNP in population with high serum IL-33 (AUC: 0.88 vs. 0.83, P<0.01).

CONCLUSIONS Serum sST2 could serve as a satisfactory biomarker for HF-pEF diagnosis, especially for patients with high serum IL-33 concentrations.

GW31-e0398

Validity and efficacy of a new classification for heart failure based on extravascular overflow and intravascular overload

Thach Nguyen[1,2], Chau Chi Nha[3], Phuong M. Nguyen[1], Tra T. Ngo[1], Duy Chung[1], Luan Ngo[1], Thai Truong[1], Ernest Talarico Jr.[2], Gianluca Rigatelli[4], Ho Thuong Dung[5], Cao Van Thinh[6], Phuoc T. Nguyen[1]
[1]Methodist Hospital, Merrillville, IN
[2]Tan Tao University School of Medicine
[3]University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam
[4]Cardiovascular Diagnosis and Endoluminal Interventions Unit, Rovigo, General Hospital, Rovigo, Italy
[5]Thong Nhat Hospital, Ho Chi Minh City, Vietnam
[6]Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Vietnam

OBJECTIVES Heart Failure (HF) is the end stage of the disease spectrum with many confounders and no specific symptoms and signs. There is a need for a test to confirm the diagnosis of volume overload in HF at its earliest in order to guide the management. This study aimed to evaluate the effectiveness of a new test, the Size and Expansion of Femoral Vein (SEFV), in the diagnosis of HF patients with co-morbidities or hypotension and in the classification into severely and moderately sick patients.

METHODS The patients who arrived to the emergency room with diagnosis of HF or suspected HF were enrolled. All patients received a standard physical examination (PE) and underwent the ultrasound test to measure the size of the common femoral vein (CFV) and artery (CFA). Then the patients were separated into 2 groups for diagnosis based on clinical findings and the results of the SEFV.

RESULTS The study enlisted 167 patients who underwent detailed review looking for locations of fluid overload. The results showed that for patients with severely abnormal SEFV test (enlarged CFV and non-expanding CFV upon cough), the majority of these locations of edema was in the intravascular compartment and located in the upper part of the body. The areas with abnormalities included hepatomegaly, splenomegaly, the mesenteric arterial system (positive hepato-jugular reflux), the pulmonary arteries (crackles on auscultation) and the jugular veins (jugular venous distention). As the patient had severe HF, they had edema in the extravascular compartment in both upper and lower parts of the body. The areas with extravascular fluid overflow were at the abdominal wall, the peritoneal cavity (ascites), the scrotum (for men), labia (for women), pre-sacral area for patients on prolonged supine position and lower extremities. The fact that the edema was pitting proved that the fluid was in the interstitial tissue or extravascular space. In contrary, if the SEFV test was moderately abnormal (enlarged CFV and non-expanding CFV upon cough) the edema was mainly in the lower extremities.

CONCLUSIONS This SEFV test was best for patients with prominent clinical confounders due to the presence of severe co-morbidities or concomitant hypotension. More importantly, a strongly abnormal the SEFV test (enlarged CFV and non-expanding CFV upon cough) could differentiate accurately the severely sick patient with fluid overload in the intravascular compartment and fluid overflow in the extravascular compartment of the whole body (upper and lower part of the body). In contrast, the less sick patients with moderately abnormal SEFV test (enlarged CFV and non-expanding CFV upon cough) had only fluid overload in the lower extremities. Randomized trials with higher number of patients could confirm the benefits of the new classification of patients with HF.

GW31-e0422

Risk stratification and efficacy of spironolactone in patients with heart failure with preserved ejection fraction: secondary analysis of the TOPCAT randomized clinical trial

Yifen Lin[1,2], Xiangbin Zhong[1,2], Xinxue Liao[1,2]
[1]Cardiology Department, First affiliated Hospital of Sun Yat-Sen University
[2]NHC Key Laboratory of Assisted Circulation, Sun Yat-Sen University

OBJECTIVES Better risk stratification tool for patients with preserved ejection fraction (HFpEF) are required to assist clinical decision making. No therapy can convincingly improve the outcome of HFpEF. We aimed to develop a simple risk score for patients with HFpEF and assessed the efficacy of spironolactone across baseline risk.

METHODS We developed risk stratification scheme for cardiovascular death in placebo arm of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist trial (TOPCAT). We screened candidate risk indicators and determined strong risk predictors using maximum likelihood estimate based on consistency of forward and backward variable selection procedures (P<0.05). The risk score for cardiovascular death in patients with HFpEF was defined as the sum of weighted points by estimate in COX model of each risk indicator. The individuals were further reformed into 4 risk groups with approximated equal sample size based on the distribution of risk scores across the derivation cohort: 0–1 points (low risk), 1.5–2 points (intermediate risk), 2.5–3.5 points (high risk) and ≥4 points (very high risk). The absolute risk reduction (ARR) in cardiovascular death with spironolactone were evaluated across risk groups. COX regressions were performed to assess the hazard ratios (HR) of spironolactone therapy for cardiovascular death and drug discontinuation in each risk categories.

RESULTS A simple risk score scheme was constructed based on five risk indicators weighted by estimates from the model, including age, diastolic blood pressure, renal dysfunction, white blood cell and left ventricular ejection fraction. The risk score scheme showed good discrimination in placebo cohort (C index=0.70). ARR with spironolactone therapy was observed only in patients at very high risk (7.9%). Spironolactone therapy significantly reduced the risk of cardiovascular death in very high risk group (HR: 0.57; 95% CI, 0.39–0.84; P=0.005 and P for interaction 0.03) but showed similar risk of drug discontinuation across risk categories (P for interaction=0.928).

CONCLUSIONS This simple risk score tool stratifies patients with HFpEF by their baseline risk of cardiovascular death. Patients at very high risk derive great benefits from spironolactone therapy. This easy-to-use risk score provides a practical tool that can facilitate risk stratification and tailoring therapy for those benefit most from spironolactone.

GW31-e0533

The therapeutic effect of lyophilized recombinant human brain natriuretic peptide on acute myocardial infarction with acute heart failure after percutaneous coronary intervention

Yujie Xing, Yu Xiang, Bo Liu, Jing Liu, Junkui Wang
Department of Cardiology, Shannxi Provincial People's Hospital, Xi'an, Shaanxi 710004, People's Republic of China

OBJECTIVES To investigate the therapeutic effect of lyophilized recombinant human brain natriuretic peptide on acute myocardial infarction with acute heart failure after percutaneous coronary intervention (PCI).

METHODS Sixty patients of acute myocardial infarction with acute heart failure after PCI were randomly divided into control group and experimental group, 30 cases in each group, the control group received conventional therapy, and the experimental group was given lyophilized recombinant human brain natriuretic peptide treatment on the basis of conventional drug treatment. The drug treatment effect and adverse reaction of two groups were observed. All patients were detected the level of cTnI, CK-MB, and BNP. The cardiac function was detected by echocardiography.

RESULTS The total effective rate of the experimental group after treatment was significantly higher than the control group. Compared with the control group, cTnI, CK-MB and BNP levels of patients in experimental group decreased significantly, while left ventricular ejection fraction and left ventricular fractional shortening increased significantly. The differences were statistically significant (P<0.05). And there was less adverse reaction.

CONCLUSIONS Lyophilized recombinant human brain natriuretic peptide can significantly improve the therapeutic effect of acute myocardial infarction patients with acute heart failure after PCI, reduce myocardial damage, improve cardiac function, and have fewer adverse reaction.

GW31-e0611

Therapeutic value of treating central sleep apnea by adaptive servo-ventilation in patients with heart failure: a systematic review and meta-analysis

Jingting Wang[1], Naima Covassin[2], Jiang Xie[1]
[1]Beijing Anzhen Hospital, Capital Medical University, Beijing
[2]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, USA

OBJECTIVES Despite the efficacy of adaptive servo-ventilation (ASV) in suppressing central sleep apnea (CSA), its impact on long-term outcomes is debatable. We aim to identify subjects with specific features who might benefit from ASV therapy.

METHODS Randomized clinical trials and comparative observational studies investigating the effects of ASV on cardiovascular (CV) and all-cause mortality and major adverse cardiovascular events (MACEs) in CSA patients were searched from PubMed, EMBASE, Cochrane library and Web of Science. Eligible studies were identified with relative risks (RR) of death and MACEs compared between patients treated by ASV and usual care.

RESULTS A total of seven studies (three randomized controlled trials and four observational studies) including 2128 participants were selected for analysis.

All-cause and CV mortality were not significantly reduced by ASV. Patients with nadir nocturnal saturation ≤80% (mean value) had lower risk of MACEs by ASV treatment compared with by usual care (RR, 0.18; P<0.001). Patients with severe heart failure (HF), defined as left ventricular ejection fraction (LVEF) ≤35% (mean value), or HF of New York Heart Association (NYHA) classification of III/IV, did not have reduced risk of MACEs post ASV therapy. However, subjects with LVEF >35% (RR, 0.19; P=0.004) or NYHA I/II (RR, 0.30; P<0.001) had significantly lower risk of MACEs by using ASV than by usual care.

CONCLUSIONS Although ASV cannot reduce CV and all-cause death, patients with profound hypoxemia or less severe HF still benefit from ASV therapy.

GW31-e0631

Improvement of LV reverse remodeling using dynamic programming of fusion-optimized atrioventricular intervals in cardiac resynchronization therapy

Pan Li, Zhongkai Wang, Xianxian Zhao
Department of Cardiology, Changhai Hospital, Second Military Medical University

OBJECTIVES Cardiac resynchronization therapy (CRT) is an effective therapeutic modality for patients with advanced heart failure, cardiomyopathy, and left bundle branch block (LBBB). It has been demonstrated that CRT improves left ventricular remodeling and clinical symptoms, and therefore reduce hospitalization and all-cause mortality. However, these effects vary amongst individuals, with approximately one-third failing to respond to CRT. Optimizing the atrioventricular delay (AVD) guided by ultrasound or electrocardiogram (ECG) enhances the fusion of intrinsic conduction and biventricular (BiV) pacing, resulting in improved in CRT responses and clinical outcomes. Post-programmed AVD however fails to adapt to the dynamics of each patient due to heart rate variability and/or drugs. Patient-tailored SyncAV algorithm shortens the QRS duration (QRSd) beyond conventional BiV pacing; however, evidence of the ability of SyncAV to improve CRT response is lacking. The aim of the study was to evaluate the impact of CRT enhanced by SyncAV on echocardiographic and clinical responses.

METHODS Consecutive heart failure (HF) patients from three centers treated with a quadripolar CRT system (Abbott) were enrolled (*Figure* 1). According to CRT with or without SyncAV function, a total of 69 patients were divided into BiV+SyncAV (n=37) and BiV groups (n=32). Electrocardiographic, echocardiographic, and clinical data were assessed at baseline and during follow-up. Echocardiographic response to CRT was defined as ≥15% decreases in left ventricular end-systolic volume (LVESV) and clinical response was measured as a reduction in NYHA class of ≥1.

RESULTS Baseline QRSd in the BiV+SyncAV group was 163.7±17.6 ms and compared to the 169.7±17.4 ms observed in the BiV group (P=0.159). The median baseline PR-interval did not differ between BiV+SyncAV and BiV group (169.0 ms vs. 170.0 ms; P=0.535). At 6-months follow-up, the baseline QRSd and LVESV decreased more significantly in the BiV+SyncAV vs. BiV group (QRSd −36.24±18.20 ms vs. −24.84±17.86 ms, P=0.005; LVESV −46.09±37.68 mL vs. −20.20±30.87 mL, P=0.001). Compared to the BiV group, a larger number of patients in the BiV+SyncAV group were classified as echocardiographic (81.08 vs. 59.37%; P=0.047) and clinical responders (67.57 vs. 21.88%; P<0.001). During follow-up, no deaths due to HF deterioration or severe procedure related complications occurred.

CONCLUSIONS This multicenter cohort observational trial revealed that BiV pacing coupled to SyncAV function can narrow the QRSd in CRT patients and increase LV remodeling compare to conventional BiV pacing. Cardiac function improvements benefit from the dynamic fusion of instinct conduction and BiV pacing. SyncAV therefore should be applied in all CRT patients with normal instinct conduction.

GW31-e0675

Prevalence and prognostic significance of anemia in patients hospitalized with heart failure

Xuemei Zhao, Yuhui Zhang, Jian Zhang
Heart Failure Center, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College

OBJECTIVES This study aimed to evaluate the prevalence and prognostic importance of anemia in patients hospitalized with HF.

METHODS We reviewed consecutive patients (age of 18 years or older) admitted for HF between December 2009 and December 2019. Anemia was defined as hemoglobin (Hb) <12 g/dL in women and <13 g/dL in men. Cox proportional hazards model was used to investigate factors associated with 1-year all-cause mortality after clinically relevant variables were adjusted.

RESULTS A total of 4350 patients with a mean age of 57.2±15.8 years and 70.5% male were included in the final analysis. Anemia was present in 17.2% of HF patients on admission, and mean Hb was 10.5±1.3 g/dL. After adjustment for clinical and demographic variables, patients with anemia were more likely to be older (odds ratio [OR] 1.02 per year), female gender (OR 1.39, 95% confidence interval [95% CI], 1.17–1.66) and had greater New York Heart Association class (OR 1.45, 95% CI, 1.28–1.64). Compared with patients without anemia, patients with anemia had longer length of stay in hospital (14 [8, 20] d *vs.* 11[7, 15] d) (P<0.01) and higher in-hospital mortality (6.2 *vs.* 3.4%) (P<0.01). In multivariable Cox proportional hazards regression models, after adjusted for covariates, patients with anemia had significantly higher one-year all-cause mortality (hazard ratio [HR]=2.02; 95% CI, 1.69–2.42; P<0.001).

CONCLUSIONS Anemia is common in patients hospitalized with HF and patients with anemia on admission had higher risk of in-hospital mortality and one-year all-cause mortality. Anemia was an independent prognostic factor of mortality in patients hospitalized with HF.

GW31-e0730

Diagnosis of heart failure with preserved ejection fraction in patients with dyspnea and paroxysmal atrial fibrillation: a role of left atrial strain

Asim Katbeh
Cardiovascular Center OLV Aalst

OBJECTIVES Diagnosis of heart failure with preserved ejection fraction (HFpEF) in patients with dyspnea and paroxysmal atrial fibrillation (AF) is challenging. Speckle tracking-derived left atrial strain (LAS) provides an accurate estimate of left ventricular filling pressures and left atrial phasic function. However, data on clinical utility of LAS in patients with dyspnea and AF are scarce. To assess relationship between LAS and probability of HFpEF in patients with dyspnea and paroxysmal AF.

METHODS The study included 205 consecutive patients (62±10 years, 58% males) with limiting dyspnea (NYHA ³II), paroxysmal AF and preserved LVEF (≥50%), who underwent speckle tracking echocardiography and natriuretic peptide (NT-proBNP) assessment during sinus rhythm. Patients with manifest ischemic heart or valve disease, and cardiomyopathy were excluded. Probability of HFpEF was estimated using H2FPEF and HFA-PEFF scores, which combine clinical characteristics, echocardiographic parameters and natriuretic peptides.

RESULTS A total of 61 (30%), 115 (56%) and 29 (14%) had high, intermediate and low, respectively, probability of HFpEF. Patients with high probability of HFpEF were significantly older, had higher body mass index, NT-proBNP, E/e′, pulmonary artery pressure and larger LA volume index than patients in low-to-intermediate probability groups (all P<0.05). Two distinct patterns of LA phasic function were observed. Firstly, reservoir LAS showed close inverse association with increasing probability of HFpEF (Figure 1). Secondly, contractile LAS showed initial decrease with subsequent compensatory increase in intermediate probability category with final decrease in patients with high HFpEF probability (Figure 1). In contrast, LV global longitudinal strain was similar between groups (NS). In multivariable regression analysis, reservoir LAS emerged as the strongest independent predictor of HFpEF defined by using both scores. Reservoir LAS with optimal cut off value of 24% showed sensitivity of 86% and specificity of 70% to identify high probability of HFpEF. Combination of LAS with NT-proBNP did not increase the accuracy of each parameter alone.

CONCLUSIONS Reservoir LAS shows strong independent association with probability of HFpEF in patients with dyspnea and paroxysmal AF. This advocates for more liberal use of LAS assessment to distinguish cardiac from non cardiac dyspnea in patients with history of AF.

GW31-e0745

Comparative treatment of the actual dose of sacubitril-valsartan versus target dose of ACEI in heart failure patients with reduced ejection fraction: a real-world cohort study

Cong Dai, Ren Qiang Yang
The Second Affiliated Hospital of Nanchang University

OBJECTIVES The aim of this study was to compare real-world dosing of Sacubitril-Valsartan with the target dose of angiotensin-converting enzyme inhibitors (ACEI) for the treatment of heart failure patients with reduced ejection fraction (HFrEF).

METHODS This was a prospective, registered, observational cohort study, which included 223 patients with dilated cardiomyopathy (DCM) and HF treated between September 2017 and December 2018. Patients were divided into observation group and standard group. The observation group was initially orally administrated with Sacubitril Valsartan Sodium tablets, 50 mg twice daily; the dose was adjusted according to the patient's blood pressure, tolerance, and doctor's willingness. The standard group orally received ACEI, which was gradually increased. Patients were followed-up for 18 months.

RESULTS The average dose of Sacubitril-Valsartan was 138.96±67.22 mg, and the target dose rate was 1.8%. The target dose achieved in the standard group

was 47.3%. The time of hospital stay, MLHFQ score, and BNP after treatment were all lower, while the 6 min walking test and effective clinical rate were higher in the observation group than the standard group (P<0.05). Total protein decreased in both groups before and after treatment. The decrease of SBP in the observation group was higher, while the reduction of platelet count before and after treatment was lower compared to the standard group. In the subgroup analysis, the average dose of Sacubitril-Valsartan in the observation group was 115.27±53.65 mg, and no patients reached the target dose. After treatment, the left ventricular end-diastolic diameter, MLHFQ score, and BNP in the two groups were all lower. In contrast, the left ventricular ejection fraction and 6 min walking test increased compared with that before Sacubitril-Valsartan treatment.

CONCLUSIONS In the treatment of HFrEF, most patients treated with Sacubitril-Valsartan did not reach the target dose. Yet, compared with the target dose of ACEI, the commonly used dose of Sacubitril-Valsartan was not inferior to the target dose of ACEI in the treatment of patients with chronic heart failure, leading to the more prominent improvement of clinical symptoms. Patients with HF with SBP of less than 100 mmHg may benefit from Sacubitril-Valsartan.

GW31-e0863

The additional prognostic value of ghrelin for mortality and readmission in elderly patients with acute heart failure

Yin Yuan[1,2,3,4], Siyang Lin[2], Feng Huang[1,2,3,4], Chaochao Deng[2], Pengli Zhu[1,2,3,4]
[1]Department of Geriatric Medicine, Fujian Provincial Hospital
[2]The Shengli Clinical Medical College, Fujian Medical University
[3]Fujian Provincial Institute of Clinical Geriatrics
[4]Fujian Provincial Key Laboratory of Geriatrics

OBJECTIVES Prognostic factors for acute heart failure (AHF) may differ from those used routinely for stable chronic HF. Ghrelin is a gut-derived 28-amino acid peptide that acts as an endogenous ligand for the growth hormone secretagogue receptor (GHS-R). The cardiovascular protective effects of ghrelin have been recently suggested, and are mediated through both GH-dependent and independent mechanisms, providing improvements in energy balance, regulation of autonomic nervous activity, and direct effects on the heart and blood vessels. However, the prognostic value of ghrelin has not been thoroughly studied, especially for AHF. Older AHF patients are more prone to frailty, comorbidities, and impaired nutritional status that can impact HF outcomes. Thus, in the present study, we aimed to investigate plasma ghrelin levels in elderly patients with AHF, and evaluate their prognostic value for adverse AHF events. We hypothesized that ghrelin would exert additional value in improving prognostic risk classifications in older AHF patients.

METHODS We measured plasma ghrelin and pro B-type natriuretic peptide (NT-proBNP) levels upon emergency admission in 241 prospectively recruited elderly AHF patients (61.0% men). Patient demographics, lifestyle habits, medical history, vital signs, nutritional status, physical examinations, laboratory tests and echocardiography data were also collected. The outcomes were all-cause mortality and/or readmission due to heart failure (HF). Multivariate Cox proportional hazards regression analyses were used to evaluate the prognostic value of ghrelin. Discrimination, calibration, and reclassification indices were compared between models, with or without ghrelin. Statistical analyses were performed using Stata 15.1, MedCalc, and R 3.5.0 statistical software. A two-sided P value <0.05 was considered statistically significant.

RESULTS Two hundred and forty one elderly patients with AHF were included (mean age=68.6 years, 61.0% men). During 1.2 years of follow-up, we observed 90 events (57 deaths and 33 readmissions due to HF). Plasma ghrelin levels were significantly elevated in elderly AHF patients, when compared to healthy control subjects (P<0.001). Patients with events had significantly higher baseline ghrelin levels, when compared to those without (P<0.001). Ghrelin levels were positively correlated with NT-proBNP levels and HF severity, whereas they were negatively correlated with nutritional status (all P<0.05). Log transformed ghrelin levels were independently associated with AHF events (hazard ratio=2.64, 95% confidence interval=1.11–6.25, P=0.028). The incorporation of ghrelin into the reference model, or reference with the NT-proBNP model, both improved C-statistics (from 0.742–0.780 and 0.836–0.857; P=0.074 and 0.044, respectively), resulting in an improvement in net reclassification index (14.42 and 10.45%, P=0.020 and 0.025, respectively), and integrated discrimination index (5.64 and 3.60%, both P<0.001). Patients who displayed the above NT-proBNP and ghrelin median levels had a markedly higher risk of AHF adverse events (P<0.001).

CONCLUSIONS Plasma ghrelin levels are elevated in elderly AHF patients, and are associated with mortality and readmission due to HF. They provide an additive value to clinical parameters, or NT-proBNP for AHF risk stratification. Therefore, ghrelin represents a promising therapeutic target for HF.

GW31-e0872

The relationship between mean ventricular heart rate of dynamic electrocardiogram and all-cause mortality among patients with non-valvular atrial fibrillation and NYHA class III or IV

Zefeng Chen, Lin Chen
Department of Cardiovascular Medicine, The Third Affiliated Hospital of Sun Yat-sen University

OBJECTIVES To investigate the relationship between mean ventricular heart rate of dynamic electrocardiogram and all-cause mortality among patients with non-valvular atrial fibrillation and NYHA class III or IV.

METHODS One hundred and seventy one patients with non-valvular atrial fibrillation and NYHA class III or IV at the Third Affiliated Hospital of Sun Yat-sen University between October 2012 and July 2016 who underwent dynamic electrocardiogram were enrolled. Patients were divided into 2 groups based on mean heart rate of dynamic electrocardiogram (Group A: mean heart rate no higher than 80 b.p.m. and Group B: mean heart rate higher than 80 b.p.m.). The median following up time was 28 months and all-cause mortality was recorded. Propensity score matching was used to control confounding factors (136 patients were matched) and then the relationship between mean heart rate and all-cause mortality was investigated.

RESULTS In this atrial fibrillation population, all-cause mortality is statistically lower in group A (mean heart rate no higher than 80 b.p.m.) then group B (mean heart rate higher than 80 b.p.m.) (OR=0.422, 95% CI: 0.184–0.971, P=0.042).

CONCLUSIONS Mean heart rate of dynamic electrocardiogram no higher than 80 b.p.m. predict a lower all-cause mortality in patients with non-valvular atrial fibrillation and NYHA class III or IV.

GW31-e1045

MTP and ROS in peripheral blood mononuclear cells are short-term indicators of coenzyme Q10 in patients with chronic heart failure

Bingxue Song, Yingying Zhang, Junjie Guo, Xin Liu, Haichu Yu
The Affiliated Hospital of Qingdao University

OBJECTIVES Observing levels of membrane potential (MTP) and lymphocyte active oxygen radicals (ROS) in peripheral blood of chronic heart failure patients with or without CoQ10 in addition to standard therapy. Exploring new biological indicators of short term treatment efficacy of Coenzyme Q10 in CHF patients.

METHODS Fifty four CHF patients were enrolled in this prospective study, who received standardized drug therapy for 3 months before the administration of Coenzyme Q10, and the medication regimen was fixed. Then, they were randomly divided into two groups. One group was normalized treatment with Coenzyme Q10 group (20 mg tid, Nengqilang, eisai pharmaceutical), as HF-CoQ10 group, and the other group was the standardized treatment for heart failure, as control. On the basis of standard treatment, patients with chronic heart failure were given oral administration of Coenzyme Q10 to collect clinical indicators. The MTP and ROS levels of lymphocytes were evaluated by flow cytometry and reported as the JC-1 fluorescence ratio and DCF fluorescence intensity, respectively. Serum NT-proBNP levels and biochemical parameters were also examined. All the participants received follow-up to evaluate clinical end-points after 3 months.

RESULTS Chronic heart failure patients with short-term intervention of Coenzyme Q10 with standardised management based on guidelines had lower levels of DCF fluorescence intensity of lymphocytes, higher level JC-1 fluorescence ratios compared and better evaluation in the Minnesota Living with Heart Failure questionnaire (all P<0.05), while there was no significant difference in NT-proBNP between groups.

CONCLUSIONS In CHF, the MTP and ROS levels of the lymphocytes showed a significant change with intervention of Coenzyme Q10.

GW31-e1060

Pulmonary hemodynamic correlates and prognostic value of cardiopulmonary exercise score in patients with left heart failure

Wande Yu, Hang Zhang
Nanjing First Hospital

OBJECTIVES Secondary pulmonary hypertension in left heart failure (PH-LHF) is associated with abnormal ventilatory response on exercise and poor prognosis. Our study sought to develop an algorithm, using cardiopulmonary exercise testing (CPET) data, to assess pulmonary hemodynamic severity and predict clinical worsening and mortality in heart failure (HF) patients.

METHODS A total of 102 HF patients prospectively participated in the study underwent CPET and invasive right heart catheterization, and tracked for

composed clinical events for at least 1 years. Using CPET data, including VO2 peak/Kg, the minute ventilation/carbon dioxide production (VE/VCO2) slope, resting end-tidal CO2 (PET CO2), VO2/WR flattening, exercise oscillatory ventilation (EOV), Oxygen Uptake Efficiency Slope (OUES), a Heart Failure Cardiopulmonary Exercise (HFCE) Score was developed.

RESULTS The high HFCE score group had a higher prevalence of NYHA class III-IV, higher NT-proBNP level, lower 6-mimute-walk-distance, worse hemodynamic parameters. The high HFCE score correlated well with the high level of pulmonary vascular resistance (PVR), pulmonary artery wedge pressure (PAWP) and mean pulmonary artery pressure (mPAP), and the low level of cardiac output (CO). Moreover, 46 patients developed 54 composed clinical events, which corresponding to an increase in HFCE score. In the multivariate model, the HFCE Score was an independent predictor of composed clinical events. Kaplan–Meier analysis showed a significantly higher probability of composed clinical events in the patients with a higher HFCE score.

CONCLUSIONS The HFCE score, obtained from cardiopulmonary exercise testing, indicates hemodynamic severity and provides prognostic information for predicting clinical worsening and mortality in patients with PH-LHF.

GW31-e1078

The effect of sacubitril–valsartan in heart failure patients with mid-range and preserved ejection fraction: a meta-analysis

Xiong Bo, Qian Jun, Rong Shunkang, Yao Yuanqing, Huang Jing
Department of Cardiology, The Second Affiliated Hospital of Chongqing Medical University, No. 76, Linjiang Road, Chongqing 400010, China

OBJECTIVES The effect of sacubitril–valsartan in heart failure patients with mid-range (HFmEF) and preserved (HFpEF) ejection fraction remains unclear. We aimed to investigate the clinical benefits of sacubitril–valsartan in HFmEF and HFpEF patients.

METHODS We searched the PubMed, Embase, Cochrane Library and China National Knowledge Infrastructure (CNKI) from inception to February 29, 2020 to identify pertinent articles. Studies meeting the inclusion criteria were included and analyzed.

RESULTS Six studies, with a total of 5201 patients, were included. Compared with ACEI/ARB, sacubitril–valsartan significantly reduced the rate of HF hospitalization (RR 0.84, 95% CI 0.77–0.91, P<0.001) and improved the NYHA class (RR 1.25, 95% CI 1.10–1.43, P=0.001) in HFmEF and HFpEF patients. But both the cardiovascular mortality and the all-cause mortality were not significantly decreased by sacubitril–valsartan. In addition, there were also no significant differences in the NT-ProBNP and left ventricular ejection fraction changes between the two groups. Regarding safety, sacubitril–valsartan was likely to increase the risk of hypotension, but the incidence of serum creatinine elevation was significantly lower in sacubitril–valsartan group than in ACEI/ARB group.

CONCLUSIONS This meta-analysis suggests that sacubitril–valsartan may be an effective and safe strategy to improve the clinical symptoms and reduce the HF hospitalization in HFmEF and HFpEF patients.

GW31-e1080

The effect of sacubitril/valsartan on cardiac remodeling by echocardiography in patients with heart failure

Xiong Bo, Yang Gang, Huang Jing
Department of Cardiology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing 400010, China

OBJECTIVES The aim of our study was to investigate the cardiac remodeling effect of sacubitril/valsartan in patients with heart failure.

METHODS Randomized controlled trials (RCTs) were searched before Jan 31, 2020 and were strictly selected according to the inclusion and exclusion criteria. Weight mean difference (WMD) with 95% confidence interval (CI) was used to analysis.

RESULTS Ten RCTs with a total of 1186 heart failure patients, were included in our meta-analysis. According to the results, in comparison with ACEI/ARB, sacubitril/valsartan significantly improved the left ventricular ejection fraction (LVEF, WMD=−3.12, 95% CI −4.51 to −1.73, P<0.001), left ventricular end-diastolic dimension (LVEDD, WMD=−3.12, 95% CI −4.51 to −1.73, P<0.001), left ventricular end-systolic dimension (LVESD, WMD=−2.43, 95% CI −3.96 to −0.90, P=0.002), left ventricular mass index (LVMI, WMD=−5.92, 95% CI −10.37 to −1.47, P=0.009) and interventricular septum thickness (IVS, WMD=−0.83, 95% CI −1.40 to −0.26, P=0.004). However, the left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV) and left atrial volume (LAV) were not significantly different between the two groups.

CONCLUSIONS Sacubitril/valsartan could furtherly improve or reverse the cardiac remodeling of heart failure patients.

GW31-e1091

Identification of potential prognostic biomarkers related to the development of heart failure using weighted gene co-expression network analysis

Qixin Chen, Hong Chen, Sufang Li
Department of Cardiology, Beijing Key Laboratory of Early Prediction and Intervention of Acute Myocardial Infarction, Center for Cardiovascular Translational Research, Peking University People's Hospital, Beijing 100044, China

OBJECTIVES A considerable amount of patients develop heart failure (HF) after suffering from acute myocardial infarction (AMI). Early recognition of patients at risk of developing HF after AMI would be a powerful strategy to improve the prognosis of AMI. The propose of this study was to identify significant prognostic biomarkers for the progression of HF following AMI via weighted gene co-expression network analysis (WGCNA).

METHODS The whole-blood gene expression dataset GSE11947, containing 32 patients with or without HF after AMI (termed post-AMI HF and non-HF, n=16 per group) was selected from the Gene Expression Omnibus (GEO) database. The co-expression network consisting of top 10,000 highly-variable genes in dataset GSE11947 was constructed using 'WGCNA' R package. Genes with similar expression profiles were merged into the same modules using the DynamicTreeCut algorithm. Modules significantly correlated with HF were identified based on Module Eigengenes (MEs) and Module Significance (MS). The Gene Ontology (GO) enrichment and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses were performed on genes identified in HF-related modules by Metascape. Hub genes in significant modules were screened according to the criterion of gene significance (|GS|) >0.2 and modular membership (|MM|) >0.8. The expressions of hub genes were validated in the dataset GEO59867 (post-AMI HF: n=9; post-AMI non-HF: n=8). The diagnostic performance of the genes were assessed by receiver operating characteristic (ROC) curve analysis.

RESULTS A total of 17 modules were identified between post-AMI HF and non-HF groups. Among them, the greenyellow (positive correlation) and yellow module (negative correlation) were the most significantly correlated with post-AMI HF. Functional enrichment analyses showed that the greenyellow module was primarily related to autophagy, inflammatory response, immunity and cell death, while the yellow module was mainly associated with oxidative phosphorylation, mitochondrial translation initiation, formation of ATP by chemiosmotic coupling and fatty acid metabolism. Sixty eight out of 218 genes of the greenyellow module and 163 out of 502 genes of the yellow module were identified as the hub genes. After the validation of the hub genes expressions and ROC curve analysis in dataset GEO59867, 4 hub genes, including SPRED2, SDCBP, PRKAR1A and VAMP3, were finally proved to have predictive value for post-AMI HF.

CONCLUSIONS Our study identified SPRED2, SDCBP, PRKAR1A and VAMP3 as potential prognostic biomarkers of the progression of post-AMI HF. These findings provided new clues for the early recognition of patients at risk of development of HF after AMI.

GW31-e1092

Impact of systolic blood pressure on clinical outcomes in patients hospitalized for heart failure

Xinghe Huang, Jiamin Liu, Lihua Zhang, Shuang Hu, Fengyu Miao, Yan Li, Jing Li
NHC Key Laboratory of Clinical Research for Cardiovascular Medications, National Clinical Research Center for Cardiovascular Diseases, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China

OBJECTIVES High systolic blood pressure (SBP) is a major risk factor for progression of heart failure (HF); however, the association between SBP and prognosis among patients with established HF remains uncertain. The study aimed to investigate the association between SBP in a stable phase during hospitalization and short- and long-term clinical outcomes in patients hospitalized for HF.

METHODS The China Patient-centered Evaluative Assessment of Cardiac Events Prospective Heart Failure Study prospectively enrolled patients hospitalized for HF in 52 hospitals from 20 provinces in China between August 2016 and May 2018. SBPs were measured in a stable phase during hospitalization according to the standard research protocol. Outcomes were all-cause death and HF readmission at 1 month, 6 months and 1 year. The associations between SBP and outcomes were assessed using multivariable Cox proportional hazards regression models. Restricted cubic splines were used to examine the non-linear association between SBP and outcomes.

RESULTS The 4564 patients had a mean age of 65.3±13.5 years and 37.9% were female. Patients with lower SBP were younger, having lower left

ventricular ejection fraction, less frequently having comorbidities, while more frequently receiving β-blockers, aldosterone antagonists and diuretics. SBP <110 mmHg was associated with a higher risk of all-cause death at 1 month (adjusted hazard ratio [HR], 2.78; 95% confidence interval [CI], 1.43–5.40; P=0.003), 6 months (adjusted HR, 1.87; 95% CI, 1.41–2.49; P<0.001) and 1 year (adjusted HR, 1.58; 95% CI, 1.27–1.96; P<0.001). The association between SBP <110 mmHg and higher risk of 1-month HF readmission existed (adjusted HR 1.56; 95% CI 1.11–2.17; P=0.009), and persisted at 6 months (adjusted HR 1.36; 95% CI 1.13–1.63; P<0.001) and 1 year (adjusted HR 1.24; 95% CI 1.06–1.45; P=0.006). In restricted cubic spline models, the risks of 1-year all-cause death and HF readmission increased significantly at SBP<110 mmHg, and no associations between higher SBP and higher risk of outcomes have been found.

CONCLUSIONS In patients hospitalized for HF, low SBP (<110 mmHg) in a stable phase during hospitalization portends increased risks of all-cause death, as well as HF readmission. Our findings suggested that the lowest SBP possible might not be optimal for HF patients.

GW31-e1093

Systolic blood pressure at admission and long-term clinical outcomes in patients hospitalized for heart failure

Xinghe Huang, Jiamin Liu, Shuang Hu, Lihua Zhang, Fengyu Miao, Jing Li
NHC Key Laboratory of Clinical Research for Cardiovascular Medications, National Clinical Research Center for Cardiovascular Diseases, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China

OBJECTIVES Blood pressure is one of the most important predictors for developing heart failure (HF). However, there is still uncertainty about the association between admission systolic blood pressure (SBP) and clinical outcomes in patients hospitalized for HF. The study sought to investigate the association between SBP at admission and one-year clinical outcomes in patients hospitalized for HF and in subgroups.

METHODS This study was based on the China Patient-centered Evaluative Assessment of Cardiac Events Prospective Heart Failure Study (China PEACE 5p-HF Study), which prospectively enrolled patients hospitalized for HF in 52 hospitals from 20 provinces in China between August 2016 and May 2018. Patients were divided into four groups according to the quartiles of SBP at admission (<117, 117–130, 131–148, and >148 mmHg). The multivariable Cox proportional hazards regression models were fitted to examine the association between admission SBP and all-cause death and HF readmission within one year after the index of hospitalization. Restricted cubic splines were used to explore the non-linear association between SBP and the clinical outcomes.

RESULTS Among 4896 patients, those with lower admission SBP were younger, more likely to be male, have left ventricular ejection fraction <40%, and receive β-blockers, aldosterone antagonists, and diuretics. After adjustment for potential confounders, compared with the 4th SBP quartile (SBP >148 mmHg), patients in the 1st SBP quartile (SBP <117 mmHg) had higher risk of all-cause death (HR, 1.92; 95% CI: 1.54–2.41; P<0.001) and HF readmission (HR, 1.43; 95% CI 1.22–1.68, P<0.001). In restricted cubic spline models, higher admission SBP was associated with significantly lower all-cause death, with no upper threshold; the risk of HF readmission was higher in patients with a lower SBP, while above a SBP of approximately 120 mmHg, the risks were similar. The associations were consistent in most subgroups, such as age, sex, left ventricular ejection fraction, etiology, and medications for HF.

CONCLUSIONS In patients hospitalized for HF, low SBP (<117 mmHg) at admission portended an increased risk of one-year all-cause death and HF readmission, and the associations were consistent among subgroups.

GW31-e1103

Prediabetes and the association with one-year mortality in acute heart failure: China PEACE prospective heart failure study

Guangda He, Jing Li
National Clinical Research Center of Cardiovascular Diseases, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China

OBJECTIVES To examine the association between prediabetes and one-year all-cause mortality risk in patients hospitalized for heart failure (HF).

METHODS We prospectively enrolled patients primarily hospitalized for HF and discharged alive from 52 hospitals in 20 provinces of China. Patients with plasma glucose ≥11.1 mmol/L, glycosylated hemoglobin (HbA_{1c}) ≥6.5%, or diabetes mellitus history were excluded, only patients without diabetes mellitus at baseline were included in the present analysis. Prediabetes was defined as i) random plasma glucose 7.8–11.0 mmol/L, or ii) HbA_{1c} 5.7–6.4%, and the rest patients were defined as normal glycemic group. All patients were followed up face-to-face or via telephone call at 1, 6, and 12 months, death events were ascertained according to death certificates, investigators' report and national death registration. We used a Cox regression model to evaluate the 1-year mortality risk for prediabetes, candidate covariates including age (≤65-year, >65-year), gender (male, female), systolic blood pressure (<110, 110–130, >130 mmHg), New York Heart Association class (II, III, IV), previous HF (yes, no), chronic kidney disease (yes, no), primary etiology for HF (ischemic, non-ischemic), level of left ventricular ejection fraction (LVEF) (≤45, >45), N-terminal pro-brain natriuretic peptide, discharge use of ACEI/ARBs (yes, no), β-blockers (yes, no). In order to further assess the prediabetes effect across various LVEF groups, patients were divided into low-LVEF (LVEF ≤45) and high-LVEF (LVEF >45) subgroups.

RESULTS Three thousand, one hundred fifty-four eligible HF patients with random glucose and HbA_{1c} data at baseline were included in the current analysis, whose median (interquartile range) age was 67 (56, 75) and 1146 (36.3%) were female. There were 704 (22.3%) patients with prediabetes at baseline. The 1-year mortality of normal glycemic, prediabetes patients were 15.0% (367/2450), 19.3% (136/704). Prediabetes patients had significant higher risk of 1-year mortality (unadjusted HR, 1.33 95% CI, 1.09–1.62) than normal glycemic patients, though the influence was attenuated after multi-variable adjustment (adjusted HR, 1.26 95% CI, 1.04–1.54). In addition, the prediabetes effect was only significant among patients in high-LVEF subgroup (adjusted HR, 1.42, 95% CI, 1.03–1.98), not in low-LVEF subgroup (adjusted HR, 1.26, 95% CI, 0.95–1.66).

CONCLUSIONS Among the non-diabetic patients hospitalized for HF, over one-fifth were affected by prediabetes at baseline. We observed that the adverse effect of prediabetes was only significant in patients with LVEF >45, but not in those with LVEF ≤45.

GW31-e1119

International physical activity questionnaire: assessing effects of daily physical activity on left ventricular diastolic function

Lina Su, Songna Yang
Department of Cardiology, Peking University People's Hospital

OBJECTIVES Left ventricular diastolic dysfunction may lead to ejection fraction preserved heart failure (HFpEF). Compared to ejection fraction reduced heart failure (HFrEF), there is no effective drug therapies to decrease morbidity and mortality of HFpEF. Though some data suggested that intensive exercise training can have a positive effect on diastolic indices, few studies have investigated the effects of daily exercise on diastolic function. Our study is to evaluate the influences of daily physical activities on left ventricular diastolic function.

METHODS A total of 432 patients were enrolled from March 2018 to July 2019 in Peking University People's Hospital. Patients elder than 18 years old were included if they had stable physical activities in recent six months and normal left ventricular systolic function. Echocardiography was performed to assess left ventricular diastolic function by tissue Doppler parameters e′, which were more sensitive and accurate than traditional echocardiographic transmitral flow velocity indices. We took international physical activity questionnaire to evaluate recent daily physical activities as well as to collect demographic characteristics and medical history. According to the physical activity guidelines for Americans, we identified these patients into low intensity exercise (LIE) group and moderate-high intensity exercise (MHIE) group. Propensity score matching (PSM) was underwent. Quantitative data were analyzed using student's t-test, while categorical variables were compared using the χ^2 test.

RESULTS After matching potential risk factors through PSM with matching ratio 1:3, 83 cases in MHIE group and 249 cases in LIE group were included in the final analysis. Between LIE and MHIE group, age (49±14 vs. 50±14, P=0.258), sex (52 vs. 46%, P=0.341) and body mass index (23.5±3.5 vs. 24.0±3.8) were not different. Compared with LIE group, MHIE group showed significantly higher septal e′ (8.0±2.9 cm/s vs. 7.3±2.6 cm/s, P=0.042). In addition, left ventricular ejection fraction was similar between the two groups (70.8±5.8% vs. 70.3±6.5%, P=0.458).

CONCLUSIONS Our study showed that Moderate-high intensity daily physical activities can improve septal e′. It implied that moderate-high intensity daily physical activities may improve left ventricular diastolic function.

GW31-e1139

Prevalence and risk factors of heart failure with reduced ejection fraction in northwest China: a cross-sectional study

Min Han, Ma Yi Tong
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi, P. R. China

OBJECTIVES Heart failure (HF) remains a rising global health burden across different racial regions, of which heart failure with reduced ejection fraction (HFrEF) is the worst phenotype. However, the HF phenotypes are not distinguished in most epidemiological studies, and there is limited epidemic data on HFrEF in the Chinese general population.

METHODS A four-stage stratified cluster random sampling scheme was adopted to recruit represented participants among Han, Uygur, and Kazak population in northwest China. HFrEF was diagnosed by meeting the signs or symptoms of heart failure and EF ≤40%. Multiple logistic regression was applied to identify associated factors of HFrEF.

RESULTS A total of 14,618 participants aged 35–101 years were included and 170 (1.2%) of them had HFrEF. The prevalence rate of HFrEF increased strikingly with age (all P<0.05) and was higher in males than that in females (1.5 vs. 0.8%, P=0.001). There exist significantly racial differences in HFrEF prevalence across Han, Uygur, and Kazak population (0.9, 1.4, and 1.3%, P<0.05). After multiple regression, age, hypertension, hyperuricemia, atrial fibrillation, valvular heart disease, and low HDL-C were identified as risk factors, while female sex was identified as a protective factor for HFrEF.

CONCLUSIONS HFrEF differed significantly by age, sex, and ethnicity in the natural population from Xinjiang. The exploration of prevalence and risk factors of HFrEF helps determine subjects 'at risk' of developing HFrEF and make ethnicity-specific strategies for the prevention of HFrEF

GW31-e1144

Plasma CA-125 or BNP: which predicts acute heart failure better in patients with acute myocardial infarction?

Weiqi Wang, Xiaokang Hu, Zhouqing Huang
The Key Laboratory of Cardiovascular Disease of Wenzhou, Department of Cardiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, China

OBJECTIVES Previous studies have shown that plasma CA-125 and BNP are closely related to acute heart failure in patients with acute myocardial infarction, but they comprised small-sample studies. On this basis, this study aimed to more comprehensively explore the relationship between plasma CA-125 and BNP using a larger dataset.

METHODS This cohort study enrolled 2025 patients from the Coronary Care Unit of the First Affiliated Hospital of Wenzhou Medical University between January 2016 and October 2019. We used the ROC curve to evaluate the predictive ability of CA-125 and BNP for AHF, and multivariate regression analysis was also used to determine its predictive ability. Additionally, to balance the associated baseline characteristics, a propensity score-matched cohort design was used, yielding 864 patients.

RESULTS Among the 2025 patients hospitalized for AMI, acute heart failure was found in 30.02%. ROC analysis revealed that BNP, CA-125 and BNP+CA-125 significantly predicted the development of AHF (area under the ROC curve [AUC]: BNP, 0.762; CA-125, 0.660; BNP+CA-125, 0.760; all P<0.001). However, multivariate regression analysis showed that CA-125 was not a good predictor of acute heart failure in the overall cohort (P=0.157), while BNP was a powerful predictor (P=0.001). After propensity score matching, 864 patients were included. The ability to predict AHF was also shown, with AUC values of 0.621 for BNP, 0.564 for CA-125, and 0.619 for BNP+CA-125 (all P<0.01). In the matched cohort (n=432 in each group), the results of multivariate analysis still revealed that BNP was a powerful predictor (P=0.001) and CA-125 had no predictive power (P=0.357).

CONCLUSIONS The BNP levels have good predictive value for the occurrence of AHF in patients with AMI. However, the prediction of AHF by the CA-125 levels is limited by factors such as age, heart rate, blood pressure, stroke history and CKD history.

GW31-e1236

Daily physical activities based on questionnaire improve tissue Doppler indices of left ventricular diastolic function

Lina Su, Songna Yang
Department of Cardiology, Peking University People's Hospital

OBJECTIVES Left ventricular diastolic dysfunction may lead to ejection fraction preserved heart failure (HFpEF). Compared to ejection fraction reduced heart failure (HFrEF), there is no effective drug therapies to decrease morbidity and mortality of HFpEF. Though some data suggested that intensive exercise training can have a positive effect on diastolic indices, few studies have investigated the effects of daily exercise on diastolic function. Our study is to evaluate the influences of daily physical activities on left ventricular diastolic function.

METHODS A total of 432 patients were enrolled from March 2018 to July 2019 in Peking University People's Hospital. Patients elder than 18 years old were included if they had stable physical activities in recent six months and normal left ventricular systolic function. Echocardiography was performed to assess left ventricular diastolic function by tissue Doppler parameters e′, which were more sensitive and accurate than traditional echocardiographic transmitral flow velocity indices. We took international physical activity questionnaire to evaluate recent daily physical activities as well as to collect demographic characteristics and medical history. According to the physical activity guidelines for Americans, we identified these patients into low intensity exercise (LIE) group and moderate-high intensity exercise (MHIE) group. Propensity score matching (PSM) was underwent. Quantitative data were analyzed using student's t-test, while categorical variables were compared using the χ^2 test.

RESULTS After matching potential risk factors through PSM with matching ratio 1:3, 83 cases in MHIE group and 249 cases in LIE group were included in the final analysis. Between LIE and MHIE group, age (49±14 vs. 50±14, P=0.258), sex (52 vs. 46%, P=0.341) and body mass index (23.5±3.5 vs. 24.0±3.8) were not different. Compared with LIE group, MHIE group showed significantly higher septal e′ (8.0±2.9 cm/s vs. 7.3±2.6 cm/s, P=0.042). In addition, left ventricular ejection fraction was similar between the two groups (70.8±5.8% vs. 70.3±6.5%, P=0.458).

CONCLUSIONS Our study showed that Moderate-high intensity daily physical activities can improve septal e′. It implied that moderate-high intensity daily physical activities may improve left ventricular diastolic function.

GW31-e1251

Long-term performance and risk factors analysis after permanent his-bundle pacing and atrioventricular node ablation in patients with atrial fibrillation and heart failure

Mengxing Cai[1,2,3], Weijian Huang[1,2]
[1]Department of Cardiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China
[2]The Key Lab of Cardiovascular Disease of Wenzhou, Wenzhou, China
[3]Department of Cardiology, Virginia Commonwealth University Health System, Richmond, VA (K.A.E.)

OBJECTIVES His bundle pacing (HBP) combined with atrioventricular node (AVN) ablation has been demonstrated to be effective in patients with atrial fibrillation (AF) and heart failure (HF) during medium-term follow-up and there was limit data on the risk analysis of adverse prognosis in this population. In this study, we aimed to evaluate the long-term performance of HBP following AVN ablation in AF and HF.

METHODS From August 2012 to December 2017, consecutive AF patients with HF and narrow QRS who underwent AVN ablation and HBP were enrolled. The clinical and echocardiographic data, pacing parameters, all-cause mortality and heart failure hospitalization (HFH) were tracked.

RESULTS A total of 94 patients were enrolled (age 70.1±10.5 years; LVEF 45.3±14.9%). Permanent HBP and AVN ablation was successfully performed in 81 (86.2%) patients, with a mean follow-up of 3.3±1.7 years. LVEF improved from 44.9±14.9% at baseline to 57.6±12.5% during last follow-up. NYHA functional class improved from 2.79±0.62 to 1.41±0.73 (both P<0.001). HFH or all-cause mortality occurred in 21 (25.9%) patients. Lower LVEF, higher pulmonary artery systolic pressure (PASP), or higher serum creatinine (Scr) at baseline were significantly associated with higher composite endpoint of HFH or death (P<0.05). The pacing threshold was 1.0±0.7 V@ 0.5 ms at implant and remained stable during follow-up.

CONCLUSIONS During long-term follow-up, HBP combined with AVN ablation was effective in patients with AF and drug-refectory HF. Higher PASP or Scr, or lower LVEF at baseline were independent predictors of composite endpoint of all-cause mortality or HFH.

GW31-e1253

Gender-specific disparities in health status and 1-year clinical outcomes among patients hospitalized for heart failure in China

Danli Hu, Jing Li
National Clinical Research Center of Cardiovascular Diseases, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China

OBJECTIVES We aim to evaluate gender-related disparity in patient characteristics, treatment pattern, health status, 1-year survival and hospitalization among Chinese patients with heart failure (HF) in a prospective cohort.

METHODS We evaluated adult patients hospitalized for HF from 52 geographically diverse hospitals in China and followed up them for one year. Health status was measured by Kansas City Cardiomyopathy Questionnaire (KCCQ) and EQ-5D-5L questionnaire at baseline, 1-month, 6-month and 1-year visit. Multivariable Cox regression model were fitted to investigate difference in prognosis across men and women.

RESULTS Totally 4866 patients were included in final analysis. Women accounted for 37.5% and were 5 years older than men (68.4±12.1 vs. 63.3±13.8, P<0.001). Proportion of HFpEF in women was higher than men compartment (52.3 vs. 29.1%). Ischemic heart disease was the most frequent comorbidity in both women and men (53.4 vs. 52.8%), women were less likely to have cardiomyopathy (28.4 vs. 44.7%) than men, but more likely to have hypertension (60.9 vs. 54.9%), atrial fibrillation (40.5 vs. 35%) and diabetes (34 vs. 29%). There was no significant difference in NYHA (III/IV, 85.4 vs. 85.9%) and NT-proBNP levels (1430 pg/mL vs. 1485 pg/mL) in women and men.

Women received less treatment of β-blockers, ACEI/ARB, aldosterone antagonists (AldA) both in-hospital and at discharge. Women reported obviously worse health status than men at baseline and 1-year visit (KCCQ: 40.5±22.3 vs. 46.2±22.8; <0.001; EQ-5D index: 0.57±0.29 vs. 0.64±0.27; <0.001). There was no significant difference in one-year crude all-cause survival and hospitalizations (16.4 vs. 16.9%, P=0.65; 45.4 vs. 47.5%, P=0.25, respectively) between women and men. After adjusting for age, socioeconomic status, medical history, NYHA, ejection fraction and NT-proBNP, treatment and health status, women had significant better 1-year survival than men (HR 0.80; 95% CI 0.65–0.99; P=0.04), but similar risk of hospitalization as men (HR 1.03; 95% CI 0.96, 1.11; P=0.35).

CONCLUSIONS Men and women with HF differ significantly in clinical characteristics and management. Despite worse symptoms and health status, women had better survival and similar rates of hospitalization. Clinical physician should pay more attention to women's health status besides clinical outcomes.

GW31-e1307

Impact of serum uric acid on left ventricular diastolic function in patients with autoimmune diseases

Zixuan Yang, Yu Kang, Tong Wang, Jiayi Lin, Qiaowei Chen, Xiaojing Chen, Qing Zhang
Department of Cardiology, West China Hospital, Sichuan University

OBJECTIVES Asymptomatic left ventricular dysfunction (LVDD) is underestimated in patients with autoimmune diseases (AD). There are inconsistent evidence regarding whether elevated serum uric acid (SUA) becomes a new cardiovascular risk factor. This retrospective study aimed to assess cardiac abnormalities in patients with AD, and to explore the association between SUA and cardiac function.

METHODS The patients who had been discharged from Department of Rheumatology with a definite AD diagnosis during Jan 2011 to Dec 2017 were retrospectively enrolled, if they also had echocardiography and SUA measurement. Data were automatically extracted from hospital information system. LVDD was defined by at least one of the following features as (1) LV hypertrophy, and/or (2) left atrial enlargement, and/or (3) E/e′ ≥13.

RESULTS A total of 5873 patients (45±16 years, 78.9% female) without primary cardiac diseases were analyzed. LVDD was the most predominant abnormality that found in 2417 (41.2%) patients, followed by valvular lesion in 21.8%, pericardial effusion in 15.2% and pulmonary hypertension in 4.2% patients. When the patients were grouped according to the SUA quartiles (Q1–Q4), the prevalence of LVDD showed a trend to increase with the SUA level (Table 1). After adjusted for other risk factors, the patients in Q2, Q3 and Q4 had 1.354 fold, 1.447 fold and 2.009 fold of the chance in LVDD when those in Q1 served as a reference.

CONCLUSIONS LVDD was commonly observed in AD patients that independently associated with SUA elevation. It warrants further investigation whether SUA elevation would become the target of treatment for LVDD.

GW31-e1324

Evaluation of criteria to distinguish left bundle branch pacing from left ventricular septal pacing

Shengjie Wu
Department of Cardiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China

OBJECTIVES To evaluate the electrocardiogram (ECG) and intracardiac eletrogram (EGM) characteristics of left bundle branch pacing (LBBP) compared to left ventricular septal pacing (LVSP).

METHODS An HBP lead, LBBP lead and multielectrode catheter at LV septum were placed. Direct LBB capture was defined as demonstration of retrograde His potential (P_{His}) on the HBP lead and/or anterograde left conduction system potentials (P_{LCS}) on the multielectrode catheter immediately after stimulus by LBBP lead. We analyzed the ECG and EGM characteristics from LBBP lead with or without LBB capture at various depths and outputs.

RESULTS Thirty patients (21 non-LBBB and 9 LBBB) were included and all demonstrated LBB capture using defined criteria. From LVSP to LBB capture with increasing output, the proportion of paced RBBB pattern increased from 23.4% (5/21) in non-LBBB and 44.4% (4/9) in LBBB group to 100% in both groups, while the stimulus to left ventricular activation time (Stim-LVAT) decreased abruptly with all of the decreasements ≥10 ms. All patients with characteristics of selective(S)-LBBP demonstrated direct LBB capture. S-LBBP showed longer paced QRS duration than those in LVSP and nonselective LBBP. LBB potential was recorded in all patients during intrinsic rhythm (non-LBBB group) or His corrective pacing (LBBB group) when the LBB capture threshold was <1 V/0.5 ms.

CONCLUSIONS Direct LBB capture can be confirmed by recording retrograde P_{His} and anterograde P_{LCS}. Stim-LVAT and SLBBP could be used as a simple criterion to confirm LBB capture.

BLOOD LIPIDS AND ATHEROSCLEROSIS

GW31-e0017

Relationship between plasma lipoprotein-associated phospholipase A2 concentrations and apolipoprotein in stable coronary artery disease patients

Yang Ling[1], Shengxing Tang[2], Cong Fu[1,3]
[1]Department of Cardiology, Yi Ji Shan Hospital Affiliated to Wan Nan Medical College
[2]Department of Nephrology, Yi Ji Shan Hospital Affiliated to Wan Nan Medical College
[3]Key Laboratory of Non-coding RNA Transformation Research of Anhui Higher Education Institution (Wann Nan Medical College)

OBJECTIVES Both the plasma lipoprotein-associated phospholipase A2 (Lp-PLA2) and apolipoprotein particles have been viewed as risk maker for cardiovascular heart disease. However, the relationship between Lp-PLA2 and apolipoprotein particles in patients with stable coronary heart disease has not been evaluated yet.

METHODS There are a sum of 569 patients, who never took lipid-lowering drugs, engaged in this research (angiographically proven CAD: n=291; non-CAD: n=278). Plasma Lp-PLA2 concentrations were calculated by Elisa Kit, while the apolipoprotein particles were measured by department of laboratory.

RESULTS The plasma concentration of Lp-PLA2 was significantly higher in CAD patients than non-CAD patients (136.0±60.5 ng/mL vs. 113.2±65.6 ng/mL, P<0.001). Pearson correlation analyses explained the plasma Lp-PLA2 concentration is correlated with apoB (r=0.390, P<0.001) and apoB/apoA1 (r=0.450, P<0.001), not associated with apoA1 (r=–0.099, P=0.101). Nevertheless, no similar results were observed in non-CAD group except apoA-1. Furthermore, multiple linear regression indicated that the plasma Lp-PLA2 concentrations were positively correlated with the apoB (β=0.390, P<0.001) and apoB/apoA1 (β=0.450, P<0.001), but not apoA1 (β=–0.099, P=0.121). After adjusting for age, gender, smoking, hypertension and DM, the plasma Lp-PLA2 concentration was positively associated with apoB (β=0.364, P<0.001) and apoB/apoA1 (β=0.390, P<0.001).

CONCLUSIONS The plasma Lp-PLA2 concentrations was positively associated with apoB, apoB/apoA-1 in patients with stable CAD, denoting an interaction between Lp-PLA2 and apolipoprotein particles in the status of CAD.

GW31-e0154

Retrospective analysis of enhanced external counterpulsation on blood lipids and carotid plaque in patients with coronary heart disease and type 2 diabetes

Xin Huang[1], Hongjiao Kong[2], Hui Zhang[1]
[1]The Second Affiliated Hospital of Zhengzhou University
[2]The Third Affiliated Hospital of Zhengzhou University

OBJECTIVES Enhanced external counterpulsation (EECP) is a green, safe, economical, and effective non-invasive treatment for coronary heart disease. This retrospective study was designed to investigate the effects of EECP on blood lipid profile and carotid plaque in patients with coronary heart disease and type 2 diabetes.

METHODS This study included patients who were treated in our hospital from January 2019 to January 2020 and were diagnosed with coronary heart disease and type 2 diabetes. Forty patients who received EECP treatment+conventional treatment were selected as the EECP group, and 40 patients who received conventional treatment within the same period were randomly selected as the conventional treatment group. Blood lipid profiles and carotid ultrasonic data of the patients before and after a 7-week treatment were compared and analyzed between those two treatment groups. Consequently, the clinical efficacy and safety were evaluated and compared in two treatment groups. The blood lipid profiles included lipoprotein-associated phospholipase A2 (Lp-PLA2), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and carotid ultrasound data included carotid intima-media thickness (IMT), carotid plaque Crouse score, and carotid plaque grade score.

RESULTS After a 7-week standard treatment, blood lipids and carotid plaques in both conventional treatment group and the EECP group were significantly improved as compared with that before treatment (P<0.05). However, blood Lp-PLA2, TC, TG, and LDL-C in the EECP group were significantly lowered compared with that in the conventional treatment group (P<0.05). Compared with that before treatment, the HDL-C level was significantly increased in the EECP group (P<0.05), but not in the conventional treatment group (P>0.05). Both carotid plaque scores improved after a 7-week treatment (P<0.05), but the EECP group was superior to the conventional treatment group in reducing carotid plaque scores (P<0.05). In the adverse reactions of the EECP group, some patients did not adapt to the external counterpulsation in the early stage

of treatment and did not report any discomfort after adjusting the therapeutic pressure.

CONCLUSIONS Our results showed that EECP has substantial improvements in blood lipid profiles and carotid plaques formation in patients with coronary heart disease and type 2 diabetes, suggesting it is superior to conventional drugs in reducing blood lipids and carotid plaques.

GW31-e0201

Value of cardiometabolic index, lipid accumulation product, and body adiposity index in predicting the risk of hypertension: findings from a large Asian population

Haoyu Wang
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES Adiposity, defined by higher cardiometabolic index (CMI), lipid accumulation product (LAP), and body adiposity index (BAI), has conferred increased metabolic risk. However, the incremental utility of CMI, LAP, and BAI in association with prevalent hypertension has not been well described in a population-based setting. We hypothesized that CMI, LAP, and BAI would provide important insight into hypertension risk.

METHODS Blood pressure (BP), fasting lipid profiles, and anthropometric parameters were recorded in a cross-sectional study of 11,400 participants (mean age, 54 years; 53% women) from China. Logistic regression models were used to assess associations of CMI, LAP, and BAI with prevalent hypertension. BAI was evaluated according to hip (cm)/[height (m) 1.5]−18; LAP was calculated separately for men [(WC-65)×TG] and women [(WC-58)×TG]; and CMI was defined by TG/HDL-C×waist-to-height ratio.

RESULTS CMI, LAP, and BAI were independently correlated with higher SBP and DBP, with nonstandardized (B) coefficients ranging from 1.827 to 4.590 mmHg and 1.475 to 2.210 mmHg (all P<0.001). After adjustment for hypertension risk factors and potential confounders, CMI, LAP, and BAI, modeled as continuous measures, carried hypertension odds (95% CI) of 1.356 (1.259–1.459), 1.631 (1.501–1.771), and 1.555 (1.454–1.662) in women, respectively, per SD increment. In men, each SD increase in CMI, LAP, and BAI experienced a 31, 65, and 53% higher hypertension risk, respectively. Moreover, among women, the odds ratio (95% CI) for hypertension were 2.318 (1.956–2.745), 3.548 (2.985–4.217), and 3.004 (2.537–3.557) in the 4th quartile vs. the first quartile of CMI, LAP, and BAI, respectively. For men, the corresponding figures were 2.200 (1.838–2.635), 3.892 (3.238–4.677), and 3.288 (2.754–3.927), respectively.

CONCLUSIONS Our findings supported the use of CMI, LAP, and BAI for estimating obesity-related hypertension burden in clinical practice and in adiposity research. Greater emphasis should be placed on reinforcing the notion that focusing on total body fat (defined by elevated BAI) and abdominal VAT compartments (quantified by increased CMI and LAP) when screening for adiposity may be helpful to better estimate cardiometabolic risk given the importance of hypertension in the pathogenesis of CVD.

GW31-e0203

Value of triglyceride-glucose index for the estimation of ischemic stroke risk: insights from a general population

Haoyu Wang
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES Recent studies have recognized triglyceride-glucose index (TyG) as a practical surrogate of insulin resistance. Previous studies have demonstrated that insulin resistance contributes to ischemic stroke via multiple mechanisms. Our study aimed to investigate the association between TyG and prevalent ischemic stroke, exploring the value of TyG to optimize the risk stratification of ischemic stroke.

METHODS This cross-sectional study included 10,900 subjects (mean age: 59.95 years, 59.8% females) from rural areas of northeast China between September 2017 to May 2018. TyG was calculated as ln[fasting triglyceride (mg/dL)×fasting plasma glucose (mg/dL)/2]. Ischemic stroke was diagnosed by 2 independent neurologists according to the World Health Organization recommendations with confirmation of computed tomography and/or magnetic resonance imaging.

RESULTS The prevalence of ischemic stroke was 5.49%. After adjusting for all covariates, each SD increment of TyG caused 22.8% additional risk for ischemic stroke. When dividing TyG into quartiles, the top quartile had a 1.776 times risk for ischemic stroke against the bottom category. Furthermore, smoothing curve fitting demonstrated this association was linear in the whole range of TyG. Finally, AUC revealed an improvement when introducing TyG into clinical risk factors (0.746 vs. 0.751, P=0.029). Consistently, category-free net reclassification index (0.195, 95% CI: 0.112–0.277, P<0.001) and integrated discrimination index (0.003, 95% CI: 0.001–0.004, P<0.001) confirmed the improvement by TyG to stratify ischemic stroke risk.

CONCLUSIONS The prevent ischemic stroke correlated proportionally with the increment of TyG, implicating the linearity of TyG as an indicator of ischemic stroke. Our findings suggest the potential value of TyG to optimize the risk stratification of ischemic stroke in a general population.

GW31-e0352

Plasma lipidomic profiling identifies lipids that predict major adverse cardiac event in acute coronary syndrome patients

Yuxin Yuan, Haiyi Yu, Lequn Zhou, Wei Zhao, Han Xiao, Youyi Zhang, Wei Gao
Peking University Third Hospital

OBJECTIVES In recent years, with the progress in coronary interventional therapy and secondary prevention of coronary artery disease (CAD), the short- and long-term prognosis of acute coronary syndrome (ACS) has been significantly improved. But the incidence of recurrent major adverse cardiovascular events (MACE) is still high. Furthermore, there are few reports on whether there were any biomarkers for the early warning of recurrent MACE to ACS patients in long-term follow-ups. Lipidomic profiles has been increasingly recognized as an enabling technique with the potential to identify key lipidomic features in an attempt to understand the pathophysiology and differentiate different types of CAD. We hypothesized that lipidomic profiles would provide insight into early warning or prognostic indicators before MACE occurs in ACS patients during follow-ups.

METHODS Our study is a multicenter, prospective, nested case-control study. ACS patients met inclusion and exclusion criteria were recruited (n=429). All patients were followed up monthly by clinics in 12 months after recruitment. When final follow-ups were completed, patients who had recurrent major adverse cardiovascular events within 12 months were enrolled in MACE group. Those patients who did not have MACE in 12 months were involved in the control group. Then these subjects were matched at a 1:1 ratio for sex, age, types of ACS, treatment at baseline and medical history including hypertension, diabetes mellitus, and dyslipidemia. Subsequently, we performed liquid chromatography-tandem mass spectrometry in human plasma. Analytes were tested for association with longitudinal changes in lipidomic traits using general linear models, and multi-marker panels were selected using forward selection.

RESULTS Twenty-two patients who had recurrent major adverse cardiovascular events within 12 months were enrolled in MACE group, whose average time from discharge to MACE occurred was 5.0±1.6 months, and 10 of them had MACE events after 3 months of recruitment. Among them, there were 4 cases of all-cause mortality, 8 cases of non-fatal myocardial infarction, 7 cases of unplanned revascularization and 3 cases of unstable angina re-hospitalization. Discovery liquid chromatography-tandem mass spectrometry profiling of 464 lipids was conducted on plasma samples. At the time point of 1 month before MACE occurrence, total plasmalogens PC and plasmalogens PC species (PC36:1p, PC36:3p, PC36:4p, PC38:2p, PC38:3p, PC38:4p, PC40:1p PC40:2p, PC40:3p and PC40:4p) levels in plasma were significantly lower in MACE group compared to controls (P<0.05). While at 3 month before MACE, 3 plasmalogens PC species (PC36:1p, PC38:2p and PC40:2p) started to show a decline in MACE group compared to controls (P<0.05).

CONCLUSIONS We identified plasmalogen PC of longitudinal changes in lipid trait in ACS patients during follow-ups. Reduced levels of plasmalogen PC before MACE occurrence may be an early warning marker of major adverse cardiovascular events for ACS patients.

GW31-e0365

The effects of obesity on the proteome and cholesterol efflux of HDL subclasses in young adults

Zhijian He, Runlu Sun, Yuling Zhang
Sun Yat-sen Memorial Hospital

OBJECTIVES HDL subclasses function and protein composition may better measure HDL's cardioprotective effects than its cholesterol content. However, whether obesity affects HDL subclasses proteomic composition and functions are not fully understood. In this study, we used fast protein liquid chromatography (FPLC) to separate HDL subclasses and study the effects of obesity on its proteomic compositions and functions in young adults.

METHODS Young males with simple obesity (n=6) and healthy control (n=6) were studied. HDL were fractionized by fast protein liquid chromatography (FPLC) into 18 fractions and examined for the concentration of total cholesterol (TC), triglyceride (TG), phospholipid (PL) and protein. Small, medium and large (S/M/L)-HDL subclasses were collected for proteomic analysis by label-free mass spectrometry. HDL functions (cholesterol efflux capacity and anti-oxidative ability) were examed. The correlation of alteration in HDL subclasses protein and HDL function were assessed with Pearson correlation analysis.

RESULTS Cholesterol efflux capacity in obesity group were significantly impaired by 34.5% in L-HDL, 30.6% in M-HDL and 31.2% in total-HDL. Antioxidative capacity had no significant impaired in L/M/S subclasses but significantly impaired in total-HDL of obesity group. S/M/L-HDL subclasses were collected for proteomic analysis and 123 HDL related proteins were identified which can be grouped into 6 functional categories (lipid metabolism, immune response, coagulation, proteolysis inhibition, metal binding and others). Lipid metabolism related proteins such as ApoA-1, ApoA-4, ApoM and CLU were decreased in L-HDL in obesity group, which was positively correlated with the impairment of L-HDL cholesterol efflux capacity.

CONCLUSIONS Obesity leads to a significant decrease of cholesterol efflux capacity in L-HDL which was correlated with the decrease of lipid metabolism related proteins such as ApoA-1, ApoA-4, ApoM and CLU in L-HDL. The dysregulation of lipid metabolism-related proteins and functions in HDL of obesity may provide HDL compositional goals for evaluating novel and existing HDL-modification therapies in obesity population.

GW31-e0378

Incidence and predictors of neoatherosclerosis in patients with early in-stent restenosis determined using optical coherence tomography

Xianglan Liu, Guosheng Fu
Sir Run Run Shaw Hospital, Zhejiang University School of Medicine

OBJECTIVES In-stent restenosis (ISR) still exists after drug-eluting stent (DES) implantation, even up to one year. The incidence and risk factors for neoatherosclerosis in patients with early ISR remain unclear. Here, we used optical coherence tomography (OCT) to evaluate the incidence and predictors of neoatherosclerosis in patients with early ISRs.

METHODS OCT was performed on ISR lesions in 185 patients to identify neoatherosclerosis. The median follow-up was 180 days, and neoatherosclerosis was detected in 37% of early ISR lesions. According to the presence of neoatherosclerosis, patients with ISR were divided into two groups: neoatherosclerosis (group A, n=69) and non-neoatherosclerosis (group B, n=116) groups.

RESULTS Risk factors were similar, except for hypercholesterolaemia. The tissue characteristics were not significantly different between patients with and without neoatherosclerosis. Follow-up low-density lipoprotein-cholesterol (LDL-C) levels were divided into three grades (LDL<70 mg/dL, 70 mg/dL≤LDL<100 mg/dL, and LDL≥100 mg/dL). The incidence of neoatherosclerosis was significantly lower (23 vs. 57%, P<0.0001) in the LDL<70 mg/dL group. No significant difference was observed in the incidence of neoatherosclerosis in patients with lipid levels between 70 and 100 mg/dL (P=0.53). However, neoatherosclerosis was significantly more common in patients with a follow-up LDL-C level >100 mg/dL (45 vs. 15%, P<0.0001).

CONCLUSIONS In patients with early ISR lesions, LDL-C levels may be related to the formation and progression of early neoatherosclerosis, and poor LDL-C control may be a risk factor for the occurrence of early-stage neoatherosclerosis after DES implantation.

GW31-e0411

Lipoprotein(a) level in early adulthood and nonalcoholic fatty liver disease in middle age

Zhenyu Xiong[1], Jinshen He[2], Xiaodong Zhuang[1], Xinxue Liao[1]
[1]Department of Cardiology, the First Affiliated Hospital, Sun Yat-Sen University
[2]Department of Gastroenterology, The First Affiliated Hospital of Sun Yat-sen University

OBJECTIVES Both NAFLD and Lp(a) are early risk factors of CVD. However, whether there is an association or mutual affect between them at the early onset of coronary heart disease is currently unclear. We aim to determine whether different concentration of lipoprotein(a) [Lp(a)] in young adulthood is associated with prevalence of NAFLD at midlife.

METHODS We analyzed data the Coronary Artery Risk Development in Young Adults (CARDIA) study, which enrolled 5115 healthy black and white American aged 18–30 years at baseline. LP (a) was measured by a double monoclonal antibody enzyme-linked immunosorbent assay method at year 5. NAFLD is defined as liver attenuation ≤51 Hounsfield Units by abdominal computed tomography (CT) measured at year 25. The association between Lp(a) levels at baseline and prevalence of NAFLD at follow-up were assessed via Logistic regression models.

RESULTS Among 2097 participants, the mean concentration of Lp(a) was 10.47 (8.44) mg/dL, the prevalence of NAFLD was 517 (24.7%). Significant rise-up was observed in the prevalence of NAFLD as the serum Lp(a) level went up (23.3 vs. 27.0 vs. 30.3%, <30 vs. 30–50 vs. >50 mg/dL). After multivariable adjustment, the odds ratio for NAFLD associated with LP (a) was 1.282 (95% CI, 1.068–1.539). The higher Lp(a) concentration level is associated with risk of NAFLD: for 30–50 mg/dL (1.41 [95% CI 1.011–1.984]), for more than 50 mg/dL (1.57 [95% CI 1.064–2.318]). Subgroup analysis showed no significant interactions between demographic and medication-related variables and change of Lp(a) level to the incidence of NAFLD.

CONCLUSIONS We found that Lp(a) levels in healthy young adults were independently associated with prevalent NAFLD in midlife, showing that high Lp(a) level is the potential risk factor of NAFLD in adults. Early identification and intervention of high serum Lp(a) level may potentially contribute to the prevention of NAFLD and CVD.

GW31-e0660

Inactivation of SERCA2 cysteine 674 accelerates atherosclerosis by induction of endoplasmic reticulum stress in macrophages

Hang Su, Xiaoyong Tong
Chongqing University

OBJECTIVES The purpose of this study was to elucidate whether inactivation of the redox site C674 of SERCA2 in pathological situations affects atherosclerosis and the possible atherosclerotic pathogenesis of SERCA2 in macrophages involved.

METHODS The heterozygous SERCA2 C674S knock-in mice (SKI) were used herein, where half of C674 was substituted by serine to represent partial irreversible oxidation of C674.

RESULTS Our research found that compared with WT mice, SKI mice had more severe atherosclerotic features. Increased levels of ER stress markers and inflammatory response from SKI macrophages compared with WT macrophages. While inhibition of ER stress could downregulate the expression of ER stress and reduced atherosclerotic plaque deposition in susceptible areas in SKI mice.

CONCLUSIONS The inactivation of SERCA2 C674 promotes the development of atherosclerosis by inducing ER stress and inflammatory response in macrophages. Our study highlights the importance of C674 redox status in the progression of atherosclerosis and the contribution of SERCA2 activity to sustain the normal morphology and function of macrophaes.

GW31-e0732

Comparison of the reduction of LDL-C or nonHDL-C induced by Xuezhikang, between fasting and postprandial states in patients with coronary artery disease

Liyuan Zhu[1,2,3,4], Xingyu Wen[5], Qunyan Xiang[1,2,3,4], Liling Guo[1,2,3,4], Jin Xu[1,2,3,4], Shuiping Zhao[1,2,3,4], Ling Liu[1,2,3,4]
[1]Department of Cardiovascular Medicine, The Second Xiangya Hospital, Central South University
[2]Research Institute of Blood Lipid and Atherosclerosis, The Second Xiangya Hospital, Central South University
[3]Modern Cardiovascular Disease Clinical Technology Research Center of Hunan Province
[4]Cardiovascular Disease Research Center of Hunan Province
[5]Xiangya School of Medicine, Central South University

OBJECTIVES Xuezhikang, an extract of red yeast rice, effectively lowers fasting and postprandial triglyceride (TG) levels. It was unknown that whether Xuezhikang could contribute the lipid management goals, low-density lipoprotein cholesterol (LDL-C) and non-high-density lipoprotein cholesterol (nonHDL-C) at fasting and postprandial states in patients with coronary artery disease (CAD).

METHODS Fifty CAD patients were divided into Xuezhikang (XZK, n=25) group and control (CON, n=25) group randomly to receive red yeast rice exact, 1200 mg/d Xuezhikang capsules or not for 6 weeks (6w). Blood lipids were detected repeatedly before and after 6w at 0, 2, 4 and 6 hours (h) after a standard breakfast with 800 kcal.

RESULTS When taking all patients as a whole (n=50), LDL-C level decreased significantly after a high-fat meal (P<0.05), especially at 4 h postprandially. Postprandial nonHDL-C level increased significantly but mildly (P<0.05). Xuezhikang induced a significant drop of around 28.4% LDL-C level in fasting and postprandial states (P<0.05). So did nonHDL-C level, with a higher drop of about 30% (P<0.05). More importantly, there was no significant difference in the percentage reduction in LDL-C or nonHDL-C level among four time points.

CONCLUSIONS Xuezhikang significantly decreased LDL-C or nonHDL-C level with similar percentages of reduction between fasting and postprandial states in patients with CAD, indicating that postprandial blood lipids detected at the same time point after a daily meal could replace fasting blood lipids to evaluate the efficacy of cholesterol-lowering therapy in CAD patients, unwilling or unable to keep a fasting state.

GW31-e0761

Nuclear magnetic resonance (NMR) spectroscopy on the effects of PCSK9 inhibitor on lipoprotein particles subfractions

Tingting Li, Yingyi Zhang, Hongliang Cong
Tianjin Chest Hospital

OBJECTIVES To assess the effects of PCSK9 inhibitor (evolocumab) on blood lipid level, lipoprotein particles, and their subfractions with Nuclear Magnetic Resonance (NMR) spectroscopy.

METHODS A total of 99 consecutive patients with acute coronary syndrome (ACS) and poor lipid control were enrolled and assigned to either the experimental group (n=54) or the control group (n=45). The combination therapy of PCSK9 inhibitor (Repatha, 140 mg, q2w) and moderate statin (rosuvastatin, 10 mg, qn) was administered in the experimental group, with moderate statin therapy (rosuvastatin, 10 mg, qn) alone in the control group. The therapeutic effects on blood lipid levels and lipoprotein particle subfractions were assessed with NMR after eight weeks of treatment, and the blood lipid control result was analyzed in both groups.

RESULTS In the experimental group, after eight weeks of evolocumab and moderate statin combination therapy, the level of blood lipids (TC, LDL-C and its subfractions [LDL-1–6], VLDL-C and its subfractions [VLDL-1–5], IDL-C, and HDL-C), lipoprotein particles, and their subfractions (VLDL-P, IDL-P, LDL-P, and its subfractions [LDL-P1–6], apoB, and LP(a)) demonstrated therapeutic benefits with statistical significance (P<0.05). Lowered level of LDL-P was attributed to the significant decrease of small LDL-P ($LDL\text{-}P_{5+6}$), which was significantly more prominent than the decrease in medium LDL-P ($LDL\text{-}P_{3+4}$) and large LDL-P ($LDL\text{-}P_{1+2}$) (P<0.001). According to lipid control target recommended by the latest China Cholesterol Education Program (CCEP) Expert Consensus in 2019, the percentage of patients reaching the treatment target differed significantly between the experimental group and the control group 96.3 vs. 13.3%, respectively (P<0.001).

CONCLUSIONS PCSK9 inhibitor treatment for 8 weeks could significantly improve the lipid profiles in patients with ACS and poor lipid control, and significantly decrease the concentration and fraction of particles which could result in atherosclerotic plaque.

GW31-e1001

Association of circulating PCSK9 concentration with cardiovascular metabolic markers and outcomes in stable coronary artery disease patients with or without diabetes: a prospective, observational cohort study

Jia Peng, Mingming Liu, Yuanlin Guo, Naqiong Wu, Chenggang Zhu, Qian Dong, Jing Sun, Ruixia Xu, Jianjun Li
State Key Laboratory of Cardiovascular Diseases, Fu Wai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College

OBJECTIVES Whether plasma proprotein convertase subtilisin/kexin type 9 (PCSK9) levels are a predictor for cardiovascular outcomes has currently been controversial. No data is currently available regarding the relation of PCSK9 to cardiovascular metabolic markers (CVMMs) and major adverse cardiovascular events (MACEs) in stable coronary artery disease (CAD) patients with diabetes or without diabetes.

METHODS A total of 1225 untreated patients with stable CAD before admission were consecutively enrolled and their baseline plasma PCSK9 levels were determined by ELISA. Patients were divided into high and low PCSK9 groups according to PCSK9 median. All patients followed up for the occurrence of MACEs and received standard therapy after admission. The associations of PCSK9 with CVMMs and MACEs were evaluated.

RESULTS PCSK9 levels were positively correlated with multiple CVMMs including total cholesterol, low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol and hemoglobin A_{1c} at baseline (all P<0.05). During a median follow-up of 3.3 years, 103 (8.4%) events occurred. PCSK9 levels were higher in patients with events compared to those without (P<0.05). The Kaplan-Meier analysis displayed that patients in high PCSK9 group had lower event-free survival than that in low group (P<0.05). Multivariable Cox regression analysis revealed that PCSK9 levels were independently associated with MACEs in diabetic patients (adjusted hazard ratio [HR]: 1.361, 95% confidence interval [CI]: 1.037–1.785, P<0.05). When added the combination of PCSK9 levels and diabetic status to stratifying factors, patients in high PCSK9 group appeared to have an extremely high risk of subsequent MACEs with diabetes (adjusted HR: 5.233, 95% CI: 2.546–10.757, P<0.01).

CONCLUSIONS The present study firstly showed that elevated PCSK9 levels were related to multiple CVMMs and MACEs in stable CAD with diabetes and high PCSK9 levels plus diabetes help identify CAD patients at higher cardiovascular risk, which needs more studies to explore.

GW31-e1070

Supravalvular and valvular aortic stenosis in 21-year-old female with heterozygous familial hypercholesterolemia: a case report

Zhuang Tian[1], Yong-Jian Xu[1], Da-Chun Zhao[2], Shu-Yang Zhang[1]
[1]Department of Cardiology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing 100730, China
[2]Department of Pathology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing 100730, China

OBJECTIVES Familial hypercholesterolemia (FH) is an autosomal dominant disorder, mainly due to mutations of low-density lipoprotein (LDL) receptor genes, characterized by high serum level of LDL-cholesterol (LDL-C), xanthoma and premature coronary artery atherosclerosis. Aortic supravalvular and valvular stenosis have been reported in homozygous familial FH (HoFH); however, it seems to be rare in HeFH. We report a patient with HeFH, who underwent both aortic valve replacement and coronary artery bypass graft due to severe aortic supravalvular and valvular stenosis as well as coronary atherosclerosis.

METHODS A 21-year-old female presented to our hospital complaining of dyspnea and angina with no other coronary risk factors but heterozygous FH(HeFH). Echocardiography and coronary angiography revealed severe aortic supravalvular and valvular stenosis as well as critical coronary atherosclerosis, which is rare in HeFH. Unfortunately, the patient died after the operation of aortic valve replacement and coronary artery bypass graft.

RESULTS The patient developed recurrent ventricular fibrillation and couldn't wean from cardiopulmonary bypass for persistent hypotension at the end of surgery treatment. Intra-aortic balloon pump, extracorporeal membrane oxygenation and vasoactive agents were used. Unfortunately, she died of circulatory collapse on the second day.

CONCLUSIONS Early intensive statin treatment in FH patients decrease progression of coronary atherosclerosis while have little effect on aortic valve stenosis evolvement. PCSK9 inhibitors may slow the progression of aortic valve stenosis. High-risk surgery should be cautiously performed due to severity of the disease and complex surgical procedures.

GW31-e1084

The difference between fasting and non-fasting lipid measurements is not related to statin treatment

Mingming Liu, Ying Gao, Jia Peng, Yuanlin Guo, Naqiong Wu, Chenggang Zhu, Jianjun Li
State Key Laboratory of Cardiovascular Diseases, Fu Wai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College

OBJECTIVES To evaluate the impact of statin use on non-fasting measurements.

METHODS In this cross-sectional study, a total of 686 hospitalized patients with normal triglyceride (TG) due to chest pain were enrolled. Their fasting (8–12 h) and non-fasting (2–4 h after breakfast) lipid panels were measured on the second day of admission. Patients were divided into two groups: non-statin (n=499) and statin treatment (n=187) groups. The differences in lipid profiles between fasting and non-fasting lipid measurements in statin and non-statin groups were compared.

RESULTS The mean age of participants was 57±13 years, and 54.4% were male. A linear correlation was observed between fasting and non-fasting lipid panels. Though a postprandial impact on available lipid parameters was observed, the general pattern of differences between fasting and non-fasting lipids were similar in both groups. Besides, the diff (%) of lipid panels did not vary across statin treatment. Moreover, no effects of statin types and duration on non-fasting lipid profiles were found.

CONCLUSIONS The current study found that the differences between fasting and non-fasting lipids were similar in individuals with or without statin treatment. Non-fasting lipid panels were not significantly affected by statin types or durations, suggesting that non-fasting lipid measurement is an acceptable test for patients receiving statin treatment.

GW31-e1095

Whole exome sequencing identifies three novel gene mutations in patients with the triad of diabetic ketoacidosis, hypertriglyceridemia and acute pancreatitis

Zhenyan Xu[1], Zixi Huang[2,3], Xiang Xu[4], Xiaoyang Lai[3]
[1]Department of Cardiovascular Medicine, The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi 330006, China
[2]Department of General Medicine, The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi 330006, China
[3]Department of Endocrinology, The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi 330006, China

[4]Department of Ultrasound Medicine, The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi 330006, China

OBJECTIVES This study aimed to analyze the genetics and treatments of the patients with the triad of diabetic ketoacidosis (DKA), hypertriglyceridemia and acute pancreatitis (AP).

METHODS We conducted a retrospective study of six patients with the triad of AP, hypertriglyceridemia and DKA at our hospital. All patients underwent plasmapheresis as part of their treatment. The clinical characteristics of the patients were obtained from the hospital information system and analyzed. Whole exome sequencing was performed using samples of one patient (case 6) and his family members.

RESULTS The average triglyceride level before plasmapheresis was 3282.17±2975.43 mg/dL (range: 1646–9332 mg/dL). The triglyceride levels dropped by approximately 80% after plasmapheresis. None of the patients developed complications related from plasmapheresis. During follow-up, patients 5 and 6 developed recurrent pancreatitis for several times, and showed the formation of pancreatic pseudocysts. We identified three novel heterozygous missense mutations in the family of patient 6, including c.12614C>T (p.Pro4205Leu) in *APOB*, c.160G>C (p.Glu54Gln) in *CILP2*, and c.1199C>A (p.Ala400Glu) in *PEPD*.

CONCLUSIONS Three novel heterozygous missense mutations, including c.12614C>T (p.Pro4205Leu) in *APOB*, c.160G>C (p.Glu54Gln) in *CILP2*, and c.1199C>A (p.Ala400Glu) in *PEPD* were first identified in a patient with the triad of DKA, hypertriglyceridemia and AP. The combination of plasmapheresis, hydration and insulin therapy may have the greatest clinical benefits for these patients.

GW31-e1147

High-intensity statin therapy induced better outcomes compared with standard statin treatment in patients with acute coronary syndromes: a meta-analysis of 16 randomized controlled trials involving 26,497 patients

Shiyong Yu, Jun Jin
Department of Cardiology, Xinqiao Hospital, Army Medical University (Third Military Medical University)

OBJECTIVES To compare the efficacy and safety of high-intensity statin administration in ACS compared with standard statin, aiming to produce more powerful evidence on high-intensity statin optimal utilization in clinic practice.

METHODS Data Sources: The PubMed, EMBASE, and the Cochrane Controlled Trials Register were searched for relevant articles published in English from their inception through February 2019. Data Extraction and Synthesis: The primary end points were the combined outcome of myocardial infarction (MI), stroke, and death or the MACE defined by the individual investigator. The fixed-effects or random-effects models, according to heterogeneity across studies, were used to calculate the RR with 95% confidence intervals (CI) for all end points in the high-intensity and standard dose groups. Subgroups analyses were stratified by statin treatment duration and race. Sensitivity analyses were pre-specified by repeating the analyses using random-effects models and fixed-effects models and by excluding studies with unclear or high risk of bias in sequence generation.

RESULTS A total of 16 randomized clinical trials were pooled; 26,497 patients were included in the analysis. Compared with the standard statin therapy, high-intensity statin significantly reduced MACE participants with ACS (RR=0.81; 95% CI, 0.75–0.87; P<0.00001) without heterogeneity among the 16 trials (I2=40%, P=0.05). A sensitivity analysis by repeating the analyses using random-effects models and the result obtained was highly consistent with the main finding above (RR=0.77; 95% CI, 0.68–0.86; P<0.00001). By subgroup analysis of 5092 patients in Asia, we observed a significant reduction in MACE in high-intensity participant compared with standard statin treatment (RR=0.77; 95% CI, 0.61–0.98; P=0.03). There was no reduction in the risk of MACE during the first month by high-intensity statin treatment (RR=0.84; 95% CI, 0.63–1.13; P=0.25). By the 12th month, there was a trend in the reduction of the risk of MACE (RR, 0.85; 95% CI, 0.73–0.99; P=0.03, I2=18% in fixed-effects Model; RR, 0.80; 95% CI, 0.58–1.09; P=0.16 in random-effects Model), a benefit from high-intensity statin that persisted through 12 months and (RR, 0.74; 95% CI, 0.65–0.83) and no heterogeneity between trials (I2=44%, P=0.05). Meta regression suggested race couldn't explain the source of heterogeneity. Safety data showed comparable tolerability for high-intensity statin and the standard arm.

CONCLUSIONS Based on available evidence, high-intensity statin therapy compared with standard statin therapy produces significant reductions in major adverse cardiovascular event in patients with ACS. Adverse events were acceptable in patients with ACS under high-intensity statin therapy.

GW31-e1159

Use of lipid parameters to identify healthy men at a higher risk of arterial stiffness progression

Yu Sang, Lei Ruan, Cuntai Zhang
Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology

OBJECTIVES Dyslipidemia contributes to the development and progression of arterial stiffness. We aimed to confirm the superiority of the serum lipids and their calculated ratios in predicting arterial stiffness progression.

METHODS Total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and brachial-ankle pulse wave velocity (baPWV) of 612 healthy males were measured at baseline. Values for non-HDL-C, TC/HDL-C, TG/HDL-C, LDL-C/HDL-C, and non-HDL-C/HDL-C were calculated. baPWV was re-performed after 4.1 years follow-up. A baPWV cutoff of 1400 cm/s was used to diagnose arterial stiffness.

RESULTS Over the follow-up period, 309 individuals increased/persisted with high baPWV (outcome 1) and 90 arterial stiffness events occurred (outcome 2). Only logTG (OR 1.65 [95% CI: 1.14–2.40] for outcome 1; 2.08 [1.24–3.52] for outcome 2) and logTG/HDL-C (1.56 [1.15–2.13] for outcome 1; 1.69 [1.10–2.62] for outcome 2) were significantly associated with arterial stiffness progression after adjusting for confounding factors. Adding logTG or logTG/HDL-C to age and blood pressure improved the accuracy of risk predictions for arterial stiffness progression. These associations remained significant when lipids were analyzed as categorical variables.

CONCLUSIONS Baseline serum TG and TG/HDL-C were independently associated with increases in/persistently high baPWV and incident arterial stiffness, and they performed more effectively than other lipid variables in identifying healthy men at a higher risk of arterial stiffness progression.

GW31-e1228

The influence of exercise on glycolipid metabolism of statins

Baihua Zhou, Jun Yan, Lijun Wang
Department of Cardiology, Affiliated Zhongshan Hospital, Dalian University

OBJECTIVES To investigate the effect of exercise on Statin-induced lipid-lowering effect and changes in glucose metabolism and its possible mechanism, we study the effects of exercise on blood glucose and blood lipids of the statin-intervened patients with coronary heart disease after the percutaneous coronary intervention (PCI) and high-fat diet fed rats, as well as the changes of the intestinal microbiome in rats.

METHODS 1. We followed up 501 patients who underwent PCI from 2016 to 2018 and were on statins consistently post-surgery. According to their level of exercise, these patients were divided into three groups: the none-exercise group, the not reach the standard group, and the reach the standard group. We collected data consisting of FPG, HbA_{1c}, TG, TC, HDL-C and LDL-C before and after statins treatment, and we compared the changes in blood sugar and blood lipid levels in each individual group. 2.40 male SD rats fed with high-fat diets were randomly divided into 4 groups: the control group (group A), the statin-only group (group B), the exercise and statin group (group C), and the exercise-only group (group D). The rats in group C and D were made to swim 60 min/day for a period of 5 weeks. The rats in group B and group C were given Rosuvastatin 2 mg/(kg day) for a period of 5 weeks and a period of 10 weeks respectively. Collected blood and fecal specimens from all four groups at the end of the 5th week after gavage, and from group C at the end of the 10th week after gavage. All the blood specimens collected were tested for FPG and blood lipid levels. Intestinal microbiome DNA was extracted from the fecal specimens, and the differential analysis was carried out through 16S rRNA high-throughput sequencing.

RESULTS 1. Clinical cases analysis: FPG and HbA_{1c} in the NE and the NS groups increased compared with those before Statins treatment, but decreased in the RS group. The changes of HbA_{1c} in the NE group and FPG in the RS group are statistically significant (P<0.01, P<0.05). The decrease of FPG in the RS group is more significant than that in the NE and NS groups (P<0.05, P<0.01). The increase of HbA_{1c} in the NE group is 3.93% higher than that in the RS group (P<0.05). The decrease of TC in the RS group is higher than that in the NE and NS groups (all P<0.01) and the amplitude of declining of LDL-C is 42.17% higher than that in the NE group (P<0.01). The level of new-onset diabetes demonstrates a downward trend as the amount of exercise decreases, but there is no statistical difference among the three groups. 2. Animal experiments: FPG is the highest in group B, which is different compared with group C (P<0.01). TC and LDL-C levels show a sequence of group C<group B<group D<group A. After stopping exercise, FPG and LDL-C are significantly higher in group C, compared with the results at 5 weeks after exercise (all P<0.05). The 16S rRNA high-throughput sequencing shows that the number of Akkermansia muciniphila is significantly higher in group C compared to group B. The number of Akkermansia muciniphila decreases after the rats in group C stop exercising for 5 weeks.

CONCLUSIONS 1. Adequate exercise can improve the Statin-induced blood sugar increase as well as enhance the lipid-lowering effects of Statins in patients with PCI treatment. This also applies to rats with high-fat diets. 2. The mechanism by which exercise affects blood sugar and blood lipid levels in rats given statins may be related to the fact that exercise can induce an increase of Akkermansia muciniphila.

GW31-e1299

Reversed L-shaped association between baseline brachial-ankle pulse wave velocity and risk of first stroke in patients with hypertension: a population-based cohort study

Lihua Hu, Jianping Li
Department of Cardiology, Peking University First Hospital, Beijing, China

OBJECTIVES Brachial–ankle pulse wave velocity (baPWV) is available as a noninvasive measure of arterial stiffness. However, little information is available on the association between baPWV and the risk of stroke in patients with hypertension. The study aimed to assess the association between baseline baPWV and risk of first stroke in Chinese community-dwelling population.

METHODS From January 1, 2017, to December 31, 2017, a total of 9787 individuals without history of stroke from the CHRS (China Hypertension Registry Study) were included in this analysis. Follow-up continued until December 31, 2018. The primary outcome was first stroke. The crude and adjusted risks of first stroke were estimated by hazard ratios (HRs) and 95% Cis using Cox proportional hazards models, without or with adjusting for pertinent covariates, respectively.

RESULTS During a median follow-up of 20.8 months, there were 138 total first strokes including 123 first ischemic strokes and 15 first hemorrhagic strokes. The Kaplan-Meier curves showed that unadjusted first stroke and first ischemic stroke curves of Q1, Q2 and Q3 were virtually superimposable. Subjects in baPWV Q4 displayed significantly greater first stroke and first ischemic stroke than those in Q1, Q2 and Q3. Adjusted smooth curve showed that the relationship between baPWV and risk of first stroke and first ischemic stroke was curvilinear and reversed L-shaped. High baPWV levels (≥21.31 m/s) was associated with increased risk of first stroke (HR=1.52; 95% CI: 1.05–2.21) and first ischemic stroke (HR=1.53; 95% CI: 1.03–2.26) compared to low baPWV levels (<21.31 m/s). E-value analysis suggested robustness to unmeasured confounding.

CONCLUSIONS High baPWV levels (≥21.31 m/s) were associated with increased first stroke risk among Chinese hypertensive adults, compared to low baPWV levels, supporting a reversed L-shaped association between baPWV and risk of first stroke. Our findings warrant additional investigation.

GW31-e1300

Association between plasma copper levels and first stroke: a community based nested case-control study

Lihua Hu[1,2], Xiaoshu Cheng[2], Jianping Li[1]
[1]Department of Cardiology, Peking University First Hospital, Beijing, China
[2]Department of Cardiovascular Medicine, the Second Affiliated Hospital of Nanchang University, Nanchang of Jiangxi, China

OBJECTIVES Uncertainty remains regarding the association between the risk of stroke and plasma copper levels in population with copper mostly in normal range due to limited data. To this end, we examined the association between baseline plasma copper and risk of first stroke in Chinese community-dwelling population.

METHODS We conducted a nested case control study from hypertensive participants in "China Hypertension Registry Study". A total of 1255 first stroke cases and 1255 controls matched for age, sex and study site were included in the final analysis. Conditional logistic regression analyses were performed to evaluate the association between plasma copper and first stroke.

RESULTS The overall mean (SD) of copper was 1.01 (0.17) μg/mL. 94.26% participants' copper concentration was in the normal range by Mayo Clinic laboratory reference values. Smoothing curve showed that the associations of plasma copper with first stroke and its subtypes were linear. Each SD increment of plasma copper was independently and positively associated with risk of first stroke [OR: 1.17, 95% confidence interval (CI): 1.07–1.28]. The multivariable ORs with 95% CIs for total stroke, ischemic stroke and hemorrhagic stroke in the highest versus the lowest quartile of plasma copper were 1.49 (1.16–1.90; P-trend=0.001), 1.46 (1.12–1.92; P-trend=0.004) and 2.05 (0.95–4.38; P-trend=0.050), respectively.

CONCLUSIONS Baseline plasma copper was positively associated with risk of first stroke in an approximately linear fashion among Chinese community population (80.32% hypertensives), although their copper levels were mostly within the normal range according to current reference values. Our findings warrant additional investigation.

STRUCTURAL HEART DISEASE

GW31-e0222

Identification of key genes involved in calcific aortic valve disease based on integrated bioinformatics analysis

Yehong Liu[1], Weifeng Shen[2], Qi Zhang[1]
[1]Department of Cardiology, Shanghai East Hospital, Shanghai Tongji University School of Medicine, Shanghai 200120, China
[2]Department of Cardiology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 200025, China

OBJECTIVES Calcific aortic valve disease (CAVD) includes the process from initial aortic valve sclerosis to more advanced aortic valve stenosis. Bioinformatics has become an emerging important part of many areas of biology. We use bioinformatics analyses for gene function and pathway exploration to discover key mechanism involved in CAVD.

METHODS Gene expression profile dataset GSE51472 was downloaded from the GEO database. The analysis was carried out by using a web-based online tool called Gene-Cloud of Biotechnology Information (GCBI). We used a classical ANOVA to identify DEGs with P<0.01 and q<0.01 as being statistically significant. The P-value<0.05 was considered as the threshold. Series Test of Cluster analysis for DEGs was performed on GCBI. DEGs with the same variable features were clustered in a trend profile to discover the most representative gene group in the process of cardiac valve calcification. The identified DEGs in profiles selected after STC analysis were performed Go enrichment and KEGG pathway analysis. P-value<0.05 was used as the cutoff criterion for the functional enrichment analysis. We used the GCBI database to generate gene co-expression network and pathway network. GCBI laboratory utilize the express profile of different genes to construct the gene co-expression network. The network reveals the key genes of regulation and shows the relationship of genes. Pathway network showed the top and bottom pathways in the diagram and could help us deeply understand the relationship of all involved pathways. For pathway network construction, pathway is taken as the subject unit according to the method of graph theory. The interaction in KEGG database is used to construct the interaction network between pathways.

RESULTS After standardization, the gene expression data were within an acceptable range. And these data were screened for the DEGs among sclerotic aortic valve, calcified aortic valve samples and normal samples. Two thousand and nine hundred and seventy-eight DEGs were extracted from the expression profile datasets GSE51472. To further narrow down the target genes which harbor great significance among the declared 2978 genes, we chose to use the 16 model profiles to summarize the expression pattern of the genes. Among these patterns, the two most significant ones were profiles No. 9 whose expression increased constantly and No. 11 whose expression reduced constantly. Gene Ontology (GO) functional enrichment analysis was performed in order to explore the biological process (BP), molecular function (MF) and cell compound (CC) of the DEGs depending on the result of the STC analysis. "Chronic inflammatory response", "T cell receptor complex", "antigen binding" exhibited highest significant enrichment within the BP, CC and MF category of DEGs. KEGG pathway enrichment analysis was then used to understand the signaling pathway enrichment of DEGs. With the criterion of P<0.05, the top enriched biological pathways associated with CAVD included "Chemokine signaling pathway", "Cytokine-cytokine receptor interaction", "Tuberculosis", "PI3K-Akt signaling pathway" and "Transcriptional misregulation in cancer".

CONCLUSIONS Finally, construction of gene co-expression network and pathway network were performed to shed light on further insights toward CAVD. TLR2, CD86 and TYROBP was found to be key genes for CAVD. Furthermore, several pathways (i.e., "MAPK signaling pathway", "Apoptosis", "Pathways in cancer") presented the core pathways among normal, sclerotic aortic valve, calcified aortic valve samples.

GW31-e0312

Clinical relevance of endogenous tissue-plasminogen activator in patients with aortic valve sclerosis

Zhongli Chen[1], Yehong Liu[2], Ke Yang[1]
[1]Department of Cardiology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China
[2]Department of Cardiology, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China

OBJECTIVES Impaired fibrinolysis with elevated tissue plasminogen activator (t-PA) induces coronary artery disease progression, myocardial infarction and cardiac mortality. Aortic valve sclerosis (AVSc) shares certain similar aspects of pathophysiology of atherosclerosis and correlates with adverse cardiovascular events. We investigated whether endogenous t-PA is associated with AVSc and clinical outcomes of these patients.

METHODS Plasma levels of t-PA were measured in 155 patients with AVSc and 140 non-AVSc counterparts. Expression of t-PA was also determined in human aortic valves with and without sclerosis by histological and immunochemical analysis. To assess the prognostic value of plasma t-PA for the major adverse cardio-cerebral events (defined as cardiovascular death, nonfatal myocardium infarction, stroke, and re-hospitalization because of heart failure or unplanned revascularization) in AVSc patients, we prospectively followed up all patients with AVSc (median 6.5 years). After excluding 12 patients (7.7%) who lost to follow-up, 143 patients with AVSc were enrolled in the final analysis. The best cutoff of t-PA in predicting the survival outcome was calculated by the X-tile software according to the highest chi-square value defined by the Kaplan-Meier survival analysis and the log-rank test.

RESULTS Plasma levels of t-PA were significantly higher in AVSc patients than in non-AVSc counterparts (median, 2163.10 pg/mL vs. 1403.17 pg/mL, P<0.001). In the multivariate regression, plasma t-PA (log 10 per standard deviation (SD)) remained an independent factor for AVSc after adjusting for demographic and known cofounders (Odd ratio (OR): 1.66, 95% confidence intervals (CI): 1.18–2.34, P=0.004). When included as a categorical variable, compared with lowest tertile, the highest tertile of t-PA indicated higher risk for AVSc, either adjusted for demographic features (OR: 3.24, 95% CI 1.49–7.04, P=0.003), or the potential cofounders (OR: 2.94, 95% CI 1.32–6.53, P=0.008). Higher plasma levels of t-PA remained associated with increased risk for AVSc in various subgroup. Furthermore, immuno-histochemical staining also showed that the expression levels of t-PA was three times higher in the human sclerotic aortic valves than in the non-sclerotic valves. Among 143 patients with AVSc who have completed clinical follow-up (median, 6.5 years), the composite MACCE rate of 60.5%. Based on the optimal cut-off value of 1787.8 pg/mL, AVSc patients with low t-PA levels displayed better survival free from MACCE than those with high t-PA levels (P=0.0018). After full adjustment, t-PA (lg per SD) remained independently associated with MACCE (Hazard ratio (HR): 1.33, 95% CI 1.07–1.66, P=0.009). Furthermore, time-dependent receiver operating characteristics (ROC) curve showed that with the landmark time of 3 years, t-PA demonstrated a decent predictive capability for MACCE, with an area under the curve of 0.71 (95% CI: 0.63–0.80).

CONCLUSIONS Elevated endogenous t-PA in plasma may serve as an indicator of AVSc and is associated with adverse long-term clinical outcomes in patients with AVSc.

GW31-e0498

Visit-to-visit glycemic variability is associated with left ventricular adverse remodeling in diabetic patients with STEMI

Chendie Yang, Xiaoqun Wang
Department of Cardiology, Ruijin Hospital, Shanghai Jiao-Tong University School of Medicine, Shanghai, P.R. China

OBJECTIVES Patients with type 2 diabetes mellitus (T2DM) are predisposed to poor cardiovascular outcomes after ST-segment elevation myocardial infarction (STEMI). Left ventricular adverse remodeling (LVAR) triggered upon myocardial infarction is recognized as the predominant pathological process in the development of heart failure. In the present study, we sought to investigate whether visit-to-visit glycemic variability (GV) is a potential predictor of LVAR in T2DM patients after STEMI.

METHODS From January 2014 to December 2018 in Ruijin Hospital, T2DM patients with STEMI who underwent primary percutaneous coronary intervention were consecutively enrolled and followed up for ~12 months. The changes in left ventricular geometric and functional parameters between baseline and 12-month follow-up were assessed by echocardiography. The incidence of LVAR, defined as 20% increase in indexed left ventricular end-diastolic volume (LVEDV), and its relationship with visit-to-visit fasting plasma glucose (FPG) variability were analyzed. Multivariate regression models were constructed to test the predictive value of GV for post-infarction LVAR.

RESULTS A total of 437 patients with type 2 diabetes and STEMI were included in the final analysis. During a mean follow-up of 12.4±1.1 months, the incidence of LVAR was 20.6% and mean enlargement of indexed LVEDV was 3.31±14.4 mL/m², which was significantly increased in patients with higher coefficient variance (CV) of FPG (P=0.002) irrespective of baseline glycemic levels. In multivariate analysis, FPG variability was independently associated with incidence of post-infarction LVAR after adjustment for traditional risk factors, baseline HbA_{1c} as well as mean FPG during follow-up (OR: 2.282 [95% CI: 1.041~5.109] for highest vs. lowest tertile of CV of FPG). Assessing GV by two measures, including standard deviation (SD) and variability independent of the mean (VIM), yielded similar findings.

CONCLUSIONS This study suggests that visit-to-visit GV is an independent predictor of incidence of LVAR in T2DM patients with STEMI.

GW31-e0546

Outcomes in patients with congenital heart disease (left-to-right shunt) and pulmonary arterial hypertension treated under "treat-repair-treat" strategy

Yuan He, Qiangqiang Li, Hong Gu
Bejing Anzhen Hospital

OBJECTIVES With the advancement of PAH targeted therapy, a therapeutic strategy was proposed in recent years as "treat-repair-treat" strategy (Targeted medications and subsequent shunt closure with continuously targeted therapy) for patients with heart defect and PAH who are considered non-correctable. This study retrospective reviewed the outcomes of patients treated in this strategy.

METHODS This is an retrospective study and the data were obtained from electronic data system.

RESULTS Sixty-six patients (women 48 (67%), 24.75±12.84 years) who were confirmed pulmonary arterial hypertension (PAH) by right heart catheterization (RHC) prior to defect closure and then received targeted therapy were enrolled. Before defect closure, thirty-four patients received PAH-specific medications (treat-repair-treat group) and thirty-two patients did not (repair-treat group). Initially, treat-repair-treat group had more patients with severe clinical symptoms (WHO-FC≧III) and higher PVR (17.30±7.54 vs. 8.85±4.19 wood*units) compared with repair-treat group. After targeted therapy, PVR in this group decreased to 8.34±4.52 wood*units (P<0.05) with no statistical significance compared with repair-treat group. At late follow-up (median 26 months), there were more patients with WHO-FC I and mean PAP significantly decreased than that when defect closure (39.45±18.14 vs. 67.25±15.77 mmHg, P<0.001). By the time of data collection, more patients received regular combined PAH-specific medications in treat-repair-treat group (44 vs. 16%, P<0.05) and less patients had adverse events (3 vs. 6) compared with repair-treat group, which suggested the necessity of targeted therapy with PAH-specific medications after defect closure.

CONCLUSIONS The results demonstrated that "treat-repair-repair" strategy could be an effective approach for patients with heart defect and PAH who are considered non-correctable initially. However, targeted therapy and close follow-up are necessary after the shunt closure.

GW31-e0548

Outcomes in patients with arterial septal defect and significant pulmonary arterial hypertension treated in "treat-repair-treat" strategy

Yuan He, Qiangqiang Li, Hong Gu
Being Anzhen Hospital

OBJECTIVES As the advancement of PAH targeted therapy, a therapeutic strategy was proposed in recent years as "treat-repair-treat" strategy (Targeted medications and subsequent shunt closure with continuously targeted therapy). This study aimed to describe the effects of this strategy in these patients.

METHODS In this study, we retrospectively reviewed 15 ASD patients (mean age of 30.2±11.55 years) with significant pulmonary arterial hypertension who underwent the defect closure in our hospital between 2010 and 2018. All patients received targeted medications prior to the defect closure.

RESULTS After a period of targeted therapy, all patients got clinically improved. PVR and mean PAP were significantly decreased after targeted therapy of PAH-specific medications compared with baseline (PVR: 8.47±2.97 vs. 5.83±1.76 wood*units P<0.05; mean PAP: 57.93±8.73 vs. 50.87±8.64 mmHg, P<0.05). Eventually, all 15 patients achieved defect closure successfully without adverse events. The median follow-up duration was 12 months. Thirteen cases visited doctors on a regular basis after defect closure. Among them, no patients got deteriorated clinically and their hemodynamics improved. Five patients were confirmed having normal pulmonary artery pressure (mPAP≦25 mmHg) measured by RHC. Two cases stopped targeted medical therapy without prescription and both of their exercise capacity worsened at the last follow up (6MWTD decreasing >50 meters). RHC showed they still had severe pulmonary arterial hypertension.

CONCLUSIONS The results demonstrated that "treat-repair-repair" strategy may be an effective approach for patients with ASD and significant PAH. However, targeted therapy of PAH-specific medications and close follow-up are necessary after the shunt closure.

GW31-e0622

Comparing efficacy and safety of transcatheter versus surgical aortic valve replacement for low-intermediate surgical risk patients: a meta-analysis

Yake Lou, Xiaomin Nie, Wei Liu
Beijing Anzhen Hospital

OBJECTIVES We aimed to investigate the efficacy and safety of transcatheter aortic-valve replacement (TAVR) versus surgical aortic valve replacement (SAVR) for low-intermediate surgical risk patients.

METHODS PubMed, Cochrane Library, and Embase databases were searched to identify potential references. Only randomized controlled trials (RCTs) or observational studies that matched using propensity score matching were eligible for screening. The primary endpoint was all-cause death. The secondary outcomes were bleeding, stroke, myocardial infarction (MI) and other complications of aortic-valve replacement. In addition, we performed subgroup analysis based on surgical risk and study type.

RESULTS Eight RCTs and 13 observational studies covering 12,467 patients were included in the current meta-analysis. For patients with low-surgical risk, compared with SAVR, TAVR was found to be associated with a lower mortality at a follow-up period of 30-day (odds ratio (OR): 0.62, 95% confidence interval (CI): [0.39, 0.99], P=0.05) and 1-year (OR: 0.66, 95% CI: [0.46, 0.96], P=0.03). This benefit disappeared when the follow-up was extended to 2-year (OR: 0.89,

9% CI: [0.61, 1.30], P=0.55). For patients with intermediate-surgical risk, TAVR showed to have similar mortality with SAVR regardless of follow-up period (30-day, 1-year or 2-year). TAVR could reduce the incidence of bleeding, AF, AKI. For complications, such as MI and stroke, TAVR exhibited to have similar safety with SAVR. However, TAVR was found to be associated with a higher incidence of reintervention, major vascular complication, paravalvular leak, and PPI.

CONCLUSIONS For patients with a low-surgical risk of AVR, TAVR showed to have a superior clinical efficiency than SAVR in a follow-up period of within 1-year, while this benefit disappeared when the follow-up period was extended to 2-year. For patients with an intermediate-surgical risk, TAVR and SAVR exhibited to have similar efficacy and safety regardless of the follow-up period. TAVR can be alternatively used in lieu of SAVR for low- to intermediate-surgical risk patients.

GW31-e0629

Preliminary study of composite clinical worsening definitions in patients with pulmonary arterial hypertension associated with congenital heart disease – a single center experience

Zhuoyuan Xu, Qiangqiang Li, Chen Zhang, Hongsheng Zhang, Hong Gu
Beijing Anzhen Hospital, Capital Medical University

OBJECTIVES Composite clinical worsening (cCW) outcomes might allow measurement of disease progression in patients with pulmonary arterial hypertension (PAH). The use of composite CW outcomes is increasingly encouraged in PAH clinical research. This study investigated the relevant factors affecting the prognosis and their predictive strength for lung transplantation/death.

METHODS Patients with CHD-PAH referred to Beijing Anzhen Hospital between Jan 2007 and Jul 2018 were included. Patients from at least 27 regions and hundreds of medical centers in China were referred to our center. CW was defined as PAH-related hospitalization, NYHA cardiac function deterioration (cCW1, 2 and 3), syncope (cCW2 and 3), and the occurrence/worsening of ≥2 PAH symptoms at diagnosis and during follow-up (cCW3). The primary endpoint events were defined as all-cause death and lung transplantation.

RESULTS Five hundred and twenty-five consecutive patients (children and adults, with or without Down syndrome) with CHD-PAH were included. All patients met the clinical definition of PAH with mean pulmonary arterial pressure (mPAP)≥25 mmHg and a pulmonary artery wedge pressure ≤15 mmHg measured by right heart catheterization (RHC) and/or invasive PAP monitoring. The median age at diagnosis was 20.7 (11.2, 30.3) years. Children (<18 years) accounted for 43.8%, women accounted for 68.8%. Two hundred and forty-nine patients with Eisenmenger syndrome, 43 patients with PAH associated with prevalent systemic-to-pulmonary shunts, 48 with PAH with small/coincidental defect, and 185 with PAH after defect correction were included. The median follow-up time was 4.5 years. Forty-seven patients (9.0%) died, and heart failure was the most common cause of death (27.7%). Survival rates of end-point-free events at 1, 3, 5 and 10 years after diagnosis were 98.0, 95.4, 89.9, and 84.4%, respectively (Log-rank P=0.016). Cox multivariate analysis showed that NYHA cardiac function deterioration, occurrence/worsening of ≥2 PAH symptoms, PAH-related hospitalization and syncope has a high predictive value for lung transplantation or death. Composite clinical worsening was associated with significantly increased risk of lung transplantation or death (P<0.0001), with cCW2 having the highest predictive value (HR: 15.476, 95% CI: 4.346–37.576, P<0.0001).

CONCLUSIONS These data support the use of cCW outcomes in CHD-PAH research. Composite clinical worsening events are initially considered as clinical endpoints in clinical trials. NYHA cardiac function deterioration, occurrence/worsening of ≥2 PAH symptoms, PAH-related hospitalization and syncope may be important for risk assessment during clinical management.

GW31-e0636

Survival of Chinese patients with pulmonary arterial hypertension associated with congenital heart disease in the modern treatment era – a single center experience

Zhuoyuan Xu, Qiangqiang Li, Chen Zhang, Hongsheng Zhang, Hong Gu
Beijing Anzhen Hospital, Capital Medical University

OBJECTIVES New pulmonary arterial hypertension (PAH)-specific drugs with the high costs of treatment and financial constraints were available in China from 2006. In 2020, as some of the PAH-specific drugs are covered by medical insurance, the choice and efficacy of patient treatment will surely be greatly improved. This study was to summarizes the baseline clinical characteristics and follow-up data in patients with PAH in a single center for observing modern treatment status (defined in China as between 2006 and 2020), survival rates and predicting prognosis, exploring the relevant factors affecting the prognosis of the patients.

METHODS A retrospective cohort study was undertaken in 525 consecutive patients diagnosed pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD) between 2007 and 2019. Patients from at least 27 regions and hundreds of medical centers in China were referred to our center. A contemporary group of idiopathic PAH/familial PAH patients was utilized for comparison. Their baseline clinical data of demographic, clinical manifestations, auxiliary examination, and right heart catheterization were collected. The primary endpoint events were defined as all-cause death and lung transplantation.

RESULTS Of 525 patients, 249 had Eisenmenger syndrome; 43 had PAH associated with prevalent systemic-to-pulmonary shunts; 48 were diagnosed with PAH with small/coincidental defect; and 185 had PAH after defect correction. The median age at diagnosis was 20.7 (11.2, 30.3) years. Children (<18 years) accounted for 43.8%, women accounted for 68.8%. The median follow-up time was 4.5 years. One hundred and eighty patients had PAH symptoms at diagnosis, and 350 (84.3%) patients received PAH targeted medication at the last follow-up, including 141 with irregular medication. Because of financial constraints, 78 patients were NYHA III-IV at diagnosis but none of them accepted initiation of i.v./s.c. prostanoids. At the last follow-up, only 1.7% (6 cases) (NYHA FC at the first visit were II) received continuous subcutaneous prostanoids for more than 3 months. Forty-seven patients (9.0%) died, and heart failure was the most common cause of death (27.7%). Survival rates of end-point-free events at 1, 3, 5 and 10 years after diagnosis of PAH patients were 98.0, 95.4, 89.9, and 84.4%, respectively; there were statistically significant differences in survival among the subgroups (Log-rank P=0.016). NYHA cardiac function was grade III and IV, frequently occurrences syncope occurred and only one-time syncope at diagnosis are independent risk factors for lung transplantation or death. Cox multivariate analysis showed that NYHA cardiac function deterioration, occurrence/worsening of ≥2 PAH symptoms, PAH-related hospitalization and syncope has a high predictive value for lung transplantation or death. The survival of the 41 IPAH/HPAH patients with PAH related gene mutations appeared to be worse when compared with the PAH-CHD subgroups.

CONCLUSIONS The overall long-term prognosis of CHD-PAH patients in this study is relatively good, and the survival status of patients in each subgroup is significantly different. Earlier use of PAH targeted combination therapy and improved compliance with PAH-specific therapy are expected to improve the prognosis of patients with CHD-PAH.

GW31-e0736

Transcatheter device closure of secundum atrial septal defect in adult

Abdel Fatah Abu Haweleh[1,2]
[1]Queen Alia Heart Institute
[2]Arab Medical Center

OBJECTIVES Atrial septal defect (ASD) is the second most common congenital cardiac anomaly seen in adult, accounting for 10% of all congenital heart disease,70% of those are ASD secundum. There is a growing body of literature that suggests the benefits of ASD closure are not restricted to younger populations.

METHODS This is a literature review discussing the indications, guidelines, contra-indications, age specific complications, technique of transcatheter closure of ASD in adult and comparing it to the surgical outcome.

RESULTS The presence of the following factors are strong indications of ASD closure: (1) symptoms such as exercise intolerance, heart failure, atrial arrhythmias; (2) RV or RA dilatations on echo, cardiac CT/MRI; (3) Paradoxical embolism regardless of the defect size; (4) Orthodeoxia-platypnea.

CONCLUSIONS Given the low rate of complications and virtual lack of mortality, isolated secundums ASDs which are larger than 5 mm should be considered for percutaneous device closure.

GW31-e1042

Incidence, risk factors and outcomes of coronary obstruction following valve-in-valve transcatheter aortic valve replacement: a systematic review and meta-analysis

Zhichun Gao, Yong Wang, Dehui Qian, Jun Jin
Xinqiao Hospital, Army Medical University (Third Military Medical University)

OBJECTIVES There is scant information about the incidence, risk factors and outcomes of coronary obstruction (CO) following valve-in-valve transcatheter aortic valve replacement (VIV-TAVR). We aimed to perform a meta-analysis and systematic review on the incidence, risk factors and outcomes of CO following VIV-TAVR in a bid to elucidate the differences between CO in native and VIV-TAVR.

METHODS Studies including case series, case-control studies, cohort studies and randomized controlled trials (RCTs) published from January 2000 to April 2020 describing CO following VIV-TAVR were collected. Two authors separately screened the studies eligible for the study. All analyses were conducted using the Review Manager (RevMan) software (version 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, 2014, Copenhagen) and the R

software (version 3.6.0; The R Foundation for Statistical Computing Platform, Vienna, Austria).

RESULTS A total of 2858 patients were enrolled in this study. The mean age was 77.7±9.8, and 39.9% of them were female. The society of thoracic surgeon (STS) score, European system for cardiac operative risk evaluation (EuroSCORE) and Logistic EuroSCORE were 8.9±7.8, 16.0±10.9 and 26.3±16.3, respectively. The overall incidence of CO was 2.58%. CO incidence between patients with prior stented and stentless valves were significantly different (1.67 vs. 7.17%), with an odds ratio (OR) of 0.25 and a 95% confidence interval (CI) of 0.14–0.44 (P<0.00001). The first-generation valves were significantly associated with higher CO incidence compared with second-generation valves (7.09 vs. 2.03%, OR=2.44, 95% CI, 1.06–5.62, P=0.04), while no statistical difference was found between self-expandable valves and balloon-expandable valves (2.45 vs. 2.60%, OR=0.99, 95% CI 0.55–1.79, P=0.98). Virtual transcatheter to coronary ostia (VTC) distance (3.3±2.1 mm, n=29 vs. 5.8±2.4 mm, n=169, mean difference: −2.70, 95% CI, −3.46 to −1.95, P<0.00001) and sinus of Valsalva (SOV) diameter (27.5±3.8 mm, n=23 vs. 32.3±4.0 mm, n=101, mean difference: −3.80, 95% CI, −6.55 to −1.05, P=0.007) were enormously shorter in patients with CO. The 24-hour, in-hospital and 30-day mortality of patients with CO were 10.5, 30.8 and 37.1%, respectively.

CONCLUSIONS In VIV-TAVR, patients receiving original stentless bioprosthetic valves were independently associated with CO. The CO incidence was higher in old generation valves group than new generation valves group. A shorter VTC distance and SOV diameter were significant risk factors for CO following VIV-TAVR. The early mortality of CO was high in VIV procedure.

GW31-e1120

Modified transannular patching palliation versus modified blalock-taussig shunt in severe tetralogy of fallot with diminutive pulmonary arteries

Yuehu Han, Jincheng Liu, Chunhu Gu
Xijing Hospital

OBJECTIVES An initial palliation followed by complete repair continues to be an important option in the staged management of patients with severe tetralogy of Fallot (TOF). However, modified Blalock-Taussig shunt (mBTS) may not be the best therapeutic strategy because of its certain drawbacks and the failing stimulate growth of the pulmonary artery. In patients with a severe form of TOF with diminutive pulmonary arteries, we performed modified transannular patching palliation (mTAP) as the initial palliation. The purpose of this study was to compare pulmonary arterial (PA) growth, morbidity, mortality, reintervention, and complete repair rates after mTAP versus mBTS for palliation in patients with severe tetralogy of Fallot with diminutive pulmonary arteries.

METHODS This was a retrospective case review study evaluating 107 patients (64 males) with severe TOF who underwent palliation with either mTAP (n=55) or mBTS (n=52) over a 10-year period. Procedure-related PA growth, morbidity, mortality, reintervention, and complete repair rates were assessed and compared.

RESULTS Two death occurred in mBTS group due to sudden cardiac arrest and five patients needs reintervention after mBTS procedure because of shunt thrombosis or stenosis, and post-mBTS complications include sudden cardiac arrest, shunt thrombosis/stenosis, vocal cord palsy and diaphragmatic palsy. Compared with the mBTS group, no death and severe complications and reintervention occurred in mTAP group. Oxygen saturations post mTAP and mBTS were significantly higher, which improved from 67.73±4.36% to 94.33±2.19% in the mTAP group and from 68.24±3.87% to 86.87±3.38% in the mBTS group respectively. The rise in oxygen saturation (pre-post palliation) was significantly better with mTAP compared with mBTS palliation (P<0.01). All 55 patients after mTAP reached complete repair and Length of palliation was significantly shorter in the mTAP group.

CONCLUSIONS In a very severe form of TOF with the hypoplastic PA tree, the mTAP seems to be a better strategy that can be accomplished safely and facilitates satisfactory pulmonary arterial growth until complete repair compared with mBTS procedure.

CARDIOMYOPATHY

GW31-e0184

Fibroblast growth factor 21 correlates with the prognosis of dilated cardiomyopathy

Lingyun Gu[1,2], Genshan Ma[1]
[1]Department of Cardiology, Zhongda Hospital, Medical School of Southeast University
[2]Department of Cardiology, Jiangyin Hospital Affiliated to Southeast University

OBJECTIVES Dilated cardiomyopathy (DCM) is the most common disease of the myocardium. The occurrence and development of DCM are complicated processes that involve inflammation, metabolic alterations and neurohormonal disturbances. Numerous study demonstrated that fibroblast growth factor 21 (FGF21), which is an important regulator of glycolipid metabolism, has anti-inflammatory and anti-oxidant properties. However, the relationship between FGF21 and DCM has not been previously investigated. Therefore, in this study, we assessed the relationship between serum FGF21 and DCM and evaluated the clinical outcomes in patients with DCM.

METHODS Two hundred and forty one patients with DCM and 80 control subjects were recruited and followed up for an average of 16.12 months. All-cause mortality and readmission were the endpoints of this study. A 2-D echocardiography technique was performed to calculate the left ventricular end-diastolic diameter (LVEDD) and the left ventricular ejection fraction (LVEF) percentage. The levels of N-terminal proBNP (NT-proBNP) and creatinine were measured in routine clinical laboratory tests. Serum FGF21 levels were measured by enzyme-linked immunosorbent assay (ELISA).

RESULTS The levels of serum FGF21 were significantly higher in the DCM groups than in the control groups (225.85±32.57 *vs.* 145.36±30.57, P<0.001). Serum FGF21 levels were positively correlated with the NYHA functional classification of heart failure (HF) (r=0.610, P<0.001) and NT-proBNP levels (r=0.741, P<0.001). Moreover, a negative correlation was observed between the serum FGF21 levels and the LVEF (r=–0.402, P<0.001). FGF21, NT-proBNP, the LVEF and a history of atrial fibrillation (AF) correlated significantly with NYHA class IV (P<0.05). The AUC of NT-proBNP for predicting NYHA class IV in DCM patients was larger than that of FGF21 (0.830 *vs.* 0.772, P<0.001). Overall, 133 patients with DCM were recorded at the endpoint. Kaplan-Meier analysis results showed that the survival probability of those individuals with high levels of FGF21 and NT-proBNP was significantly lower than that of those with low levels of these factors (P<0.001). Cox analysis showed that FGF21 (HR: 2.561, 95% CI: 1.705–3.849) and NT-proBNP (HR: 4.458, 95% CI: 2.645–7.513) were independent predictors of a poor prognosis in DCM patients.

CONCLUSIONS In this study, we demonstrated that serum FGF21 levels were significantly elevated in DCM patients, particularly in those with HF, and was independently associated with NYHA class IV. Moreover, serum FGF21 levels were associated with adverse cardiovascular events and showed a prognostic value for DCM similar to that of NT-proBNP. Therefore, FGF21 may serve as a novel biomarker for DCM and subsequent HF independent of traditional risk factors and biomarkers.

GW31-e0224

The effect of trimetazidine on cardiac function in patients with dilated cardiomyopathy combined with chronic heart failure

Yujie Xing, Meijuan Ma, Yu Xiang, Yong Zhang
Department of Cardiology, Shannxi Provincial People's Hospital, Xi'an, Shaanxi

OBJECTIVES To investigate the effect of trimetazidine on cardiac function in patients with dilated cardiomyopathy combined with chronic heart failure.

METHODS Forty cases of dilated cardiomyopathy patients with chronic heart failure were randomly divided into two groups: the experimental group and the control group, with 20 cases in each group. The experimental group was given trimetazidine treatment on basis of conventional drug treatment, and the control group received conventional therapy. All patients were followed up for half a year. Then the general conditions and clinical characteristics of the two groups were analyzed. The level of BNP was examined and the changes of heart function was detected by echocardiography. Six min walking distance was used to test the exercise tolerance of patients in two groups. At the same time, the adverse reactions of the two groups should be observed.

RESULTS There was no significant difference in general conditions and clinical characteristics between the two groups. Compared with control group, the BNP levels of patients in experimental group decreased significantly, 6 min walking distance increased significantly, left ventricular ejection fraction (LVEF) increased significantly, while left ventricular end systolic diameter (LVESD) and left ventricular end diastolic diameter (LVEDD) decreased significantly. All the differences were statistically significant (P<0.05).

CONCLUSIONS Trimetazidine can significantly improve the cardiac function in patients with dilated cardiomyopathy combined with chronic heart failure.

GW31-e0247

Left ventricular pressure-strain–derived myocardial work in patients with multiple myeloma with preserved EF value

Zhiyue Liu, Mei Liu, Fang Wang, Qiuchen Lu, Zhuoqin Tang, He Huang
West China Hospital

OBJECTIVES The aim of this study was to investigate cardiac performance in multiple myeloma (MM) with preserved EF value by 3D strain and LWMWI.

METHODS A total of 39 subjects were included. These subjects comprised of 26 patients with MM with preserved EF value and 23 healthy controls. All patients

had undergone comprehensive two-dimensional and three-dimensional echocardiographic examinations. The global area strain (GAS), global circumferential strain (GCS), global longitudinal strain (GLS) and global radial strain (GRS) were analyzed by 3D Speckle-tracking imaging. Laboratory data and clinical history of all patients were also collected.

RESULTS Patients with MM showed lower LV myocardial work efficiency (LVMWE), LVGAS, higher longitudinal peak strain dispersion (PSD) and myocardial mass index than controls (P<0.05 for all). However, there was no significance difference in LVGLS, LVGCS, LVGRS and LVMWI between MM and control group. The LVMWE of MM patients in apical, middle and basal segments were lower than controls. Compared among apical, middle and basal segments in MM patients, the longitudinal strain, LVMWI, and LVMWE in apical segments were all higher than basal segment. Furthermore, patients with MM had higher LAVmin and LAVpreA and lower LAEF compared with control group. Light chain level was positively related to myocardial mass index (P=0.0003, r=0.711) and PSD (P<0.001 r=0.850) and negatively correlated with LVMWE (P<0.001, r=−0.755). β2 microglobulin was negatively related to LVWME (P=0.042 r=−0.448) and positively correlated with PSD (P=0.0, r=0.546).

CONCLUSIONS Patients with MM with preserved EF may have subclinical systolic left ventricular dysfunction, as well as a decreased left atrial conduct and reservoir function. The reduced cardiac performance is negatively correlated with the light chain level and β2 microglobulin in MM patients.

GW31-e0401

Distribution of type 2 diabetes mellitus and analysis of lipotoxicity in patients with dilated cardiomyopathy

Haifeng Zhang[1,2], Qingyuan Gao[1,2], Zhiteng Chen[1,2], Shaohua Wang[1,2], Wenhao Liu[1,2], Yangxin Chen[1,2], Jingfeng Wang[1,2]
[1]Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong 510120, PRC
[2]Laboratory of Cardiac Electrophysiology and Arrhythmia in Guangdong Province, Guangdong 5101120, PRC

OBJECTIVES To investigate the distribution of type 2 diabetes mellitus (T2DM), myocardial lesions with features of dilated cardiomyopathy (DCM) and secondary lipotoxicity, and the influence on patients' cardiac function.

METHODS A total of 259 patients with DCM were enrolled. Their T2DM situation and serum free fatty acid (FFA) level were analyzed, so as to get to know the influence of T2DM and FFA on patients with DCM. Besides, cardiac function was evaluated by left ventricular ejection fraction and left ventricular end-diastolic diameter.

RESULTS The incidence of T2DM was high in patients with DCM, especially secondary DCM. The cardiac function of DCM patients with T2DM combined with high levels of FFA was poor.

CONCLUSIONS The morbidity of T2DM and its secondary lipotoxicity are high in patients with DCM, and it should be seriously considered in clinical work.

GW31-e0435

The role of TTN gene mutation in Mongolian dilated cardiomyopathy

Yu Hou[1], Shengnan Liu[1], Qingyan Zhang[2], Xiaozhen Sun[1], Buihui Zhang[2], Xiaoshuang Shi[2], Hanqimuge Wu[1], Tu Ba[1], Chen Xiaochun[1], Xiaochun Chen[1]
[1]Inner Mongolia Autonomous Region International Mongolian Medical Hospital
[2]Inner Mongolia Medical University

OBJECTIVES To investigate the role of TTN gene mutation in Mongolian nonalcoholic primary dilated cardiomyopathy (DCM).

METHODS: Forty-five patients with primary DCM who were hospitalized in the Inner Mongolia International Mongolian Hospital were selected and divided into groups based on nationality: Mongolian DCM group and Han DCM group. Another 20 cases from the healthy control group were treated as a normal control group. The patients were selected according to the diagnostic and exclusion criteria of DCM jointly developed by the European Heart Association (ESC) and the World Health Organization/International Federation of Cardiology Associations (WHO/ISFC), of which included 20 Mongolian DCM patients and 25 Han DCM patients. All patients were evaluated for cardiac function (NYHA), chest X-ray, echocardiography and NT-proBNP, whole blood was collected for detection of TTN gene mutation, serum for anti-ANT (Adenine nucleotide translocator) antibody and anti-β1AR (β1-adrenergic receptor) antibody detection, standardized anti-heart failure treatment, followed up for 2 years, and the prognosis of DCM patients was observed.

RESULTS The mutation rate of the TTN gene was 15.56% in the DCM group (7 out of 45 people) and 0% in the healthy group (0 out of 20 people). The mutation rate of the Mongolians was 30% (6 out of 20 people) and that of Han was 4% (1 out of 25 people). In the Mongolian nationality, 2 cases were pathogenic (rs147879266, exon 46, nucleotide variation: c.G13250A, amino acid variation: p.S4417N), 3 cases were probable pathogenicity (2 cases were rs56071233, exon 154, nucleotide variation: c.G43712A, amino acid variation: p.R14571H. 1case was rs368914555, exon 154, nucleotide variation: c.C47839T, amino acid variation: p.R15947W). Three cases were not reported in the database, in which there was no sequence number and another case had a possible pathogenic mutation at the same time (sequence number: none, rs773072591, rs781139091, exon 88, exon 154, exon 53, nucleotide variation: c.T22480A, c. A43966G, C.G14087A, amino acid variation: p.F7494I, p. I14656V, p. R4696H), One case of Han nationality mutation was not reported in database (rs765925142, exon: 90, nucleotide variation: c.T21965C, amino acid variation: p.V7322A). There are differences in mutation sites between Mongolian and Han nationalities. There were 17 cases of terminal events in the two groups, 9 cases in the Mongolian DCM group and 8 cases in the Han DCM group. Although the rate of terminal events in the Mongolian group was higher than that in the Han group, there was no significant difference between the two groups (P>0.05).

CONCLUSIONS 1. The mutation rate of the TTN gene in the Mongolian DCM group was significantly higher than that in the Han DCM group. 2. It was found that 3 cases of Mongolian and 1 case of Han nationality were new mutations of the TTN gene. 3. The incidence of DCM endpoint events in the Mongolian group was higher than that in the Han group (P>0.05).

GW31-e0461

Functional advanced atrio-ventricular block as cause of death in patients with dilated cardiomyopathy

Thach Nguyen[1,2], Vy Le[2], Nguyen Thanh Luan[2], Duy Chung[1], Luan Ngo MD[1], Tra Ngo[2], Phuong M. Nguyen[1], Phuoc T. Nguyen[1], Thai Truong[1], Hoang C. Nguyen[1], An T. Ngo[1], Quang N. N. Do[2], Hien D. N. Duong[2], Vu Tri Loc[2], Tran P. H. Nhan[3], Cao Van Thinh[4], Ho Thuong Dung[5], Gianluca Rigatelli[6]
[1]Methodist Hospital, Merrillville IN
[2]Tan Tao University School of Medicine
[3]Tam Duc Hospital, Hochiminh City, Vietnam
[4]Pham Ngoc Thach School of Medicine, Hochiminh City, Vietnam
[5]Thong Nhat Hospital, Hochiminh City, Vietnam
[6]Cardiovascular Diagnosis and Endoluminal Interventions, Section of Adult Congenital Interventions, Rovigo General Hospital, Rovigo, Italy

OBJECTIVES In the care of patients with dilated cardiomyopathy, the patient could have chest pain, syncope or sudden cardiac death (SCD) with patent coronary arteries. However, it is not clearly understood how these patients can present with chest pain, syncope and SCD while their coronary arteries have no lesions? The aim of our study was to use the coronary flow abnormalities to explain the cause of chest pain, syncope or SCD in patients with dilated cardiomyopathy and patent coronary arteries.

METHODS All the patients were enrolled if they were diagnosed with dilated cardiomyopathy. The coronary arteries should be normal or minimally diseased. A group of patients who were admitted with normal coronary arteries and left ventricular function served as control. In order to assess accurately the dynamic flow during angiography, this new technique required angiographers to inject the contrast until all the coronary arteries were completely filled. As the injection of contrast stopped, the blood in white color moved in and flew down along the vessel. The angiogram was recorded from the beginning of injection until all the contrast was cleared from the artery. Thia was the arterial phase and it was compared with control.

RESULTS From January 2017 to December 2019, one hundred patients (mean age=65, 56% female) met the inclusion criteria and were enrolled. Eighty patients with dilated cardiomyopathy were selected. Ten patients with normal coronary arteries and left ventricle (LV) function served as control. Prolonged arterial transit time caused ischemia in the control group, the duration of the arterial phase was 24–30 frames (2 seconds). In contrast, in patients with dilated cardiomyopathy, the duration of the arterial phase was averaged at 120 frames or more than 8 seconds (p

CONCLUSIONS In the diagnosis of patients with ischemia, syncope, and possible SCD due to dilated cardiomyopathy, the extreme prolonged arterial phase deprived the myocardium of highly oxygenated blood, triggered ischemia and ventricular arrhythmia leading to sudden death. With the new understanding of the mechanism of ischemia, effective strategies for prevention and management of ischemia, syncope and SCD could be developed.

GW31-e0577

Left ventricular noncompaction in the monozygotic twins presented 7 years apart with heart failure

Zhe Zhang
Zhuhai People's Hospital

OBJECTIVES We reported 47 years old monozygotic twins with LVNC who presented with similar clinical symptoms but 7 years apart with heart failure.

METHODS We retrospectively reviewed the family history and echocardiograms of 2 adults of monozygotic twins with LVNC.

RESULTS A 47 years old man was diagnosed and treated for onset heart failure. His cardiac history was unremarkable before the admission. No features were suggesting a systemic disease or other before the onset of symptoms. However, echocardiography showed an LV end-diastolic diameter of 65 mm with a global ejection fraction (EF) of 28%. We observed the increased and prominent left ventricular trabeculation and deep recesses with perfusion of the intertrabecular spaces and a thin, compacted layer. Doppler echocardiography presented mild mitral and aortic valve regurgitation. The ratio between noncompacted and compacted myocardium in telediastole was greater than 2 in the apex. No other valve abnormalities were observed. The heart function was New York Heart Association function class II (NYHA II) after receiving heart failure management, including furosemide 40 mg i.v. bid the clinical conditions improved, and the medications were raised to metoprolol 6.25 mg bid, furosemide 20 mg qd, antisterone 20 mg qd, sacubitril valsartan 50 mg bid, warfarin 3 mg qn and atorvastatin 20 mg qn. He was discharged and followed-up for 3 months. Even though he did not experience any heart failure, the EF was reduced to 14% in recently and ICD would be highly recommended to this patient. We collected the family history and learned that the patient's twin brother was diagnosed with alcoholic cardiomyopathy and left ventricular and atrial enlargement with a EF of 27% 7 years ago. Also, echocardiography presented moderate mitral and severe tricuspid valve regurgitation and the function was NYHA IV. He received heart failure therapy, quitted alcohol and followed-up for 7 years regularly. He took medications including digoxin 0.125 mg qd, furosemide 20 mg qd, antisterone 20 mg bid, carvedilol 2.5 mg bid, aspirin 100 mg qd and atorvastatin 20 mg qn. At present, his heart function was NYHA I and with a global EF of 43%, moderate mitral and mild tricuspid valve regurgitation. However, noncompacted myocardium was observed in the apex and lateral wall of the left ventricular, which was not described in previous echocardiography.

CONCLUSIONS Efforts are necessary to distinguish genetic LVNC from nongenetic ones. The outcome of LVNC may be better treated if diagnosing and managing at the early stages.

GW31-e0590

The predictive value of late gadolinium enhancement by cardiac magnetic resonance for atrial fibrillation in hypertrophic cardiomyopathy patients: a systematic review and meta-analysis

Tingting Fang
West China Hospital Sichuan University

OBJECTIVES Objective – We performed a meta-analysis to evaluate the predictive value of late gadolinium enhancement (LGE) cardiac magnetic resonance for atrial fibrillation (AF) in patients with hypertrophic cardiomyopathy (HCM).

METHODS We systematically searched for cohort studies of patients with HCM with either prospective or retrospective follow-up data regarding post-MRI adverse cardiovascular outcomes.

RESULTS We identified 4 studies of 639 subjects (mean age 55.3±23.5; 63.2% men). Four hundred and seventy-two patients (74%) were LGE-positive, 167 LGE-negative subjects (26%). AF occurred in 90 LGE-positive versus 18 LGE-negative subjects (Events rate 19.1 versus 11.4%). LGE correlated with AF event in the different patient groups. In the overall population, the pooled OR was 2.12 (95% confidence interval [CI]: 1.17–3.84).

CONCLUSIONS LGE is a powerful predictor of AF in patients with HCM.

GW31-e0994

Meta-analysis global group in chronic heart failure risk score predicted adverse events in a cohort of dilated cardiomyopathy patients: a single-center study

Yang Dong, Xiaogang Guo
Department of Cardiology, The First Affiliated Hospital of Zhejiang University School of Medicine

OBJECTIVES Meta-analysis global group in chronic heart failure (MAGGIC) risk score emerging in 2013 has been validated by several studies as a good risk stratification tool for predicting prognosis of HF patients. However, there is lack of validation on prognostic value of MAGGIC risk score in nonischemic dilated cardiomyopathy (DCM) patients. In this study, we aimed to perform a MAGGIC risk score on the baseline of DCM patients, and study the prognostic value of the risk score.

METHODS DCM patients were prospectively recruited and underwent clinical assessments. MAGGIC risk score was calculated. Patients were followed up for adverse events and echocardiography. Primary endpoints were all-cause mortality and first rehospitalization due to heart failure (HF). Secondary endpoint was left ventricular remodeling, defined as a decline in left ventricular ejection fraction (LVEF)>10% or an increase in left ventricular end-diastolic diameter (LVEDD)>10%. Survival status was examined using univariate and multivariate Cox regression analyses. The model's ability to discriminate adverse events and left ventricular remodeling was calculated using receiver operating characteristics curve.

RESULTS There were 217 patients recruited according to echocardiography. One hundred and three patients excluded due to coronary artery disease according to coronary angiography or coronary computed tomography angiography. Finally, a total of 114 DCM patients were included in our study. The median follow-up time was 31 months (26–34 months). After follow up adverse events of all DCM patients included, ten patients died within the first year after inclusion while 21 patients died within the first 2 years after inclusion. And there were 31 patients suffered from first hospitalization due to HF in the first year after inclusion while there were 44 patients suffered from first hospitalization due to HF in the first 2 years after inclusion. Age, gender, BMI, systolic blood pressure (SBP), N-terminal Pro brain natriuretic peptide (NT-Pro-BNP), ratio of current smoker, ARB use, left ventricular end-diastolic diameter (LVEDD), and MAGGIC risk score demonstrated significant difference between different endpoint groups. MAGGIC risk score of all DCM patients were divided into four groups by inter-quartile range from Q1 to Q4 (Q1:5–16 points, N=25; Q2:17–19 points, N=28; Q3:20–24 points, N=29; Q4: 25–37 points, N=32). When comparing the survival curves of Q1-Q2 and Q3-Q4, the former group performed significantly better survival status (All $P<0.05$). Cox regression also showed that MAGGIC risk score was independently related to adverse events of DCM patients (2-year all-cause mortality: HR=1.122 (1.043–1.208); 1-year rehospitalization due to HF: HR=1.094 (1.032–1.158); 2-year rehospitalization due to HF: HR=1.088 (1.033–1.147)). However, MAGGIC risk score showed weak ability for discrimination in adverse events (All area under curve ranged from 0.6 to 0.7).

CONCLUSIONS MAGGIC risk score was related with adverse events and demonstrated weak discrimination ability on adverse events and LVR in DCM patient. MAGGIC risk model could be a good choice for evaluating prognosis on DCM patients.

GW31-e1312

Novel discovery of an epicardial origin of a subset of intra-myocardial cells in arrhythmogenic cardiomyopathy

Ping Yuan, Ali J Marian
Department of Cardiovascular Medicine, The Second Affiliated Hospital of Nanchang University

OBJECTIVES To determine the effects of epicardial and epicardial deprived cells (EPDCs) in an epicardial cell-specific desmoplakin (*Dsp*) gene deficiency adult mice model on fibro-adipogenesis as well as cardiac function and the incidence of arrhythmias events.

METHODS The *Dsp* gene, encoding desmosome protein DSP was conditionally deleted in the epicardial cells in mice under the transcriptional regulation of Wilms tumor 1 (*Wt1*) locus. The cardiac function was assessed by echocardiography. Picric Red and Masson Trichrome staining were used to show the myocardium morphology, especially, the myocardial fibrosis. Adipogenesis in the heart was assessed using complementary methods of staining of the thin myocardial sections with Oil Red O (ORO), immunostaining for CEBPA, a transcription factor of adipocytes, and staining for PLIN1, a specific marker of adipocytes. In terms of the cell fate mapping analysis, both myocardium and isolated epicardial cells were stained with specific cell markers.

RESULTS Epicardial cells were enriched with desmosomes proteins. Heterozygous deletion of *Dsp* was associated with premature death, the *Wt1-Cre*^{ERT2}*: Dsp*$^{W/F}$ mice showed a gradual increase in premature death, reaching a 30% mortality by 12 months of age, as compared to <3% mortality in the wild type (WT) and *Wt1-Cre*^{ERT2} mice. The *Dsp* insufficiency mice manifested a dilated cardiomyopathy, indicated by a reduced interventricular septum and posterior wall thicknesses, while increased left ventricular (LV) end-diastolic diameter (EDD) and end-systolic diameter (ESD). Subsequently, LV fractional shortening (FS) and ejection fraction (EF) was reduced. Myocardium gross analysis showed accumulated myocardial fibrosis in the *Wt1-Cre*^{ERT2}*: Dsp*$^{W/F}$ mice (3.00±0.59% *vs.* 0.5±0.08%) when compared with the WT group at 6 months old age. All the markers of adipocytes were increased in the *Wt1-Cre*^{ERT2}*: Dsp*$^{W/F}$ mouse myocardium, as compared to WT or *Wt1-Cre*^{ERT2} mice. A small part of EPDCs was positive staining with fibroblast cells marker PDGFRA, and smooth muscle marker SM22α, moreover a small cluster of cells expressed molecular markers of cardiac myocytes.

CONCLUSIONS EPDCs specific *Dsp* insufficiency adult mice mimic the phenotype of arrhythmogenic cardiomyopathy (ACM). EPDCs give rise to multiple cell types, which would be the mechanism of mediating fibroadipogenesis in ACM.

GW31-e1376

Long-term effect of catheter ablation of hypertrophic obstructive cardiomyopathy

Dong Chang
Xiamen Cardiovascular Hospital, Xiamen University

OBJECTIVES Catheter ablation guided by intracariac echo is a novel therapy for hypertrophic obstructive cardiomyopathy (HOCM). However, the long-term efficacy and safety has not been elucidated.

METHODS Thirty-six patients with symptomatic HOCM (mean age 43.7 15.6 years, five males) and significant left ventricular outflow tract (LVOT) gradient despite optimal drug therapy were recruited in the present study. Radiofrequency catheter ablation was performed at the maximal bulge of left ventricular septal hypertrophy under the guidance of 3D electro-anatomical system and intracardiac echocardiography. Patients were followed up at 1, 6, and 12 months post-procedure. Patients were followed up 3 days and 6 months after procedures.

RESULTS After 8.2±3 radiofrequency pulses, a significant and sustained LVOT gradient reduction could be achieved (68% reduction of resting gradients, P<0.0001). The 6-min walking distance increased significantly from 352.9±116 m to 512.7±126 m after 1 year, P<0.0001); and New York Heart Association functional class was improved from 3.2 to 1.6 (P<0.01). No atrioventricular block or requirement of pacemaker implantation.

CONCLUSIONS Even long-term following up, catheter ablation of HOCM could refer favorite results.

CARDIOVASCULAR SURGERY

GW31-e0871

Moderate hypothermic circulatory arrest does not increase the risk of brain injury

Lei Li, Ming Gong, Xinliang Guan
Beijing Anzhen Hospital Affiliated to Capital Medical University

OBJECTIVES The effect of temperature on cerebral injury during hypothermic circulatory arrest has never been specifically studied. This study aimed to compare the effects of two different temperatures used for hypothermic circulatory arrest on the degree of brain injury in pig models.

METHODS Thirteen pigs were randomly assigned to a deep hypothermic circulatory arrest group (n=5), moderate hypothermic circulatory arrest group (n=5) or control group (n=3).

RESULTS No significant differences in immunohistochemical assay results, including Bax, Bcl-2, and Caspase 3 staining and a TUNEL assay, were observed between the deep and moderate hypothermic circulatory arrest groups. Furthermore, no significant difference was found for biomarkers of brain injury (Soluble protein-100B) between the 2 experimental groups. Similarly, no significant difference was observed in the trend of changes in inflammatory factors, including TNF-α, IL-2 and IL-6, between these 2 groups (P>0.05). However, in coagulation factors, including FXI and FVII, were different between the deep and moderate hypothermic circulatory arrest groups (P>0.05).

CONCLUSIONS Therefore, it can be concluded that moderate hypothermic circulatory arrest does not increase the risk of cerebral injury. Considering the adverse effects of deep hypothermic circulatory arrest on the coagulation system, moderate hypothermic circulatory arrest is more suitable for current clinical practice.

GW31-e0992

Is fibrinogen plasma level a risk factor for the first 24-hour death of medically treated acute Type A aortic dissection patients

Yuan Xue[1], Wenjian Jiang[2], Hongjia Zhang[2]
[1]Department of Cardiac Surgery, Beijing Anzhen Hospital, Capital Medical University, Beijing, China
[2]Department of Cardiac Surgery, Beijing Chaoyang Hospital, Capital Medical University, Beijing, China

OBJECTIVES The present study aims to assess the risk factors which affect the first 24-hour death of medical treatment in acute type A aortic dissection (ATAAD) patients.

METHODS This is a retrospective cohort study in a single center. From January 2009 to January 2018, 2379 patients with type A aortic dissection were admitted to Beijing Anzhen Hospital, of which 243 patients who received medical intervention in ATAAD were involved in the final analysis. Multivariable regressions were used to analyze the association of fibrinogen on in-hospital mortality and the first 24-hour mortality.

RESULTS The total in-hospital mortality rate was 92 (37.9%) in patients with ATAAD, and 33 (13.6%) of patients died within 24 hours of onset. We found no significant association between fibrinogen plasma level and in-hospital death (HR, 0.91; 95% CI, 0.78, 1.06; P=0.23), but a fibrinogen plasma level of ≤4.0 g/L was an independent risk factor for the first 24-hour mortality (HR, 5.92; 95% CI, 1.40, 25.08, P=0.02).

CONCLUSIONS ATAAD patients with a fibrinogen plasma level of >4.0 g/L have lower first 24-hour mortality when treated medically, while patients with a fibrinogen plasma level of ≤4.0 g/L are more likely to die without surgery in the first 24 hours.

GW31-e1010

Effect of LVEF on total arch replacement in Subacute/chronic Type A aortic dissection

Zhou Fang[1,2], Yuan Xue[2,3], Hongjia Zhang[1,2]
[1]Department of Cardiac Surgery, Beijing Chaoyang Hospital, Capital Medical University, Beijing 10020, China
[2]Beijing Lab for Cardiovascular Precision Medicine, Beijing 10029, China
[3]Department of Cardiac Surgery, Beijing Anzhen Hospital, Capital Medical University, Beijing 10029, China

OBJECTIVES Preoperative low left ventricular ejection fraction (LVEF) is a risk factor for cardiovascular surgery postoperative mortality. We investigated the relationship between LVEF and the outcome of total arch replacement in patients with subacute/chronic type A aortic dissection.

METHODS One hundred thirty-six patients with subacute/chronic TAAD were included in the analysis. All patients received total arch replacement in Beijing Anzhen hospital from January 2015 to January 2018. Univariable and multivariable Cox proportional hazards regression analyses were performed to assess the relationship between LVEF and surgical outcome.

RESULTS In-hospital mortality was 4.4%, and 6.6% of patients experienced neurologic complications. During a median (interquartile range) period of 3.97 (3.20–4.67) years of follow-up, the all-cause mortality was 10.3% (14/136). Multivariable Cox proportional hazards analysis demonstrated that low LVEF was an independent predictor of midterm mortality (HR=0.93; 95% CI: 0.86–0.99; P=0.03).

CONCLUSIONS The midterm follow-up showed a satisfactory surgical survival rate of total arch replacement in subacute/chronic TAAD. Low LVEF had a negative relationship to the surgical mortality after total arch replacement in subacute/chronic TAAD. Subacute/chronic TAAD patients with low LVEF should be evaluated carefully if they will receive the total arch replacement.

GW31-e1041

Prognostic value of preoperative hemoglobin levels for long-term outcomes of acute Type B aortic dissection post-thoracic endovascular aortic repair

Zhichun Gao, Zhexue Qin, Zhixia An, Changchun Hou, Luyu Wang, Jun Jin
Xinqiao Hospital, Army Medical University (Third Military Medical University)

OBJECTIVES There is scant information available about the prognostic value of preoperative hemoglobin (Hb) levels on the long-term outcomes of acute type B aortic dissection (ABAD) following thoracic endovascular aortic repair (TEVAR). The present study aims to examine the association between Hb concentration and the long-term outcomes of ABAD patients who have undergone TEAVR in a relatively large population with a long follow-up period.

METHODS A retrospective analysis of consecutive patients from 2010 to 2018 regarding the relationship between Hb level and long-term outcomes was conducted. The primary endpoint was all-cause mortality. Major adverse cardiovascular events (MACEs) included all-cause death, recurrent ruptures and secondary procedures.

RESULTS In total, 391 subjects treated by TEVAR were enrolled, with a mean age of 57.1±12.0 years; 79.5% of them were male. Cox multivariate analysis showed that the preoperative Hb level was independently associated with all-cause death [adjusted hazard ratio (HR) 0.797 (per 1 g/dL), 95% confidence interval (CI) 0.693–0.918, P=0.002] and MACEs (adjusted HR 0.795, 95% CI 0.672–0.871, P=0.000). The area under the receiver operating characteristic curve of Hb for all-cause death and MACEs were 0.617 (95% CI 0.548–0.687, P=0.008) and 0.617 (95% CI 0.551–0.684, P=0.005), respectively. In the linear trend test, Hb concentration was significantly related to all-cause mortality (P for trend=0.001) and MACEs (P for trend=0.000). Moreover, in Kaplan-Meier analysis, lower Hb levels (<12 g/dL) were significantly different from higher Hb (≥12 g/dL) levels for both all-cause death (log-rank P=0.001) and MACEs (log-rank P=0.001). Similar results were found when assessing the prognostic value of red blood cell count and anemia.

CONCLUSIONS Hb level may serve as a good predictor of long-term adverse events in ABAD patients undergoing TEVAR. A higher Hb concentration may

indicate a better outcome and similar results were found when assessing the prognostic value of RBC and anemia. Hb levels might be taken into consideration when risk-stratifying ABAD patients. Nutrition support to increasing preoperative Hb might be one of the additional treatments in patients with Hbs lower than 12 g/dL and anemia.

CLINICAL DRUG RESEARCH AND DEVICE DEVELOPMENT

GW31-e0022

Metformin may not reduce the mortality, cardiac, or vascular risk of people with Type 2 diabetes mellitus

Tian Li, Heng Ma
Department of physiology and pathophysiology, School of Basic Medicine, Fourth Military Medical University, Xi'an 710032, China

OBJECTIVES Given the global changes of lifestyle and eating habits, numerous strategies have been employed in the management of diabetes. Metformin is a first-line drug in type 2 diabetes mellitus (T2DM) treatment, whereas there remains uncertainty concerning whether metformin increases all-cause or cardiovascular mortality among them. A meta-analysis was designed to evaluate the effects of metformin monotherapy/combined therapy in mortality, cardiac, and vascular risk of T2DM people.

METHODS We searched PubMed and Embase for RCT published from inception to Apr 14, 2020. Data search and extraction were completed with a standard Excel and was evaluated by Cohen's kappa coefficient. Risk ratio (RR) with 95% CI was pooled across trials by a random-effects model. Primary outcomes are all-cause mortality and cardiovascular mortality. Secondary outcomes include non-cardiovascular mortality, macrovascular events (myocardial ischemia, stroke, hypertension, and peripheral vascular diseases), heart failure, and microvascular events (nephropathy and oculopathy). Risk of bias was is according to the Cochrane guidelines. Heterogeneity analysis was performed by subgroup analysis, Labbe and Galbraith plot, and meta-regression. Sensitivity analysis was analyzed by funnel plot and leave-one-out methods. Publication bias was implemented by Begg's funnel plot and Egger's test.

RESULTS We enrolled 34 articles (1991–2018) for qualitative synthesis and identified 18 articles (29 studies in total, 8627 patients) for final quantitative synthesis, with 371 all-cause and 227 cardiovascular death. Compared with the controls, metformin treatment has no meaningful actions on all-cause mortality (RR: 0.98; 95% CI: 0.69, 1.38; P=0.90), cardiovascular mortality (RR: 1.15; 95% CI: 0.57, 2.30; P=0.70), as well as macrovascular events, heart failure, and microvascular events. Combination of metformin with another hypoglycemic drug increase the all-cause (RR: 1.49; 95% CI: 1.02, 2.16) and cardiovascular mortality (RR: 2.21; 95% CI: 1.22, 4.00) vs. the hypoglycemic drug alone.

CONCLUSIONS Metformin may not reduce the mortality, macrovascular and microvascular events. The combination of metformin treatment increases all-cause and cardiovascular mortality. This finding, at least in part, shows no evidence for benefits of metformin in terms of all-cause/cardiovascular mortality and cardiovascular events. However, the conclusion must be interpreted with caution considering the number and quality of available RCT.

GW31-e0024

Intravascular ultrasound (IVUS) guided percutaneous coronary intervention (PCI)–our experiences at Evercare Hospital Dhaka

Dr. Azfar Hossain Bhuiyan, AHM Waliul Islam, Shams Munwar
Evercare Hospital Dhaka

OBJECTIVES Intravascular Ultrasound (IVUS) is an invasive imaging modality used to visualize coronary cross-sectional anatomy. IVUS technology accurately determines vessel size/lesion severity and allows a detailed plaque composition. With the availability of IVUS coronary intervention might provide better stent placement covering the proximal and distal landing zone with apposition and hence, in-hospital outcome and reduces ISR and repeat hospitalization. Although, Coronary angiography is considered as the gold standard for coronary artery disease assessment, this technique might have some limitation in assessing plaque composition. IVUS can provide information about vessel and lumen dimension, plaque burden, plaque morphology and vulnerability. Therefore, we have carried out this observational prospective cohort of IVUS guided PCI.

METHODS Patients were enrolled in this observational non-randomized prospective cohort, who underwent routine CAG and subsequent PCI with the uses of IVUS. Total 35 patient (Female 5, Male 30), has IVUS guided PCI was done, as IVUS enrolled in our Cath lab very lately and financial costing also an issue. Average age of the patient population was (61), BMI (26). Average stent diameter was 3.3.

RESULTS Total 35 patient PCI done by using IVUS; Male 30(85.7%), Female 5(14.3%). Female were more obese (Female 28: Male 25), developed CAD at advance age (Female 70: Male 59). Among the CAD risk factors: DM 21(60%), HTN 21(60%), Dyslipidemia 18(51.4%), Smoking 18(51.4%) and FH 12(34.3%). Total 44 stent deployed. Common Stented territory were, LM 3(6.8%), LM-LAD 22(50%), LM-LCX 4(9%), LCX 6(13.6%), LAD 7(15.9%) and RCA 2(4.5%). Common DES were, Everolimus 36(81.8%), Zotarolimus 5(11.3%) and sirolimus 3(6.8%). No acute or late complications noted in this small group of patients and doing well at 12 months OPD follow-up.

CONCLUSIONS We found that in this very primitive observational cohort study that IVUS guided PCI provides better in-hospital and 12-month follow-up outcomes. Thus, we recommend uses of IVUS to treat coronaries with better lesion coverages and stent optimization. Thus, to reduce procedure related acute or late complications.

GW31-e0198

Efficacy and safety of low intensity Vitamin K antagonists in Western and East-Asian populations of left-sided mechanical heart valve patients

Ke Xu[1], Arjun K Pandey[2], Li Zhang[3], Saurabh Gupta[3,4], John Eikelboom[5,6], Emilie P BelleyCote[4,5,7], Richard P Whitlock[3,4,5]
[1]Department of Cardiology, Shanghai Chest Hospital affiliated to Shanghai Jiao Tong University, Shanghai, China
[2]Department of Medicine, McMaster University, Hamilton, ON, Canada
[3]Division of Cardiac Surgery, Department of Surgery, McMaster University, Hamilton, ON, Canada
[4]Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada
[5]Population Health Research Institute, Hamilton, ON, Canada
[6]Division of Hematology, Department of Medicine, McMaster University, Hamilton, ON, Canada
[7]Division of Cardiology, Department of Medicine, McMaster University, Hamilton, ON, Canada

OBJECTIVES The optimal INR target with vitamin K antagonist (VKA) therapy in patients with mechanical heart valves is unclear. Although higher INR targets are often used in Western compared with East Asian countries, data from randomized controlled trials (RCTs) have suggested that lower INR targets may offer reduced bleeding rates without a significant difference in thromboembolic rates. The objective of this systematic review and meta-analysis was to summarize the evidence for the efficacy and safety of lower versus higher INR targets in Western and East-Asian patients with a left-sided mechanical heart valve.

METHODS We searched Western databases including Cochrane CENTRAL, Medline, and Embase as well as Chinese databases including SinoMed, CNKI, and Wanfang Data in addition to grey literature for RCTs and observational studies evaluating effects of lower versus higher INR targets in patients with left-sided contemporary mechanical heart valves. We pooled the data overall and separately for Western and East-Asian data using a random-effects model.

RESULTS We identified nine RCTs (n=5705) including three (n=120) from East Asia, as well as 17 observational studies (n=8684), including 15 (n=5485) from East Asia. The median INR target of the low INR groups was ≤2.0 in 16 of 18 East-Asian studies and 5 of 9 Western studies. In the RCTs, lower compared with higher INR targets were associated with similar rates of thromboembolism (2.4 vs. 2.3%; RR: 1.14, 95% CI: 0.82, 1.60, I^2=0%) and lower rates of bleeding (21.9 vs. 40.9%, RR: 0.46, 95% CI: 0.28, 0.78, I^2=88%), with no statistical evidence of heterogeneity by region (Western vs. East Asian). In observational studies, lower INR targets, compared with higher INR targets, were also associated with similar rates of thromboembolism (3.2 vs. 5.1%; RR: 0.92, 95% CI: 0.60, 1.39, I^2=36%) and lower rates of bleeding (4.5 vs. 12.3%, RR: 0.30, 95% CI: 0.23, 0.38, I^2=22%). There was significant heterogeneity in thromboembolism by region (P-for-interaction=0.0005). Lack of reporting on major bleeding and mortality in East-Asian studies precluded analysis of these outcomes.

CONCLUSIONS In patients with left-sided contemporary mechanical heart valves, lower INR targets, compared with higher INR targets, are associated with similar rates of thromboembolism and lower rates of bleeding.

GW31-e0623

Sodium-glucose cotransporter 2 inhibitors and fracture risk in patients with Type 2 diabetes mellitus: a meta-analysis of randomized controlled trials

Yake Lou, Wei Liu, Xiaomin Nie
Beijing Anzhen Hospital

OBJECTIVES We aimed to investigate whether sodium-glucose co-transporter 2 inhibitors (SGLT2i) are associated with increased risk of fracture.

METHODS We retrieved articles from PubMed, Embase, Cochrane Library database, and other sources up to October 24, 2019. We included randomized controlled trials (RCTs) that reported fractures and analyzed the fracture incidence of SGLT2i, canagliflozin, dapagliflozin and empagliflozin. Subgroup analysis was also performed based on baseline characteristics.

RESULTS A total of 78 RCTs with 85,122 patients were included in our analysis. The overall SGLT2i fracture incidence was 2.56 versus 2.77% in the control group (OR, 1.03; 95% CI [0.95, 1.12]; P=0.49). Compared to control treatment, treatment with canagliflozin led to a higher rate of fractures (OR, 1.17; 95% CI [1.00, 1.37]; P=0.05), but no significant difference was observed when compared with dapagliflozin (OR, 1.02; 95% CI [0.90, 1.15]; P=0.79) or empagliflozin (OR, 0.89; 95% CI [0.73, 1.10]; P=0.30). Subgroup analysis showed that, in a follow-up of less than 52 weeks, SGLT2i decreased the incidence of fracture by 29% (OR, 0.71; 95% CI [0.55, 0.93]; P=0.01), but this benefit was lost when the follow up extended to more than 52 weeks (OR, 1.08; 95% CI [0.98, 1.18]; P=0.12).

CONCLUSIONS Canagliflozin seems to increase the risk of fracture, while other SGLT2i are not associated with a higher incidence of fracture.

GW31-e1112

Choice of percutaneous patent foramen ovale closure devices for recurrent stroke: a network meta-analysis

Hao Nie, Cuntai Zhang
Department of Geriatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan Hubei 430030, P. R. China

OBJECTIVES Randomized controlled trials directly comparing safety and efficacy of percutaneous PFO closure devices are lacking. We performed a network meta-analysis and found out the most and least recommended occluder at present.

METHODS We searched Embase, PubMed, and Cochrane Library databases (from 1st, January, 2000 to 1st, May, 2018) for RCTs involving percutaneous closure device (STARFlex, GORE and Amplatzer) and medical therapy in cryptogenic cerebral ischemic patients with PFO. Occurrence rate of recurrent stroke, atrial fibrillation, major vascular complication, headache, transient ischemic attack and bleeding were compared with frequentist and Bayesian methods using R statistics.

RESULTS Three thousand and seven hundred and forty-seven patients from 6 RCTs were included in the network meta-analysis. GORE and Amplatzer showed significant association with a decrease in the risk of recurrent stroke (RR 0.37, 95% CI 0.17–0.81 and 0.49, 0.29–0.83, respectively). STARFlex increased the risk of postoperative atrial fibrillation and major vascular complications by 10 and 6 times (RR 11.66, 95% CI 4.87–21.91, and RR 7.63 95% CI 2.34–24.88, respectively). There was no difference in the occurrence of headache, transient ischemic attack or bleeding between different treatments.

CONCLUSIONS GORE occluder can be considered the most appropriate choice among three closure devices to prevent secondary stroke in patients with PFO. Amplatzer also behaves well. STARFlex is the least recommended devices for it could not decrease recurrent stroke risk compared with medical therapy, as well as it is most likely to have adverse reactions.

GW31-e1218

Non-vitamin K antagonist oral anticoagulants for the treatment of ventricular thrombus

Qing Yang, Yan Liang
Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES This article reviews the effectiveness and safety of NOACs in the treatment of ventricular thrombus.

METHODS We used "ventricular thrombus" or "intraventricular thrombus", "direct/new/noval oral anticoagulants" or "non-vitamin K antagonist oral anticoagulants" and combination of these terms as keywords. Fifty-two case reports or series describing 90 cases were found by searching Medline, Embase, Cochrane Library Web of Science and Pubmed databases from inception to August 2020, which represented the best evidence to explore the efficacy of NOACs for ventricular thrombus.

RESULTS Among the 90 cases, rivaroxaban (n=46, 51.1%) was the most common used NOACs, and 28.9% (n=26), 17.8% (n=16), 2.2% (n=2) patients received apixaban, dabigatran and edoxaban. At a median follow-up period of 60(28–111) days, 92.5% (74/80) patients had complete thrombus resolution. Patients who were treated with dabigatran and edoxaban achieved 100% ventricular thrombus resolution, while those with apixaban and rivaroxaban therapy had 88.4 and 95.8% resolution dependently. There was a total of 5(5.5%) embolic events and 3(3.3%) deaths while being treated with rivaroxaban and dabigatran, and 3(3.3%) bleeding events only occurred in the rivaroxaban group.

CONCLUSIONS According to the evidence from previous case reports, the application of NOACs showed a great complete resolution of thrombus, with few thromboembolic or hemorrhagic events. Given that the sample size of NOACs in ventricular thrombosis is small and the studies are most case reports or series, there is an urgent need for further randomized controlled trials to assess the efficacy and safety of NOACs in patients with ventricular thrombus.

GW31-e1254

Empagliflozin improves cardiac dysfunction by alleviating cardiac hypertrophy in heart failure-rat model

Chang Wang, Ping Yang
China-Japan Union Hospital of Jilin University

OBJECTIVES Sodium-glucose cotransporter 2 inhibitor (SGLT-2i) is a new type of hypoglycemic agent which has proven to be cardiovascular protective. Among these SGLT-2is, the efficacy of empagliflozin is the best in improving cardiac dysfunction. However, the accurate mechanisms are still under research.

METHODS In this study, we established the heart failure (HF) rat model by left anterior descending coronary ligation. In the middle stage of HF, empagliflozin was administered orally for 2 weeks. First, we evaluated the heart function by echocardiography. Then, we obtained the left ventricle tissue samples from the control and therapy group and performed transcriptomics and proteomics analyses. These results were then used to determine correlation between transcriptome and proteome and potential molecular mechanisms.

RESULTS The results of echocardiography showed an improvement in cardiac function after empagliflozin therapy, and higher dose led to better outcome. And we detected 75 differentially expressed genes and 80 differentially expressed proteins. The sequencing results involved in aspects such as fibrosis, hypertrophy, energy metabolism, and so on.

CONCLUSIONS The result revealed that empagliflozin improves cardiac dysfunction by alleviating cardiac hypertrophy, and this study is first to report the molecular evidence supporting this mechanism.

GW31-e1365

Endothelium-protective role of acute Beraprost sodium administration

Yumin Qiu[1,2,3], Yuanya Liu[1,2,3], Xing Liu[1,2,3], Jun Tao[1,2,3]
[1]Department of Hypertension and Vascular Disease, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China
[2]National-Guangdong Joint Engineering Laboratory for Diagnosis and Treatment of Vascular Diseases, Guangzhou, China
[3]Key Laboratory on Assisted Circulation, Ministry of Health, Guangzhou, China

OBJECTIVES Endothelial dysfunction plays a pivotal role in the initiation and progression of atherosclerotic cardiovascular diseases. Beraprost sodium (BPS) has a beneficial effect on endothelium, but limited data are available on BPS-mediated protective role in endothelial function detected by endothelial microparticles (EMPs) and Endo-PAT in healthy volunteers. In the present study, we aim to investigate the effect of acute oral BPS therapy in endothelial homeostasis.

METHODS Six healthy volunteers (1 female, 5 males, aged 29.5±3.9 years) were enrolled and given BPS tablets 20 μg once a day. The number of EMPs in peripheral blood was measured at baseline, 1 hour, 8 hours and 24 hours after therapy. Endo-PAT was used to evaluate vascular endothelial function by detecting reactive hyperemia index (RHI).

RESULTS The number of circulating EMPs showed a downward trend, and the difference was statistically significant in 8 h and 24 h compared with the baseline. In addition, RHI increased markedly at 1 h and 8 h after taking the drug.

CONCLUSIONS Our study demonstrated that BPS has a beneficial effect on maintaining endothelial homeostasis. Acute BPS administration may be an effective pharmacologic intervention for improving endothelial function.

CARDIOVASCULAR DISEASES IN SPECIAL POPULATIONS (CHILDREN, WOMEN, ETC.)

GW31-e0165

Prevalence and characteristics of the b-type natriuretic peptide in pregnant women with heart disease

Manzura Uzakova[1], Guljahon Babadjanova[1], Jamol Uzokov[2]
[1]Tashkent Medical Academy
[2]Republican Specialized Scientific and Practical Medical Center of Therapy and Medical Rehabilitation

OBJECTIVES Heart disease in pregnancy is one of the problem of the current obstetrics and gynecology. Aim of the study was to estimate prevalence and characteristics of the B-type natriuretic peptide (BNP) in pregnant women with heart disease in the third trimester of the pregnancy and after childbirth.

METHODS Thirty-five pregnant women with heart disease (aortal stenosis, mitral stenosis and mitral incompetence rheumatic etiology) and 15 healthy pregnant women were enrolled in the study. Initial characteristics of the

groups did not significantly differ from each other. All anthropometric parameters, biochemistry including BNP, instrumental analysis were done at the third trimester of the pregnancy and after delivery (till 3 months). All statistical analysis were done at the STATA.

RESULTS The first group pregnant women's age were 24±4.8 years and second groups' mean age were 25.2±5.2 years. Mean BMI in the pregnant women with heart disease were 22.4±4.2 kg/m² and in healthy pregnant women were 21.6±3.8 kg/m² (P>0.05). Average BNP concentration were high in the first group than second one at the third trimester of the pregnancy (82±26.4 pg/mL vs. 35±25 p/mL Po.05), nevertheless in women with heart disease BNP was significantly higher than healthy women as in pregnancy (78.4±23.1 pg/mL vs. 31.2±22.5 p/mL P<0.05).

CONCLUSIONS Plasma levels of BNP is high in pregnant women with heart disease in the third trimester of pregnancy and after delivery.

GW31-e0216

Features of changes in coronary arteries in young women with retrosternal pain during coronary angiography with various risk factors

Sevindzh Najafova[1], Mekhman Mamedov[2]
[1]Clinical Medical Center, Baku, Azerbaijan
[2]National Medical Research Center for Preventive Medicine, Moscow, Russia

OBJECTIVES The aim of this study is to identify the relationship between risk factors and coronary angiography in a group of young patients with different risk factors for coronary heart disease.

METHODS The study included 40 women aged 38–45 years (42.3±2.5) who had various risk factors for coronary heart disease with typical and atypical chest pains. All women have preserved reproductive function. To exclude gynecological pathology, a gynecological history and clinical examination were collected. The study evaluated anthropometric and hemodynamic parameters, laboratory data (total Ch, HDL, LDL, triglycerides, fasting glucose level, C-reactive protein (CRP)). Non-invasive research methods (ECG, echocardiography, Holter monitoring, treadmill test) were carried out. Coronary angiography was performed to clarify the condition of the coronary arteries.

RESULTS According to the results hemodynamically significant narrowing of the coronary arteries was detected in 7 patients (4 women having a lesion of one vessel, and 3 women having multivascular lesions). All these women had a history of different risk factors for CHD, and women with multivascular lesions showed a combination of several risk factors: AH, hyperlipidemia, and hereditary factor. 8 women have hemodynamically insignificant narrowing >50%. In 15 women were discovered the coronary muscle bridge and pronounced convoluted coronary arteries, which are considered coronary anomalies. The coronary muscle bridge was detected in 5 women. In all women, he was in a typical place – in the middle segment of the left descending coronary artery. When conducting a coronary angiography in 6 women, such a feature of coronary blood flow as delayed coronary blood flow (syndrome Y) was found. Moreover, in 4 women it is found in isolation in one vessel LAD, in the other 2 in two (LAD, CX) and three vessels (LAD, CX, RCA). These women had a history of hypertension, smoking, and hyperlipidemia. In 2 women, vasospastic angina was detected. There is a local spasm in RCA>50%, passing after the resolving test (nitroglycerin). In 4 women, intact vessels without anatomical abnormalities were found. Of these, 2 women have a positive stress test for physical activity, which can be assessed as coronary syndrome X.

CONCLUSIONS In young women, a direct correlation was found between the quantitative lesion of the coronary arteries and risk factors for coronary artery disease. Identification of convoluted coronary arteries and coronary muscle bridges should be considered as a risk group for the development of CHD. Syndrome X and the phenomenon of slow blood flow (Syndrome Y) can be a potential cause of recurrent chest pain and myocardial ischemia during stress.

GW31-e0582

Stress at workplace and risk of acute cardiovascular diseases in population 25-64 years in Russia/Siberia: gender issues. MONICA-psychosocial epidemiological study

Valery Gafarov[1,2], Elena Gromova[1,2], Dmitiry Panov[1,2], Igor Gagulin[1,2], Almira Gafarova[1,2]
[1]Institute of Internal and Preventive Medicine – branch of Institute of Cytology and Genetics SB RAS
[2]Collaborative Laboratory of Cardiovascular Disease Epidemiology

OBJECTIVES To determine gender differences in the impact of stress at work on the risk of cardiovascular disease over 16-years of follow-up in an open population of 25–64 years in Russia/Siberia

METHODS Under the third screening of the WHO MONICA-psychosocial program (MOPSY) random representative sample including both genders aged 25–64 years was surveyed in Novosibirsk in 1994 (n=1346, 48.8% males; mean age 44.9±0.4 years; response rate was 77.3%). Stress at work was assessed by means Karazek scale. New-onset cases of myocardial infarction (MI), stroke were identified from 1994 to 2010. This longitudinal survey performed in frame budgetary issue # AAAA-A17-117112850280-2.

RESULTS A high level of stress at work was in 29.5% of men and in 31.6% of women. The middle level was in 48.9% of men and in 50.7% of women (χ^2=2.574 υ=2 p=0.276). The risk of MI over 16-years period in persons experiencing stressful situations at work was as follow: in men HR=3.592 and women HR=3.218 (95%CI 1.146-9.042); stroke risk was in men HR=2.603 (95%CI, 1.06-4.153) and in women HR was 1.956 (95%CI 1.008-3.795). In multivariate analysis risk of MI in men was HR=1.15 (95%CI 0.6-2.2) and in women HR=2.543 (95%CI 1.88-7.351); risk of stroke in men was HR=3.8 (95%CI 1.6-8.8) and in women it was HR=1.95 (95%CI 0.984-3.887). The risk of stroke was higher in those who are living alone, divorced and widowed men HR=4.2 (95% CI 1.5-13.2) and in women with high school or primary education degree HR=3 (95%CI 0.852-11.039).

CONCLUSIONS It was established that a high level of stress at work is not gender-specific. The risk of MI incidence over a 16-years period is higher in women than in men but stroke in men; the risk of myocardial infarction and stroke is affected by the social gradient in both genders.

GW31-e0592

Clinical scenario and long-term outcome of childhood takayasu arteritis undergoing 121 endovascular interventions: the largest cohort over a 15-year period

Luyun Fan[1], Lirui Yang[2], Dongmei Wei[1], Wenjun Ma[1], Ying Lou[1], Lei Song[1], Jin Bian[1], Huimin Zhang[1], Jun Cai[1]
[1]Fuwai Hospital, Peking Union Medical College&Chinese Academy of Medical Sciences
[2]Beijing Anzhen Hospital, Capital Medical University, China

OBJECTIVES Evidence-based studies on endovascular approaches for childhood Takayasu arteritis (c-TA) are limited. This study presents the largest real-world scenario up-to-date for c-TA patients undergoing interventions and their post-interventional outcomes.

METHODS Data were collected for c-TA patients admitted from 2002 to 2017. Complication/Re-intervention-free survival were projected by Kaplan-Meier methods. Associated factors for intervention and predictors for post-interventional complications/re-interventions were assessed via regression models.

RESULTS Among 101 patients enrolled, 69(68.3%) underwent 121 interventions (Angioplasty 95; Stenting 26) during 3.1-year follow-up. Compared with non-intervention group, the intervention group independently associated with male population (OR=0.27, P=0.035) and type IV disease (OR=17.92, P=0.001). Male sex also marginally indicated risk for re-intervention (HR=3.22, P=0.05). Baseline retinopathy, delay in diagnosis and descending thoracic aorta involvement associated with stent insertion (<0.05). Hypertension secondary to renal artery stenosis (RAS, 59.4%) or mid-aorta stenosis (MAS, 14.5%), heart failure (21.7%), claudication (21.7%) were leading clinical hints for interventions. Technical success rate was 96.7%. Over 2.88 years since intervention, 36 lesions occurred complications in 28 patients and 22 lesions in 17 patients, majorly on renal artery or mid-aorta. The 5-year complication-free and re-intervention survivals were 50.7 and 65.8%. Peri-interventional dual antiplatelet therapy (DAPT, HR=0.31), concurrent surgery (HR=26.5), and technical failure (HR=3.65) were independent predictors for complications (P<0.05). Male sex (HR=2.52), retinopathy secondary to hypertension (HR=3.41), and pulmonary artery hypertension (PAH, HR=3.64) were baseline indicators for complications (P<0.05).

CONCLUSIONS Over two-thirds c-TA patients require interventions and 5-year complication-free survival is 50.7%. Male sex, retinopathy, and PAH at baseline alert unfavorable outcomes. Interventions on MAS or RAS in c-TA need specific concerns. DAPT peri-intervention appears to protect c-TA from post-interventional complications.

GW31-e0742

Elevated resting heart rates are a risk factor for mortality among patients with COVID-19 in China

Han Jin, Jianping Li
Peking University First Hospital

OBJECTIVES We evaluated the association between higher resting heart rates (RHRs) and adverse events in COVID-19 patients

METHODS One hundred thirty-six patients with laboratory-confirmed COVID-19 were admitted. Outcomes of patients with different RHRs were compared.

RESULTS Twenty-nine patients had RHRs of <80 bpm, 85 had RHRs of 80–99 bpm, 22 had RHRs ≥100 bpm as tachycardia. Those with higher RHRs had lower SpO_2 and higher temperatures, a higher proportion of men upon admission (all P<0.05). Patients with higher RHRs showed higher white blood cell counts and D-dimer, TnI, N-terminal pro-B-type natriuretic peptide and hypersensitive C-reactive protein levels but lower albumin levels (all P<0.05) after admission. During follow-up, 26 patients died (mortality rate, 19.1%). The mortality rate was significantly higher among patients with tachycardia

than among the moderate and low RHR groups (all P<0.001). Kaplan-Meier survival curves showed that the risks of death and ventilation use increased for patients with tachycardia (P<0.001). Elevated RHR as a continuous variable and a mean RHR as tachycardia were independent risk factors for mortality and ventilator use (all P<0.05) in the multivariable adjusted Cox proportional hazards regression model.

CONCLUSIONS Elevated average RHRs during the first 3 days of hospitalization were associated with adverse outcomes in COVID-19 patients. Average RHRs as tachycardia can independently predict all-cause mortality.

GW31-e0804

Clinical characteristics and thinking of children's myocarditis in the epidemic of COVID-19

Xi Yang, Qian Zhou, Jia Li, Ying Sun, Guiying Liu
Department of Pediatrics, Beijing Anzhen Hospital, Capital Medical University, Beijing 10029, China

OBJECTIVES Analyze the impact of the coronavirus disease 2019 (COVID-2019) epidemic on the clinical characteristics of children with myocarditis, consider the reasons and summarize relevant laws.

METHODS A retrospective cross-sectional study was used to analyze the clinical data of children with myocarditis diagnosed and treated in Beijing Anzhen Hospital of Capital Medical University within 6 months after the start of response to public health emergencies in Beijing and the same period in 2019, and summarize their clinical manifestations and etiological characteristics, ECG, echocardiogram and cardiac magnetic resonance characteristics, and analyze these changes.

RESULTS Within 6 months of the initiation of response to public health emergencies in Beijing, the number of children diagnosed with myocarditis decreased significantly compared with the same period in 2019 (134 cases vs. 377 cases, P<0.05). A total of 134 cases were diagnosed from February to July 2020, of which 26 cases completed the magnetic resonance examination (CMR) examination, and 377 children with myocarditis were diagnosed from February to July 2019, of which 89 cases completed the CMR examination, and the age of diagnosis increased compared with the same period in 2019 (6.33±1.19 vs. 12.71±3.36, P<0.05). In terms of symptoms, during the epidemic of COVID-19, the circulatory system symptoms of children with myocarditis were more obvious than the same period last year, chest pain (84.7 vs. 30.3%, P<0.05), fatigue (54.3 vs. 17.9%, P<0.05), and other symptoms such as rash in children were significantly increased (41.3 vs. 7.9%, P<0.05), and symptoms of infection such as fever, cough, vomiting and diarrhea were significantly reduced compared with the previous ones. The proportion of chest radiographs and echocardiograms indicating heart enlargement increased (80.4 vs. 60.6%, P<0.05), and compared with the previous, the number of cases whose LVED in echocardiograms increased ≥3mm in the short term (3–6 months) increase (24, 1 vs. 38.4%). The ECG is more common with V1 ST-segment arch elevation (63 vs. 3.3%, P<0.05), and cTnI in myocardial markers is significantly increased (1.15±1.69 vs. 0.07±0.15, P<0.05). In CMR performance, compared with the same period in 2019, the proportion of T2 hyperintensity (58.7 vs. 37.1%, P<0.05), pericardial effusion (32.6 vs. 7.9%, P<0.05), LGE (41.3 vs. 23.6%, P<0.05) is higher. Pathogen examination shows that all children with myocarditis are excluded from COVID-19 infection. The mixed infection of multiple pathogens has increased significantly compared with the same period in 2019. The co-infection ratio of CoxA, echo, influenza virus A, and B has increased significantly (43.5 vs. 2%, P<0.05).

CONCLUSIONS Under the influence of the 2020 epidemic, the clinical characteristics of children with myocarditis showed different changes. The number of children diagnosed with myocarditis was significantly less than before, but the clinical symptoms were more obvious. The prominent manifestation was chest pain and fatigue, and the number of children with enlarged heart was significantly increased. V1 ST Segmental arched back elevation in ECG is more common, and myocardial markers are significantly increased in the early stage. CMR indicates that the severity and extent of myocardial pathology are more serious than in the same period in 2019. Mixed infections of multiple pathogens can be seen at the same time.

GW31-e1043

Association of uterine fibroids and hypertension: a case-control study and a meta-analysis of observational studies

Nianling Xiong[1,2], Jiaxin Xiao[1], Xuerui Tan[1,2]
[1]The First Affiliated Hospital of Shantou University Medical College, Shantou, China
[2]Shantou University Medical College, Shantou, China

OBJECTIVES Previous studies have revealed that uterine fibroids are associated with the increased risk of hypertension. The findings, however, are not consistent, and there is no meta-analysis for this issue. Therefore, we conducted a case-control study and a meta-analysis to assess the association of uterine fibroids with hypertension.

METHODS Eight thousand and four hundred and one participants who took physical examination in the First Affiliated Hospital of Shantou University Medical College from June 2011 to June 2013 were enrolled in this study. They were divided into uterine fibroids group (1617 cases) and control group (6784 cases). Then a systematic search was conducted for published articles which explored the association of uterine fibroids with hypertension in PubMed, Embase, the Cochrane library using search formula "((("Leiomyoma"[Mesh]) OR (Leiomyomas OR Fibroid Tumor OR Fibroid Tumors OR Tumor, Fibroid OR Tumors, Fibroid OR Fibromyoma OR Fibromyomas OR Fibroid OR Fibroids OR Fibroid Uterus OR Uterus, Fibroid OR Fibroma, Uterine OR Fibromas, Uterine OR Uterine Fibroma OR Uterine Fibromas OR Fibroids, Uterine OR Fibroid, Uterine OR Uterine Fibroid OR Uterine Fibroids OR Leiomyoma, Uterine)) AND (("Hypertension"[Mesh]) OR (OR Blood Pressure, High OR Blood Pressures, High OR High Blood Pressure OR High Blood Pressures))". The retrieval period was from the establishment of the databases to May, 2020. The outcome for this analysis was hypertension incidence. The articles would be included if they: (1) were published in English (2) compared the incidence of hypertension among patients with and without uterine fibroids (3) reported relative risks with 95% CIs, or data to calculate them. Studies that only abstract was available were excluded. In addition, we manually searched the references of the retrieved literature in order to avoid missing potential eligible studies.

RESULTS The results of our case control study showed that uterine fibroids were associated with the increased rate of hypertension [OR=1.435, 95% confidence interval (CI): 1.199–1.717]. As for, 604 citations were retrieved by database searches and 2 citations were retrieved by reference screening. Most papers were excluded based on titles and/or abstract because clearly not relevant or duplicated. According to the inclusion criteria, 10 studies enrolling 8361 patients were eventually included in the systemic review and meta-analysis (figure 1). Data sets were heterogeneous (I^2=69%), therefore, random-effects models were used for analyses. The meta-analysis of the included studies and our study revealed a significant association between uterine fibroids with hypertension incidence [pooled OR=1.44, 95% CI: 1.19–1.74, P=0.0002; I^2=69%] (figure 2). When we excluded one study at each time in the sensitivity analysis, none of the individual studies substantially influenced the results. And we also did subgroup analysis to investigate heterogeneity results (figure 3). The result shows that continent may be the source of heterogeneity.

CONCLUSIONS The case control study and meta-analysis show that uterine fibroids are associated with the increased incidence of hypertension. Blood pressure of women with uterine fibroids should be closely monitored, and hypertension preventive measures are crucial.

GW31-e1146

Atrial performance in healthy subjects following high altitude exposure at 4100m: 2D speckle-tracking strain analysis

Shiyong Yu, Lan Huang
Department of Cardiology, Xinqiao Hospital, Army Medical University (Third Military Medical University)

OBJECTIVES High altitude (HA) exposure has been considered as a cardiac stress. However, the atrial performance to HA exposure is poorly understood. This study aimed to evaluate the effect of HA exposure on bi-atrial phasic functions and the determinants.

METHODS Physiological parameters, conventional and speckle-tracking echocardiography were collected in 82 healthy men at sea level (SL, 400 m) and 4100 m after an ascent within 7 days.

RESULTS Following HA exposure, significant decreases of total emptying fraction (SL: 59.7±11.6 vs. HA: 54.5±12.3%, P=0.001), active emptying fraction (SL: 41.7±13.9 vs. HA: 35.4±12.2%, P=0.001), strain and strain rate during contractile phase were observed in right atrium (RA) but not in left atrium (LA), although decreases of strain and strain rate during reservoir and/or conduit phases were observed in bi-atria. Correlation analysis showed that the decreases in RA emptying fractions were correlated with age, mean pulmonary arterial pressure (mPAP) and tricuspid E/A, whereas the decreases in RA strain derived parameters were correlated with body mass index (BMI) and arterial pulse oxygen saturation (SpO2). Moreover, the decreases in RA function were pronounced in subjects with tricuspid regurgitation (TR) at HA, but not in those without TR.

CONCLUSIONS For the first time, our results suggested that bi-atrial performance was decreased following HA exposure, mostly observed in RA in subjects with TR. Furthermore, age, BMI, SpO2, mPAP and tricuspid E/A were also associated with the HA exposure induced decreases in RA function.

GW31-e1343

Elderly people with low handgrip strength and low gait speed have higher risk of orthostatic hypotension

Siyang Lin[1], Yin Yuan[1,2,3], Feng Huang[1,2,3], Pengli Zhu[1,2,3]
[1]Provincial Clinical Medical College, Fujian Medical University, Fuzhou, Fujian, China

[2]Department of Geriatric Medicine, Fujian Provincial Hospital, Fuzhou, Fujian, China
[3]Fujian Key Laboratory of Geriatrics, Fujian Provincial Center for Geriatrics, Fuzhou, Fujian, China

OBJECTIVES Orthostatic hypotension (OH) is a prevalent problem in older adults. Meanwhile, it is reported that handgrip strength (HGS) and gait speed (GS) decrease with age. The association among HGS, GS and OH is not clearly established, especially for the elderly. Therefore, the goal of this study was to investigate the association among HGS, GS and OH in the elderly population.

METHODS This was a study of 408 older patients aged ≥60 years, in which all participants performed HGS tests and GS tests. Patients with HGS <28 kg for men and <18 kg for women were diagnosed as low HGS, and GS <1 m/s were diagnosed as low GS. OH was assessed by measuring systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the supine and standing positions at 3 minutes.

RESULTS Among 408 patients (207 men and 201 women, mean age 72.4±8.2 years), 78 patients (19.1%) were diagnosed with OH. There were 172 (42.2%) older adults with low HGS, 234 (57.4%) with low GS and 137 (33.5%) with low HGS and low GS. OH was not associated with low HGS (OR: 1.694, P=0.083) and low GS (OR: 1.644, P=0.101) alone. Compared with the normal HGS and normal GS group, older adults with low HGS and low GS had a higher risk of OH (OR: 2.176, P=0.038).

CONCLUSIONS Neither low HGS nor low GS was associated with OH in the elderly population, but older adults who had both low HGS and low GS might have a higher risk of OH.

CARDIOVASCULAR-DISCIPLINARY RESEARCH

PULMONARY VASCULAR DISEASE

GW31-e0088

Genome-wide prioritization reveal novel signatures associated with cardiotoxicity effects of tyrosine kinase inhibitors

Yilan Li, Xueming Xu, Yao Zhang
The 2nd Affiliated Hospital of Harbin Medical University

OBJECTIVES Tyrosine kinase inhibitors (TKIs) are characterized by multi-targeted anticancer agent and lack of enough specificity leading to cardiovascular adverse effects. To date, there is no reliable means to predict cardiotoxicity of TKIs in development. In this article, we faultlessly explored usual variants of genes an eye to molecular targets of TKIs for association with heart failure (HF).

METHODS Gene or gene products to be affected by TKIs were explored by Drug Gene Interaction Database (DGIdb) and we studied these genes in genome-wide association studies (GWAS) datasets associated with HF at a genome-wide significant level (P-value<1E-5). We next investigated single-nucleotide polymorphisms (SNPs) which reached the established GWAS threshold (P-value<5E-8) for genome-wide significance. Based on a threshold of score 3, 9 gene loci yielded significant associations according to their biological function using RegulomeDB. At last, we faultlessly performed a comprehensive functional analysis of SNPs using complicated bioinformatics databases to identify potential drug targets.

RESULTS Using rSNPBase, rs7115242, rs143160639 and rs8870064 interfere in proximal transcription regulation, rs7115242, rs143160639 and rs117153772 involved in the distal regulation and most of these SNPs participate in the post-transcriptional RNA binding protein mediated regulation. Rs191188930 on PDGFRα is associated with many TKI drugs (Sunitinib, Pazopanib, Sorafenib, Dasatinib, Nilotinib). Using RegulomeDB and HaploReg v4.1, rs191188930 was predicated to locate in enhancer histone marks and we found that rs191188930 is also associated with other diseases or phenotypes apart from HF in PhenoScanner GWAS analysis. Then Genotype-Tissue Expression (GTEx) indicated that gene PDGFRα had the highest median expression in Cells-Transformed fibroblasts and STRING database revealed protein-protein interaction (PPI) network of PDGFRα including a total of 11 nodes and 39 edges and there are three genes affected by sunitinib administration in this functional pathway.

CONCLUSIONS Our findings demonstrate overlap of TKIs-induced genes and those mediating HF risk, suggesting deep mechanisms potentially responsible for TKIs-induced HF risk. Meanwhile, our genetic studies may be helpful to further explore the clinical application of off-target drug effects.

GW31-e0103

Borderline mean pulmonary arterial pressure is associated with a higher risk of developing pulmonary hypertension and increased mortality: a systematic review and meta-analysis

Lin Xue, Yicheng Yang, Bo Sun, Bingyang Liu, Qixian Zeng, Changming Xiong
Fuwai Hospital

OBJECTIVES Pulmonary hypertension (PH) is defined by a mean pulmonary arterial pressure (mPAP) ≥25 mmHg measured by right heart catheterization (RHC) at rest. Actually, it is 20 mmHg rather than 25 mmHg that is the upper limit of a normal mPAP. There was a knowledge gap between 20 mmHg, the upper limit of normal mPAP, and 25 mmHg, our threshold for diagnosing PH. The 6th World Symposium on Pulmonary Hypertension emerged the controversial proposal of a new hemodynamic definition of PH, which lowered the threshold of mPAP from ≥25 mmHg to >20 mmHg. What threshold value of mPAP should be used for diagnosing PH is still under debate. Therefore, our study aimed to investigate whether individuals with borderline mPAP, which is defined as 20 mmHg<mPAP<25 mmHg, are at higher risk of developing PH or suffering from increased mortality than those with normal mPAP.

METHODS We reviewed studies evaluating the risk of developing PH and/or mortality of people with borderline mPAP versus those with normal mPAP. The mPAP value of each participant was confirmed by RHC. A systematic search was conducted of publications published before March 31, 2020 in PubMed, EMBASE, Web of Science, the Cochrane Library, and Ovid. Other resources including unpublished grey literature (OpenGrey) and up-to-date literature from one specific journal (The European Respiratory Journal) were also searched. Additionally, the reference lists of key articles were reviewed as well.

RESULTS We identified 1213 studies through our search method, and 8 of them fulfilled our inclusion criteria. A total of 2015 participants were enrolled in the 8 studies (802 with normal mPAP, 333 with borderline mPAP, and 880 diagnosed with PH). Four studies investigated the incidences of developing PH during follow-up in the borderline mPAP group versus the normal mPAP group. Pooled relative risk (RR) for the development of PH showed a higher risk of developing PH in the borderline mPAP group (RR=1.81, 95% CI, 1.21–2.71, P=0.004, I^2=0%, when only participants who had repeated RHCs were considered as the total number for calculating the incidence of developing PH; RR=2.45, 95% CI, 1.55–3.87, P=0.0001, I^2=0%, when all participants in each group were regarded as the total number, regardless of whether they had repeated RHCs) than the normal mPAP group. Seven studies were included to analyze the hazard ratio (HR) for mortality, and the pooled HR of the borderline mPAP group versus the normal mPAP group was 2.48 (95% CI 1.69–3.64, P<0.00001, I^2=26%). We also pooled survival probabilities in each arm to obtain a summary survival curve for each group, and the pooled 1-, 3-, 5-, 7- and 9-year survival rates in the borderline mPAP group (97.0, 89.4, 77.0, 64.5 and 49.6%) were obviously lower than those in the normal mPAP group (97.7, 93.3, 88.8, 81 and 74.9%). There was no evidence of significant heterogeneities or publication biases in our analyses.

CONCLUSIONS Our study revealed that individuals with borderline mPAP were at higher risk of developing PH and suffered from increased mortality than those with normal mPAP. The pooled survival rates and the corresponding 95% CIs at 1, 3, 5, 7 and 9 years of follow-up in the borderline mPAP population were 97.0% (93.7%; 100.0%), 89.4% (84.0%; 95.2%), 77.0% (67.2%; 88.3%), 64.5% (55.4%; 75.0%) and 49.6% (35.5%; 69.4%), respectively.

GW31-e0251

One-year morbidity and risk factors of pulmonary hypertension in hemodialysis patients: an observational study

Jingyuan Chen[1], Bin Sheng[1,2], Jiang Li[1]
[1]Second Xiangya Hospital of Central South University
[2]Changsha Central Hospital

OBJECTIVES Pulmonary hypertension (PH) is the newly recognized complication in patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis (HD). High morbidity of PH was found in ESRD patients suffered long term HD. PH was found to be an independent prognostic factor of HD patients. We demonstrated an observational study to investigate the one-year morbidity of PH in ESRD patients undergoing HD via arteriovenous fistula (AVF) and to analyze the associated risk factors of PH and its correlation with pulmonary artery systolic pressure (PASP).

METHODS Clinical data including age, sex, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), glomerular filtration rate (GFR), mean arterial pressure (MBP) and other general information were obtained from all patients. Laboratory data included a clinical routine blood test, renal and liver function tests, serum electrolyte, lipids, N-terminal B-type natriuretic peptide (NT-proBNP), parathyroid hormone (iPTH), as well as inflammation parameters such as erythrocyte sedimentation rate (ESR), procalcitonin (PCT), c-reactive protein (CRP), D-Dimer and other indicators were all measured. All patients were examined with doppler echocardiography 1 day after the AVF creation or peritoneal dialysis catheter implantation and after one-year followed up.

RESULTS Compared with peritoneal dialysis, HD patients showed a high rate of PH after 1 year, with the morbidity 27.3%. Comparisons between patients with or without PH found differences in AVF flow, mean arterial pressure, left atrial systolic diameter, left ventricular diastolic diameter, and left ventricular ejection fraction. Logistic regression analysis showed that mean arterial pressure (OR=1.118, P=0.045) and AVF flow (OR=1.032, P=0.036) are risk factors for PH. Linear correlation analysis showed that MBP (r=0.622, P<0.0001) and AVF flow (r=0.68, P<0.0001) were highly positively correlated with PASP.

CONCLUSIONS Our study showed a high morbidity rate of PH, even in the first year of HD. MBP and AVF flow showed positively correlated with PASP. We recommend ESRD patients who have risk factors and tendencies to have PH should consider the way to have renal replacement therapies.

GW31-e0650

Inactivation of SERCA2 redox cysteine 674 promotes pulmonary artery remodeling by activating IRE1α-XBP1 pathway

Weimin Yu, Li Xiao, Xiaoyong Tong
School of Pharmaceutical Sciences, Chongqing University

OBJECTIVES Sarcoplasmic/endoplasmic reticulum Ca^{2+} ATPase 2 (SERCA2) is a key enzyme for maintaining Ca^{2+} homeostasis in vasculature. The decrease of SERCA2a (one of SERCA2 subtypes) is related to pulmonary arterial hypertension (PAH). Cysteine 674 (C674) of SERCA2 is the key redox regulatory site to maintain SERCA2 activity. Its irreversible oxidation (C674-SO_3H) significantly increased in the lung of PAH mice induced by hypoxia. We hypothesize that inactivation of SERCA2 redox cysteine 674 promotes pulmonary artery remodeling and PAH.

METHODS We previously generated a SERCA2 C674S knock-in (SKI) mice to mimic the irreversible oxidation of C674, whose homozygotes were embryo lethal. Heterozygous SKI mice and their littermate control wild type (WT) mice were used.

RESULTS We found that SKI mice had significant pulmonary arterial remodeling, right ventricular hypertrophy and increased right ventricular pressure which were in an age-dependent manner. In lung and pulmonary arterial smooth muscle cells (PASMC), SKI mice compared with WT mice had: (1) activated IRE1α-XBP1 (spicing XBP1, XBP1s) pathway; (2) decreased PASMC contractile markers and increased synthetic markers; (3) activated cell cycle related proteins; (4) higher proliferation rate. The increased XBP1s and proliferation rate in SKI PASMC was abolished by 4μ8C, an IRE1α-RNAse inhibitor, or CDN1163, a non-specific SERCA activator in vitro and vivo. In WT PASMC, overexpression of either SERCA2a C674S or SERCA2b C674S upregulated XBP1s and cell cycle related proteins, and promoted cell proliferation. In addition, the overexpression of XBP1s promoted cell proliferation.

CONCLUSIONS Our study is the first to confirm that inactivation of SERCA2 redox cysteine 674 promotes pulmonary artery remodeling by activating IRE1α-XBP1 pathway.

GW31-e0682

The prognostic accuracy of three-dimensional echocardiography in patients with pre-capillary pulmonary hypertension

Yicheng Yang, Bingyang Liu, Changming Xiong
Fuwai Hospital

OBJECTIVES To investigate the prognostic accuracy of three-dimensional echocardiographic (3DE) right ventricular (RV) data and compare it with that of risk stratification based on 2015 ESC Guidelines in pre-capillary pulmonary hypertension (PcPH) patients.

METHODS We prospectively enrolled PcPH patients from March 2017 to May 2018. 3DE sequences were analyzed by semi-automatic software (TomTec 4D RV-Function 2.0). RV end-diastolic volume (EDV), end-systolic volume (ESV), ejection fraction, longitudinal strain of septum and free wall, tricuspid annular plane systolic excursion were obtained. All participants were classified into low and intermediate-high risk groups based on 2015 ESC Guidelines. Patients were followed-up till May 2019 for death due to RV failure as an end-point.

RESULTS Finally 112 PcPH patients were enrolled (average 36 years, 39 males and 73 females) in our study. Mean follow-up time was 18 months, and 11 patients died. Multivariate Cox proportional regression analyses indicated RV-3D-EDV>150 mL and RV-3D-ESV>109 mL were independent predictors of mortality after adjusted by age, gender, BMI or Risk stratification. McNemar-Bowker test revealed that compared with risk stratification based on 2015 ESC Guidelines, RV-3D-EDV>150 mL (67.3 vs. 44.6%, P<0.01) and RV-3D-ESV>109 mL (62.4 vs. 44.6%, P<0.01) had better predictive specificities for end-point.

CONCLUSIONS RV volumes detected by three-dimensional echocardiography had the potential to predict death due to RV failure in PcPH patients, and their prognostic accuracy were non-inferior to that of risk stratification recommended by 2015 ESC Guidelines.

GW31-e0733

Left atrium function analysis in patients with unexplained giant T-wave inversion and thicken apex but less than 15 mm of the left ventricular: results from cardiac magnetic resonance imaging

Hui Wang[1], Xin Du[1], Sanshuai Chang[1], Lei Xu[1], Jianzeng Dong[1], Yi He[2]
[1]Beijing Anzhen Hospital, Capital Medical University
[2]Beijing Friendship Hospital, Capital Medical University

OBJECTIVES Patients with apical hypertrophy cardiomyopathy (ApHCM) morphological features but apical thickness less than 15 mm has been proposed as preclinical scope of ApHCM (Pre-ApHCM). However, left atrial (LA) function in these patients has not been studied. In this study we aimed to evaluate LA volumetric and function parameters in Pre-ApHCM patients by cardiac magnetic resonance (CMR).

METHODS Thirty-one Pre-ApHCM, 40ApHCM patients and 31 normal controls were retrospectively included. Left ventricle (LV) function, LV wall thickness, LA volumetric and function parameters were acquired by CMR and compared among the three groups.

RESULTS Compared with normal controls, all LA volumetric parameters in both ApHCM and pre-ApHCM group were higher (P<0.05). LA reservoir (LA total EF, εs) and conduit function (LA passive EF, εe) parameters in pre-ApHCM group were significantly impaired compared with normal controls but higher than ApHCM (P<0.05). In ApHCM group, compared with the control group, both the LA booster pump strain (εa) and LA booster EF were impaired (P<0.05). By contrast, in Pre-ApHCM group, only the LA booster pump strain (εa) was impaired (P<0.05) while LA booster EF was not (P>0.05). Neither εa nor the booster EF show difference between the ApHCM and Pre-ApHCM (P>0.05).

CONCLUSIONS Pre-ApHCM patients had enlarged LA volume and impaired LA function. In Pre-ApHCM and ApHCM patients, the LA reservoir and conduit function impaired earlier before the left atrium enlarged and decreased progressively as apex wall thickening while the booster function independently decreased.

GW31-e1031

Retrospective study on microalbuminuria in tibetan patients with high-altitude pulmonary hypertension

Qian Zhang[1], Aili Fan[2], Qian Zhang[1]
[1]Peking University People's Hospital Heart Center
[2]Department of High Altitude Sickness and Cardiovascular Disease, The People's Hospital of the Tibet Autonomous Region Heart Center

OBJECTIVES To investigate the level and influencing factors of microalbuminuria in Tibetan patients with high-altitude pulmonary hypertension.

METHODS One hundred and twenty patients with high altitude pulmonary hypertension admitted to the heart center of the people's Hospital of Tibet Autonomous Region from November 2018 to August 2019 were selected as the observation group, and 120 patients without definite organic disease who were hospitalized for physical examination at the same time were selected as the control group for retrospective analysis. The cardiac function was evaluated according to the WHO cardiac function classification established in 1998 and measure their urine albumin/creatinine ratio (UACR). According to the UACR, patients were divided into a non-microalbuminuria group (UACR≤30 mg/g) and a microalbuminuria group (300 mg/g>UACR≥30 mg/g). The WHO cardiac function classification, 6-minute walking test (6MWT), resting heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), pulmonary artery systolic pressure (PASP), fasting blood glucose (FBG), blood lipids (total cholesterol, low-density lipoprotein cholesterol, triacylglycerol and high-density lipoprotein cholesterol), renal function (BUN, SCR, UA), estimated glomerular filtration rate (EGFR) And N-terminal pro-B-type natriuretic peptide (NT-pro BNP). Binary logistic regression analysis was used to analyze the influencing factors of microalbuminuria.

RESULTS The incidence of microalbuminuria in all subjects was 29.58% (71/240), and the remaining 169 cases were in the normal urine protein group. The incidence of microalbuminuria in patients with High-altitude pulmonary hypertension was 57.5% (69/120). SBP, DBP, NT-pro BNP, hemoglobin, FBG, SCr, and pulmonary artery pressure in the microalbuminuria group were higher than those in the normal group, and the end-of-digital blood oxygen saturation (SaO2) and 6-min walking distance were lower than those in the normal group. Binary logistic regression analysis of independent risk factors for MAU are, pulmonary artery systolic pressure, end-of-finger blood oxygen saturation (SaO2).

CONCLUSIONS The level of microalbuminuria in Tibetan patients with high-altitude pulmonary hypertension has increased, and the occurrence of microalbuminuria in Tibetan patients with High-altitude pulmonary hypertension is related to hypoxia and increased pulmonary systolic blood pressure.

GW31-e1106

Baseline NO concentration/eNOS SNP and ET-1 were independent predictors for high-altitude de-acclimatization syndrome after de-acclimatization from 4400 m

Dehui Qian, Lan Huang
Department of Cardiology, Second Hospital Affiliated to the Army Medical University, Xinqiao Hospital, Chongqing 400037, China

OBJECTIVES We aimed to identify the associations and predictors between high-altitude de-acclimatization syndrome (HADAS) and the nitric oxide (NO)-related axis after de-acclimatization from high altitude.

METHODS A total of 67 volunteers were recruited after arrival at 4400 m for two-month acclimatization and were followed up after descent to sea level. HADAS symptoms, demographic data, heart rate and oxygen saturation were measured. Venous blood samples were also taken to measure eNOS SNPs and the concentrations of NO, endothelin-1 (ET-1), malondialdehyde (MDA) and asymmetric dimethylargininase (ADMA)

RESULTS NO and MDA concentrations dramatically increased after de-acclimatization from high altitude, whilst ET-1 and ADMA concentrations significantly decreased (P<0.001). Both the baseline and follow-up NO concentrations were significantly higher in the non-HADAS group. Furthermore, HADAS score was associated with baseline NO (r=–0.276; P=0.029) and follow-up NO (r=–0.306; P=0.035) concentrations. Finally, baseline NO concentration (OR: 0.828; P=0.033) and the rs9901734 SNP of eNOS (OR: 0.372; P=0.018) were independent predictors of a protective effect against HADAS, while ET-1 concentration (OR: 1.414; P=0.038) was an independent predictor of a hazardous effect. HADAS was closely with NO concentrations at baseline and follow-up.

CONCLUSIONS Baseline NO concentration and the rs9901734 SNP of eNOS combined with ET-1 concentration were independent predictors for HADAS.

GW31-e1125

Myocardial extracellular volume fraction analysis in doxorubicin-induced beagle models: comparison of dual-energy CT with equilibrium contrast-enhanced single-energy CT

Zhen Zhou[1], Yifeng Gao[1], Hongwei Wang[1], Wenjing Wang[1], Shuanzhuang Zhu[1], Zhonghua Sun[2], Lei Xu[1]
[1]Department of Radiology, Beijing Anzhen Hospital, Capital Medical University, Beijing, China
[2]Department of Medical Radiation Sciences, Curtin University, Perth, WA 6845, Australia

OBJECTIVES The purpose of this study was to test the proof of the concept that DECT allows for quantification of myocardial extracellular volume (ECV) in comparison with single-energy CT (SECT).

METHODS Fifteen doxorubicin-induced beagle models cared for in compliance with the Local Animal Care and Use Committee were selected in this study. We quantified myocardial ECV using DECT and SECT before and after doxorubicin administration. Magnetic resonance imaging (MRI) was performed to assess cardiac function and strain. The histological collagen volume fraction (CVF) was calculated as the gold standard. The Bland-Altman analysis was used to compare the agreement between DECT-ECV and SECT-ECV. The associations among DECT-ECV, SECT-ECV, CVF, cardiac function, and strain indexes were determined by correlation analysis.

RESULTS The DECT and SECT-ECV values were increased with the elongation of modeling time (pre-modeling vs. 16-week models vs. 24-week models: DECT-ECV 24.1±1.1%, 35.1±1.3% and 37.6±1.4%; SECT-ECV 22.9±0.8%, 33.6±1.2% and 36.3±1.0%; n=30 in per-subject analysis, all P<0.05). Both ECV values of DECT and SECT correlated well with the CVF results (R=0.935 and 0.952 for the DECT-ECV and SECT-ECV; all P<0.001; n=13). Bland-Altman plots showed no significant differences between DECT and SECT-ECV.

CONCLUSIONS DECT-ECV correlated well with both SECT-ECV and histology, showing the feasibility of DECT in evaluating the doxorubicin-induced diffuse myocardial interstitial fibrosis.

GW31-e1256

The determinants and impacts of mechanical right ventricular dyssynchrony in young healthy men at high altitude

Yuanqi Yang, Chuan Liu, Lan Huang
Institute of Cardiovascular Diseases of PLA, The Second Affiliated Hospital, Third Military Medical University (Army Medical University), Chongqing, China

OBJECTIVES Recent data focus on the mechanical right ventricular dyssynchrony in different kinds of cardiovascular diseases. However, the importance of mechanical right ventricular dyssynchrony on young healthy men is still a lack of evidence. This study aimed to detect the effect on the incidence of right ventricular dyssynchrony and its determinants and impacts in young healthy men following high altitude exposure.

METHODS In 108 healthy young men, physiological and echocardiographic variables were recorded at both sea level and 4100 m. By using 2-dimensional speckle-tracking echocardiography, right ventricular dyssynchrony was evaluated by calculating the R-R interval corrected the standard deviation of the times to peak systolic strain for the 4 mid-basal RV segments (RVSD4) according to the Bazett's formula, and using the upper 95% limit of young healthy subjects at sea level in our study, a cut-off value of 18.7 ms was defined as the criterion for right ventricular dyssynchrony.

RESULTS RVSD4 was significantly increased following high altitude exposure, and the incidence of right ventricular dyssynchrony was about 32.4%. Moreover, Subjects with right ventricular dyssynchrony showed lower oxygen saturation and right ventricular global longitudinal strain, higher systolic pulmonary artery pressure than those without right ventricular dyssynchrony, and myocardial acceleration during isovolumic contraction was increased in total subjects and those without right ventricular dyssynchrony but not in those with right ventricular dyssynchrony. Meanwhile, multivariate logistic regression identified oxygen saturation and right ventricular global longitudinal strain were the independent determinants of right ventricular dyssynchrony at high altitude. In addition, mean pulmonary artery pressure was linearly correlated with the magnitude of right ventricular dyssynchrony in the presence of Notch. No additional changes had been found in RV fractional area change, tricuspid annular motion and tricuspid s' velocity between subjects with right ventricular dyssynchrony and those without right ventricular dyssynchrony.

CONCLUSIONS We firstly demonstrated that high altitude exposure could induce right ventricular dyssynchrony in healthy young subjects, which may be mainly attributed to hypoxaemia; the incidence of RVD at HA was associated with the reduced right ventricular regional function and blunted myocardial acceleration.

DIABETES, CEREBROVASCULAR DISEASES, KIDNEY DISEASES, CARDIO-ONCOLOGY

GW31-e0056

Repolarization discordance and calcium handling dysfunction caused by ibrutinib, a targeted medication for treating lymphomas

Beibei Du[1,2], Xingtong Wang[3], Praloy Chakraborty[2], Mohammed Ali Azam[2], Stephane Masse[2], Patrick Lai[2], Ahmed Niri[2], Daoyuan Si[1,2], Ou Bai[3], Paaladinesh Thavendiranathan[2], Kumaraswamy Nanthakumar[2], Ping Yang[1]
[1]Department of Cardiology, China-Japan Union Hospital of Jilin University, Jilin Provincial Cardiovascular Research Institute, Changchun 130031, China
[2]The Hull Family Cardiac Fibrillation Management Laboratory, Peter Munk Cardiac Center, Toronto General Hospital, Toronto M5G 2N2, Canada
[3]Department of Hematology, First Hospital of Jilin University, Jilin Provincial Institute of Hematology, National Key Discipline, Changchun 130021, China

OBJECTIVES Bruton's tyrosine kinase (BTK) inhibitor Ibrutinib has been used more and more widely because of its remarkable efficacy in B-cell lymphoma. The subsequent cardiac complications such as atrial fibrillation (AF) and more life-threating ventricular arrhythmias (VA) have resulted in raising concerns in the field of Cardio-oncology, for which the usage has been limited. The pro-arrhythmic electrophysiological dysregulation that results from Ibrutinib with age and cardiovascular disease is unknown. This study sought to investigate the acute effects of Ibrutinib on left ventricular (LV) VA vulnerability, cytosolic calcium dynamics and membrane electrophysiology in old and young spontaneous hypertensive rats (SHR).

METHODS The hearts of young (age: 10–14 weeks) and old (age: 10–14 months) spontaneously hypertensive rats (SHR) were harvested under anesthesia and retrogradely perfused in a Langendorff perfusion system through the aorta. Ibrutinib (0.1 μM) or vehicle (DMSO) was added to the perfusion system and the hearts were exposed to the drug for 30 minutes. During this period, calcium and voltage-sensitive fluorescent dyes were added to the perfusion system for staining. Through a pacing device connected to the rat's heart "seat", the SHR heart was paced incrementally (9.0 Hz–12.5 Hz, every 0.5 Hz) for 30 s. Signals of the 4 seconds including the last two seconds of pacing and first two seconds after the pacing stopped were collected. Calcium dynamics and action potentials changes the LV epicardial of SHR hearts were analyzed with a custom program made by Matlab (MathWorks), calcium transient parameters and action potential duration (APD) parameters were selected and processed. VA susceptibility was assessed by burst pacing induced ventricular fibrillation (VF). A ventricular fibrillation episode with a duration of ≥10 seconds after a burst pacing is defined successful induced VF. Western blot was done to find the molecular pathways involved.

RESULTS Ibrutinib was found to increase significantly the susceptibility to VA in old SHR (27.5 vs. 5.71% [control group], P=0.015), but in young SHR, this increase was not statistically significant (8 vs. 0% [control group], P=0.49). In old SHR, after Ibrutinib treatment, the calcium transient duration 50 (CaTD50) was prolonged (P=0.007), calcium transient amplitude alternans ratio was significantly reduced (P=0.03), and time to peak (TPP) of calcium transient was shortened (P<0.001). In young SHR, no differences in calcium dynamics parameters between the two groups were observed. Membrane electrophysiological parameters show that in old SHR rats, the left ventricular epicardial action potential duration 80 (APD80) alternation (P<0.001) and APD alternation discordance in the Ibrutinib treatment group (P<0.001) were more prominent. However, Western blot results related to aged SHR rats showed that there was no difference between the two groups in RyR2 receptor phosphorylation, PLB phosphorylation, AMPK activation, PI3K expression, and Akt activation.

CONCLUSIONS Ibrutinib can increase the inducibility of ventricular arrhythmias, especially in the elderly and those with existing cardiac diseases. Abnormal calcium handling and dysregulated membrane repolarization are important electrophysiological mechanisms.

GW31-e0065

Folic acid attenuates contrast-induced nephropathy in patients after coronary arteriography or percutaneous coronary intervention

Long Peng, Zexiong Li, Suhua Li
The Third Affiliated Hospital, Sun Yat-Sen University

OBJECTIVES The present study aimed to investigate whether folic acid administration could reduce the incidence of CIN in patients with hyperhomocysteinemia after coronary arteriography (CAG) or percutaneous coronary intervention (PCI).

METHODS A total of 412 patients underwent CAG or PCI were prospectively enrolled after screening for eligibility from Jan 2018 to August 2019 at the Department of Cardiovascular Medicine, the Third Affiliated Hospital, Sun

Yat-sen University. Patients with high homocysteine (Hcy) were randomly divided into 2 groups: treatment group (n=203) taking 5 mg of folic acid orally three times a day at admission until discharge and control group (209) without folic aid. All patients also received additional hydration. Serum creatinine (Scr) were measured for **immediately before**, 24 hours, 48 hours and 72 hours after completion of CAG or PCI. CIN was defined as an increase in Scr of more than 25% or 44.2 mmol/L 48 to 72 hours after contrast medium administration.

RESULTS Administration of folic acid significantly attenuated the incidence of CIN compared with control group (8.87 vs. 16.75%; P=0.017). A higher Homocysteine (Hcy) level was observed in patients in CIN group compared with non-CIN group (18.31±5.55 vs. 16.30±5.85, P=0.04). Further univariate and multivariate logistic regression analysis indicated that folic acid treatment was a protective factor against CIN after CAG or PCI (OR 0.706 [95% CI: 0.247–0.844]; P=0.012).

CONCLUSIONS Administration of folic acid might be associated with reduction in the incidence of CIN in patients with hyperhomocysteinemia after CAG or PCI.

GW31-e0142

Association of hemorrhagic stroke and dairy intake in Inner Mongolia

Min Liu, Xingguang Zhang
Inner Mongolia Medical University

OBJECTIVES Dairy consumption is a common dietary habit in Inner Mongolia, a region with high incidence of hemorrhagic stroke. We examined whether an association exists between dairy product consumption and risk of hemorrhagic stroke, based on the Early Screening and Comprehensive Intervention Project for High-Risk Groups of Cardiovascular Diseases in Inner Mongolia.

METHODS During 2015–2017, we enrolled 31,968 participants age 35–75 years without cardiovascular disease from six cities in Inner Mongolia. We conducted a survey, physical examination, and laboratory testing. We performed univariate and multivariate logistic regression to identify the association between dairy intake and hemorrhagic stroke and calculated odds ratios (ORs) and 95% confidence intervals (CIs).

RESULTS Among 31,968 participants, 275 (0.86%) had hemorrhagic stroke and 13,651 (42.70%) had the dietary habit of consuming dairy. Multivariate logistic regression analysis revealed that male sex (OR: 1.65, 95% CI: 1.29–2.11), older age (OR: 1.04 95% CI: 1.03–1.06), hypertension (OR: 1.86, 95% CI: 1.35–2.56), dyslipidemia (OR: 1.35, 95% CI: 1.06–1.72), family history of stroke (OR: 3.23, 95% CI: 2.29–4.57), and dairy consumption (OR: 1.68, 95% CI: 1.32–2.14) were associated with hemorrhagic stroke. Compared with primary school education or below, secondary school education (OR: 0.64, 95% CI: 0.49–0.83) and higher education levels (OR: 0.46, 95% CI: 0.27–0.78) showed lower risk of hemorrhagic stroke. In subgroup analysis, dairy consumption was associated with hemorrhagic stroke.

CONCLUSIONS This study suggested that dairy product intake is associated with hemorrhagic stroke. The association was robust in different subgroups.

GW31-e0145

The role of psychological risk factors in type 2 diabetic patients in the development of hypertension in the population of Azerbaijan

Mehdiyev Samir Khasay[1], Mustafaev Isakh Ismail[1], Mamedov Mehman Niyazi[2]
[1]Azerbaijan State Advanced Training Institute for Doctors Named After A. Aliyev, Baku, Azerbaijan
[2]National Medical Research Center of Therapy and Preventive Medicine, Moscow, Russia

OBJECTIVES The study of the psychological status of patients with type 2 diabetes mellitus (DM2), depending on the level of blood pressure (BP) in the Azerbaijani population.

METHODS A one-time cohort study included 528 patients aged 30–69 years (mean age 54.1±0.3 years, 30.5% men and 69.5% women). The mean values and frequency of occurrence of anxiety, depression and stress in hypertension and normotension were studied in these patients. Hypertension was classified according to the recommendations of ESC 2018. According to the international questionnaire ARİC, the symptoms of anxiety and depression were calculated on a hospital scale, according to which 0–7 points were considered the norm, 8–10 points – subclinical and ≥11 points – clinical manifestations of anxiety and depression. The presence of 1.0–1.9 points indicated the presence of severe stress, 2.0–2.9 – moderate and 3–3.9 points about the light degree of stress. Statistical analysis was carried out using the methods of variation, dispersion and discriminant.

RESULTS The average anxiety and depression consistent with their subclinical manifestations, regardless of the level of BP. Despite the high occurrence of these parameters in hypertensive patients (78.5 and 68.2%, respectively), a significant difference depending on the level of BP was detected only among the anxiety indicators (78.5 vs. 72.1%, respectively, P<0.05).

CONCLUSIONS In the Azerbaijani cohort of patients with DM2 in the formation of hypertension, the most important role is played by the state of clinically expressed anxiety.

GW31-e0270

Protective effect of Danggui Buxue decoction on myocardial injury induced by adriamycin in mice and its effect on autophagy of cardiomyocytes through PI3K-mediated pathway

Qiyuan Mao, Lanchun Liu, Yong Wang
Beijing University of Chinese Medicine

OBJECTIVES Combining theoretical and experimental research, we hoped to investigate the protective effect of Danggui Buxue Decoction on myocardial injury induced by adriamycin, and to study its effect on myocardial autophagy through PI3K-mediated pathway.

METHODS Firstly, based on the network pharmacology, we searched TCMSP database, GeneCard database to obtain the intersection target of the drugs and disease, used Cytoscape 3.7.2 software to draw the ingredient-target-disease interaction network diagram. The PPI network of target interaction is constructed by String database and analyzed by R software, including the function of GO (Gene Ontology) and the enrichment of KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway. Then we designed an animal experiment to verify the pathway. Forty male ICR mice were randomly divided into control group (CON), the group intervened by adriamycin (ADR), the group intervened by adriamycin and bafilomycin A1 (ADR+Baf), the group intervened by Danggui Buxue Decoction, adriamycin and bafilomycin A1 (DBD+Baf) and the group intervened by Danggui Buxue Decoction and adriamycin (DBD), with 8 mice in each group. Experimental period was 4 weeks. The general condition, body weight, cardiac function, serological markers, pathological changes and autophagy-related protein levels of the mice were observed and measured.

RESULTS A total of 59 potential active ingredients and 707 targets of Danggui Buxue Decoction, 2943 targets related to myocardial injury, 157 targets for the intersection of drugs and disease, and 47 active ingredients were screened out. Go function enrichment showed that the target was mainly involved in the biological process of adrenaline receptor activity. The enrichment of KEGG pathway showed that the decoction was mainly involved in the signal pathways of phosphatidylinositol 3-kinase/protein kinase B (PI3K/Akt). The animal experiment results are as followed. Compared with the CON, the ADR had weak activity, weight loss, disordered myocardial cells, edema, vacuolar degeneration, left ventricular ejection fraction (EF%, 74.33±7.89% versus 87.06±5.05%), fractional shortening (FS%, 45.72±4.25% versus 56.13±6.82%), left ventricular posterior wall end-diastolic (LVPW d), left ventricular posterior wall end-systolic (LVPW s) were reduced, left ventricular internal diastolic end-diastolic (LVID d, 3.57±0.55 mm versus 3.03±0.24 mm), left ventricular internal diastolic end-systolic (LVID s, 1.96±0.42 mm versus 1.35±0.31 mm) was increased, serum LDH (2106.9±603.43 U/L versus 700.65±223.91 U/L) and CK-MB (340.9±50.31 U/L versus 63.15±45.09 U/L) were increased (P<0.05). Compared with the ADR, the general condition of the DBD were improved, the body weight was increased, EF% (86.05±4.92% versus 74.33±7.89%), FS% (54.89±6.89% versus 45.72±4.25%) were increased, LVID s (1.45±0.20 mm versus 1.96±0.42 mm) and CK-MB (132.95±9.42 U/L versus 340.9±50.31 U/L) was decreased (P<0.05). Western-Blot results showed that compared with the CON, the autophagic flow of the ADR was increased, and the PI3K protein expression was decreased (P<0.01). Compared with ADR and ADR+Baf, the autophagic flow of DBD and DBD+Baf was decreased, and the expression of PI3K protein was increased (P<0.05).

CONCLUSIONS Both from theoretical and experimental level, Danggui Buxue Decoction has protective effects on myocardial injury in adriamycin-treated mice, and its mechanism may be related to activation of PI3K-mediated pathway and inhibition of cardiomyocyte autophagy.

GW31-e0295

Meteorin-like protein, a newly identified myokine, attenuates doxorubicin-induced cardiotoxicity by decreasing oxidative stress and apoptosis in mice

Xin Zhang[1,2], Can Hu[1,2], Qizhu Tang[1,2]
[1]Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan 430060, China
[2]Hubei Key Laboratory of Metabolic and Chronic Diseases, Wuhan 430060, China

OBJECTIVES Myokines are kinds of peptides or cytokines produced by muscle fibres and mediate multiple cardiovascular benefits of physical exercise. Our previous studies identified the myokines, fibronectin type III domain-containing 5 and osteocrin as cardioprotectants in the context of doxorubicin

(DOX) chemotherapy. Meteorin-like (METRNL) protein is a newly identified myokine that functions to modulate energy expenditure and inflammation in adipose tissue. Herein, we aim to investigate the potential role and molecular basis of METRNL in DOX-induced cardiotoxicity.

METHODS Mice received an intravenous injection of adeno-associated virus 9 or an intramyocardial injection of adenovirus to overexpress or knock down METRNL in murine hearts, respectively, which were then injected intraperitoneally with DOX (4 mg/kg/week) for consecutive 4 weeks to imitate the cardiotoxicity upon chronic DOX exposure. H9C2 cell lines were cultured to verify the effects of METRNL in vitro. To validate the necessity of SIRT1 in the cardioprotection by METRNL, cardiac-restrict *Sirt1* knockout mice were constructed. Besides, DOX-sensitive 4T1 breast cancer cells and tumor-bearing mice were used to evaluate the influence of METRNL on DOX-mediated chemotherapeutic capacity in vitro and in vivo.

RESULTS ETRNL was abundantly expressed in cardiac muscle under physiological conditions that was decreased upon DOX exposure. Cardiac-specific overexpression of METRNL markedly improved oxidative stress, apoptosis, cardiac dysfunction and survival status in DOX-treated mice. Conversely, knocking down endogenous METRNL in the heart exacerbated DOX-induced cardiotoxicity and mouse death. Meanwhile, METRNL overexpression attenuated, while METRNL silence promoted oxidative damage and apoptosis in DOX-treated H9C2 cells. Systemic METRNL depletion by a neutralizing antibody aggravated DOX-related cardiac injury and dysfunction in vivo, which were notably alleviated by METRNL overexpression within the cardiomyocytes. In addition, we detected robust METRNL secretion from isolated rodent hearts and cardiomyocytes, but to a less extent in those with DOX treatment. And the beneficial effects of METRNL in H9C2 cells disappeared after the incubation with a METRNL neutralizing antibody. Mechanistically, METRNL activated SIRT1 via the cAMP/PKA pathway, and its antioxidant and antiapoptotic capacities were blocked by SIRT1 deficiency. More importantly, METRNL did not affect the tumor-killing action of DOX in 4T1 breast cancer cells and tumor-bearing mice.

CONCLUSIONS Cardiac-derived METRNL activates SIRT1 via cAMP/PKA signaling axis in an autocrine manner, which ultimately improves DOX-elicited oxidative stress, apoptosis and cardiac dysfunction. Targeting METRNL may provide a novel therapeutic strategy for the prevention of DOX-associated cardiotoxicity.

GW31-e0296

Osteocrin, a novel myokine, prevents diabetic cardiomyopathy via restoring proteasomal activity

Can Hu[1,2], Xin Zhang[1,2], Qizhu Tang[1,2]
[1]Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan 430060, China
[2]Hubei Key Laboratory of Metabolic and Chronic Diseases, Wuhan 430060, China

OBJECTIVES Proteasomal activity is compromised in diabetic hearts that contributes to proteotoxic stresses and cardiac dysfunction. Osteocrin (OSTN) acts as a novel exercise-responsive myokine and is implicated in various cardiac diseases. Herein, we aim to investigate the role and underlying molecular basis of OSTN in diabetic cardiomyopathy (DCM).

METHODS Mice received a single intravenous injection of the cardiotrophic adeno-associated virus serotype 9 to overexpress OSTN in the heart and then were exposed to intraperitoneal injections of streptozotocin (STZ, 50 mg/kg) for consecutive 5 days to generate diabetic models. Neonatal rat cardiomyocytes were isolated and stimulated with high glucose to verify the role of OSTN in vitro.

RESULTS OSTN expression was reduced by protein kinase B/forkhead box O1 dephosphorylation in diabetic hearts, while its overexpression significantly attenuated cardiac injury and dysfunction in mice with STZ treatment. Besides, OSTN incubation prevented, whereas OSTN silence aggravated cardiomyocyte apoptosis and injury upon hyperglycemic stimulation in vitro. Mechanistically, OSTN treatment restored protein kinase G (PKG)-dependent proteasomal function, and PKG or proteasome inhibition abrogated the protective effects of OSTN in vivo and in vitro. Furthermore, OSTN replenishment was sufficient to prevent the progression of pre-established DCM and had synergistic cardioprotection with sildenafil.

CONCLUSIONS OSTN protects against DCM via restoring PKG-dependent proteasomal activity. OSTN is a promising therapeutic target for treating DCM.

GW31-e0414

The sodium-glucose cotransporter-2 (SGLT-2) inhibitors effect on contrast-induced nephropathy: study design and protocol for a prospective cohort study

Xiaopu Wang, Xinqun Hu
Second Xiangya Hospital of Central South University

OBJECTIVES Sodium-glucose co-transporter-2 (SGLT-2) inhibitor is one kind of novel hypoglycemic agent to restrain glucose reabsorption in the proximal tubule which can suppress intraglomerular pressure and renal hyperfiltration, thereby results a transient eGFR decreasing and serum creatinine increasing. Although findings from EMPA-REG OUTCOME and DECLARE TIMI-58 trials showed that SGLT-2 inhibitors can significantly alleviate the progression of kidney disease and reduce rates of clinically relevant renal events, the effect of SGLT-2 inhibitors on contrast-induced nephropathy (CIN) which considered as one of the most common causes of iatrogenic acute renal failure is unclear. This study is designed to investigate whether type 2 diabetes (T2DM) patients taking SGLT-2 inhibitors have a higher incidence of CIN after percutaneous coronary angiography.

METHODS This study is a multi-center, prospective, controlled cohort study. It will recruit patients with a T2DM and in need of a coronary angiography. The SGLT-2 inhibitor group and the control group will be matched 1:1 according to risk scores of CIN and baseline data, and divided into low-risk, moderate-risk, high-risk, and extremely high-risk according to CIN risk score scale. Patients attended study will be obtained serum creatinine, eGFR and cystatin C within 1 day and 1 week, and postprocedural in 72 hours.

RESULTS The primary outcome measure is defined as the incidence of CIN, 72 hours after a successful percutaneous coronary angiography. The secondary outcome measures are the persistent renal damage, major adverse cardiovascular events (MACE), major post-procedure in-hospital adverse clinical events, length of hospitalization and postoperative complication.

CONCLUSIONS This study is testing the hypotheses that SGLT-2 inhibitors may increase the occurrence of CIN.

GW31-e0480

Superoxide in doxorubicin-induced acute cardiotoxicity: toll-like receptor 5 and spleen tyrosine kinase-dependent activation of NADPH oxidase 2

Zhenguo Ma, Chunyan Kong, Qizhu Tang
Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan 430060, PR China

OBJECTIVES The clinical application of doxorubicin (DOX) is limited by the cardiovascular toxic effects. NADPH oxidase (NOX) isozymes served functional roles in toll-like receptor (TLR)-mediated biological actions. However, the molecular mechanism between TLR5 and NOX-mediated superoxide production in DOX-induced acute cardiotoxicity remains unclear.

METHODS Heterozygous TLR5 deficiency mice were interbred to establish homozygous TLR5 knockout mice and their wild-type littermates. To mimic an acute cardiotoxicity, these mice were subjected to a single intraperitoneal injection of DOX (15 mg/kg) or the same volume of normal saline. Male mice were injected with flagellin (an agonist of TLR5, 1 μg/mouse, every other day) via orbital venous plexus to activate TLR5.

RESULTS The data in our study demonstrated that TLR5 expression was markedly increased in response to DOX injection. TLR5 deficiency exerted potent protective effects against DOX-related cardiac injury, whereas activation of TLR5 by flagellin exacerbated DOX injection-induced cardiac toxic effects in mice. Mechanistically, the effects of TLR5 were largely attributed to the direct interaction with spleen tyrosine kinase to activate NOX 2, thus increasing the production of superoxide and subsequent activation of p38. The toxic effects of TLR5 activation in DOX-related acute cardiac injury were abolished by NOX2 deficiency in mice. Our further study showed that neutralizing antibody-mediated TLR5 depletion blunted DOX-induced acute cardiotoxicity in mice.

CONCLUSIONS These findings suggested that TLR5 deficiency attenuated DOX-induced acute cardiotoxicity in mice. Targeting TLR5 may provide feasible therapies for DOX-induced acute cardiotoxicity.

GW31-e0482

Revsolvin D1 protects against doxorubicin-induced cardiotoxicity via regulation of inflammation, oxidative stress, autophagy, endoplasmic reticulum stress and apoptosis

Mengmeng Zhao, Menglong Wang, Jishou Zhang, Jing Ye, Di Ye, Jun Wan
Renmin Hospital of Wuhan University

OBJECTIVES Resolvin D1 (RvD1) is a lipid mediator, which can attenuate the pro-inflammatory response and promote inflammation resolution through different mechanisms. However, the function of RvD1 in doxorubicin- (Dox-) induced cardiotoxicity has not been clarified. This study aimed to investigate whether RvD1 could attenuate Dox-induced cardiac injury.

METHODS The mice were divided into three groups: control, Dox and Dox+RvD1. RvD1 (2.5 μg/kg, i.p.) was injected 30 minutes and daily after Dox injection. Five days later, echocardiography was applied to evaluate cardiac function and then heart tissue and blood samples were collected for further analysis.

RESULTS The results showed that cardiac dysfunction and cardiac injury were induced by Dox. However, these effects were attenuated by RvD1 treatment.

In addition, RvD1 attenuated the increased inflammation, oxidative stress, autophagy and endoplasmic reticulum stress induced by Dox. Furthermore, the severity of apoptosis induced by Dox were attenuated by RvD1.

CONCLUSIONS RvD1 could protect against Dox-induced cardiotoxicity in mice via multiple mechanisms, which indicates the potential therapeutic effects of RvD1 in Dox-induced cardiotoxicity.

GW31-e0483

Resolvin E1 protects against doxorubicin-induced cardiotoxicity by inhibiting oxidative stress, autophagy and apoptosis by targeting AKT/mTOR signaling

Jishou Zhang, Menglong Wang, Yao Xu, Mengmeng Zhao, Zhen Wang, Jun Wan
Renmin Hospital of Wuhan University

OBJECTIVES Doxorubicin (DOX)-induced cardiotoxicity impairs the quality of life of cancer patients during or after DOX treatment, and it is imperative to explore a novel strategy to address this problem. Resolvin E1 (RvE1) is derived from eicosapentaenoic acid (EPA) that has been reported to exert beneficial effects on DOX-induced oxidative stress in cardiomyocytes. This study was designed to investigate whether RvE1 protects against DOX-induced cardiotoxicity, and the underlying mechanism was explored.

METHODS In this study, DOX (20 mg/kg, one injection, i.p.) was used to induce DOX-induced cardiotoxicity in C57BL/6 mice. At 5 days after DOX administration, the effect of RvE1 was assessed by measuring cardiac function, oxidative stress, autophagy and apoptosis in cardiac tissue. We used an AKT inhibitor and rapamycin to investigate the underlying mechanisms.

RESULTS Our results showed that RvE1 inhibited the DOX-induced decrease in body weight and heart weight, the reduction in LVEF and FS, and the increase in LDH, CK-MB and cardiomyocyte vacuolization. Compared to the control group, the DOX group exhibited increased oxidative stress, autophagy and apoptosis in cardiac tissue, which were alleviated by treatment with RvE1. The AKT/mTOR signaling pathways were responsible for RvE1-mediated regulation of DOX-induced oxidative stress, autophagy and myocardial apoptosis.

CONCLUSIONS RvE1 protected against DOX-induced cardiotoxicity via the regulation of AKT/mTOR signaling.

GW31-e0487

Apolipoprotein C-III is independently associated with incidence of diabetes: a 5-year follow-up of the Chinese multi-provincial cohort study

Jiangtao Li, Dong Zhao, Jing Liu, Miao Wang, Jiayi Sun, Jun Liu, Yan Li, Qjuju Deng, Yue Qi
Department of Epidemiology, Beijing Anzhen Hospital, Capital Medical University, Beijing Institute of Heart, Lung and Blood Vessel Diseases, Beijing 100029, China

OBJECTIVES This study was aimed to evaluate the impact of serum apoCs levels on the risk of developing diabetes in a middle-aged population.

METHODS Study participants were recruited from the Chinese Multi-Provincial Cohort Study (CMCS)-Beijing Project, which is a population-based prospective cohort study. Totally, 1085 participants aged 45–74 years and free of diabetes at baseline were investigate development of diabetes with a 5 year follow-up. Multivariate logistic regression was performed to examine the independent association of serum apoC-II and apoC-III levels with 5-year incident diabetes.

RESULTS During the 5-year period of follow-up, 97 (8.9%) participants had developed new-onset diabetes. Baseline median levels of apoC-II and apoC-III were 3.95 (2.71–5.47) mg/dL and 9.92 (7.55–12.76) mg/dL, respectively. After adjusting for traditional risk factors and parental history for diabetes, apoC-II (odds ratio [OR]=1.37; 95% confidence interval [CI]: 1.06–1.77) and apoC-III (OR=1.56; 95% CI: 1.22–1.98) were both significantly and positively associated with the risk of incident diabetes. However, only apoC-III was still significantly associated with the risk of developing diabetes after further adjustment for baseline fasting blood glucose (OR=1.36; 95% CI: 1.04–1.77).

CONCLUSIONS ApoC-III levels were associated with 5-year risk of incident diabetes in the Chinese population. More attention should be paid to preventive strategies of diabetes targeting apoC-III.

GW31-e0517

Intermittent artificial gravity alleviates blood-brain barrier dysfunction and cognitive impairment induced by simulated weightlessness in rats

Jiahui Li[1], Jijun Li[1], Fang Kuang[2], Jing Chen[3], Feng Gao[1], Ling Dong[1]
[1]School of Aerospace Medicine, The Fourth Military Medical University
[2]Department of Neurobiology, The Fourth Military Medical University
[3]Department of Anatomy, The Fourth Military Medical University

OBJECTIVES Previous studies have indicated that long-term spaceflight led to extensive volumetric gray matter decrease and cognitive dysfunction, but the underlying mechanism remains unknown. Considering the importance of cognition for crewmembers' health and performance both in- and post-flight, our study was aimed to investigate the effects and mechanism of the action of weightlessness on cognition and the role of intermittent artificial gravity intervention in a model of simulated weightless rats.

METHODS Eight-week-old male SD rats were randomly divided into control group (CON), 4-week tail suspended (SUS) and intermittent artificial gravity group (IAG) in which tail-suspended rats were allowed to stand for 1 hour per day for 4 weeks. The open field test and the new object recognition test were performed to assess cognitive function, and Hematoxylin-eosin (HE) staining, Nissl staining, immunofluorescence and TUNEL were applied to analyze the neuron morphology and apoptosis in hippocampus. Blood-brain barrier (BBB) permeability in hippocampus were analyzed by immunofluorescence staining and western-blot.

RESULTS Compared with the control, 4-week tail suspended rats exhibited cognitive dysfunction as manifested by the significant reduction in overall distance traveled, the time spent and distance traveled in the center area, and total object exploration time. Notably, the simulated weightlessness induced an increased BBB permeability as evidenced by increased albumin exudation and reduced occludin expression in the hippocampus of the SUS rats compared with CON ($P<0.05$). Furthermore, GLUT1 and CD31 double labeling results showed that the vessel diameter decreased significantly, and the expression of VEGF and VEGFR2 were increased after SUS, suggesting angiogenesis in the hippocampus. Interestingly, only 1 hour per day IAG intervention alleviated the weightlessness-induced cognitive impairment together with the attenuated morphological changes and apoptosis in the hippocampus.

CONCLUSIONS Our findings demonstrate that 4-week simulated weightlessness induces cognitive impairment which may be attributable to blood-brain barrier dysfunction. Intermittent artificial gravity can alleviate simulated weightlessness-induced blood-brain barrier dysfunction and partly reverse the cognitive impairment.

GW31-e0624

Alzheimer's disease risk prediction for hypertension adults of age from 45 to 65

Bochen Che, Huijuan Yin, Jinpeng Wu, Yingxin Li
CAMS & PUMC (Chinese Academy of Medical Science, Peking Union Medical College) Institute of Biomedical Engineering. Lab of Intelligent Photomedicine and Health Engineering

OBJECTIVES To design a model for assessing Alzheimer's disease (AD) risk among hypertension adults from 45 to 65.

METHODS We analyzed baseline information and Ultra wide field (UWF) fundus images of 1828 patients enrolled from March 2018 to March 2020. (1) Baseline information consist of sex, age, MMSE scores, systolic blood pressure (SBP), diastolic blood pressure (DBP), average blood pressure in one week [(ABPW), SBP and DBP included], body mass index (BMI), heart rate (HR), SBP/DBP ratio, which is analyzed for designing numeric model with logistics regression method and radial basis function in artificial neural net (ANN) via SAS 9.4M6 software. (2) We programmed algorithm to perform ultra wide field (UWF) fundus image segmentation by calculating main vessel bifurcation degree. The algorithm theory bases on method as follows: firstly we merge the ultra wide field (UWF) fundus image into a larger 2D cube background which is segmented into 81 small cubes, then calculate the proportion area of ultra wide field (UWF) fundus image in the 2D cube with fractal web equation; secondly we calculate the angles and bifurcation degree of the different main vessels which take optic disc centre as common focus in the eye fundus field. (3) We mark the ultra wide field (UWF) fundus image with main weight factor calculated from step (1) (2) to pre-train deep learning model in Tensor Flow Quantum.

RESULTS (1) We calculate a logistic regression formula with MMSE as dependent variance and BMI, S/D ratio, heart rate as independent variance. The main formula is Logit V (D)=–0.101+0.921 V(I)1+0.826V(I)2+0.671 V(I)3. BMI and S/D ratio shows more weight (0.857 and 0.842, respectively). (2) We mark UWF fundus image with main vessel bifurcation degree, S/D ratio, BMI and establish a deep learning model in Tensor Flow Quantum (TFQ) data frame, in which UWF fundus image is set as input value with estimated MMSE score as output value, we compare the deep learning model-estimated results with physicians' assessment in terms of MMSE scores, the AUC is 90%.

CONCLUSIONS Alzheimer's disease (AD) risk prediction for hypertension adults of age from 45 to 65 can be performed and estimated initially with fundus image artificial intelligence model.

GW31-e0663

The incidence of contrast-associated acute kidney injury in observational research about studying risk factors: a systematic review and meta-analysis

Zhubin Lun[1,2,3], Liwei Liu[1], Guanzhong Chen[1], Shiqun Chen[1], Jin Liu[1], Jianfeng Ye[2], Yong Liu[1], Jiyan Chen[1]
[1]Department of Cardiology, Guangdong Provincial Key Laboratory of Coronary Heart Disease Prevention, Guangdong Cardiovascular Institute, Guangdong Provincial People's Hospital, The Affiliated Guangdong Provincial People's Hospital of South China University of Technology, Guangdong Academy of Medical Sciences, Guangzhou, 510100, China
[2]Department of Cardiology, Dongguan TCM Hospital, Dongguan, 523209, China
[3]The First School of Clinical Medicine, Guangdong Medical University, Zhanjiang, 523808, China

OBJECTIVES Contrast-associated acute kidney injury is a common complication after coronary angiography (CAG) or percutaneous coronary intervention (PCI), which not only increases the economic burden of the disease, but also has poor prognosis. But up to now, previous studies have not discussed the incidence of CA-AKI comprehensively. Therefore, we explore the incidence of CA-AKI after CAG or PCI through a database of meta-analysis of CA-AKI about risk factors (PROSPERO register number: CRD42019121534).

METHODS Until 30th June 2019, we searched MEDLINE, Embase and the Cochrane Database of Systematic Reviews for observational articles researching risk factors related to CA-AKI. All articles reporting the definition and incidence of CIN in the original text are included in our analysis. We excluded conference abstract, meta-analysis and reviews. We evaluate the quality of the article by two people, and the third party resolves controversial reviews. Through in-depth reading, we extracted the country, study year, study population, number of people, incidence of CIN and deaths in the article. Random or fixed meta-analysis was performed to derive the incidence of CA-AKI.

RESULTS After screening (not studying in CAG/PCI) and deleting duplicated articles, a total of 141 articles (1,319,229 participants) and 89 research articles on PCI (1,262,580 participants) were included in our analysis. The incidence and mortality rate of CA-AKI after CAG/PCI were 12.5% (95% CI: 11.7–13.3%) and 22.3% (95% CI: 17.2–27.4%). The incidence of CA-AKI of patients with chronic kidney disease, diabetes mellitus and ST-segment elevation myocardial infarction were 14.4, 11.9 and 12.6%, respectively. The incidence of CA-AKI$_A$ (an increase in serum creatinine by 25% or ≥0.5 mg/dL (≥44.2 μmol/L) within 48–72 hours after contrast exposure), CA-AKI$_B$ (an increase in serum creatinine by 50% or ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours after contrast exposure) and CA-AKI$_C$ (as per the Acute Kidney Injury Network or RIFLE definitions) were 12.8, 15.0 and 16.6%, respectively. In addition, their mortality rates were 20.5, 27.1 and 17.6%, respectively. The country with the highest incidence was Germany, followed by Iran and Brazil. The incidence in China, the United States, Turkey and Japan were 13.7, 10.9, 15.3 and 14.5%, respectively. The country with the highest mortality rate was Italy, followed by the United States and Japan. The mortality rate in China, the United States, Turkey and Japan were 3.1, 29.9, 12.7 and 29.9%, respectively. The incidence of CA-AKI were 11.6 and 14.8% in high-income countries and upper middle-income countries, and the pooled mortality rate were 29.3 and 8.2%.

CONCLUSIONS We are the first meta-analysis in the world to comprehensively discuss the incidence and mortality of CA-AKI. The results of the meta-analysis show that no matter how CA-AKI is defined, it is always a common complication after CAG/PCI. With the addition of risk factors, the incidence of CA-AKI increased. Similarly, we find that the incidence of high income countries is slightly lower than that of upper middle income countries, but the mortality rate is converse, which may be related to the perfect medical security system and higher life expectancy. The meta-analysis provides a platform that can increase the awareness of CA-AKI among the public, medical and health personnel, and government officials.

GW31-e0750

Galectin-3 inhibitor modified citrus pectin prevents fibrosis mediated atrial remodeling in alloxan-induced diabetes mellitus rabbits

Ruimeng Liu[1], Jian Li[2], Ya Suo[2], Guangping Li[2], Tong Liu[2], Changle Liu[2]
[1]Xintai Institute of Cardiology, Department of Cardiology, The People's Hospital of Xintai, Xintai City 271200, Shandong Prov, China
[2]Department of Cardiology, Tianjin Institute of Cardiology, Second Hospital of Tianjin Medical University, Tianjin 300211, China

OBJECTIVES In diabetes mellitus, fibrosis activated by inflammation leading to atrial remodeling, resulting in electrical, biochemical as well as structural change within the atria, is key in the development of atrial fibrillation (AF). In this study, we investigate the relationship between Galectin-3(Gal-3), atrial electrical, structural remodeling and Calcium imbalance, even the potential beneficial effects of Gal-3 inhibitor modified citrus pectin on these pathological changes. In diabetes mellitus, fibrosis activated by inflammation leading to atrial remodeling, resulting in electrical, biochemical as well as structural change within the atria, is key in the development of atrial fibrillation (AF). In this study, we investigate the relationship between Galectin-3(Gal-3), atrial electrical, structural remodeling and Calcium imbalance, even the potential beneficial effects of Gal-3 inhibitor modified citrus pectin on these pathological changes.

METHODS A total of 72 healthy male New Zealand rabbits, weighing about 2.1 kg at the beginning of the study, were randomly and equally divided into normal control group (NC, n=24), diabetes mellitus group (DM, n=24), and modified citrus pectin-treated DM group (MCP, n=24), rabbits in the MCP group received Modified citrus pectin (380 mg/kg/d) for 8 weeks orally. Isolated heart electrophysiology technique was used to obtain electrophysiological index and characteristics. Echocardiographic were performed by Professional cardiologist. Tissue markers of atrial fibrosis and inflammation, including the protein expression were examined. Atrial interstitial fibrosis and tissue morphology was evaluated by Masson trichrome staining and HE staining. Isolated left atrial cardiomyocytes adopting Langendorff system with collagenase solution applied to voltage-clamp techniques, confocal microscopy and fluorescence staining technique.

RESULTS Compared with the normal control group, conduction time and atrial fibrillation inducibility in the diabetes mellitus group were significantly increased (P<0.01). LAD, IVST and PWT in the diabetes mellitus group were significantly increased (P<0.01). The protein expression levels of inflammatory and fibrosis-related factors in left atrial tissue in the diabetes mellitus group were significantly up-regulated (P<0.05). The representative photomicrographs of HE staining and Masson staining indicated the disorders in arrangement of atrial myocytes in the diabetes mellitus group, and atrial interstitial fibrosis in the diabetes mellitus group was significantly increased (P<0.01). The calcium mean fluorescence intensity and the I_{Ca_1L} maximum current density of atrial myocytes in the diabetes mellitus group significantly increased (P<0.01). These abnormalities were alleviated by modified citrus pectin treatment.

CONCLUSIONS MCP, via its antifibrotic effects, reduces atrial mechanical, structural and ion channel remodeling induced by DM-related, thereby reducing the vulnerability to AF.

GW31-e0763

HbA1c variability to predict diabetic complications and mortality: a 10-year single-center cohort study

Sharen Lee[1], Tong Liu[2], Wing Tak Wong[3], Gary Tse[2,3]
[1]Laboratory of Cardiovascular Physiology, Li Ka Shing Institute of Health Sciences, Hong Kong, China
[2]Tianjin Key Laboratory of Ionic-Molecular Function of Cardiovascular disease, Department of Cardiology, Tianjin Institute of Cardiology, Second Hospital of Tianjin Medical University, Tianjin 300211, P.R. China
[3]School of Life Sciences, Chinese University of Hong Kong, Hong Kong S.A.R., P.R. China

OBJECTIVES Emerging evidence suggests that HbA1c variability, in addition to HbA1c itself, can be used as a predictor for complications and mortality. The present study aims to examine the predictive power of both HbA1c value and variability towards the prognosis of diabetic patients and evaluate the interrelationship between hypoglycemia, HbA1c variability, and mortality.

METHODS The retrospective observational study analyzed diabetic patients at the Prince of Wales Hospital prescribed with insulin from January 1st to December 31st, 2008. The predictive value of HbA1c baseline and variability towards all-cause and cardiovascular mortality, in addition to secondary outcomes of diabetes-related complications, were assessed. The association between hypoglycemia with both HbA1c variability and mortality was evaluated. Mean, standard deviation (SD), root mean square (RMS) and coefficient of variation were used to represent the variability of HbA1c.

RESULTS The study cohort consists of 3424 patients, including 3137 patients with at least three HbA1c measurements. The low mean HbA1c subgroup had significantly shorter time-till-death for all-cause mortality, (P<0.001), but not cardiovascular mortality (P=0.920). On the other hand, the time-till-death was significantly shorter for the high HbA1c variability subgroup for both all-cause (P<0.001), and cardiovascular mortality (P<0.001). In terms of prediction of secondary outcomes, both baseline HbA1c and HbA1c variability are significant positive predictors for the following: 1) diabetic ketoacidosis (DKA)/hyperosmotic hyperglycemic state (HHS) (baseline: odds ratio [OR]=1.16, P=0.006; mean: OR=1.32, P<0.001; SD: OR=1.27, P=0.018; RMS: OR=1.29, P<0.001); 2) neurological diabetic complications (baseline: OR=1.07, P=0.033; mean: OR=1.16, P=0.003; SD: OR=1.23, P=0.004; RMS: OR=1.15, P=0.002; CV: OR=1.02, P=0.006); 3) ophthalmological diabetic complications (baseline: OR=1.10, P<0.001; mean: OR=1.32, P<0.001; RMS: OR=1.28, P<0.001). Furthermore, significant association was found between dichotomized HbA1c variability and hypoglycemia frequency (P<0.0001), whilst hypoglycemia frequency was found to be a positive predictor for both mortality (OR=1.11, P<0.001) and time-till death of all cause (hazard ratio [HR]=1.08, P<0.001), in addition to cardiovascular-specific time-till-death (HR=1.07, P=0.044).

CONCLUSIONS The association between high HbA1c variability and increased risk for both all-cause and cardiovascular mortality, in addition to various diabetic complications, is demonstrated. The association between hypoglycemic frequency, HbA1c variability, and mortality suggests that intermittent hypoglycemia resulting in poorer outcomes in diabetic patients.

GW31-e0852

PXDN reduces autophagic flux in insulin-resistant H9C2 cells via modulating FoxO1

Chan Li, Ruizheng Shi
Department of Cardiovascular Medicine, Xiangya Hospital, Central South University

OBJECTIVES Autophagy, a well-observed intracellular lysosomal degradation process, is particular important to the cell viability in diabetic cardiomyopathy (DCM). Peroxidasin (PXDN) is a heme-containing peroxidase that augments oxidative stress and plays an essential role in cardiovascular diseases, while whether PXDN contributes to the pathogenesis of DCM remains unknown.

METHODS Palmitate acid (PA) was applied to induce insulin resistance in H9C2 cell line, and DC661 (a dimeric chloroquine) was used to inhibit lysosomal acidification. H9C2 cells were infected with small-silencing RNAs (siRNAs) to achieve inhibition of PXDN or forkhead box-1 (FoxO1). Glucose consumption, cell viability and indicators of autophagic flux including transmission electron microscopy (TEM), LC3II and p62 were measured subsequently, protein level of PXDN, AKT, p-AKT, FoxO1 and p-FoxO1 were detected by western blot as well.

RESULTS In cultured H9C2 cardiomyocytes treated with PA, glucose consumption decreased in a time and dose manner. Cell death and PXDN protein level increased significantly after treated with 400 μM PA for 24 hours. Obstructed autophagic flux was observed under PA stimulation, as shown by accumulation of autophagosomes and increasing of LC3-II and p62 protein level. Cell death, autophagosomes accumulation, as well as the increase of p62 expression were suppressed after PXDN silence. In addition, knockdown of PXDN reversed PA-induced down-regulating of forkhead box-1 (FoxO1) and reduced FoxO1 phosphorylation, whereas did not affect the decrease of AKT phosphorylation. Not consistent with the effects of si-PXDN, double-silence of PXDN and FoxO1 significantly increased p62 expression, declined the level of FoxO1 and PXDN, while the expression of LC3-II was unchanged under PA stimulation. Furthermore, inhibition of FoxO1 in PA-untreated cells up-regulated the levels of LC3-II and p62, and inhibited the expression of FoxO1 and PXDN.

CONCLUSIONS PXDN plays a key role in PA-induced cell death by impairing autophagic flux through inhibiting FoxO1, and FoxO1 may affect PXDN through negative feedback regulation. Our findings may provide a novel target for further investigation of autophagy in DCM.

GW31-e1055

Remote ischemic conditioning reduces perihematomal edema after intracerebral hemorrhage: first proof-of-concept randomized controlled trial

Wenbo Zhao, Xunming Ji
Department of Neurology, Xuanwu Hospital, Capital Medical University

OBJECTIVES The prognosis of intracerebral hemorrhage (ICH) is poor because of the mass effect arising from the hematoma and the associated perihematomal edema (PHE). Remote ischemic conditioning (RIC) has been shown to promote hematoma clearance and reduce PHE in animal models, however it remains unknown whether RIC is safe and effective in reducing PHE in ICH patients. This study aimed to evaluate the safety and efficacy of RIC in reducing PHE after ICH.

METHODS In this open-label, rater-blind, randomized control trial, 40 subjects with supratentorial ICH (hematoma volume: 10–30 mL) diagnosed between 24 and 48 hours of onset were assigned to the RIC group or control group. All subjects received standard background medical therapy. Subjects in the RIC group underwent repeated daily RIC (4 cycles of 5 minutes inflation [200 mmHg]/deflation [0 mmHg] of cuff on one arm) for 7 consecutive days. The primary efficacy outcome was PHE volume at 7 days, and both absolute PHE volume and relative PHE volume (defined as absolute PHE volume divided by hematoma volume) were measured. Safety outcome included death, neurological deterioration, hematoma expansion, and any other severe adverse events.

RESULTS All 40 subjects completed this study. Mean age was 59.3±11.7 years, and 57.5% were male. At baseline, the median National Institutes of Health Stroke Scale score was 9.5 (range 1–28), median Glasgow Come Score was 15 (range 10–15), and mean ICH volume was 13.9±4.5 mL. The mean relative PHE volume was 1.11±0.26 in the control group and 1.05±0.23 in the RIC group at baseline; and 1.49±0.30 vs. 1.33±0.32 at Day 3 (P>0.05 each), respectively. After 7 days of treatment, RIC significantly reduced the relative PHE volume as compared to the control (1.77±0.39 vs. 2.02±0.27, P=0.02). The absolute PHE volume and hematoma volume at Day 3 and Day 7 had no significant difference between groups (P>0.05 each). No subject died or suffered from neurological deterioration or hematoma expansion. No adverse event was associated with RIC.

CONCLUSIONS RIC seemed to be safe in patients with ICH and induced a significant reduction in the relative PHE volume after 7 day of treatment. These results warrant a further study with large sample to examine the effect of RIC on functional outcome after ICH.

GW31-e1149

AdipoRon, an adiponectin receptor agonist, protects contrast-induced nephropathy by suppressing oxidative stress and inflammation via activation of the AMPK pathway

Daqian Gu, Chunyu Zeng
Department of Cardiology, Daping Hospital, The Third Military Medical University, Chongqing, P.R. China

OBJECTIVES Contrast-induced nephropathy (CIN), a complication caused by using contrast medium (CM) during diagnostic and interventional procedures, occurs frequently and lacks effective treatment. AdipoRon, the agonist of adiponectin receptors, has been shown to benefit many organs including the kidney. This study aimed to investigate the role of AdipoRon in treating CIN.

METHODS CIN model was established via infusing iopromide (1.8 g/kg) in Sprague-Dawley rats; NRK52E cells were treated with iopromide (5–50 μM). Renal function, renal histopathology, levels of LDH release, cell vitality, oxidative stress and inflammatory markers were measured to evaluate the protective effects of AdipoRon. The protein expression levels of pAMPK/AMPK were determined by western blot analysis.

RESULTS AdipoRon (50 mg/kg) significantly reversed Serum creatinine (Cr), blood urea nitrogen (BUN), creatinine clearance (CrCl) and urinary kidney injury molecule-1 (uKIM-1) levels induced by iopromide in SD rats. Besides, it decreased the renal injury score and apoptosis of renal cells. AdipoRon also reversed the changes of antioxidant markers, pro-oxidant and inflammatory markers induced by iopromide. Moreover, the in-vitro studies showed that AdipoRon decreased lactate dehydrogenase (LDH) release and increased cell vitality in NRK52E cells treated with iopromide. Then, we demonstrated that the protection of AdipoRon was accompanied by augmented AMPK phosphorylation. Thus, we used compound c (CC), an AMPK inhibitor, to demonstrate the role of AMPK in the protective effects of AdipoRon in CIN. Both in-vivo and in-vitro studies demonstrated that CC reversed the AdipoRon-mediated improvement in the CIN model.

CONCLUSIONS Our data indicate that AdipoRon protects against the CIN by suppressing oxidative stress and inflammation via activating the AMPK pathway, showing that AdipoRon might be a potential candidate for the prevention and therapy of CIN.

GW31-e1195

Association between 24-hour urinary sodium to potassium ratio and mild cognitive impairment in community-based general population

Zhongrong Wang[1,2,3], Nanfang Li[1,2,3], Mulalibieke Heizhati[1,2,3], Lin Wang[1,2,3], Mei Li[1,2,3], Fengyu Pan[1,2,3], Zhikang Yang[1,2,3], Reyila Abudureyimu[1,2,3], Jing Hong[1,2,3], Le Sun[1,2,3], Jing Li[1,2,3], Wei Li[1,2,3]
[1]National Health Committee Key Laboratory of Hypertension Clinical Research
[2]Hypertension Center of People's Hospital of Xinjiang Uygur Autonomous Region
[3]Xinjiang Hypertension Institute

OBJECTIVES High sodium low potassium intake, a well-established risk factor of cardio-cerebrovascular disease, is also a suggested risk factor for mild cognitive impairment (MCI), whereas inconclusive, owing to diverse methods for estimating sodium and potassium intake (food frequency questionnaire, three-day food diary, or spot urine), low powered sample size, enrollment of specific study population (older, single gender, or patients). Therefore, the aim of this study is to explore the relationship between parameters of sodium and potassium intake and excretion using gold standard method "24-hour urine collection" and MCI in community-based general population.

METHODS With a multistage proportional random sampling method in community-based population in Xinjiang China between March and June 2019, totally 1147 subjects aged ≥18 years were selected to complete the study. Cognitive status was assessed with Mini Mental State Examination (MMSE) questionnaire and timed 24-hour urine specimens were collected. MCI was defined as total MMSE score <17 for subjects with no formal education, <20 for subjects with 1–6 years of education and <24 for subjects with ≥7 years of education. The completeness of urine samples were evaluated as: (1) total urine volume ≥500 mL; (2) 20 hours or more duration; (3) reported no more than a

few drops of urine lost during collection; (4) 24-hour urinary creatinine per kilogram of body weight ≥20 mg/kg in men and ≥15 mg/kg in women aged <50 years and ≥10 mg/kg in men and ≥7.5 mg/kg in women aged ≥50 years. Finally, subjects aged ≥35 years with qualified urine sample and complete data on MMSE were included for the current analysis and divided into three groups by tertiles of 24-hour urinary sodium to potassium ratio (24-h UNa/K). Multiple linear regression was used to examine the association between parameters of sodium and potassium intake and excretion and MMSE score and multivariable logistic regression for the association between above parameters and the odds of prevalent MCI. Sensitivity analysis was performed after excluding subjects taking anti-hypertensive agents.

RESULTS Finally 561 participants aged 52.7±9.3 years with 42.6% men were enrolled, with a median salt intake of 8.6 gram and a median total MMSE score of 26. The MMSE score decreased significantly in the T3, compared with the T1 group (26.0 vs. 25.0, P=0.002) and the prevalent MCI was significantly higher in T3 than in T1 group (11.7 vs. 25.8%, P<0.001). In multiple linear regression, 24-h UNa/K [β: −0.184, 95% CI: (−0.319, −0.050), P=0.007] and salt intake [β: −0.122, 95% CI: (−0.229, −0.015), P=0.025] were negatively associated with MMSE score, while 24-hour urinary potassium (24-h UK) showed a positive effect [β: 0.028, 95% CI: (0.001, 0.055), P=0.045]. In multivariable logistic regression, compared with T1 group, 24-h UNa/K in the T2 and T3 group showed 2.01 (95% CI: 1.03–3.93, P=0.041) and 3.38 (95% CI: 1.77–6.44, P<0.001) fold odds for presence of MCI, even after adjustment for confounders. Additionally, when compared with T3 group, the odds for MCI in T1 and T2 groups of 24-h UK were 3.23 (95% CI: 1.58–6.57, P=0.001) and 3.04 (95% CI: 1.52–6.09, P=0.002), respectively. More augmented results were demonstrated in sensitivity analysis by excluding individuals taking anti-hypertensive agents.

CONCLUSIONS Higher sodium intake and lower potassium intake is in an independent association with prevalent MCI.

GW31-e1199

A cross-sectional study of the contemporary (2019) prevalence of cardiovascular disease in adults with type 2 diabetes in China

Tianpei Hong[1], Ke Cao[2], Li Li[3], Lin Qj[4], Jiangong Ren[5], Wei Tang[6], Qin Wan[7], Wenhua Xiao[1], Zongxun Yan[8], Jianhua Ye[9]
[1]Peking University Third Hospital, Beijing, China
[2]Novo Nordisk China Pharmaceutical Co. Ltd., Beijing, China
[3]Ningbo First Hospital, Ningbo, China
[4]Beijing Yanhua Hospital, Beijing, China
[5]Lanzhou University Second Hospital, Lanzhou, China
[6]Geriatric Hospital of Nanjing Medical University, Nanjing, China
[7]Affiliated Hospital of Southwest Medical University, Luzhou, China
[8]Affiliated Hospital of North Sichuan Medical College, Nanchong, China
[9]The First Affiliated Hospital of Clinical Medicine of Guangdong Pharmaceutical University, Guangzhou, China

OBJECTIVES There are limited data on the prevalence of cardiovascular disease (CVD) in people with type 2 diabetes mellitus (T2DM). The CAPTURE study estimated the contemporary (2019) prevalence of established CVD in a sample representing the general T2DM population across 13 countries. Here, we report the findings from China.

METHODS CAPTURE (NCT03811288; NCT03786406) was a multinational, cross-sectional, non-interventional study. Detailed, standardized demographic and clinical data were collected from adults aged ≥18 years with T2DM, attending a single routine healthcare visit in primary or specialist care between December 2018 and September 2019. In China, all data were collected from endocrinologists. Across all 13 countries, CVD prevalence estimates were weighted to account for the size of the T2DM population of each country. CAPTURE also prespecified a secondary analysis to assess the proportion of adults with T2DM and CVD using glucose-lowering medication with approved CVD benefit such as glucagon-like peptide-1 receptor agonist (GLP-1RA): dulaglutide or liraglutide; sodium-glucose cotransporter-2 inhibitor (SGLT2i): canagliflozin, dapagliflozin, empagliflozin; lipid-lowering medication; and anti-platelet agents. Data were analyzed descriptively.

RESULTS In the CAPTURE China subgroup, 805 adults with T2DM from eight different sites participated with the following median characteristics: age 59.0 years, diabetes duration 9.24 years, glycated hemoglobin (HbA_{1c}) 7.3% and body mass index 24.5 kg/m²; 38.1% were female. CVD prevalence was 33.9% [30.6; 37.3]$_{95\%\ CI}$, with most (95.0%) categorized as atherosclerotic CVD (32.2% [29.0; 35.5]$_{95\%\ CI}$). Coronary heart disease prevalence was 16.0% [13.6; 18.7]$_{95\%\ CI}$, carotid artery disease was 9.6% [7.6; 11.8]$_{95\%\ CI}$, cerebrovascular disease was 7.7% [6.0; 9.8]$_{95\%\ CI}$, and heart failure was 0.2% [0.0; 0.9]$_{95\%\ CI}$. The prevalence for peripheral artery disease was 1.4% [0.7; 2.4]$_{95\%\ CI}$, for arrhythmias and conduction disorders it was 3.4% [2.2; 4.8]$_{95\%\ CI}$ and for aortic diseases it was 0.2% [0.0; 0.9]. Of 259 participants with atherosclerotic CVD status, 1.5% were prescribed GLP-1RA, 5.4% were prescribed SGLT2i, 38.6% received lipid-lowering medication, and 36.3% received anti-platelet agents. The prevalence of CVD in China compared with the global prevalence estimates of CVD was 33.9 vs. 34.8%, respectively.

CONCLUSIONS CAPTURE was the first multinational, cross-sectional study to estimate CVD prevalence in adults with T2DM and demonstrated that in China, approximately one in three adults with T2DM had established CVD. The prevalence of CVD in China was similar to the global prevalence. Most participants with T2DM and atherosclerotic CVD in China did not receive glucose-lowering medication with approved CVD benefit, lipid-lowering medication and/or anti-platelet agents.

PERIPHERAL VASCULAR DISEASE

GW31-e0249

Preliminary evaluation of a novel retrievable self-expandable drug-eluting stent in a canine peripheral artery model

Xiuyue Jia, Houliang Chen, Minghong Wang, Xue Zhao
The Third Affiliated Hospital of Navy Medical University

OBJECTIVES Retrievable stent may be an alternative choice to achieve "nothing left" intervention. This pilot study was to observe the retrievable stent related pathology in canine iliac artery to primarily evaluate the feasibility of retrieving a stent in vivo.

METHODS Five retrievable stents (Figure 1), characterized by the structure of point-to-point overlapped double-layer scaffolds and a retrieval hook, were deployed into the left iliac arteries of 5 Labrador dogs and retrieved at day 14, 21, 28, 35 or 42 after implantation, respectively. The stent implanted for 14 days was firstly removed by dissection to evaluate the adhesion degree, while the others were removed by designed retrieval device. Angiography was performed before and after procedures. The dogs were euthanized immediately after stent retrieval, expect for the dog with stent implanted for 28 days, which was sacrificed 14 days after stent retrieval. HE, SMA, CD31 and Masson trichrome staining were used for histopathologic analysis.

RESULTS The stent implanted for 14 days was retrieved by dissection. Distinct stent footprints were left on the artery wall, and the stent was intact with tiny semitransparent tissue adhering on its inner surface. Straight internal elastic lamina and decreased smooth muscle cells were noted around the struts by microscopic detection (Figure 2). The stent implanted for 28 days was retrieved by retrieval device. The mean lumen diameter decreased by 10% before retrieval and 21% on day 14 after retrieval comparing with that before stent implantation (Figure 3). The retrieved stent showed structural integrity with a thin layer of semitransparent membranous tissue covering on its inner surface. A focal injury was noted at the distal arterial segment by gross. For microscopic detection, the primary intima with CD31(-) was completely covered by uneven neointima with CD31(-) and SMA(-), and focal ruptured internal elastic lamina was noted (Figure 4). The stent implanted for 35 days was retrieved by retrieval device. Angiography before stent retrieval showed the mean lumen diameters of the stented vessel decreased by 9% comparing with that before stent implantation (Figure 5). For gross observation, the retrieved stent showed structural integrity with a thick layer of semitransparent membranous tissue covering on its inner surface. The harvested vessel showed intact with distinct strut footprints, and focal thrombus trace and punctuate bleeding points were observed in its proximal segment. For microscopic detection, ruptured internal elastic lamina, fewer endothelial cells with positive CD31and decreased smooth muscle cells were noted around the strut footprints (Figure 6). The neointima adhered on the inner surface of the stent, mainly composed of collagen fibers, smooth muscle cells and endothelial cells, and angiogenesis was also noted in the gap between adjacent struts (Figure 7). Two stents failed to be retrieved due to stent displacement or loss to capture retrieval hook.

CONCLUSIONS This pilot study demonstrated the feasibility of retrieving a stent from iliac artery after implantation for 35 days. The operational injuries implied the designs of the stent and retrieval technique need to be modified in order to improve the retrieval safety and efficiency. Neointima formation would still be challenging for further study.

GW31-e0290

Alamandine inhibits pathological neovascularization in oxygen-induced retinopathy along with a downregulation of HIF-1α and VEGFA expression

Kun Zhao, Chuanxi Yang, Peng Li, Wei Sun, Xiangqing Kong
The First Affiliated Hospital of Nanjing Medical University

OBJECTIVES Alamandine, a heptapeptide, is closely related to the vasodilator Ang (1-7). As they have similar amino acid sequence and structure, their effects are highly likely to be similar. It has reported that Ang (1-7) may exert an anti-angiogenic role by decreasing proangiogenic agents such as vascular endothelial growth factor-A. However, it is still unclear whether Alamandine can alleviate neovascularization. Here, we investigated the potential effect of Alamandine on the hypoxia-induced retinal neovascularization and the possible mechanisms.

METHODS The C57BL/6J mice with oxygen-induced retinopathy were injected intravitreally with Almandine (physiological saline solution, 5 mg/mL per eye). Real-time PCR and western were used to determine the expression of hypoxia-inducible factor-1α (HIF-1α) and vascular endothelial growth factor A (VEGFA). In vitro, human umbilical vein endothelial cells (HUVECs) were used to study the proliferation, apoptosis, migration, tubular formation without (–) (control) or with (+) Almandine (PBS, 5 μg/mL, 10 μg/mL, 20 μg/mL) and/or VEGF (10 ng/mL). Real-time PCR and western were used to determine the expression of HIF-1α and VEGFA.

RESULTS Alamandine decreased the mRNA and protein expression of VEGFA and HIF-1α significantly (P<0.01) under hypoxia condition in mice compared with the control eyes. In a vitro system, the addition of Alamandien to the cell cultures attenuated the proliferation, scratch-wound healing and tube formation of vascular endothelial cells induced by VEGF (10 ng/mL) significantly. Meanwhile, Alamandine decreased the mRNA and protein expression of VEGFA and HIF-1α via inhibition of the signaling pathway under hypoxia condition. In addition, Alamandine inhibited hypoxia-induced accumulation of nuclear HIF-1α protein.

CONCLUSIONS Alamandine, via its receptor, ameliorates retinal neovascularization through inhibition of the HIF-1α/VEGF signaling pathway, implying that Alamandine is an antiangiogenic agent in pathophysiological settings and may be developed as a potential drug for the prevention and treatment of diabetic retinopathy.

GW31-e0651

Underwent primary percutaneous coronary intervention in a 29-year-old male Buerger's disease with acute myocardial infarction: 5-year follow-up outcomes

Xianguan Zhu[1], Jianchang Wang[2], Xuejun Xiang[1]
[1]Department of Cardiology, Affiliated Anqing Hospital of Anhui Medical University, Anqing, Anhui, China
[2]Geriatrics Research Center, General Hospital of Air Force, PLA, Beijing 100142, China

OBJECTIVES Buerger's disease or thromboangiitis obliterans is a non-atherosclerotic segmental inflammatory disease that ordinarily affects the small and medium-sized arteries. There were few cases of patients with Buerger's disease and comorbidities in coronary and the treatment strategies are varied and the long-term outcome is lack of evidence, especially for primary percutaneous coronary intervention (PCI). We report a case of acute myocardial infarction in a 29-year-old male patient with Buerger's disease treated with primary PCI and anticoagulant and the good outcomes of 5-year follow-up. Therefore in this article we discuss the clinical treatment strategy and outcomes of Buerger's disease with acute myocardial infarction and give insight to clinicians how to manage patients with Buerger's disease and acute myocardial infarction.

METHODS Case Report

RESULTS A 29-year-old male with previous history of Buerger's disease, a right wrist-level amputation one year ago and smoking was admitted to the emergency department due to acute persistent chest pain for 2 hours. Electrocardiography demonstrated ST segment elevation in precordial leads (V2–V5). After aspirin (300 mg) and clopidogrel (300 mg) were administered, the emergency coronary angiography was performed immediately, which indicated that the proximal and middle segments of left anterior descending (LAD) artery was completely occluded. By underwent thrombus aspiration in 4 times intermittently and intracoronary tirofiban through the aspiration catheter, stenting of the infarct-related LAD were completed and the TIMI flow grade were improved from 0 to 3 eventually. At 1-year follow-up, the left distal brachial artery was nearly completely occluded and thrombolysis was executed by catheter to relieve the pain of left forearm. Two years later, the left wrist-level amputation was performed. After three years, he appreciated that the progression of burger's disease was slow by reason of no more pain in the upper/lower extremities. During the past 5 years, the patient has not complained of chest distress or pain, the occurrence of syncope and malignant arrhythmia events. At present, he is able to engage in raising sheep and his current Seattle Angina Questionnaire (SAQ) score is 87.7 of physical limitation, 93.8 of angina stability, 87.5 of angina frequency, 89.8 of treatment satisfaction, 88.6 of disease perception. The quality of life is in good condition.

CONCLUSIONS Underwent primary percutaneous coronary intervention in Buerger's disease with acute myocardial infarction is safety and efficacy in long-term.

GW31-e0853

Trends in hypertension prevalence, awareness, treatment and control among the middle-aged and elderly: the China health and retirement longitudinal study

Lili Liu[1], Lu Xu[1], Siyan Zhan[1,2], Shengfeng Wang[1]
[1]Department of Epidemiology and Biostatistics, School of Public Health, Peking University, 38 Xueyuan Road, Haidian District, Beijing 100191, China
[2]Research Center of Clinical Epidemiology, Peking University Third Hospital, 49 Huayuan North Road, Haidian District, Beijing 100191, China

OBJECTIVES Trends in prevalence, awareness, treatment and control of hypertension among the middle-aged and elder can inform new strategies for hypertension management. However, no such information in China existed since 2010. This study aims to describe trends in the prevalence, awareness, treatment, and control of hypertension in Chinese middle-aged and elderly population.

METHODS A national population-based study was conducted among adults aged 45 years and older between 2011 and 2015 using data in the China Health and Retirement Longitudinal Study (CHARLS) during three periods: May 2011 to March 2012, July 2013 to August 2013 and July 2015 to August 2016. Hypertension was considered as a mean systolic blood pressure ≥140 mmHg or a mean diastolic blood pressure ≥90 mmHg, self-reported use of antihypertensive medications or self-reported hypertension. Control of hypertension was defined as a measured blood pressure <140/90 mmHg.

RESULTS The prevalence rose from 44.08% (95% CI 42.41–45.75%) to 48.84% (47.53–50.14%). The proportion of patients with hypertension aware of their condition increased from 61.04% (58.02–63.98%) to 77.00% (75.15–78.75%). The proportion of patients receiving treatments witnessed an increase from 51.60% (48.74–54.46%) to 57.30% (55.29–59.28%). Sharp climb was observed in the control rate, with only 23.80% (22.04–25.66%) of patients controlling disease progression effectively in 2011 versus 40.11% (38.18–42.08%) in 2015. In terms of treatment, the prevalence of medication use and lifestyle intervention showed a similar rise (approximately 7% compared to baseline). In 2011, 92.36% (88.15–95.15%) and 13.77% (10.70–17.55%) of patients with hypertension took western medicine and traditional Chinese medicine (TCM), respectively. 6.13% (5.13–7.30%) of those treated with medication combined western and TCM, the rates of each had increased to 92.66% (90.91–94.10%), 15.08% (13.34–17.00%) and 7.74% (6.75–8.87%) respectively in 2015.

CONCLUSIONS Increases in prevalence, awareness, treatment and control of hypertension have been observed among Chinese middle-aged and elderly population. But the treatment and control rates are far lower than developed countries. In the future, additional strategies in prevention and management of hypertension among the middle-aged and elder should be adopted.

PSYCHO-CARDIOLOGY

GW31-e0159

The impact of the Type D personality pattern on prehospital delay in patients suffering from acute myocardial infarction findings from the multi-center MEDEA FAR-EAST study

Youyang Zhang[1], Shihao Wu[2], Jiangqi Pan[3], Sophia Hoschar[4,5], Zhen Wang[6], Rongxiang Tu[1], Karlheinz Ladwig[4,7], Wenlin Ma[1,2]
[1]Department of Cardiology, Shanghai Tongji Hospital, Tongji University School of Medicine, Shanghai, China
[2]Department of Geriatrics, Shanghai Tongji Hospital, Tongji University School of Medicine, Shanghai, China
[3]Department of Cardiology, Gongli Hospital, Navy Military Medical University, Shanghai, China
[4]Institute of Epidemiology, Mental Health Research Unit, Helmholtz Zentrum München, German Research Center for Environmental Health (HMGU), Ingolstädter Landstr 1, 85764 Neuherberg, Germany
[5]Department of Psychosomatic Medicine and Psychotherapy, Medical Center, University of Freiburg, Faculty of Medicine, Freiburg, Germany
[6]Department of General Practice, Jiangning Hospital, Nanjing Medical University, Shanghai, China
[7]Department of Psychosomatic Medicine and Psychotherapy, University Hospital Rechts der Isar, Technische Univerität Munich (TUM)

OBJECTIVES The Type D Personality (TDP) has been specifically linked to acute myocardial infarction (AMI). However, the impact on prehospital delay of AMI patients is unclear. The aim (PHT) in a Chinese population.

METHODS A total of 256 AMI patients (47 women and 209 men) were taken from the Multicenter Delay in Patients Experiencing AMI in Shanghai (MEDEA FAR-EAST) study. Sociodemographic and psycho-behavioral characteristics were assessed by bedside interviews and questionnaires. TDP was evaluated according to the Type D Personality Scale (DS14) subdivided in social inhibition (SI) and negative affectivity (NA). Based on a significant interaction analysis of TDP and sex on PHT, all analyses were stratified by sex.

RESULTS PHT of female patients with TDP were substantially shorter compared to non-TDP female patients (108 min vs. 281 min, P=0.029). In male patients, no effect of TDT on PHT was found. Spearman correlation analysis suggests that NA was negatively correlated with PHT (r=–0.358, P=0.014). Further age-adjusted logistic regression analyses showed that female patients with TDP were generally less likely to delay compared with non-TDP patients (OR=0.28, 95% CI=0.08–0.98) and had a lower risk of delaying more than 360 minutes (OR=0.10, 95% CI=0.01–0.91). However, statistical significance

disappeared after adjustment for psychological factors (anxiety, depression, suboptimal wellbeing, cardiac denial and stress event).

CONCLUSIONS Type D Personality is associated with less prehospital delay in female patients during AMI – an effect which may be particularly mediated by NA.

GW31-e0862

Factors associated with insomnia symptoms in patients with coronary heart disease using machine learning method: a retrospective case-control study

Sizhi Ai, Binbin Han, Guohua Li, Xuehui Wang, Shanshan Wang, Peicheng Li, Meng Li, Zhigang Chen, Fei Lin, Guoan Zhao
The First Affiliated Hospital of Xinxiang Medical University

OBJECTIVES The present study aims to investigate factors that associated with insomnia symptoms in patients with coronary heart disease by using a novel machine learning (ML) algorithm and provide an interpretable risk prediction model.

METHODS A total number of 826 subjects with coronary heart disease (CHD) was retrospectively collected from Medical admission record system of the First Affiliated Hospital of Xinxiang Medical University. They were separately divided into the insomnia group and non-insomnia group according to the self-reported insomnia questionnaire assessment, and the demographic, examination and biochemical data of these subjects were also collected. The ML model based gradient boosting framework was trained using these clinical characteristics, and validated though 10-fold cross-validation.

RESULTS Subjects with insomnia symptoms more likely to be older, longer hospitalized days, and had more use of diuretic and sedative medication compared with subjects without insomnia symptoms. ML random forest method identified serum levels of creatinine, albumin, uric acid, and diuretic medication use as the top factors that associated with insomnia symptoms in patients with CHD, and suggested that diuretic medication use is a risk factor of insomnia symptoms in CHD patients. ML interaction analysis indicated a significant interaction between diuretic medication use and serum levels of albumin on the risk of insomnia. In subjects who use diuretic medication, a lower levels of serum albumin was associated with more insomnia symptoms. We also provide an interpretable risk prediction model for a given subject, and showed how the clinical characteristics such as diuretic medication use, serum levels of creatinine, albumin, and uric acid affect the risk of insomnia symptoms in patients with CHD.

CONCLUSIONS Diuretic medication use is a risk factor of insomnia in CHD patients, higher albumin levels may be less prone to insomnia in those patients who use diuretics.

GW31-e1075

The value of Chinese version GAD-7 and PHQ-9 to screen anxiety and depression in Chinese outpatients with atypical chest pain

Qjuzhen Lin, Keke Wu, Qjming Liu, Ling Liu
Department of Cardiovascular Medicine, The Second Xiangya Hospital, Central South University

OBJECTIVES Atypical chest pain in some outpatients could derive from mental disorders if they had been ruled out organic diseases, such as coronary heart disease. We aimed to compare the validity between the Chinese version of the seven-item scale for General Anxiety Disorder (GAD-7)/Self-rating Anxiety Scale (SAS), the nine-item Patient Health Questionnaire (PHQ-9)/Self-rating Depression Scale (SDS) in screening anxiety and/or depression, and to provide better diagnosis for those patients in the outpatient department of cardiovascular clinic.

METHODS The study included 122 Chinese outpatients with atypical chest pain in the department of Cardiology. All participants accepted routine enquiry, body examination, the examination of electrocardiogram, treadmill test and pulmonary function test and there was no abnormal findings to explain the chest pain that they felt. After that, patients with normal findings were judged by the three-question method as highly likely to have emotional disorders. And then a standard questionnaire package containing GAD-7, SAS, PHQ-9 and SDS were administered to all of them to evaluate anxiety and depression.

RESULTS The percentages of anxiety evaluated by GAD-7 and SAS were 62.3 and 26.2%, respectively. The percentage of GAD-7 was significantly higher than that of SAS in evaluating moderate (21.3 vs. 4.9%) or severe (15.6 vs. 2.5%) anxiety (P<0.0167). Analogously, the assessment by PHQ-9 showed a significant higher percentage of depression when compared to that by SDS (61.5 vs. 29.5%) (P<0.05). The percentage of PHQ-9 was significantly higher than that of SDS in evaluating moderate (16.4 vs. 5.7%) or severe (9.8 vs. 2.5%) depression (P<0.0167). Kappa analysis showed that the consistency between GAD-7 and SAS (Kappa coefficient was 0.295), or that between PHQ-9 and SDS (Kappa coefficient was 0.356) was not very good. About 73% (89 of total 122) of outpatients with atypical chest pain suffered from emotional disorders, presenting as anxiety and/or depression evaluated by GAD-7 and PHQ-9. Furthermore, sleep disorders accounted for more than 80% of patients with mental illness. Finally, there was not to be ignored that the suicidal tendency of depression patients was about 17%.

CONCLUSIONS This study showed a high prevalence of mental disorders in patients with atypical chest pain. Compared with SAS and SDS, GAD-7 and PHQ-9 detected more participants with emotional disorders in the Chinese outpatients with atypical chest pain, indicating that GAD-7 and PHQ-9 could be briefly well-validated tools to distinguish emotional disorders in the outpatients department of Cardiology. In addition, sleep disorder and suicidal thoughts should be paid closely attention in patients with atypical chest pain that cannot be explained by an organic etiology.

CARDIOVASCULAR IMAGING

GW31-e0151

Correlation analysis of n-terminal b-type natriuretic peptide precursor and cardiac troponin I on myocardial fibrosis in patients with different degrees of hypertrophic cardiomyopathy

Yan Zhang[1], Mingjie Pang[2], Mingjie Pang[2]
[1]Department of Magnetic Resonance, affiliated Hospital of Kunming University of Science and Technology, the first people's Hospital of Yunnan Province, Kunming 650032, China
[2]Department of Cardiovascular Medicine, affiliated Hospital of Kunming University of Science and Technology, the first people's Hospital of Yunnan Province, Kunming 650032, China

OBJECTIVES To study the value of high sensitivity cardiac troponin I and b-type natriuretic peptide in (HCM) myocardial fibrosis in hypertrophic cardiomyopathy and their correlation with myocardial fibrosis in different degrees of hypertrophic cardiomyopathy.

METHODS The concentrations of NT-proBNP and cTnI in peripheral blood of patients with HCM (N=46; age=46.2±11.8 years old) were measured. Contrast-enhanced CMR was used to identify and quantify myocardial fibrosis, and the late gadolinium enhancement ratio was calculated by visual analysis.

RESULTS 1. Of the 48 patients, 34 (73.9%) had LGE, classified according to left ventricular end-diastolic volume, including 15 mild (15 mm≤LVEDTH<20 mm), The late gadolinium enhancement segment LGE (n) was 0.12±0.20, and the late gadolinium enhancement ratio LGE (%) was 0.06±0.04.10 moderate (20 mm≤LVEDTH<25 mm), The late gadolinium enhancement segment LGE (n) was 0.15±0.16, and the late gadolinium enhancement ratio LGE (%) was 0.21±0.09. There were 9 cases of poisoning (25 mm≤LVEDTH<30 mm). The late gadolinium enhancement segment LGE (n) was 0.12±0.20, and the late gadolinium enhancement ratio LGE (%) was 0.06±0.04. There was significant difference between late gadolinium enhancement segment LGE (n) and late gadolinium enhancement ratio LGE (%) among the three groups. The levels of NT-proBNP and cTnI in 2. LGE positive patients were significantly higher than those in LGE negative patients (2487.68±1361.72 vs. 747.63±410.44 pmol/L). The degree of LGE (%) of 0.56±1.52 vs. 0.15±0.16 ng/mL, P<0.001 pmol/L) was positively correlated with cTnI and NT-proBNP. There was a significant correlation between NT-proBN, cTnI and LVEDTH.

CONCLUSIONS Serum high sensitivity cardiac troponin I and b-type natriuretic peptide are significantly correlated with cardiac fibrosis in hypertrophic cardiomyopathy, and the degree of LGE and cTnI increases with the increase of left ventricular hypertrophy.

GW31-e0152

Application of cardiac magnetic resonance feature tracking in myocardial fibrosis in patients with hypertrophic cardiomyopathy

Yan Zhang[1], Mingjie Pang[2], Kunhua Wu[1], Yan Zhao[2], Mingjie Pang[2]
[1]Department of Magnetic Resonance, affiliated Hospital of Kunming University of Science and Technology, the first people's Hospital of Yunnan Province, Kunming 650032, China
[2]Department of Cardiovascular Medicine, affiliated Hospital of Kunming University of Science and Technology, the first people's Hospital of Yunnan Province, Kunming 650032, China

OBJECTIVES Myocardial fibrosis in hypertrophic cardiomyopathy was evaluated by Cardiac magnetic resonance feature tracking.

METHODS Eighty six patients with hypertrophic cardiomyopathy in the first people's Hospital of Yunnan Province from November 2016 to April 2020 were retrospectively analyzed. Cardiac magnetic resonance imaging was performed. Myocardial fibrosis was judged by late gadolinium-enhanced (LGE). Three-dimensional global and local longitudinal, radial and circumferential strain (S) and strain rate (SR) were obtained by CMR-FT software. The FT findings of HCM patients with and without delayed enhancement were compared.

RESULTS 1. Among 86 patients with HCM (mean age 45±7.9 years, male 83%), 64 patients (mean age 38±5.6 years) had delayed enhancement. There was no significant difference in left ventricular ejection fraction, left ventricular mass and left ventricular end-diastolic volume between patients with delayed enhancement and patients without delayed enhancement. 2. The overall longitudinal, circumferential and radial S and SR of patients with delayed enhancement were lower than those of patients without delayed enhancement (−7.6±3.4 vs. 14.3±2.5, −9.4±1.9 vs. −17.2±1.6, 10.3±2.1 vs. 17.9±3.5, P<0.01; 89±16.3 vs. −123.5±13.1, −92.5±13.5 vs. −137±12.6, 80.9±9.9 vs. 129.1±22.3, P<0.00). 3. In 64 patients with delayed enhancement, there were 1024 segments except apical enhancement, of which 256 segments had delayed enhancement. The myocardium with delayed enhancement was significantly lower than that without delayed enhancement on longitudinal, circumferential and radial S and SR (−8.1±2.2 vs. −15.2±3.9, −9.7±1.1 vs. −16.8±1.3, 11.7±3.0 vs. 19.7±2.6, P<0.01). −92.7±18.4 vs. −127.1±12.71, −90.5±11.2 vs. −129.4±11.7, 81.6±7.9 vs. 135.7±19.5, P<0.00).

CONCLUSIONS Myocardial fibrosis is an independent risk factor for sudden cardiac death in patients with hypertrophic cardiomyopathy. In view of the differences in longitudinal, circumferential and radial strain between patients with and without fibrosis, feature tracking technique can be used to evaluate the prognosis of patients without contrast agent.

GW31-e0153

The value of T1 mapping and ECV in the diagnosis of hypertrophic cardiomyopathy and H-type hypertensive ventricular hypertrophy

Yan Zhang[1], Mingjie Pang[2], Mingjie Pang[2]
[1]Department of Magnetic Resonance, affiliated Hospital of Kunming University of Science and Technology, the first people's Hospital of Yunnan Province, Kunming 650032, China
[2]Department of Cardiovascular Medicine, affiliated Hospital of Kunming University of Science and Technology, the first people's Hospital of Yunnan Province, Kunming 650032, China

OBJECTIVES To investigate the diagnostic value of cardiac magnetic resonance T1 mapping imaging and extracellular volume (ECV) in hypertrophic cardiomyopathy (HCM) and H-type hypertensive ventricular hypertrophy.

METHODS From January 2017 to December 2019, 42 patients who were treated in the first people's Hospital of Yunnan Province and underwent cardiac MRI examination in the Department of Magnetic Resonance, including 16 patients with H-type hypertension and 26 patients with hypertrophic cardiomyopathy. Left ventricular mass (LVM), left ventricular ejection fraction (LVEF), heart rate (HR), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV) and stroke volume were compared between the two groups. According to the presence of late gadolinium enhancement (LGE), the patients in the two groups were divided into LGE group and non-LGE group, and the values of T1, T1 mapping and ECV were measured before and after enhancement.

RESULTS 1. There was no significant difference in age, sex, heart rate, creatinine and other basic parameters between patients with H-type hypertension and patients with hypertrophic cardiomyopathy, but there were significant differences in systolic blood pressure, diastolic blood pressure and left ventricular mass (P<0.05). Ejection fraction, stroke volume and ventricular thickness were lower than those in hypertrophic cardiomyopathy (P<0.05). 2. Late gadolinium enhancement of myocardium was found in 8 patients with H-type hypertension and 18 patients with hypertrophic cardiomyopathy, NativeT1, T1 and ECV in hypertrophic cardiomyopathy were significantly increased, T1 and ECV in patients with H-type hypertension and non-LGE cardiomyopathy were significantly lower than those in LGE group, while ECV in patients with H-type hypertension was significantly lower than that in patients with hypertrophic cardiomyopathy in LGE group. 3. ROC curve analysis showed that the area under the curve of NativeT1 and T1 was 0.721 and 0.803, the sensitivity was 0.692 and 0.769, the specificity was 0.875 and 0.750, the area under the curve (AUC) was 0.808, the sensitivity was 0.615 and the specificity was 1.000.

CONCLUSIONS T1 mapping and ECV are of great value in the differential diagnosis of H-type hypertensive ventricular hypertrophy and hypertrophic cardiomyopathy, especially ECV has high efficiency in differential diagnosis.

GW31-e0237

Morphological characteristics and geometric models of coronary bifurcation core in left main and left anterior descending coronary artery

Yifan Chen[1,2], Genshan Ma[1,2]
[1]Cardiology department of Nanjing Zhongda Hospital
[2]School of Medicine, Southeast University

OBJECTIVES The study aimed to determine the geometric models of the polygon of confluence (POC) of coronary bifurcation regions (CBR) in left main and left anterior descending artery (LMCB, LADB), in order to optimize coronary bifurcation lesions (CBL) intervention.

METHODS In the retrospective observational study, 94 participants with normal coronary angiography (CAG) were enrolled in Zhongda Hospital from Jan 2015 to Dec 2019. Target CBR included LMCB-CBR and LADB-CBR. Two-dimensional quantitative coronary angiography analysis (2D-QCA) was performed on the end-diastolic stage of optimal angiographic images for maximal diameter (D_{POC}), maximal height (H_{POC}), diameter of proximal main-branch (D_{PMB}), distal main-branch (D_{DMB}), side-branch (D_{SB}) and distal bifurcation angle (DBA). The difference between D_{POC} and D_{PMB} ($D_{POC\text{-}PMB}$) was calculated. Relation of D_{PMB}, D_{DMB} and D_{SB} was explored to verify whether it conformed to Murray's-, Finet's- or HK law. Geometric model of D_{POC}, H_{POC}, D_{DMB}, D_{SB} and DBA was obtained by correlation and regression analysis.

RESULTS (1) Demographic features: 94 participants with 184 target CBRs were enrolled. Among which, 51 (54.3%) were male, the average age was 58.3±10.2 (years old). (2) Different CBRs: 1) D_{POC}, H_{POC}, $D_{POC\text{-}PMB}$ and DBA in different sites of CBR varied greatly. D_{POC} was 5.00±1.27 mm in LMCB, 3.72±0.82 mm in LADB. H_{POC} was 3.53±0.88 mm in LMCB, 4.89±0.65 mm in LADB. $D_{POC\text{-}PMB}$ was 1.20±0.91 mm in LMCB, 0.89±0.35 mm in LADB. DBA was 75.0±26.1° in LMCB, 50.0±21.4° in LADB (P<0.01 for all). 2) D_{POC} of Y- (DBA<70°) or T-CBR (70°≤DBA<90°) varied greatly, but H_{POC} and $D_{POC\text{-}PMB}$ varied little. D_{POC} was 4.15±1.07 mm in Y-CBR, 4.53±1.12 mm in T-CBR (P<0.05). H_{POC} was 3.37±0.84 mm in Y-CBR, 3.17±0.65 mm in T-CBR. $D_{POC\text{-}PMB}$ was 1.00±0.42 mm in Y-CBR, 0.96±0.58 mm in T-CBR (P>0.05 for both). (3) QCA results: 1) Relation of D_{PMB}, D_{DMB} and D_{SB} was explored to verify whether it conformed to Murray's-, HK- or Finet's law. The fitting results were $D_{PMB}{}^{2.6}=D_{DMB}{}^{2.6}+D_{SB}{}^{2.6}$ (R^2=0.93) or $D_{PMB}=0.641(D_{DMB}+D_{SB})$ (R^2>0.92), which conformed to HK- and Finet's law better. 2) Relation of D_{POC}, H_{POC}, D_{DMB}, D_{SB} and DBA: A) D_{POC}, D_{DMB} and DSB: $D_{POC}{}^{1.3}=D_{DMB}{}^{1.3}+D_{SB}{}^{1.3}$ or $D_{POC}=0.860(D_{DMB}+D_{SB})$ (both R^2=0.72). The relationship among D_{POC}, D_{DMB} and D_{SB} varied greatly from previous laws. B) H_{POC}, D_{DMB} and D_{SB}: positive correlation could be seen in H_{POC} with D_{DMB} (r_s=0.542, P<0.001), with D_{SB} (r_s=0.584, P<0.001) and with ($D_{DMB}+D_{SB}$) (r_s=0.600, P<0.001), however, no remarkable regression relationship could be seen among them (R^2<0.5 for all). C) D_{POC}, H_{POC} and DBA: positive correlation could be seen in D_{POC} with DBA (r_s=0.214, P=0.04) whereas negative correlation in H_{POC} with DBA (r_s=−0.154, P=0.04). No remarkable regression relationship could be seen among them (R^2<0.5 for all). Stratified analysis which grouped DBA by 30 degrees suggested H_{POC} decreased step by step with the increase of DBA stratification in LABD. No similar trend could be seen in D_{POC}.

CONCLUSIONS D_{POC} is significantly larger than D_{PMB} with close relating to D_{DMB} and D_{SB}. New geometric models show 2.6 is the exponent in the exponential function of D_{POC}, D_{DMB} and D_{SB} and 0.641 is the ratio of D_{PMB} to the sum of D_{DMB} and D_{SB}, which makes it easy to calculate any of the three indexes when those of the other two are known. In LADB, H_{POC} decreases step by step with the increase of DBA. These could provide theoretical fundamentals for CBL intervention optimization.

GW31-e0262

A novel methodology for automatic measurement of aortic stiffness by doppler ultrasound

Wang Zhen[1], Yang Yong[2], Gao Feng[1]
[1]School of Aerospace Medicine, Fourth Military Medical University, Xi'an 710032, China
[2]Department of Ultrasound Medicine, Tangdu Hospital, Fourth Military Medical University, Xi'an 710038, China

OBJECTIVES Aortic stiffness (AS) has been increasingly claimed as a robust predictor of cardiovascular events and all-cause mortality in various populations. Carotid-femoral PWV (cfPWV) is a simple, robust and reproducible parameter and has been regarded as the "gold standard" for measuring AS. Given the accuracy and simplicity, Doppler ultrasound has been well accepted as a preferable method for cfPWV measurement. However, conventional cfPWV measurement can only be done by manual method, which inevitably brings intrinsic limitations such as considerable time-consuming, operator-dependence (especially for the wave foot recognition) and substantial measurement errors. Hence, exploring an automated algorithm for aortic PWV measurement by Doppler ultrasound would eliminate these problems and thus warrants high priority. In this study, we aimed to investigate the reproducibility and clinical applicability of a novel Doppler ultrasound automatic measurement of arterial stiffness (AMAS) system.

METHODS Fifty consecutive patients with suspected coronary artery disease (aging 59.2±10.0 years; 36 males) were enrolled. Carotid-femoral pulse wave velocity (cfPWV) assessment was performed by three observers, two experienced sonographers and one cardiologist. The results measured by AMAS system ($cfPWV_A$) were compared with that by standard manual method ($cfPWV_M$) to evaluate the agreement and reproducibility. This study was approved by Ethics Committee of Tangdu Hospital, Fourth Military Medical University (No. 201909-01) and conformed to the principles of the Declaration of Helsinki.

RESULTS Measurements of cfPWV showed no significant difference neither between methods nor observers (P>0.05), and the agreement between $cfPWV_A$ and $cfPWV_M$ was excellent with an intraclass correlation coefficient (ICC) of 0.915 (95% CI: 0.876–0.942). Specifically, the ICCs between $cfPWV_M$ and

cfPWV$_A$ measured by the sonographers were 0.941 and 0.889. The cfPWV$_A$ by the cardiologist was 8.04±1.29 m/s, showing an ICC of 0.866 with cfPWV$_M$ by a well-trained sonographer (8.07±1.39 m/s). Bland-Altman plots further showed the good agreement between the two methods. In addition, time consumption of AMAS system was significantly less than that of manual method (122±35 s *vs.* 455±105 s, P<0.0001), saving about 73% of the time. The intra- and inter-observer variability demonstrated both methods had excellent reproducibility in practice.

CONCLUSIONS The Doppler ultrasound AMAS system may be used as an automatic, reliable, time-saving and reproducible method for aortic PWV measurement and AS evaluation in routine clinical settings.

GW31-e0415

Visit-to-visit fasting glucose variability in young adulthood and cardiac structure and function at midlife

Zhenyu Xiong[1], Peihan Xie[1], Xiaodong Zhuang[1], Jiaying Li[2], Xinxue Liao[1]
[1]Department of Cardiology, the First Affiliated Hospital, Sun Yat-sen University
[2]Department of Cardiology, Nanfang Hospital of Southern Medical University, Guangzhou, China

OBJECTIVES To investigate whether visit-to-visit fasting glucose (FG) variability in young adulthood is associated with cardiac structure and function at midlife.

METHODS Participates from the community-based cohort study of Coronary Artery Risk Development in Young Adult (CADIA) were included at the baseline age of 18–30 during 1985–1986 (Year 0). FG was measured at Year 0, 2, 10, 15, 20 and 25. And echocardiographic evaluation of cardiac structure and function was conducted at year 25.

RESULTS A total of 2601 young adults mean (SD) aged at 24.9 (3.6) of which 57.3% were women and 46.7% were black had been included in the study. After multivariable adjusted, Higher FG variability (one-SD increase) was associated with higher E/e' (SD$_{FG}$, β [SE], 0.307 [0.094], P<0.01; CV$_{FG}$, β [SE], 0.204 [0.078], P<0.01; ARV$_{FG}$, β [SE], 0.178 [0.085], P<0.05), higher SD$_{FG}$ and CV$_{FG}$ (one-SD increase) are associated with lower e' respectively (SD$_{FG}$, β [SE], −0.214 [0.080], P<0.01; CV$_{FG}$, β [SE], −0.141 [0.066], P<0.05;), and higher ARV$_{FG}$ is associated with higher LVMI (β [SE], 1.240 [0.618], P<0.05).

CONCLUSIONS Higher fasting glucose variability in adulthood is associated with more hypertrophic left ventricular (LV) myocardium and poorer LV diastolic function in midlife.

GW31-e0560

Quantitative analysis of renal blood flow during thoracic endovascular aortic repair in Type B aortic dissection using syngo iFlow

Kun Fang[1], Jiawei Zhao[1], Mingyao Luo[1], Yunfei Xue[1], Hui Wang[2], Luming Ye[3], Xuelan Zhang[4], Liancun Zheng[4], Chang Shu[1,2]
[1]Department of Vascular Surgery, National Center for Cardiovascular Disease, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
[2]Department of Vascular Surgery, The Second Xiangya Hospital of Central South University, Changsha, Hunan, China
[3]Department of Advanced Therapy, Siemens Healthineers, Beijing, China
[4]School of Mathematics and Physics, University of Science and Technology Beijing, Beijing, China

OBJECTIVES To quantitatively assess the haemodynamic changes in the renal artery and parenchyma during thoracic endovascular aortic repair (TEVAR) in patients with type B aortic dissection (TBAD) by *syngo* iFlow.

METHODS From April 2017 to September 2019, medical records of 51 patients (43 men and 8 women) with TBAD undergoing TEVAR were recruited. Their pre- and post-procedural digital subtraction angiography (DSA) images were converted into colour-coded maps by *syngo* iFlow for quantitative comparison. Time–intensity curves and related parameters including the average peak ratio (avg. Pr), average delayed time to peak (avg.dTTP), and average area under the curve ratio (avg.AUCr) of the renal arteries and renal cortex were obtained and analysed.

RESULTS One hundred two series including 51 pre-operative and 51 post-operative image datasets were successfully post-processed. For the renal arteries, no significant difference was found between the pre- and post-operative avg.dTTP (P=0.179), but the avg. Pr increased from 0.56±0.28 to 0.75±0.32 (P<0.001) and the avg.AUCr increased from 0.66±0.26 to 0.90±0.38 (P<0.001). For the renal cortex, statistical differences were detected between pre- and post-procedural parameters: the avg.dTTP decreased from 6.52±2.09 to 5.73±2.04 (P=0.001), the avg. Pr increased from 0.30±0.13 to 0.37±0.14 (P=0.001) and avg. AUCr increased from 0.72±0.32 to 0.99±0.80 (P=0.017).

CONCLUSIONS *syngo* iFlow provides a novel quantitative method for evaluating renal haemodynamic changes in patients with TBAD undergoing endovascular treatment. Time-intensity curve parameters may facilitate intraprocedural evaluation of renal blood flow and perfusion to complement the colour-coded map.

GW31-e0581

Study on the characteristics of carotid artery wall shear stress in patients with Type 2 diabetes mellitus using ultrasound vector flow imaging

Zhaohuan Li, Lixue Yin
Cardiovascular Ultrasound and Non-invasive Cardiology Department, Sichuan Academy of Medical Sciences, Sichuan Provincial People's Hospital, 610072

OBJECTIVES To quantitatively analyze the characteristics of carotid artery wall shear stress (WSS) in patients with type 2 diabetes mellitus (T2DM) using ultrasound vector flow imaging (V-flow) and to elucidate the relationship between WSS and atherosclerosis.

METHODS Forty nine patients with type 2 diabetes (age 63.47±11.87 years, 25 males) who were treated in our hospital from November 2018 to February 2019 were selected as the DM group, while 20 healthy volunteers (age 57.60±12.10 years, 13 males) were the control group. V-flow examination of bilateral common carotid artery was performed with Mindri Resona 7 color doppler ultrasound diagnostic instrument and l9-3u linear array probe (frequency 3.0–9.0 MHz). The maximal wall shear stress (WSSmax) and mean wall shear stress (WSSmean) in the middle and near the bifurcation of the bilateral common carotid artery were obtained. According to the combination of hypertension (HPT), the DM group was further divided into DM+HPT group (n=26) and DM+ non-HPT group (n=23), and the differences of WSSmax and WSSmean in the corresponding common carotid artery between the DM group and each subgroup and the control group were compared. The relationship between WSS and IMT were analyzed.

RESULTS Both WSSmax and WSSmean in the middle segment of the common carotid artery in the DM group were significantly lower than those in the control group (WSSmax: 2.39±0.51 Pa and 2.63±0.53 Pa, P=0.014; WSSmean: 0.81±0.25 Pa and 1.03±0.24 Pa, P=0.000). WSSmean near the bifurcation of the common carotid artery in the DM group was significantly lower than that in the control group (0.73±0.26 Pa and 0.88±0.23 Pa, P=0.002). WSSmean in the middle and near the bifurcation of the common carotid artery in the DM+HPT group and the DM+ non-HPT group were all lower than that in the control group (at the middle: 0.76±0.24 Pa, 0.87±0.25 Pa and 1.03±0.24 Pa, P<0.05; near the bifurcation: 0.69±0.26 Pa, 0.77±0.25 Pa, and 0.88±0.23 Pa, P<0.05). WSSmean at the middle and near the bifurcation of the common carotid artery was negatively correlated with IMT at the same site (r=−0.158, P=0.009).

CONCLUSIONS In the patients with T2DM combined with hypertension or not, WSSmean in the middle and near the bifurcation of the common carotid artery was significantly decreased. The sensitivity of WSSmean may be superior to WSSmax. There was a weak negative correlation between WSSmean and IMT, which suggests that WSSmean might be related to the occurrence and development of atherosclerosis.

GW31-e0609

Left ventricle energy loss in normal and hypertensive subjects

Xiaowen Zuo[1,2], Huaping Jia[1], Xiao Zhou[3], Jing Wang[3], Yang Mu[3], Manli Yuan[1], Can Zhang[1], Guang Zhi[3]
[1]Department of Ultrasound Medicine, PLA Strategic Support Force Characteristic Medical Center, Beijing, China
[2]Medical School of Chinese PLA, Beijing, China
[3]Department of Cardiology, First Medical Center of Chinese PLA General Hospital, Beijing, China

OBJECTIVES Vector flow mapping (VFM) is a novel echocardiographic technique that enables visualization of the intraventricular flow. We aimed to evaluate the index of hemodynamic dissipative energy loss in patients with hypertension and to compare it with normal subjects.

METHODS Transthoracic echocardiography was performed in eighty-nine hypertensive patients with preserved left ventricular ejection fraction, fifty-one with left ventricular hypertrophy (LVH group) and thirty-eight without LVH (non-LVH group). Forty-two healthy volunteers were enrolled as the control group. Four points during the cardiac cycle were determined: rapid filling period, slow filling period, atrial contraction period, and LV rapid ejection period.

RESULTS The average energy loss of diastole in the LVH group increased significantly (controls vs. non-LVH vs. LVH: 7.07±0.91 vs. 12.44±3.14 vs. 16.29±3.17 [J/(s m^3)]). The value of EL during each period of the cardiac cycle in the LVH group was much higher than that in the control group. As a consequence of the abnormalities, the fluid dynamics increase the instability of the

flow during the LV rapid filling period and slow filling period. Therefore, EL in the LVH group was the highest among the three groups during these two periods. The most appreciable difference during the atrial contraction period was observed in the non-LVH group and was the greatest among the three groups. (controls vs. non-LVH vs. LVH: 6.96±3.64 vs. 8.66±2.55 vs. 10.64±2.88 [J/(s m^3)]). With the low early diastolic atrioventricular gradient and reduction in LA conduit volume, reduction in early diastolic emptying is compensated by forceful atrial contraction to maintain an optimal end-diastolic volume. The source of flow acceleration in the LV is enhanced, which makes the flow more turbulent. Therefore, EL in the non-LVH group was found to be significantly increased during the atrial contraction period.

CONCLUSIONS A new index, EL, was employed in this study to evaluate the impaired blood flow dynamics during diastole. The diastolic EL may be a sensitive indicator of early LV cardiac dysfunction in patients without hypertrophy.

CARDIOVASCULAR NURSING

GW31-e0131

Discussion on the level of protection, knowledge, behavior and nursing measures of patients with cardiovascular disease under the novel coronavirus pneumonia

Tiantian Cui, Pengbo Zhu, Xiaoli Wu, Qing Li
The Third Affiliated Hospital of Sun Yat-sen University

OBJECTIVES To understand the knowledge, attitude and practice of novel coronavirus pneumonia in inpatients in cardiovascular medicine, summarize and analyze the existing nursing deficiency factors, and implement related nursing measures based on this to improve the level of knowledge, attitude and practice in inpatients in cardiovascular medicine.

METHODS Randomly selected 30 inpatients with cardiovascular medicine in a third-level hospital to conduct a questionnaire survey, statistical analysis of the survey results, and based on PDCA management method to take care intervention measures for inpatients in cardiovascular medicine. P (plan stage): Based on the investigation results, analyze the main problems found and formulate corresponding care plans. D (implementation stage): (1) The primary nurses use one-on-one, face-to-face methods to teach epidemic knowledge to the inpatients. For older or lower-educated patients, use TV to broadcast the epidemic prevention video to help them learn more. (2) Explain the correct steps of teaching the seven-step washing method and taking off the mask. And to produce and distribute propaganda pictures. (3) Strengthen protective attitude and psychological care: Based on the health belief model, psychological care is given to enable patients to actively cooperate with prevention and control. (4) Medical staff should strictly implement ward management measures. C (inspection stage): the head nurse supervises the implementation of nursing measures, and records problems in a timely manner in order to improve in the follow-up nursing work. A (evaluation stage): one week after the implementation of the corresponding nursing measures, the patients were again surveyed on the questionnaire of knowledge, belief, behavior, and the relevant results were analyzed. The results were statistically analyzed using SPSS21.0 software.

RESULTS Analysis of the survey results revealed that the current knowledge, behavior, and behavior of the patients were at a moderate level, with a score rate of 78.99%. The main problems are as follows: (1) The patient's protection knowledge is poor, and the score rate is 76.50%. Age is inversely related to protection knowledge. (2) The patient has panic about the outbreak and epidemic of pneumonia. (3) The patient's compliance with protective behavior is more general, and he does not understand the correct method and steps of washing hands and taking off the mask, and has wrong habits and cognition. After the implementation of nursing measures, the total score of the patient's knowledge, belief and behavior has improved significantly, with a score rate of 85.64%. Among them, the scores of each part of protection knowledge, belief and attitude and protection behavior have improved. The difference was statistically significant (P<0.05).

CONCLUSIONS Cardiovascular disease patients generally have a low level of knowledge, attitude and practice in response to the novel coronavirus pneumonia epidemic. Effective nursing interventions can improve the patient's protection level and attitude, which has positive significance for the novel coronavirus pneumonia epidemic.

GW31-e0138

Effect of different pre-operative educational methods on cardiac autonomic nervous function in patients with coronary angiography

Yehui Jin, Zhiyi Xie
Department of Cardiology, the Second Hospital of Hebei Medical University, Shijiazhuang 050000, China

OBJECTIVES To investigate the effect of different pre-operative educational methods on cardiac autonomic nervous function in patients with coronary angiography

METHODS A total of 400 patients with coronary atherosclerotic heart disease (CHD) admitted at our hospital from September 2018 to September 2019 successfully undergoing coronary angiography was selected, whose clinical data were recorded. All patients were randomly divided into two groups, including 200 cases in routine pre-operative education group and 200 cases in diversified pre-operative education group. And then, all patients were measured for heart rate variability (HRV) within 48 hours of admission and within 48 hours after pre-operative education. Self-rating anxiety scale (SAS) and pre-operative education effect questionnaire were performed.

RESULTS There was no significant difference in HRV indicators, SAS scores before pre-operative education and questionnaire's scores after pre-operative education between groups (P>0.05). After pre-operative education, the SDSD showed significant difference between groups, however, the other HRV indicators did not show any difference. Meanwhile, the SAS scores were significantly decreased in diversified pre-operative education group than in routine pre-operative education group (P<0.05).

CONCLUSIONS Diversified pre-operative education can improve cardiac autonomic nervous function and SAS scores in patients undergoing coronary angiography in the superiority of traditional pre-operative education mode.

GW31-e0355

Effect of a telephone-based self-management program Led by nurses on quality of life and cardiac autonomic nervous function

Yehui Jin, Zhiyi Xie
Department of Cardiology, the Second Hospital of Hebei Medical University

OBJECTIVES To investigate the effect of a telephone-based self-management program led by nurses on quality of life and cardiac autonomic nervous function.

METHODS A total of 60 patients with heart failure underwent medical treatment admitted to our hospital from January 2019 to December 2019, including 30 heart failure patients in the experimental group and 30 heart failure patients in the control group, whose clinical data were recorded. The experimental group received the telephone-based self-management program, which included a 30-minute face-to-face education talking and six telephone consultation and education talkings. The face-to-face education talking was performed at the first visit to the outpatient clinic. Thereafter, biweekly telephone consultations and education talkings were done for 3 months. And then, all patients were measured for heart rate variability (HRV) within 48 hours before discharge and after 3 months. Health-related quality of life will be measured by the Minnesota Living Heart Failure Questionnaire (MLHFQ).

RESULTS The baseline clinical characteristics and health-related quality of life of the patients from both groups were observed to be statistically similar. Three months after discharge, both groups showed statistically significant improvements in the baseline parameters based on the MLHFQ (P<0.05). The patients followed up through the telephone-based self-management program showed a greater increase in MLHFQ after 3 months, although the increase was not significantly greater than that of the control group. There was no significant difference in HRV indicators between groups. After 3 months of discharge, the SDNN, PNN50, RMSSD, HF and LF/HF showed significant difference between groups, however, the other HRV indicators did not show any difference (P<0.05).

CONCLUSIONS The telephone-based self-management program is an effective method to improve quality of life and cardiac autonomic nervous function in heart failure patients.

GW31-e0368

Effect of a nurse-coordinated prevention program on cardiovascular risk and lipid management in very high-risk atherosclerotic cardiovascular disease patients

Yaqui Jin, Zhiyi Xie
Department of Cardiology, the Second Hospital of Hebei Medical University

OBJECTIVES To investigate the effect of a nurse-coordinated prevention program on cardiovascular risk and lipid management in very high-risk atherosclerotic cardiovascular disease patients.

METHODS A total of 100 patients with very high-risk atherosclerotic cardiovascular disease underwent medical treatment admitted to our hospital from January 2019 to December 2019, including 50 patients in the experimental group and 50 patients in the control group, whose clinical data were recorded. The experimental group received the nurse-coordinated prevention program, consisting of six outpatient nurse clinic visits with a 30-minute face-to-face education session and six telephone consultation and education sessions, focusing on healthy lifestyles, biometric risk factors and medication adherence, in addition to usual care. Lipid and 10-year cardiovascular mortality risk as estimated by Systematic Coronary Risk Evaluation (SCORE) were evaluated at discharge and at 6 months in both groups.

RESULTS The baseline clinical characteristics from both groups were observed to be statistically similar. Six months after discharge, both groups showed statistically significant improvements in the lipid management (P<0.05). The patients followed up through the nurse-coordinated prevention program showed a greater increase in lipid goal completion rate after 6 months of discharge, although it was not significantly different than that of the control group. The experimental group showed a decreased SCORE after 6 months of discharge, however, it was not significantly different than that of the control group.

CONCLUSIONS The study showed a trend reduction of lipid goal completion rate and 10-year cardiovascular mortality risk with the nurse-coordinated prevention program in very high-risk atherosclerotic cardiovascular disease patients.

GW31-e0625

Psychometric properties of the Chinese (Mandarin) version of HeartQoL among patients post-acute coronary syndrome

Huijing Zou, Xi Cao, Sek Ying Chair
The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong

OBJECTIVES Assessment of health-related quality of life is an important component and increasingly used in contemporary clinical practice and research trials. The HeartQoL, a recently developed core heart disease-specific questionnaire, allows assessment and comparison of disease-sensitive health-related quality of life across the spectrum of cardiac diseases. The aim of this study was to evaluate the psychometric properties of the Chinese version of the HeartQoL among patients post-acute coronary syndrome.

METHODS This study involved a cross-sectional survey and a test-retest survey. Eligible patients were invited to complete the Chinese HeartQoL, 9-item Patient Health Questionnaire (PHD-9), 7-item Generalized Anxiety Disorder (GAD-7), 10-item Perceived Stress Scale (PSS-10), and sociodemographic and clinical questionnaire. Internal consistency reliability, convergent and divergent validity, and discriminative validity were assessed using cross-sectional data and then test-retest reliability was assessed using longitudinal data in a subsample of 50 patients.

RESULTS Floor and ceiling effects were absent from each subscale and global scale of the Chinese HeartQoL. Internal consistency (Cronbach's alpha ranging from 0.829 to 0.870) and test-retest reliability (intra-class correlation >0.90) were satisfactory. Convergent and divergent validity were supported as emotional HeartQoL strongly correlated with PHD-9 (r=–0.518) and GAD (r=–0.573) and physical HeartQoL moderately correlated with PHD-9 (r=–0.369) and GAD-7 (r=–314) (all P<0.001). Discriminative validity was largely verified as ten of twelve (83.3%) known-group comparisons were confirmed.

CONCLUSIONS The Chinese HeartQoL showed sound psychometric properties in patients post-acute coronary syndrome, suggesting its potential as a reliable and valid instrument for clinicians and researchers to measure HRQL.

CLINICAL LABORATORY OF CARDIOVASCULAR DISEASE

GW31-e0023

Clopidogrel resistance in patient undergoing percutaneous coronary intervention (PCI): a single center experience in Evercare Hospital Dhaka

Dr. Azfar Hossain Bhuiyan, Ahm Waliul Islam, Shams Munwar
Evercare Hospital Dhaka

OBJECTIVES Dual antiplatelet (DAPT) treatment with Clopidogrel and Aspirin after percutaneous coronary intervention (PCI) is common practice for the interventionist to prevent thrombotic event after coronary stent placement. In spite of this, a significant number of thrombotic events still occur. Exact data on our population regarding the thrombotic events after successful PCI and uses of DAPT not yet available. Therefore, we have carried out this study to see sensitivity resistance in our population by measuring Clopidogrel resistance test (CYP2C19 assay).

METHODS Total 311 patients have enrolled in this observation non-randomized prospective cohort. The patient who had a single-center percutaneous coronary intervention (PCI) at our center or elsewhere, and on Aspirin, were selected for the study. Clopidogrel resistance was measured by CYP2C19 assay at our hospital molecular lab.

RESULTS Among the 311 patients, male 252 and female 59. The average age for the male: female was 59:61 years. Clopidogrel resistant test was performed by Real-Time PCR. Total 176 (56.6%) patients are Clopidegrol resistant or positive and 135 (43.4%) patients are Negative. Among the resistant case, 26 (8.4%) patients are Homozygous Positive with probable genotype CYP2C19*2 (*2/*2) and 150 (48.2%) patients were Heterozygous positive with probable genotype CYP2C19 (*1/*2).

CONCLUSIONS In this single-center, observational prospective cohort, we found quite a significant (56.6%) number of patients are Clopidegrol resistant. Therefore, we may need to double the Clopidogrel dose and or to swap to other antiplatelet such as Ticagrelor or prasugrel, thus to prevent stent thrombosis or restenosis.

GW31-e0255

Environment play a key role in the number of platelet?

Liying Gong, Xiaoli Wu, Hongliang Kong
The People's Hospital of Liaoning Province

OBJECTIVES The number of platelets is associated with many disease, which is influenced by many factors, such as race, environment, gender, age and so on. But what is the key factor?

METHODS The present study is conducted on three healthy population: 3210 Tibetan in plateau (altitude: 4507 m), 1708 plain people after 6 months settled in plateau (altitude: 4507 m), 2501 plain Han in Shenyang (altitude: 0 m). The numbers of platelets in the mentioned three groups are tested by Automatic Hematology Analyzers. Each population was divided into groups based on gender and then on age range, from 21 to 70 years old, every 10 years old as a group. Regardless of gender and age, each population was also divided into four group base on HGB concentration. HGB concentration are the lowest in group1, while highest in group 4.

RESULTS Constituent decline in platelet count was observed with age in each population, whether in male or female. In male, the Han population who migrated to the plateau decreased the most in platelet count (48.2 *vs.* 22.7% in Tibetan, P<0.001, and 14.7% in plain Han, P<0.001). In female, the results are similar (38.9 *vs.* 27.0% in Tibetan P<0.001, and 11.3% in plain Han, P<0.001). The number of platelet in female is higher than that in male at the same age range of each population. Plain female, age at 21–30 y, have the highest platelet count ((273±67.3)×10^9/L), while platelet count is the lowest ((109±60.6)×10^9/L) in immigrated male, age at 61–70 y. Constituent decline in platelet count was observed with increase of HGB concentration in plain population and Tibetan. In immigrated population, the number of platelet decreased by 25.5% from group 1((217.7±65.1)×10^9/L) to group 4 ((162.6±72.3)×10^9/L), has no significant difference with the decrease (27.6%, P>0.05) in Tibetan (group1: ((271.2±93.6)×10^9/L), group4: (196.3±61.8)×10^9/L), but significant difference with the decrease (2.4%, P<0.001) in plain population (group1: (254.6±64.7)×10^9/L, group4: (248.8±58.4)×10^9/L).

CONCLUSIONS The trend of platelet count in the three population is similar when grouped as gender or age range. But regardless the two factors, the platelet count in immigration population has the significantly diffident to plain population, so this implies that environment may be the main factor affecting platelet count, rather than geography or race. It may be caused by the feedback mechanism of the self-regulation in order to adapt to the harsh environment of the plateau. The conclusion remind us that the number of platelet should be take attention in immigrated population to plateau to avoid causing thrombosis or bleeding.

TRADITIONAL CHINESE MEDICINE

GW31-e0039

Virtual screening and network pharmacology-based synergistic mechanisms identification of multi-components contained in Guanxin V against coronary artery disease

Bo Liang[1], Xiaoxiao Zhang[1], Ning Gu[2]
[1]Nanjing University of Chinese Medicine
[2]Nanjing Hospital of Chinese Medicine Affiliated to Nanjing University of Chinese Medicine

OBJECTIVES Guanxin V (GXV), a traditional herbal mixture, has been widely used to treat coronary artery disease (CAD) in clinical practice in China. However, the research on the active components and underlying mechanisms of GXV for CAD is still scarce.

METHODS A virtual screening and network pharmacological approach was utilized for predict pharmacological mechanism of GXV for CAD. The active compounds of GXV based on various TCM-related databases were picked out and then the potential targets of these compounds were fished. Then after the CAD target were built through nine databases, a PPI network was constructed based on the matching GXV and CAD potential targets to analyze the interactions among these targets and the hub targets were screened by MCODE. Moreover, Metascape was applied to GO and KEGG functional enrichment. Finally, HPLC fingerprints of GXV were established.

RESULTS A total of 119 active components and 121 potential targets shared with CAD of GXV were obtained. The results of functional enrichment indicated several GO biological processes and KEGG pathways of GXV mostly

participated in the therapeutic mechanisms. Furthermore, 7 hub MCODEs of GXV were collected as potential targets, implying the complex effects of GXV mediated protection against CAD. Six specific chemicals were identified.

CONCLUSIONS GXV could employ for CAD through the molecular mechanisms, which involved complex interactions between multiple compounds and targets, predicted by virtual screening and network pharmacology. Our study provided a new herbal medicine against CAD and has increased the understanding on the molecular mechanisms of GXV against CAD.

GW31-e0040

Guanxin V for coronary artery disease: a retrospective study

Bo Liang[1], Ning Gu[2]
[1]Nanjing University of Chinese Medicine
[2]Nanjing Hospital of Chinese Medicine Affiliated to Nanjing University of Chinese Medicine

OBJECTIVES Guanxin V (GXV), a traditional herbal mixture, has been widely used in clinical practice for the treatment of coronary artery disease (CAD). This retrospective study was designed to assess the safety and effectiveness of GXV for CAD.

METHODS In our study, December 2006 to January 2009, 101 patients with CAD from Nanjing Hospital of Chinese Medicine Affiliated to Nanjing University of Chinese Medicine were enrolled of whom 52 patients received GXV plus guideline-recommended medical therapy (GMT) (GXV group), 49 patients received GMT alone (GMT group). The general clinical information, traditional Chinese medicine syndrome score (TSS), the therapeutic effects, 6-minute walk test (6MWT), adverse events, echocardiography and laboratory information were collected and analyzed pre-and post-treatment.

RESULTS We did not find differences in the information between the two groups before treatment. Patients in the GXV group had decreased TSS ($P<0.0001$) and increased therapeutic effects ($P=0.763$) and 6MWT ($P<0.0001$) than those in the GMT group and there were no significant differences in safety between the two groups. Moreover, Patients in the GXV group improved ejection fraction, cardiac output, and stroke volume ($P=0.2113$, 0.0001, 0.0002, respectively), and dropped BNP ($P=0.3856$) compared with those in the GMT group.

CONCLUSIONS Superiority in the GXV group for patients with CAD was demonstrated over the GMT group for both the safety and effectiveness endpoints. This suggests that GXV is a potentially safe and effective treatment for GAD patients.

GW31-e0269

Therapeutic efficacy and safety of traditional Chinese medicine herbal formula BushenHuoxue decoction for coronary heart disease: a systematic review and meta-analysis

Lanchun Liu[1,2], Qiyuan Mao[1], Chao Liu[1,2], Lian Duan[1,2]
[1]Department of Cardiology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China
[2]Graduate School, Beijing University of Chinese Medicine, Beijing, China

OBJECTIVES This systematic review and meta-analysis aimed to evaluate the efficacy and safety of BushenHuoxue Decoction (BSHXD), which can nourish kidney and promote blood circulation in coronary heart disease.

METHODS This study has been registered on the PROSPERO platform (ID: CRD42020173741). Medline, EMBASE, Cochrane Central Register of Controlled Trials, Chinese National Knowledge Infrastructure, and Wanfang Database were searched up to March 1, 2020 for randomized control trials in treating coronary heart disease. Two reviewers screened the literature separately, extracted information and assessed the risk of bias in the included studies, then conducted a meta-analysis using STATA software. We assessed funnel plot asymmetry using Egger's test, and defined significant publication bias as a P value <0.1.

RESULTS A total of 901 patients were included in 10 randomized controlled trials (RCTs). Compared with antianginal drugs, BushenHuoxue decoction plus antianginal drugs (BPAD) significantly reduced the frequency of angina attacks [SMD=−1.25, 95% CI (−1.79, −0.71), P=0.016], shortened the duration of angina [SMD=−1.37, 95% CI (−1.92, −0.81), P=0.015]. A subgroup analysis was conducted according to the year of publication and studies in the past five years had shown no difference in the electrocardiogram (ECG) efficacy between the test group and the control group [OR=1.42, 95% CI (0.79, 2.53), P=0.24]. Compared with antianginal drugs, BPAD could also reduce low density lipoprotein cholesterol (LDL-C) [SMD=−0.75, 95% CI (−1.07, −0.42)]. There were no significant differences in the effects of total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C) and the results had high heterogeneity ($I^2 \geq 75\%$), the sensitivity analysis found that its efficacy might be associated with the baseline levels of TC, TG, and HDL. Five studies reported adverse reactions and safety indicators such as blood, urine, liver and kidney function. Among them, 2 cases of nausea occurred in the treatment group and 1 case of diarrhea in the control group, but it could not be proved to be related to the effect of BSHXD. In view of the very limited reports on adverse reactions, no meta-analysis was conducted. Egger's test indicated that there was no significant publication bias in this analysis (P=0.024).

CONCLUSIONS Limited by the quality of the included studies, as well as potential reporting bias, the above conclusions still need to be verified by higher quality studies. Although further studies are needed to establish the optimal approach to the application of this treatment in practice, our findings clearly lend support to the use of Chinese Medicine Herbal Formula BSHXD in combination with antianginal drugs in the clinical management of patients with coronary heart disease.

GW31-e0417

The novel mechanism of Danqi pill against post-acute myocardial infarction heart failure through restoring autophagy flux

Yanyan Jiang, Xiaoping Wang, Qian Zhang, Weili Li, Yong Wang
Beijing University of Chinese Medicine

OBJECTIVES Autophagy plays an essential role in cardiac function, and disordered autophagy is associated with the progression of HF. Danqi pill, which is composed of Salvia miltiorrhiza Bunge and Panax notoginseng, has been proved to exert a definite effect on improving cardiac function in many large-scale randomized and controlled clinical trials. However, the effect of Danqi pill on autophagy has not been reported yet. This study aims to elucidate whether Danqi pill restores autophagy to protect against HF and its potential mechanism.

METHODS Left anterior descending ligation was performed to induce a HF rat model, H_2O_2-stimulated H9C2 cardiomyocytes model was conducted to clarify the effects and potential mechanism of Danqi pill. In vivo, Danqi pill (1.5 g/kg) were orally administered for four weeks and Fenofibrate (10 mg/kg) was selected as a positive group. In vitro, Danqi pill (10~200 μg/mL) was pre-cultured for 24 h and co-cultured with H_2O_2 stimulation for 4 h. Echocardiography, HE staining, Masson staining and serum detection were used to evaluate cardiac function. The regulatory effects of Danqi pill on key proteins of autophagy (including Beclin1, Atg3, Atg5, Atg7, LC3 II, P62, p-AMPK, p-mTOR, p-ULK1 and p-TSC) were detected by PCR, Western blot and Immunohistochemical techniques. Importantly, transmission electron microscopy and fluorescence GPF-mRFP-LC3 reporter system were combined to monitor autophagy flux. Furthermore, we utilized Compound C, a specific AMPK inhibitor, to validate the mechanism.

RESULTS Twenty-eight days after surgery, echocardiography results displayed that Danqi pill restored cardiac function in post-AMI HF rats evidenced by the increased values of EF and FS, and the reduced values of LVIDs and LVIDd. In vivo, HE staining and Masson staining photomicrographs suggested that Danqi pill could improve myocardial pathological changes. Meanwhile, Danqi pill alleviated the increased levels of BNP, CKMB and LDH in the model group. Transmission electron microscopy showed that Danqi pill increased the amount of autophagosomes. PCR, Western blot and Immunohistochemical results suggested that Danqi pill treatment could increase the levels of Beclin1, ATG3, ATG5, ATG7, LC3 II, p-AMPK and p-TSC, while decrease the levels of p62, p-mTOR and p-ULK1. These results indicated that Danqi pill could restore initiation of autophagy and autophagic flux, enhance the formation of autophagosomes, the mechanism was closely related to AMPK-TSC2-mTOR signaling pathway. In vitro, Western blot results of LC3 II, p62, p-AMPK, p-TSC, p-mTOR and p-ULK1 were consistent with those in vivo. The transfection of GFP-mRFP-LC3 adenovirus in H9C2 cells furtherly confirmed that Danqi pill could promote the formation of autophagosomes. Interestingly, utilization of Compound C abolished the effects of Danqi pill on autophagy flux and the expressions of p-TSC2, p-mTOR and p-ULK1, which demonstrated that Danqi pill could restore autophagic flux via AMPK-TSC2-mTOR signaling pathway.

CONCLUSIONS Danqi pill could improve cardiac function and protect against cardiomyocytes injury by restoring autophagy via regulating the AMPK-TSC2-mTOR signaling pathway. This study provides new insights into therapeutic strategies for clinical management of HF.

GW31-e0529

Network pharmacology based approach into the effect and mechanism of Qingre Jiedu recipe against heart failure

Qian Zhang[1], Xiaoping Wang[1], Weili Li[2], Yanyan Jiang[2], Linghui Lu[1], Qiyan Wang[2], Yong Wang[1,2], Wei Wang[1]
[1]College of Chinese Medicine, Beijing University of Chinese Medicine, Beijing 100029, China
[2]School of Life Sciences, Beijing University of Chinese Medicine, Beijing 100029, China

OBJECTIVES Heart failure (HF) remains a prevalent disease that contributes a high morbidity and mortality, while Qingre Jiedu (QJ) recipe (contains Lonicera japonica Thunb. And Scrophularia ningpoensis Hemsl.) has been

demonstrated to have remarkable cardio-protective efficacy against HF. The aim of this study is to observe the efficacy of QJ in HF model rats and H9C2 cells induced by hydrogen peroxide (H_2O_2), and to verify the underlying mechanisms.

METHODS The key components of QJ and its targets against HF were analyzed and selected by network pharmacology. The potential mechanisms that QJ regulates the progress of myocardial inflammation and fibrosis were verified in left anterior descending (LAD) artery ligation induced HF rats and H_2O_2-induced H9C2 cell lines. QJ at a dose of 0.823 g/kg/day was administrated to rats intragastrically for 28 days after surgery. After CCK-8 assay, QJ at a dose of 400 μg/mL was selected to treat H9C2 cells induced by H_2O_2.

RESULTS A screening of 31 components in QJ had led to the acquisition of 277 targets, while 814 genes from the Disgenet-Gene relating to the pathophysiology of HF were also collected. Eighty five common targets were shared between known HF-related targets and potential targets of QJ. *In vivo* experiment, echocardiography results showed that QJ could significantly improve heart function and attenuate inflammatory infiltration as well as collagen deposition. QJ could alleviate inflammatory responses evidenced by down-regulating the expressions of NF-κB and IL-6. Furthermore, QJ could effectively attenuate cardiac fibrosis through the inhibitions of expressions and depositions of collagen I and collagen III and regulated expressions of key proteins including Signal transducer and activator of transcription 3 (STAT3) and Matrix metalloproteinase 9 (MMP-9). Further experiments demonstrated that the effects of QJ were mediated through upregulation of Phosphatidylinositol 3 kinase (PI3K). The PI3K inhibitor LY294002 could abrogate the therapeutic effect of QJ *in vitro*.

CONCLUSIONS In conclusion, QJ protects cardiomyocytes and improves cardiac function by inhibiting inflammation and fibrosis via activation of the PI3K-AKT signaling pathway.

GW31-e0542

Experimental study on Bushen Kangshuai tablet regulating inflammation and autophagy in atherosclerosis through Sirt1-FoxO1 pathway

Xiaochen Guo[1], Peng Yuan[2], Xinnong Chen[2], Junping Zhang[1]
[1]First Teaching Hospital of Tianjin University of Traditional Chinese Medicine
[2]Tianjin University of Traditional Chinese Medicine

OBJECTIVES We established high-fat diet induced atherosclerosis model in ApoE$^{-/-}$ mice and observed the effect of Bushen Kangshuai Tablet on the expression of ICAM-1, IL-1β, LC3B, Sirt1 and FoxO1 in early atherosclerosis in order to explore whether Bushen Kangshuai Tablet can induce autophagy and inhibit inflammatory response during atherosclerosis development.

METHODS Twenty-four ApoE$^{-/-}$ mice with C57BL/6J background were randomly divided into model group, Bushen Kangshuai Tablet group and simvastatin group. All three groups were given a high-fat diet (21% fat and 0.15% cholesterol) and C57BL/6J mice were used as control group and given an ordinary diet. After 12 weeks of administration, blood samples were taken to determine biochemical indicators of lipids. Pathological morphological changes of the aorta were observed by HE staining. The expression of ICAM-1, IL-1β, LC3B, Sirt1 and FoxO1 in aorta was detected by immunohistochemistry.

RESULTS After 12 weeks of high-fat diet, compared with control group, the expression of TC, TG, and LDL-C in model group was significantly increased, HDL-C was significantly decreased; the intima of the aorta was significantly thickened and formed AS plaques. The inflammation-related markers ICAM-1 and IL-1β were significantly increased, the autophagy protein LC3B was significantly decreased, and Sirt1 and FoxO1 protein expression were decreased ($P<0.01$). Compared with model group, Bushen Kangshuai Tablet group and simvastatin group up-regulated the level of HDL-C ($P<0.05$ or $P<0.01$), and the pathological morphology of aorta was improved. At the same time, the inflammation-related markers ICAM-1 and IL-1β were significantly decreased, the expression of autophagy protein LC3B was increased, and Sirt1 and FoxO1 protein expression were increased ($P<0.01$).

CONCLUSIONS Bushen Kangshuai Tablet can inhibit the formation of atherosclerosis, and have protective effects on the aorta. The mechanism may be achieved through regulating Sirt1-FoxO1 pathway to play an anti-inflammatory role and promote autophagy during atherosclerosis development.

GW31-e0603

Mechanism of Wenxin decoction in treating coronary heart disease based on network pharmacology and transcriptome sequencing

Yawen Deng, Jun Li
Guang'an men Hospital of China Academy of Chinese Medical Sciences

OBJECTIVES To screen WXT medicinal ingredients and core targets of treatment on CHD, to explore mechanism of Wenxin Decoction (WXT) in the treatment of coronary heart disease (CHD) through omics and sequencing methods to validate the possible therapeutic mechanism of WXT intervening in CHD.

METHODS By querying 15th edition of Chinese Pharmacopoeia, using ETCM, SymMap, and TCMSP databases to screen the medicinal ingredients; through GeneCards, CHD@ZJU V3.0 databases to screen the human target of CHD. Using Coxpedia database to find co-expressed genes with similar gene expression profiles of WXT and CHD, and KEGG pathways obtained from Metascape. By selecting one case of peripheral blood samples of subjects with CHD observed in ethically approved clinical studies using WXT, one case was set as the blood sample of CHD patients who did not use WXT as a control, using transcriptome second-generation sequencing methods to isolate the white blood cells, extract the RNA, and detect the differentially expressed genes for bioinformatics analysis. Using GSEA to find the differentially expressed gene significance GO entries and the involved KEGG signaling pathway.

RESULTS A total of 137 human targets of WXT were obtained. The top pivot targets screened after PPI interaction network of WXT: IL-6, TP53, PTGS2, INS, MYC, MMP9, TNF, CSF2, ALB, IL4. Cluster analysis showed that there were 8 clusters in the therapeutic target network, and the largest cluster consisted of 39 target proteins. Gene co-expression analysis showed that 4 co-expressed genes of Wenxin Decotion and CHD have in common, namely CYP1A2, F2, CYP2C8 and APOM. The significant biological processes involving: inflammatory response, lipid metabolism, cytokines, oxygen levels, biological metabolic processes of reactive oxygen species, blood circulation, cell migration, apoptosis pathways, oxidative stress, lipid biosynthesis. Significant KEGG pathways including: PPAR signaling pathway, PI3K-Akt signaling pathway, MARK signaling pathway, adipocytokine signaling pathway, thyroid hormone signaling pathway, estrogen signaling pathway, cGMP-PKG signaling pathway ($P<0.01$). Analyzed the clinical blood samples of one patient twice before and after by transcription sequencing method, and 769 differentially expressed genes obtained from WXT intervention in CHD.347 genes were up-regulated and 422 genes were down-regulated. GSEA were used to perform GO enrichment and KEGG enrichment on differentially expressed genes. By comparing the network pharmacology prediction, the two have five target intersections, namely FLT4, PKIA, ACHE, SEC14L2 and NR3C2. Comparing the signal pathways of transcriptome sequencing with differential genes predicted by the network pharmacology, 8 overlapping signal pathways obtained: AGE-RAGE signaling pathway, PPAR signaling pathway, PI3K-Akt signaling pathway, and MARK signaling pathway in diabetic complications, Adipokine signaling pathway, thyroid hormone signaling pathway, estrogen signaling pathway, cGMP-PKG signaling pathway.

CONCLUSIONS There are 10 pivot targets for WXT in the treatment of CHD: IL6, INS, TNF, TP53, PTGS2, JUN, MYC, IL4, MMP9, ICAM1. WXT and CHD have four co-expressed targets in common. The mechanism of WXT intervention of CHD possibly correlated with regulating lipid metabolism, reducing inflammatory response, circulate blood flow and apoptosis pathway.

GW31-e0614

Functional gene module based identification of phillyrin as an anti-cardiac fibrosis agent

Lei Wang[1], Wuxia Zhang[2], Ziwen Lu[1], Baofu Wang[1], Yang Li[1], Jingjing Yang[1], Peng Li[2], Mingjing Zhao[1]
[1]Key Laboratory of Chinese Internal Medicine of Ministry of Education and Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing 100700, China
[2]College of Arts and Sciences, ShanXi Agricultural University, Taigu, Shanxi Province 030801, PR China

OBJECTIVES This study aimed to construct a gene functional module to represent the core pathological process of cardiac fibrosis (CF) and screen anti-fibrotic agents capable of decreasing the expression of the gene functional module.

METHODS First, three CF marker genes Postn, Ddr2, and Pdgfra were selected to identify the corresponding highest co-expressed genes in the genome-based transcriptional profiles of human hearts. Both the marker genes and the co-expressed genes formed the CF-related gene functional module (CFGM). Second, the correlation of the module with the CF process was measured in a collection of gene expression profiles of heart diseases to evaluate the participation of the functional module in heart diseases. Third, the anti-CF effects of phillyrin were predicted by the enrichment analysis of the module in the phillyrin-induced transcriptional profile. Finally, the myocardial infarction animal model was used to validate the cardioprotective and anti-CF effects of phillyrin experimentally.

RESULTS CFGM in the heart disease induced transcriptional profiles was analyzed, confirming the positive association of the fibrosis module with some heart diseases, including cardiomyopathy, heart failure, and MI. Phillyrin significantly decreased the expression of CFGM, suggesting that phillyrin might be a potential anti-CF agent. In terms of heart function, phillyrin could significantly improve the value of EF, FS, and LVAWs and reduce the value of LVIDs and LVESV, which was consistent with the effect of enalapril. In terms of

the heart structure, smaller infarction area and aneurysm, lower heart/weight ratio, orderly and smaller cardiomyocytes, and less amount of collagen were found in phillyrin-treated rats.

CONCLUSIONS The results showed that phillyrin was a novel antifibrotic agent in heart diseases.

GW31-e1183

Artificial intelligence and network pharmacology based investigation of Pharmacological mechanism of Qingying Huayu decoction in treating deep venous thrombosis

Jian Chen[1,2], Yongbing Cao[1,2], Yemin Cao[1,2], Cheng Zhao[1,2], Shikai Zhang[1,2], Zhiqiang Liang[1]
[1]Shanghai TCM-Integrated Hospital, Shanghai University of Traditional Chinese Medicine
[2]Institute of Vascular Anomalies, Shanghai Academy of Traditional Chinese Medicine

OBJECTIVES Qingying Huayu decoction (QYHY) is a typical Traditional Chinese medicine (TCM) for deep venous thrombosis (DVT) and contains various natural chemicals, such as quinones, saponins, flavonoids, and alkaloid. But its effective constituents and action mechanism are unknown. Therefore, this paper aims to explore the possible constituents and mechanism of QYHY in treating DVT.

METHODS In the current study, a highly efficient system for screening efficacy constituents of QYHY has been developed with the integration of intelligent data acquisition, data mining, network pharmacology, computer assisted target fishing, molecular docking and bioinformatics analysis. Then, TCM constituents and the related mechanisms have been preliminary verified by in vivo and vitro experiments.

RESULTS 1. 275 chemical components of QYHY were screened by network pharmacology. For the main drugs of QYHY (Jun herbs in Chinese), a total of 95 active components of rhubarb and 45 active components of buffalo horn were selected from TCM database, with a total of 355 targets. Network topology analysis and molecular docking revealed the important active components of TCM (deoxycorticosterone, cortisol, Cortexolone, triptolide, cincofen, etc.), target protein (PTGS2) and signal pathways (serotonergic synapses and oxytocin signaling pathways). The toxicity prediction of active components showed that the half lethal dose (LD50) of 17 active components were all above 495 mg/kg. MicroRNA enrichment analysis showed that there were 26 regulatory miRNA of rhubarb, 26 regulatory miRNA of buffalo horn, 12 regulatory miRNA of moutan bark, 11 regulatory miRNA of licorice, 23 regulatory miRNA of motherwort, 12 regulatory miRNA of purple grass and 10 regulatory miRNA of Radix Paeoniae Rubra. Among them, buffalo horn has the most specific regulatory miRNA. 2. We further found that QYHY can treat DVT by repairing vascular endothelial cells, controlling inflammation, dissolving and organizing thrombus in DVT rat. Compared to the DVT group, QYHY can significantly decrease the expression of miR-126a and miR-150, which may be regulated by JAK2/STAT3 signal pathway. Next, the differential gene analysis of two microarray data sets of HUVEC with knock-down miRNA-126 expression showed that there were 7 common up-regulated and 7 common down-regulated genes. Functional enrichment analysis of these 14 differential genes were involved in biological processes such as cell division, chromosome separation and regulation of chromosome segregation; molecular functions included extracellular matrix binding, death receptor binding and fibronectin binding; and cell components included condensed chromosome kinetochore, Ndc80 complex and chromosome. KEGG pathway includes Apoptosis – multiple species, small cell lung cancer and human papillomavirus infection. Finally, the molecular docking results showed that the STAT3 can be regulated by miR-126a due to the number of stable hydrogen atoms and the favorable amino acids identified in the binding pocket of the argonaute protein.

CONCLUSIONS In summary, the above results indicated that the application of both intelligent recognition technology and computerized network pharmacology might provide a pioneering approach for investigating the substance basis of TCM and searching lead compounds from natural sources, which specifically target miRNA-mRNA interactions.

GW31-e1191

Effect of Berberine on the oxidative stress of human coronary endothelial cells induced by intermittent high glucose

Wei Zhuang, Jianbin Gong
Jinling Hospital

OBJECTIVES In this study, a model was established for the damage of human coronary endothelial cells (HCAECs) by high glucose fluctuation, to investigate the protective effect of Berberine on the oxidative stress of human coronary endothelial cells injury induced by intermittent high glucose and explore the possible molecular mechanism.

METHODS HCAECs were cultured and divided into 5 groups: Group A was the normal blood glucose group (5.5 mmol/L glucose, NG); Group B was the persistent hyperglycemia group (25 mmol/L glucose, PHG); Group C was the intermittent high glucose group (5.5 mmol/L and 25 mmol/L glucose fluctuated every 24 hours, IHG); Group D was the fluctuation of hyperglycemia+Berberine intervention group (5.5 mmol/L and 25 mmol/L glucose +50 μmol/L Berberine fluctuated every 24 hours, IHG+BBR); Group E was a fluctuating hypertonic environment (without glucose, mannitol with the same concentration as IHG was added to maintain the same fluctuating hypertonic environment as IHG, OC). The cells of each group were changed into maintenance solution containing 2% serum concentration once every 24 hours, and were co-cultured for 7 days for later experiments. The cell viability of HCAECs was determined by MTT assay; TUNEL staining and flow cytometry were used to detect apoptosis; The levels of oxidative stress markers such as reactive oxygen species (ROS), malonic dialdehyde (MDA) and superoxide dismutase (SOD) were measured with corresponding detection kits. Western blotting was used to detect the expressions of NADPH oxidase 4 (Nox4), mRNA expression levels of Nox4 was detected by qRT-PCR.

RESULTS 1. Cell viability: Compared with the NG group, the PHG group decreased cell viability ($P<0.05$). Compared with the PHG group, the IHG group showed a more significant decrease in cell viability ($P<0.05$). After intervention with Berberine, the cell viability of IHG+BBR group was significantly enhanced compared with that of IHG group ($P<0.05$). 2. Apoptosis: Compared with the NG group, apoptosis was significantly increased in the PHG group ($P<0.05$), and apoptosis was more significant in the IHG group ($P<0.05$). Berberine was added into the intermittent high glucose, and the apoptosis of cells in the IHG+BBR group was significantly reduced compared with that in the IHG group ($P<0.05$). However, no significant apoptosis was observed in OC group ($P>0.05$). 3. Oxidative stress: Compared with the NG group and the OC group, ROS, Nox4 and MDA contents increased in the PHG group and the IHG group, while SOD activity decreased ($P<0.05$). However, comparing the PHG group with the IHG group, ROS, Nox4 and MDA levels in the IHG group were significantly higher than those in the PHG group, and SOD activity was significantly decreased ($P<0.05$). Compared with the IHG group, the production of ROS, Nox4 and MDA in the IHG+BBR group decreased, and SOD activity showed a significant increase trend ($P<0.05$).

CONCLUSIONS 1. Compared with persistent hyperglycemia, fluctuating hyperglycemia is more likely to cause oxidative stress in human coronary endothelial cells, reduce cell viability, and promote apoptosis. The effect of fluctuating high glucose on human coronary endothelial cells was more obvious, and the damage was independent of osmotic pressure. 2. Berberine has a significant protective effect on human coronary endothelial cells induced by fluctuating hyperglycemia. This mechanism may be related to the fact that Berberine alleviates oxidative stress of human coronary endothelial cells.

CARDIOVASCULAR PREVENTION & REHABILITATION

EPIDEMIOLOGY AND EVIDENCE-BASED MEDICINE

GW31-e0034

The comparison among different intensive statins or combination therapies with Niacin/Ezetimibe on carotid intima-media thickness: a network meta-analysis of randomized controlled trials

Hongwei Li[1,2], Xiaolin Xu[3], Runlu Sun[1,2], Qian Chen[1,2], Qi Guo[1,2], Junjie Wang[1,2], Zhijian He[1,2], Yuling Zhang[1,2]
[1]Cardiovascular Medicine Department, Sun Yat-sen Memorial Hospital, Sun Yat-sen University
[2]Guangdong Province Key Laboratory of Arrhythmia and Electrophysiology
[3]Department of Ultrasound, Sun Yat-sen Memorial Hospital, Sun Yat-sen University

OBJECTIVES Whether high-intensity statins are superior to combination therapies with niacin/ezetimibe on carotid intima-media thickness (CIMT) reduction remains unclear.

METHODS PubMed, EMBASE, Cochrane Library and Web of Science were searched, and 3539 articles published from 1992 to 2020 were retrieved. Randomized controlled trials (RCTs) for statins reporting CIMT levels in primary and secondary prevention were included. The quality of included studies was assessed by the Cochrance Collaboration's tool for assessing risk of bias. Stata software was utilized to perform traditional and network meta-analyses.

RESULTS Eighteen studies and twelve studies were included for traditional meta-analysis to compare the CIMT reduction between statins and no statins, as well as high-intensity statins/combination therapies and moderate/low-intensity statins, respectively. Both statin groups (standard mean difference, SMD=–0.207, 95% confidence interval, CI: –0.291 to –0.123, P<0.001) and the group of high-intensity statins, combination therapies (SMD=–0.270, 95% CI: –0.428 to –0.111, P=0.001) showed a significant CIMT reduction compared to control groups. Thirty-three studies including 8762 individuals were included in the network meta-analysis. The combination therapy with niacin ranked the first (mean rank: 1.7) to reduce CIMT, followed by high-intensity statins (mean rank: 2.2), the combination therapy with ezetimibe (mean rank: 2.3), and moderate/low-intensity statins (mean rank: 4.0). No significant publication bias was found in both traditional and network meta-analysis.

CONCLUSIONS Statins combined with niacin performed greater CIMT reduction compared to high-intensity statins and combination therapies with ezetimibe, which were more effective than moderate/low-intensity statins. The advantage of niacin-combined statin therapies to improve cardiovascular endpoint needs further validation RCTs.

GW31-e0083

Associations of long-term exposure to ambient air pollution with cardiac conduction abnormalities in Chinese adults: the CHCN-BTH cohort study

Han Cao, Bingxiao Li, Ling Zhang
Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University, and Beijing Municipal Key Laboratory of Clinical Epidemiology, Beijing, China

OBJECTIVES To investigate the associations of long-term exposure to air pollution and cardiac conduction abnormalities in Chinese adults and explore the susceptibility characteristics.

METHODS In 2017, a total of 27,047 participants aged 18–80 years were recruited from the baseline survey of the Cohort Study on Chronic Disease of Communities Natural Population in Beijing, Tianjin and Hebei (CHCN-BTH). The three year (2014–2016) average pollutant concentrations were assessed by a spatial statistical model for $PM_{2.5}$ and air monitoring stations for PM_{10}, SO_2, NO_2, O_3 and CO. Residential proximity to a roadway was calculated by neighborhood analysis. Associations were estimated by two-level generalized linear mixed models. Stratified analyses related to demographic characteristics, health behaviors, and cardiometabolic risk factors were performed. Two-pollutant models were used to evaluate the possible role of single pollutants.

RESULTS We detected significant associations of long-term air pollutant exposure with increased heart rate (HR), QRS and QTc, such that an interquartile range increase in $PM_{2.5}$ was associated with 3.63% (95% CI: 3.07, 4.19%), 1.21% (95% CI: 0.83, 1.60%), and 0.13% (95% CI: 0.07, 0.18%) changes in HR, QRS and QTc, respectively. Compared to the other pollutants, the estimates of $PM_{2.5}$ remained the most stable across all two-pollutant models. Similarly, significant associations were observed between living closer to a major roadway and higher HR, QRS and QTc. Stratified analyses showed generally greater association estimates in older people, males, smokers, alcohol drinkers, and those with obesity, hypertension and diabetes.

CONCLUSIONS Long-term exposure to ambient air pollution was associated with cardiac conduction abnormalities in Chinese adults, especially in older people, males, smokers, alcohol drinkers, and those with cardiometabolic risk factors. $PM_{2.5}$ may be the most stable pollutant to reflect the associations.

GW31-e0113

Elevated Lipoprotein(a) and risk of coronary heart disease according to different lipid profiles in the general Chinese community population: the CHCN-BTH study

Chunyue Guo[1], Han Cao[1], Guangliang Shan[2], Wei Zhao[3], Han Zhang[4], Kaijun Niu[5], Ze Cui[6], Naijun Tang[7], Kuo Liu[1], Li Pan[2], Xiaoyan Han[3], Zhengfang Wang[4], Ge Meng[5], Jixin Sun[6], Anqi Shan[7], Yuxiang Yan[1], Huijing He[2], Zhiyuan Xu[3], Yajing Cao[6], Wenjuan Peng[1], Yanyan Sun[1], Ling Zhang[1]
[1]Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University and Beijing Municipal Key Laboratory of Clinical Epidemiology, Beijing, China
[2]Department of Epidemiology and Statistics, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, School of Basic Medicine, Peking Union Medical College, Beijing, China
[3]Department of Chronic and Noncommunicable Disease Prevention and Control, Chaoyang District Center for Disease Prevention and Control, Beijing, China
[4]Health Management Center, Beijing Aerospace General Hospital, Beijing, China
[5]Nutritional Epidemiology Institute and School of Public Health, Tianjin Medical University, Tianjin, China
[6]Department of Chronic and Noncommunicable Disease Prevention and Control, Hebei Provincial Center for Disease Prevention and Control, Shijiazhuang, Hebei Province, China
[7]Department of Occupational and Environmental Health, School of Public Health, Tianjin Medical University, and Tianjin Key Laboratory of Environment, Nutrition, and Public Health, Tianjin China

OBJECTIVES Several studies have reported that elevated lipoprotein(a) [Lp(a)] concentration is associated with a higher risk of coronary heart disease (CHD). However, due to different assays of Lp(a), racial differences and heterogeneity and the complexity of the structure of Lp(a), studies have reported inconsistent results. There are limited data regarding the association between Lp(a) and CHD in China. Moreover, the role of Lp(a) in subjects with well-controlled lipid levels remains unclear. Therefore, the aim of our study was to investigate the contributions of elevated Lp(a) to the risk of CHD and to explore the synergistic effect between Lp(a) and lipid profiles in a large-scale general Chinese community population.

METHODS We recruited individuals aged over 18 years old from the baseline survey of the Cohort Study on Chronic Diseases of the General Community Population in Beijing, Tianjin and Hebei (CHCN-BTH) using a stratified, multistage cluster sampling method. Data were collected through questionnaire surveys, anthropometric measures and laboratory tests. Participants were categorized into four groups according to predetermined percentiles of Lp(a): <50^{th} (<119.0 mg/L), 51^{st}–80^{th} (119.0–281.2 mg/L), 81^{st}–95^{th} (281.2–607.9 mg/L), and >95^{th} (>607.9 mg/L). Restricted cubic spline functions, multivariate logistic regression, sensitivity and stratified analyses were used to evaluate the association between Lp(a) levels and CHD.

RESULTS A total of 25,343 participants were included, with 1364 (5.38%) identified as having CHD. Elevated Lp(a) levels were linearly related to increased risk of CHD (P for overall association test <0.0001 and P for nonlinear association test=0.8468). Multivariate analysis indicated that subjects with Lp(a)≥300 mg/L had a higher risk of CHD [OR (95% CI): 1.36 (1.17, 1.57)] than did individuals with Lp(a) <300 mg/L. Compared with individuals with Lp(a) <119.0 mg/L (<50^{th} percentile), the OR (95% CI) for CHD in the 51^{st}–80^{th}, 81^{st}–95^{th} and >95^{th} percentiles was 1.07 (0.93, 1.23), 1.26 (1.07, 1.50) and 1.68 (1.30, 2.17), respectively (P for trend<0.0001). The association was also found among the subgroup of subjects with no dyslipidemia, including normal TC (<6.2 mmol/L), TG (<2.3 mmol/L), HDL-C (≥1.0 mmol/L) and LDL-C (<4.1 mmol/L). Elevated Lp(a) and dyslipidemia made a significant contribution to a higher risk of CHD with synergistic effects. In the multivariate ROC curve analysis, the AUC of Lp(a) was almost equal to that of other lipid indexes (AUC=0.837). The sensitivity and specificity of Lp(a) were 84.1 (82.0, 86.0) and 69.3 (68.7, 69.9), respectively. The optimal cutoff value of Lp(a) for evaluating the diagnostic ability of CHD was 295.0 mg/L. Stratified analyses showed that elevated Lp(a) concentrations were significantly associated with an increased risk of CHD in subgroups of noncurrent drinkers, individuals with overweight, hypertension and moderate physical activity, and those without diabetes mellitus and individuals in Beijing and Tianjin.

CONCLUSIONS Elevated Lp(a) concentrations were linearly associated with a higher risk of CHD in the general Chinese community population, which was more significant in normolipidemic subjects. Both dyslipidemia and elevated Lp(a) independently or synergistically contributed to the risk for CHD. Our results suggest that more attention should be paid to the level of Lp(a) in normolipidemic subjects, which may be an early predictor for the occurrence of CHD.

GW31-e0168

Metabolic syndrome as a predictor of type 2 diabetes mellitus and future cardiovascular disease

Baxrom Alyavi, Jamol Uzokov, Akbar Abdullaev
Republican Specialized Scientific and Practical Medical Center of Therapy and Medical Rehabilitation

OBJECTIVES Metabolic syndrome is a characterized by constellation of the several risk factors such as, abdominal obesity, hypertension, dyslipidemia, insulin resistance and impairment of the glucose tolerance and considered risk for the future cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM). Aim of the present study was to investigate the predictive value of the metabolic syndrome components for the future T2DM and CVD.

METHODS Three Hundred Fifty six patients diagnosed with metabolic syndrome (MetS) were enrolled in this study. Mean age of the patients was 48.4±16.2 years at admission (aged 32–65 years, male=41%). Mean follow-up period was 60.0±20.0 months. Anthropometric, laboratory and instrumental data were performed at baseline and during the follow-up.

RESULTS During the median follow-up period in 56 patients T2DM have occurred and in 32 patients CVD occurred. Multivariable analysis revealed that abdominal obesity – AO (Hazard ratio – HR 2.1 Correlation Interval – CI 95% 1.12–3.24, P=0.02), insulin resistance – IR (HR 1.8 CI 95% 1.09–2.46, P=0.01), impairment of glucose tolerance – IGT (HR 1.7 CI 95% 1.19–2.54, P=0.03) were strong predictors for the T2DM whereas dyslipidemia (HR 2.8 CI 95% 1.46–4.12, P=0.04), high blood pressure – HBP (HR 1.4 CI 95% 1.05–2.28, P=0.04) were predictors for CVD. The findings were modified by gender and it was noted that AO was strong predictor for men and IR and IGT was strong predictors for women for T2DM. There were no differences between sexes among risk factors for the development of CVD.

CONCLUSIONS This study show that AO, IR and IGT were predictors for the T2DM whereas dyslipidemia and HBP for CVD. The association were modified by gender and in men AO and in women IR, IGT remained the strong predictors for the development of T2DM whilst there were no differences between sexes for CVD.

GW31-e0199

The prevalence of left ventricular hypertrophy assessed by echocardiography in a general Chinese population

Lv Tingting[1], Yuan Yifang[1], Yang Jing[1,2], Kong Lingyun[1,2], Li Huijuan[3], Li Xingjie[4], Yingxian Sun[5], Li Xuewen[6], Zhang Zheng[7], Cheng Xiaoshu[8], Wu Lirong[9], Tan Xuerui[10], Han Bing[11], Li Hua[1,2], Wang Yanfang[3], Wang Jiayu[3], Zhang Zhaoguo[12], Wu Yangfeng[3], Guo Jihong[2], Zhang Ping[1]
[1]Department of Cardiology, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University
[2]Peking University People's Hospital
[3]Peking University Clinical Research Institute
[4]Jining No. 1 People's Hospital
[5]The First Hospital of China Medical University
[6]Shanxi Academy of medical sciences, Shanxi Dayi Hospital
[7]The First hospital of Lanzhou University
[8]The Second Affiliated Hospital of Nanchang University
[9]The Affiliated Hospital of Guiyang Medical College
[10]The First Affiliated Hospital of Shantou University Medical College
[11]Xuzhou Central Hospital
[12]Beijing First Hospital of Integrated Chinese and Western Medicine

OBJECTIVES Left ventricular hypertrophy (LVH), which is defined by increased left ventricular mass (LVM), is usually regarded as a response to chronic pressure and volume load, and it has been reported as an independent risk factor for subclinical atherosclerosis and heart failure. However, its prevalence of LVH in general Chinese population is limited.

METHODS A multi-stage, stratified cluster sampling across China was performed and 7415 representative Chinese adults aged 18–85 years were analyzed in the study. LVH was assessed by echocardiography and left ventricular mass (LVM) was estimated by cube formula: $0.8\times1.04\times[(IVSd+LVIDd+PWTd)^3-LVIDd^3]+0.6$ g, which was indexed by body surface area (BSA) calculated as $0.007184\times Height^{0.725}\times Weight^{0.425}$ reported by Devereux et al. Cutoff values were defined as 115 g/m² for male, 95 g/m² for female according to American Society of Echocardiography.

RESULTS LVH was detected in 11% of the sample population with an average left ventricular ejection fraction (EF) of 68% and LVM indexed by BSA of 80 g/m². Furthermore, the prevalence of Echo-LVH and its distribution according the traditional and the newly 4-titers methods stratified by age, gender, BMI and blood pressure was calculated in the study. Echo-LVH was more distributed in the elderly (≥20%), female (16%), obesity (>30 kg/m², 16%) and those with hypertension (17%). The prevalence of concentric remodeling was generally much higher than eccentric or concentric hypertrophy in each subgroup, and it had increased trend in older, female, obese and hypertensive individuals. Similarly, according to the newly-proposed 4-tiered classification of LVH, dilated, thick or 'dilated and thick' type of LVH also showed the increased rate in elderly, female, obese and hypertensive individuals.

CONCLUSIONS The prevalence of LVH assessed by echocardiography was 11% in our general population. The prevalence of Echo-LVH warranted the importance of prevention of Echo-LVH for the elder, female, obesity and hypertensive individuals.

GW31-e0202

Four-tiered classification of left ventricular hypertrophy based on ventricular concentricity and dilatation identifies ischemic stroke in the general population

Haoyu Wang
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES Left ventricular hypertrophy (LVH) is traditionally classified as concentric or eccentric based on LV relative wall thickness. We evaluated the prediction of ischemic stroke in a new 4-group LVH classification based on LV concentricity (mass/end-diastolic volume 0.67) and indexed LV end-diastolic volume (EDV) in the general Chinese population

METHODS The cross-sectional study consisted of 11,037 general Chinese population (mean age 54 years; 54% women) from Northeast China Rural Cardiovascular Health (NCRCH) study who underwent echocardiography measurement. A 4-tiered classification of LVH was proposed where eccentric LVH is subdivided into "indeterminate hypertrophy (n=484)" and "dilated hypertrophy (n=386)" and concentric LVH into "thick hypertrophy (n=246)" and "both thick and dilated hypertrophy (n=138)" based on the presence of increased LV end-diastolic volume.

RESULTS Compared with normal LV geometry (2.6%), indeterminate (7.4%) and thick hypertrophy (10.2%) showed a higher prevalence of ischemic stroke (P<0.05). Ischemic stroke was significantly greater in participants with indeterminate (adjusted odd ratio [OR]: 1.635, 95% confidence interval [CI]: 1.115–2.398) and thick (2.143 [1.329–3.456]) hypertrophy but not significantly in those with dilated (1.251 [0.803–1.950]) and both thick and dilated hypertrophy (0.926 [0.435–1.971]) compared with normal geometry in multivariable analysis. Additionally, the continuous parameters of LV concentricity 0.67 (OR, 1.067; 95% CI, 1.024–1.113 per 1 SD increment) was independently associated with the presence of ischemic stroke in multivariable analysis adjusted for age, sex, race, physical activity, current smoking and drinking status, BMI, TC, hypertension and diabetes, while LVEDV/BSA was not (OR, 0.957; 95% CI, 0.859–1.065 per 1 SD increment).

CONCLUSIONS In a large-scale Asian population, we identified that thick hypertrophy carried the greatest odd for ischemic stroke, independently of traditional risk factors, followed by indeterminate hypertrophy. The new 4-tiered categorization of LVH can permit a better understanding of which subjects are at high enough risk for ischemic stroke to warrant early targeted therapy.

GW31-e0204

Fuster-BEWAT score versus American Heart Association's life's simple 7 to predict subclinical target organ damage: findings from a large-scale Asian population

Haoyu Wang
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES The AHA's Life's Simple 7 score is recommended for use in primordial prevention. Simpler tools not requiring laboratory tests, such as the Fuster-BEWAT score (FBS) (blood pressure [B], exercise [E], weight [W], alimentation [A], and tobacco [T]), are also available. We aimed to investigate the relationships of FBS and Life's Simple 7 with several subclinical markers of target organ damage (TOD) representing myocardial structure and function (i.e., ECG-LVH and LV diastolic dysfunction), carotid structure (i.e., carotid intima-media thickness), and vascular function (i.e., arterial stiffness) in the framework of general Chinese population.

METHODS The study population consisted of 11,163 community-based adults (mean age 53.9 years; 54% female) who were recruited in the NCRCH (Northeast China Rural Cardiovascular Health) study between January 2013 and August 2013. A SD+SV4 ≥2.3 mV for female subjects and ≥2.8 mV for male subjects were considered positive for LVH according to Peguero–Lo Presti criteria. Participants with LV diastolic dysfunction was defined as septal e′ velocity

<7 cm/s, average E/e' ratio>14, or left atrial volume index>34 mL/m². Carotid intima-media thickness >0.9 mm was assessed for the detection of carotid wall thickness. The highest tertile of pulse pressure/stroke volume indexed to height 2.04 (>2.76 mmHg/mL) was chosen to reflect increased arterial stiffness.

RESULTS With poor Life's Simple 7 and FBS as references, subjects with ideal Life's Simple 7 and FBS presented substantially lower adjusted odds of having ECG-LVH (OR, 0.57; 95% CI, 0.49–0.66 vs. OR, 0.54; 95% CI, 0.46–0.64), LV diastolic dysfunction (OR, 0.34 [0.26–0.45] vs. OR, 0.43 [0.33–0.57]), carotid wall thickness (OR, 0.66 [0.51–0.87] vs. OR, 0.68 [0.50–0.93]), and arterial stiffness (OR, 0.22 [0.19–0.26] vs. OR, 0.21 [0.18–0.25]). In a similar model, per each additional metric at recommended optimal level of Life's Simple 7 (0–7) and FBS (0–5) was predictive to a similar degree of reduced odds of all subclinical TOD. Similar levels of significantly discriminating accuracy were found for Life's Simple 7 and FBS with respect to ECG-LVH (Life's Simple 7: C-statistic of 0.623; FBS: C-statistic of 0.625), LV diastolic dysfunction (FBS C-statistic of 0.729; CVHS C-statistic of 0.721), carotid wall thickness (FBS: C-statistic of 0.720; Life's Simple 7: C-statistic of 0.721) and arterial stiffness (FBS: C-statistic of 0.701; Life's Simple 7: C-statistic of 0.704).

CONCLUSIONS Both scores exhibited comparable discriminatory values for detection of subclinical TOD in a large sample of middle-aged adults, highlighting the potential usefulness and clinical relevance of FBS as an easy, practical, and affordable option for elucidating the impact of CV risk behaviors and factors on subclinical CVD in settings where limited access to laboratory analysis and resource-constrained health-care areas hinder the possibility of estimating CV risk.

GW31-e0207

Usefulness of triglyceride-glucose index for estimating hyperuricemia risk: insights from a general population

Haoyu Wang
Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES Hyperuricemia is a metabolic abnormality that has cast an enormous burden on global healthcare. Previous studies have revealed the close association between insulin resistance and hyperuricemia. Therefore, monitoring insulin sensitivity may be a possible way to prevent hyperuricemia. Recent studies have demonstrated the usefulness of triglyceride-glucose index (TyG) as a simple surrogate of insulin resistance. Hence, our study aimed to explore the impact of TyG on hyperuricemia and its value to improve the risk stratification and prevention of hyperuricemia.

METHODS This cross-sectional study included 6466 subjects (mean age: 59.57 years, 60.19% females) from northeast China between September 2017 to May 2018. TyG was determined as ln[fasting TG (mg/dL)×FPG (mg/dL)/2]. Hyperuricemia was defined as serum uric acid ≥357 μmol/L for females and ≥417 μmol/L for males.

RESULTS The prevalence of hyperuricemia was 5.24%. In the full model, each SD increment of TyG caused a 12.528 μmol/L elevation of serum urate concentration and a 54.1% additional risk for hyperuricemia. When dividing TyG into quartiles, the top quartile had a 2.730 times risk for hyperuricemia than the bottom one. Moreover, smooth curve fitting demonstrated this association was linear. Additionally, subgroup analysis revealed the association was robust to several risk factors of hyperuricemia. Finally, AUC displayed an improvement when introducing TyG into clinical risk factors (0.751 vs. 0.772, P<0.001), category-free net reclassification index (0.304, 95% CI: 0.195–0.413, P<0.001) and integrated discrimination index (0.009, 95% CI: 0.004–0.013, P<0.001) also showed the improvement from TyG.

CONCLUSIONS Our work revealed the linear and robust association between TyG and hyperuricemia. Furthermore, our results suggest the importance of simultaneous glycemic and lipids control in the prevention of hyperuricemia. Most importantly, our findings implicate the value of TyG to optimize the risk stratification and prevention of hyperuricemia.

GW31-e0230

Is hypoxia the strongest determinant of hypertension among Chinese Han adults who having worked in the very high altitude region?

Hongliang Kong[1,2], Xiaohong Chen[1]
[1]The People's Hospital of Liaoning Province
[2]The People's Hospital of Naqv City, Tibet

OBJECTIVES The study aimed to assess the prevalence and awareness of hypertension, and its key risk factors among Tibetan adults living on Seni town with a very high altitude of 4507 m.

METHODS It was a cross-sectional study in Seni town. A total of 3440 native Tibetan adults were voluntarily enrolled in this survey. In the study, each participant had their blood pressure and body mass index measured, completed two self-report questionnaires.

RESULTS Hypertension was defined according to the criteria from JNC-7. The prevalence of hypertension was 42.1% in the current populations. Overall awareness, treatment, and control of hypertension was low, which was 17.6, 7.0, and 1.8% in patients with hypertension. Participants, knowing their hypertension, had a significantly higher mean level of systolic pressure, diastolic pressure, and pulse pressure. The prevalence of sleep disorder was 34.13%, in which 88.4% was hypertensive. The prevalence of hypertension and the level of systolic pressure, diastolic pressure, and pulse pressure were significantly increased with the aggravation of sleep disorder. In multiple logistic regression analyses, sleep disorder, age, drinking, and men were all associated independently with hypertension.

CONCLUSIONS Prevalence of hypertension was high in native Tibetan adults living on the very high altitude. Awareness of hypertension was low, and a number of individuals with hypertension did not receive treatment and control. Sleep disorder may be independently risk factors of hypertension.

GW31-e0231

Is hypoxia the strongest determinant of altitude-related hypertension among Chinese Han adults in the very high altitude region?

Hongliang Kong[1,2], Xiaohong Chen[1]
[1]The People's Hospital of Liaoning Province, Shenyang City
[2]The People's Hospital of Naqv City, Tibet

OBJECTIVES The study aimed to assess the prevalence of altitude-related hypertension (ARH) and identify the role of hypoxia in ARH among Chinese Han adults, having been working at a very high altitude of 4507 m.

METHODS Each participant had their blood pressure (BP) and oxygen saturation (SaO2) measured, and had two self-report questionnaires performed. Hypertension was defined according to the criteria from JNC-7. BP difference is defined as BP at high altitude – BP at low altitudes.

RESULTS In all Chinese Han adults (n=1241), being voluntarily enrolled, the prevalence of ARH was 33.9% (male 45.9%, female 14.3%). Male, age, work years, drinking, classification of sleep disorder, and SaO_2 were all associated independently with ARH. Overall awareness, treatment, and control of hypertension was 32.3%, 15.0%, and 5.5% in patients with ARH, respectively. Participants, knowing their hypertension, had a significantly higher mean level of systolic BP (SBP), diastolic BP (DBP), and pulse pressure. After all patients with ARH returning hometown at low altitudes <200 m, along with their SaO_2 to normal, 206 (48.9%) individuals restored BP to normal and the remaining 215 patients had BP improved; There existed negatively correlative between work years and BP difference between two altitude, including SBP difference and DBP difference.

CONCLUSIONS There was a high prevalence of ARH, along with a low awareness, treatment and control, in Chinese Han adults living on the very high altitude. Hypoxia may be the independently strongest determinant of ARH.

GW31-e0395

Appraisal of guidelines for non-cardiac surgery in patients on dual antiplatelet therapy

Shaozhao Zhang[1,2], Xiaodong Zhuang[1,2], Zhengzhipeng Zhang[3], Xinxue Liao[1,2]
[1]Cardiology department, First Affiliated Hospital of Sun Yat-Sen University
[2]NHC Key Laboratory of Assisted Circulation (Sun Yat-Sen University)
[3]Zhongshan School of Medicine, Sun Yat-Sen University

OBJECTIVES Dual antiplatelet therapy (DAPT) is important for patients with coronary stent placement. However, it may increase the risk of bleeding when patients receive surgery. Relevant recommendations are inconsistent in current guidelines. We aimed to systematically review guidelines with recommendations for non-cardiac surgery during DAPT, highlight their commonalities and differences to facilitate clinical decision-making and improvement of guidelines.

METHODS Guidelines published in English were searched in MEDLINE, Embase, and websites of professional societies. Guideline quality was appraised by two reviewers with the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. Besides, 18 items from the Reporting Item for Practice Guidelines in Healthcare (RIGHT) checklist are used to assess the report of guidelines as supplementary. Relevant recommendations were extracted.

RESULTS Seven guidelines were included with overall AGREE II scores varied from 67 to 84%. Most guidelines received high scores, though shortage exists in "Stakeholder Involvement" and "Applicability". The report of COI is elaborated in most guidelines. Slight differences still exist in recommendations for the timing of non-cardiac surgery, and the level of evidence was not satisfying in general. The recommendations for perioperative management of antiplatelet agents and clinical decision-making could be improved by being more detailed.

CONCLUSIONS Only a few guidelines developed recommendations for non-cardiac surgery in patients on DAPT. The quality of these guidelines is generally satisfying. Discrepancy on the optimal timing of non-cardiac surgery still exists, and more evidence is required to guide the perioperative management of antiplatelet therapy.

GW31-e0428

Efficacy of statin treatment based on cardiovascular outcomes in elderly patients: a Bayesian network analysis

Chuannan Zhai[1,2], Hongliang Cong[1,2]
[1]NanKai University School of Medicine
[2]Tianjin Chest Hospital

OBJECTIVES Statins have been shown to be beneficial for the prevention of cardiovascular events. In elderly individuals, the efficacy of statins remains controversial and the comparative effect of statins has not been assessed.

METHODS MEDLINE, Embase and the Cochrane Central database were searched for randomized controlled trials, which assessed statins in older patients. The odds ratios (ORs) and 95% confidence intervals (CIs) were used to evaluate dichotomous outcomes. The inverse variance and Mantel-Haenszel techniques were used to combine the separate statistics. Heterogeneity was investigated using the Q statistic, and P values<0.05 was regarded as statistically significant. In order to control for the risks of random type I and II errors due to sparse data and repetitive testing of accumulating data and to assess the reliability and conclusiveness of the present evidence, trial sequential analysis (TSA) of any statin versus placebo/usual care was conducted on each clinical outcome with at least two trials. The Bayesian network meta-analysis (NMA) was conducted using the aggregate data drug information system (ADDIS) v1.16.5.

RESULTS Seventeen trials were analyzed. When used for secondary prevention, statins were associated with reduced risk of cardiovascular events, all-cause mortality, cardiovascular mortality, revascularization, and stroke. When used for primary prevention, statins reduced the risk of myocardial infarction and revascularization, but did not significantly affect other outcomes. A modest difference between pharmaceutical statin products was found, and high-quality evidence indicated that intensive atorvastatin had the greatest benefits for secondary prevention.

CONCLUSIONS In secondary prevention, evidence strongly suggests that statins are associated with a reduction in the risk of all-cause mortality, cardiovascular events, cardiovascular mortality and revascularization. However, differences in the effects of various statins do not appear to have significant effects on therapy in secondary prevention for the elderly.

GW31-e0437

Association between plasma level of retinol-binding protein 4 and coronary artery disease: a meta-analysis of case-control studies

Jun Wang, Xiangfeng Lu
Key Laboratory of Cardiovascular Epidemiology & Department of Epidemiology, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

OBJECTIVES The association between retinol-binding protein 4 (RBP4) and risk of coronary artery disease (CAD) remains controversial. We performed a meta-analysis of published case-control studies to clarify this association.

METHODS We systematically searched databases, including PubMed, Web of Science, CNKI, Wan fang, and VIP, up to June 2020 without language publications. Original articles of case-control studies on association between RBP4 and CAD were included. Study selection, quality assessment, and data extraction were completed by two independent investigators. The study quality was evaluated by the Newcastle-Ottawa scale. Multivariable adjusted odds ratios (ORs) and 95% confidence intervals of CAD incidence for the highest versus the lowest level of serum RBP4 was used as a measure of the effect size for all studies. We calculated the combined OR by the random-effects model. Heterogeneity between studies was assessed using Q and I^2 statistics. The publication bias was estimated using Egger's test. Sensitivity analyses were also conducted by excluding each study individually to test its influence on the total result.

RESULTS We identified 125 articles, of which 5 were used in this study. There were 2639 patients and 2906 control subjects. The design of one article was nested case-control study with two follow-ups, and effect estimates were evaluated separately at each follow-up. Another article conducted analyses independently between female and male. Therefore, the meta-analysis included seven studies. The pooled effect showed that higher serum RBP4 concentration had significant positive effect on the incidence of CAD, with the OR of 1.395 (95% CI 1.054–1.863). Sensitivity analyses indicated that after removing two studies, the result of the combined *OR* tended to be stable. Publication bias was not observed.

CONCLUSIONS The study suggests that elevated serum RBP4 level may increase the risk of CAD. However, due to limited number of case-control studies it is necessary to collect more evidence to detect the real association.

GW31-e0445

Dietary carbohydrate intake and right ventricular structure and function: the mesa-right ventricle study

Xiaodong Zhuang[1,2], Shaozhao Zhang[1,2], Zhimin Du[1,2], Xinxue Liao[1,2]
[1]Cardiology Department, First Affiliated Hospital of Sun Yat-Sen University
[2]NHC Key Laboratory of Assisted Circulation (Sun Yat-Sen University)

OBJECTIVES The relationship between dietary carbohydrate intake and right ventricular (RV) morhpology is unclear. We aimed to evaluate the association between carbohydrate intake and RV structure and function in a large multi-ethnic population-based cohort.

METHODS We included 3776 participants (age, 61.5±10.1 years; 47.5% male) who completed a dietary questionnaire and cardia MRI examination in the MESA-Right Ventricle Study. Participants were divided into three categories based on carbohydrate intake: low (≤45%), medium (45–55%), and high (≥55%). Multivariable linear regression was used to assess the associations between carbohydrate intake and RV parameters (mass, volumes, ejection function) and results were expressed using least squares means.

RESULTS After adjustment for traditional cardiovascular risk factors, higher carbohydrate intake (1-SD increase) was associated with higher RV stroke volume (β, 0.91; 95% CI, 0.36–1.46; 2 and 3% greater, respectively) and higher RV ejection fraction (β, 0.35; 95% CI, 0.14–0.56; 0.2 and 1% greater, respectively).

CONCLUSIONS Higher dietary carbohydrate intake is associated with high RV stroke volume and RV ejection fraction independently.

GW31-e0583

An update of antithrombotic therapy for patients with atrial fibrillation and percutaneous coronary intervention

Huiling Huang, Chen Liu, Xing Wang, Xumiao Chen
The First Affiliated Hospital of Sun Yat-Sen University

OBJECTIVES Patients with atrial fibrillation undergoing percutaneous coronary intervention (PCI) are recommended for antithrombotic strategy with antiplatelet drugs plus anticoagulant. Obviously, triple therapy with non-vitamin K dependent oral anticoagulant (NOAC) and dual antiplatelet seems better than warfarin in current. Hence we try to combined all current evidence to make a fully understanding about the new strategy.

METHODS We searched in Medline, Embase, Cochrane databases, and proceedings of major international meetings for randomized controlled trials (RCTs) that comparing different strategies. The titles and abstracts were reviewed. Conflicts between reviewers were resolved by discussion. Internal validity of randomized controlled trials was assessed. The primary endpoints were cardiovascular mortality, myocardial infarction, stroke, all cause mortality, major bleeding or clinically relevant clinically relevant nonmajor bleeding (CRNM). Risk ratios (RR) and 95% confidence interval (CI) were used as the summary statistic. Fixed-effects model was used in our analysis when heterogeneity was acceptable.

RESULTS Four RCTs enrolling 8474 participants were included. Surprisingly, dual therapy halved the risk in the rate of major bleed or CRNM (RR 0.53, 95% CI 0.46–0.60). We found no statistically significant difference in the rate of cardiovascular mortality or acute myocardial infarction (RR 1.07, 95% CI 0.76–1.53 and RR 1.19, 95% CI 0.95–1.50 respectively) for dual therapy compared with triple therapy. Similarly, the rate of stroke was comparable in both groups (RR 0.98, 95% CI 0.66–1.46). With respect to all cause mortality, there seemed to have a moderate trend towards favoring dual therapy (RR 0.94, 95% CI 0.61–1.43). Dual therapy reduces bleeding events and non inferior in the ischemia events. There was nearly 50% risk reduction for major or CRNM bleeding with dual therapy. Interestingly, there was almost 20% relative risk increased in the rate of acute myocardial infarction. We deduce that there might be still roll for aspirin in such patients. Our combined data showed no significant difference between dual therapy and triple therapy.

CONCLUSIONS We recommend that dual therapy should be the better choice for patients with atrial fibrillation after PCI since dual therapy benefit from less CRNM bleeding events with no increase in thrombotic complication.

GW31-e0608

Geographical distribution and temporal trends in incidence rate of acute coronary events from 2007 to 2012 in Beijing

Jie Chang, Qiuju Deng, Jing Liu
The Department of Epidemiology, Beijing An Zhen Hospital, Capital Medical University; Beijing Institute of Heart, Lung and Blood Vessel Diseases

OBJECTIVES To examine the geographical distribution and temporal trends of incidence of acute coronary events (ACEs) in Beijing from 2007 to 2012, and explore the difference in trends across gender and age groups.

METHODS A total of 161,026 ACEs events were identified from 1 January 2007 to 31 December 2012 by the Beijing Monitoring System for Cardiovascular Diseases. ACEs included non-fatal acute myocardial infarction cases and all coronary deaths. Numbers of residents by age, gender and region were obtained from the Beijing Statistics Bureau. The crude ACEs incidence per 100,000 population were calculated and directly age-standardized with 2010 China Standard Population. The trend and its corresponding 95% confidence interval (CI) in ACEs events rates were calculated for crude and age-standardized annual rates by using the regression model log r_t=a+bt, where log denotes the natural logarithm and t is the year. The estimate 100b was expressed as average annual percentage changes in the ACEs events rate.

RESULTS The crude and age-standardized ACEs incidence rates per 100,000 population increased from 180.6 to 238.5 and 132.6 to 147.5 from 2007 to 2012, with an annual increase rate of 5.0% (95% CI: 2.5–7.5) and 1.7% (95% CI: –0.7–4.0), respectively. The ACEs incidence rate increased by 4.7% (95% CI: 0.1–11.6) and 4.9% (95% CI: 1.8–7.9) annually for males aged 40–49 and 50–59, and by 4.5% (95% CI: 0.5–8.4) annually for females aged 50–59. Compared with core area and urban area, increasing trends of the age-standardized incidence of ACEs were noticed in outskirts from 2007 to 2012, with an annual increase rate of 5.2% (95% CI: 1.6–8.7). The most rapid increase in age-standardized incidence of ACEs was in the Fangshan district in the southwest outskirts, with a 12.4% (95% CI: 6.0–18.8) increase annually, followed by the Shunyi district (8.9%, 95% CI: 3.5–14.4) and the Miyun district (8.3%, 95% CI: 2.1–14.6) in the northeast outskirts.

CONCLUSIONS The crude incidence of ACEs increases significantly in Beijing. The increases in age-standardized incidence of ACEs were not statistically significant for the total population, whereas the increases in the middle-aged and those in the southwest and the northeast outskirts were significant. Targeted actions on primary ACEs prevention in these specific high-risk populations and areas are needed.

GW31-e0638

Midlife to late-life blood pressure patterns and cardiovascular risk: findings from the Chinese multi-provincial cohort study

Shuai Liu, Dong Zhao, Yue Qi, Miao Wang, Jiayi Sun, Jun Liu, Ningning Zhang, Guoliang Hu, Jing Liu
Department of Epidemiology, Beijing An Zhen Hospital, Capital Medical University; Beijing Institute of Heart, Lung and Blood Vessel Diseases

OBJECTIVES To investigate the association of midlife to late-life blood pressure (BP) patterns with the long-term risk of cardiovascular disease (CVD).

METHODS Data from the Chinese Multi-Provincial Cohort Study were analyzed. 2525 participants (aged 45–59 years at entry in 1992) with two BP recorded in 1992 and 2007 and free of CVD in 2007 were included. Participants were grouped into one of the four categories based on longitudinal patterns of normotension and hypertension (SBP/DBP>140/90 mmHg) in 1992 and 2007: midlife and late-life normotension, midlife normotension and late-life hypertension, midlife hypertension and late-life normotension, and midlife and late-life hypertension. Cardiovascular events (including coronary heart disease and stroke) occurred during 2007 and 2018 were registered. Cox proportional hazards regression models were used to obtain hazard ratios (HRs) of CVD incidence associated with midlife to late-life BP patterns, adjusting for age, sex, smoking status, diabetes, levels of low-density lipoprotein cholesterol and high-density lipoprotein cholesterol, and antihypertensive drug use in 2007.

RESULTS Among 2525 participants (1397 [55.3%] men; mean (SD) age in 1992, 51.5 (4.1) years), there were 297 (11.8%) incident CVD cases during 11 years of follow-up. The incidence rate for participants with midlife and late-life normotension, midlife normotension and late-life hypertension, midlife hypertension and late-life normotension, and midlife and late-life hypertension was 794.3, 1, 513.4, 1589.2, and 2230.4 per 100,000 person-years, respectively. Compared with midlife and late-life normotension, midlife normotension and late-life hypertension (hazard ratio [HR], 1.83; 95% confidence interval [CI], 1.34–2.49), midlife hypertension and late-life normotension (HR, 1.96; 95% CI, 1.26–3.05), and midlife and late-life hypertension (HR, 2.97; 95% CI, 2.12–4.17) were significantly associated with increased CVD risk.

CONCLUSIONS Midlife normotension and late-life hypertension, midlife hypertension and late-life normotension, and midlife and late-life hypertension are all associated with increased CVD risk in the Chinese population. Lifetime normal BP levels are ideal for controlling cardiovascular risk.

GW31-e0642

Status of sleep disorders among elderly hypertensive patients in new rural communities

Yulin Huang[1], Dong Zhao[1], Zhenqi Gao[2], Miao Wang[1], Yue Qi[1], Zhenquan Yang[2], Huan Jin[2], Xuejuan Jin[3], Jun Zhou[3], Shuai Liu[1], Jing Liu[1]
[1]Department of Epidemiology, Beijing Anzhen Hospital, Capital Medical University, Beijing Institute of Heart, Lung and Blood Vessel Diseases
[2]Community Health Service Center of Langxia, Jinshan, Shanghai
[3]Department of Cardiology, Zhongshan Hospital, Fudan University, Shanghai Institute of Cardiovascular Diseases

OBJECTIVES To investigate the status of sleep disorders among elderly hypertensive patients in new rural communities of Shanghai.

METHODS A total of 2224 elderly hypertensive patients from Langxia, Shanghai were enrolled from the Multi-provincial Cohort for Hypertension (MUCH) of the National Key Research and Development Project during May to July 2018. Questionnaires, physical examinations, and laboratory tests were conducted, and demographic and sleep-related information was collected. The sleep status of the participants were analyzed, and sleep disorders among patients with different characteristics were compared.

RESULTS The mean age of the participants was 69.4±6.9 years, and 38.9% were males. The treatment, control, and therapeutic control rates for hypertension were 77.3, 26.1 and 33.1%, respectively. Overall, 59.0% of the participants had sleep disorders. The prevalence rates of snoring and obstructive sleep apnea (OSA) in men were higher than those in women. However, short sleep time at night, insomnia symptoms and daytime fatigue were more prevalent in women than in men (P<0.05). The proportion of subjects with sleep disorders raised with the increase of body mass index (BMI), with a percentage of 51.7, 62.2 and 63.1% among participants of normal weight, overweight and obesity, respectively. The prevalence rates of snoring and OSA were significantly higher in overweight and obese subjects (P<0.05).

CONCLUSIONS The antihypertensive treatment is widely received among elderly hypertensive patients in developed new rural areas. However, the control rate for those on treatment is still not satisfactory and these patients often have sleep problems. Sleep health of elderly patients with hypertension and the potential of improvement in blood pressure control through sleep management are worthy of attention.

GW31-e0673

Association between educational attainment and risk for out-of-hospital coronary death in Beijing, China

Qiuju Deng, Jie Chang, Jiayi Sun, Jing Liu
Beijing An Zhen Hospital, Capital Medical University, Beijing Institute of Heart, Lung, and Blood Vessel Diseases, No. 2 An Zhen Rd, Chaoyang District, Beijing 100029, China

OBJECTIVES Many fatal events still occur out of the hospital despite the advances in coronary heart disease prevention, emergency transport systems, and medical treatment. To develop targeting prevention strategies, knowledge about the risk and risk factors for out-of-hospital coronary death (OHCD) is needed. While traditional risk factors of coronary heart disease are well-established, the evolving role of non-traditional risk factors, including socioeconomic and psychosocial factors, is increasingly recognized. However, the impact of educational attainment on OHCD are poorly described. We therefore aimed to evaluate the relationship between individual educational attainment and risk for OHCD compared to the in-hospital coronary death in China.

METHODS All coronary deaths from 1 January 2007 to 31 December 2012 in Beijing were identified from the Beijing Vital Registration Monitoring System, according to the underlying causes of death, with ICD-10 codes of I20–I25. OHCD was defined as a coronary death occurring before hospital admission, including at home, at work and other public places, during transportation, and at the emergency room, based on the location of death in vital registration. Education attainment was classified into four categories: uneducated, primary education (primary school), secondary education (including middle or high school), and college or higher education. Multilevel logistic regression models were used to estimate the association between education attainment and OHCD risk, adjusted for age, sex, marital status, and location of residence and results were expressed as odd ratio (OR) and 95% confidence interval (CI).

RESULTS From 2007 to 2012, 90,922 coronary deaths occurred in Beijing. The mean (SD) age was 75.1 (12.5) years and 46.2% were female. Among all coronary deaths, OHCD accounted for 75.2%. Secondary education, primary education, and uneducated were all associated with higher risk for OHCD after adjustment for covariates compared to college or higher education (OR=1.15, 95% CI 1.09–1.22; OR=1.42, 95% CI 1.34–1.52; OR=2.39, 95% CI 2.23–2.56, P for trend<0.001). Similar results were observed in the sensitivity analysis restricted to 43,949 acute myocardial infarction cases or 17,149 patients without previous hospital admission for acute myocardial infarction in the past five years. When stratified by sex and age group (<60 and ≥60 years), the inverse relation between education attainment and OHCD persisted in both sexes and age groups. However, the ORs on OHCD were higher if the patients with coronary heart disease were young and male.

CONCLUSIONS This study provides individual-level estimates of the association of educational attainment with OHCD. Clinical and public health interventions targeting these high-risk groups with low education attainment are needed to reduce the burden of OHCD.

GW31-e0766

Chinese ASCVD risk equations rather than pooled cohort equations are better to identify macro- and microcirculation abnormalities

Qiaowei Li[1,2,3,4], Feng Huang[1,2,3,4], Fan Lin[1,2,3,4], Pengli Zhu[1,2,3,4]
[1]Department of Geriatric Medicine, Fujian Provincial Hospital
[2]Shengli Clinical Medical College of Fujian Medical University
[3]Fujian Provincial Center for Geriatrics
[4]Fujian Provincial Key Laboratory of Geriatric Disease

OBJECTIVES We hypothesized that discriminating the early subclinical organ damage would serve as a great opportunity for prevention against atherosclerotic cardiovascular disease (ASCVD). Brachial-ankle pulse wave velocity (baPWV), low retinal vascular fractal dimension, and albuminuria are surrogates of subclinical vascular changes. The aim of this study was to use Pooled Cohort Equations (PCE) and ASCVD risk equations derived from "Prediction for ASCVD Risk in China project (CHINA-PAR)" to observe the prevalence of macro- and microcirculation abnormalities.

METHODS A total of 2166 subjects were involved. Characteristics were investigated using questionnaire and physical examinations. We calculated the urine albumin to creatinine ratio (UACR). The baPWV was measured using a fully automatic arteriosclerosis detector. The retinal vascular fractal dimension was measured by a semiautomated computer-based program. The 10-year ASCVD risk was estimated using the PCE and CHINA-PAR model.

RESULTS The cut-off values for the elevated baPWV were 2.82 and 2.92% in the PCE model and CHINA-PAR model, respectively, with nearly 85% sensitivity and an average specificity of 74%. For low retinal fractal dimension, at the cut-off point of 3.8%, we acquired an acceptable sensitivity of 66.27–68.24% and specificity of 62.57–67.45%. All the C-statistics presented a significant improvement from the PCE model to the CHINA-PAR model (P<0.05). For all categories-net reclassification improvement (NRI) values were significant and clearly varied (0.329, 0.183, and 0.104, respectively) depending on the cut-off set at 3%.

CONCLUSIONS Our study demonstrated that the CHINA-PAR equations rather than PCE could provide better identification of macro- and microcirculation abnormalities. A lower cut-off point for the subclinical vascular changes may be selected in a population from southeast China.

GW31-e0767

Combination of endoglin and ASCVD risk assessment improves carotid subclinical atherosclerosis recognition

Qiaowei Li[1,2,3,4], Fan Lin[1,2,3,4], Feng Huang[1,2,3,4], Pengli Zhu[1,2,3,4]
[1]Department of Geriatric Medicine, Fujian Provincial Hospital
[2]Shengli Clinical Medical College of Fujian Medical University
[3]Fujian Provincial Center for Geriatrics
[4]Fujian Provincial Key Laboratory of Geriatric Disease

OBJECTIVES Our study aimed to investigate the association between soluble endoglin and carotid subclinical atherosclerosis.

METHODS We used the endoglin as an adjunct to atherosclerotic cardiovascular disease (ASCVD) risk in recognition for carotid clinical atherosclerosis in order to explore a new model to refine risk assessment. Nine hundred and seventy-eight subjects with soluble endoglin levels detection out of the 3452 participants by random sampling of a cross-sectional investigation in Fujian Province were enrolled. Soluble endoglin concentration in serum samples was evaluated using an enzyme-linked immunosorbent assay method. Carotid ultrasonography was used to detect intima-media thickness and carotid plaque.

RESULTS The mean 10-year ASCVD risk by the new Pooled Cohort Equations accounted for 10.04% (±12.35). The mean soluble endoglin level was 15.35 ng/mL (±6.64). Multivariable regression demonstrated that age, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol and serum uric acid were independent determinants of soluble endoglin. Adding tests of ASCVD and endoglin together in parallel will increase the sensitivity and decrease specificity in recognition of carotid subclinical atherosclerosis. Evaluating the added value of endoglin to the ASCVD risk model showed significantly improved discrimination with analysis of C-statistics, continuous net reclassification index and integrated discrimination index. Both ASCVD risk and soluble endoglin showed positively linear correlation with carotid intima-media thickness (cIMT) (β=0.006, P<0.001; β=0.485, P<0.001). Even with adjustment for other factors, the relationship between log-transformed soluble endoglin with cIMT was still significant (β=0.369, P<0.001).

CONCLUSIONS The combination of ASCVD risk and endoglin levels serves to higher carotid atherosclerosis recognition.

GW31-e0786

Effects of metabolically healthy and unhealthy obesity on prolongation of corrected QT interval

Xiaofan Guo, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Although obesity and the metabolic syndrome (MS) often co-occur, many obese (OB) subjects have a favorable metabolic profile. It is unclear whether these factors independently influence cardiac electrophysiology including prolongation of the QT interval.

METHODS We examined associations among obesity, MS, and prolonged corrected QT (QTc) interval in a large sample of Chinese research participants aged ≥35 years recruited from rural areas of Liaoning Province during 2012–2013.

RESULTS Of the 11,209 participants, 6364 (56.8%) were nonobese and metabolically healthy (OB–/MS–), 2853 (25.5%) were OB–/MS+, 493 (4.4%) were OB+/MS–, and 1499 (13.4%) were OB+/MS+. Mean (±SD) QTc intervals were higher in OB–/MS+ (436.3±24.3) and OB+/MS+ (436.6±25.9) participants but not OB+/MS– participants (425.4±24.0) than in OB–/MS– participants (426.8±21.5, P<0.001), and the prevalence of QTc prolongation was higher in OB–/MS+ and OB+/MS+ participants (adjusted odds ratios [aOR] 1.68, 95% confidence interval [CI] 1.52–1.85; aOR 1.92, 95% CI 1.69–2.17, respectively) compared with OB–/MS– group but not in OB+/MS– participants (aOR 0.92, 95% CI 0.73–1.15). Prevalence increased with each MS component (aOR 1.27, 95% CI 1.22–1.32) but not with body mass index (aOR 1.01, 95% CI 0.99–1.02).

CONCLUSIONS In conclusion, prolonged QTc interval is associated with the MS and not independently associated with obesity.

GW31-e0787

Metabolic profile for prediction of ischemic stroke in Chinese hypertensive population

Xiaofan Guo, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Stroke burden is extremely high in Chinese hypertensive population. Novel biomarkers for cardiovascular diseases can be detected by metabolomic profiling of human fluids. We aim to find a panel of distinctive plasma metabolites for predicting incident ischemic stroke in hypertensive patients.

METHODS This is a nested case-control study from a prospective cohort design. Baseline plasma samples were collected from 66 newly developed ischemic stroke cases and 66 matched controls. Untargeted metabolomics was performed by ultra-high performance liquid chromatography-tandem mass spectrometry, and data were analyzed by multivariate and univariate statistics.

RESULTS Plasma metabolite profiles clearly differed between hypertensive patients with incident ischemic stroke and without. A total of 12 metabolites were screened and identified as potential biomarkers. The altered metabolic pathways included retinol metabolism, sphingolipid metabolism, glycerophospholipid metabolism, lysine degradation, tyrosine metabolism, and tryptophan metabolism. For prediction of hypertensive ischemic stroke, the panel of specific metabolomics-based biomarkers provided area under the curve of 0.848 (95% confidence interval: 0.783–0.913).

CONCLUSIONS Our study identified a metabolic signature of incident ischemic stroke in hypertension. Differences in small-molecule metabolites hold translational value in prediction and provide insights into potential new mechanisms of this condition.

GW31-e0788

Sex-specific association between serum uric acid and prolonged corrected QT interval: result from a general rural Chinese population

Xiaofan Guo, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Recently, it has been found that high level of serum uric acid (SUA) is causally related to sudden cardiac death (SCD). We examined the sex-specific associations of SUA with prolonged heart rate-corrected QT (QTc) interval in a general Chinese population.

METHODS A large sample of 11,206 Chinese research participants aged 35 years and older was recruited from rural areas of Liaoning Province during 2012–2013. SUA were divided into quartiles separated for males and females. Prolonged QTc interval, assessed by the Bazett formula, was defined as cut points of 460 ms or longer in females and 450 ms or longer in males.

RESULTS Mean (±standard deviation) QTc intervals were 422.1±24.2 ms among 5104 males and 436.1±23.5 ms among 6102 females, respectively.

In both sexes, SUA showed significant correlations with QTc interval (both P<0.001). Among male participants, the highest quartile of SUA (>379 μmol/L) was related to an increased risk for prolonged QTc interval (odds ratios: 1.402, 95% confidence interval: 1.073–1.831) compared to the lowest quartile (≤276 μmol/L) after fully adjustment. However, there were no significant relationships between SUA and prolonged QTc interval among females in all the models. Males with high SUA are prone to a higher risk for prolonged QTc interval.

CONCLUSIONS This study provides novel explanation for population-based findings on SUA and SCD, as well as important implications for management strategies for hyperuricemic patients in clinical practice.

GW31-e0789

The relation of moderate alcohol consumption to hyperuricemia in a rural general population

Zhao Li, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Although alcohol abuse is known to increase serum uric acid, the relation between moderate drinking and uric acid have remained poorly understood. We performed this study to evaluate whether different alcohol consumption level has different effects on the risk of hyperuricemia based on a rural general population.

METHODS Multi-stage cluster sampling method was used to select a representative sample of individuals aged 35 years or older. Participants were asked to provide information about their alcohol consumption. Data regarding the demographic and lifestyle characteristics and the blood biochemical indexes of these participants were collected by well-trained personnel.

RESULTS In total, 11,039 participants aged 35 years or older were included (4997 men and 6042 women). The prevalence of hyperuricemia in the different male alcohol consumption groups was 11.9% in non-drinkers, 12.6% in moderate drinkers, and 16.3% in heavy drinkers (P<0.001). In females, the rates were 6.3% in non-drinkers, 8.1% in moderate drinkers, and 6.6% for heavy drinkers (P=0.818). In males, multivariate logistic regression analyses shows heavy drinkers had an approximately 1.7-fold higher risk of hyperuricemia (OR: 1.657, 95% CI: 1.368–2.007, P<0.001) than non-drinkers; moderate drinkers did not experience a significant increase in risk (OR: 1.232, 95% CI: 0.951–1.596, P=0.114). Multivariate logistic regression analyses of females showed that, compared with non-drinkers, neither moderate nor heavy drinkers had a significantly increased risk of hyperuricemia (OR: 1.565, 95% CI: 0.521–4.695, P=0.425 for heavy drinkers; OR: 0.897, 95% CI: 0.117–6.855, P=0.916 for moderate drinkers).

CONCLUSIONS Heavy alcohol consumption increased the risk of hyperuricemia for males but not for females. Among both males and females, moderate alcohol consumption did not increase the risk of hyperuricemia.

GW31-e0790

Alcohol consumption and cardiovascular diseases in rural China

Zhao Li, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES This study aimed to update the current information on alcohol consumption and evaluate the associations between drinking status and cardiovascular diseases in a general population from rural China.

METHODS The study examined a total of 11,269 adults using a multi-stage cluster sampling method to select a representative sample of individuals 35 years or older. Related medical histories were obtained using a standard questionnaire, and blood biochemical indexes were collected by well-trained personnel. Participants were asked for information about whether they regularly consumed alcohol, their average alcohol consumption per day, and the number of days per month that they consumed alcohol.

RESULTS This population consisted of 75.8% non-drinkers, 7.5% moderate drinkers, and 16.7% heavy drinkers. And the mean alcohol consumption per day for the total population was 15.29±0.35 g/d (women: 1.0±0.11 g/d and men 32.5±0.69 g/d, P<0.001). Multivariate logistic regression analysis showed that heavy drinkers had an approximately 1.3-fold and 1.7-fold greater risk for coronary heart disease and hypertension, respectively (OR: 1.252, 95% CI: 1.012–1.549; OR: 1.741, 95% CI: 1.519–1.994, respectively) compared with that of the non-drinking group. After fully adjusting the data for all variables, the data showed no significant association between moderate alcohol consumption and CHD, HT or ischemic stroke.

CONCLUSIONS Alcohol consumption in rural populations is high, particularly in men. Heavy drinking is a risk factor for coronary heart disease and hypertension, but not for ischemic stroke. There was no significant association between moderate alcohol consumption and CHD, HT or ischemic stroke.

GW31-e0791

The association between alcohol consumption and left ventricular ejection fraction: an observational study on a general population

Zhao Li, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES The results of previous studies on the relation between alcohol consumption and heart failure (HF) have been inconsistent. This study aimed to evaluate the association between alcohol consumption and left ventricular ejection fraction (LVEF) in a general population.

METHODS A total of 10,824 adults were examined using a multistage cluster sampling method to select a representative sample of individuals who were at least 35-years old. The participants were asked to provide information about their alcohol consumption. Echocardiograms were obtained, and LVEF was calculated using modified Simpson's rule.

RESULTS Of the 10,824 participants included in the present study, 46.1% were males, and the mean participant age was 54 years; age ranged from 35 to 93 years. The overall prevalence of LVEF <0.50 and LVEF <0.40 in the studied population was 11.6 and 2.9%, respectively. The prevalence of LVEF <0.5 and LVEF <0.04 was higher in both the moderate and heavy drinker groups than in the nondrinker group (P<0.05). Multivariate logistic regression analyses corrected according to the different levels of alcohol consumption showed that moderate and heavy drinkers had an ~1.3-fold and 1.2-fold higher risk of LVEF <0.5, respectively, than nondrinkers (OR: 1.381, 95% CI: 1.115–1.711, P=0.003 for moderate drinkers; OR: 1.246, 95% CI: 1.064–1.460, P=0.006 for heavy drinkers). Heavy drinkers had an approximately 1.5-fold higher risk of decreased LVEF <0.4 than nondrinkers (OR: 1.482, 95% CI: 1.117–1.965, P=0.006). Moderate drinkers did not show a risk of decreased LVEF <0.4 that was significantly higher than that of nondrinkers (OR: 1.183, 95% CI: 0.774–1.808, P=0.437).

CONCLUSIONS According to these results, we concluded that increased alcohol consumption was associated with decreased LVEF compared with no alcohol consumption in this general population.

GW31-e0792

Diagnosed but not undiagnosed diabetes is associated with depression in rural areas

Zhao Li, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES There is a lack of study on the relation between undiagnosed diabetes and depression in the general population.

METHODS A total of 11,531 adults were examined using a multistage cluster sampling method to select a representative sample of individuals who were at least 35 years old. Subjects were classified into three groups: no diabetes (ND), diagnosed diabetes (DD), and undiagnosed diabetes (UD). The participants were surveyed with the Patient Health Questionnaire-9 (PHQ-9).

RESULTS Of all the 11,531 participants, the prevalence of depression was higher in the DD group than in the other two groups. Multi variable logistic regression analyses show that the DD group had significantly higher odds for depression compared with the ND group (P<0.01), while the UD group showed no significant differences compared to the ND group. Subgroup analyses show that diagnosed diabetes in subjects with a lower educational level, compared with subjects with an educational level of high school or above, had higher odds for a PHQ-9 score ≥5 (P<0.01).

CONCLUSIONS In this general population, diagnosed but not undiagnosed diabetes was significantly associated with depression. Much higher odds for depression were found among diagnosed diabetic individuals with a lower level of education.

GW31-e0794

Plasma homocysteine levels associated with a corrected QT interval

Zhao Li, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Little is known about the relationship between homocysteine (Hcy) levels and the QT interval. We examined the association of different Hcy levels with corrected QT (QTc) intervals in a general population.

METHODS Plasma levels of Hcy were assessed in a population-based study of 7002 participants 35 years of age and older from 2012 to 2013. Twelve-lead ECGs were performed on all participants and analyzed automatically.

RESULTS The distribution of Hcy levels was determined for an entire population after the data were grouped into quartiles (Q1: ≤11.1 μmol/L; Q2: 11.1–13.8 μmol/L; Q3: 13.8–18.2 μmol/L; Q4>18.2 μmol/L). The mean

value of the QTc interval in each quartile was 433.2±23.8 ms, 430.0±24.6 ms, 429.2±24.5 ms and 430.6±25.7 ms. Multiple logistic regression analyses showed that, compared with the second quartile, and after fully adjusting for potential confounding factors, the odds for QTc>440 ms in the first and fourth quartile increased (P<0.05), (OR: 1.23, 95% CI: 1.05–1.43 for Q1; OR: 1.40, 95% CI: 1.19–1.65 for Q4).

CONCLUSIONS QTc interval was associated with the Hcy level in this general population.

GW31-e0795

Metabolism rather than obesity is associated with ischemic stroke: a cross-sectional study in rural northeastern China

Zhao Li, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Little is known about stroke with different obesity phenotype as determined using the Adult Treatment Panel-III criteria with metabolic health or not. This study aimed to investigate the effects of metabolically healthy and unhealthy obesity on ischemic stroke in a general population.

METHODS A total of 11,150 adults were examined using a multi-stage cluster sampling method to select a representative sample of individuals 35 years or older. Ischemic stroke was defined as history of a cerebrovascular event, as documented by doctors via either cranial CT or MR scan within the past 2 years. All subjects were categorized as having metabolically healthy non-obesity (MHNO), metabolically unhealthy non-obesity (MUNO), metabolically healthy obesity (MHO) or metabolically unhealthy obesity (MUO) using the Adult Treatment Panel-III criteria. Stratified analysis were done based on different body mass index group.

RESULTS For the total population, multiple regression analyses revealed that individuals with MUNO and MUO were more likely to experience ischemic stroke compared with those with MHNO (OR 2.136, 95% CI 1.677–2.720; OR 2.712, 95% CI 1.798–4.092; all P<0.001). The OR for ischemic stroke did not significantly differ between MHO and MHNO. Stratification based on different BMI group showed that, compared with people who were normal weight without Mes, participants who were in Mes with overweight or obesity had significantly higher OR for ischemic stroke (both P<0.05); participants who were not in Mes with overweight or obesity did not showed OR significantly higher.

CONCLUSIONS Ischemic stroke is likely associated with poor metabolic health rather than with obesity itself.

GW31-e0796

Relation of heavy alcohol consumption to QTc interval prolongation

Zhao Li, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Until now, few studies have examined QT intervals in subjects who consume alcohol. We performed this study to evaluate the associations between alcohol consumption and the QTc interval based on a general population.

METHODS A total of 11,269 adults were examined using a multistage cluster sampling method to select a representative sample of subjects aged ≥35 years. Participants were asked to provide information about their alcohol consumption, and all participants received electrocardiograms and echocardiograms. A prolonged QTc interval was defined according to the national guidelines, which specify thresholds of ≥460 ms in women and ≥450 ms in men.

RESULTS Patients were divided into 3 categories, based on the amount of alcohol they consumed: heavy drinkers (>15 g/d for women and >30 g/d for men), moderate drinkers (≤15 g/d for women and ≤30 g/d for men), and nondrinkers (0 g/d). The results showed that the heavy drinkers had longer QTc intervals than did the nondrinkers. Multivariate logistic regression analyses revealed that men who were heavy drinkers had approximately 1.4-fold higher odds of having a prolonged QTc interval (odds ratio 1.431, 95% confidence interval [CI] 1.033–1.982, P=0.031) than nondrinkers; in women, heavy drinkers had approximately 2.3-fold higher odds of having a prolonged QTc interval (odds ratio 2.344, 95% CI 1.202–4.571, P=0.012) than nondrinkers.

CONCLUSIONS Neither men nor women who were moderate drinkers exhibited a significant increase in risk for prolonged QTc interval. In conclusion, heavy alcohol consumption was found to be a risk factor for a prolonged QTc interval.

GW31-e0807

Assessing the performance of monocyte to high-density lipoprotein ratio for predicting ischemic stroke: insights from a population-based Chinese cohort

Haoyu Wang[1,2], Yingxian Sun[2]
[1]Fuwai Hospital
[2]The First Hospital of China Medical University

OBJECTIVES Monocyte to high-density lipoprotein cholesterol ratio (MHR) is a recently emerged measure of inflammation and oxidative stress and has been used to predict multiple cardiovascular abnormalities, but data relative to ischemic stroke are lacking. The goal of this study was to estimate the associations of MHR and prevalent ischemic stroke among a large cohort of general Chinese population.

METHODS The study analyzed 8148 individuals (mean age: 54.1 years; 45.7% males) enrolled in a cross-sectional population-based Northeast China Rural Cardiovascular Health Study (NCRCHS). We identified 194 patients admitted from January and August 2013 with ischemic stroke.

RESULTS After adjustment for age, sex, and potential confounders, each standard deviation (SD) increment of MHR was predictive to a greater odd of ischemic stroke (odds ratio, 1.276; 95% confidence interval [CI], 1.082–1.504), with subjects in the highest quartile of MHR levels having a 1.6-fold higher risk of prevalent ischemic stroke (95% CI, 1.045–2.524) as compared with those in the lowest quartile. Moreover, smoothing curve showed a linear positive pattern of this association. The area under the curve (AUC) significantly increased (P=0.042) to 0.808 (95% CI, 0.779–0.837) when the combined MHR was added to the baseline logistic regression model with ischemic stroke risk factors. Also, MHR (0.004) significantly improved integrated discrimination improvement when added to the baseline model.

CONCLUSIONS The present study demonstrated for the first time a linear relation between MHR levels and the odds of ischemic stroke in a large community-based population. The MHR, a marker of high atherosclerotic burden, demonstrated incremental predictive value over traditional clinical risk factors, thus providing clinical utility in risk stratification in subjects presenting with ischemic stroke. These findings had implications for strategies aimed at lowering MHR to prevent adverse cardiovascular and cerebrovascular outcomes.

GW31-e0808

Usefulness of cardiometabolic index for the estimation of ischemic stroke risk among general population in rural China

Haoyu Wang[1,2], Yingxian Sun[2]
[1]Fuwai Hospital
[2]The First Hospital of China Medical University

OBJECTIVES Cardiometabolic index (CMI) has been recognized as a novel and practical marker for the assessment of cardiometabolic risk as it is independently related to diabetes and atherosclerotic progression. This study tested the hypothesis that CMI represents a risk of ischemic stroke in a general population of rural China.

METHODS From July 2012 to August 2013, we examined data from a large cross-sectional study of 11,345 participants (mean age 53.8 years; 60.8% females) who underwent biochemical determinations and anthropometric measurements in rural areas of northeast China. Ischemic stroke was documented as a history of cerebrovascular events and verified by medical record review.

RESULTS The prevalence of ischemic stroke was given to 3.1% of females and 3.2% of males. The cardio-metabolic profile was notably more adverse in ischemic stroke groups, irrespective of gender. A dose-response manner was detected for the prevalence of ischemic stroke, exhibiting a significant increase from the lowest to the highest quartiles of CMI (1.2–6.4% in females, P for trend <0.001; 2.3–4.3% in males, P for trend=0.017). In multivariable analysis, for every 1 SD increment in CMI, the probability of ischemic stroke increased by 18% in females and 14% in males, respectively. The odds ratios for ischemic stroke comparing the top versus bottom quartiles of CMI were 2.047 (95% CI: 1.168–3.587) for females and 1.722 (95% CI: 1.019–2.910) for males. According to the area under receiver operating characteristic (AUC), the discrimination power of CMI in predicting ischemic stroke was relatively higher for females (AUC: 0.685) than males (AUC: 0.573).

CONCLUSIONS The strong and independent association of CMI with ischemic stroke in females, in comparison with the much lesser degree in males, provides further insight to better stratify by sex in investigations of ischemic stroke and solidly corroborates the potential role of ischemic stroke prevention targeted at CMI.

GW31-e0809

The impact of nontraditional lipid profiles on left ventricular geometric abnormalities in general Chinese population

Haoyu Wang[1,2], Yingxian Sun[2]
[1]Fuwai Hospital
[2]The First Hospital of China Medical University

OBJECTIVES Despite current interest in the unfavorable impact of nontraditional lipid profiles on cardiovascular disease, information regarding its relations to abnormal left ventricular (LV) geometry has not been systemically elucidated. This study sought to understand predictive implication of nontraditional lipid profiles in specific LV geometric patterns in the general population of rural China.

METHODS Analyses were based upon a cross-sectional study of 10,756 participants (mean age 53.8 years; 54.0% females) who underwent assessment of biochemical, anthropometric, and blood pressure variables in rural areas of China. Participants were classified into four groups of LV morphologic pattern according to left ventricular mass index (LVMI) and relative wall thickness with quantitative echocardiographic data.

RESULTS By multivariable-adjusted linear regression models, nontraditional lipid profiles were positive determinants of concentricity index and LV wall thickness (all P<0.05), with modest effects on LVMI. Non-high-density lipoprotein cholesterol (non-HDL-C) emerged as an independent correlate of concentric LV hypertrophy (LVH) (adjusted odds ratio [OR]: 1.174 per 1 SD increment in non-HDL-C, 95% confidence interval [CI]: 1.075–1.281), followed by low-density lipoprotein cholesterol (LDL-C)/HDL-C ratio (1.158 [1.059–1.266]), total cholesterol (TC)/HDL-C ratio (1.150 [1.050–1.260]), and triglyceride (TG)/HDL-C ratio (1.134 [1.030–1.249]). The ORs for concentric LVH by tertiles further provided insight into that excess risk was associated with the highest tertile of nontraditional lipid profiles. The areas under the ROC curves to predict concentric LVH were statistically identical among nontraditional lipid parameters.

CONCLUSIONS Nontraditional lipid profiles, easily measured in the everyday routine examination, were responsible for increased risk of concentric LVH, potentially providing enhanced clinical utility at no additional cost, which emphasized the beneficial effect of these markers to supplement and improve CVD risk stratification.

GW31-e0810

Validity of cardiometabolic index, lipid accumulation product, and body adiposity index in predicting the risk of hypertension in Chinese population

Haoyu Wang[1,2], Yingxian Sun[2]
[1]Fuwai Hospital
[2]The First Hospital of China Medical University

OBJECTIVES Adiposity, defined by higher cardiometabolic index (CMI), lipid accumulation product (LAP), and body adiposity index (BAI), has conferred increased metabolic risk. However, the incremental utility of CMI, LAP, and BAI in association with prevalent hypertension has not been well described in a population-based setting. We hypothesized that CMI, LAP, and BAI would provide important insight into hypertension risk.

METHODS Blood pressure (BP), fasting lipid profiles, and anthropometric parameters were recorded in a cross-sectional study of 11,400 participants (mean age, 54 years; 53% women) from China. Logistic regression models were used to assess associations of CMI, LAP, and BAI with prevalent hypertension. BAI was evaluated according to hip (cm)/[height (m)(1.5)]−18; LAP was calculated separately for men [(WC-65)×TG] and women [(WC-58)×TG]; and CMI was defined by TG/HDL-C×waist-to-height ratio.

RESULTS CMI, LAP, and BAI were independently correlated with higher SBP and DBP, with nonstandardized (B) coefficients ranging from 1.827 to 4.590 mmHg and 1.475 to 2.210 mmHg (all P<0.001). After adjustment for hypertension risk factors and potential confounders, CMI, LAP, and BAI, modeled as continuous measures, carried hypertension odds (95% CI) of 1.356 (1.259–1.459), 1.631 (1.501–1.771), and 1.555 (1.454–1.662) in women, respectively, per SD increment. In men, each SD increase in CMI, LAP, and BAI experienced a 31, 65, and 53% higher hypertension risk, respectively. Moreover, among women, the odds ratio (95% CI) for hypertension were 2.318 (1.956–2.745), 3.548 (2.985–4.217), and 3.004 (2.537–3.557) in the 4th quartile vs. the first quartile of CMI, LAP, and BAI, respectively. For men, the corresponding figures were 2.200 (1.838–2.635), 3.892 (3.238–4.677), and 3.288 (2.754–3.927), respectively.

CONCLUSIONS Measurements of CMI, LAP, and BAI provide a more complete understanding of hypertension risk related to variation in body fat distribution and pinpoint hypertensive participants in great risk of cardiovascular disease in the future.

GW31-e0811

Estimate of ischemic stroke prevalence according to a novel 4-tiered classification of left ventricular hypertrophy: insights from the general Chinese population

Haoyu Wang[1], Yingxian Sun[2]
[1]Fuwai Hospital
[2]The First Hospital of China Medical University

OBJECTIVES Recently, a novel 4-tiered classification of left ventricular hypertrophy (LVH) based on ventricular dilatation (indexed LV end-diastolic volume [EDV]) and concentricity (mass/EDV (0.67)) has improved all-cause and cardiovascular mortality risk stratification. However, their possible association with ischemic stroke has not been extensively evaluated in the general population.

METHODS We evaluated a cross-sectional study of 11,037 subjects from the general population of China in whom echocardiographic and ischemic stroke data were available to subdivide patients with LVH into four geometric patterns: indeterminate, dilated, thick and both thick and dilated hypertrophy.

RESULTS Compared with normal LV geometry, indeterminate and thick hypertrophy showed a higher prevalence of ischemic stroke (P<0.05). Ischemic stroke was significantly greater in participants with indeterminate (adjusted odd ratio [OR]: 1.635, 95% confidence interval [CI]: 1.115–2.398) and thick (2.143 [1.329–3.456]) hypertrophy but not significantly in those with dilated (1.251 [0.803–1.950]) and both thick and dilated hypertrophy (0.926 [0.435–1.971]) compared with normal geometry in multivariable analysis.

CONCLUSIONS Indeterminate and thick hypertrophy were significantly associated with the presence of ischemic stroke in the general Chinese population. The new 4-tiered categorization of LVH can permit a better understanding of which subjects are at high enough risk for ischemic stroke to warrant early targeted therapy. Key messages this was the first study to investigate whether a 4-tiered classification of LVH defines subgroups in the general population that are at variable risks of ischemic stroke. We identified that thick hypertrophy carried the greatest odd for ischemic stroke, independently of traditional risk factors, followed by indeterminate hypertrophy. The new 4-tiered categorization of LVH emerged as a valuable operational approach, a potential alternative to LVM, to refine ischemic stroke stratification in general population.

GW31-e0812

Sex-specific association between serum uric acid and self-reported snoring in rural China: a cross-sectional study

Haoyu Wang[1,2], Yingxian Sun[2]
[1]Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College
[2]The First Hospital of China Medical University

OBJECTIVES Until now, information has been rare on the association of serum uric acid (SUA) with self-reported snoring. Therefore, the purpose of this study was to explore the sex-specific relationship between SUA and self-reported snoring in a general Chinese population.

METHODS A large cross-sectional study of 10,912 participants aged ≥35 years old were recruited from rural areas of Liaoning Province in China during 2012–2013. SUA were divided into quartiles separated for males and females. Anthropometric measurements and blood biochemical indexes were examined according to standard protocols. Sleep duration and self-reported snoring status were investigated by trained personnel using a structured questionnaire.

RESULTS The prevalence of self-reported snoring was 37.9% (n=2197) among females and 47.4% (n=2420) among males, respectively. The proportion of self-reported snoring presented a significant linear increase across the quartile of SUA level in both sexes. In multivariate logistic regression analysis adjusted for possible confounders, the odds ratio (OR) for SUA with regard to self-reported snoring was significantly higher in females. The OR of self-reported snoring associated with per 1 SD increase in SUA was 1.208 (95% CI 1.118–1.305, P<0.001). The highest quartile of SUA (>293 μmol/L) conferred an independently increased risk for self-reported snoring with OR of 1.643 (95% CI 1.384–1.950, P<0.001) compared to the lowest quartile of SUA (<209 μmol/L). However, there were no significant relationships between SUA and self-reported snoring among males in all the models.

CONCLUSIONS Our study showed that in rural China, SUA was positively correlated with an increased risk for self-reported snoring in females but not in males. The strong association of SUA levels with self-reported snoring in females emphasizes the necessity of stratifying the sex in investigations of self-reported snoring and encourages exploration of SUA as an effective clinical tool of self-reported snoring risk.

GW31-e0813

Relation of four nontraditional lipid profiles to diabetes in rural Chinese H-type hypertension population

Haoyu Wang[1,2], Yingxian Sun[2]
[1]Fuwai Hospital
[2]The First Hospital of China Medical University

OBJECTIVES Mounting evidence suggested that nontraditional lipid profiles have been recognized as a reliable indicator for unfavorable cardiovascular events. The purpose of this study was to explore the role of nontraditional lipid profiles as potential clinical indices for the assessment of prevalent diabetes in rural Chinese H-type hypertension population.

METHODS During 2012–2013, we conducted a large cross-sectional study of 2944 H-type hypertension participants (≥35 years of age) from rural areas in northeast China. Subjects underwent accurate assessment of lipid profiles, fasting plasma glucose (FPG), homocysteine (Hcy) according to standard protocols.

RESULTS The proportion of diabetes showed a graded and linear increase across the quartiles for all four nontraditional lipid parameters. Nontraditional lipid variables were independent determinants of FPG, and its correlation for TG/HDL-C was strongest, whether potential confounders were adjusted or not. Multivariable logistic regression analysis established that the highest triglycerides (TG)/high-density lipoprotein cholesterol (HDL-C) quartile manifested the largest ORs of prevalent diabetes (OR: 3.275, 95% CI: 2.109–5.087) compared with the lowest quartile. The fully adjusted ORs (95% CI) were 2.753 (1.783–4.252), 2.178 (1.415–2.351), 1.648 (1.097–2.478) for the top quartile of total cholesterol (TC)/HDL-C, low-density lipoprotein cholesterol (LDL-C)/HDL-C, and non-high-density lipoprotein cholesterol (non-HDL-C), respectively. On the basis of the area under receiver-operating characteristic curve (AUC), TG/HDL-C showed the optimal discriminating power for diabetes (AUC: 0.684, 95% CI: 0.650–0.718).

CONCLUSIONS Nontraditional lipid profiles (TG/HDL-C, TC/HDL-C, LDL-C/HDL-C and non-HDL-C) were all consistently and independently correlated with prevalent diabetes among the H-type hypertension population in rural China. TG/HDL-C was prone to be more profitable in assessing the risk of prevalent diabetes and should be encouraged as an effective clinical tool for monitoring and targeted intervention of diabetes in H-type hypertension adults.

GW31-e0814

Contribution of non-traditional lipid profiles to reduced glomerular filtration rate in H-type hypertension population of rural China

Haoyu Wang[1,2], Yingxian Sun[2]
[1]Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College
[2]The First Hospital of China Medical University

OBJECTIVES Despite current interest in the unfavourable impact of non-traditional lipid profiles on cardiovascular disease, information regarding its relations to reduced glomerular filtration rate (GFR) in H-type hypertension population has not been systemically elucidated.

METHODS Analyses were based upon a cross-sectional study of 3259 participants with H-type hypertension who underwent assessment of biochemical, anthropometric and blood pressure values. Reduced GFR was considered if meeting estimated GFR <60 mL/min/1.73 m(2).

RESULTS A stepwise multivariate regression analysis indicated that non-traditional lipid parameters remained as independent determinants of estimated GFR (all P<0.001). In multivariable models, we observed a 50, 51, 31, and 24% higher risk for decreased GFR with each SD increment in TC/HDL-C, TG/HDL-C, LDL-C/HDL-C ratios and non-HDL-C levels, respectively. The highest quartile of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C ratios carried reduced GFR odds (confidence intervals) of 5.50 (2.50–12.09), 6.63 (2.58–17.05) and 2.22 (1.15–4.29), respectively. CONCLUSIONS: The relative independent contribution of non-traditional lipid profiles, as indexed by TC/HDL-C, TG/HDL-C, LDL-C/HDL-C ratios and non-HDL-C, towards reduced GFR putting research evidence at the very heart of lipoprotein-mediated renal injury set a vital example for applying a clinical and public health recommendation for reducing the burden of chronic kidney disease.

CONCLUSIONS Non-traditional lipid profiles has been linked with the occurrence of cardiovascular disease, but none of the studies that address the effect of non-traditional lipid profiles on reduced GFR risk in H-type hypertension population has been specifically established. A greater emphasis of this study resided in the intrinsic value of TC/HDL-C, TG/HDL-C, LDL-C/HDL-C ratios and non-HDL-C that integrate atherogenic and anti-atherogenic lipid molecules to predict the risk of reduced GFR among H-type hypertension population and provide insight into the pathophysiology of subsequent cardiocerebrovascular outcomes. In a large Chinese H-type hypertension adults, the relative independent contribution of non-traditional lipid profiles, as indexed by TC/HDL-C, TG/HDL-C, LDL-C/HDL-C ratios and non-HDL-C, towards reduced GFR putting research evidence at the very heart of lipoprotein-mediated renal injury set a vital example for applying a clinical and public health recommendation for reducing the burden of CKD.

GW31-e0815

Value of reduced glomerular filtration rate assessment with cardiometabolic index: insights from a population-based Chinese cohort

Haoyu Wang[1,2], Yingxian Sun[2]
[1]Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College
[2]The First Hospital of China Medical University

OBJECTIVES Recent studies have suggested that cardiometabolic index (CMI), a novel estimate of visceral adipose tissue, could be of use in the evaluation of cardiovascular risk factors. However, the potential utility and clinical significance of CMI in the detection of reduced estimated glomerular filtration rate (eGFR) remains uncertain. The purpose of this study was to investigate the usefulness of CMI in assessing reduced eGFR in the general Chinese population.

METHODS This cross-sectional analysis included 11,578 participants (mean age: 53.8 years, 53.7% females) from Northeast China Rural Cardiovascular Health Study (NCRCHS) of general Chinese population (data collected from January 2013 to August 2013). CMI was calculated by triglyceride to high density lipoprotein cholesterol ratio multiply waist-to-height ratio. Reduced eGFR was defined as eGFR<60 mL/min per 1.73 m(2). Multivariate regressions were performed to determine CMI's association with eGFR value and eGFR reduction, ROC analyses were employed to investigate CMI's discriminating ability for decreased eGFR.

RESULTS The prevalence of reduced eGFR was 1.7% in males and 2.5% in females. CMI was notably more adverse in reduced eGFR groups, regardless of genders. In fully adjusted multivariate linear models, each 1 SD increment of CMI caused 3.150 mL/min per 1.73 m(2) and 2.411 mL/min per 1.73 m(2) loss of eGFR before CMI reached 1.210 and 1.520 in males and females, respectively. In logistic regression analyses, per 1 SD increase of CMI brought 51.6% additional risk of reduced eGFR in males while caused 1.347 times of risk in females. After divided into quartiles, people in the top quartile of CMI had higher adjusted ORs of having reduced eGFR, with ORs of 4.227 (1.681, 10.627) and 3.442 (1.685–7.031) for males and females respectively. AUC of CMI was revealed to be 0.633 (0.620–0.646) in males and 0.684 (0.672–0.695) in females.

CONCLUSIONS Higher CMI was independently associated with greater burden of reduced eGFR, highlighting VAT distribution and dysfunction as a potential mechanism underlying the association of obesity with kidney damage and adverse cardiovascular outcomes. The findings from this study provided important insights regarding the potential usefulness and clinical relevance of CMI in the detection of reduced eGFR among general Chinese population.

GW31-e0831

Atherogenic index of plasma predicts hyperuricemia in rural population: a cross-sectional study from northeast China

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES We aimed to determine the association of atherogenic index of plasma (AIP) with hyperuricemia (HUA) in the rural population of northeast China.

METHODS This cross-sectional study was conducted in the rural areas of northeast China from January 2012 to August 2013, and the final analysis included data obtained form 5253 men and 6092 women.

RESULTS One thousand and one hundred and four participants (9.7%) suffered from HUA. Spearman rank test showed that AIP was positively correlated with uric acid in both sexes (r=0.310 for men and r=0.347 for women, both P<0.001). AIP was classified into three groups: the low (<0.11), the intermediate (0.11–0.21) and the increased (>0.21) risk. The prevalence of HUA increased with AIP. Multivariate logistic regression analysis showed that, compared to the low AIP group, participants in increased AIP group had a 2.536-fold risk for HUA (2.164-fold in male and 2.960-fold in female) after adjustment for covariates. Results of receiver operating characteristic curves showed that the area under the curve (95% confidence intervals) was 0.686 (0.665–0.707) for male and 0.730 (0.706–0.755) for female.

CONCLUSIONS We indicated that increased AIP was associated with higher serum uric acid levels and could be identified as an independent risk factor of HUA in the rural population of northeast China.

GW31-e0833

A body shape index and body roundness index: two new body indices to identify left ventricular hypertrophy among rural populations in northeast China

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Recently, two new anthropometric indices, the A Body Shape Index (ABSI) and Body Roundness Index (BRI) have been developed as possible improved alternatives to body mass index (BMI) and waist circumference (WC). The main research aim is to assess the capacity of the ABSI and BRI to identify subjects with left ventricular hypertrophy (LVH) and the secondary aim is to determine whether ABSI and/or BRI is superior to BMI, WC, and waist-to-height ratio (WHtR).

METHODS This cross-sectional study was conducted among the rural population in northeast China and finally included 10,907 participants. Pearson rank test showed that BRI showed the highest correlation coefficient for LVH.

RESULTS Body Roundness Index had the highest AUCs for eccentric and concentric LVH (AUC: 0.74, 95% CI: 0.72–0.75; AUC: 0.67, 95% CI: 0.64–0.70, respectively). A multivariate logistic regression analysis also showed that BRI was the best predictor of eccentric and concentric LVH (OR: 5.11, 95% CI: 3.62–7.22; OR: 2.48, 95% CI: 1.40–4.40, respectively). In the five anthropometric indices, only BRI had predictive ability for concentric LVH.

CONCLUSIONS We have shown that BRI, not ABSI was superior measure compared to BMI, WC and WHtR for determining the presence of LVH, especially for eccentric LVH.

GW31-e0835

The association of ideal cardiovascular health and left ventricle hypertrophy in rural population of northeast China: a cross-sectional observational study

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES In 2010, the American Heart Association (AHA) published a new concept "ideal cardiovascular health" (CVH), which consisted of 4 behaviors (smoking, body mass index [BMI], physical activity, and diet score) and 3 health factors (total cholesterol [TC], blood pressure [BP], and fasting plasma glucose [FPG]). This study was aimed to investigate the association between CVH with left ventricle hypertrophy (LVH) in a rural general population.

METHODS From January 2012 to August 2013, we conducted this cross-sectional study using a multi-stage cluster sampling method. A representative sample of individuals who were at 35 years or older was selected. All the 7 CVH metrics were estimated for ideal, intermediate, and poor levels. LVH was accessed by echocardiography and classified into concentric remodeling, concentric LVH, and eccentric LVH. The association between CVH and LVH was determined.

RESULTS The final data were obtained from 10,684 adults (5497 men and 5187 women) in the rural areas of northeast China. Overall, the prevalence rates of concentric remodeling, concentric LVH, and eccentric LVH were 5.1, 4.9, and 12.8%, respectively. The prevalence of concentric/eccentric LVH was inversely related to the numbers of ideal CVH metrics. Multivariate logistic regression analysis indicated that only poor BP was associated with concentric remodeling among the 7 CVH metrics; poor BP was highly associated with concentric LVH (OR: 8.49; 95% CI: 4.59–15.7); poor BMI was highly associated with eccentric LVH (OR: 5.87; 95% CI: 4.83–7.14). Compared to subjects with 5–7 ideal CVH metrics, subjects with 4, 3, 2, 1, and 0 ideal CVH metrics had an increased risk for both concentric and eccentric LVH in a number-dependent manner. The subjects with poor CVH status had a 5.90-fold higher risk of developing concentric LVH and a 3.24-fold higher risk of developing eccentric LVH, compared to subjects with ideal-intermediate CVH.

CONCLUSIONS Our study found that an inversely gradient relationship existed between the prevalence of concentric/eccentric LVH with the numbers of ideal CVH metrics. Although not all the 7 CVH metrics were associated with LVH, the components of CVH metrics carried a synergistic effect beyond the risk related to the component alone.

GW31-e0836

The prevalence of hypertension accompanied by high homocysteine and its risk factors in a rural population: a cross-sectional study from northeast China

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Previous studies found that hypertension and high homocysteine (HHcy) exhibited a synergistic effect on the risk of cardiovascular diseases. This study aimed to investigate the prevalence of hypertension accompanied by HHcy and its risk factors in the rural areas of northeast China.

METHODS This study was conducted using a stratified cluster random sampling method, and included 6529 subjects with complete data. Demographic characteristics were obtained from a questionnaire. Blood pressure and anthropometric indices were measured, and serum indices were analyzed. Hypertension accompanied by HHcy was defined as hypertension plus HHcy [homocysteine (Hcy)>10 μmol/L].

RESULTS The mean concentration of Hcy was 17.29 μmol/L in the general population. The prevalence of hypertension accompanied by HHcy was so high that it reached 45.1% of our study population and accounted for 86.8% of the total participants with hypertension. Multiple logistic regression analysis indicated that the modifiable risk factors of hypertension accompanied by HHcy included obesity, diabetes, dyslipidemia, and inactive physical activities.

CONCLUSIONS We found that the mean level of Hcy, and the prevalences of HHcy and hypertension accompanied by HHcy were very high among the rural population of northeast China. Obesity, diabetes, dyslipidemia, and inactive physical activities were modifiable risk factors of hypertension accompanied by HHcy.

GW31-e0837

Comprehensive comparison between empty nest and non-empty nest elderly: a cross-sectional study among rural populations in northeast China

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES This study aimed to comprehensively compare the general characteristics, lifestyles, serum parameters, ultrasonic cardiogram (UCG) parameters, depression, quality of life, and various comorbidities between empty nest and non-empty nest elderly among rural populations in northeast China.

METHODS This analysis was based on our previous study which was conducted from January 2012 to August 2013, using a multistage, stratified, random cluster sampling scheme. The final analyzed sample consisted of 3208 participants aged no less than 60 years, which was further classified into three groups: non-empty nest group, empty nest group (living as a couple), and empty nest group (living alone).

RESULTS More than half of the participants were empty nest elderly (60.5%). There were no significant statistical differences for serum parameters, UCG parameters, lifestyles, dietary pattern, and scores of Patient Health Questionnaire-9 (PHQ-9) and World Health Organization Quality of Life questionnaire, abbreviated version (WHOQOL-BREF) among the three groups. Empty nest elderly showed no more risk for comorbidities such as general obesity, abdominal obesity, hyperuricemia, hyperhomocysteinemia, diabetes, dyslipidemia, left atrial enlargement (LAE), and stroke.

CONCLUSIONS Our study indicated that empty nest elderly showed no more risk for depression, low quality of life and comorbidities such as general obesity, abdominal obesity, hyperuricemia, hyperhomocysteinemia, diabetes, dyslipidemia, LAE, and stroke among rural populations in northeast China.

GW31-e0838

The feasibility of two new anthropometric indices to identify hypertension in rural China: a cross-sectional study

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Recently, 2 new anthropometric indices, the A Body Shape Index (ABSI) and Body Roundness Index (BRI), have been developed. Our study was to compare the associations between different anthropometric indices, including ABSI, BRI, body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR), and hypertension in a rural population of northeast China.

METHODS This cross-sectional study was conducted in the rural areas of northeast China from January 2012 to August 2013 using a multistage, stratified random cluster-sampling scheme. All eligible permanent residents aged ≥35 years (a total of 14,016 individuals) in each village were invited to participate in the study.

RESULTS A final sample size of 11,345 (5253 males and 6092 females) were included in this study. All the 5 anthropometric measures were positively correlated with hypertension. The prevalence of hypertension increased across quartiles for ABSI, BMI, BRI, WC, and WHR. Multivariable logistic regression analysis of the presence of hypertension for the highest quartile versus the lowest quartile of each anthropometric measure, showed that BRI had the largest values of ORs (OR: 3.49, 95% CI: 2.86–4.21 in men; OR: 3.06, 95% CI: 2.56–3.67 in women) and ABSI had the smallest ORs (OR: 1.30, 95% CI: 1.06–1.58 in men; OR: 1.19, 95% CI: 1.04–1.34 in women). BRI had the highest AROCs for hypertension (AROC: 0.65, 95% CI: 0.64–0.67 for men and AROC: 0.68, 95% CI: 0.67–0.70 for women), while ABSI had the lowest AROCs for hypertension

(AROC: 0.60, 95% CI: 0.58–0.61 for men and AROC: 0.59, 95% CI: 0.58–0.61 for women).

CONCLUSIONS Our results showed that ABSI, BMI, BRI, WC, and WHR were all associated with hypertension. ABSI showed the weakest association with hypertension, while BRI showed potential for use as an alternative obesity measure in assessment of hypertension.

GW31-e0839

Prevalence and metrics distribution of ideal cardiovascular health: a population-based, cross-sectional study in rural China

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES The American Heart Association (AHA) introduced definitions of "ideal," "intermediate," and "poor" cardiovascular health (CVH) based on seven cardiovascular health metrics (smoking, body mass index, physical activity, diet score, total cholesterol, blood pressure, and fasting glucose). This study used this construct to assess the prevalence and metric distribution of CVH in a rural population with traditional lifestyles and investigate the relationship of CVH with socio-demographic characteristics of participants.

METHODS From January 2012 to August 2013, a representative sample of 11,113 adults (mean age 53.8±10.6 years; 53.8% women) was enrolled from a rural population in Northeast China using a multi-stage, stratified random cluster-sampling scheme.

RESULTS According to the adjusted AHA criteria for CVH health metrics, there was 0.1% prevalence of ideal CVH (all seven health metrics at ideal levels), 11.7% of intermediate CVH (at least one health metric at intermediate level, but no poor health metrics), and 88.2% of poor CVH (at least one of seven health metrics at poor level). Women and young/middle-aged adults were more likely to have all of the ideal CVH metrics, behaviours, factors and CVH status.

CONCLUSIONS Our study showed extremely low (0.1%) prevalence of ideal CVH in the rural population of northeast China. The poor CVH status, particularly among men and older individuals, underscores the need for urgent action on modifiable risk factors, especially blood pressure and smoking.

GW31-e0840

The association of ideal cardiovascular health and atherogenic index of plasma in rural population: a cross-sectional study from northeast China

Ye Chang, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES In 2010, the American Heart Association has proposed a new concept "ideal cardiovascular health" (CVH) based on seven CVH metrics: smoking, body mass index, physical activity, diet score, total cholesterol, blood pressure, and fasting plasma glucose. We aimed to determine the association of CVH with atherogenic index of plasma (AIP), a strong marker for atherosclerosis (AS).

METHODS This cross-sectional study was conducted in the rural areas of northeast China and 11,113 middle-aged subjects were enrolled. Seven CVH metrics were classified into ideal, intermediate, and poor groups. AIP was calculated as log (TG/HDL) (triglycerides/high-density lipoprotein cholesterol).

RESULTS AIP>0.21 was classified into the high AIP group and served as dependent variable. All seven CVH metrics were correlated with AIP. A gradient relationship between the number of poor CVH metrics and the prevalence of high AIP existed. Log binomial regression analysis showed that compared to those with five to seven ideal CVH metrics, individuals with four, three, two, one, and no ideal CVH metrics had 1.67, 2.66, 4.00, 5.30 and 6.50 times higher prevalence for high AIP. The subjects with poor CVH status had 2.73 times higher prevalence for high AIP.

CONCLUSIONS We found an inversely gradient relationship between the number of ideal CVH metrics and lower prevalence of high AIP.

GW31-e0841

Independent influence of blood pressure on QTc interval: results from a general Chinese population

Guozhe Sun, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES We performed the current study primarily to characterize the independent association of blood pressure with heart rate-corrected QT (QTc) interval after adjusting for cardiovascular confounding factors and left ventricular mass (LVM) in a large general population in China.

METHODS All enrolled 10,553 permanent residents with age ≥35 years from Liaoning Province were investigated by a questionnaire and then subjected to physical examinations, laboratory analyses, and electrocardiogram (ECG) as well as echocardiogram at the same visit. Multivariate linear and logistic regression analyses were conducted to assess the independent association of blood pressure with QTc interval.

RESULTS Hypertensive subjects had significantly longer QTc interval and higher prevalence of prolonged QTc interval compared with normotensive ones in all subgroups stratified by gender and left ventricular hypertrophy (LVH) (all Ps ≤ 0.001). Multiple relevant clinical confounding factors and LVM were all adjusted in the multivariate linear and logistic regression analyses. As a result, both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were independently associated with QTc interval (β=0.12 and 0.16, respectively; Ps<0.001). Furthermore, as categorical variables, hypertension was independently associated with prolonged QTc interval (OR=1.71; P<0.001). Sex-specific analyses revealed that the independent associations were detected in both males and females (all Ps<0.001).

CONCLUSIONS These key findings of the current study highlighted the fact that hypertension was significantly associated with prolonged QTc interval and the correlations were independent of confounding factors and LVM.

GW31-e0842

Early repolarization pattern in the general population: prevalence and associated factors

Guozhe Sun, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES To evaluate the prevalence of early repolarization pattern (ERP) in the general rural Chinese population and identify the contributing risk factors.

METHODS A cross-sectional study of 11,956 permanent residents of Liaoning Province ≥35 year of age was conducted between January and August 2013 (response rate 85.3%). ERP was diagnosed if there was J-point elevation of ≥0.1 mV in ≥2 leads in the inferior (II, III, aVF) or lateral (I, aVL, V(4-6)) territory, or both. Risk factors for ERP were evaluated with a stepwise logistic regression analysis.

RESULTS The overall prevalence of ERP was 1.3%, and it was higher in men than women (2.6 vs. 0.2%, P<0.001), decreasing with increasing age. Percent of ERP positive in lateral leads, inferior, and both was 73.0, 15.3, and 11.7%, respectively. Stepwise logistic regression demonstrated that independent clinical factors for ERP included age (odds ratio [OR] 0.68; P<0.001), male sex (OR 17.09; P<0.001), systolic blood pressure (SBP) (OR 0.77; P=0.022), stroke (OR 0.14; P=0.055), RR interval (OR 1.27; P=0.001), QTc interval (OR 0.76; P=0.008), QRS duration (OR 0.67; P=0.001), Cornell voltage (OR 0.28; P<0.001), and Sokolow-Lyon voltage (OR 2.03; P<0.001).

CONCLUSIONS Although the prevalence of ERP in general rural Chinese population is low, younger age, male sex, lower SBP, non-stroke history, longer RR interval, shorter QTc interval, shorter QRS duration, lower Cornell voltage, and higher Sokolow-Lyon voltage are independent risk factors.

GW31-e0843

The protective role of the TOPK/PBK pathway in myocardial ischemia/reperfusion and H_2O_2-induced injury in H9C2 cardiomyocytes

Guozhe Sun, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES T-LAK-cell-originated protein kinase (TOPK) is a PDZ-binding kinase (PBK) that was recently identified as a novel member of the mitogen-activated protein kinase (MAPK) family. It has been shown to play an important role in many cellular functions. However, its role in cardiac function remains unclear. Thus, we have herein explored the biological function of TOPK in myocardial ischemia/reperfusion (I/R) and oxidative stress injury in H9C2 cardiomyocytes.

METHODS I/R and ischemic preconditioning (IPC) were induced in rats by 3-hour reperfusion after 30-min occlusion of the left anterior descending coronary artery and by 3 cycles of 5-min I/R. Hydrogen peroxide (H_2O_2) was used to induce oxidative stress in H9C2 cardiomyocytes. TOPK expression was analyzed by western blotting, RT-PCR, immunohistochemical staining, and immunofluorescence imaging studies.

RESULTS The effects of TOPK gene overexpression and its inhibition via its inhibitor HI-TOPK-032 on cell viability and Bcl-2, Bax, ERK1/2, and p-ERK1/2 protein expression were analyzed by MTS assay and western blotting, respectively. The results showed that IPC alleviated myocardial I/R injury and induced TOPK activation. Furthermore, H_2O_2 induced TOPK phosphorylation in a time-dependent manner. Interestingly, TOPK inhibition aggravated the H_2O_2-induced

oxidative stress injury in myocardiocytes, whereas overexpression relieved it. In addition, the ERK pathway was positively regulated by TOPK signaling.

CONCLUSIONS In conclusion, our results indicate that TOPK might mediate a novel survival signal in myocardial I/R, and that its effect on anti-oxidative stress involves the ERK signaling pathway.

GW31-e0844

Assessment of novel Peguero-Lo Presti electrocardiographic left ventricular hypertrophy criteria in a large Asian population: newer may not be better

Guozhe Sun, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Recently, the novel Peguero-Lo Presti electrocardiographic criteria to diagnose left ventricular hypertrophy (LVH) were developed from Caucasian American population with a relatively high sensitivity. However, further validation on a large Asian population has never been conducted. Thus, this study was to test and validate the overall performance of this index in a general population from China.

METHODS A total of 10,614 permanent residents ≥35 years of age were included in this study. All participants completed 12-lead electrocardiography and echocardiography at the same visit. A receiver-operating characteristic curve was used for comparing the performance of electrocardiographic indices in diagnosing echocardiographic LVH.

RESULTS The Peguero-Lo Presti criteria had higher sensitivity but lower specificity than Cornell and Sokolow-Lyon voltage according to the recommended criteria. The area under the curve of this novel Peguero-Lo Presti voltage was lower than that of Cornell for predicting LVH defined by both left ventricular mass/body surface area (0.665 vs. 0.699 in males; 0.689 vs. 0.721 in females) and left ventricular mass/height (2.7) (0.623 vs. 0.681 in males; 0.642 vs. 0.709 in females) (all Ps<0.05). By changing cutoff values, Cornell voltage outperformed Peguero-Lo Presti whether to achieve a relatively high sensitivity or specificity.

CONCLUSIONS The novel Peguero-Lo Presti voltage may not be a better screening tool for LVH in Asian population. In comparison with this new index, Cornell voltage could be a better screening test for LVH by changing its cutoff values to obtain maximum sensitivity.

GW31-e0845

Association between CHADS(2) score, depressive symptoms, and quality of life in a general population

Guozhe Sun, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES To investigate the association between CHADS(2) score, depressive symptoms, and quality of life in a large general population from China.

METHODS A cross-sectional study of 11,956 permanent residents of Liaoning Province in China ≥35 years of age was conducted between January and August 2013 (response rate 85.3%). All participants completed a questionnaire, had a physical examination, and underwent blood examination. Depressive symptoms were assessed with the Patient Health Questionnaire-9 (PHQ-9), while the quality of life (QoL) was measured using the World Health Organization Quality of Life Brief Scale (WHOQOL-BREF).

RESULTS With increasing CHADS(2) score, the prevalence of depressive symptoms increased from 4.9 to 27.8% (P<0.001), and all scores of WHOQOL-BREF decreased significantly (all Ps<0.001). After adjusting for confounding risk factors, subjects with CHADS(2) score ≥3 had higher risk of depressive symptoms than those with CHADS(2) score=0 (all Ps<0.05). Also, CHADS(2) score was negatively associated with all scores of WHOQOL-BREF (all Ps<0.001). Furthermore, subjects with any item in CHADS(2) had higher prevalence of depressive symptoms (all Ps<0.001). Heart failure and stroke remained independently associated with depressive symptoms after adjusting for confounding risk factors and other items (Ps<0.001), while heart failure, age ≥75 years, diabetes mellitus, and stroke were all independently negatively associated with the total score of WHOQOL-BREF (all Ps<0.05).

CONCLUSIONS The CHADS(2) score is significantly associated with depressive symptoms and impaired quality of life in the general population.

GW31-e0846

10-Year ASCVD risk is positively correlated with depressive symptoms in a large general population

Guozhe Sun, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES To explore the potential correlation between 10-year atherosclerotic cardiovascular disease (ASCVD) risk and depressive symptoms in a general population.

METHODS A cross-sectional study involving 11,956 permanent residents of Liaoning Province in China ≥35 years of age was conducted. Depressive symptoms were assessed with the Patient Health Questionnaire-9 (PHQ-9) while 10-year ASCVD risk was calculated using the tool suitable for China.

RESULTS Males had significantly higher 10-year ASCVD risk than females (14.2±10.7% vs. 9.3±9.1%; P<0.001) but lower PHQ-9 score (2.34±3.13 vs. 3.63±4.02; P<0.001). The mean PHQ-9 score increased significantly with advancing 10-year ASCVD risk category in both males (from 2.03 to 2.61; P for trend <0.001) and females (from 3.04 to 4.61; P for trend <0.001), and the increasing trend was more apparent in females (P<0.001). Pearson correlation analyses showed that 10-year ASCVD risk positively correlated with PHQ-9 score in both sexes (Ps<0.001). In multivariate linear regression analyses adjusting for confounding risk factors, the independent associations of 10-year ASCVD risk with PHQ-9 score were all significant in the total (β=2.61; P<0.001), male (β=1.64; P=0.001), and female subjects (β=3.71; P<0.001). Further, the interaction analysis proved the impacts of 10-year ASCVD risk on PHQ-9 score were more apparent in females than males (Ps<0.001).

CONCLUSIONS The 10-year ASCVD risk was positively associated with depressive symptoms in both males and females, which was more apparent in the latter. These findings provided some novel data about the value of 10-year ASCVD risk in estimating depressive symptoms.

GW31-e0847

Independent associations of blood pressure and body mass index with interatrial block: a cross-sectional study in general Chinese population

Guozhe Sun, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES This current study was performed to characterise the independent associations of obesity and hypertension with interatrial block (IAB) after adjusting for cardiovascular risk factors, echocardiographic left atrial diameter (LAD) and left ventricular mass index (LVMI) in a large general Chinese population. DESIGN: A cross-sectional study.

METHODS A total of 11,956 permanent residents (≥35 years of age) from Liaoning Province in China were included in this study. Following the completion of a questionnaire, the enrolled participants were subjected to physical examinations, laboratory analyses, ECG and echocardiogram. Linear and logistic regression analyses were performed to evaluate the associations of hypertension and obesity with IAB. IAB was defined as a prolongation of the P wave duration ≥120 ms on a digital 12-lead ECG.

RESULTS The prevalence of IAB in hypertensive individuals was higher than the normotensive in both men (9.5 vs. 5.9%; P<0.001) and women (6.6 vs. 3.6%; P<0.001). In addition, the prevalence of IAB exhibited a sharp increase with advancing body mass index (BMI) in both men (from 4.9 to 13.0%) and women (from 3.5 to 6.9%) (ps – for trend <0.001). Multiple relevant clinical covariates, echocardiographic LAD and LVMI were adjusted in the multivariate linear and logistic regression analyses. The results revealed that systolic blood pressure, diastolic blood pressure and BMI were all independently associated with P wave duration (β=0.02, 0.09 and 0.25, respectively; all ps <0.005). Furthermore, hypertension was found to be independently associated with IAB (OR=1.27; P=0.018), while both overweight and obesity exhibited higher odds of IAB (OR=1.42 and 1.67, respectively; ps <0.005), compared with BMI <24.0 kg/m(2).

CONCLUSIONS The key findings of this study highlighted that hypertension and overweight/obesity were independently and significantly associated with IAB in general Chinese population.

GW31-e0848

Diabetes mellitus is an independent risk factor for atrial fibrillation in a general Chinese population

Guozhe Sun, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES To explore the association between atrial fibrillation (AF) and diabetes mellitus in a general Chinese population, and the influence of hypertension.

METHODS From January 2013 to August 2013, we carried out a cross-sectional study involving 11,956 permanent residents aged ≥35 years from the general population in the Liaoning province of China (response rate 85.3%). Each participant completed a questionnaire, had a physical examination, and underwent an electrocardiogram and echocardiogram. AF was diagnosed on the basis of the electrocardiogram findings. Logistic regression analyses were carried out to estimate the associations between diabetes mellitus and AF. The associations were also analyzed in hypertensive and normotensive subgroups.

RESULTS There was a higher prevalence of AF in participants with diabetes mellitus than those without diabetes mellitus (1.2 vs. 0.5%; P=0.004). In the hypertensive subgroup, the prevalence of AF in participants with diabetes mellitus was significantly higher than in participants without diabetes mellitus (1.5 vs. 0.6%; P=0.008); however, the prevalences were similar in the normotensive subgroup (0.3 vs. 0.4%; P=1.000). Similar trends were present in both men and women. After adjustment for cardiovascular risk factors, the independent association between diabetes mellitus and AF remained in the total sample (odds ratio 2.33, 95% confidence interval 1.20–4.54) and hypertensive subgroup (odds ratio 3.15, 95% confidence interval 1.52–6.56), but not in the normotensive subgroup (odds ratio 0.64, 95% confidence interval 0.08–5.31).

CONCLUSIONS Diabetes mellitus is an independent risk factor for AF in the general population in China, this association was present in total and hypertensive participants, but not in normotensive participants.

GW31-e0849

Self-reported snoring patterns predict stroke events in high-risk patients with obstructive sleep apnea: post-hoc analyses of the SAVE study

Jingwei Li[1], Craig Anderson[2]
[1]Department of Cardiology, Xinqiao Hospital, Third Military Medical University, Chongqing, China
[2]The George Institute for Global Health, Faculty of Medicine, University of New South Wales, NSW, Australia

OBJECTIVES The relation of snoring to risks of stroke and other major cardiovascular (CV) events is uncertain. We aimed to determine associations of snoring patterns and major CV events in relation to the obstructive sleep apnea (OSA), among participants of the international Sleep Apnea cardiovascular Endpoints (SAVE) trial.

METHODS Post-hoc analyses of the SAVE trial, which involved 2687 patients with co-existing moderate-severe OSA and established coronary or cerebral CV disease, who were randomly allocated to continuous positive airway pressure (CPAP) treatment plus usual care or usual care alone, and followed up for a median 3.5 years. Associations of self-reported snoring patterns (frequency and loudness) and breathing pauses collected on the Berlin questionnaire at baseline and multiple times during follow-up, and adjudicated composites of CV outcomes (primary, CV death, non-fatal myocardial infarction, non-fatal stroke, and hospitalization for unstable angina, heart failure, or transient ischemic attack; and separately of cardiac and cerebral events), were evaluated in time-dependent Cox proportional hazards models adjusted for various confounders including apnea-hypopnea index.

RESULTS Increase (per category) of snoring frequency (adjusted hazard ratio [HR] 1.10, 95% confidence interval [CI] 1.02–1.20; P=0.015), loudness (HR 1.16, 95% CI 1.06–1.27; P=0.001), and breathing pauses (HR 1.16, 95% CI 1.08–1.25; P<0.001) at any timepoint during follow-up were each associated with the primary composite CV outcome. These associations were driven by significant associations for cerebral rather than cardiac events, and positive interactions between the three snoring patterns for cerebral events. There is no significant interaction between CPAP treatment and snoring variables for cerebral events.

CONCLUSIONS Snoring in OSA patients with established CV disease is associated with greater risks of cerebral but not cardiac events, independent of CPAP treatment and frequency of apnea and hypopnea events.

GW31-e0864

Green space exposure on mortality and cardiovascular outcomes in older adults: a systematic review and meta-analysis of observational studies

Yin Yuan[1,2,3,4], Siyang Lin[2], Feng Huang[1,2,3,4], Pengli Zhu[1,2,3,4]
[1]Department of Geriatric Medicine, Fujian Provincial Hospital
[2]The Shengli Clinical Medical College, Fujian Medical University
[3]Fujian Provincial Institute of Clinical Geriatrics
[4]Fujian Provincial Key Laboratory of Geriatrics

OBJECTIVES The previous literature has shown that green spaces are beneficial to a range of health-related outcomes in adults. However, associations of greenness with mortality and cardiovascular outcomes may differ depending on the age class, which makes the associations are less certain in the elderly. To our knowledge, no other systematic review has synthesized the evidence, nor are there precise estimates of reductions in mortality risks or cardiovascular outcomes in relation to green space exposure in older adults. This review aimed to systematically evaluate the association of green space exposure with mortality and cardiovascular outcomes in older adults based on observational studies.

METHODS We systematically searched PubMed, Embase, Web of Science, EBSCOhost, and Scopus, from 1st January 2000 to 1st July 2020. Qualitative evaluation and meta-analyses of included studies were conducted. A systematic narrative synthesis of the evidence was applied, and primary study characteristics were summarized and discussed. The meta-analysis was performed in "Stata 15.0" software. A random effects model was chosen as it represented a more conservative approach for studies with high heterogeneity [39]. All results were presented as forest plots with 95% CI. We quantified heterogeneity between studies using the coefficient of inconsistency (I^2). We evaluated the impact of individual studies by conducting sensitivity analysis, excluding one study at a time. Begg's funnel plots and the Egger's test were performed to detect publication bias.

RESULTS Of the 8143 records identified, we finally included 22 studies. In a narrative systematic review, we observed that the majority of studies showed reductions in the risk of all-cause mortality and total cardiovascular disease. For the meta-analysis, we included only cohort studies that investigated associations between green space exposure as measured by NDVI and mortality. Altogether, eight articles revealed a significantly lower risk of all-cause mortality of 0.1 unit increase in NDVI (pooled HR (95% CI)=0.99 (0.97, 1.00), I^2=87.6%, N=8). For a 0.1 unit increase in NDVI, there was a statistically significant reduction in the risk of stroke mortality (pooled HR (95% CI)=0.77 (0.59, 1.00), I^2=78.8%, N=4), but not for CVD mortality (pooled HR (95% CI)=0.99 (0.89, 1.09), I^2=76.4%, N=4), IHD mortality (pooled HR (95% CI)=0.96 (0.88, 1.05), I^2=54.6%, N=3), and respiratory disease mortality (pooled HR (95% CI)=0.99 (0.89, 1.10), I^2=64.6%, N=5). Despite the limited number of studies, Begg's funnel plots and Egger's tests did not reveal any publication bias for all selected outcomes. Sensitivity analyses, excluding one study at a time, exhibited reliable findings for all outcomes.

CONCLUSIONS This review provides some evidence for associations between increased greenness exposure and reduced risk of all-cause and stroke mortality, as well as major CVD outcomes in elderly populations. However, our results are limited by data heterogeneity and should be interpreted with caution. In an aging society, this review suggests that increased greenness exposure may be promising measures for mortality and cardiovascular prevention and provides evidence for urban planners and policymakers to create optimal natural environments for older populations.

GW31-e0882

Prevalence of hyperuricemia and its correlates in rural northeast Chinese population: from lifestyle risk factors to metabolic comorbidities

Shasha Yu, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES The increasing trend of hyperuricemia in urban areas of China has been noted in the past decade. However, the prevalence of hyperuricemia in rural China has not been extensively investigated. We aimed to estimate the prevalence and risk factors of hyperuricemia and the associated comorbidities in rural Northeast China.

METHODS This survey was conducted from July 2012 to August 2013. In this study, a total of 11,576 residents from the rural Northeast China were randomly selected and examined. Hyperuricemia was defined as serum uric acid ≥416 μmol/L in men and ≥357 μmol/L in women. Data regarding the demographic and lifestyle characteristics and the blood biochemical indexes of these participants were collected by well-trained personnel.

RESULTS The prevalence of hyperuricemia was 10.9% and was more prevalent in men than in women (15.0 vs. 7.3%, P<0.001). Multivariate logistic regression models revealed that besides age, hyperuricemia in men was associated with ethnic minority [OR (95%): 0.683 (0.472, 0.989)], physical activity [moderate, OR (95%): 0.716 (0.596, 0.859); high, OR (95%): 0.527 (0.354, 0.786)], current smoking [OR (95%): 1.380 (1.179, 1.616)], and current drinking [OR (95%): 0.705 (0.603, 0.825)], while in women was only associated with ethnic minority [OR (95%): 0.485 (0.262, 0.896)]. After adjusting for possible confounders, hyperuricemia was related to different subtypes of cardiometabolic comorbidities in both gender like abdominal obesity, general obesity, hypertriglyceridemia, hypertension, hypercholesterolemia, and low HDL-C.

CONCLUSIONS Besides, in women only, hyperuricemia was related to diabetes and high LDL-C. Hyperuricemia was common among residents living in rural Northeast China especially among men. Ethnic minority, physical activity, current smoking, and drinking contributed to hyperuricemia in this population.

GW31-e0885

Metabolic syndrome associated with the onset of depressive symptoms among women but not men in rural northeast China

Shasha Yu, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES The present study aimed to assess the cumulative incidence of major depressive disorder (MDD) among rural Chinese residents. Furthermore, we intended to estimate whether metabolic syndrome (MetS) was associated with MDD by both cross-sectional and prospective analysis.

METHODS Data of 11,675 residents (46.3% men) was used for cross-sectional analysis. The residents were followed up with median 4.66 years. MDD was diagnosed using the Patient Health Questionnaire-9 (PHQ-9). The data of 2796 individuals without any depressive symptoms was used for prospective analysis.

RESULTS With median of 4.66 years follow-up, the cumulative incidence of MDD among rural residents was 3.9%. Women had significantly higher cumulative incidence of MDD than men (5.3% for women and 2.9% for men, P<0.01). The incidence of MDD was significantly higher among women with MetS (7.3 vs. 3.8%, P<0.001), hypertriglyceridemia (7.0 vs. 4.5%, P<0.001) or elevated blood pressure (6.4 vs. 3.4%, P<0.001) at baseline compared with those without them. There was no incidence difference of MDD among men with or without baseline metabolic disorders. In prospective study, after adjusting possible confounders, baseline MetS was associated with higher incidence of MDD (OR: 1.82, 95% CI: 1.01, 3.27, P=0.045) in women but not men (OR: 1.84, 95% CI: 0.88, 3.83, P=0.104).

CONCLUSIONS Cumulative incidence of MDD in rural China was higher among women than among men. Baseline MetS was associated with higher cumulative incidence of MDD in women but not men. More concern should be put on women with MetS in case of onset depressive symptom in future.

GW31-e0888

Association between obese phenotype and mildly reduced eGFR among the general population from rural northeast China

Shasha Yu, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Obesity contributes to reduced kidney function; however, whether this is due to obesity itself or the metabolic abnormalities that accompany it is unclear. Besides, most previous studies enrolled participants with moderate or severe stage of chronic kidney disease. In the present study, we aim to investigate the possible relationship between obesity, metabolic abnormalities and mildly reduced estimated glomerular filtration rate (eGFR).

METHODS A total of 11,127 Chinese participants (age ≥35 years) were enrolled in a survey conducted from January 2012 to August 2013. eGFR 60–90 mL/min/1.73 m^2 was defined as mildly reduced eGFR. Obese phenotype was divided into four types: metabolically healthy non-obese (MHNO), metabolically healthy obese (MHO), metabolically abnormal non-obese (MANO) and metabolically abnormal obese (MAO).

RESULTS Among all participants, 1941 (17.4%) of them had mildly reduced eGFR (16.7% for men and 18.1% for women, P=0.025). The prevalence of obese phenotype was 22.5% for MHNO, 9.1% for MHO, 32.1% for MANO and 36.4% for MAO. The prevalence of mildly reduced eGFR was 9.0% among MHNO, 7.0% among MHO, 22.6% among MANO and 20.7% among MAO (P<0.001). Multivariate logistic regression analysis revealed that obese phenotype did not statically contributed to mildly reduced eGFR (MHO: OR=1.107, P=0.662; MANO: OR=0.800, P=0.127; MAO: OR=1.119, P=0.525). However, gender (OR=1.475, P<0.001), aging (OR=1.283, P<0.001), dyslipidemia (OR=1.544, 95% CI: 1.315, 1.814, P<0.001) and hyperglycemia (OR=1.247, 95% CI: 1.068, 1.455, P=0.005) was associated with increased risk of mild reduced eGFR.

CONCLUSIONS Among the general population from rural Northeast China, mildly reduced eGFR was associated with metabolic disorders like dyslipidemia and hyperglycemia, but not obesity.

GW31-e0902

Influence of relative wall thickness on electrocardiographic voltage measures in left ventricular hypertrophy: a novel factor contributing to poor diagnostic accuracy

Ning Ye, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES To characterize the influence of relative wall thickness (RWT) on Cornell, Sokolow-Lyon and Peguero-Lo Presti voltages and elucidate its potential impacts on their diagnostic accuracy for LVH in a large general Chinese population.

METHODS A total of 10,614 permanent residents aged ≥35 years were recruited for this study. All the participants were subjected to ECG and echocardiogram during the same visit. Multivariate linear and logistic regression analyzes were conducted to assess the influence of RWT on the voltages and their diagnostic performance for LVH detection.

RESULTS A distinct correlation was identified between RWT and Cornell and Peguero-Lo Presti voltages following adjustments for age, gender and left ventricular mass (LVM) (β=0.675 and 1.342, respectively; Ps<0.001). Besides, subjects with RWT >0.42 exhibited higher rates of LVH diagnosed by Cornell (OR=1.78, 95% CI: 1.45–2.20), Sokolow-Lyon (OR=1.30, 95% CI: 1.08–1.56), and Peguero-Lo Presti voltage (OR=1.48, 95% CI: 1.29–1.70) after adjustments for age, gender and echocardiographic LVH. Furthermore, concentric remodeling or concentric hypertrophy displayed higher rates of LVH diagnoses via Cornell and Peguero-Lo Presti voltage criteria, as compared with normal geometry or eccentric hypertrophy, respectively (all Ps<0.05), findings of which were independent of age, gender and LVMI.

CONCLUSIONS Echocardiographic RWT was independently correlated with electrocardiographic voltage measures of LVH, which influenced their positive rates and contributed to poor diagnostic performance.

GW31-e0925

Prevalence of abnormal serum liver enzymes in patients with type 2 diabetes mellitus: a cross-sectional study from China

Shuang Chen, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES This cross-sectional study aimed to determine the prevalence of elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in Chinese type 2 diabetic patients and identify contributing risk factors.

METHODS This cross-sectional study was conducted in rural areas of China, and 1198 type 2 diabetic patients with complete data were recruited. Elevated ALT and AST levels were defined as >40 U/L. Prevalence of abnormal liver enzymes was analyzed and multivariable analysis was used to identify independent risk factors.

RESULTS 10.3% and 6.1% diabetic patients had elevated ALT and elevated AST, respectively. The prevalence of elevated liver enzymes was gender-related; it was 13.8% in men and 7.5% in women for elevated ALT, and 7.4% in men and 3.1% in women for elevated AST. High triglyceride was positively associated with both elevated ALT (OR 1.80, 95% CI 1.08–3.01, P=0.024) and elevated AST (OR 2.24, 95% CI 1.08–4.65, P=0.031), while taking anti-diabetes medicine was inversely related to both elevated ALT (OR 0.48, 95% CI 0.29–0.80, P=0.005) and elevated AST (OR 0.37, 95% CI 0.17–0.82, P=0.014). The risk of elevated ALT in diabetic patients increased with the presence of obesity (OR 2.54, 95% CI 1.07–6.01, P=0.034), and was lower in women (OR 0.37, 95% CI 0.19–0.72, P=0.003). Hypertension (OR 4.33, 95% CI 1.41–13.30, P=0.011), current drinking status (OR 2.90, 95% CI 1.21–6.96, P=0.017) and national minority (OR 3.26, 95% CI 1.31–8.12, P=0.011) were risk factors for elevated AST.

CONCLUSIONS A relatively high prevalence of abnormal serum liver enzymes in diabetic patients was demonstrated in China, especially in males. More attention should be paid to preventing liver injuries in diabetic patients.

GW31-e0926

Hypertriglyceridemic waist phenotype and metabolic abnormalities in hypertensive adults: a STROBE compliant study

Shuang Chen, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES The aim of this study was to evaluate the relationship between the hypertriglyceridemic waist (HTGW) phenotype and metabolic abnormalities in hypertensive adults.

METHODS A cross-sectional study, with a sample of 5919 hypertensive adults (2892 men and 3027 women) aged 35 years or older, was recruited from rural areas of China. The participants underwent anthropometric measurements and laboratory examinations. The self-reported information was collected by trained personnel. The HTGW phenotype was defined as elevated triglycerides and elevated waist circumference. The logistic regression analysis was used to evaluate the associations of interest.

RESULTS Hypertensive adults with the HTGW phenotype had significantly higher prevalences of all cardiometabolic risk factors than those without the HTGW phenotype (P<0.001). Compared with the normal waist normal triglyceride (NWNT) group, hypertensive adults with the HTGW phenotype had much higher possibilities to have all cardiometabolic risk factors, especially for 8.35 times more likely of having ≥3 cardiometabolic risk factors [95% confidence interval (95% CI) 5.92–11.79], 6.14 times more likely of having low HDL cholesterol (95% CI 4.98–7.58), 5.49 times more likely of having hyperuricemia (95% CI 4.40–6.86), and 4.32 times more likely of having 1–2 cardiometabolic risk factors (95% CI 3.68–5.07) (P<0.001). Multivariate analysis indicated that the HTGW phenotype was positively associated with metabolic abnormalities (P<0.05).

CONCLUSIONS This study concluded that the HTGW phenotype was positively associated with metabolic abnormalities in hypertensive adults. The HTGW phenotype showed to be an important tool for monitoring of hypertensive adults with metabolic abnormalities, which is low cost, simple, and useful in clinical practice, especially in primary health care in the rural area of China.

GW31-e1061

Child-to-adult cumulative burden of blood pressure and cardiac conduction abnormalities in midlife

Yu Yan, Jianjun Mu
The First Affiliated Hospital of Xi'an Jiaotong University

OBJECTIVES Hypertension is the most common preventable risk factor for all-cause morbidity and mortality and is associated with cardiovascular diseases, including coronary disease, valvular heart diseases, and cardiac arrhythmias. Elevated blood pressure (BP) causes insidious multi-organ injuries and may represent a chronic exposure that injures the cardiac conduction system. A significant body of literature indicates that high blood pressure is one of the most important factors for incident atrial fibrillation. While most prior studies focused predominantly on blood pressure from a single time-point or separated time-points, data are limited regarding the impact long-term burden of BP on cardiac conduction system. This study aims to examine the influence of child-to-adult cumulative BP burden on cardiac conduction function in midlife.

METHODS This study utilized data derived from the Hanzhong Adolescent Hypertension Cohort, an ongoing prospective cohort that was established in 1987. We enrolled participants who had received blood pressure measurements at least four times from childhood (age: 6–15 years) to adulthood (age: 36–45 years). Growth curves of SBP and DBP measured multiple times across life were constructed using a random-effects mixed model. The area under the curve (AUC) was calculated as a measure of long-term burden (total AUC; AUCt) and trends (incremental AUC; AUCi) of systolic blood pressure (SBP) and diastolic blood pressure (DBP). Twelve-leading electrocardiograms (ECGs) were performed. The cardiac conduction function was recorded as heart rate (HR), and the PR, QRS and QT intervals. Multiple linear regression models were used to assess the association of cumulative BP exposure with ECG parameters of interest.

RESULTS A total of 2131 participants (1173 males; median age=42.3 years at follow-up) who had available BP measurements from childhood and ECG data in adulthood were enrolled in this study. Generally, we detected significant associations of child-to-adult cumulative BP burden with increased heart rate (HR) and QTc in midlife. An interquartile range increase in AUCt and AUCi of SBP was associated with 1.207 (95% CI: 0.773, 1.641) and 1.181 (95% CI: 0.750, 1.611) changes in HR, and 1.852 (95% CI: 0.998, 2.706) and 1.731 (95% CI: 0.884, 2.578) changes in QTc, respectively. Similarly, significant associations were observed between higher AUCt and AUCi of DBP and higher HR and QTc. All associations were independent of sex, age, smoking and drinking status, prevalence of hypertension, diabetes and hyperlipidemia, and biochemical parameters at the last follow-up. However, we did not detect significant associations between cumulative BP burden and the PR and QRS intervals.

CONCLUSIONS The observations of this study indicate that child-to-adult cumulative burdens of blood pressure were associated with cardiac conduction abnormalities in middle-aged Chinese adults. Adverse influence of elevated BP exposure on cardiac conduction system begins in childhood. Controlling elevated BP early and throughout life may improve cardiac conduction function in the long run.

GW31-e1081

Impact of monocyte to high-density lipoprotein ratio on prevalent hyperuricemia: findings from a rural Chinese population

Mengqi Chen, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Monocyte to high-density lipoprotein cholesterol ratio (MHR) is a novel inflammatory marker that has been used to predict various inflammation-related diseases. This study aims to explore the association between MHR and prevalent hyperuricemia in a rural Chinese population.

METHODS Eight thousand and one hundred sixty-three eligible participants (mean age: 54.13 years, males: 45.71%) from northeast China were enrolled in this cross-sectional study between 2012 and 2013. MHR was determined as blood monocyte count ratio to high-density lipoprotein cholesterol concentration.

RESULTS The prevalence of hyperuricemia was 12.86%. After adjusting for potential confounding factors, per SD increase of MHR caused a 25.2% additional risk for hyperuricemia, and the top quartile of MHR had an 82.9% increased risk for hyperuricemia compared with the bottom quartile. Additionally, smooth curve fitting and subgroup analyses showed a linear and robust association between MHR and prevalent hyperuricemia respectively. Finally, after introducing MHR into the established model of risk factors, the AUC displayed a significant improvement (0.718 vs. 0.724, P=0.008). Furthermore, Category-free net reclassification improvement (0.160, 95% CI: 0.096–0.224, P<0.001) and integrated discrimination improvement (0.003, 95% CI: 0.002–0.005, P<0.001) also demonstrated significant improvements.

CONCLUSIONS The present study suggests that MHR was positively and independently correlated with prevalent hyperuricemia among rural Chinese adults. Our results also implicate an important value for MHR in optimizing the risk stratification of hyperuricemia.

GW31-e1082

The impact of monocyte to high-density lipoprotein ratio on reduced renal function: insights from a large population

Wenrui Shi, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES To investigate whether monocyte to HDL cholesterol ratio (MHR) can improve the risk stratification of reduced renal function by estimating atherosclerosis.

METHODS The cross-sectional study included 8159 subjects (males: 45.73%, mean age: 54.12 years) from Northeast China in 2013.

RESULTS Each standard deviation increase of MHR brought 42.9% additional risk of reduced renal function in males. In females, MHR strongly correlated with reduced renal function before it reached a breakpoint (MHR=0.25). Additionally, net reclassification improvement identified the value of MHR (0.199; 95% CI: 0.030–0.369; P=0.021) to improve the risk classification of renal function reduction.

CONCLUSIONS This study implicates that MHR is independently associated with reduced renal function and can refine the risk stratification of renal function reduction.

GW31-e1083

Estimate of prevalent diabetes from cardiometabolic index in general Chinese population: a community-based study

Wenrui Shi, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Cardiometabolic index (CMI) defines adiposity based on triglycerides (TG) to high-density lipoprotein cholesterol (HDL-C) ratio and waist-to-height ratio (WHtR). This newly proposed metric has been used to detect multiple cardiovascular risk factors, but data relative to diabetes in the general population are lacking. This study aims to validate CMI's utility of discriminating diabetes and compares it with other indexes among general Chinese population.

METHODS Analyses were based on a cross-sectional study of 11,478 participants that underwent assessment of metabolic and anthropometric parameters in rural areas of northeastern China in 2013. CMI was calculated by TG/HDL-C×WHtR. Multivariate logistic regressions were performed to clarify CMI's association with diabetes, ROC analyses were engaged to investigate CMI's discriminating ability for diabetes.

RESULTS The prevalence of diabetes was 9.93% in males while 10.76% in females, and increased with CMI's increment. After full adjustment, each SD increment of CMI had odds ratios (ORs) for diabetes of 1.471 (1.367–1.584) and 1.422 (1.315–1.539) in females and males, respectively. Compared with bottom categories of CMI, the top quartiles had ORs of 3.736 (2.783–5.015) in females and 3.697 (2.757–4.958) in males. The ROC results showed an excellent discriminating power of CMI (AUC: 0.702 for females, 0.664 for males).

CONCLUSIONS An increasing CMI was correlated with higher odds of diabetes, supporting CMI as a useful and economic measure to screen and quantify diabetes in general Chinese population. Monitoring and promoting achievement of dyslipidemia and abdominal obesity based on CMI may improve subclinical and cardiovascular outcomes.

GW31-e1133

Trends in status of hypertension in rural northeast China: results from two representative cross-sectional surveys, 2013–2018

Liying Xing, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES To investigate the long-term natural trends in the status of hypertension in rural northeast China from 2013 to 2018.

METHODS Two successive cross-sectional surveys were conducted in Liaoning rural areas in 2013 and 2018, which included 10,753 and 10,926 participants aged at least 40 years from different villages, respectively. A multistage, stratified, and cluster random sampling method was used to ensure that the samples of the two studies were representative. Hypertension was defined as a mean

SBP at least 140 mmHg or a mean DBP at least 90 mmHg, and/or self-reported use of antihypertensive medication within the past 2 weeks. The prevalence and control rate of hypertension were also estimated according to the 2017 American College of Cardiology/American Heart Association high blood pressure guideline.

RESULTS Overall, the age-standardized prevalence of hypertension increased from 52.3 to 53.6%, while the age-specified DBP level increased by 5.2% (82.4 vs. 86.7 mmHg) during the study period. However, the control rate unfortunately remained low (4.1 vs. 3.6%), despite unsatisfied awareness and treatment rates of hypertension in rural northeast China. Under the 2017 American College of Cardiology/American Heart Association guideline, the prevalence of hypertension increased from 73.9 to 79.1%; however, the control rate decreased sharply from 1.8 to 0.5% between 2013 and 2018.

CONCLUSIONS Despite the high prevalence of hypertension during the past 5 years, blood pressure levels increased significantly, especially the DBP level. Awareness, treatment, and control of hypertension remained unacceptably low. Therefore, strategies targeting the management of hypertension should be emphasized in rural northeast China.

GW31-e1134

C-R relationship between fasting plasma glucose and unfavorable outcomes in patients of ischemic stroke without diabetes

Liying Xing, Yingxian Sun
The First Hospital of China Medical University

OBJECTIVES Limited data are available on the impact of fasting plasma glucose (FPG) on outcomes in nondiabetic acute ischemic stroke patients.

METHODS The prospective, multi-center, and observational study was performed at 8 hospitals in the Liaoning Province between 2015 and 2016, sought to elucidate the relationship between FPG and the 6-month functional outcomes in nondiabetic acute ischemic stroke patients. The primary effect measure was the adjusted odds ratio for a shift in the direction of unfavorable outcome on the modified Rankin Scale (mRS) score at 6 months, estimated with an ordinal logistic regression, and adjusted for common prognostic factors. Finally, we employed a restricted cubic spline function of linear model to characterize concentration-response (C-R) relationships between FPG and outcomes.

RESULTS A total of 1260 consecutive patients were enrolled, 48.9% of patients had FPG levels >6.1 mmol/L. A total of 282 (22.4%) patients achieved an unfavorable neurologic outcome. Patients achieving an unfavorable neurologic outcome had significantly higher levels of FPG than those achieving a favorable neurologic outcome (6.47 mmol/L versus 7.02 mmol/L). FPG was significantly related to an unfavorable neurologic outcome in nondiabetic acute ischemic stroke patients. The C-R curve showed a nonlinear relation between FPG and 6-month mRS with the nadir at 5.9 mmol/L. Moreover, the likelihood of unfavorable outcome increased by 8.5% for each 1 mmol/L increase in FPG.

CONCLUSIONS Early identification and prompt hyperglycemia management should be considered to improve the functional outcomes during the early poststroke stage.

GW31-e1189

Maternal exposure to cold spells during pregnancy is associated with higher blood pressure and hypertension in offspring later in life

Nanfang Li[1,2,3], Li Cai[1,2,3], Mulalibieke Heizhati[1,2,3], Lin Wang[1,2,3], Mei Li[1,2,3], Delian Zhang[1,2,3], Suofeiya Abulikemu[1,2,3], Xiaoguang Yao[1,2,3], Jing Hong[1,2,3], Bo Zou[1,2,3], Jianxin Zhao[1,2,3]
[1]Hypertension Center of People's Hospital of Xinjiang Uygur Autonomous Region
[2]Xinjiang Hypertension Institute
[3]National Health Committee Key Laboratory of Hypertension Clinical Research

OBJECTIVES We aimed to investigate if month of birth is associated with blood pressure (BP) and prevalent hypertension in adults from a region with frost-free days of <150 days, and average temperatures −13 °C in winter Xinjiang China.

METHODS We analyzed data for 6158 subjects from several surveys. We divided subjects into April to August (n=2624) and September to March (n=3534) groups, based on length of maternal exposure to cold months and analyzed BP, prevalent hypertension and related factors.

RESULTS Diastolic BP in total subjects and systolic and diastolic BP in male subjects born between April and August were significantly higher than in those born in September and March. In sensitivity analysis, untreated males born between April to August showed significantly higher systolic and diastolic BP than did their counterparts. Subjects born between April to August showed significantly higher prevalence of hypertension (31.3 vs. 27.8%, P=0.003), and isolated systolic (23.3 vs. 20.8%, P=0.018) and diastolic hypertension (24.5 vs. 21.4%, P=0.004), than those born between September to March, which is similar for men. Birth between April to August showed 1.68 (95% CI: 1.06–2.67, P=0.027) fold increased odds for the prevalence of hypertension, independent of gender, age, body mass index, waist circumference, cigarette consumption, alcohol intake and family history, compared with their counterparts.

CONCLUSIONS In conclusion, maternal exposure to cold spells during pregnancy may be associated with the increased risk of hypertension in offspring later in life, particularly among males, suggesting the involvement of maternal cold exposure during pregnancy in offspring hypertension development.

GW31-e1258

The profile of cardiovascular disease among 15 million health check-up participants in China

Mingkun Tong[1,2], Bo Wang[1,2], Cheng Jin[1,2], Xiaofang Lan[1,2], Wei Guo[1,2], Jing Liu[3], Liming Li[2,4], Yi Ning[1,2,4]
[1]Peking University Health Science Center Meinian Public Health Institute, Beijing 100191, China
[2]Meinian Institute of Health, Beijing 100191, China
[3]Department of Epidemiology, Beijing Anzhen Hospital, Capital Medical University Beijing 100029, China
[4]Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, Beijing 100191, China

OBJECTIVES It was estimated that more than 200 million people participate in health check-up annually. However, cardiovascular health status was less studied in such population. Therefore, the aim of current study was to investigate the status of cardiovascular diseases (CVD) and their risk factors and target-organ damage using medical records of a large health checkup population.

METHODS We analyzed the medical records of 15,604,275 adults (≥18 years old) who underwent routine checkup from January 1 to December 31, 2018, in 459 Meinian Health Screening Centers covering all provinces nationwide, except Tibet, Hong Kong, Macao and Taiwan. Prevalence of important CVDs were analyzed and compared between different sexes and geographical areas. Major types of CVDs included valvular heart disease (VHD, stenosis or incomplete closure of aortic value, mitral valve, tricuspid valve, and pulmonary valve), atrial flutter and atrial fibrillation, second degree type II and third degree atrioventricular block, and pathological Q wave or R wave poor progression. In addition, we also analyzed the prevalence of target-organ damage, such as left ventricular hypertrophy (LVH), carotid artery plaque and moderate to severe stenosis (the degree of stenosis >30%), chronic kidney disease (CKD, defined as eGFR <60 mL/min/1.73 m^2), and retinal arteriosclerosis. All prevalence rates were standardized by age and gender according to the sixth national census data. SAS 9.4 and R 3.6.4 were used for the analysis.

RESULTS The average age was 41.3±13.5 years old and 52.9% were males in this population. The prevalence of VHD was 1.30%, which was higher in female than that in male (1.44 vs. 1.16%), showing an increasing trend with geographic latitude. Prevalence of atrial flutter and atrial fibrillation was 1.70%, male had higher rate than female (2.77 vs. 1.52%), and the prevalence were relatively higher in central China than in other regions. Of all participants, 0.84% were detected with second degree type II and third-degree atrioventricular block (male: 1.09%; female: 0.58%), and the top three prevalent provinces were Qinghai, Hunan and Xinjiang. The prevalence of pathological Q wave or R wave poor progression was 0.88% (male: 0.94%; female: 0.83%), and the top three prevalent provinces were Hunan, Xinjiang and Shaanxi. For target-organ damage, the prevalence of LVH, carotid artery plaque, carotid artery moderate to severe stenosis, CKD, and retinal arteriosclerosis were 2.31, 13.54, 0.74, 1.45, and 0.78%, respectively. The prevalence of LVH and CKD were higher in the south while carotid artery plaque, moderate to severe stenosis, and retinal arteriosclerosis were more prevalent in the north. For all cardiovascular diseases and target-organ damage, the prevalence increased with age. Overall, approximately 20.14% of physical examination population had above CVDs and/or target-organ damage.

CONCLUSIONS CVDs pose a significant burden with large geographical variation in China. The cardiovascular health issues should be further studied, and health education or management needs to be strengthened immediately.

GW31-e1260

Prevalence of dyslipidemia in a 10 million health checkup population in China

Yuan Ma[1,2], Mingkun Tong[1,2], Bo Wang[1,2], Cheng Jin[1,2], Xiaofang Lan[1,2], Jing Liu[3], Liming Li[2,4], Yi Ning[1,2,4]
[1]Peking University Health Science Center Meinian Public Health Institute, Beijing 100191, China
[2]Meinian Institute of Health, Beijing 100191, China

[3]Department of Epidemiology, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China
[4]Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, Beijing 100191, China

OBJECTIVES Dyslipidemia is one of the most important risk factors for cardiovascular disease. The aim of this study was to investigate the prevalence of dyslipidemia among general health checkup population.

METHODS From January 1 to December 31, 2018, a total of 10,274,986 adults (≥18 years old) were included from a medical checkup population in Meinian Health Screening Centers nationwide, covering all provinces except Tibet, Hong Kong, Macao and Taiwan. The prevalence of dyslipidemia was calculated, and the distribution of dyslipidemia by age, gender, and geographic locations were explored. The prevalence was standardized by age and gender according to the sixth national census data. Dyslipidemia was defined as any one of the following: (1) total cholesterol (TC) ≥6.2 mmol/L; (2) triglyceride (TG) ≥2.3 mmol/L; (3) low-density lipoprotein cholesterol (LDL-C) ≥4.1 mmol/L; (4) high-density lipoprotein cholesterol (HDL-C<1.0 mmol/L); or (5) Self-reported history of dyslipidemia. Awareness rate was defined as the proportion of people with self-reported dyslipidemia in people diagnosed as dyslipidemia according to above definition.

RESULTS The average age was 43.4±13.3 years and 52.3% were men among all participants. The median (interquartile) level was 1.20 (0.83–1.82) mmol/L (men: 1.45 (1.00–2.18) mmol/L, women: 1.00 (0.73–1.46) mmol/L) for TG. Mean±SD was 4.85±0.98 mmol/L for TC (men: 4.90±0.98 mmol/L, women: 4.79±0.98 mmol/L), 2.75±0.83 mmol/L for LDL-C (men: 2.86±0.83 mmol/L, women: 2.64±0.83 mmol/L), and 1.37±0.33 mmol/L for HDL-C (men: 1.28±0.29 mmol/L, women: 1.46±0.33 mmol/L). The prevalence of dyslipidemia was 30.01% (standardized prevalence: 29.26%) for all participants, 38.90% (standardized prevalence: 38.96%) for men and 20.29% (standardized prevalence: 19.24%) for women. It showed an inverted V-shaped trend in both men and women with the highest age-specific prevalence at the age of 40–44 in men (45.22%) and at the age of 65–69 in women (38.54%). The geographical distribution of dyslipidemia in both men and women were: northern region> southern region> central region. The provinces with top three prevalence rates were Heilongjiang, Gansu, and Inner Mongolia, with the standardized prevalence of 42.42, 36.73, and 36.19% respectively, and Jiangsu Province had the lowest prevalence of 22.53%. The standardized prevalence was 7.88% for TC≥6.2 mmol/L, 15.54% for TG ≥2.3 mmol/L, 5.84% for HDL-C<1.0 mmol/L, 9.52% for LDL-C≥4.1 mmol/L. There were 26.57, 9.58, 2.13, and 0.14% of men with one, two, three, all of above four dyslipidemia, respectively. Among women, the percentages were 13.38, 5.57, 0.97, and 0.03% respectively. The awareness rate of dyslipidemia was 4.26, 4.19, 4.40% in all, men and women, respectively.

CONCLUSIONS The prevalence of dyslipidemia is high and varied by age, gender, and geographic locations, but the awareness rate was low. It calls for urgent need to improve preventive and educational strategies for dyslipidemia control in China.

GW31-e1261

Prevalence, awareness, treatment, and control of hypertension in 14 million health check-up participants

Lu Meng[1,2], Mingkun Tong[1,2], Cheng Jin[1,2], Sailimai Man[1,2], Bo Wang[1,2], Jing Liu[3], Liming Li[2,4], Yi Ning[1,2,4]
[1]Peking University Health Science Center Meinian Public Health Institute, Beijing 100191, China
[2]Meinian Institute of Health, Beijing 100191, China
[3]Department of Epidemiology, Beijing Anzhen Hospital, Capital Medical University Beijing 100029, China
[4]Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, Beijing 100191, China

OBJECTIVES Hypertension contributes to heart disease, stroke, kidney failure and premature mortality and disability. However, the issue has been less investigated in health checkup population. Therefore, we analyzed rates of prevalence, awareness, treatment, and control of hypertension in a large health check-up population.

METHODS The study participants included adults who participated in an annual physical examination in 459 health check-up centers in all provinces across the country, except Tibet, Hong Kong, Macao and Taiwan. Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg, or a history of hypertension, or taking antihypertensive drugs. Age and sex standardized weighted rates were estimated based on the sixth population census in China in 2010. SAS 9.4 and R 3.6.4 were used for data analysis.

RESULTS A total of 14,254,382 participants were included in the study. The average age was 41.3±13.4 years and 47.0% of the participants were females. The average SBP/DBP was 123.0±18.4/74.9±12.0 mmHg. The average SBP/DBP in males was 127.0±17.1/78.0±12.0 mmHg, higher than that in females (119.0±18.8/71.8±11.2 mmHg, both P<0.01). With the increase of age, SBP showed a rising trend, while DBP rose at first and then fell slowly. The crude prevalence of hypertension was 22.01%. The age and sex standardized prevalence was 21.50%. The standardized prevalence was higher among males (26.11 vs. 16.75%, P<0.01) than females. The prevalence of hypertension of northern region in China, particularly Northern, Northeast, and Eastern China was higher than southern region (P<0.01). Among the hypertensive participants, the rates of awareness, treatment, and control of hypertension were 34.60, 25.76, and 7.30%, respectively. Each of these rates appeared higher in females than in males (37.42 vs. 32.70%, 30.13 vs. 22.83% and 8.06 vs. 6.83%).

CONCLUSIONS In China, the prevalence of hypertension increased with age, being higher in males and in northern regions than their counterpart. Especially, the awareness, treatment, and control rates of hypertension remained relatively low. Therefore, comprehensive strategies should be developed and implemented to improve the prevention and control of hypertension.

PREVENTION RESEARCH

GW31-e0008

Aspects of somatogenic asthenic syndrome in patients with increased cardiovascular risk

Mazur Tetyana[1], Demikhov Oleksii[1], Sklyar Serhiy[2], Cherkashyna Lidiya[2], Nei Sandra[3], Demikhova Nadiia[1]
[1]Sumy State University, Ukraine
[2]Kharkiv Medical Academy of Postgraduate Education, Ukraine
[3]Tartu University Hospital, Estonia

OBJECTIVES To study frequency and nature of psychopathological symptoms in various forms of somatogenic asthenic syndrome in patients with high cardiovascular risk.

METHODS The primary information base for the implementation of research was the result of complex clinical and anamnestic survey of young patients, the part of whom had non-psychotic mental disorders (NPMD) and who were previously stratified by the level of cardiovascular risk (CVR), defined by the «SCORE» method. The usage of this method involved taking into account: age, gender, presence of smoking, blood pressure levels. Among the 199 persons with high cardiovascular risk (hCVR) and NPMD-31 patients had somatogenic asthenic syndrome (SAS), stratified by clinical variants: asthenic (1n2=14); asthenic-anxious (2n2=8); asthenic-subdepressive (3n2=6) and dyssomniac (4n2=3).

RESULTS Neurotic complaints were typical for patients with high CVR and existing SAS, they happened gradually over time after diagnosis of comorbid somatic disease with high CVR, without actual stressful indirect phenomena with prevalence of physical and mental asthenia. Therefore, neurotoxic and traumatic impact of physical illness on CVR rising cannot be excluded. The frequency and emphasis of SAS grew with increasing of antiquity of comorbid disease and its severity. Emotional and volitional disorders increased gradually: morbid irritability, irascibility, mood swings with a prevalence of negative emotions, depression, despondency, anguish, and inner discomfort with elements of anxiety. At the same time, the symptoms were fairly pale, indistinct; patients did not pay attention on it, seeing it as a secondary, albeit unpleasant "add-on" to their current physical condition. The degree of intensity of psychopathological symptoms in this group was at the level of 2.7–3.6 points. Each variant of SAS in patients with high CVR has its features of symptomological structure. More, than in half of cases in asthenic variant of SAS in patients with high CVR, registered a headache, a feeling of heaviness in the head 6.4±12.8%, intolerance to loud sounds and bright lights 57.1±13.2% and low mood 50.0±13.4%. Patients with high CVR and asthenic-anxious variant of SAS on the first place by the frequency of diagnosing was also weakness 87.5±11.7%, lack of vigor after a night's sleep 87.5±11.7% and almost with the same frequency were registered fatigue 75.0±15.3%, memory impairment 62.5±17.1%, which in 1.5–3 times exceeded the average in patients with SAS by the frequency; anxiety, absentmindedness were diagnosed in 50.0±17.7% of cases in this subgroup.

CONCLUSIONS The frequency and kind of pathopsychological symptoms in young people with increased cardiovascular risk and somatogenic asthenic syndrome was studied. Most common symptom in patients with high CVR and asthenic variant of SAS was a weakness – in 92.9±6.9%, and the prevalence was significantly higher, than on the average in group of patients with SAS. More than ¾ of patients diagnosed: fatigue 85.7±9.4%, tearfulness 85.7±9.4%, irritability 63.4±12.8%, difficulty falling asleep 57.1±13.2%. In patients with high CVR and asthenic-anxious version of SAS on the first place by the frequency of diagnosis was also weakness 87.5±11.7%, lack of vigor after a night's sleep 87.5±11.7% almost on the same frequency was registered fatigue 75.0±15.3%, memory impairment 62.5±17.1%, which in 1.5–3 times exceeded the average in patients with SAS by the frequency.

GW31-e0160

Genetically determined education attainment associates with atrial fibrillation: a mendelian randomization study

Songzan Chen, Guosheng Fu
Sir Run Run Shaw Hospital, Zhejiang University School of Medicine

OBJECTIVES Education attainment is a well-established risk factor for cardiovascular diseases. However, few if any study has investigated the relation between education attainment and atrial fibrillation.

METHODS In current study, we utilized two-sample Mendelian randomization analyses to study the causal effect of education attainment on atrial fibrillation. The inverse-variance-weighted (IVW) method was employed for the main analysis. Single-nucleotide polymorphisms (SNPs) associated with education attainment were extracted from a large genome-wide association study (GWAS) of 1,131,881 European individuals. The summary statistics for atrial fibrillation were obtained from Atrial Fibrillation Consortium with 537,409 (55,114 cases and 482,295 non-cases) European individuals.

RESULTS In total, 264 SNPs were identified as genetic instruments for education attainment. Using the IVW, we found a 1-SD genetic elevation of education attainment was associated with decreased risk of atrial fibrillation (OR=0.90; 95% CI 0.82–0.99; P=0.03). This main result was robust in the follow-up sensitivity analyses.

CONCLUSIONS Our findings clarify the causal association of poor education attainment with the increased risk of atrial fibrillation, supporting the large body of evidence that education attainment has a lifelong impact on health outcomes.

GW31-e0161

The impact of birth weight on atrial fibrillation: evidence from a mendelian randomization study

Songzan Chen, Guosheng Fu
Sir Run Run Shaw Hospital, Zhejiang University School of Medicine

OBJECTIVES Birth weight has been reported to be associated with the risk of atrial fibrillation, but controversy remains. In current study, we aimed to investigate the causal associated between birth weight and atrial fibrillation using a two-sample Mendelian randomization study.

METHODS The inverse-variance-weighted (IVW) method was employed for the main analysis. Single-nucleotide polymorphisms (SNPs) associated with birth weight were obtained from a large-scale genome-wide association study (GWAS) with 321,223 individuals. Summary statistics for atrial fibrillation were derived from Atrial Fibrillation Consortium with up to 537,409 (55,114 cases and 482,295 non-cases) individuals.

RESULTS A total of 132 SNPs was selected as genetic instruments for birth weight. Positive causal association were found between genetically elevated birth weight and increased risk of atrial fibrillation (OR=1.30; 95% CI 1.18–1.44; $P=4.0\times10^{-7}$). This main result was robust in the follow-up sensitivity analyses.

CONCLUSIONS There was positive causal effect of elevated birth weight on the risk of atrial fibrillation incident.

GW31-e0363

Effect of influenza vaccination on the prognosis of heart failure patients: a systematic review and meta-analysis

Miao Wang[1,2,3], Wei Guo[2], Heze Han[2], Siyan Zhan[1]
[1]Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Centre
[2]Beijing Anzhen Hospital, Capital Medical University
[3]Department of Epidemiology, Beijing Institute of Heart, Lung and Blood Vessel Diseases

OBJECTIVES Heart failure (HF) is a serial of clinical manifestations of many cardiovascular diseases at end-stage, including dyspnea, edema, decreased mobility et al. People with HF, who characterized as high re-hospitalization and case-fatality rates, need long-term medication to improve prognosis. Currently, several systematic reviews and meta-analysis show influenza vaccination could improve the prognosis of HF, meanwhile, some studies enrolled participants with cardiovascular disease but no HF. Furthermore, the heterogeneity of studies did not be paid enough attention. This systematic review and meta-analysis aimed to evaluate the effect of influenza vaccination on all-cause mortality and rate of hospitalization by systematically searching and summarizing the studies reported in Chinese and English. The discrepancy of research methods and their effect on the results were also explored.

METHODS A literature search was conducted in four databases (PubMed, OVID, China National Knowledge Infrastructure, and Wanfang Data. The latter two databases were used to search Chinese literature). References in the published reviews were also browsed for checking leakage. The research was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines. The Newcastle-Ottawa Scale was used for appraising the research quality. Manager 5.3 software was used to conduct meta-analyses and combine effect sizes. A random-effect model was used when the heterogeneity was more than 50%.

RESULTS Among 189 literature, eight studies (N=237,819) were eligible for inclusion. The results show during the observation period, compared to HF patients no vaccination, influenza vaccination both associated with low risk of all-cause mortality (HR: 0.82, 95% confidence interval [CI]: 0.81–0.83, P<0.001, I^2=0%) and hospitalization (HR=0.96, 95% CI: 0.95–0.97, P<0.001, I^2=87%). This study also found current studies were not the same in the duration of observation, the number of vaccination, confounder control (such as medication treatments), study adjustment factors, and outcome indicators.

CONCLUSIONS Influenza vaccination could improve the prognosis of HF patients which had a better effect on preventing all-cause mortality than hospitalization. High heterogeneity was observed when explored the benefit of influenza vaccination on preventing hospitalization which deserved to explore thoroughly when enough studies were conducted in the future. Medication or other treatments used during the period of observation and their influence should be paid more attention in future studies. Currently, no high quality and large sample size study conducted in China was seen.

GW31-e0678

Efficacy of the fixed amlodipine-benazepril combination in the treatment of patients with essential hypertension

Qingan Jiang, Tao Xu
Department of Cardiology, No.2 Affiliated Hospital of Guizhou University of traditional Chinese Medicine

OBJECTIVES To evaluate the clinical application of therapy with the fixed combination of amlodipine-benazepril combination in patients with essential hypertension in daily practice.

METHODS The data of 120 essential hypertension patients in our department with a mean age of 62 years and a mean body mass index (BMI) of 28 kg/m^2 were evaluated. They were randomly divided into the amlodipine therapy group (n=40), the benazepril therapy group (n=40) and the amlodipine-benazepril combination therapy (n=40), compared the efficacy of drug after treatment 4 weeks. The amlodipine (YBH10950224, 5 mg) is Produced by Pfizer Pharmaceuticals Limited, the benazepril (YBH10332005, 10 m) by Novartis pharmaceutical company, and The fixed combination (YBH20090309, amlodipine 5 mg/benazepril 10 mg) by Chengdu Di'ao Pharmaceutical Group Co., Ltd. China.

RESULTS The average mean decrease in blood pressure was 28.4 mmHg systolic/13.5 mmHg diastolic in amlodipine-benazepril combination therapy, however 20.5 mmHg/11.3 mmHg in amlodipine therapy and 18.7 mmHg/10.5 mmHg in benazepril therapy (P<0.05). The treatment enabled 79% of the patients to reach the target blood pressure in the amlodipine-benazepril combination therapy, 50% in amlodipine therapy, 61% in benazepril therapy, respectively (P<0.05). There was a mean reduction here of 3 beats/min from 76 to 73 beats/min in the amlodipine-benazepril combination therapy, but Heart rate did not change or even increase in other 2 groups (P<0.05).

CONCLUSIONS The amlodipine-benazepril combination therapy in patients with essential hypertension in daily practice is convenient and effective.

CARDIAC REHABILITATION

GW31-e0043

Survey of the readiness for hospital discharge and its influencing factors among patients with cardiac valve replacement

Limin Liang, Huan Li, Youdi Cai
The Third Affiliated Hospital of Sun Yat-sen University

OBJECTIVES To describe the status of readiness for hospital discharge among patients with cardiac valve replacement and to explore its influencing factors.

METHODS A cross-sectional survey was conducted. A self-designed general information questionnaire, the Readiness for Hospital Discharge Scale and the Quality of Discharge Teaching Scale were delivered to 130 cardiac valve replacement patients from a hospital in GuangZhou.

RESULTS The total score of Readiness for Hospital Discharge Scale was 163.88±39.082, and Quality of Discharge Teaching Scale was 194.09±40.643, which were at moderate level. The multiple linear regression analysis revealed that the quality of discharge guidance, age, occupation were influencing factors of readiness for hospital discharge.

CONCLUSIONS The level of cardiac valve replacement patients' readiness for hospital discharge is at moderate level, and healthcare workers should provide specific interventions according to different influencing factors. Especially, the quality of discharge guidance has a positive effect on discharge readiness. Therefore, in clinical work, we should pay attention to patients' discharge guidance, implement personalized health education, and improve the quality of patients' guidance.

GW31-e0155

Effects of aerobic exercise on cardiac remodeling and endoplasmic reticulum stress-related proteins in spontaneously hypertensive rats

Hongtai Li, Zixin Zhang
China Medical University

OBJECTIVES By using the spontaneously hypertensive rats (SHR), the experiment of aerobic exercise was designed to analyze the myocardial structure and the effect of aerobic exercise on SHR. At the same time, measure the expression of GRP78, CHOP and Caspase12 protein in myocardial tissue of each group, to explore the relationship between the effects of aerobic exercise on myocardial remodeling and ERS in hypertensive rats.

METHODS SHR rats (n=6) were used as aerobic exercise group (SHR-E), and SHR rats (n=6) were used as resting control group (SHR-R), WKY (n=6) as a non hypertensive non exercise control group, rats in SHR-E group were given moderate intensity aerobic exercise for 8 weeks (the speed was set at 2 m/min, reaching to ~55–65% of the maximum aerobic speed, 60 min/day, for 5 days/week). The blood pressure, heart rate were recorded simultaneously before and after the experiment, and then the rats were executed painlessly. The myocardial tissue was taken, paraffin section was made, and the content of collagen fiber in each group was compared with Masson staining. The expression of GRP78, CHOP and Caspase12 protein in myocardial cells in each group was compared with immunohistochemical method, and the expression of GRP78, CHOP and Caspase12 protein in myocardial cells in each group was compared with Western blot method.

RESULTS Compared with the baseline, after 8 weeks of aerobic exercise, (1) in terms of blood pressure, both the SHRs had a significant increase. Besides, the increase of SHR-E group was less than SHR-R group in systolic blood pressure ($P<0.05$), in terms of heart rate, SHR-E group had a increase; in terms of the ratio of left ventricle to body weight, there was no significant difference between the groups ($P>0.05$). (2) Pathological changes of collagen content in myocardial tissue, the collagen content in SHR-R group was the most, followed by that in SHR-E group, and that in WKY group was the least ($P<0.05$). (3) Immunohistochemical results, the expression of GRP78 protein in WKY group was the least (AOD value 0.139±0.078), and that expressed in SHR-E group was the most (AOD value 2.491±0.578). The expression of GRP78 protein in SHR-R group was stated between the two groups above (AOD value 0.139±0.078). The AOD value of each group was statistically different ($P<0.05$). The expression level of CHOP protein in WKY group was the lowest (AOD 0.31±0.302), SHR-R group was the highest (AOD 4.49±0.613), SHR-E was stated between the two groups above (AOD 2.28±0.404), AOD value of each group was statistically significant ($P<0.05$). The expression of Caspase12 protein in WKY group was the lowest (AOD 1.15±0.159), SHR-R group was the highest (AOD 3.87±0.435), and SHR-E group was stated between the two groups above (AOD 2.41±0.474). The results of Western blot were consistent with the results of immunohistochemistry.

CONCLUSIONS Hypertension can lead to the increase of collagen fiber content as well as the expression of ERS related proteins. Aerobic exercise, to some extent, can inhibit the increase of collagen fibers, and improving myocardial remodeling. At the same time, the adverse reaction of ERS can be inhibited, including increasing the expression of protective factor GRP78, reducing the expression of damaging factors CHOP and Caspase12, slowing down the apoptosis of myocardial cells. Besides, aerobic exercise can improve blood pressure, especially the rise of systolic blood pressure and the heart damage caused by it.

GW31-e0388

Endothelial cells responses to shear stress under atheroprone conditions by modulating cell-cell and cell-substrate interactions

Tingting Zhong[1,2], Yanling Li[1,3], Xiaohong He[1], Yongdong Liu[4], Yugang Dong[1], Hong Ma[1], Zhensheng Zheng[1], Yan Zhang[1]
[1]Department of Cardiology, NHC Key Laboratory of Assisted Circulation, First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China
[2]Department of Cardiology, Fuwai Hospital, Chinese Academy of Medical Sciences, Shenzhen, China
[3]Department of Emergency, Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China
[4]Department of Pathology, First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

OBJECTIVES Endothelial cells play a pivotal role in cardiovascular physiology and pathology by contributing a barrier to the bloodstream. In the current study, we investigated the phenotype and barrier function of endothelial cells in response to shear stress under pro-atherogenic conditions.

METHODS Human umbilical endothelial cells (HUVEC) were exposed to laminar shear stress at low (5 dynes/cm^2) or high (25 dynes/cm^2) level in a parallel-plate flow chamber and pump system. To mimic atheroprone conditions, human oxidized Low-Density Lipoprotein (oxLDL) was added into the perfusion medium at a concentration of 100 μg/mL. No flow and no oxLDL conditions served as static control. To evaluate the integrity of endothelial monolayers, transendothelial electrical resistance (TEER) was measured using an electrical cell-substrate impedance sensor (ECIS) system. Endothelial permeability was evaluated by measuring the passage of fluorescein isothiocyanate-dextran (FITC-dextran, 40,000 Da) through the endothelial monolayer. Interendothelial gap area within disrupted vascular endothelial cadherin (VE-cadherin) junctions was determined from immunofluorescence imagines. To exam cell-substrate interactions, endothelial monolayers were trypsinized after the intervention. Membrane and cytoplasmic protein extracts were prepared for immunoblotting analysis.

RESULTS Our results showed that oxLDL stimulation and static conditions synergized to enhance endothelial barrier disruption. Under the same oxLDL challenge, the application of 25 dynes/cm^2 laminar shear stress on the endothelial monolayer can reduce the passage of FITC-dextran by 37.79%, increased the TEER by 24.97% compared with the static cells ($P<0.05$), which was accompanied by reduced intercellular gap formation, relatively solid cell-substrate adhesion, less small size focal adhesions (FAs), less monocyte transmigration, meanwhile, attenuated internalization of VE-cadherin and vinculin.

CONCLUSIONS Static conditions favor, whereas physiologically higher levels of LSS ameliorate endothelial barrier disruption under proatherogenic stress. Shear stress alters endothelial cell-cell interactions, also affects endothelial cell-substrate interactions and attenuates focal adhesion remodeling evoked by oxLDL, contributes to protect the availability of VE-cadherin and vinculin on the endothelial cell surface under atheroprone conditions. Intervention strategy targeting appropriate elevation in shear stress can be used as therapeutic approaches to protect endothelial barrier function, prevent and treat atherosclerotic diseases.

GW31-e0589

Comparison of functional exercise capacity, respiratory muscle strength, pulmonary functions in patients with chronic stable angina and healthy controls

Irem Huzmeli[1], Aysel Yildiz Ozer[2], Oguz Akkus[3], Nihan Katayifci[1], Fatih Sen[3], Saadet UfukYurdalan[2], Mine Gulden Polat[2]
[1]Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Hatay Mustafa Kemal University, Hatay, Turkey
[2]Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Marmara University, Istanbul, Turkey
[3]Department of Cardiology, Tayfur Ata Sokmen Faculty of Medicine, Hatay Mustafa Kemal University, Hatay, Turkey

OBJECTIVES Chronic Stable angina is a disturbing and life restricting disease of coronary heart diseases. Tissue oxygenation in the human body is conveyed by the coordinated action of the cardiovascular and respiratory system. No studies investigated respiratory and peripheral muscle strength and pulmonary function that were important for respiratory systems in patients with chronic stable angina. Therefore, this study was aimed to evaluate respiratory and peripheral muscle strength, functional capacity, and pulmonary function in patients with chronic stable angina.

METHODS Sixteen patients with chronic stable angina (51.31±5.52 years, Canada Class 2) and left ventricular ejection fraction-LVEF 63.57±6.68% and 16 age-matched healthy controls (48.18±4.79 years) were compared. Respiratory muscle strength (maximal inspiratory pressure-MIP, maximal expiratory pressure-MEP) with mouth pressure device, peripheral muscle strength with a dynamometer, pulmonary function with spirometry, functional capacity with a six-minute walking test (6MWT) were evaluated.

RESULTS Demographic and clinical characteristics were similar between the groups ($P>0.05$). Cigarette exposure was higher in patients with angina ($P<0.05$). MIP [89.75±23.09 cmH2O versus 118.62±30.44 cmH2O]; MEP [88.25±20.16 cmH2O versus 139.81±53.42 cmH2O], quadriceps femoris muscle strength, hand-grip strength, predicted %MEP, 6-MWT distance, predicted %6MWT, PEF(L), and %PEF were significantly lower in chronic stable angina patients compared with controls ($P<0.05$).

CONCLUSIONS Respiratory and peripheral muscle weakness, reduced functional capacity and impaired pulmonary function are obvious in patients with chronic stable angina. Therefore, the impairments in outcomes especially exercise capacity, pulmonary functions, respiratory, and peripheral muscle strength should be investigated in detail to plan appropriate cardiac rehabilitation programs.

GW31-e0626

Effects of listening to music while exercising on physical activity adherence and health outcomes among patients with coronary heart disease: a systematic review

Huijing Zou, Xi Cao, Sek Ying Chair
The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong

OBJECTIVES Exercise training is a key facet of cardiac rehabilitation and is associated with irrefutable benefits for patients with coronary heart disease. However, compliance and adherence to such interventions are challenging among this population. The incorporation of music into exercise training is suggested as a potential approach to address this issue. This study aimed to evaluate the effects of listening to music while exercising on adherence to physical activity and health outcomes in patients with coronary heart disease.

METHODS A systematic review was conducted by searching seven English databases. Randomized controlled trials and quasi-experimental studies that evaluated the effects of listening to music while exercising on adherence to physical activity and physical, psychological, and cognitive outcomes in adults with coronary heart disease were included. Two reviewers independently screened records for eligibility, extracted data, and assessed the quality using the EPHPP tool.

RESULTS We identified seven studies involving 293 participants (mean age: 62.6–72 years, male: 57–80%). All but one study utilized relatively small samples (17–56). The overall quality varied as weak for three studies, moderate for two studies, and strong for two studies.

CONCLUSIONS We identified seven studies involving 293 participants (mean age: 62.6–72 years, male: 57–80%). All but one study utilized relatively small samples (17–56). The overall quality varied as weak for three studies, moderate for two studies, and strong for two studies. Several reviewed studies showed significant effects on adherence to physical activity (two out of three studies), perceived exertion (two out of three studies), exercise capacity (one out of three studies), heart rate during exercise (one out of two studies), male waist circumference (one out of two studies), mood (two out of three studies), and cognitive function (one study) as compared to controls.

GW31-e0816

Comparison of home-based versus center-based exercise training and usual care in patients with heart failure: a systematic review and meta-analysis

Yuanzheng Ye, Ping Fan, Baopeng Tang
The First Affiliated Hospital of Xinjiang Medical University

OBJECTIVES This study is to assess the effect of home-based cardiac rehabilitation (CR) on functional capacity, quality of life and readmission rates in patients with heart failure.

METHODS Randomized controlled trials (RCTs) were initially identified from previous systematic reviews of CR. Literature retrieval was performed in MEDLINE, EMBASE, CINAHL and Cochrane Library to July 2019. The intervention group included a home-based standardized CR or a comprehensive rehabilitation strategy that included home-based CR. The control group received CR at a hospital rehabilitation center or usual care without rehabilitation.

RESULTS The main outcome measurements included patient quality of life, exercise capacity, mortality and re-hospitalization. A total of 20 RCTs were included, in which 16 studies compared home-based CR with usual care and four studies compared home- and center-based CR. Compared to the usual care, the home-based CR improved the total Minnesota Living with Quality of Life score [MD=−5.85, 95% CI (−9.76, −1.94), P<0.0001, I^2=75%] and VO_{2max} [MD=1.05 mL/kg/min, 95% CI (0.35, 1.75), P=0.06, I^2=46%], 6-min Walk distance [MD=11.84, 95% CI (7.41, 16.28), P=0.83, I^2=0%] and 6-min Walk feet [MD=98.93, 95% CI (26.79, 171.08), P=0.13, I^2=56%]. However, there was no difference in mortality, re-hospitalization or anxiety and depression.

CONCLUSIONS The outcomes and costs were similar between home-based and center-based rehabilitation. Home-based CR can prevent early cardiovascular death, reduce hospitalization, and improve quality of life of patients with heart failure.

OTHERS

OTHERS

GW31-e0014

Epidemiological investigation and analysis of SARS-CoV-2 on cardiovascular disease

Li Jinliang, Sun Qi
Harbin Sixth Hospital

OBJECTIVES To study and analyze the impact of SARS-CoV-2 on cardiovascular system which can provided a basis for further timely and effective treatment.

METHODS The clinical data of 42 patients with SARS-CoV-2 in our hospital were retrospectively analyzed.

RESULTS Of the 42 patients with SARS-CoV-2, there were 13 patients had a previous history of cardiovascular disease, including 3 patients with common pneumonia (2 patients had aggravated cardiovascular disease after infection, which improved after treatment with creatine phosphate), 7 patients with severe pneumonia (1 patient had aggravated cardiovascular disease after infection, which improved after treatment with creatine phosphate), and 3 patients with critical pneumonia (2 patients with aggravated cardiovascular disease after infection, all died); There were 29 patients without a previous history of cardiovascular disease, including 24 patients with common pneumonia (4 patients developed cardiovascular injury after infection, improved after treatment with creatine phosphate), 1 patient with severe pneumonia (this example cardiovascular injury appears after the infection, improved after treatment with creatine phosphate), 4 patients with critical pneumonia (1 patients suffered cardiovascular injury after the infection, died).

CONCLUSIONS On the one hand, the SARS-CoV-2 can cause or aggravate the possibility of cardiovascular injury, on the other hand, patients with cardiovascular disease will aggravate the SARS-CoV-2 pnemonia and increase mortality. The timely use of creatine phosphate can effectively protect the cardiovascular system.

GW31-e0045

Phenotypes of coronary artery disease patients with boderline coronary artery stenosis at Siberian Industrial City

Davyd Yakhontov, Julia Ostanina
Novosibirsk State Medical University

OBJECTIVES Borderline (50–70%) coronary artery (CA) stenosis are at high risk of myocardial infarction (MI). Diabetes mellitus (DM), hypertension (Ht) and obesity indicate a "metabolic adverse" phenotype (MAP) in these patients (pts). *Aim*: To determine the frequency various phenotypes in Coronary artery disease (CAD) pts with borderline stenosis – Siberian Industrial Center citizens.

METHODS Retrospective analysis 236 stable CAD pts with borderline stenosis underwent general clinical examinations, heart ultrasound and coronary angiography.

RESULTS All pts were divided into 4 groups: 1st (29.7%): CAD pts without MI; 2nd (15.7%): CAD pts suffered MI more 6 months ago without DM and obesity; 3rd (33.9%): CAD and MAP without DM, 4th (20.8%): CAD and DM type 2. Hypertension was diagnosed in all patients. CAD duration was comparable in all groups, MI occurrence age was lower in MAP group. MI frequency in DM and obesity groups did not differ; repeated MI frequency in DM, MAP, and MI without DM and obesity groups were also comparable. 1-Vascular CA lesion detected more often in pts, who have had MI without DM and obesity than in other three groups; in stable CAD group without MI 1-vascular lesion detected more often than in MAP and DM groups. Multivessel CA lesion were significantly more often detected in MAP and DM groups compared with other pts. The LDL values increasing frequency was comparable between groups and occurred >90% pts, average LDL values also did not differ in all groups, and the frequency of statins intake was >60% in all groups.

CONCLUSIONS We found the predominant phenotypes among stable CAD pts with borderline CA stenosis, large Siberian industrial center citizens. Among them pts with MAP had more MI frequency and an earlier age of its onset comparable with the other groups pts. The LDL levels and statin intake frequency were the same at different phenotypes groups.

GW31-e0110

Identification of lncRNA-NR_104160 as a biomarker and construction of a lncRNA-related ceRNA network for essential hypertension

Wenjuan Peng[1], Han Cao[1], Kuo Liu[1], Chunyue Guo[1], Yanyan Sun[1], Han Qi[2], Zheng Liu[3], Yunyi Xie[1], Xiaohui Liu[1], Bingxiao Li[1], Ling Zhang[1]
[1]Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University, and Beijing Municipal Key Laboratory of Clinical Epidemiology, Beijing 100069, China
[2]The National Clinical Research Center for Mental Disorders & Beijing Key Laboratory of Mental Disorders & The Advanced Innovation Center for Human Brain Protection, Beijing Anding Hospital, School of Mental Health, Capital Medical University, Beijing 100088, China
[3]Science Department, Peking University People's Hospital, Beijing 100044, China

OBJECTIVES To identify long noncoding RNAs (lncRNAs) and construct a competing endogenous RNA (ceRNA) network for essential hypertension.

METHODS An RNA microarray and two-step quantitative real-time PCR were applied to identify differentially expressed RNAs (DE-RNAs), and a luciferase assay was performed to explore the binding relationship between RNAs. A generalized linear model and logistic regression model were used to analyze the associations between different RNAs and of RNAs with hypertension. Receiver operating characteristic curve analysis was executed to evaluate the diagnostic performance. Bioinformatics analysis was applied for network construction.

RESULTS In total, 439 DE-RNAs (387 lncRNAs and 52 mRNAs) were identified in the microarray, and 71 'lncRNA-miRNA-mRNA' loops formed the ceRNA network. The first validation confirmed that five RNAs (NR—104160, lnc-GPR63-8:1, lnc-HPRT1-9:1, *ID1* and *RSL24D1*) were significantly upregulated in hypertensives (P<0.05). NR—104160 was significantly associated with hypertension (OR=2.863, 95% CI: 1.143–7.172; P=0.025) after adjusting for confounding factors. NR—104160 was included in the hypertension diagnostic model, with an area under the curve of 0.852 (95% CI: 0.761–0.944). In the second validation, NR—104160 showed a constant significant difference (P=0.001). An elevated expression level of NR—104160 was associated with the expression of *ID1* (β=0.2235, P=0.005). Luciferase assays showed hsa-miR-101-3p stimulation significantly inhibited the reporter gene activation ability of the NR—104160 wild-type plasmid (P<0.001).

CONCLUSIONS Our study constructed a ceRNA network to provide hypotheses regarding the mechanism of hypertension development. lncRNA-NR—104160 was identified as a hub element that participates in hypertension transcriptional regulation and as a potential biomarker.

GW31-e0112

Discrepant acute effect of saline loading on blood pressure, urinary sodium and potassium according to salt intake level: EpiSS study

Wenjuan Peng[1], Yunyi Xie[1], Kuo Liu[1], Han Qi[2], Zheng Liu[3], Juan Xia[1], Han Cao[1], Chunyue Guo[1], Yanyan Sun[1], Xiaohui Liu[1], Bingxiao Li[1], Fuyuan Wen[1], Ling Zhang[1]
[1]Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University, and Beijing Municipal Key Laboratory of Clinical Epidemiology, Beijing 100069, China
[2]The National Clinical Research Center for Mental Disorders & Beijing Key Laboratory of Mental Disorders & the Advanced Innovation Center for Human Brain Protection, Beijing Anding Hospital, School of Mental Health, Capital Medical University, Beijing 100088, China
[3]Science Department, Peking University People's Hospital, Beijing 100044, China

OBJECTIVES Acute saline loading is one of the methods to determine the salt-sensitivity of blood pressure (BP). The study aimed to assess the acute effect of saline loading on BP in subjects with different levels of salt intake.

METHODS This study is based on the baseline survey of systemic epidemiology of salt sensitivity study. The sodium excretion in the 24-hour urine was calculated for estimating the level of salt intake. Subjects received 1000 mL normal saline orally. Multivariate linear regression and stratified analyses were performed to identify the associations between 24-hour urinary sodium (24hUNa) with changes of BP.

RESULTS A total of 2019 participants were performed an acute oral saline loading test, and the systolic BP (SBP), pulse pressure and spot urinary sodium concentration were significantly increased, while diastolic BP and spot urinary potassium concentration were significantly decreased. The increment of SBP were more significant in subjects with lower salt intake, normotensives, elders, males, smokers and drinkers. After adjusting for confounders, there was a significant linear negative dose-response association between SBP increment with 24hUNa (β=–0.901 mmHg, 95% confidence interval, CI: –1.253, –0.548),

especially in subjects with lower salt intake (β=−1.297 mmHg, 95% CI: −2.338, −0.205) and hypertensive patients (β=−1.502 mmHg, 95% CI: −2.037, −0.967).

CONCLUSIONS Acute salt loading leads to an increment in SBP, and the increased SBP was negatively related with 24hUNa especially in lower salt intake individuals. This study indicated maintaining a stable low-sodium diet and avoiding acute salt loading were important to control BP.

GW31-e0156

A meta-analysis of the adverse reactions in patients using sacubitril/valsartan

Yun Huang[1], Lili Ma[1], Yuyu Zhang[1], Chongbo Fang[1], Hong Yuan[2]
[1]Ningbo Medical Center Lihuili Hospital
[2]The Third Xiangya Hospital of Central South University

OBJECTIVES This review aimed to summarize the prevalence and type of adverse events reported during the use of sacubitril/valsartan.

METHODS Studies containing safety outcomes or adverse reactions during the use of sacubitril/valsartan were retrieved from Medline, Embase, Cochrane library databases and Clinical trials. From the selected studies, the ES and 95% confidence intervals (CI) of prevalence of adverse reactions included was assessed weighted random effects model in our meta-analysis.

RESULTS The available data of 22,667 patients in 30 literatures were included in this review. The prevalence of total adverse events was 36% and most of that were common and not serious. The top three adverse reactions involving system-organ were cardiovascular disorders (12.4%), infection and infestation (11.1%) and respiratory system disorders (10.8%). The top five adverse reactions were hypotension (12.4%), hyperkalaemia (7.3%), nasopharyngitis (7.0%), renal dysfunction (5.4%) and dizziness (4.7%). In addition, large doses (≥400 mg/d), long course of treatment (>12 W), n-RCT and primary disease of HF (HErHF, HEpHF) resulted in a higher prevalence of adverse events and discontinuation due to adverse events.

CONCLUSIONS The most common adverse effects of sacubitril/valsartan were not serious. Besides common adverse reactions, we should also pay attention to adverse effects involved infection and infestation.

GW31-e0197

CURB-65 may serve as a useful prognostic marker in COVID-19 patients with in Wuhan, China: a retrospective cohort study

Boda Zhou, Ping Zhang
Beijing Tsinghua Changgung Hospital

OBJECTIVES A recently developing pneumonia caused by SARS-CoV-2 has quickly spread across the world. Unfortunately, simplified risk score which could easily be used in primary care or general practice settings has not been developed. The objective of this study is to identify simplified risk score which could easily be used to quick triage COVID-19 patients.

METHODS All severe and critical adult patients with laboratory confirmed COVID-19 in West campus of Union Hospital, Wuhan, China, from January 28, 2020 to February 29, 2020, were included in this study. Clinical data and laboratory results were obtained. CURB-65 pneumonia score was calculated. Univariate logistic regression was applied to explore risk factors associated with in-hospital death. We used ROC curve and multi-variate COX-PH model to analyze risk factors for in-hospital death.

RESULTS A total of 74 patients (31 died, 43 survived) were finally included in the study. We observed that: Compared with survivors, non-survivors were older in age and illustrated higher respiratory rate, neutrophil-to-lymphocyte ratio, D-dimer and LDH, but lower SpO2 as well as impaired liver function especially synthesis function. CURB-65 showed good performance for predicting in-hospital death (AUC 0.81, 95% CI 0.71–0.91). CURB-65 ≥2 may serve as a cut-off value for prediction of in-hospital death in severe patients with COVID-19 (Sensitivity 68%, Specificity 81%, F1 score 0.7). CURB-65 (HR 1.61; 95% CI 1.05–2.46), LDH (HR 1.003; 95% CI 1.001–1.004) and albumin (HR 0.9; 95% CI 0.81–1) were risk factors for in-hospital death in severe patients with COVID-19.

CONCLUSIONS Our study indicates CURB-65 may serve as a useful prognostic marker in COVID-19 patients which could be used to quick triage patients in primary care or general practice settings.

GW31-e0226

RyR2 inhibition by dantrolene can attenuate pressure-overload induced cardiac hypertrophy

Yi Gao, Huan Sun, Shuai Li, Ping Yang
China Japan Union Hospital of Jilin University

OBJECTIVES Cardiac ryanodine receptors (RyR2) has been proved to be critical to cardiac function and arrhythmia. However, the role of RyR2 in pressure-overload induced cardiac hypertrophy is still controversial. We aimed to assess the effect of dantrolene, a RyR2 inhibitor, treatment on pressure-overload with transverse-aortic constriction (TAC) mice as well as its potential mechanism.

METHODS TAC surgery was performed on 8-week C57/B6 mice, and dantrolene treatment was given following the surgery. Invasive hemodynamic measurements, cardiac hypertrophy indices, histology change, as well as RNA sequencing for hypertrophy signaling change were assessed after 4 weeks' treatment of dantrolene.

RESULTS The cardiac hypertrophy was successfully induced by TAC. The treatment of dantrolene significantly attenuated the cardiac remodeling marked with decreased heart weight, fibrosis and expression of hypertrophy biomarkers in dantrolene-treated TAC mice with the similar left ventricle pressure compared with vehicle-treated ones. The following RNA sequencing showed dramatical gene expression change in inflammation as well as cardiac metabolism.

CONCLUSIONS RyR2 inhibition can attenuate cardiac remodeling induced by pressure overload, and the potential mechanism may associated to calcium-handling related inflammation and metabolism changes.

GW31-e0287

Improving echocardiogram reporting speed to expedite clinical decision making on cardiac wards: a quality improvement project

Michela Martinuzzi, Saajan Ramji, Siddarth Raj
King's College London

OBJECTIVES This quality improvement project aimed to expedite delivery of key echocardiogram information to doctors by applying two strategies; (1) introduce a provisional report, and (2) reduce the number of referral requests by implementing a new echocardiogram triage system.

METHODS Baseline data were gathered during a 9-week period aimed at understanding and calculating the median time needed to order, perform and report an echocardiogram, as well as monitoring the total number of echocardiogram requests made. The first intervention (strategy 1), lasting 6 weeks, involved a provisional report (PR) containing key clinical information such as left ventricular function and, if present, any valvular, wall motion or any other relevant abnormalities. This was then given by echocardiographers to doctors soon after an echocardiogram was completed. The number of requests, rate of PR uptake and the time from referral to echocardiogram completion to PR availability were monitored during this period. A second intervention (strategy 2), aimed at reducing unnecessary requests, was implemented 4 weeks after the conclusion of the first intervention and it involved a consultant cardiologist triaging the echocardiogram requests daily, for a 6-week period. The number of requests, and the time from referral to full report availability were again monitored. Semi-structured questionnaires were proposed to doctors (FY2 to consultant level) in a cardiac ward at the beginning and end of both cycles to explore participants' subjective opinion. We enhanced staff motivation and adherence through visual aids on wards and stakeholder involvement through regular weekly meetings and constant feedback.

RESULTS The provisional report (PR) reduced the median time for key information to be available to clinicians from 227 to 48.5 minutes, without negatively affecting the time needed to obtain a full report. However, uptake of the PR varied widely across the intervention window being at best, 40% of the total number of echocardiograms performed. Triaging resulted in a decrease in the median number of referrals per week, from 47 to 27.5, and a reduction from 2.73 days to 1.87 days in the median time from referral to full report availability. The results were stable across the observation window. Sixty-two percentage of interviewed doctors reported they noticed significant improvements in speed of echocardiogram information delivery after strategy 1 which increased to 71% after the application of strategy 2.87% of participants felt strategy 1 and 71% felt strategy 2 improved patient outcomes and timely discharge.

CONCLUSIONS Substantial improvements in reporting times for a key diagnostic procedure can be achieved as shown by the application of strategy 1, while strategy 2 demonstrated how eliminating inappropriate referrals can streamline the process of obtaining investigation results. Furthermore, qualitatively, staff acknowledged significant improvements in the availability of echocardiogram results leading to better support in clinical decision making and patients' outcomes. However, sustainability and staff engagement were variable, especially when additional duties, like the formation of a provisional report, are introduced as in the first intervention (strategy 1). Pilot experiences such as this reported experiment and subsequent positive feedback, could become key elements to achieving higher rates of adherence and sustained positive changes.

GW31-e0298

Harpagoside alleviated doxorubicin-induced cardiotoxicity by modulating mitochondrial homeostasis through Pink1/Parkin-mediated mitophagy

Weili Li, Yong Wang
Beijing University of Chinese Medicine

OBJECTIVES Doxorubicin (DOX)-induced cardiotoxicity (DIC) remains a growing healthy problem to be solved. It was extensively reported that

dysregulation of Pink1/Parkin-mediated mitophagy in DIC subsequently leads to excessive deposition of damaged mitochondria. Harpagoside (Har) is considered to have the attractive effect on mitophagy in previous studies. This study aims to explore whether Har can alleviate DIC by controlling Pink1/Parkin-mediated mitophagy in removing damaged mitochondria, and thus improve mitochondrial homeostasis.

METHODS A DIC mice model via tail vein injection with DOX (5 mg×kg^{-1}) once weekly for 4 weeks and a DOX-induced H9C2 cell injury model with DOX (1 μmol/L) were established. In vivo, the mice were divided into saline-injected group, DOX-injected group, DOX+Har-treated group. Echocardiographic assessment of cardiac function, histological examination and western blot analysis of Pink1/Parkin-mediated mitophagy related proteins (Pink1, Parkin, LC3II, p62) were collectively implemented for evaluating the cardioprotective effect of Har on mitophagy. In vitro, DHE fluorescence staining and ATP measurement were used to evaluate mitochondrial injury; Parkin siRNA was applied to detect the changes of ROS, ATP, mRNA level of Parkin and Pink1/Parkin-mediated mitophagy related proteins in the whole cell and mitochondria, so as to authenticate reversely that Har acts on Parkin-mediated mitophagy thus improving mitochondrial injury.

RESULTS Har exerted protective effect on DOX-induced zebrafish heart injury. In vivo, the results of echocardiography and HE staining showed that Har improved cardiac function and alleviated myocardial irregular arrangement compared with the model group. Western blot results showed that the expression of Pink1, p62 and LC3II were increased and Parkin was declined in the model group compared with saline group, while Har greatly reversed these changes. In vitro, Parkin siRNA greatly reduced mRNA level of Parkin. DHE fluorescence staining and ATP measurement displayed that Har remedied the accumulation of ROS and reduced ATP production caused by DOX. Western blot showed that the protein expressions in whole cells were consistent with in vivo, and all these proteins in mitochondria were reduced in the model group, and were increased with Har treatment. Intriguingly, co-incubation with Parkin siRNA abolished the effects of Har on ROS, ATP and protein expressions, demonstrating that Har contributed on Pink1/Parkin-mediated mitophagy and thus improved mitochondrial homeostasis.

CONCLUSIONS The results partially revealed that Har exerts cardioprotective effects against DIC by promoting Pink1/Parkin-mediated mitophagy to remove damaged mitochondria and thus improves mitochondrial homeostasis. Har may potentially be used for treating anti-cancer drug DOX-induced cardiotoxicity. This paper provided the mechanistic underpinnings for Har's further clinical application on DIC.

GW31-e0382

Analysis of influencing factors related to elevated serum troponin I level for COVID-19 patients in Yichang, China

Zhixing Fan, Chaojun Yang, Jun Yang
Department of Cardiology, the First College of Clinical Medical Sciences & Yichang Central People's Hospital, China Three Gorges University, Yichang, Hubei 443000, P.R. China

OBJECTIVES Cardiac injury is a common condition among hospitalized coronavirus disease 2019 (COVID-19) patients, and is associated with a higher risk of mortality. However, the mechanism of myocardial injury in COVID-19 remains unclear. In this retrospective study, we compared the clinical characteristics of COVID-19 patients with different troponin I (TnI) levels during hospitalization to provide a clinical reference for the identification of those at high-risk.

METHODS In total, 218 patients diagnosed with COVID-19 in Yichang Central People's Hospital and Yichang Third People's Hospital between January 23 and February 19, 2020 were initially included. Of these patients, 89 underwent TnI testing during hospitalization and were finally included in the study. The medical history, clinical signs and symptoms at the time of admission, and laboratory test results were recorded. The patients were assigned to the normal TnI group (TnI<0.01 μg/L; n=67) or the elevated TnI group (TnI>0.01 μg/L; n=22).

RESULTS The incidence of elevated TnI in our patient cohort was 24.7%. There were significant differences between the two groups in the following factors: history of coronary heart disease, age, lymphocyte count, prothrombin time (PT), activated partial thromboplastin time (APTT), and levels of interleukin (IL)-6, C-reactive protein, myoglobin (MYO), lactate dehydrogenase (LDH), and albumin (all P<0.05). Binary logistic analysis showed that a history of coronary heart disease, age, lymphocyte count, IL-6, APTT, and MYO were influencing factors of elevated serum TnI.

CONCLUSIONS A history of coronary heart disease, advanced age, decreased lymphocyte count, increased IL-6, increased MYO, and prolonged APTT were independent influencing factors of elevated TnI in COVID-19 patients. COVID-19 patients with these characteristics are prone to myocardial injury.

GW31-e0430

Application of CEASE standard nursing in CCU nurses in electrocardiogram monitoring alarm fatigue

Jinlian Li, Liqin Feng, Liyuan Zhan, Dongling Chen
The Third Affiliated Hospital of Sun Yat-sen University

OBJECTIVES To analysis of the application effect of "CEASE standard nursing mode" in CCU nurses in electrocardiogram monitoring alarm fatigue.

METHODS Forty-two patients with acute myocardial infarction hospitalized in CCU after the implementation of standard nursing mode from January 2019 to December 2019 were selected as the observation group, and 39 patients with acute myocardial infarction who underwent conventional electrocardiogram nursing mode from January 2018 to December 2018 were selected as the control group. The average number of patient alarms per hour and the alarm fatigue scores of 15 nurses in the departments before and after the implementation of THE CEASE standard nursing mode were compared between the two groups.

RESULTS Control group of 42 cases of hospitalized patients with acute myocardial infarction electrocardiogram monitoring average alarm number per hour (2.95±0.854) significantly less than conventional electrocardiogram monitoring nursing in 2018 (5.97±1.013), the difference was statistically significant (P<0.001), the alarm fatigue score of ICU nurses decreased from (19.07±2.764) to (9.53±1.407) before the implementation of standard care, and the difference was statistically significant (P<001).

CONCLUSIONS The CEASE standard nursing mode reduced the average number of alarms per hour in electrocardiogram monitoring and reduced the alarm fatigue of nurses, which is worthy of promotion in clinical practice.

GW31-e0465

Beneficial influence of transurethral resection of prostate on hypertensive patients with benign prostatic hyperplasia

Wenbiao Li[1], Wanwen Lin[2], Xiangfu Zhou[1]
[1]Department of Urology, The Third Affiliated Hospital of Sun Yat-sen University
[2]Department of Cardiology, The Third Affiliated Hospital of Sun Yat-sen University

OBJECTIVES To assess the influence of transurethral resection of prostate (TURP) on mean blood pressure and blood pressure rhythm in hypertensive patients with benign prostatic hyperplasia (BPH).

METHODS From October 2015 to June 2019, total 126 patients with hypertension and benign prostatic hyperplasia underwent transurethral resection of prostate in the third affiliated hospital of Sun Yat-sen University. The age of these patients range from 53 to 81 years, average of (65.3±7.9) years. All patients have suffered hypertension for 6 months to 32 years, average of (10.2±3.1) years. Before operation, systolic pressure was control stable and less than 150 mmHg by oral antihypertensive agents. 24-hour ambulatory blood pressures were tested in all patients before operation and 6 months after operation. 24 hour-mean systolic blood pressure (24 h-sBP), 24 hour-mean diastolic blood pressure (24 h-dBP), daytime mean systolic blood pressure (d-sBP), daytime mean diastolic blood pressure (d-dBP), night mean systolic blood pressure (n-sBP), night mean diastolic blood pressure (n-dBP), cases of dipper hypertension, cases of non-dipper hypertension, amount and dose of antihypertensive agents needed were compared before and 6 months after TURP. Antihypertensive drugs were no more needed and the basic blood pressure <140/90 mmHg counted as recovery, the amount or dose of antihypertensive drugs had been reduced and the basic blood pressure still <140/90 mmHg counted as improved, amount and dose of antihypertensive drug were taken as usual and no significant change in blood pressure was counted as stable, more amount or large dose of antihypertensive drugs needed to control blood pressure to the target <140/90 mmHg was counted as progression.

RESULTS The mean blood pressure were significantly decrease after TURP [(24 h-sBP, 135.2±13.3 mmHg vs. 131.8±12.8 mmHg, P<0.05), (24 h-dBP, 85.3±7.7 mmHg vs. 83.1±7.2 mmHg, P<0.05), (d-sBP, 138.8±13.8 mmHg vs. 135.1±13.2 mmHg, P<0.05), (d-dBP, 88.3±8.2 mmHg vs. 85.5±6.7 mmHg, P<0.05), (n-sBP, 130.2±11.3 mmHg vs. 126.7±10.1 mmHg, P<0.05), (n-dBP, 82.3±5.1 mmHg vs. 80.1±4.5 mmHg, P<0.05)]. There were 51 cases of dipper hypertension and 75 cases of non-dipper hypertension before surgery and 29 cases of non-dipper hypertension converted to dipper hypertension after surgery, the change was statistically significant (P<0.05). Nine cases were recovered, 51 cases were improved, 66 cases were stable and no patients were progress 6 months after TURP.

CONCLUSIONS Benign prostatic hyperplasia is risk factor for hypertension. For hypertensive patients with BPH, transurethral resection of prostate is benefit to reduce blood pressure levels and recover of normal blood pressure rhythm.

GW31-e0540

Effect of TMAO on the interaction between endothelial cells and adventitial fibroblasts

Zhibo Zhu[1], Jianqiang Guo[2]
[1]Chifeng Hospital
[2]The Affiliated Hospital of Inner Mongolia Medical University

OBJECTIVES To investigate the effect of trimethylamine N-oxide (TMAO) on the interaction between endothelial cells and fibroblasts and its related mechanism.

METHODS Rat endothelial cells and adventitial fibroblasts were isolated from the aortas of Sprague-Dawley rats (150–180 g). First, we investigated the influence of TMAO on the phenotypic modulation of adventitial fibroblasts. Western blot method was used to detect the expression of Collagen I and alpha smooth muscle actin (a-SMA) in adventitial fibroblasts stimulated by TMAO. The ability of cell migration was detected by transwell method. Second, endothelial cells and adventitial fibroblasts were cultivated in a co-culture system and endothelial cells were treated with or without TMAO to observe the effect of endothelial cells on phenotypic modulation of adventitia fibroblasts. Third, Endothelial cells were stimulated by TMAO, and the survival rate of endothelial cells was measured by CCK-8 method. Intracellular ROS generation was monitored by using Reactive Oxygen Species Assay Kit. The expression of eNOS, Bcl-2 and Lc3 in endothelial cells were detected by Western blot method to observe the effect of TMAO on endothelial cells.

RESULTS (1) TMAO upregulated the expression of collagen I and a-SMA and the migration of adventitial fibroblasts (P<0.05). (2) Adventitial fibroblasts–endothelial cells co-culturing attenuated the effects of TMAO. TMAO-treated endothelial cells, which were functionally impaired, were less inhibitory of the phenotypic modulation of adventitial fibroblasts (P<0.05). TMAO changed the morphology of endothelial cells, and the nucleus expanded and enlarged, intracellular ROS increased, eNOS decreased, the expression of Bax in endothelial cells increased, and the expression of Bcl-2 decreased to induce apoptosis. (3) TMAO can also up-regulate the proportion of Lc3II in endothelial cells and induce autophagy.

CONCLUSIONS TMAO promotes phenotypic modulation of adventitial fibroblasts, which may be related to endothelial cell dysfunction induced by TMAO.

GW31-e0567

Association between premenopausal weight and waist circumference with age at menopause: a cohort study

Yan Li[1,2], Min Liu[1]
[1]Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing, China
[2]Department of Epidemiology, Beijing An Zhen Hospital, Capital Medical University, Beijing Institute of Heart, Lung and Blood Vessel Diseases, Beijing, China

OBJECTIVES The causality between weight and waist circumference with age at menopause is uncertain. The purpose of this study was to investigate whether premenopausal weight and waist circumference influence age at onset of menopause.

METHODS We used data from Chinese Multi-provincial Cohort Study. Participants aged 35–64 years were enrolled from Beijing communities in 1992 and followed until 2018. A total of 1433 women who were premenopausal at study entry and who reached natural menopause at the end of follow-up were included in the study. Normal- or over-weight were defined by body mass index. Central obesity was defined by waist circumference. Age at menopause was categorized as <45 years (early menopause), 45–49 (relatively early menopause), 50–51 (reference), and >51 years (relatively late menopause). Multinomial logistic regression models were used to estimate relative risk ratios (RRRs) and 95% confidence intervals (CIs) for the association between weight and waist circumference with age at menopause after adjusted for age and cardiovascular disease risk factor levels at baseline.

RESULTS The mean (standard deviation) age at menopause was 50.6 (3.1) years. There were 38.9% of women having relatively early and 35.2% having relatively late menopause. Compared with women with normal BMI (<24 kg/m^2), overweight women had higher risk of relatively early (RRR 1.76, 95% CI 1.25–2.47; P=0.001) and relatively late menopause (RRR 1.70, 95% CI 1.21–2.39; P=0.002). Overweight women with normal waist circumference (<80 cm) had a higher risk of relatively late menopause (RRR 1.64, 95% CI 1.10–2.45; P=0.01), while overweight women with increased waist circumference (≥80 cm) had higher risk of early (RRR 3.13, 95% CI 1.20–8.13; P=0.02), relatively early (RRR 2.76, 95% CI 1.71–4.46; P<0.001), and relatively late menopause (RRR 1.82, 95% CI 1.13–2.93; P=0.01).

CONCLUSIONS Compared with women who had normal weight and normal waist circumference, overweight women with central obesity had higher risk of relatively early and relatively late menopause.

GW31-e0648

Cadmium exposure causes endothelial dysfunction by interfering with lipid metabolism in human microvascular endothelial cells

Hao Liang[1], Zaiyong Zheng[1], Mingming Lv[1], Xiaobo Wang[1], Dan Qin[1], Jing Zeng[1], Jun Pu[1], Yulong Zhang[2], Houxiang Hu[1]
[1]Department of Cardiology, Affiliated Hospital of North Sichuan Medical College
[2]Department of Anesthesiology, Affiliated Hospital of North Sichuan Medical College

OBJECTIVES Cadmium (Cd), an occupational and environmental heavy metal pollutant derived from many sources, is directly connected with vascular endothelial homeostasis. Since the vascular endothelium represents an important site of Cd deposition, increasing evidence has revealed the close relationship between endothelial dysfunction and abnormal lipid metabolism. However, the effects of the alterations in lipid metabolism on vascular endothelial cells after Cd exposure still remain unclear.

METHODS Human microvascular endothelial cells were obtained from American Type Culture Collection (Manassas, VA, USA). HMEC-1 were treatment with $CdCl_2$ at concentrations of 10 μM, 20 μM and 40 μM for 24 hours. Lactate dehydrogenase (LDH) release assay and Cell Counting Kit-8 (CCK-8) were used to assess the cell viability. The nitric oxide (NO) levels, endothelial nitric oxide synthesis (NOS) and endothelial nitric oxide synthesis (eNOS) activities were used to assess the endothelial function. Triglyceride (TG), total cholesterol (TC) and free fatty acid (FFA) were used to verify the degradation of lipid droplets. ATP content, mitochondrial membrane potential (MMP) and reactive oxygen species (ROS) were used to be assess the mitochondrial function. They were all detected by colorimetric assays. The expression of lipogenic genes (ACACA, FASN, FADS1 and SREBF1), lipolysis genes (PNPLA2, LIPE and ABDH5) and fatty acid β-oxidation (CPT1A, CPT1B and CPT2) were quantified by Real-time PCR. The expression of ET1 protein and eNOS protein were evaluated by Western blotting. Oil red O and BODIPY 493/503 were utilized to stain neutral lipids as a mean to evaluate the intuitive changes in HMEC-1.

RESULTS Cell viability was decreased to 67% of the control at 40 μM (P<0.01) after treatment with $CdCl_2$ for 24 h. LDH release increased by 1.4-fold following treatment with 40 mM $CdCl_2$ (P<0.01). NO levels and eNOS activity markedly decreased in a dose-dependent manner (P<0.01). The expression of ET1 protein and eNOS protein were also markedly decreased in a dose-dependent manner (P<0.05). The result from real-time PCR demonstrated that ACACA, FADS1, SREBF1 expression were decreased to 70% of control (P<0.05). However, the in apparent change was observed in the expressions of FASN. Additionally, LIPE and ABDH5 level increased by approximately 3-fold compared control level (P<0.01), PNPLA2 level increased to 1.5-fold of the control (P<0.01). On the other hand, CPT1A, CPT1B and CPT2 expressions decreased to 70% of the control (P<0.05). Just like the changes mentioned above, the neutral lipid staining of cells via Oil red O and BODIPY 493/503 revealed that the size of lipid droplets in HMEC-1 was significantly reduced with the highest Cd exposure (40 μM). Consistent with the results of cell staining, the TG content decreased by approximately 2-fold compared with control in the group treated with $CdCl_2$ 40 μM (P<0.05). The FFA content increased to 1.5-fold of the control (P<0.05). As such a change in lipid droplet, Cd exposure to 40 μM Cd for 24 h markedly increased intracellular ROS production which caused the significant decrease of MMP and ATP (P<0.05).

CONCLUSIONS This study is the first to report that Cd exposure induces endothelial dysfunction by disturbing lipid metabolism in HMEC-1 cells. These changes were accompanied by FFA accumulation and ROS generation, which ultimately led to mitochondrial dysfunction in the HMEC-1 cells.

GW31-e0668

The research on the effect of exercises combined with equol on breast cancer tissue in DMBA Induced Wistar Rat Breast Cancer model

Yuanxun Huang[1], Junxuan Li[2], Yuanyuan Liu[3], Xiaofei Han[4], Yuanwu Chen[2]
[1]Wuhan University of Bioengineering
[2]Hubei University
[3]Wuhan Sports University
[4]Hubei Sports Vocation College

OBJECTIVES The aim of the research is to study the effect of exercises combined with equol on breast cancer tissue in DMBA Induced Wistar Rat Breast Cancer Model and discuss the mechanism.

METHODS For the construction of induced mammary gland, Six-week-old female Wistar rat were received gavage on a dosage of 10 mg/mL DMBA for eight weeks. After successful modeling, the rat were randomized into four groups: the control group (group C), the females of phenol group (group E), exercise group (P group), motion plus females phenol group group (PE).

Among them, C and P group normal feeding water daily. E and PE group per 200 mg daily females of phenol in sesame oil into 1000 g solution, which is 200 mg dose females of phenol in rats of females of phenol by gastric lavage. Set the movement of P and PE group to swim, sink depth of 50 cm, water temperature 30 °C or so, exercise every day 30 min 5 min rest, a day four groups, sports eight weeks.

RESULTS Compared with group C, other groups were very significant differences (P<0.01), Bax protein expression levels, Caspase-3 increased significantly; The NF-kappa B p65 expression. Compared with P group, group C and PE group had very significant difference (P<0.01), and E group there was no significant difference (P>0.05). Compared with PE group, other groups were very significant differences (P<0.01), PE group than other groups of Bax protein expression levels, Caspase-3 increased significantly; the NF-kappa B p65 express declined significantly. Prompt aerobic exercise combined with females of phenol can cause DMBA breast tissue cell apoptosis in rat model of breast cancer, reduce inflammation of the body.

CONCLUSIONS Long-term the intensity of movement joint females phenol can inhibit DMBA induced the growth of breast cancer in rats. Improve Bax protein in breast cancer tissue, Caspase-3 protein, regulating the activity of NF-kB P65, promote cell apoptosis may be movement joint females of phenol on induced rat breast cancer growth of one of the important physiological mechanism.

GW31-e0672

Echocardiographic cardiac output-based exercise pulmonary vascular function in obesity

Na Zhou[1,2], Corentin Scoubeau[2], Yoshiki Motoji[2], Jean Closset[3], Vitalie Faoro[2], Na Zhou[1,2]
[1]Department of Cardiology, Yunnan BOYA Hospital
[2]Laboratory of Cardio-Pulmonary Exercise Physiology, Faculty of Motorskills Sciences, Université Libre de Bruxelles
[3]Department of Surgery, Erasmus Hospital, Free University of Belgium

OBJECTIVES The cardiac output (CO) increases during exercise in response to oxygen uptake by working muscles, and pulmonary vascular pressures at any given resistance are determined by CO. Previous studies have shown that the mean pulmonary artery pressure (mPAP) and CO measured by exercise stress echocardiography (ESE) can assess pulmonary vascular function and predict exercise capacity and the future development of pulmonary hypertension (PH). However, little is known about echocardiographic CO-based pulmonary vascular function in obese subjects.

METHODS Seventeen pairs of subjects (obese vs. healthy matched control subjects, gender: 25% men, age: 44±11 vs. 46±12 years, height: 1.7±0.1 vs. 1.7±0.1 m, weight: 111±17 vs. 64±11 kg, BMI: 38±4 vs. 22±2 kg/m^2) performed an ESE on a semi-recumbent cycle ergometer. Pulmonary artery pressure (PAP) and CO were taken during the last minute of each workload until exhaustion. Total pulmonary vascular resistance (TPR) was calculated as mPAP/CO, total pulmonary vascular resistance index (PVRi) as mPAP/CI and pulmonary vascular distensibility coefficient α was mathematically determined from the slight natural curvilinearity of multipoint mPAP–CO plots.

RESULTS There was no difference in pulmonary vascular function at rest between the two groups, but at common maximum exercise level, the mPAP and PVRi were higher in obesity with a higher mPAP/CI slope. As shown in Table 1.

CONCLUSIONS In obese subjects, the echocardiographic CO-based pulmonary vascular function is preserved at rest, but exacerbated at common maximum exercise, following with an higher exercise mPAP.

GW31-e0765

Cardiac sequelae of COVID-19 can be detected in patients with mild infection

Wanjun Liu, Xingwei He, Fen Huang, Hesong Zeng
Department of Cardiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology

OBJECTIVES The purpose of this study was to assess whether cardiac sequelae of COVID-2019 can be detected in patients with mild infection at convalescent stage.

METHODS Between January 18, 2020 and February 24, 2020, 18 convalescent patients (median age 38.5 years, 63.6% female) with mild COVID-19 who were presenting with cardiovascular symptoms (chest congestion, palpitations, or shortness of breath were enrolled prospectively. Cardiac function evaluation was performed on all patients, including blood test, electrocardiogram, echocardiogram, and cardiac magnetic resonance (CMR) examination.

RESULTS All patients had no prior cardiac diagnosis and recovered from COVID-19. The median time from recovery to cardiac examination was 27 (23–30) days. Holter ECG showed an average heart rate of 72 (76–84) bpm without serious arrhythmia. Although the hs-cTnI and NT-proBNP were normal in all patients, abnormalities on echocardiogram and CRM were found in 7/18 (38.9%) and 12/18 (66.7%) patients. All the 7 patients with abnormal echocardiogram showed lower global longitudinal strains, especially in basal longitudinal. For patients with abnormal CRM, myocardial edema was found in 8/12 (66.7%) based on visual inspection of T2-weighted images, while late gadolinium enhancement was found in 12/12 (100%). Five cases demonstrated both, echocardiogram and CRM abnormalities.

CONCLUSIONS The findings of this study show that cardiac sequelae of COVID-19 patients can be detected in mild patients at convalescent stage with cardiovascular symptoms. More attention needs to be paid to cardiac function in not only severe cases, but also mild ones.

GW31-e0784

The role of sepsis in clinical outcomes of coronary care unit patients

Tienan Sun, Chenghui Cai, Yujie Zhou
Beijing Anzhen Hospital Affiliated to Capital Medical University, Beijing, China

OBJECTIVES Sepsis, defined as systemic inflammatory response syndrome cause by infection, is the most common cause of death in critically patients. Cardiovascular system is one of the most important organ systems frequently effected by sepsis. Global ischemia, the changes in level of cytokines, inflammatory factors and myocardial depressant substance caused by sepsis can all lead to the damage of cardiovascular system. Previous studies have shown that sepsis significantly increases mortality in coronary care unit (CCU) patients. This study aimed to explore the role of sepsis in clinical outcomes of CCU patients.

METHODS All data of this study was extracted from Medical Information Mart for Intensive Care III (MIMIC-III, version 1.4) database. Propensity score-matched analysis (PSM) was used to reduce the effects of biases and confounding variables. Binary logistic regression analysis was performed to determine the independent effect of sepsis and different causative agents on clinical outcomes.

RESULTS Three thousand seven hundred and eighty-nine CCU patients were included in this study. PSM resulted in 529 matched pairs. After PSM, all baseline parameters were well matched. In matched patient population, sepsis was found to be independently associated with in-hospital mortality after adjusting for possible confounding variables (OR, 95% CI: 2.02, 1.45–2.83, P<0.001). Staphylococcus was the most common causative agent of sepsis which had a 2.23 fold increased risk of in-hospital mortality compared with no-sepsis. The highest risk of in-hospital mortality was from yeast (OR, 95% CI: 3.39, 2.17–5.29, P<0.001). The risk of in-hospital mortality of multiple causative agents (OR, 95% CI: 2.53, 1.65–3.87, P<0.001) was obviously higher than single causative agent (OR, 95% CI: 1.69, 1.13–2.52, P=0.011). In most subgroups, we did not observe obvious interactions. Sepsis was also found to be independently associated with increased risk of acute kidney injury (OR, 95% CI: 1.41, 1.05–1.88, P=0.022) and vasopressin (OR, 95% CI: 3.08, 1.97–4.79, P<0.001) after PSM. The length of CCU and hospital stay were prolonged significantly in sepsis group.

CONCLUSIONS Sepsis was independently associated with in-hospital all-cause mortality, acute kidney injury and vasopressin in CCU patients after PSM. The risk of in-hospital mortality of multiple causative agents was higher than single causative agent. Length of CCU and hospital stay were prolonged significantly in sepsis group.

GW31-e1305

High-density lipoprotein cholesterol: its association with atherosclerotic cardiovascular disease and cancer risk among Chinese people in a Kailuan cohort

Xumin Guan[1], Gary Tse[1], Rongfeng Zhang[1], Guangming Gu[1], Shuang Xu[1], Xiaolei Yang[1], Shouling Wu[2], Yunlong Xia[1]
[1]First Affiliated Hospital of Dalian Medical University
[2]Kailuan General Hospital

OBJECTIVES The aim of this study is to investigate the relationship between high-density lipoprotein cholesterol (HDL-C) and atherosclerotic cardiovascular disease (ASCVD) or cancer.

METHODS A total of 92,376 Chinese subjects who had a standardized medical examination between 2006 and 2007 from the Kailuan cohort were included. Demographic, socioeconomic and laboratory data were collected at baseline and were followed up for approximately 11 years until occurrence of ASCVD, cancer, death, or December 31, 2017. Univariable and multivariable Cox regression analyses were performed to examine the association of HDL-C with ASCVD or cancer.

RESULTS A total of 5178 (5.6%) subjects developed ASCVD, whereas 3848 (4.2%) subjects developed cancer. Through multivariable analysis, HDL-C (1.28–1.51 mmol/L) and HDL-C (1.51–1.77 mmol/L) respectively decreased risk of ASCVD occurrence by 8% compared with the first quartile of HDL-C

(<1.28 mmol/L). While there was no significant association between HDL-C concentration and cancer risk in the general population. Hazard ratio curves for HDL-C levels associated with ASCVD or cancer were shown by spline functions (Figure 1). A significant interaction was found between diabetes mellitus and HDL-C on the incidence cancer risk (P for interaction=0.001). Compared with the lowest quartile of HDL-C (<1.28 mmol/L), the upper-most quartile (≥1.77 mmol/L) decreased cancer risk by 26% (HR: 0.74, 95% CI: 0.55–0.98) in diabetic participants, while increased cancer risk by 11% (HR: 1.11, 95% CI: 1.01–1.22) in participants without diabetes mellitus. The relationships of HDL-C to overall and individual cancer incidence in participants with or without diabetes mellitus were shown in Figure 2. Gastrointestinal and esophagus cancers were the predominant cancer types for non-diabetic subjects with high HDL-C. By contrast, gastrointestinal and respiratory cancers are found in diabetic subjects with low HDL-C levels.

CONCLUSIONS Low HDL-C levels are associated with a higher incidence of ASCVD in the overall population, and with higher incidences of gastrointestinal cancer and respiratory cancer in the diabetic population. High HDL-C levels are associated with a higher incidence of gastrointestinal and esophagus cancers in the non-diabetic population.

GW31-e1309

Large animal model of ischemic mitral regurgitation established by percutaneous coronary occlusion in rhesus monkey

Qiaowei Chen[1], Yu Kang[1], Mian Wang[1], Xiaojing Chen[1], Mingqiang Rong[2], Qing Zhang[1]
[1]Department of Cardiology, West China Hospital, Sichuan University, Chengdu, Sichuan, China
[2]College of Life Sciences, Hunan Normal University, Changsha, Hunan, China

OBJECTIVES Ischemic mitral regurgitation (IMR) is a major predictor of poor prognosis in coronary artery disease. Establishment of IMR model in large animals is indispensable to explore its underlying mechanisms and facilitate innovating more effective therapies, which unfortunately is lacking. This study aimed to explore the feasibility and effectiveness of percutaneous coronary occlusion in creating rhesus monkey model of IMR.

METHODS Twenty male rhesus monkeys received 2 types of percutaneous transcatheter intervention to the left circumflex coronary artery (LCX), i.e., the ischemia-reperfusion (IR) method by inflating and deflating occlusion balloon in the target artery (n=9), or the permanent ischemia (PI) method by injecting gelatin sponge for a total occlusion of the LCX (n=11). Transthoracic echocardiography and cardiac magnetic resonance (CMR) were used to assess the IMR severity, left ventricle (LV), and mitral apparatus including annular dimension, tenting height and tenting area at baseline and 4-week follow up.

RESULTS Six monkeys in the IR group and 8 monkeys in the PI group survived at 4-week follow up who received cardiac imaging examination. IMR was observed in 10 animals (2 in the IR group, 8 in the PI group), while there was no IMR created in 4 cases of the IR group (Table 1). In contrast to the IR group where LV ejection fraction (LVEF) less than 50% was only recorded in one case, the PI group showed remarkable increase in LV volumes and decrease in LVEF. Six in 8 cases had a LVEF of <50%, including 2 cases with a LVEF of ≤35%. The mitral apparatus was also more deformated (Table 1). Among the 11 monkeys with good quality CMR images for late gadolinium enhancement (LGE) assessment, 4 in the IR group and 7 in the PI group revealed positive LGE that located at the LV inferior and posterior walls). One animal in the IR group showed negative LGE.

CONCLUSIONS Percutaneous LCX occlusion is feasible in establishing rhesus monkey model of IMR. Permanent occlusion could create satisfactory IMR with obvious LV and mitral apparatus remodeling.

GW31-e1325

Correlation between TGFβ pathway-associated genes ACTAT2 and CYP2A13 gene polymorphisms on the occurrence and prognosis of Debakey type III AD

Peipei Jiang, Xiang Ma
The First Affiliated Hospital of Xinjiang Medical University

OBJECTIVES This study was to investigate the association of TGFβ (transforming growth factor-β) pathway-related genes ACTA2 (α-smooth muscle actin) and CYP2A13 (cytochrome oxidase 2A13) polymorphism with Debakey type III AD (aortic dissection) in Chinese Han population.

METHODS A case-control study was conducted in 157 cases of aortic dissection Debakey III, and 323 cases in the control group without angiography. Real-time PCR was used to identify genotypes of 6 sites of ACTA2 (rs2119685, rs3781211, rs2028493) and CYP2A13 (rs3968432, rs1645694, rs34178072), and the case group was followed up for 2 years to analyze the occurrence and prognosis of type III AD.

RESULTS There were differences in the genotype and allele frequency distribution of ACTA2 (rs2119685) between the case group and the control group (P<0.05). After adjusting for confounding factors, logistic regression analysis showed that the association between ACTA gene polymorphism and type III aortic dissection was associated (OR=0.369, 95% CI: 0.202–0.672, P=0.001). In the 2-year follow-up of the case group, the mortality distribution of the ACTA2 (rs2119685) dominant model (TT vs. TC+CC) in Debakey type III AD patients was statistically significant (P<0.05).

CONCLUSIONS The ACTA2 (rs2119685) gene polymorphism in Chinese Han population is associated with the occurrence and prognosis of Debakey type III AD. The five sites of ACTA2 (rs3781211, rs20284933) and CYP2A13 (rs3968432, rs1645694, rs34178072) are not associated with Debakey type III AD. The results of this study provide reference value for screening and prognosis assessment of Debakey type III AD patients.

GW31-e1329

Association with gene polymorphisms in MYH11 and TGFBR1 gene with DeBakey aortic dissection

Yafei Chang, Xiang Ma
The First Affiliated Hospital of Xinjiang Medical University

OBJECTIVES Vascular smooth muscle cells (VSMCs) are the main structure of the middle layer of the aorta. The proteins encoded by myosin heavy chain (MYH) 11 and transforming growth factor-beta receptor I (TGFBR1) genes are involved in the regulation of the structure and function of VSMCs. This study aims to investigate the association of MYH11 and TGFBR1 gene polymorphisms with DeBakey III aortic dissection (AD).

METHODS A total of 159 patients with DeBakey III aortic dissection and 305 subjects without vascular abnormality in control group. Three SNPs (MYH11 gene rs115364997 and rs117593370, and TGFBR1 gene rs1626340) were selected and genotyped. T-test, chi-square test and unconditional logistic regression were performed to investigate assess the association between the different genotypes of each locus and the genetic susceptibility and the effects of SNPs on the risk of DeBakey III AD.

RESULTS There were significant differences in recessive model of rs117593370 (TT vs. CT+CC, P=0.002), additive model of rs1626340 (GA vs. AA+GG, P=0.019) between the AD and control groups. Common risk factors were adjusted such as age, hypertension, smoking, drinking, hypertension and triglyceride. Logistic regression analysis showed that the recessive model of MYH11 gene rs117593370 was the risk of DeBakey III AD, and there was still correlation after removing the confounding factors (OR=7.896, 95% CI: 1.636–38.109, P=0.010).

CONCLUSIONS This study indicated that variations in the TGF-beta pathway and Vascular smooth muscle contraction unit gene (MYH11 gene rs115364997 and rs117593370, and TGFBR1 gene rs1626340) are associated with DeBakey III AD. Carriers of GA genotype in TGFBR1 rs1626340 have a higher risk of DeBakey III AD.

GW31-e1337

Discovery and validation of novel protein biomarkers in acute aortic dissection patient tissue

Mengmeng Wang, Xiang Ma
The First Affiliated Hospital of Xinjiang Medical University

OBJECTIVES Acute aortic dissection (AAD) is a serious life-threatening cardiovascular disease. Currently, its diagnosis depends on clinical and radiological investigation, no fit-for-purpose biomarkers have yet been identified for early and rapid diagnosis of AAD. In this study we aimed to identify potential biomarker candidates in aorta tissue from AAD patients.

METHODS We conducted a pilot study consisting of 20 patient ascending aorta tissue samples (10 from each group), using 4D label-free quantitative (4D-LFQ) mass spectrometry, to identify potential biomarker candidates in aorta tissue from individual AAD patient. And we performed protein annotation, unsupervised hierarchical clustering, functional classification, functional enrichment and cluster, and protein–protein interaction analyses. To validate these changes, we selected 20 significantly enriched differential proteins to study their abundance using Parallel Reaction Monitoring (PRM).

RESULTS 4D-LFQ analyses identified 3985 proteins in a discovery set of 10 ascending aorta tissue samples. Among them 139 were upregulated and 108 were downregulated as compared to the control groups. Several proteins, including LBP, SAA1, ITGAM, MPO, and SCGB1A1 were confirmed to be enriched in the aorta tissue of AAD patients using PRM.

CONCLUSIONS This is the first application of a 4D-LFQ-PRM workflow to identify and validate AAD biomarkers in patients ascending aorta tissue.

GW31-e1381

Research on the improvement of liability for medical malpractice in the civil code

Tao Mi
Doctor in Civil and Commercial Law, Dalian Maritime University

OBJECTIVES This paper aims to give detailed interpretations of the latest provisions on medical malpractice liability in Civil Code, and provides reference & guidance for medical institutions to take reasonable measures to deal with medical disputes.

METHODS A comparative study has been made between the provisions of Civil Code and the original Tort Liability Law concerning medical malpractice liability, with an analysis of the similarities and differences between the two, as well as the main reasons and ideas behind such modifications.

RESULTS The main content and corresponding clauses in the original Tort Liability Law concerning Liability for Medical Malpractice are basically continue in the Civil Code, with several modifications focused on the following four aspects: (i) Protecting patients' rights to be informed and consent. The adjustments in Civil Code gives medical staff and patients more communication options and confirmation methods. (ii) Clarifying medical institutions' liability as an employer in medical malpractices. Whether the harm to the patient is caused by the fault of medical institution itself or its medical staff, the medical institution shall bear the corresponding liability for damages compensation in accordance with the law. (iii) Optimizing the application of presumed-default liability doctrine in medical malpractice. The presumed fault of medical institutions is limited to the damage that occurs during the diagnosis and treatment of patients, which is well aligned with the juridical practice. The application of presumed-default liability doctrine, if the medical institution destroyed medical records, shall be limited to the conditions of "illegal destruction". (iv) Protecting the legal rights of medical personnel. The Civil Code has added a comprehensive liability clause concerning infringements on the legal rights of medical staff.

CONCLUSIONS The Civil Code definitely provides judicial guarantee for building a harmonious doctor-patient relationship and promoting the construction of a healthy China.

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