The 33rd Great Wall International Congress of Cardiology
Asian Heart Society Congress 2022
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ABSTRACTS

This Supplement contains the selected Abstracts presented at the 33rd Great Wall International Congress of Cardiology, Asian Heart Society Congress, held October 26–30, 2022.
Dear Fellow Cardiologists, Ladies and Gentlemen,

Fragrant olive perfume the air in this golden autumn. Great Wall International Congress of Cardiology 2022 and Asian Heart Society Congress 2022 will be held on October 24–30, 2022 in Beijing. As one of the most fascinating academic event in Chinese cardiological world, the online sessions will make a rewarding trip for you.

Time flies. Thirty-two years has past since the first congress in 1990. Our mission is to make “healthy China” not just as a campaign, but one day as reality. From innovation to application, from standardized medicine to personalized medicine, We've made every redouble efforts to provide our people with life-cycle healthcare. One of our best approach to realize our duty is for the patients, by the patients, and with the patients.

Through these years, we've witnessed the transformation and development of the Great Wall Society and embarked on a path of international academic congress with Chinese characteristics. The road ahead is full of twists and turns. Despite the profound changes in the way of academic exchanges due to the COVID-19 pandemic, Great Wall International Congress of Cardiology never hesitate. We now stand at a fresh start. A new chapter of carrying on the past and opening a way for the future, will be written.

This international renowned academic congress will shoulder the mission and responsibility of academic development in the field of cardiology by promoting the latest achievements and supporting multidisciplinary and comprehensive subjects. We welcome with open arms to the hottest research topics and spirited debate of ideas. Lets strive together to tackle regional, national, and global challenges of cardiovascular disease in our generation.

On behalf of the Organizing Committee, I sincerely invite you to attend Great Wall International Congress of Cardiology 2022 and Asian Heart Society Congress 2022 online and on-site. Hereby, I would like to express my great appreciation and respect to you all, especially to the health professional who was or still as a fighter against COVID-19. This “Great Wall” of global health is built by you.

We look forward to meet you in 2022!

Signature
Shao-Liang Chen
President of GWICC 2022
The 33rd Great Wall International Congress of Cardiology
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**BASIC AND TRANSLATIONAL MEDICINE**

**BASIC RESEARCH OF CARDIOVASCULAR DISEASE**

**GW33-e0014**
Intensive exercise induces atrial fibrillation in an autophagy-necroptosis-inflammation dependent manner
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2 Northwestern Polytechnical University

**OBJECTIVES** The role of exercise in atrial fibrillation (AF) is complicated, presenting a J-shaped phenomenon which means intensive exercise raises the risk of AF, whereas the underlying mechanisms haven’t been fully illustrated. Emerging evidence reveals altered autophagy in AF patients but the role of autophagy in AF genesis is still controversial, thus requiring further exploration.

**METHODS** Male C57BL/6J mice were divided into sedentary group (Sed), moderate-intensity exercise group (MIE) and high-intensity exercise group (HIE) to investigate the role of exercise intensity and time on AF and underlying mechanisms. Then verifying in AF patients and using 3-methyladenine (3-MA) to inhibit autophagy in mice, we explored the relationship between autophagy and AF. AF inducibility test was performed by transesophageal atrial pacing. Atrial electrical remodeling was evaluated by ion channel genes and connexins expression. And atrial structural remodeling was assessed by echocardiographic measurement of left atrial diameter, Masson trichrome and Sirius red staining of atrial fibrosis, respectively. Western blot, real-time PCR, TUNEL staining and histological staining were performed to reveal molecular mechanisms.

**RESULTS** AF frequency and duration increased in a swim time course-dependent manner in HIE group and the differences were most significant at the 8th week, while in MIE group, swim training protected mice against AF at the 3rd week yet this effect gradually disappeared as swim time increasing. Thus, we established an intensive exercise-induced AF mouse model by 8 weeks of high-intensity swim training. Real-time PCR results showed altered ion channel expression, especially K+-related ion channels in intensively exercised mice and western blot analysis showed downregulated connexin 40 and 43, indicating obvious structural electrical remodeling. Besides, we observed left atrial enlargement and atrial fibrosis in HIE group, consistent with AF-related atrial structural remodeling. Furthermore, to investigate the mechanisms, we found upregulated atrial pro-inflammatory cytokines especially IL-18 but decreased granulocyte colony-stimulating factor (G-CSF) expression in HIE model. Decreased G-CSF expression was also found in patients with AF. Interestingly, inhibiting autophagy via 3-MA partially reversed exercise-induced AF susceptibility and atrial fibrosis. Mean while, blocking necroptotic signaling and downregulating pro-inflammatory cytokines activated by exercise suggested a critical role of autophagy in AF genesis, probably via activating necroptosis-inflammation signaling.

**CONCLUSIONS** Our results identify autophagy as a novel potential therapeutic target for AF in endurance athletes or even other AF population and highlight autophagy-necroptosis-inflammation axis as the underlying regulate mechanism in this process.

**GW33-e0056**
Endothelial Foxp1 restricts tumor angiogenesis and protects against tumor growth through Hif1α-Hk2 glycolysis signal pathway
Jiangjing Pi
Shanghai East Hospital, Tongji University School of Medicine

**OBJECTIVES** Angiogenesis is critical for physiological and pathological processes, Endothelial cells (ECs) rely on glycolysis for energy production to maintain vascular homeostasis and normalization of hyperglycemia. We analyzed the TCGA database of the NIH Cancer Genome Atlas Program and found reduced Foxp1 expression in lung carcinoma. Immunostaining demonstrated that the reduced expression was more restricted at tumor vascular ECs, and EC-Foxp1 deletion mice exhibited a significant increase of xenograft tumor angiogenesis for tumor growth. Through data mining of ECs-Foxp1 Chip sequence results and confirmed by ChIP and luciferase assays, we identified hypoxia-inducible factor 1 (Hif1α) as the Foxp1 target gene, for the regulation of EC glycolytic metabolism to govern tumor angiogenesis.

**RESULTS** Moreover, we identified Hk2 as the Hif1α target gene for regulation of tumor EC metabolism. RGD-peptide magnetic nanoparticles EC target delivery of Hif1α-siRNAs or Hk2-siRNAs reduced the hyperglycolysis to suppress ECs growth. Finally, simvastatin, a strong inducer of ECs-HIF1α-Foxp1, as well as EC-Foxp1 gain-of-function, significantly reduced the hyperglycolysis of ECs and inhibited the pro-angiogenic activity to protect against tumor growth.

**CONCLUSIONS** Foxp1 regulation of a Hif1α-Hk2 pathway in the endothelium advances our understanding of EC metabolism for tumor angiogenesis, and meanwhile provides evidence for future therapeutic intervention of hyperglycolysis in tumor ECs for suppression of tumor growth.

**GW33-e0059**
CB1R-stabilized NLRP3 inflammasome drives antipsychotics cardiotoxicity
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2 Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital and Institute of Biomedical Sciences, Fudan University

**OBJECTIVES** Long-term use of antipsychotics is a common cause of myocardial injury and even sudden cardiac deaths. The mechanisms underlying antipsychotics cardiotoxicity remain largely unknown. The present study aimed to investigate the toxic effects of common antipsychotics on hearts and designed a cell-based small-molecule compound screen to identify cardioprotectants during antipsychotics use.

**METHODS** Representative antipsychotics including clozapine (Clz) and olanzapine (Olv) were intraperitoneally injected into mice for 7, 14, and 21 days, respectively, with doses comparable to clinical use. Analysis of left-ventricle function, QT interval, heart histopathology and myocardial injury markers were conducted. Transcriptomic and proteomic analyses were conducted to identify enriched molecular pathways.

**RESULTS** Clz and Olv time-dependently concentrated in hearts and induced cardiotoxicity by preceding lipopolysaccharide (LPS)-induced myocardial inflammation, apoptosis and oxidative stress after swim training. Apoptosis and oxidative stress significantly reduced heart rate and mean arterial pressure (MAP), decreased creatine kinase (CK)-MB and aspartate aminotransferase (AST) levels, as well as ECs-Foxp1 Chip sequence results and confirmed by ChIP and luciferase assays, we identified hypoxia-inducible factor 1 (Hif1α) as the Foxp1 target gene, for the regulation of EC glycolytic metabolism to govern tumor angiogenesis.

**RESULTS** Moreover, we identified Hk2 as the Hif1α target gene for regulation of tumor EC metabolism. RGD-peptide magnetic nanoparticles EC target delivery of Hif1α-siRNAs or Hk2-siRNAs reduced the hyperglycolysis to suppress ECs growth. Finally, simvastatin, a strong inducer of ECs-HIF1α-Foxp1, as well as EC-Foxp1 gain-of-function, significantly reduced the hyperglycolysis of ECs and inhibited the pro-angiogenic activity to protect against tumor growth.

**CONCLUSIONS** Foxp1 regulation of a Hif1α-Hk2 pathway in the endothelium advances our understanding of EC metabolism for tumor angiogenesis, and meanwhile provides evidence for future therapeutic intervention of hyperglycolysis in tumor ECs for suppression of tumor growth.

**GW33-e0060**
Nesfatin-1 protects cardiac damages in a streptozotocin-induced diabetes mice
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**OBJECTIVES** Nesfatin-1 is a novel anorexigenic peptide that has been recently found to possess an antihyperglycemic effect. However, the role of nesfatin-1 in diabetic cardiomyopathy (DC) has not been fully investigated.

**METHODS** The aim of this article was to bring a different perspective on the effect of nesfatin-1 on diabetes-associated cardiac dysfunction in a mice model.

**RESULTS** In this study, we found that nesfatin-1 expression was significantly downregulated in a high-fat diet (HFD) retoptozocin (STZ)-induced diabetic mice. Nesfatin-1 treatment elevated the insulin sensitivity and attenuated the diabetic dyslipidemia with the reduced levels of total cholesterol (TC), triacylglycerol (TG) and low-density lipoprotein (LDL) in diabetic mice. Nesfatin-1 improved the diabetes-caused alternations in cardiac function and structure, as proved by reduced heart rate and mean arterial pressure (MAP), decreased creatine kinase (CR)-MB and aspartate aminotransferase (AST) levels, as well as...
as mitigated myocardial hypertrophy. Nesfatin-1 exerted an antioxidant activity in STZ-induced diabetic mice with decreased ROS and MDA levels, as well as increased SOD and GSH levels in heart tissues. Nesfatin-1 also attenuated the cardiac inflammation, as shown by decreased cardiac and plasma IL-1β and TNF-α levels. In addition, we also found that p38 MAPK was markedly activated in diabetic mice, while nesfatin-1 significantly inhibited its activation.

CONCLUSIONS Collectively, nesfatin-1 exerted protective effects against diabetes-mediated cardiac damages via regulating p38 MAPK. These results indicated that targeting nesfatin-1 might be a good approach for therapeutic intervention of DC.

GW33-e0071 Single-cell RNA sequencing of the rat carotid arteries uncovers potential cellular targets of NIH
Xiao-Fei Gao, Ai-Qun Chen, Zhen Ge, Jun-Jie Zhang
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OBJECTIVES In-stent restenosis (ISR) remains an Achilles heel of drug-eluting stents despite technical advances in devices and procedural techniques. Neointimal hyperplasia (NIH) is the most important pathophysiological process of ISR. The present study mapped normal arteries and stenotic arteries to uncover potential cellular targets of neointimal hyperplasia.

METHODS By comparing the left (control) and right (balloon injury) carotid arteries of rats, we mapped 11 clusters in normal arteries and 11 mutual clusters in both the control and experimental groups. Different clusters were categorized into 6 cell types, including vascular smooth muscle cells (VSMCs), fibroblasts, endothelial cells (ECs), macrophages, unknown cells and others. An abnormal cell type expressing both VSMC and fibroblast markers at the same time was termed a transitional cell via pseudotime analysis.

RESULTS Due to the high proportion of VSMCs, we divided them into 6 clusters and analyzed their relationship with VSMC phenotype switching. Moreover, N-myristoyltransferase 1 (NMT1) was verified as a credible VSMC synthetic phenotype marker. Finally, we proposed several novel target genes by disease susceptibility gene analysis, such as Cyp7a1 and Cdkg, which should be validated in future studies.

CONCLUSIONS Maps of the heterogeneous cellular landscape in the carotid artery were defined by single-cell RNA sequencing and revealed several cell types with their internal relations in the ISR model. This study highlights the crucial role of VSMC phenotype switching in the progression of neointimal hyperplasia and provides clues regarding the underlying mechanism of NIH.

GW33-e0072 Therapeutic exosomes in prognosis and developments of coronary artery disease
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OBJECTIVES Exosomes, with an diameter of 30–150 nm, could be released from almost all types of cells, which contain diverse effective constituent, such as RNAs, proteins, lipids, and so on. In recent years, exosomes have been verified to play an important role in mechanism, diagnosis, treatment, and prognosis of cardiovascular disease, especially coronary artery disease (CAD).

RESULTS Exosomes from human umbilical cord mesenchymal stem cells (hUCMSCs) have been used to deliver therapeutic genes and proteins to cells. Exosomes can selectively deliver genes and proteins to target cells, avoiding the immunogenicity and toxicity of naked DNA. Exosomes can also be used to deliver therapeutic agents to target cells, such as siRNA, miRNA, and proteins.

CONCLUSIONS Exosomes can selectively deliver therapeutic genes and proteins to target cells, avoiding the immunogenicity and toxicity of naked DNA. Exosomes can also be used to deliver therapeutic agents to target cells, such as siRNA, miRNA, and proteins.
GW33-e0093
LncRNA FGDS-AS1 aggravates myocardial ischemia-reperfusion injury by sponging miR-129-5p
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OBJECTIVES LncRNA FGDS-AS1 has been found to regulate the pathogenesis of many human diseases. Thus this study aims to elucidate the function of LncRNA FGDS-AS1 and the regulatory mechanism of LncRNA FGDS-AS1/miR-129-5p in myocardial ischemia-reperfusion (I/R) injury.

METHODS Myocardial I/R injury mouse model and H/R treated H9c2 cells were established. RT-qPCR and Western blot analysis were used to detect the mRNA and protein expression. Cell viability was detected by MTT assay. Dual luciferase reporter assay was applied to confirm the relationship between LncRNA FGDS-AS1 and miR-129-5p. Data were analyzed SPSS 19.0 and expressed as mean±SD. Graphs are made by Graphpad Prism 6. Student t-test was adopted to compare the difference between two groups, and multiple comparison was performed by one-way analysis of variance followed by Tukey's post hoc test. P<0.05 indicates statistically significant difference.

RESULTS LncRNA FGDS-AS1 was upregulated in myocardial I/R injury mice models and H/R treated H9c2 cells. Functionally, knockdown of LncRNA FGDS-AS1 promoted cell viability and inhibited apoptosis in H/R treated H9c2 cells. In addition, LncRNA FGDS-AS1 directly targets miR-129-5p. And upregulation of lncRNA FGDS-AS1 weakened the protective effect of miR-129-5p on myocardial I/R injury.

CONCLUSIONS LncRNA FGDS-AS1 aggravates myocardial I/R injury by downregulating miR-129-5p.

GW33-e0128
Biomineralization of nanoceria alleviates isoproterenol-induced myocardial impairment by regulating mitochondrial oxidative stress
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OBJECTIVES The exact evidence has indicated that concentrations of catecholamine are elevated in the development of chronic heart failure (CHF). Isoproterenol (ISO), one of the catecholamine adrenergic receptor agonists, has been proved to cause myocardial necrosis, cardiac hypertrophy, fibroblast proliferation and abnormality of cardiac function. Mitochondrial dysfunction and ROS are important role in the pathogenesis of ISO-induced CHF. Cerium oxide nanoparticles (NPs) recently have received extensive attention in biomedical applications due to their excellent antioxidation performance. The biomineralization-based synthesis method is green, environmentally friendly, simple and efficient compared to traditional methods. Herein, we develop a novel therapeutic nanoparticle via the biomineralization process and assessed its effectiveness for ISO-induced CHF.

METHODS We synthesized albumin-based cerium oxide nanoparticles (CeO2@BSA) via a biomineralization process and polyethylene glycol (PEG) modified hydrophobic cerium oxide NPs (CeO2@PEG) as a comparison. Then the physicochemical and biological properties of NPs were characterized. The Cc content in the purified solution was determined by an X Series quadrapole inductively coupled plasma mass spectrometry (ICP-MS) instrument. Cellular uptake, cytotoxicity test, intracellular mitochondrial membrane potential (MMP) and reactive oxygen species (ROS), were verified with H2DCF cell lines. Thereafter the distribution of CeO2@BSA in C57/B16F1 mouse ventricular tissue cells were observed by transmission electron microscope (TEM) and optical in vivo Imaging. The cardiac function of C57/B16F1 mouse male was evaluated. Fibrosis for assessment of myocardial structural remolding was stained by Masson. Finally, the histocompatibility of CeO2@BSA was evaluated.

RESULTS TEM revealed the CeO2@BSA are ∼2–4 nm in diameter and remain stable in deionized water. X-ray diffraction and X-ray photoelectron spectroscopy characterized the other properties successfully. MTT assay show that H9c2 cell viabilities were not influenced by CeO2@BSA even at high doses of Ce of up to 200µM and CeO2@BSA had better efficacy and better biocompatibility compared to CeO2@PEG. H2DCF treatment led to increased ROS and decreased intracellular MMP in H9c2 cells. CeO2@BSA and CeO2@PEG improved the above changes. TEM found CeO2@BSA both in cytoplasm and mitochondrion in mice ventricular at 12 hours after injection through the tail vein and lasting >24 hours by optical in vivo Imaging. ISO mice showed increased myocardial fibrosis, abnormality of diastolic and systolic functions. All these abnormal changes were improved in the ISO+CeO2@BSA group but none significant improvement was observed in group ISO+CeO2@PEG however. Finally, CeO2@BSA show excellent biosafety after 14 days treatment.

CONCLUSIONS These consistent biochemical and histopathological results suggest that, biomimetic mineralization of CeO2@BSA could be used as effective antioxidant in prophylactic protocols for management of cardiogenic disorders associated with oxidative stress. Compared with PEG modification, biomimetic mineralization shows advantages such as narrow size distribution, good biocompatibility, high stability and ability to control drug release.

GW33-e0151
Quercetin protects endothelial function from inflammation induced by localized disturbed flow by inhibiting NR2P
Feng Wang, Junjie Zhang
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OBJECTIVES The present research aims to elucidate the mechanism underlying the regulation of Neuruplin (NRP) 2 under DF in endothelial cells (ECs) in an inflammatory state.

METHODS The mRNA and protein levels of NRP family members were observed by shear stress stimulation, and were verified in animal and human tissue samples. Possible therapeutic targets were predicted using bioinformatic methods and verified by luciferase reporting assay and chip-qPCR assay. The model of deranged flow in mice was established by carotid artery ligation. Quercetin and NR2P adeno-associated virus were used to observe the inflammatory level of endothelial cells in the disturbed flow area.

RESULTS We observed that NR2P expression was significantly upregulated in DF-stimulated human umbilical vein endothelial cells (HUVECs). Knockdown of NR2P in HUVECs significantly ameliorated cell inflammation induced by DF. In addition, quercetin inhibited NR2P expression as well as endothelial inflammation. Animal experiments suggested that NR2P knockdown or intraperitoneal injection of quercetin affected the expression of inflammation-related genes. Moreover, the upstream transcription factor GATA2 was found to regulate NR2P transcription by binding to the −1100 to −100 bp region of the NR2P promoter.

CONCLUSIONS These findings suggest that NR2P plays a essential proinflammatory role and that NR2P is a promising therapeutic target for the treatment of atherosclerotic disorders.

GW33-e0157
Endothelial PHACTR1 promotes endothelial activation and atherosclerosis by repressing PPAP4 activity under disturbed flow
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OBJECTIVES Numerous genome-wide association studies revealed that SNPs at phosphatase and actin regulator 1 (PHACTR1) locus are strongly correlated with coronary artery disease (CAD). However, the mechanism linking these variants to CAD remains uncertain. Here, we identified PHACTR1 as the causal gene and demonstrated biological functions and molecular mechanisms of endothelial PHACTR1 in atherosclerosis.

METHODS We generated global (Phacr1−/−) and endothelial cell (EC)-specific (Phacr1−/−ECs) Phacr1 knockout mice and crossed these mice with apolipoprotein E-deficient (apoE−/−) mice. Atherosclerosis models were built by feeding the high-fat/high-cholesterol (HF-HC) diet for 12 weeks or partially ligation carotid arteries combined with a 2-week HF-HC diet. Atherosclerotic lesions were analyzed in whole aorta, aortic sinus or ligated carotid arteries. PHACTR1 localization was identified by immunostaining of overexpressed PHACTR1 in human umbilical vein endothelial cells (HUVECs) exposed to different types of flow. The molecular function of endothelial PHACTR1 was explored by RNA-seq using EC-enriched mRNA from global or EC-specific Phacr1 knockout mice. Endothelial activation was evaluated in HUVECs transfected with siRNA targeting PHACTR1 and in Phacr1−/− mice after partial carotid ligation.

RESULTS Global or EC-specific Phacr1 deficiency significantly inhibited atherosclerosis in regions of disturbed flow. PHACTR1 was enriched in ECs and located in the nucleus of disturbed flow area but shuttled to cytoplasm under laminar flow in vitro. RNA-seq using EC-enriched RNA showed that Phacr1 depletion affected vascular function and peroxisome proliferator-activated receptor gamma (PPARγ) was the top transcription factor regulating
differentially expressed genes. PHACTR1 functioned as a PPARY/transcriptional corepressor by binding to PPARY through the corepressor motifs. PPARY activation protects against atherosclerosis by inhibiting endothelial activation. Consistently, PHACTR1 deficiency remarkably reduced endothelial activation induced by disturbed flow in vivo and in vitro. PPARY antagonist GW9662 ablated the effects of PHACTR1 knockdown on EC activation and atherosclerosis in vivo.

CONCLUSIONS Our results identified endothelial PHACTR1 as a novel PPARY corepressor to promote atherosclerosis in disturbed flow region. Endothelial PHACTR1 is a potential therapeutic target for atherosclerosis treatment.

GW33-e0159 A lymph node-targeted drug delivery system for effective immunomodulation to prolong the long-term survival of heart transplantation
Yanjia Che 
Renmin Hospital of Wuhan University

OBJECTIVES Despite scientific and clinical advances in cardiac transplant surgery and immune regulation, the chronic rejection response and the ensuing side effects of systemic administration of immunosuppressant have been the main obstacles for heart allograft and patient survival. In addition, the development of xenotransplantation also urgently requires more efficient immune regulation strategies with minimized effects of immunosuppressant. To develop more effective immune regulation strategies and minimize the side effects associated with long-term use of immunosuppressive drugs are of critical importance for improved prognosis and prolongation of survival time. The purpose of this study is to develop an aptamer functionalized lymph node (LN) targeted drug delivery system with high targeting efficiency and ideal biocompatibility to effectively prolong the long-term survival after heart transplantation.

METHODS First, we synthesized the FTY720 loaded nanoparticles-FTY720@NP and lymph node targeted FTY720 loaded nanoparticles-FTY720@TNP using the biotin-avidin interaction connected the CCL21-aptamer with the particles. In vivo fluorescence imaging was used to verify the ability of FTY720@TNP to target lymph nodes. We designed the hybrid nanoparticles loading the novel immunosuppressant FTY720 in the model of full-MHC mismatch acute heart transplantation and analyzed the immune infiltration of allografts. Then we transplanted the hearts of C57BL/6 mice into C57BL/6 mice, in this chronic heart transplantation model, we explored the role of FTY720@TNP in preventing CAV, and we analyzed the CD4+ T effector cells, CD8+ T effector cells and CD4+ Treg cells of draining the lymph nodes and spleens derived from recipients by FCM.

RESULTS In vivo live fluorescence imaging studies confirmed the lymph-targeting capability of the targeting drug delivery system (FTY720@TNP) using the MHCII fully mismatch heart transplantation model. FTY720@NP suppressed acute allografts response and significantly reduced the frequency the effector/memory T cells but increased the generation of Treg cells and in chronic heart transplantation model, LN-targeted FTY720@TNP prolongs allograft survival and improve the CAV. Prolongation of chronic graft survival treated by FTY720@TNP relies primarily on increasing the Treg/Teff ratio in draining LN.

CONCLUSIONS In this experiment, we developed a new draining lymph node targeted drug delivery system that targets CCL21-expressed by high endothelial venules and fibroblastic reticular cells of the lymphoid T cell rich zones of lymph nodes. The application of CCL21 aptamer can drive the nanoparticles into the T cell rich area of lymph nodes. We demonstrate that FTY720@TNP can efficiently deliver the novel immunosuppressant FTY720 to draining lymph nodes, thereby alleviating CAV in chronic transplant rejection. Our aptamer functionalized lymph node targeted drug delivery system can effectively deliver the immunotherapeutic drug to the draining lymph nodes to relieve immune rejection locally and thereby minimize the side effects associated the immunosuppressant. This study provides a promising strategy to overcome the key difficulties encountered in heart transplantation, which is also applicable for other organ transplantsations.

GW33-e0204 Allicin regulates P-PEKR through SHP2 to inhibit the oxidative stress of I/R mice
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China-Japan Friendship Hospital

OBJECTIVES This study aims to include an appropriate mechanism of alllicin regulating the expression of Src homology 2 domain-containing tyrosine phosphatase-2 (SHP2) in mouse ischaemia/reperfusion (I/R)-induced oxidative stress.

METHODS The mouse model of myocardial I/R injury (MIIR) was established using macrophage-specific conditional SHP2-knockout (SHP2-KO) and wild-type (WT) mice, followed by animal experiments and cell experiments. The mice were divided into three groups (control group, model group and alllicin group) in animal experiments, and divided into five groups (control group, model group, allicin group, SHP2 KO group and SHP2 KO+alllicin group) in cell experiments. The changes in myocardial fibrosis and the expressions of oxidative stress pathway-related proteins in tissues and macrophages were detected through Masson staining and Western blotting, respectively.

RESULTS The results of in vivo experiments showed that alllicin significantly reduced the area of myocardial infarction and myocardial fibrosis after myocardial injury, and up-regulated the protein expression of SHP2 in the myocardium in I/R mice, and the expressions of other proteins phosphorylated protein kinase R-like ER kinase (p-PEKR), mitofusin-1 (MFN1), NLR family pyrin domain containing 3 (NLPR3), NADPH oxidase 2 (NOX2) and NOX3 also significantly declined. The results of in vivo experiments revealed that the protein expression of SHP2 was significantly lower, while the expressions of other proteins (p-PEKR, MFN1, NLPR3, MFN2, NOX4, P47, gp91, NOX2 and NOX3) were significantly higher in WT mouse-derived macrophages in model group than those in control group. However, the expressions of these proteins were reversed by alllicin, consistent with the results of in vivo experiments. There were no obvious changes in the expressions of these proteins in SHP2-KO mouse-derived macrophages between SHP2 KO+alllicin group and SHP2 KO group. It can be seen that the deficiency of SHP2 enhances alllicin in the regulatory effect on p-PEKR and NLPR3, suggesting that alllicin acts on the expressions of oxidative stress-related proteins in I/R mice through promoting the expression of SHP2, and that the activation of p-PEKR is involved in the occurrence of oxidative stress after I/R in mice.

CONCLUSIONS In conclusion, alllicin can regulate the activation of p-PEKR by diminishing the expression of SHP2, thereby inhibiting the mouse I/R-induced oxidative stress.
GW33-e0213
Silencing mas-related G protein-coupled receptor member D (MrgD) improved hypertensive and ameliorated hypertension-induced vascular remodeling by mediating Cav1.2-CamkII gamma axis
Kun Zhao, Peng Li, Xianqing Kong
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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. Abnormal activation of the MrgD receptor, a ligand of Mas-related G protein-coupled receptor, member D (MrgD), was reported to improve hypertrophy. However, the specific physiological and pathological role of MrgD in hypertension is not yet elucidated.

METHODS The recombinant adenosine-MrgD (AD-MrgD) or adenosine-shRNA-MrgD (shRNA-MrgD) was intravenously injected in Wistar-Kyoto rats (WKY) or Spontaneous Hypertension rats (SHR), respectively. The vascular smooth muscle cells (VSMCs) was induced by AngII to mimic the cell culture model of hypertension in vitro. Then, low-intensity pulsed ultrasound (LIPUS) irradiation (0.5 MHz, 77.20 mW/cm²) was applied for 20 minutes every other day in mice received chronic AngII infusion in vivo.

RESULTS We found that MrgD overexpression increased blood pressure and induced mesenteric vascular remodeling in WKY rats, while silencing MrgD alleviated hypertension and mesenteric vascular remodeling in SHR rats. The same trends were observed in AngII-induced VSMCs. Moreover, the vasopressor effects of AngII were weakened in MrgD-KO mice. Further results indicated that shRNA-MrgD, like Ala, downregulated AngII-induced protein and mRNA expression of Cav1.2 in vitro, while Cav1.2 activator Bay-K-8644 could reversed the protective effects of silencing MrgD. Meanwhile, COIP-MP mass spectrometry showed that the expression of CamkII gamma, which is related to Cav1.2 function, was significantly increased in AngII-induced VSMCs compared with the control group. In vitro functional experiments also showed that AngII induction promoted the binding of CamkII gamma to MrgD and CamkII Gamma to Cav1.2, respectively, thus promoting the phenotypic transformation of VSMCs. Moreover, LIPUS, a novel and safe apparatus, improved AngII-induced vascular remodeling in vivo and VSMCs phenotypic switch in vitro via inhibiting MrgD expression.

CONCLUSIONS Taken together, our current study unveiled the promising protective effects of silencing MrgD expression on improving hypertension and ameliorating hypertension-associated mesenteric vascular remodeling by mediating Cav1.2-CamkII gamma axis, paving the way to develop novel therapies for treating pathological cardiac hypertrophy and heart failure.

GW33-e0232
OSMR deficiency aggravates pressure overload-induced cardiac hypertrophy by modulating macrophages and OSM/LIFR/STAT3 signaling
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OBJECTIVES Oncostatin M (OSM) is a member of interleukin (IL)-6 family mainly involved in inflammatory and cardiovascular diseases through binding to the functional receptors of common signal transducing component glycoprotein 130 (gp130) and OSM receptor β (OSMR) or leukemia inhibitory factor (LIFR) receptor. The effect and underlying specific protease 36 (USP36), a nuclear deubiquitinating enzyme (DUB), in the progress of DIC and its mechanism.

METHODS Neonatal rat cardiomyocytes and H9c2 cells were used to construct a doxorubicin-induced cardiomyocyte injury model. The expression levels of USP36 and its downstream PARP1 were analyzed by western blotting and the binding of USP36 and PARP1 was verified by co-IP experiments. DHE staining, LDH, hematoxylin and eosin (H&E) staining and western blotting were performed to evaluate cell oxidative stress injury and apoptosis. We also established a DIC model in mice, specifically knocked down USP36 by injecting AAV9 (adeno-associated virus serotype 9) – associated virus into the tail vein of mice, and analyzed mouse heart function, myocardial structural cell survival status by echocardiography, HE staining and Masson staining.

RESULTS We identified an increased expression of USP36 both in neonatal rat cardiomyocytes and H9c2 cells exposed to DOX, and USP36 silencing significantly ameliorated DOX-induced oxidative stress injury and apoptosis in vitro. Mechanistically, USP36 knockdown resulted in reduction of PARP1 levels, and its overexpression was observed to positively correlate with PARP1 expression. Further investigation showed that USP36 could bind to and mediate the deubiquitination of PARP1 and increase its protein stability in cardiomyocytes upon DOX exposure. Moreover, overexpression of wild-type (WT) USP36, but not its catalytic-inactive mutant (C131A), stabilizes PARP1 in H9c2 and cardiomyocytes. Herein, we also established DIC model in mice and observed a significant upregulation of USP36 in the heart. USP36 cardiomyocyte-specific knockdown mice showed preserved cardiac function after chronic low-dose DOX treatment and were protected against DOX-induced in terms of structural changes within the myocardium.

CONCLUSIONS DOX promotes DIC progression by activating USP36-mediated PARP1 deubiquitination. USP36/PARP1 axis may play an important regulatory mechanism in the pathogenesis of DIC.

GW33-e0254
CDK9 combined with SGK3 regulates cardiomyocyte regeneration and cardiac repair in the mouse infarcted heart by activating GSK-3β catenin pathway
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OBJECTIVES The neonatal heart maintains entire regeneration capacity in a transient regeneration window, but the adult heart loses this function. The loss of the proliferative capacity of cardiomyocytes (CMs) involves numerous core hubs regulation of gene expression and activities. SGK3 is a functional kinase we identified previously, with the capacity of promoting cardiomyocyte proliferation and cardiac repair after myocardial infarction (MI). The present study further elucidated the direct combination relationship of cyclin-dependent kinase 9-serine (CDK9) and threonine-protein kinase 3(SGK3), and explored the role and mechanism of CDK9 in cardiac regeneration after myocardial infarction.

METHODS We used quantitative phosphoproteomics data of infarct border zone in newborn hearts after MI to identify CM regeneration-associated kinases. Gain- and loss-of-function experiments were performed to determine the effect of CDK9 in CM proliferation and cardiac repair after apical resection (AR) or MI. Pulldown assay and co-immunoprecipitation (Co-IP) experiments were conducted to investigate the direct binding target proteins.
RESULTS CDK9 and SGK3 protein expression was highly expressed at postnatal day 1 (P1), reduced at P7 until adult. In, CM proliferation ratio was elevated by CDK9 overexpression, while it was decreased by CDK9 knockdown in newborn mouse cardiomyocytes. In vivo, inhibition of CDK9 shortened the time window of cardiac regeneration after AR in neonatal mice, and overexpression of CDK9 significantly promoted CM proliferation and cardiac repair after MI in adult mice. Mechanically, CDK9 could be directly combined with and activated the phosphorylation of SGK3, and the activated SGK3 further promotes CM regeneration through the GSK-3β/-catenin signal pathway. Inhibition of SGK3 partially blunted CM proliferation induced by CDK9 overexpression in vitro.

CONCLUSIONS Our study revealed the direct combination relationship of CDK9 and SGK3. As an upstream of SGK3, CDK9 plays a greater role in promoting myocardial regeneration after cardiac injury such as MI, which may reopen a novel therapeutic avenue for MI.

**GW33-e0257**

miR-455-5p promotes pathological cardiac remodeling via inhibition of PRMT1-mediated Notch1 activation

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OBJECTIVES Although microRNAs have been reported to participate in the regulation of cardiovascular diseases, the potential role of miR-455-5p on pathological cardiac remodeling remains to be elucidated. The present study focused on clarifying the function and searching the direct target of miR-455-5p, as well as exploring its underlying mechanisms in pathological cardiac remodeling.

METHODS To clarify the function of miR-455-5p in pathological cardiac remodeling, miR-455-5p mimic and inhibitor were transfected into cardiomyocytes in vitro, miR-455-5p agomir and miR-455-5p antagonist were injected to caudal vein of mice; To explore which echocardiographic parameter was significantly correlated to miR-455-5p level, quantitative primer chain reaction (Q-PCR) was utilized to measure the miR-455-5p level in patients with hypertension; To find out the direct target of miR-455-5p, luciferase binding assay was employed; Co-immunoprecipitation assay (Co-IP) was used to testify asymmetric dimethylation of Notch1 was regulated by PRMT1 and influenced by miR-455-5p level.

RESULTS miR-455-5p participated in inducing pathological cardiac remodeling suppressed both in vivo and in vitro; By exploring the correlation of miR-455-5p level and echocardiography results in hypertensive patients, miR-455-5p mainly regulated in left ventricular wall thickening via inhibition of Notch signaling pathway; By luciferase binding assay, PRMT1 was found to be a direct target of miR-455-5p; By co-immunoprecipitation, miR-455-5p was proved to impede asymmetric dimethylation of Notch1 and subsequent Notch1 activation.

CONCLUSIONS The present study reveals that miR-455-5p provokes pathological cardiac remodeling by impediment of PRMT1 transcription and subsequent Notch1 asymmetric dimethylation. Downregulation of Notch1 asymmetric level mediated by PRMT1 inhibition results in suppression of Notch signaling pathway. Thus, targeting the miR-455-5p/PRMT1/Notch1 signaling axis may suggest a novel therapeutic approach against pathological cardiac remodeling.

GW33-e0266

CHK1 pathway inhibition with gemcitabine treatment results in cardiotoxicity and worsens cardiac remodeling after myocardial infarction

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OBJECTIVES CHK1 is the core component of DNA damage response pathway and regulates multiple downstream factors, controlling cell proliferation and survival. CHK1 inhibitor AZD7762 is now in clinical trials, whereas it will potentially cause cardiotoxicity especially combined with gemcitabine. The adverse impact of CHK1 inhibition and gemcitabine on the heart is unclear. This research aims to determine whether CHK1 inhibition combined with gemcitabine affects cardiac physiology and ventricular remodeling post-MI and to elucidate the underlying molecular mechanisms.

METHODS Healthy mice were treated with AZD7762 combined with gemcitabine for 21 days and mice with MI were treated for 10 days to construct a cardiomyocyte model. Echocardiography and cardiac MRI were conducted to detect the functional and structural changes with the anti-neoplastic treatment. H&E and Masson’s trichrome staining were used to identify the histological alterations. Proteomics analysis was taken to determine the cardiotoxicity-related pathways. Western blot and RT-qPCR were used to verify the gene expression changes.

RESULTS In vivo, both chk1 inhibition and gemcitabine therapy induced weight loss, heart atrophy, exaggerated blood pressure, systolic dysfunction and myocardial inflammation in mice. After myocardial infarction, mice with the anti-neoplastic treatment showed aggravated cardiac dysfunction, adverse post-MI remodeling and greater infarct area. Proteomic analysis provided changes in the level of multiple proteins, which were further enriched in acute inflammation response-related pathways. Both AZD7762 and gemcitabine treatment resulted in DNA damage response pathway activation and worsened cardiac remodeling with reduced blood vessel density, activated inflammatory response and endothelial apoptosis. In vivo, AZD7762 and gemcitabine suppressed CHK1 activation, cell viability, proliferation, and increased cell apoptosis in human umbilical vein endothelial cells.

CONCLUSIONS The CHK1 pathway is associated with heart atrophy, cell survival and tumorigenesis in mice. CHK1 inhibition with gemcitabine worsens cardiac remodeling post-MI. The promising anti-neoplastic therapy is potentially cardiotoxic, especially in patients with myocardial infarction.
CONCLUSIONS Pex3 knockout leads to the abnormal abundance and biological function of peroxisomes, which inhibits the AKT/GSK3β signaling pathway, resulting in the impaired regenerative capacity of cardiomyocytes. Overall, our data reveal the role of Pex3 in regulating CM regeneration, emphasizing the effect of Peroxins mutations on myocardial regeneration.

GW33-e0292
METTL3 improves cardiomyocyte proliferation by mediating m6A modification of miR-17-3p/Ank2 after myocardial infarction
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OBJECTIVES Myocardial infarction (MI) leads to heart failure by causing a massive and rapid loss of cardiomyocytes. However, MI injury-induced proliferation of adult mammalian cardiomyocytes is insufficient to restore impaired cardiac function. Therefore, research on revealing the mechanism of endogenous cardiomyocyte proliferation has become crucial locally and abroad. We investigated the role of m6A modification in cardiomyocyte proliferation and apoptosis under hypoxic or MI conditions.

METHODS We performed lentiviral infection experiments in vitro and myocardial infarction experiments in vivo. We investigated the role of METTL3 in regulating m6A modification of miR-17-3p/Ank2 and its effect on cardiomyocyte proliferation and apoptosis under hypoxic or MI conditions.

RESULTS (1) METTL3 overexpression significantly upregulated miR-17-3p expression and inhibited cardiomyocyte proliferation and apoptosis under hypoxia. (2) METTL3 overexpression significantly improved cardiac function and reduced infarct size in MI-induced rats. (3) METTL3 knockdown significantly inhibited cardiomyocyte proliferation and apoptosis under hypoxia or MI conditions. (4) METTL3 overexpression significantly improved cardiac function and reduced infarct size in MI-induced rats. (5) METTL3 knockdown significantly inhibited cardiomyocyte proliferation and apoptosis under hypoxia or MI conditions.

CONCLUSIONS METTL3 overexpression significantly improved cardiac function and reduced infarct size in MI-induced rats, thereby providing evidence for the potential therapeutic effects of METTL3 overexpression in MI.

GW33-e0302
Checkpoint kinase 1 alleviates myocardial ischemia/reperfusion injury by restoring blocked autophagic flux in cardiomyocyte
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OBJECTIVES Myocardial ischemia/reperfusion (I/R) injury remains a leading cause of mortality worldwide. The role and mechanism of autophagy in myocardial I/R injury is still controversial and largely unknown. CHK1 (Checkpoint Kinase 1) is indicated to promote cardiomyocyte proliferation and cardiac repair after myocardial infarction but its role in reperfusion injury remains unclear. Here, we aim to explore the role of CHK1 in regulation of myocardial autophagy and I/R injury.

METHODS In this study, we used an in vivo and in vitro I/R model to investigate whether CHK1 regulates myocardial I/R injury and autophagy in cardiomyocyte, by subjecting mice to I/R and by exposing NCM460 cells (neonatal mouse cardiomyocytes) to OGD/R (oxygen glucose deprivation/reperfusion) models. The I/R model was established by ligation of LAD (left anterior descending) of coronary for 45 minutes, followed by removal of occlusion. We constructed cardiomyocyte-specific CHK1-knockin (CHK1-cKI) or knockout (CHK1-cKO) mouse to determine the role of CHK1 in myocardial I/R injury. We used echocardiography (LVEF, left ventricular ejection fraction, LVFS, left ventricular fractional shortening) and Evans Blue-TTC staining to evaluate cardiac function. In addition, we used AD5: cTNT-CHK1/Ad5: cTNT-CHK1sh and mCherry-GFP-LC3 puncta to monitor CHK1-mediated dynamics of autophagy in NCM460 cells. We used anti-ATG5 (TGF-β1) antibody to detect ATG5 protein expression, and mCherry-GFP-LC3 puncta to monitor CHK1-mediated dynamics of autophagy in NCM460 cells. We used anti-ATG5 (TGF-β1) antibody to detect ATG5 protein expression, and mCherry-GFP-LC3 puncta to monitor CHK1-mediated dynamics of autophagy in NCM460 cells. We used anti-ATG5 (TGF-β1) antibody to detect ATG5 protein expression, and mCherry-GFP-LC3 puncta to monitor CHK1-mediated dynamics of autophagy in NCM460 cells.

RESULTS The phosphorylation activity of CHK1 decreased in myocardium with I/R injury, while the total expression level of which remained unchanged. Reduced myocardial autophagy and CHK1-cKI mice had a smaller infarct size and moderate cardiac function (LVEF and LVFS) deterioration. Compared with the blocked autophagic flux in wider type-I/R mice, CHK1-cKI-I/R mice showed enhanced activity of autophagy flux, manifested by higher levels of beclin, ATG5 and LC3, together with downregulated autophagy substrate, p62. In vitro, NCM460 cells exposed to OGD/R and transfected Ad5: cTNT-CHK1sh showed decreased autolysosome-to-autophagosome ratio. Moreover, CHK1-knockdown mice showed partial weakened in CHK1-cKI-I/R mice subjected with intraperitoneal injection of 3-MA and CQ. Conversely, CHK1-knockdown mice showed worse cardiac function and further aggravated by 3-MA and CQ.

CONCLUSIONS Our study revealed a key cardioprotective role of CHK1 after myocardial I/R injury through restoring impaired autophagic flux.

GW33-e0334
Repolarization heterogeneity in heart failure with preserved ejection fraction and its relation to ventricular tachyarrhythmias
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OBJECTIVES Heart failure with preserved ejection fraction (HfPEF) has a unique pathophysiological mechanism, and its mechanism of ventricular arrhythmia is in urgent need of further study. The purpose of this study was to investigate the repolarization heterogeneity in heart failure with preserved ejection fraction and its relation to ventricular tachyarrhythmias.

METHODS Twenty 3D rats were randomly divided into HfPEF group (n=12) and control group (n=8). The HfPEF group was treated with abdominal aortic constriction to establish HfPEF model, and the control group was treated with sham operation. The heart rate, PR interval, QRS interval, QTc interval, TpTe interval and so on were recorded in all 3D rats before and every 2 weeks after

GW33-e0326
Magnoflorine protects against cardiac remodeling induced by pressure overload through enhancing the Keap-1/Nrf-2/HO-1 signaling pathway
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OBJECTIVES Magnoflorine (MAG), a well-known quaternary alkaloid isolated from the herb Magnolia or Aristolochia, has been reported to possess anti-inflammatory and antioxidant activities, but the effect of MAG on pressure overload-induced cardiac remodeling remains inconclusive. In this study, we investigated the effect of MAG on cardiac remodeling in vivo and in vitro model to clarify the underlying molecular mechanisms.

METHODS C57BL/6 mice were subjected to aortic banding (AB), and treated with MAG (10 mg/kg, ip) 1 week after AB surgery (and continued for further 7 weeks). Eight weeks after AB surgery, the mice were subjected to echocardiography, and then sacrificed to harvest the hearts for analysis. For in vitro study, neonatal rat cardiomyocytes and cardiac fibroblasts were used to validate the protective effects of MAG in response to angiotensin II (Ang II) and transforming growth factor-β (TGF-β) challenge.

RESULTS We showed that MAG administration protected against pressure overload-induced cardiac hypertrophy, fibrosis, inflammation, and dysfunction in AB mice. In the in-vitro study, we showed that treatment with MAG (50 μM) blocked Ang II-induced-cardiomyocyte hypertrophy and TGF-β-induced cardiac fibroblasts activation. Furthermore, MAG treatment significantly enhanced the activation of the Keap-1/Nrf-2/HO-1 signaling pathway in response to pressure overload in vivo and extracellular stimuli in vitro. Moreover, adenoviruses infections by siRNA-mediated silencing of Nrf-2 abolished the protective effects of MAG in both in vitro and in vivo models.

CONCLUSIONS MAG improves cardiac function and alleviates cardiac remodeling induced by pressure overload through enhancing the Keap-1/Nrf-2/HO-1 signaling pathway, and provide a reference for the development and utilization of natural products in the treatment of pathological cardiac remodeling.
operation. After successful modeling, MAP recording electrode was attached to left subtrabecular myocardium and ventricular septum in body, MAP and limb lead electrocardiogram were recorded, sinus heart rate, repolarization 90% action potential duration (MAPD90) and effective response period (ERP) were measured, and ERP/MAPD90 were calculated. After that, the pacing electrode was attached to the middle part of the left ventricular free wall to induce ventricular arrhythmia.

RESULTS Routine ECG: The post-operation PR interval in HFpEF group was gradually prolonged, and reached the peak at the 28th week (57±2.33 ms), and then decreased slightly, which was statistically significant compared with the baseline (49±2.83 ms) (P<0.05). The QTC interval was significantly longer at 6 weeks (185±18.44 ms), 10 weeks (200±18.05 ms) and 16 weeks (186±17.98 ms) than the baseline level (166±18.10 ms) (all P<0.05). The duration of TpTe was significantly longer than baseline (31±10.57 ms) at 2 weeks (405±10.77 ms), 6 weeks (485±16.16 ms), 8 weeks (535±88.8 ms), 10 weeks (481±35.35 ms), and 16 weeks (49±10.55 ms) (all P<0.05). There were no significant differences in PR interphase, QTc interphase and TpTe interphase in the control group compared with baseline. ERP: HFpEF group (72±9.87 ms) was significantly shorter than control group (90±5.1) (P<0.05). Induction of ventricular arrhythmia: persistent ventricular tachycardia was found in 8 cases in HFpEF group.

CONCLUSIONS HFpEF has delayed cardiac repolarization, increased heterogeneity of ventricular repolarization, and shortened ventricular effective refractory period, leading to increased sensitivity to arrhythmias and laying a foundation for the onset of HFpEF ventricular arrhythmias.

GW33-e0344

Acetylation of PTPN1 mRNA mediates the SMCs proliferation in vivo

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OBJECTIVES The uncontrolled proliferation of SMCs (smooth muscle cells) is the major pathophysiological trait of PAH (pulmonary arterial hypertension). Previous evidence showed that mRNAs acetylation is associated with cell proliferation, leading us to explore the relationship between them.

METHODS Immunoblot, Immunohistochemistry and qRT-PCR were used to measure the protein and RNA expression level. Dot blot was used to estimate the RNA acetylation in vivo and in vitro. EDU and CCK-8 were utilized to test the cell proliferation. Viral vector (SM22-Cre-AAV2-flex) and Crispr-cas 9 were employed to specifically knock down the NAT10 (the mRNA acetylation enzyme) in vivo, acRIP-seq and RIP-seq were used to predict the downstream target gene.

RESULTS RNA acetylation level decreased obviously in SMC from lung of mice (Hyposia+Hysig446 for 4 weeks) or PAH patients, in consistent with NAT10 knockdown. Decreased NAT10 could accelerate the SMC proliferation in vitro. Specifically knocking down the NAT10 in SMC could elevate the pulmonary arterial pressure and narrow the lumen of pulmonary artery in vivo. Bioinformatic analysis of acRIP-seq and RIP-seq results showed that PTPN1 might be the downstream target of RNA acetylation, which is negatively related to the cell proliferation.

CONCLUSIONS Our above results showed that mRNA acetylation is related to the SMC proliferation in vivo and in vitro, in turn being associated with the development of PAH. PTPN1 was the main downstream target, might be a potential therapeutic agent for PAH.

GW33-e0345

Circular RNA Fbxl5 regulates cardiomyocyte apoptosis during ischemia reperfusion injury via sponging microRNA-146a

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OBJECTIVES Cardiomyocyte apoptosis critically contributes to ischemia reperfusion injury (IRI), which lacks effective therapeutic strategies. Circular RNAs (circRNAs) serve as novel diagnostic and therapeutic targets in various cardiovascular diseases. Circular Fbxl5 is one of the abundantly expressed circRNAs in the heart and its role in myocardial IRI remains elusive.

METHODS Wild-type (WT) mice and neonatal mice ventricular myocytes (NMVMs) were used and subjected to myocardial IRI and anoxia reoxygenation (AR), respectively. Molecular and histological analyses and echocardiography were used to determine the extent of apoptosis, infarct size, and cardiac function.

RESULTS We found that circRNA Fbxl5 was significantly upregulated in the myocardium, as well as in NMVMs subjected to AR. Knockdown of circRNA Fbxl5 ameliorated cardiomyocyte apoptosis, thereby decreasing infarct size and preserving cardiac function. Additionally, in vitro knockdown of circRNA Fbxl5 in NMVMs subjected to AR recapitulated the in vivo findings. Mechanistically, we identified that circRNA Fbxl5 directly sponged and suppressed the endogenous microRNA-146b (miR-146b), thereby weakening its inhibitory effect on MED1, which could further promote the apoptosis of cardiomyocytes.

CONCLUSIONS Our findings revealed a novel and critical role for circRNA Fbxl5 in regulating cardiomyocyte apoptosis, and added additional insight into the molecular mechanisms mediated during myocardial IRI. The underlying miR-146b-MED1 signaling serves as an important cascade in regulating the apoptosis of cardiomyocytes.

GW33-e0349

Reg3γ-dependent accumulation of macrophages in aging related atrial fibrillation

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OBJECTIVES Atrial fibrillation (AF) is the most common persistent arrhythmia and significantly increases the risk of stroke, heart failure and mortality in patients. Aging, however, is an independent risk factor for AF, significantly increasing its incidence. However, the mechanisms underlying the high prevalence of AF in the elderly population are not well understood. Inflammation is an important pathogenesis of AF, and the mechanisms that inflammation induced aging related AF need to be further elucidated. The aim of this study was to explore new mechanisms that inflammation induced aging related AF and to provide new directions for the clinical management of the occurrence, development and recurrence of AF in the elderly.

METHODS SD rats fed normally until 20 months of age were constructed as the young group. The young group was subjected to 20 months of aging. The atrioventricular conduction circumference (AVWCS), sinus node recovery time (SNRT), atrial expiration period (AERP) and AF induction rate were observed by electrophysiological examination. The aging rats were all divided into aging-prone and non-prone AF according to the induction of AF. RNA-seq analysis was performed on the atrial tissues. Bone marrow-derived macrophages (BMDM) were isolated and induced. Migration assays were performed to observe whether Regenerating Islet-Derived Protein3 gamma (Reg3γ) could recruit BMDMs. qPCR and cytokine array panel were performed to observe the effect of Reg3γ on production and secretion of inflammatory factors of BMDMs. RNA-seq was performed on BMDM with or without Reg3γ.

RESULTS AVWCS, SNRT, AERP, and AF inducibility were increased in aging rats compared with young controls. We performed RNA-seq analysis of AF-prone atrial tissues in the aging group compared with those in the young group and found that the differential genes were mainly concentrated in inflammation-related pathways. The most significant change in the differential genes was Reg3γ, and the expression of Reg3γ was higher in aging atrial tissues prone to AF than in those less prone to AF. And we found an increase in macrophages and associated inflammatory in aging atria. We also found that Reg3γ promoted the recruitment of BMDMs and inflammatory factor production. Using cytokine array panel, we screened that Reg3γ promoted the recruitment of BMDMs and inflammatory factor production. Using cytokine array panel, we screened that Reg3γ promoted the secretion of CCL3, CCL4, CXCL19, CXCCL10, CXCL13, IL17 by macrophages. We also determined that Reg3γ activates STAT3-JAK1 through the gp-130 receptor and then enables macrophages to function. In addition, we performed RNA-seq assays on Reg3γ-acting macrophages and control cells, and analyzed the differential genes by GO enrichment and KEGG pathway annotation and enrichment, and found that the differential genes mainly focused on MAPK pathway, IL17 signaling pathway, and protein metabolism pathway. It is suggested that Reg3γ also affect macrophages through the non-classical gp130-STAT3-JAK1 pathway.

CONCLUSIONS Reg3γ recruits macrophages and activates them through the gp130-STAT3-JAK1 pathway to promote inflammatory factor production and release, ultimately contributing to the development of aging related AF. The study provides an experimental basis for the prevention and treatment of elderly patients with AF from the perspective of Reg3γ-induced macrophage-associated inflammation.

GW33-e0352

The effects of nicotinamide mononucleotide on radiation-related cardiac injury

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However, the protective effects and the underlying mechanisms of NMN on cardiac dysfunction, among which increased oxidative stress is an important factor. However, the detailed mechanisms remain unclear and effective treatment strategies are still lacking. NMN, a mononucleotide (NMMN), the most direct precursor of nicotinamide adenine dinucleotide (NAD+), can effectively reduce reactive oxygen species (ROS) production, and thus could be a candidate to alleviate radiation-induced damage. However, the protective effects and the underlying mechanisms of NMN on radiation-related cardiac injury remain to be elucidated.

METHODS Wild-type c57 mice were divided into radiation exposure (7.2 Gy) and non-exposure groups. Wild-type C57BL/6J mice supplied with NMN for 1.2 months before radiation. Echocardiography to detect mice cardiac function. Epicardial electrical mapping technique to detect cardiac electrical conduction. Metabolomics was used to detect different metabolites. In parallel, we observed the effect of radiation on survival and mitochondrial function of H9c2 cells with or without NMN.

RESULTS In the radiation exposure group, echocardiography showed that the left ventricular ejection fraction (LVEF) and fractional shortening (FS) were reduced, whilst epicardial mapping demonstrated slowed conduction velocity and change in the direction of propagation. Non-targeted metabolomics showed the different metabolites between the radiation group and the control group were mainly in nucleotide and amino acid metabolism. Metabolic pathway enrichment analysis showed that different metabolites were implicated in the metabolism of pyruvate, folate, arginine and proline, and tryptophan. Mice with NMN before radiation showed reduced mechanical and electrical dysfunction, with non-targeted metabolomic results showed NMN rescued the radiation-induced decrease of 1-(4-aminobutyric acid, 4-aminobenzoic acid, and glycine, which ultimately exerted cardioprotective effects. We also found that radiation could reduce the survival, increase ROS production, and reduce ATP content of H9c2 cells in vitro, and these harmful effects can be partially reversed by NMN.

CONCLUSIONS The mechanical and electrical dysfunction caused by radiation were associated with altered nucleotide and amino acid metabolism in the myocardium, and these harmful effects could be partially mitigated by NMN supplementation.

GW33-e0355 The influence of diabetes duration on ischemic postconditioning
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OBJECTIVES It has been demonstrated that ischemic postconditioning (IPC) seems a largely efficient approach to enhance the myocardial resistance to the reperfusion injury. Yet the cardio-effectiveness of IPC in a diabetic state is controversial, we established an experimental model of diabetes mellitus with different stage of diabetes on the protective effect of ischemic postconditioning IPC is associated with attenuation of ischemic reperfusion injury, however, preclinical studies and some clinical trials demonstrated that IPC is associated with attenuation of ischemic reperfusion injury, however, preclinical studies and some clinical trials demonstrated that IPC still has a cardioprotective effect in the early phase of diabetes. Yet further experiments and clinical trials will be needed to confirm the results of the studies reviewed here.

METHODS 2018, 2019 and 2020 were divided into experimental group (miR-Plin4) and control group (miR-NC) according to the principle of randomization. AAV virus expressing Cre was injected into the experimental group by micro-RNA interference of Plin4 gene expression, and the control group was injected with micro-RNA control fragment. After 6 weeks of high fat diet (50% KCal), feeding, the weight of the mice was weighed to calculate the hepatoprotective weight, liver samples were collected for qPCR and WB detection. Liver weight of mice in miR-Plin4 group was significantly reduced. Liver HE staining and oil red staining indicated that the volume of liver lipid droplets decreased and the lipid change was alleviated in miR-Plin4 group.

CONCLUSIONS Reducing PLIN4 in liver of mice with Gt158 liver deficiency can significantly improve liver dysfunction, reduce the volume of liver lipid droplets, reduce liver weight, delay or even reverse the occurrence and development of NAFLD induced by high fat diet.

GW33-e0374 Mechanism of hepatic lipoprotein Plin4 on metabolic fatty liver induced by CGT-58 deficiency
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OBJECTIVES Nonalcoholic fatty liver disease (NAFLD) is an important risk factor for cardiovascular diseases such as coronary heart disease (CHD). The global prevalence rate of NAFLD is up to 24.4%, and lipid metabolism disorder is the key mechanism of its pathogenesis. How to effectively improve liver lipid metabolism will become a key link to protect liver function and reduce long-term cardiovascular and cerebrovascular events. Lipid droplet associated protein 4 (Plin4) is a rate-limiting enzyme that activates triglyceride hydrolysis, promotes lipid droplet decomposition, and is a key inhibitor of liver lipid metabolism disorders. Liver specific knockout of Gt1-58 leads to the formation of hyperlipidemia-induced fatty liver. However, its regulatory mechanism remains unclear. Low-dose continuous Plin4 promotor-lacZ and droplet formation and abnormal lipid accumulation under the regulation of overnutrition. Therefore, this study investigated whether PLIN4 interacts with Gt158 to participate in the formation and pathological progress of NAFLD.

METHODS CGT-58flox/Flox homozygous mice aged 6 weeks from the same nest were divided into experimental group (miR-Plin4) and control group (miR-NC) by using the same low dose of Gt158 high glucose diet. To establish a diabetes model with high glucose diet combined with multiple low-dose injections of STZ. After the establishment of the experimental model, the mice were randomly divided into six groups: non-diabetic (2 weeks) ischemia-reperfusion group (2NIR), non-diabetic (2 weeks) ischemia-postconditioning group (2NPost), non-diabetic (8 weeks) ischemia-reperfusion group (8NIR), non-diabetic (8 weeks) ischemia-postconditioning group (8NPost), diabetic (8 weeks) ischemia-reperfusion group (8DIR), diabetic (8 weeks) ischemia-postconditioning group (8DPost). After all, hearts underwent 30 mins of prolonged ischemia, 2NIR, 8NIR, 2DIR, and 8DIR groups received 60 minutes of continuous reperfusion. 2NPost group, 8NPost group, 2DPost group, and 8DPost group were given three cycles of 10 s reperfluations and 10 s ischemia followed by 60 mins continuous reperfusion. The levels of lactate dehydrogenase (LDH) and creatine kinase (CK) in the coronary outflow fluid at 60 min of reperfusion were measured, the left ventricular myocardium was isolated and the infarct area was measured, and immunohistochemical staining of the myocardium was performed to determine the expression of ERK1/2 to evaluate the effect of different stage of diabetes on the protective effect of ischemic postconditioning after myocardial ischemia-reperfusion.

RESULTS Compare to the 2NIR group, the 2DIR group had displayed higher LDH and CK levels (P 0.05), with larger infarct size (P 0.05), and downregulation of ERK1/2 level (P 0.05) however between 2NPost and 2DPost group, there was no significant difference (P 0.05) compare to 8 weeks normoglycemic IR group and 8DPost group, the 8DIR group, and 8DPost group showed increased LDH and CK levels, larger infarct size, and decreased ERK1/2 level (P 0.05). Yet there is no statistical significance between the 8DIR group and 8DPost group.

CONCLUSIONS Preclinical studies and some clinical trials demonstrated that IPC is associated with attenuation of ischemic reperfusion injury, however, preclinical studies and some clinical trials demonstrated that IPC still has a cardioprotective effect in the early phase of diabetes. Yet further experiments and clinical trials will be needed to confirm the results of the studies reviewed here.

GW33-e0376 Low shear stress promotes atherosclerosis via IKKε/STAT1/ NLPR3 mediated endothelial cell pyroptosis
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OBJECTIVES The initiation and progression of atherosclerosis is characterized by vascular endothelial dysfunction, and low shear stress (SSS) of blood flow is a key factor leading to endothelial dysfunction. Caspase-dependent protein CGT-58 is a novel type of inflammatory programmed cell death characterized by the activation of inflammasomes, especially NOD-like receptor protein 3 (NLPR3). Growing evidence suggests that endothelial cell pyroptosis plays an important role in the development of atherosclerosis. However, the exact mechanism by which low shear stress induces endothelial cell pyroptosis remains unknown.

METHODS At the cellular level, we investigated the effect of IKKεK on the scavenging of endothelial cells under SSS and the specific mechanism using molecular biology and immunofluorescence, and at the animal level, we
used RT-qPCR and enface staining to detect the expression of scorching-related molecules in different blood flow patterns in the aortic arch and descending aorta.

RESULTS Our cellular experiments demonstrate that low shear stress induces endothelial cell pyroptosis and promotes the phosphorylation of IkB kinase ε (IKKe). Knockdown of IKKe significantly reduces low shear stress-induced endothelial cell pyroptosis, and vice versa promotes pyroptosis. Concomitant knockdown of IKKe attenuates low shear stress-induced reactive oxygen species (ROS) accumulation in endothelial cells, IKKe promotes the expression of NLRP3 by activating its downstream signal transducer and activator of transcription 1 (STAT1) activation and nuclear translocation rather than leading to endothelial cell pyroptosis through the ROS pathway. The above results were verified by animal experiments. The phosphorylation level of IKKe in the medial curvature of the aortic arch (AA) of mice was significantly higher than that in the descending aorta (DA). IKKe knockdown significantly reduces the level of NLRP3 in the medial aortic arch and attenuates atherosclerosis in high cholesterol diet-induced ApoE−/− mice.

CONCLUSIONS These results suggest that low shear stress can play a proatherosclerotic role by causing endothelial cell pyroptosis through the IKKe/STAT1/NLRP3 pathway and provide new insights into the formation of atherosclerosis.

GW33-e0382 Soluble RAGE attenuates myocardial I/R injury by suppressing monocytes/macrophages-produced interleukin-6
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OBJECTIVES Inflammation plays a central role during myocardial ischemia/reperfusion (I/R) injury. Previous studies have demonstrated that the receptor for advanced glycation end-products (RAGE) is involved in the pro-inflammatory process of myocardial I/R injury by binding to diverse ligands. Soluble RAGE (sRAGE) is a decoy receptor for RAGE, inhibiting the inflammatory process of myocardial I/R injury. Previous studies have demonstrated that the receptor for advanced glycation end-products (RAGE) is involved in the pro-inflammatory process of myocardial I/R injury by binding to diverse ligands. Soluble RAGE (sRAGE) is a decoy receptor for RAGE, inhibiting the inflammatory response. This study aimed to investigate whether the effects of sRAGE on myocardial I/R injury was associated with a reduced inflammatory state.

METHODS Plasma levels of sRAGE and several inflammatory mediators were measured in patients with ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) and control subjects (negative coronary arteriographic findings). Myocardial I/R surgeries were operated on cardiomocyte-specific sRAGE knock-in (sRAGE-KI) mice and littermate control (sRAGE-KI/+ ) mice by ligation of the left anterior descending coronary artery. Cardiac function and infarct size were measured by echocardiography and TTC staining, respectively. Plasma levels of inflammatory mediators in the mice were measured by ELISA. Mouse peripheral blood monocytes were assessed by flow cytometry. The phenotypes of macrophages in the mouse heart were determined by immunohistochemistry.

RESULTS sRAGE levels in STEMI patients were significantly increased compared with that in the control subjects. There was a negative correlation between the plasma sRAGE level before PCI with interleukin (IL)-1, IL-6 and IL-10. Cardiac overexpression of sRAGE dramatically improved cardiac function and decreased infarct size during myocardial I/R. Furthermore, sRAGE decreased IL-6 level, but did not affect the plasma IL-1 and IL-10 levels compared with the sham group in mice. Mechanistically, sRAGE decreased the numbers of proinflammatory CD14+CD68+ monocytes in the mice. In addition, cardiac-specific overexpression of sRAGE increased CD206 M2-macrophages, and decreased pro-inflammatory iNOS M1-macrophages in the heart.

CONCLUSIONS Our data suggested that sRAGE protected the heart from myocardial I/R injuries. The process might be mediated by inhibiting the numbers of proinflammatory monocytes and infiltration of M1-macrophages, leading to decreased secretion of IL-6.

GW33-e0383 Ibrutinib induced connexins degradation contributed to atrial arrhythmia through the activation of autophagy by off-target inhibiting PI3K-AKT-mTOR signaling pathway
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OBJECTIVES Ibrutinib is a Bruton tyrosine inhibitor that has remarkable efficacy in B-cell cancers. However, according to pivotal trial results, almost 5–9% of the Chronic lymphocytic leukemia (CLL) patients developed atrial fibrillation compared to 0.5−2.4% in the comparator arms. Why ibrutinib could increase the occurrences of atrial fibrillation remained poorly understood. This study aimed to investigate the ibrutinib-related proarrhythmic mechanism in atrial.

METHODS We performed optical mapping using calcium and action potential dye to explore the intracellular calcium activity and conduction of HL-1 cells with or without ibrutinib treatment. Fluorescence imaging was used to determine the Cx43 distribution and structure of ibrutinib treated HL-1 cells. We also conducted a western blot to analyze the expression of connexins, ibrutinib targets, and autophagy-regulated proteins. The virus- Monomeric cherry (mCherry)-goose fluorescent protein (GFP)-LC3 was transplanted into cells to display autophagic flux. The structure of autophagosome and autophagolysosome was shown with electron microscopy results.

RESULTS Our results showed that Ibrutinib enhanced susceptibility to atrial arrhythmia by decreasing the conduction velocity. Compared to the control group, Ibrutinib significantly reduced the expression of connexin 43 and connexin 40 at the protein level. However, the total levels of connexin 43 and connexin 40 were not different between the two groups at the gene transcription level. The autophagy activity was enhanced in the ibrutinib intervention group, and autophagy inhibitors could reverse the degradation of Cx43. Thus, Ibrutinib could induce the connexins degradation contributing to atrial arrhythmia through the activation of autophagy by its off-target effect on the PI3K-AKT-mTOR Signaling Pathway.

CONCLUSIONS In the present study, we discovered that the concentration of 100 μm ibrutinib could increase susceptibility to AF in HL-1 cells. Further research will investigate the possible autophagic proarrhythmic mechanism, we demonstrated that the underlying effect was associated with the degradation of Connexin 43. Besides, we found that the decreased expression of Connexin 43 was due to enhanced autophagic activity, and the degradation process was significantly slowed down. At the same time, the autophagy was inhibited in HL-1 cells, suggesting that inhibiting autophagy could be a promising preventative for ibrutinib-related atrial arrhythmia.

GW33-e0391 Gut permeability promotes aortic dissection via low-grade endotoxemia
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OBJECTIVES Aortic Dissection (AD) is a severe life-threatening cardiovascular emergency with rapid onset, rapid progress, and high mortality. In recent years, with the continuous in-depth research on the Gut microbiome (GM), the potential role of GM in cardiovascular disease has been revealed. However, it is still unknown whether GM disorders are involved in AD development. This study explored the role of the innate immune inflammatory response caused by the damage of the intestinal barrier in the pathogenesis of aortic dissection.

METHODS 1. Use proteomics technology to detect the blood samples and tissue of the healthy control group, screening the differential genes and proteins when AD occurs, and through the gene ontology (Gene Ontology, GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) databases carry out enrichment analysis of the essential biological processes and critical signal pathways involved in differential genes and proteins in the occurrence of AD, revealing the critical mechanism of AD occurrence. 2. We collected blood samples from 50 healthy controls, 50 hypertensive patients, and 50 AD patients and tested the lipopolysaccharide (LPS), which is the component of the outer wall of gram-negative bacteria, also known as endotoxin, interleukin-6 (IL-6), interleukin-1α, interleukin-1β, interleukin-18, tumor necrosis factor-α, and interleukin-10. 3. To study the potential role of intestinal microbial disorders in AD, fecal samples from the above population were collected, and 16S amplicon sequencing was used for bacterial diversity analysis (including α-diversity, and β-diversity) to screen the differential flora further, analyze the species composition and abundance comparison, and predict the function of the flora.

RESULTS 1. Proteomics analysis results show that differential proteins are enriched in the Toll-like receptor signaling pathway. 2. Compared with healthy controls and hypertensive patients, AD patients have higher levels of serum LPS, IL-6, LBP, and sCD14; the difference is statistically significant (P<0.05). 3. To determine the expression of the intestinal microbiome was analyzed, and α-diversity and β-diversity were evaluated. The results show that compared with healthy controls and hypertensive patients, the intestinal flora of AD patients tends to be more inclined. It produces LPS type.

CONCLUSIONS After the intestinal barrier function is impaired, LPS-mediated low-grade endotoxemia causes the activation of immune inflammation in the blood vessels and participates in the occurrence and development of aortic dissection.
The impact of lymphangiogenesis in transplant arteriosclerosis

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OBJECTIVES
Transplant arteriosclerosis is a major limitation to long-term survival of patients with solid organ transplantation. Although lymphatic ves- sels have been recently reported to possess organ-specific features in allograft transplantation, the relationship between lymphangiogenesis and transplant arteriosclerosis remains unknown.

METHODS
Vascular allografts were obtained from wild type (BALB/c, C57BL/6), Lyve-1-CreERT2, R26-e tdTomato, severe combined immune deficiency (SCID), Cdx21, Foxn110 and lymphnode1 mice. Whole-mount staining and three-dimensional reconstruction depicted the lymphatic ves- sel regeneration within transparent grafted arteries. Multiple lineage tracing strategies were performed to delineate the cellular origin of lymphangiogen- esis within grafts. Single-cell RNA sequencing, Western blotting, quantitative polymerase chain reaction and immunohistochemical staining were used to identify the characteristics of lymphatic endothelial cells and evaluate cellular contributions of related lymphangiogenic factors AAXVEGFC, AAXVEGFR- lg and VEGFR3 inhibitor, MAZ51, were separately applied to explore the pos- sible therapeutic effect.

RESULTS
Lymphangiogenesis within allografted vessels was initiated in the anastomotic sites and primarily derived from recipient pre-existing lymphatics but not by newly derived cells. Coexistence of initial and two distinct Foxp3+ and Icam1+ collecting lymphatic endothelial cells demonstrated the heterogeneity of lymphatic vessels in vascular allografts. CCL21-expressing lymphatic vessels had a close relationship with tatty lymphatic organ formation in grafted arteries. Most critically, a positive feedback was revealed between cellular immunity and lymphangiogenesis mediated by VEGF-C released from fibroblasts. Taking advantages of a unique recipient replacement phenomenon, early inhibition of lymphangiogenesis in vascular allografts could break this vicious circle and led to a long-term alleviation of transplant arteriosclerosis.

CONCLUSIONS
Our results substantiated the importance of lymphatic ves- sels serving as a key immunosuppressive target in the treatment of transplant arteriosclerosis.

GW33-e0401
Newly-synthesized proteomic analysis of mesenchymal stem cells under OGD condition

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OBJECTIVES
Mesenchymal stem cell (MSC) is an attractive choice of regenera- tive medicine for possible development of clinical applications. The aim of this study was to understand the biochemical and metabolic mechanisms and feedback associated with response to hypoxia and ischemia in MSCs using a meta- bolic labeling method for cell-selective analysis of newly synthesized proteins.

METHODS
After culturing and identification, murine MSCs were transduced with lentivirus MetRSL274G and supplemented with azidonorucleic (ANL); targeting of a mutant methionyl-tRNA synthetase (MetRS) from MSCs permits ANL charged to initiator tRNAMet and subsequently allows ANL labeling of their nascent proteins. Bio-orthogonal non-canonical amino-acid tagging (BONCAT) and fluorescent non-canonical amino-acid tagging (FUNCAT) were performed to detect the efficiency and specificity of this labeling method. Results showed that MetRSL274G mutant MSCs with ANL treated showed fluo- rescent protein bands in the gel and strong green signal in cell culture, indic- ating efficient and specific incorporation of ANL in nascent protein synthesis. MetRSL274G-transduced MSCs were then cultured in glucose-serum-free and ANL supplemented medium under hypoxia (5% CO2 and 95% N2) for 12 h. Newly synthesized proteins were isolated by click chemistry reaction eliminat- ing the azido and identified by LC/MS.

RESULTS
As results, we found totally 1326 and 1323 of ANL-labeled proteins respectively in Sham and Oxygen and glucose deprivation (OGD) group; 1219 proteins were shared among two groups, accounting for 92.0±2.0% of all identified proteins in individual group. Notably, 50 proteins were significantly up- regulated whereas 29 proteins were significantly down-regulated in OGD vs. Sham group. These differentially expressed proteins were more pronounced in the pathways of actin cytoskeleton, oxidative phosphorylation and apoptotic process. Some factors like gelsolin and moesin may serve as a crucial role in sur- vivor MSCs under hypoxia.

CONCLUSIONS
Our results showed that mutant MetRSL274G brought about an efficient and specific labeling method of dynamic proteome in MSCs cell line. By this approach, we investigate functional and adaptive changes of MSCs in hypoxic and ischemic environment that help us better understanding how to improve stem cell therapy.

GW33-e0407
Knock down of PCSK9 can improve myocardial ischemia/ reperfusion injury by inhibiting autophagy

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OBJECTIVES
To investigate the effect and mechanism of proprotein con- vertase subtilisin/kexin type 9 (PCSK9) on myocardial ischemia-reperfusion injury (MI/R) and to provide a reference for clinical prevention and treatment of acute myocardial infarction (AMI).

METHODS
We established a rat myocardial ischemia/reperfusion (I/R) model and AC16 hypoxia/reoxygenation (H/R) model. A total of 48 adult male Sprague-Dawley rats were randomly assigned into 3 groups.

RESULTS
PCSK9 mRNA and protein levels were significantly upregulated during cardiomyocyte hypoxia in vitro and in vivo. Immunohistochemical staining experiments confirmed that PCSK9 expression was increased in rats hearts 3 days after anterior descending branch ligation. In vitro and in vivo experimental studies revealed that siRNA knockdown of PCSK9 resulted in reduced expression of autophagy protein Beclin-1, light chain 3 (LC3) compared to control treated cells and sham-operated groups, at the same time, the presentation of the autophagic pathway BNI3P was also downregulated. Furthermore, the PCSK9-mediated small interfering RNA (siRNA) group injected into the left ventricular wall significantly improved cardiac function and myocardial infarct size, as well as the expression of mRNA of Recombinant Human Interleukin-1β (IL-1β) and Nucleotide-binding oligomerization domain-like receptor protein 3 (NLRP3) was significantly downregulated and reduced the inflammatory response compared with the I/R group.

CONCLUSIONS
In ischemic/hypoxic circumstances, PCSK9 expression was dramatically increased. PCSK9 knockdown alleviated MI/R via the BNI3P-mediated autophagic pathway, and improved myocardial infarct size and cardiac function.

GW33-e0424
Novel insights of ANGPTL-3 on modulating cholesterol efflux capacity induced by HDL particle

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OBJECTIVES
Angiopoietin-like protein 3 (ANGPTL-3) modulates lipid metab- olism and the role of acute coronary syndrome (ACS) via suppressing lipopro-tein lipase (LPL). Whether there are other mechanisms are still not elucidated. The current research explored the modulatory roles of ANGPTL-3 on high-density lipoprotein (HDL) particle which further affects the atherosclerotic development.

METHODS
Two hundred individuals were enrolled in the present study. Serum ANGPTL-3 levels were detected via enzyme-linked immunosorbent assays (ELISA). Cholesterol efflux capacity induced by HDL particles was detected through H+-cholesterol loading THP-1 cells.

RESULTS
As shown, the serum ANGPTL-3 levels presented no significant discordance between ACS group with non-ACS group, whereas the serum ANGPTL-3 levels in type 2 diabetes mellitus (T2DM) group was significa- ntly decreased compared with those in the non-T2DM group (428.3 ± 306.2 vs. 736.8 mg/mL vs. 298.2 ± 55.6 mg/mL, P<0.05). Additionally, the serum ANGPTL-3 levels exhibited elevated in patients with low TG levels compared to those in patients with high TG levels (53.9 ± 37.6 vs. 80.9 ± 22.1 mg/mL, P=0.05). By comparison, the individu- als in ACS group and DM group presented decreased cholesterol efflux induced by HDL particles (ACS: (12.2±2.1±11%) vs. (15.5±2.7±26%), P<0.05; T2DM: (11.2±2.1±13%) vs. (14.6±3.3±27%), P<0.05). In addition, the serum concentrations of ANGPTL-3 were inversely associated with the cholesterol efflux capacity of HDL particles (r=-0.184, P<0.05). Via regression analysis, it is shown that the serum concentrations of ANGPTL-3 were an independ- ent modulator to cholesterol efflux capacity of HDL particle (standardized coefficient β=-0.201, P<0.05).

CONCLUSIONS
Conclusively, ANGPTL-3 exhibited a negative regulatory function on cholesterol efflux capacity induced by HDL particles.
GW33-e0431

KDM3A attenuate myocardial ischemic and reperfusion injury by ameliorating cardiac microvascular endothelial cells pyroptosis

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OBJECTIVES Even though subjected to successful revascularization therapy, microvascular endothelial cell ischemia-reperfusion (CMEC I/R) injury occurs in approximately 50% of acute myocardial infarction patients, leading to the dysfunction of the cardiac microcirculatory system. Our prior studies have characterized the participation of histone demethylase KDM3A in protecting cardiomyocytes from I/R injury, while its roles in CMEC I/R injury remain to be illustrated.

METHODS CMEC hypoxia and reoxygenation (H/R) model was established to mimic the ischemia-reperfusion process in vitro. The proliferative and migration abilities of CMEC were measured by the CCK-8 and wound healing assay. Tube formation assay and sprouting assay were performed to determine the angiogenesis ability of CMEC. Also, CMEC death were detected by Hoechst 33342/PI double fluorescent staining. Besides, the rat ischemia-reperfusion injury model was established in vivo. Myocardial infarct size, cardiac function, and cell death were measured by Evans blue and TTC staining, echocardiography assay and TUNEL staining, respectively. In addition, the no-reflow zone and capillary density were detected by thioflavin-S and CD31 fluorescent staining. Moreover, the expression of pyroptosis-associated proteins and PI3K/Akt signaling pathway-related molecules were analyzed by Western blot assay.

RESULTS Here we show that H/R treatment significantly impaired CMEC function and induced CMEC pyroptosis accompanied by the obvious down-regulation of KDM3A. Subsequently, gain- and loss-of-function experiments were performed to investigate the effects of KDM3A in the settings of CMEC I/R injury in vitro. KDM3A knockout further aggravated CMEC malfunction and accelerated the expression of pyroptosis-associated proteins including NLRP3, ASC, cleaved-caspase-1, GSDMD-N, IL-1, and IL-18. Conversely, KDM3A overexpression developed the ameliorated alterations in CMEC H/R injury. Additionally, in vivo experiments also confirmed KDM3A knockout further deterioration of heart function as well as decreased no-reflow area and capillary density. Mechanistically, our data uncovered that KDM3A could activate the PI3K/Akt signaling pathway and mitigate I/R induced CMEC pyroptosis.

CONCLUSIONS Our present study suggests that KDM3A is a potential therapeutic target for alleviating CMEC I/R injury by activating PI3K/Akt signaling pathway.

GW33-e0448

Global phosphoproteomic profiling reveals perturbed signaling in a sheep model of atrial fibrillation

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OBJECTIVES Atrial fibrillation (AF) is a common arrhythmia, but the detailed mechanism and underlying signaling networks are unclear. To fully understand the intricate pathogenesis, there are still challenges to overcome. Thus, identifying the fundamental mechanisms and targets of AF progression, then exploring possible treatments, is critically important.

METHODS In this work, precision mass spectrometry-based proteomics and phosphoproteomics were constructed to depict the pivotal abnormalities of AF, and quantified 1799 proteins and 10,476 phosphorylation sites were mapped to 2886 proteins in AF- and sham-sheep left atrial tissues. Signaling pathways of AF-associated remodeling were evaluated via global statistical enrichment analysis of differential phosphoprotein patterns. The signaling pathway alterations were confirmed via Western blotting and immunohistochemistry.

RESULTS Deep phosphoproteomic analysis of atrial tissue from sham- and AF-sheep atrial tissue demonstrated a prominent role of adrenergic signaling- and autophagy-regulating roles in AF pathophysiology. Notably, the considerably perturbed pathways included the Hippo signaling pathway, ErbB/ErbB2 and splicing signals, which have never been reported to be AF-associated. Alterations in components of these AF development-associated signaling pathway were verified via Western blotting or immunohistochemistry.

CONCLUSIONS These data reveal the unexpected relationships between cell signaling networks and AF, paving the way for investigation of AF mechanisms and drug targets.

GW33-e0458

HSP70 improves coronary microcirculation disturbance in neonatal rat with hypoxia-induced pulmonary arterial hypertension

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OBJECTIVES Right ventricular (RV) heart failure is the main cause of death in pulmonary hypertension (PH), while there is an unmet need for RV-targeted therapies to improve mortality. Heat shock protein 70 (HSP70) acts as a vasoprotective regulator in pulmonary smooth muscle and endothelial cells, while its role in the heart is unclear. This study investigated the effect of HSP70 on RV injury in PH.

METHODS HPH model was induced using 10% hypoxia, and a single intravenous injection of adenoviral vectors carrying HSP70 or luciferase gene was administered. The animals were euthanized 7 or 14 days after gene delivery to assess cardiac structure, function and myocardial perfusion. Also we measured RV microcirculation relevant measures of histology, protein, and gene expression.

RESULTS Hypoxia induced progressive RV dysfunction, fibrosis, and inflammation. HSP70 prevented hypoxia-induced RV dysfunction and remodeling, improved myocardial perfusion; Besides, HSP70 promoted microvascular neovascularization by up regulating VEGF; and promoted vasodilation by upregulating eNOS and reducing ET-1; Also, HSP70 reduced the expression of E-selectin and ICAM-1, inhibited the adhesion and aggregation of inflammatory cells in myocardium and the release of inflammatory factors IL-6 and TNF-α (P<0.05), to inhibit microcirculation inflammatory response.

CONCLUSIONS Together, HSP70 gene transduction can improve myocardial microcirculation and induce the cardioprotective effect of HPH, by promoting microvascular neovascularization and vasodilation, and attenuating microcirculation inflammation, representing a therapeutic approach for PAH and other cardiovascular/pulmonary diseases.

GW33-e0488

Deficiency of NLRC5 in macrophages promotes chronic heart failure

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OBJECTIVES Macrophages play an important role in tissue repair and inflammatory response during the process of myocardial infarction. However, the role of macrophages in the microenvironment of chronic cardiac remodeling has not been clearly elucidated. Among NOD-like receptor family members, NLRP3 receptor family is a key inflammation-related domain family containing 5 (NLRC5) was an innate immunologic protein and play important roles in chronic inflammation. However, the role of NLRC5 in heart failure (HF) remains unclear. In this study, we determine the role of macrophage NLRC5 in pressure overload-induced HF and dissect the underlying mechanisms.

METHODS Peripheral blood samples from 20 patients with hypertrophic cardiomyopathy and 20 healthy subjects and heart tissue samples from patients with heart failure were collected to explore the significantly different genes of NRLRs family members in peripheral blood monocytes and cardiac macrophages. Then, male C57BL/6 wild-type (WT) and NLRC5 knockout (NLRC5−/−) mice were subjected to pressure overload-induced heart failure using transverse aortic constriction (TAC). The numbers of macrophages, monocytes and T cells in mice with TAC was determined by flow cytometry. The myeloid conditioned knockout mice and bone marrow transplantation mice were also used to identify myeloid-specific cells NLRC5−/− mice plays a major role. The difference cytokine secretion between NLRC5 KO and WT bone marrow derived macrophages (BMDM) was detected by cytokine array and Enzyme linked immunosorbent assay. High performance liquid chromatography mass spectrometry, co-immunoprecipitation and immunofluorescence were used to investigate the target protein that interacted with NLRC5, and western blot and RNA sequencing was used to reveal the underlying mechanism of NLRC5 influencing cardiomyocytes and fibrotic cells in heart failure through macrophage.

RESULTS NLRC5 was markedly increased in circulating monocytes and cardiac macrophages from patients with hypertrophic cardiomyopathy and mice with pressure overload induced heart failure (TAC). Both global and myeloid-specific NLRC5 knockout significantly aggravates TAC-induced pathological cardiac hypertrophy and fibrosis, as shown by a series of morphological experiments in mice. More importantly, NLRC5-null mice exhibited increased infiltration of macrophages, neutrophils and T lymphocytes in failing hearts. Mechanically, we identified that NLRC5 suppressed...
the phosphorylation of IKKβ and p38 via interaction with chaperone protein HSPA8 in bone marrow-derived macrophages (BMDMs). In addition, deletion of NLRCS in BMDMs enhanced the expression and secretion of proinflammatory cytokines such as IL-6, ICAM-1 and CXCL1, while blockade of IL-6 receptor by Tocilizumab alleviated cardiomyocyte hypertrophy and cardiac fibrosis activation induced by conditioned medium from NLRCS-deficient BMDMs. Furthermore, specific IL-6 receptor antagonist Tocilizumab reversed cardiac remodeling and dysfunction caused by NLRCS deficiency in vivo.

CONCLUSIONS Our findings suggest that NLRCS in macrophages positively impacts on cardiac remodeling via interaction with HSPA8, thereby providing a strong pre-clinical foundation that the NLRCS-HSPA8-IL-6 signaling axis may serve as complementary immunomodulatory target for HF.

GW33-e0508 Exogenous rDLK1 improves neovascularization after hindlimb ischemia by modulating endothelial progenitor cell mitochondrial function
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OBJECTIVES Peripheral arterial disease (PAD) is an atherosclerosis disease characterized by impaired circulation to the lower extremities, commonly results from vascular occlusion or narrowing. Noteworthy, severe PAD leads to critical limb ischemia (CLI), characterized by high mortality and significant amputation rates. Currently, interventions aimed at enhancing angiogenesis and restoring blood flow in CLI are essential. Bone marrow-derived endothelial progenitor cells (EPCs) are a subset of circulating endothelial cells responsible for vascular and tissue repair processes after ischemia, and mitochondria regulate energy balance, and cell fate determination of EPCs. Delta-like-like non-canonical Notch ligand 1 (DLL1) is a member of the epidermal growth factor-like family of homeotic proteins, typically involved in endothelial cell function. However, its role in angiogenesis remains controversial. Therefore, the present study aimed to determine whether DLL1 could affect angiogenesis and blood flow recovery after CLI.

METHODS Mouse model of hindlimb ischemia (HLD) created by femoral artery ligation was performed on 6-8 weeks old male C57BL/6 mice. From Day 0, mice were injected intravenously with recombinant DLL1 (rDLL1) (0.1 mg/kg) or vehicle every 3 days for 14 days. Hindlimb blood flow was sequentially measured before and at 3, 7, and 14 days after surgery. Angiogenesis was detected by CD31 staining, and mature blood vessel was assessed by e-SMA staining. In addition, flow cytometry was used to evaluate the EPC/CD34+/KDR+ mobilization from bone marrow to ischemic tissues. ROS, Δψm and ATP measurement were further performed in EPCs under oxygen glucose deprivation condition.

RESULTS rDLL1-treated mice showed better recovery than vehicle control-treated mice at days 3 and 7 post-surgery. This result was further supported by increased CD34+ and e-SMA+ vessels in the ischemic muscles of rDLL1-treated mice compared to vehicle control group. In addition, the rDLL1 group exhibited significantly enhanced EPC mobilization from bone marrow to ischemic tissue during the progression of hindlimb ischemia. rDLL1 reduced ROS production, Δψm decrease of EPC mitochondrial and increased ATP levels.

CONCLUSIONS These findings suggested that rDLL1 repletion may inhibit ischemia-induced damage by promoting EPC mobilization, thus improve angiogenesis and tissue repair. This benefit of rDLL1 may lead to a new therapeutic approach for critical hindlimb ischemia. Under oxygen glucose deprivation condition, mitochondria shift their function from ATP synthesis to reactive oxygen species (ROS) production causing decrease of Δψm, which could be reversed by rDLL1.

GW33-e0512 Human antigen R regulates autophagic flux by stabilizing autophagy-associated mRNA in calcific aortic valve disease
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OBJECTIVES The incidence of calcific aortic valve disease (CAVD) has risen over the last decade and is expected to continue rising. Currently, surgical and transcatheter aortic valve replacements (TAVR) remain the most effective interventions for patients with late-stage CAVD, however, pharmacological approaches have proven ineffective. In this study, we evaluated the role and underlying mechanisms of human antigen R (HuR)-mediated post-transcriptional regulation in CAVD.

METHODS We performed quantitative real-time polymerase chain reaction and western blot to evaluate the expression of HuR in human calcific aortic valves and human aortic valvular interstitial cells upon osteogenic induction. Then we investigated the role of HuR in osteogenic differentiation and CAVD progression by silencing HuR in vitro and in vivo. Furthermore, we conducted in vivo experiments to assess the effect of HuR silencing on osteogenic differentiation between HuR and its target mRNA phosphatidylinositol-5-phosphate 4-kinase 4, kinase type II, alpha (PIP4K2A), and more functional studies proven the roles of HuR and PIP4K2A played on angiogenesis and associated pathway.

RESULTS We found that HuR was significantly upregulated in human calcified aortic valves and primary aortic valvular interstitial cells (VICS) following osteogenic stimulation. Subsequent functional studies revealed that HuR silencing ameliorated calcification both in vitro and in vivo. For the first time, we demonstrated that HuR directly interacted with the transcript of phosphatidylinositol-5-phosphate 4-kinase 4, kinase type II, alpha (PIP4K2A), which mediates phosphatidylinositol signaling, facilitates angiogenesis, and act as an mRNA stabilizer. HuR positively modulated PIP4K2A expression at the post-transcriptional level, and consequently influenced the AKT/mTOR/ATG13 pathway to regulate angiogenesis and CAVD progression.

CONCLUSIONS Our study provides new insights into the post-transcriptional regulatory role of HuR in modulating autophagy-positive factors to regulate the pathogenesis of CAVD. Our findings highlight the potential of HuR as an innovative therapeutic target in CAVD treatment.

GW33-e0530 Dapagliflozin attenuates cardiac fibrosis by suppressing cardiac fibroblasts STAT3-Grb2 signaling axis in diabetic cardiomyopathy
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OBJECTIVES Cardiac fibroblast (CF) proliferation and activation drive extracellular matrix (ECM) remodeling, leading to fibrosis and diastolic dysfunction (DD) eventually heart failure (HF). Previous study showed that dapagliflozin (DAPA), a sodium glucose transporter 2 inhibitors (SGLT2), decrease cardiac fibrosis and improved cardiac function in diabetic cardiomyopathy (DCM), which is characterized by DD and/or systolic dysfunction. Herein, we attempted to determine whether DAPA exerts antifibrotic effects on DCM by directly suppressing CF proliferation and activation.

METHODS High-glucose (HG) cultured adult mouse cardiac fibroblasts (AMCsFs) and streptozotocin (STZ)-induced diabetic mice were administrated with or without DAPA. Signaling pathway was verified through gene silencing and western blot in both vivo and vitro. The cardiac structures were determined by histopathological analysis.

RESULTS Knockdown of signal transducer and activator of transcription 3 (STAT3) or pretreatment with DAPA markedly inactivated STAT3, leading to inhibit Grb2 (growth factor receptor bound protein 2), with subsequently attenuated CF proliferation and activation and cardiac fibrosis in high glucose (HG)-treated AMCsFs. These properties of DAPA were dampened when cells were pretreated with colivelin TFA, a potent activator of STAT3. In CF isolated from hearts of db/db mice, DAPA treatment significantly mitigated diabetes induced STAT3 activation, Grb2 phosphorylation and cell proliferation and activation. Additionally, administration of DAPA significantly improved cardiac function in db/db mice. However, these effects were weakened when diabetic mice pre-subjected to intraperitoneal injection of colivelin TFA.

CONCLUSIONS DAPA-induced improvement of cardiac fibrosis in diabetic mice, may be at least in part attributable to the suppression of STAT3-Grb2 signaling axis-mediated CF proliferation and activation.

GW33-e0535 Dual GIP/GLP-1 receptor activation by tirzepatide promotes BCAA catabolism to prevent myocardial infarction
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OBJECTIVES Adverse cardiac remodeling is an important cause of heart failure. Patients with Type 2 diabetes mellitus (T2DM) have an increased risk of developing heart failure. Controlling blood glucose can reduce the incidence of cardiovascular events in diabetic patients. Tirzepatide (LY2345176, TZP), a novel dual GIPR and GLP-1R agonist, has shown superior efficacy in glycemic control and weight loss. The biological functions in myocardial infarction, however, are still unknown. We wanted to explore the role of tirzepatide in myocardial infarction and the potential mechanism.

METHODS C57/BL/6 mice underwent permanent coronary artery ligation (STAS) or pretreatment with DAPA markedly (n=10) or tirzepatide (10 nmol/kg, n=30) for 7 days. Cardiac function was assessed by using echocardiography and histological and molecular indicators of cardiac remodeling and metabolism were detected. Downstream effectors
were screened through Untargeted Metabolomics analysis. In addition, we used Molecular Docking to determine the combining sites of tirzepatide and downstream molecules. In vitro, H9c2 were exposed to hypoxia (5% O₂, 24 h) to simulate cardiac hypoxia and ischemic situation and then tirzepatide (100 nmol/L, 24 h). Molecular markers of cardiac remodeling and metabolism were tested.

**RESULTS** We found that the mortality of post-M1 mice decreased by 36.58% and M1-M2 and incidence of cardiac rupture largely diminished. Cardiac dysfunction of MI-tirzepatide group had significantly improved, accompanied by an increase in the left ventricular ejection fraction, fraction shortening, and a decrease in cardiac fibrosis and myocardial inflammation. Mechanistically, tirzepatide was associated with branched chain amino acid (BCAA) catabolism by attenuating BCAA catabolism, ultimately contributing toward the improvement of cardiac function.

**CONCLUSIONS** Taken together, these findings provide new insights into the previously unrecognized role of tirzepatide in cardiac protection via enhancing BCAA catabolism. Consequently, these findings may provide new therapeutic options for patients with heart failure.

**GW33-e0540**
The role of SGLT2 inhibitor dapagliflozin in renal protection in diabetic nephropathy use and mechanism research

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**BACKGROUND AND AIMS** Dapagliflozin is a new hypoglycemic drug, which not only has a low risk of hypoglycemia, but also has good cardiac-renal protection. Dapagliflozin can inhibit SGLT2, a sodium-glucose co-transporter, increasing urine glucose, reducing blood glucose, and achieving the purpose of blood glucose control. However, the protective effect and mechanism of dapagliflozin on diabetic nephropathy is still unclear.

**METHODS** db/db diabetic nephropathy animal model were used to investigate the effect of dapagliflozin on diabetic nephropathy. Eight-week-old diabetic mice were randomly divided into two groups: normal control group and drug-treated group, fed for 12 weeks, during which body weight and blood glucose were monitored regularly. After 12 weeks, the mice were sacrificed, and kidney tissue and serum were collected. The kidney tissue was isolated and observed at the serological and tissue levels, and the inflammatory response of diabetic mice was observed at the protein level. At the same time, AD293 cells were stimulated with hydrogen peroxide to simulate the inflammatory response in diabetic mice. Furthermore, overexpression or knockdown of SGLT2 detected the anti-inflammatory effect in AD293 with or without Dapagliflozin.

**RESULTS** Dapagliflozin increases the survival rate of diabetic mice, reduce the fasting blood glucose level of diabetic mice, alleviate the expansion of the mesangial matrix and fibrosis in the kidney tissue of diabetic mice, and improve the diabetic mice decreased renal function in db/db mice. Furthermore, dapagliflozin can reduce the inflammatory response in the kidney tissue of diabetic mice, and at the protein and tissue levels. It also can be observed that dapagliflozin can reduce the protein expression level of SGLT2. In vitro experiments, dapagliflozin can reduce the inflammatory response stimulated by hydrogen peroxide, but the expression level of SGLT2 increased. When the expression level of SGLT2 was inhibited, the protein expression level of p-P65 in the cells was also reduced when SGLT2 was over-expressed, the expression level of p-P65 in the cells also decreased rise.

**CONCLUSION** Dapagliflozin may reduce the expression of SGLT2 by reducing the inflammatory response. The reduced expression of SGLT2 also inhibits the production of some inflammatory responses, thus forming a good cycle and better exerting the kidney protection of Dapagliflozin effect.

**GW33-e0544**
Cardiac overexpression of PHD3 can alleviate the cardiac function impairment of chronic intermittent hypoxia in mice with cardiac pressure overload

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**OBJECTIVES** Obstructive sleep apnea (OSA) accelerates the development and progression of heart failure (HF). However, the underlying mechanism has not been elucidated, and effective treatments are also lacking. This study explored the chronic intermittent hypoxia (CIH) accelerates the occurrence and development of HF and identify new therapeutic directions to improve outcomes of HF.

**METHODS** Mice were modeled by transverse aortic constriction (TAC) surgery or/and CIH exposure. Tail vein injection injection of an adeno-associated virus 9 (AAV9) expressing prolyl hydroxylase 3 (PHD3) (AAV9-PHD3) for drug treatment. Echocardiography analysis, histopathology, western blotting, and Real-time PCR methods were performed to elucidate the mechanism.

**RESULTS** CIH exposure promotes long-term abnormal expression of hypoxia-inducible factor 1α (HIF-1α) in mice subjected to TAC, further inducing continuous upregulation of miR-29c expression. Together, HIF-1α and miR-29c inhibit the expression of serco/endoplasmic reticulum calcium ATPase 2a (SERCA2a) in the nucleus and cytoplasm in cardiomyocytes, Synergistically accelerate cardiomyocyte hypertrophy and cardiac dysfunction, Treatment with AAV9-PHD3 inhibited HIF-1α activation in the mouse heart while decreasing miR-29c expression, stabilizing the level of SERCA2a in the mouse heart, alleviates cardiac dysfunction and cardiomyocyte hypertrophy.

**CONCLUSIONS** CIH exposure in combination with TAC can cause further hypertrophy of mouse cardiomyocytes and promote cardiac dysfunction. Overexpression of PHD3 may be its potential therapeutic approach.

**GW33-e0557**
E3 ubiquitin-ligase Trim69 prevents D-galactose-induced cardiac aging in rats by suppressing oxidative stress and apoptosis

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**OBJECTIVES** Cardiac aging manifests as a progressive deterioration in cardiac structure and function, resulting in subsequent heart failure. The main
purpose of our study is to investigate whether the altered expression of Trim69 affects cardiac aging.

**METHODS** The aging model was constructed in SD rats by subcutaneous injection of D-gal (150 mg kg\(^{-1}\) d\(^{-1}\)) for 8 weeks. Echocardiography was used to evaluate the cardiac function. Transmission electron microscope was used to observe the ultrastructure of cardiomyocyte. SA-β-galactosidase staining was performed to assess cardiac aging. Western-blotting was applied to detect the expression of age-associated proteins (P35, P21), and Trim69. Reactive oxygen species (ROS) was evaluated through measuring 3-Nitrotyrosine by immunohistochemistry. Tunnel staining was used to measure apoptosis. Masson trichrome staining was used to assess cardiac fibrosis and WGA staining was used to assess cardiac hypertrophy.

**RESULTS** In present study, our results revealed that the expression of Trim69 was decreased while the expression of age-associated proteins (P35, P21), ROS level, and apoptosis activity was significantly increased in the heart tissue from aging rats induced by D-gal. Overexpression of Trim69 alleviates cardiac aging induced by D-gal. Meanwhile, Trim69 alleviates cardiac hypertrophy, fibrosis, and myocardial ultrastructural derangement. Echocardiography also indicated that the compromised cardiac function induced by D-gal was reversed in rats from Trim69-overexpression group. In addition, the reduced ROS level and apoptosis activity suggested that Trim69 might prevent cardiac aging through oxidative stress and apoptosis pathway.

**CONCLUSIONS** Trim69 might play a protective role on cardiac aging via the suppression of oxidative stress and apoptosis.

**GW33-e0561**

mir-3154 regulates phenotypic conversion of vascular smooth muscle cells by targeting Pax7

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**OBJECTIVES** Vascular smooth muscle cells transform from differentiated phenotype to synthetic phenotype can lead to many cardiovascular diseases, such as abdominal aortic aneurysm and vascular remodeling. Finding the regulatory molecules of smooth muscle cell phenotype transformation is crucial for the discovery of therapeutic targets for vascular injury. Currently, there are 5 literatures about mir-3154 searched on PubMed. As a prognostic biomarker of cervical cancer and leukemia, there are no literatures about the biological function of mir-3154 at present. This study is the first to find the regulatory role of mir-3154 in vascular smooth muscle cells. The purpose of this study was to explore the regulatory role of mir-3154 in phenotypic transformation of vascular smooth muscle cells.

**METHODS** Primary vascular smooth muscle cells were cultured and treated by angiotensin II (1 μmol/l) with mimic-NC or mir-3154 mimic transfection. After angiotensin II (1 μmol/l) stimulation, real-time quantitative PCR (RT-qPCR) detected a slight increase in mir-3154 expression. Cell proliferation was detected by EDU immunostaining. CXCR4 was used to detect cell proliferation activity. Cell migration was detected by Transwell Chamber analysis. The expression of PCNA, cyclinD1, 5-endo-dUTP, and the OD value of cells increased, and the number of migratory cells increased. However, this regulation is reversed by Pax7. MiR-3154 was identified as the upstream of Pax7 in abdominal aortic aneurysm mice model.

**RESULTS** Compared with the control group, the expression level of mir-3154 in mir-3154 mimic group increased (P<0.05), the positive proportion of EDU increased, the expression of PCNA, cyclinD1, 5-endo-dUTP, the OD value of cells increased, and the number of migratory cells increased. However, this regulation is reversed by Pax7. MiR-3154 was identified as the upstream of Pax7 by luciferase assay and investigated by gain-loss-of-function approaches.

**CONCLUSIONS** mir-3154 regulates phenotypic conversion of vascular smooth muscle cells through Pax7.

**GW33-e0562**

miR-193a-5p and its target genes CCND1, CCNE1 and CXCR4 modulate proliferation and migration of vascular smooth muscle cells in angiotensin II-induced the abdominal aortic aneurysm mice model

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**OBJECTIVES** AAA refers to the abdominal aortic aneurysm with a diameter greater than 3 cm and dilation of more than 50%, and its incidence is increasing year by year. Its treatment usually includes surgery and interventional vascular stents, but there is no effective drug treatment at present, so it is particularly necessary to find new therapeutic targets for abdominal aortic aneurysm. The purpose of this study is to explore the role and mechanism of miR-193a-5p in abdominal aortic aneurysm, and strive to provide a new target for the treatment of abdominal aortic aneurysm.

**METHODS** qRT-PCR were detected the expressions of mir-193a-5p in abdominal aortic aneurysm vascular tissue and AngII treated vascular smooth muscle cells. Western blot was used to detect the effects of miR-193a-5p on PCNA, CCND1, CCNE1, CCNE2, CXCR4, CCK-8 method, EdU staining method, flow cytometry, wound healing and Transwell method were used for detection effects of miR-193a-5p on proliferation and migration of vascular smooth muscle cells.

**RESULTS** In AAA patients, vascular tissue and AngII treated cells vascular smooth muscle cells, mir-193a-5p expression was significantly decreased, while CCND1, CCNE1, CXCR4 expression was significantly up-regulated. mir-193a-5p overexpression can inhibit the proliferation and migration of vascular smooth muscle cells.

**CONCLUSIONS** miR-193a-5p inhibits proliferation and migration of vascular smooth muscle cells by targeting CCND1, CCNE1 and CXCR4, thus providing an effective target for the treatment of AAA.

**GW33-e0563**

FGF21 deficiency promotes heart failure by impairing mitochondrial dynamics and inhibiting mitophagy

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**OBJECTIVES** Fibroblast growth factor 21 (FGF21) is a pleiotropic hormone, secreted mainly by the liver, considered as a major regulator of energy homeostasis. Cardiovascular disease is a serious threat to human health and life, and has become the number one killer of human health. Common cardiovascular diseases include hypertension, coronary heart disease, etc. An important cause for heart failure is cardiac remodeling. Therefore, slowing or reversing cardiac remodeling in patients is the focus of clinical treatment of cardiovascular disease. Studies have found that mitochondrial dysfunction may lead to myocardial hypertrophy, causing heart failure. Under normal circumstances, the adult heart is mainly powered by fatty acid oxidation. Studies have found that before the occurrence of left ventricular hypertrophy and heart failure, the increase of pressure load will lead to changes in the energy metabolism of myocardial mitochondria, and the myocardial energy supply from fatty acids is converted into glucose energy. This alteration in energy metabolism plays an important role in protecting the heart from irreversible damage during the early stages of cardiac remodeling. Recent research revealed that FGF21 could play an important role in cardiac pathological remodeling effects and preventing cardiomyopathy, but the underlying mechanism remained largely unknown. The aim of this study was to clarify the mechanism of FGF21 cardiac protective effects.

**METHODS** We assessed plasma FGF21 levels in patients with severe symptomatic heart failure (ejection fraction <55%, n=18) and control subjects (n=22) by ELISA analysis. Furthermore, we engineered FGF21 knock out mice and used the high-fat diet to produce a cardiac dysfunction model. The effects of FGF21 and its downstream mediators were subsequently elucidated using qRT-PCR, western blot, RT-QPCR, and mitochondrial morphological, functional and biochemical analysis.

**RESULTS** The plasma FGF21 levels were lower in patients with severe symptomatic heart failure compared with the control subjects (331.4±188.8 vs 496.2±274.7 pg/ml, P<0.05). FGF21 knock out mice resulted in cardiac dysfunction accompanied by a decline in global longitudinal strain and ejection fraction which was independently of obesity. Mitochondrial quality, quantity and functions were abnormal accompanied with the decreased levels of OA1 (optic atrophy-1)/MFN2 (mitofusin-2) in FGF21−/− mice. In contrast to FGF21 knockdown, the overexpression of FGF21 can alleviate high fat diet-induced cardiac dysfunction. In vitro study FGF21 siRNA can inhibit the cardiomyocytes mitophagy and deteriorate mitochondrial dynamics, functions impairments induced by PA1. Both recombinant FGF21 and adeno virus mediated FGF21 expression can alleviate PA induced mitochondrial impairment by restoring mitochondrial dynamics.

**CONCLUSIONS** FGF21 is essential for maintaining mitochondrial dynamics and functions in cardiomyocytes. FGF21, as an important target in regulating cardiomyocytes mitophagy under oxidative stress, will provide new therapeutic options for heart failure patients.

**GW33-e0564**

AMPKβ2 regulated macrophage migration after myocardial infarction via YY1/CXCL16/CXCR6 axis

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**OBJECTIVES** Recent years myocardial infarction (MI) has got developed therapeutic strategy, however, cardiac remodeling and dysfunction post-myocardial infarction remain common and remain keep high mortality. In the early stage...
after MI, Th1 lymphocyte secretes amounts of IFN-γ, which stimulates macrophage activation. Therefore inhibiting excessive inflammatory reaction may repress cardiac necrosis and benefit cardiac dysfunction post-MI. However, how to regulate and target macrophage migration to restrain cardiac inflammation is still needed to be elucidated.

**METHODS** Firstly, AMPKγ2 level in plasma of myocardial infarction patients was tested by Elisa assays. Experimental LAD surgery was conducted to establish myocardial infarction model in vivo. IFN-γ was employed to simulate inflammatory conditions in macrophage. To identify the mechanism by which AMPKγ2 deletion promoted migration, we performed transcriptome sequencing (RNA-seq) based on silencing AMPKγ2 and corresponding control. LY294002 specific knockout of AMPKγ2 mice were employed to test the role of AMPKγ2 in macrophage in vivo. Adeno-associated virus (AAV) carrying CMV and F4/80 promoter injection was performed to simulate AMPKγ2 specifically overexpression of macrophage in vivo.

**RESULTS** Elisa assays were performed to find AMPKγ2 was declined in myocardial infarction patients. Besides, AMPKγ2 was downregulated by inflammatory stimuli such as IFN-γ, TNFα and CoCl2. AMPKγ2 was declined as well as in bone marrow derived macrophage (BMDM) extracted from mice subjected to MI. AMPKγ2 repressed macrophage migration and inflammatory factor expression in vivo and in vitro. Besides, CXCL16/CXCR6 axis was the key contributor for macrophage migration involved in MI, which was alleviated by AMPKγ2 administration via transcriptional regulation. CXCL16 secretion in plasma of mice subjected to MI reached two folds of sham group at 7 days post-MI. AMPKγ2 downregulated by global knockdown of AMPKγ2 using AAV carrying CMV promoter. Meanwhile, AAV-CMV-AMPKγ2 group repressed CXCL16 expression in BMDM when MI-7 D. AMPKγ2-KO showed increased CXCL16 expression in BMDM under physiological condition. AMPKγ2-RO aggravated MI-induced inflammation activation, showed as elevated inflammation cytokines CXCL16 and CXCR6 expression in BMDM derived from mice post-MI. AMPKγ2 repressed CXCL16/CXCR6 axis via restraining YY1 expression to rescue cardiac dysfunction after myocardial infarction. IFN-γ induced HOXA5 downregulated, which repressed AMPKγ2 transcriptional activity. Overexpression of HOXA5 repressed YY1-mediated YY1/CXCL16/CXCR6 expression and following macrophage migration, instead. Finally, AMPKγ2 mediated the regulation of migration and inflammation in macrophage involved in MI via the YY1/CXCL16/CXCR6 pathway was dependent on AMPKγ2 activity. Our current data supported AMPKγ2 maintain the stability of AMPK complex composed of α1-β1-γ2 subunits in macrophage.

**CONCLUSIONS** In our current study, IFN-γ induced HOXA5-AMPKγ2-YY1-CXCL16-CXCR6 pathway played an important role in cardiac dysfunction following macrophage myocardial infarction, AMPKγ2 can be developed as a potential therapeutic target to ameliorate cardiac remodeling post-myocardial infarction.

**GW33-e0565**

**Endogenous S100A12 transcriptional activation of annexin A5-RAGE augments myocardial infarction injury through excessive neutrophil extracellular trap formation**

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**OBJECTIVES** Members of the S100 protein family have been reported to function as endogenous danger signals (alarmins) playing an active role in tissue inflammation and repair when released from myoid cells. However, the role of S100A12 in the etiology of Acute Myocardial Infarction (AMI) is not well understood. Neutrophil extracellular traps (NETs) are implicated in the pathogenesis of AMI and in the externalization of some S100 family members. Here, we investigated the effect of S100A12 on neutrophils’ function and myocardial injury after AMI.

**METHODS** Since S100A12 is a human specific molecule and not expressed in mice, we constructed transgenic (TG) mice expressing S100A12 in myoid cells. Myocardial infarction was induced by ligation of the left anterior descending coronary artery (LAD). Cardiac function was assessed by echocardiography. Primary neutrophils from TG and WT mice bone marrow were isolated and cultured. In vitro experiments we overexpressing plasmid to increase expression of S100A12 and small interfering RNA (siRNA) to inhibit the expression of S100A12, Western blotting, quantitative RT-PCR, immunofluorescence (IF), immune-histochemistry (IHC) and Masson’s trichrome staining were conducted. Dissection of mice aortas for biological and functional determination. Western blot, immunofluorescence, immunohistochemistry, and quantitative polymerase chain reaction were used to assess protein and gene expression. Vascular smooth muscle cells were isolated and CREG1 was overexpressed by adenovirus.

**RESULTS** The expression of CREG1 increased with Ang II stimulation in a time dependent manner in vivo and in vitro. Compared with AAA model group, CREG1 overexpressed mice significantly attenuated Ang II-induced AAA incidence, aortic dilation and severity, accompanied by preserved α-SMA expression and reduced elastin degradation, MMP2 activity, deposition of collagen and blood pressure. The CREG1 recombiant protein group had consistant results. In VSMC, Ang II leads to a transition from contractile to synthetic state, which can be reversed by overexpression of CREG1. Overexpression of CREG1 significantly increased the expression of synthetic markers SM22 and α-SMA, while decreased the expression of MMP9 and MMP2.

**CONCLUSIONS** Our results indicate that in response to Ang II stimulation, CREG1 maintains aortic VSMC phenotype, ECM homeostasis, structural integrity and reduces AAA formation. Thus, targeting CREG1 provides a potential therapeutic strategy for AAA.

**GW33-e0566**

**CREG1 attenuates abdominal aortic aneurysm formation through modulating vascular smooth muscle cell phenotype**

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**OBJECTIVES** Vascular smooth muscle cell (VSMC) phenotypic switch from a contractile to a synthetic phenotype plays a significant role in abdominal aortic aneurysm (AAA). CREG1 (Cellular Repressor Of E1A-Stimulated Genes 1) is a glycoprotein that antagonizes transcriptional activation of e1a and may contribute to AAA. In the transcriptional control of cell differentiation, it has been reported that CREG1 promotes smooth muscle cell contractile phenotype, however, the role of CREG1 in angiogenesis II (Ang II)-induced AAA remains unclear. The purpose of this article is to clarify the role of CREG1 in AAA.

**METHODS** To investigate the function of CREG1 in AAA formation, mice deficient in Apeo (Apeo−/−) or both CREG1 systemic overexpression and Apeo−/− were subjected to an angioteins II infusion model of AAA formation. To further clarify the therapeutic effect of CREG1, Apeo−/− mice were injected with the CREG1 recombinant protein subcutaneously using micropumps. Aortas were harvested at different time points and the diameter of the aortas were measured. Dissection of mice aortas for biological and functional determination. Masson staining was used to assess collagen deposition. Verhoff’s Van Gieson (EVG) staining was used to assess elastic fiber breakage. Western blot, immuno-fluorescence, immunohistochemistry, and quantitative polymerase chain reaction were used to assess protein and gene expression. Vascular smooth muscle cells were isolated and CREG1 was overexpressed by adenovirus.

**RESULTS** The expression of CREG1 decreased with Ang II stimulation in a time dependent manner in vivo and in vitro. Compared with AAA model group, CREG1 overexpressed mice significantly attenuated Ang II-induced AAA incidence, aortic dilation and severity, accompanied by preserved α-SMA expression and reduced elastin degradation, MMP2 activity, deposition of collagen and blood pressure. The CREG1 recombiant protein group had consistant results. In VSMC, Ang II leads to a transition from contractile to synthetic state, which can be reversed by overexpression of CREG1. Overexpression of CREG1 significantly increased the expression of synthetic markers SM22 and α-SMA, while decreased the expression of MMP9 and MMP2.

**CONCLUSIONS** Our results indicate that in response to Ang II stimulation, CREG1 maintains aortic VSMC phenotype, ECM homeostasis, structural integrity and reduces AAA formation. Thus, targeting CREG1 provides a potential therapeutic strategy for AAA.
RESULTS There were 24 female New Zealand rabbits, including 10 for acute experiment and 14 for chronic experiment. Epidural optical mapping was performed in both paced and normal arteries in two groups. Action potential duration (APD80) was determined during right atrial and ventricular pacing. AT-APD correlation and ventricular stability was tested before and after IKAS blockade.

CONCLUSIONS Long-term ventricular pacing leads to an increase in the intracellular Ca2+ accumulation in the paced far-right cardiomyocytes, which activates IKAS, shortens APD, and maintains uniform ventricular repolarization. APD in the paced heart has regional adaptability, IKAS participates in the repolarization reserve of APD regional distribution, and blocking IKAS increases the susceptibility of ventricular arrhythmia.

GW33-e0572 miR-22 regulates AngII-induced hypertension
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OBJECTIVES Hypertension and its complications are the primary risk factor of cardiovascular diseases. Although extensive and sustained efforts have been made to understand the pathogenesis of essential hypertension, its potential cellular and molecular mechanisms are still elusive, which need to be further clarified. Hypertension is associated with vascular changes, and the disturbance of vascular smooth muscle cell signal pathway and the change of its function play a basic and core role in the occurrence and development of hypertension. MicroRNAs (miRNAs) have been proved to regulate the level of key genes controlling contraction, remodeling, and phenotypic regulation in vascular smooth muscle cells, and plays an important role in controlling the development and function of vascular smooth muscle cells, including proliferation, differentiation, and remodeling. Among the miRNAs that can regulate the vascular smooth muscle function, which can also play an important role in systemic hypertension is not clear. Therefore, to identify miRNAs that can directly regulate blood pressure is a problem that needs to be solved in the research field. The aim of our study was to identify miRNA that directly regulates vascular smooth muscle function and blood pressure.

METHODS A mouse model of hypertension was established by subcutaneously implanting a micro-osmotic pump into the back of the mouse and continuously pumping AngII. We use the isolated vascular ring experiment to evaluate the changes of vascular ring tension and study the vasomotor function. We isolated vascular smooth muscle cells from mouse aorta and cultured them in vitro. We used cr/lox technique to construct smooth muscle specific miR-22 overexpression mice. We used luciferase reporter gene experiment to verify the target gene of miR-22. We used miR-22 mimic to transflect vascular smooth muscle cells to overexpress miR-22 in the cells.

RESULTS Through the screening and comparison of online databases, we found that miR-22 may play an important role in the regulation of hypertension. We found that the expression of miR-22 in aorta of AngII-induced hypertensive mice was down regulated. We used mice with smooth muscle specific miR-22 overexpression and wild-type mice to construct AngII-induced hypertensive mice and found that overexpression of miR-22 in smooth muscle may elevate hypertension. In isolated vascular rings, we found that overexpression of miR-22 in smooth muscle could promote vasoconstriction. After screening, we believe that PTGS1 and PLXG6, two important enzymes in arachidonic acid metabolic pathway, may be potential target genes of miR-22 to regulate hypertension. Finally, luciferase reporter gene experiment was used to verify the target genes.

CONCLUSIONS miR-22 plays a regulatory role in AngII induced hypertension by regulating the expression of arachidonic acid metabolism related genes PLAXG6 and PTGS1.

GW33-e0578 FABP5 deficiency aggravates pathological cardiac remodeling and dysfunction by impairing mitochondrial function
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OBJECTIVES Heart failure (HF) is one of the leading causes of death worldwide. Although its therapeutic strategies and drugs have made significant progress, its current therapeutic methods are still limited, so it is necessary to continuously study the pathogenesis of HF. Structural and functional impairment of mitochondria in myocardiocytes plays a basic and core role in the occurrence and development of pathological cardiac remodeling and homeostasis of energy metabolism is the basis of normal heart function. Energy metabolism disorders are associated with cardiac dysfunction. Fatty acids (FA) represent the main energy substrate of the heart. The water solubility of FA is low, and their transport into specific cells and organelles require the help of fatty acid-binding proteins (FABP). Fatty acid-binding protein 5 (FABP5) is an important member of the FABP family. The role of FABP5 in pathological cardiac remodeling and dysfunction remains unknown. We aimed to investigate the role of FABP5 in pathological cardiac remodeling and HF.

METHODS We performed TAC to establish the pressure-overload pathological cardiac remodeling and HF model in mice. Heart tissues were prepared for single-cell sequencing and the transcriptome data of single cells were obtained by 10× single-cell sequencer and analyzed by R Studio. CRISPR/cas9 technology was used to generate FABP5-deficient mice. The small animal ultrasound imaging system was used to evaluate cardiac function. Histopathological examination, transmission electron microscopy, and ATP content assay were used to further investigate the role of FABP5 in pathological cardiac remodeling and HF. We used small interfering RNA (siRNA) to downregulate FABP5 mRNA expression in cardiac fibroblasts (CFs) in vitro. Dihydroethidium (DHE) staining was performed to detect oxidative stress in CFs. The oxygen consumption rate (OCR) of adherent living cells was measured by Seahorse XF24 extracellular flux analyzer to evaluate the mitochondrial respiratory function in vitro.

RESULTS FABP5 expression was increased in pressure-overloaded hearts and mainly expressed in endothelial and cardiac fibroblasts (CFs). FABP5 deficiency aggravated pressure-overload-induced cardiac dysfunction, cardiac hypertrophy and fibrosis. FABP5 deficiency aggravated structural and functional damage of mitochondria in myocardial and cardiac fibroblasts after TAC and TGF-β treatment.

CONCLUSIONS FABP5 deficiency aggravates pressure-overload-induced pathological cardiac remodeling and dysfunction. Mechanically, FABP5 deficiency mediates structural and functional impairment of mitochondria in myocardial and cardiac fibroblasts.
CONCLUSIONS Disturbed flow-induced atherosclerotic plaques at the lateral walls of bifurcations. PLXND1 promotes in M1 macrophage at the bifurcation lesions and its level increased with the progression of atherosclerosis. PLXND1 mediates disturbed flow-induced M1 macrophage polarization. Thus, PLXND1 may be a potential target for monitoring and treatment for bifurcation lesions.

GW33-e0602 Natriuretic peptide receptor C protects vascular endothelial cells and macrophage against high glucose-induced injury by inhibiting the pyroptosis pathway

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OBJECTIVES The aim was to investigate the effect of high glucose on human umbilical vein endothelial cells (HUVECs) and macrophage, and to explore whether NPR-C signaling could alleviate HUVECs and macrophages injury induced by high glucose via regulating pyrolysis pathway.

METHODS HUVECs and macrophages were treated with high glucose, together with c-ANF (NPR-C agonist). The cell viability were detected by cell counting kit-8 (CCK-8). The toxicity of high glucose was subjected with LDH assay and Hoechst/Propidium Iodide (PI) staining. The scratch assay was utilized to detect the cell migration ability. RT-PCR and western blot were carried out to compare the levels of gene expressions and protein synthesis involved in pyrolysis.

RESULTS 1. Result of HUVECs. (1) CCK-8 indicate that cell viability decrease in a concentrations-dependant manner as glucose concentrations rise when HUVECs treated by high-glucose with various concentrations (P<0.05). In conditions of using 33 mM high-glucose, c-ANF could inhibit the decline viability of HUVEC cell induced by high-glucose in a concentrations-dependant manner when using various concentrations of c-ANF to activate NPR-C. (2) LDH detection: Compared with the control group, the secretion of lactate dehydrogenase in the cell supernatant was increased in the high glucose group, showing high-glucose toxicity to cells, and this could be alleviated by c-ANF with a lower level of the lactate dehydrogenase in the c-ANF+ high glucose group (P<0.05). (3) Hoechst/PI staining: Compared with the control group, the PI stained cells increased in the high glucose group, while compared with the high glucose group, the PI stained cells in the c-ANF+ high glucose group decreased (P<0.01). (4) RT-PCR: Compared with the control group, the mRNA expressions levels involved in pyrolysis were augmented by high glucose (P<0.05), and c-ANF could reduce the increase by high glucose (P<0.05). (5) Western blot: Compared with the control group, the protein synthesis levels involved in pyrolysis were augmented by high glucose, and c-ANF could reduce the increase by high glucose. It needs to be further verified. (6) Scratch test: After scratch injury, the migratory distance of HUVECs in the high glucose group decreased compared with the control group, while in the c-ANF+ high glucose group, the migratory distance increased compared with the high glucose group.

2. Result of macrophages. (1) CCK-8 indicate that micro phage viability will be inhibited by 33 mM high glucose (P<0.05), the cell viability of group high glucose and lipopolysaccharide (P<0.05). c-ANF take a certain effects to the survival of micro phage treated with high-glucose or lipopolysaccharide (P<0.05), but without obvious concentration dependant manner. (2) RT-PCR: Compared with the control group, the mRNA expressions levels involved in pyrolysis were augmented by high glucose, and c-ANF could reduce the increase by high glucose. This needs to be further verified.

CONCLUSIONS High glucose could cause the damage of HUVECs and macrophages. NPR-C might protect HUVECs and macrophages against high glucose-induced injury by inhibiting the pyroptosis pathway.

GW33-e0605 Pentamethylquercetin protects against angiotensin II-induced abdominal aortic aneurysm formation in mice

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OBJECTIVES Pentamethylquercetin (PMQ) is a kind of natural polymethyl flavonoids with many biological activities, such as anti-oxidation and anti-inflammatory. The purpose of this study was to investigate the role and mechanism of PMQ in the development of abdominal aortic aneurysm (AAA).

METHODS AAA model was established by continuous infusion of angiotensin II (Ang II) in ApoE−/− mice for 4 weeks. PMQ (5 mg/kg/day or 12.5 mg/kg/day) was intraperitoneally administered to mice for 5 days before administration of Ang II and continued for 4 weeks. Experimental animals were divided into four groups: control group, AAA group, PMQ low-dose group, and PMQ high-dose group. Blood pressure and body weight were measured. Real-time PCR, western blot and immunohistochemical staining was used to measure mRNA and protein levels of matrix metalloproteinases (MMP2 and MMP9), apoptosis-related proteins (Bax, Bcl-2, and active caspase-3), oxidative stress associated protein (SOD and CAT), HE, Masson staining and Verhoeff staining were used to examine the morphology of abdominal aorta. Mouse vascular smooth muscle cells (VSMCs) were used to clarify the role of PMQ in cell apoptosis and oxidative stress. Tunel staining was used to evaluate the apoptosis of vascular smooth muscle cells in vitro and in vivo. Proteomic analysis was used to screen the difference proteins between AAA group and PMQ treatment group. Real-time PCR and western blot was used to measure mRNA and protein levels of Gsk-3β and P-Gsk-3β in vitro and in vivo.

RESULTS We found that administration of PMQ dose-dependently reduced the incidence of Ang II-induced AAA, aneurysm diameter enlargement, elastin degradation, matrix metalloproteinase production, and the apoptosis of VSMCs. The oxidative stress injury was improved in PMQ-treated mice. In Ang II-stimulated VSMCs, PMQ dose-dependently reduced the expression of Gsk-3β and p-Gsk-3β, improved oxidative stress injury, Gsk-3β was found to be the most significant difference protein between the AAA group and the PMQ treatment group using by proteomics analysis. PMQ could increase the phosphorylation of Gsk-3β. The therapeutic effect of PMQ was disappeared after the application of Gsk-3β phosphorylation inhibitor.

CONCLUSIONS In our study, PMQ alleviates Ang II-induced AAA by enhancing antioxidant capacity and reducing the apoptosis of VSMCs, through regulating the phosphorylation of Gsk-3β, PMQ may be a potential treatment agent for AAA.

GW33-e0603 CREG1 attenuates doxorubicin-induced cardiotoxicity via inhibiting the ferroptosis of cardiomyocytes

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OBJECTIVES Cardiovascular diseases and cancers are two important causes of human death. Doxorubicin (DOX) is currently one of the most commonly used broad-spectrum anti-tumor drugs, it is widely used in the treatment of patients with leukemia, breast cancer and ovarian cancer. However, some cancer patients may experience obvious cardiotoxicity after the use of DOX. Cellular repressor of E1A-stimulated genes (CREG1) is an important cardioprotective factor, which plays an important role in maintaining cardiomyocyte differentiation and homeostasis regulation. However, the roles and mechanisms of CREG1 in DOX-induced cardiotoxicity have not been reported.

METHODS In vivo, the intraperitoneal injection of DOX was used to establish a mouse DOX-induced cardiotoxicity model, the mRNA and protein expression of CREG1 in the DOX-treated myocardium was examined using real-time PCR and western blot. To clarify the role of CREG1 in the development of DOX-induced cardiotoxicity, CREG1 transgenic mice, cardiac-specific CREG knock-out mice and its littermate controls were used to establish DOX-induced cardiotoxicity model, HE staining, Masson staining, WGA staining and western blot were applied to examine fibrosis, myocardial hypertrophy and ferroptosis of myocardium. In vitro, neonatal mouse cardiomyocytes (NMMCs) were cultured and stimulated with DOX, CREG1 overexpression adenovirus and small interfering RNA was used to examine the role of CREG1 on the ferroptosis of NMMCs.

RESULTS In vivo, the mRNA and protein expression of CREG1 were significantly reduced in DOX-treated myocardium. CREG1 transgenic mice significantly alleviated the myocardial damage induced by DOX, and CREG1 deficiency in heart aggravated the DOX-induced cardiotoxicity. In vitro, the mRNA and protein expression of CREG1 was also obviously reduced in DOX-treated NMMCs. Under DOX stimulation, CREG1 overexpression inhibited the ferroptosis of cardiomyocytes, and CREG1 knockdown aggravated the ferroptosis of cardiomyocyte. Mechanically, CREG1 inhibited the mRNA and protein expression of pyruvate dehydrogenase kinase 4 (PDK4). The effect of CREG1 overexpression on ferroptosis of cardiomyocytes was reversed by PDK4 overexpression.

CONCLUSIONS CREG1 alleviated DOX-induced cardiotoxicity by inhibiting ferroptosis of cardiomyocytes. Our findings might help clarify new roles of CREG1 in the development of DOX-induced cardiotoxicity.
GW33-e0607
UBC9 alleviates diabetic cardiomyopathy by inhibiting oxidative stress and mitochondrial damage in cardiomyocytes
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OBJECTIVES Oxidative stress injury is one of the important pathogenic factors of diabetic cardiomyopathy. Ubiquitin conjugating enzyme E2 I (UBC9) is the enzyme that transfers ubiquitin and plays a key role in oxidative stress. However, the role of UBC9 in the development of diabetic cardiomyopathy is poorly understood. The aim of this study is to clarify the role and mechanism of UBC9 in the development of diabetic cardiomyopathy.

METHODS Male C57BL/6J mice were injected with UBC9 overexpressed adenovirus and control virus (AAV-GFP) by tail vein injection for 21 days. Mouse diabetic cardiomyopathy model was established by high fat diet (HFD) and low-dose streptozotocin injection. Body weight, fasting glucose, glucose tolerance, insulin tolerance, cardiac function of were measured. Real-time PCR, western blot and immunohistochemical staining was used to measure mRNA and protein levels of UBC9, oxidative stress associated proteins (SirT3, SOD2 and NOX4) and mitochondrial autophagy related proteins (PINK1, PARKIN, LC3B and P62). H&E, WGA-staining, Masson staining were used to detect myocardial hypertrophy and fibrosis. In vivo, cultured cardiomyocytes were stimulated with palmitic acid (PA). UBC9-overexpressed adenovirus or small interfering RNA was used to examine the effect and mechanism of UBC9 on the oxidative stress and mitochondrial function of cardiomyocytes using Real-time PCR, western blot, DHE staining.

RESULTS In vivo, the mRNA and protein of UBC9 was significantly decreased in the myocardium of diabetic cardiomyopathy. UBC9 overexpression could improve cardiac dysfunction, decrease myocardial fibrosis and hypertrophy, and inhibit oxidative stress injury and mitochondrial damage. In vitro, PA obviously inhibited the mRNA and protein expression of UBC9, accompanied by mitochondrial dysfunction and oxidative stress damage. UBC9 overexpression improved mitochondrial function and oxidative stress of cardiomyocytes induced by PA stimulation. In contrast, UBC9 knockdown aggravated mitochondrial dysfunction and oxidative stress damage of cardiomyocytes. Moreover, SirT3 was a downstream of UBC9, accompanied by mitochondrial dysfunction and oxidative stress. In vitro, PA obviously inhibited the mRNA and protein expression of UBC9, accompanied by mitochondrial dysfunction and oxidative stress damage. UBC9 overexpression improved mitochondrial function and oxidative stress of cardiomyocytes induced by PA stimulation. In contrast, UBC9 knockdown aggravated mitochondrial dysfunction and oxidative stress damage of cardiomyocytes. Moreover, SirT3 was a downstream of UBC9, accompanied by mitochondrial dysfunction and oxidative stress damage. UBC9 overexpression improved mitochondrial function and oxidative stress of cardiomyocytes induced by PA stimulation. In contrast, UBC9 knockdown aggravated mitochondrial dysfunction and oxidative stress damage of cardiomyocytes. Moreover, SirT3 was a downstream of UBC9, accompanied by mitochondrial dysfunction and oxidative stress damage.

CONCLUSIONS In our study, UBC9 alleviates the development of diabetic cardiomyopathy by inhibiting oxidative stress and improving mitochondrial function in cardiomyocytes. This study provides new perspectives for the use of UBC9 as a therapeutic target for diabetic cardiomyopathy.

GW33-e0609
CREG inhibits vascular calcification by regulating FHL2 expression
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OBJECTIVES Vascular calcification (VC) is a common pathological feature of atherosclerosis, chronic kidney disease, vascular injury and aging. VC is characterized by different mineral deposits accumulating in blood vessels and valves. Cellular repressor of E1A-stimulated genes (CREG) is a small molecule secreted glycoprotein and is consisted by 220 amino acids. Studies have shown that CREG is involved in regulating cell growth and differentiation. The aim of this study is to clarify the role of CREG participates in the development of VC.

METHODS Male C57BL/6J mice were injected with CREG overexpressing adenovirus or small interfering RNA was used to examine the effect of CREG on VC. Primary vascular smooth muscle cells (VSMCs) were isolated and cultured, and western blotting and Alizarin red staining were used to assess the severity of VC. In vitro, mouse primary vascular smooth muscle cells (VSMCs) were isolated and cultured, and western blotting and Alizarin red staining were used to assess the severity of VC. In vitro, mouse primary vascular smooth muscle cells (VSMCs) were isolated and cultured, and western blotting and Alizarin red staining were used to assess the severity of VC. In vitro, mouse primary vascular smooth muscle cells (VSMCs) were isolated and cultured, and western blotting and Alizarin red staining were used to assess the severity of VC. In vitro, mouse primary vascular smooth muscle cells (VSMCs) were isolated and cultured, and western blotting and Alizarin red staining were used to assess the severity of VC. In vitro, mouse primary vascular smooth muscle cells (VSMCs) were isolated and cultured, and western blotting and Alizarin red staining were used to assess the severity of VC.

RESULTS In vivo, the mRNA and protein levels of CREG were significantly decreased in the aortas of ST-segment elevated myocardial infarction (STEMI) patients compared with the control group (P=0.001). The expression levels of IDO, kynurenine, kynurenine 3-monooxygenase (KMO) and 3-hydroxykynurenine were increased in the STEMI group (P<0.05). The serum KTR of STEMI patients was significantly higher than that of the control group (12.8±5.4 vs 27.0±12.1), and the difference was statistically significant (P<0.000). The incidence of MACCE in 280 patients with STEMI was 6.4% (17/266) after one-year follow-up. The KTR level of STEMI patients with MACCE events was significantly higher than that of those without MACCE events, the difference was statistically significant (40.6±17.0 vs 25.7±11.1, P=0.002).

CONCLUSIONS A total of 15 different metabolic markers were identified in the serum of STEMI patients compared with the control group (P<0.05). The serum tryptophan level was significantly decreased in STEMI patients, while the level of IDO, KTR and kynurenine (kynurenine, kynurenic acid, 3-hydroxykynurenine, 3-hydroxyanthranilic acid and xanthene acid) were significantly increased in STEMI patients. The higher the expression level of serum KTR, the higher the risk of MACCE in STEMI patients within one year.

GW33-e0610
Untargeted metabolomics identifies tryptophan/kynurenine metabolic pathway as a reliable plasma metabolic markers in ST-segment elevated myocardial infarction
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OBJECTIVES The tryptophan/kynurenine pathway plays a key role in the increase of cardiovascular disease incidence by regulating inflammation, oxidative stress and immune activation. We evaluated the predictive value of Kynurenine/Tryptophan (KTR) for the major adverse cardiac and cerebral events (MACCE) in STEMI patients.

METHODS In order to clarify the characteristics of plasma metabolism in the STEMI patients, plasma metabolite profiling of STEMI and healthy controls was analysed using nuclear magnetic resonance (1H-NMR). Ultraperformance liquid chromatography/electrospray ionization quadruple time-of-flight mass spectrometry (UPLC/Q-TOF) was used to analyze the concentration of metabolites of tryptophan/kynurenine pathway among the 504 participants. Major adverse cardiac and cerebral events were assessed in the STEMI patients followed for 1 year.

RESULTS 1H-NMR revealed 15 differential kinds of metabolites markers that were related to the plasma of STEMI patients compared with the control subjects. Targeted metabolomics results showed that serum concentration of tryptophan in STEMI group were significantly lower than those in the control group (P=0.001); the expression levels of IDO, kynurenine, kynurenic acid, 3-hydroxykynurenine were increased in the STEMI group (P<0.05). The serum KTR of STEMI patients was significantly higher than that of the control group (12.8±5.4 vs 27.0±12.1), and the difference was statistically significant (P<0.000). The incidence of MACCE in 280 patients with STEMI was 6.4% (17/266) after one-year follow-up. The KTR level of STEMI patients with MACCE events was significantly higher than that of those without MACCE events, the difference was statistically significant (40.6±17.0 vs 25.7±11.1, P=0.002).

CONCLUSIONS Untargeted metabolomics approach identifies tryptophan/kynurenine metabolic pathway as a reliable plasma metabolic markers in ST-segment elevated myocardial infarction. This study could provide a promising target for VC therapy.

GW33-e0612
S100A12 aggravates abdominal aortic aneurysm by promoting MMP9 expression in macrophages via activating JAK2/STAT3 signaling pathway
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OBJECTIVES Abdominal aortic aneurysm (AAA) is recognized as a chronic vascular inflammatory disease with no effective drug therapy. So, exploring novel target to prevent AAA is crucial. S100A12 is a calcium-, zinc- and copper-binding protein which plays a significant role in the regulation of inflammatory processes and immune response. However, whether S100A12 participates in the pathological process of AAA has not been identified yet. In this study, we identified the effect of S100A12 on AAA formation and its underlying mechanisms.

METHODS The enzyme-linked immunosorbent assay was used to detect the level of S100A12 in AAA and normal control group. For in vivo experiment, we used aortic sections from S100A12 transgenic mice (S100A12-Tg) to overexpress S100A12 and the S100A12-Tg mice received angiotensin II for 4 weeks, together with its control group. PCR, Western blotting and gelatin zymography were used to access the expression and the activity of MMP9 in the aortas of each group. In vitro, to clarify the specific signaling pathway, RAW264.7 cells were stimulated by exogenous S100A12 protein and RNA interference, respectively.
RESULTS The level of serum S100A12 in AAA patients was significantly higher than that in normal group. Interestingly, the incidence of AAA in S100A12-Tg mice was higher under AngII stimulation. Besides, loss of medial smooth muscle cells (SMCs) was severe and more elastin fragmentation, vascular inflammation and degradation of the extracellular matrix was observed in S100A12-Tg mice stimulated with Ang II. In addition, matrix metalloproteinase 9 (MMP9) expression greatly increased in the abdominal aortic tissue and spleen tissue in S100A12-Tg group. Similarly, the expression and activity of MMP9 increased in RAW264.7 cells after they were treated with S100A12. Moreover, exogenous S100A12 protein could activate JAK2 and increase the downstream STAT3 expression. Furthermore, overexpression of STAT3 increased MMP9 expression while inhibition of STATS elicited the opposite change.

CONCLUSIONS S100A12-aggravated AAA formation under AngII stimulation while inhibition of STATS elicited the opposite change. These data suggested that S100A12/JAK2/STAT3 signaling pathway could be a potential target to treat AAA.

GW33-e0616 Ginsenoside-Rg1 ameliorates heart failure by activating NR2-mediated anti-ferroptosis
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OBJECTIVES Evidence suggests that ferroptosis plays a key role in the occurrence and development of heart failure, while the Nrf2 signaling pathway regulates oxidative stress and lipid peroxidation, but its effects with ginsenoside-Rg1 on heart failure and ferroptosis remain unclear. In the present study, we aimed to determine the functional role of ginsenoside-Rg1 in heart failure and to elucidate its potential mechanisms of action.

METHODS We established an in vivo model with C57BL/6 mice using transverse aortic constriction (TAC) and stimulated neonatal mouse cardiomyocytes with phenylephrine (PE) to establish an in vitro model to determine the effect of ginsenoside-Rg1 on heart failure and to assess the anti-ferroptosis death effect of ginsenoside-Rg1.

RESULTS In this study, we observed that ginsenoside-Rg1 treatment significantly attenuated heart failure in TAC mice, including changes in cardiac ultrasound, morphologic changes in the heart and elevated expression of heart failure markers (ANP, BNP and β-MHC). Ginsenoside Rg1 also inhibited ferroptosis in the myocardium of TAC mice in vivo, including changes in mitochondrial morphology, iron accumulation, and expression associated with lipid peroxidation (increased ROS, elevated MDA levels, SOD and GSH depletion, as well as decreased GPX4 expression). Meanwhile, Nrf2 KO mice were more susceptible to ferroptosis after TAC-induced heart failure than control mice. The protective effect of ginsenoside-Rg1 against heart failure and ferroptosis was largely abolished in Nrf2 KO mice. Experiments in vitro showed that ginsenoside-Rg1 treatment remarkably ameliorated PE-induced hypertonphy in primary mouse cardiomyocytes and activated Nrf2 to inhibit ferroptosis. In addition, we down-regulated the expression level of Nrf2 in vitro using a gene-specific siRNA targeting Nrf2. The results showed that suppression of Nrf2 eliminated the protective effect of ginsenoside-Rg1 against ferroptosis in heart failure.

CONCLUSIONS Ginsenoside-Rg1 can play a regulatory role in heart failure, and its mechanism of action involves NR2-mediated anti-ferroptosis, suggesting that ginsenoside-Rg1 can be used as a potential therapeutic agent in heart failure.

GW33-e0666 Rosuvastatin enhances lymphangiogenesis after myocardial infarction by regulating the miRNAs/VEGFR3 pathway
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OBJECTIVES Several clinical studies have suggested that early administration of statins could reduce the risk of in-hospital mortality in acute myocardial infarction (AMI) patients. Recently, some studies have identified that stimulating lymphangiogenesis after AMI could improve cardiac function by reducing myocardial oedema and inflammation. This study aimed to identify the effect of rosvastatin on postinfarct lymphangiogenesis, especially the epigenetic regulation of lymphangiogenesis, and to identify the underlying mechanism of this effect.

METHODS Myocardial infarction (MI) was induced by ligation of the left anterior descending coronary artery in mice orally administered rosvastatin for 7 days. The changes in cardiac function, pathology, and lymphangiogenesis following MI were measured by echocardiography and immunostaining. EdU, Matrigel tube formation and scratch wound were used to evaluate the effect of rosvastatin on the proliferation, tube formation and migration of the lymph endothelial cell line SVEC4-10. The expression of miR-107-3p, miR-491-5p, and VEGFR3 was measured by PCR and western blotting. A gain-of-function study was performed using miR-107-3p and miR-491-5p mimics.

RESULTS The rosvastatin-treated mice had a significantly improved ejection fraction and increased lymphatic plexus density 7 days after MI. Rosuvastatin also reduced myocardial oedema and inflammatory infiltration after MI. We used a VEGFR3 inhibitor to partially reverse these effects. Rosuvastatin promoted proliferation, migration, and tube formation of SVEC4-10 cells. PCR and Western blot analysis revealed that rosvastatin intervention downregulated miR-107-3p and miR-491-5p and promoted VEGFR3 expression. The gain-of-function study showed that miR-107-3p and miR-491-5p could inhibit the proliferation, migration and tube formation of SVEC4-10 cells.

CONCLUSIONS Rosuvastatin could improve heart function by promoting lymphangiogenesis after MI by regulating the miRNAs/VEGFR3 pathway.

GW33-e0679 Interleukin 29 accelerates vascular calcification via JAK2/STAT3/BMP2 signaling
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OBJECTIVES Vascular calcification (VC), associated with enhanced cardiovascular morbidity and mortality, is characterized by osteogenic transdifferentiation of vascular smooth muscle cells (VSMCs). Inflammation promotes the initiation and progress of VC. Interleukin 29 (IL-29), a newly discovered member of type III interferon, has recently been implicated in the pathogenesis of autoimmune diseases. Therefore, we evaluated the role of IL-29 on VC process and the underlying inflammatory mechanisms.

METHODS We detected the mRNA expression of IL-29 in calcified carotid arteries from patients with coronary artery disease (CAD) or chronic kidney disease (CKD) by real-time quantitative PCR. We also investigated the effects of IL-29 on VC process and the underlying inflammatory mechanisms. In vitro, VSMCs calcification was induced by the CaP or osteogenic medium, while in vivo VC was triggered by intraperitoneally injected with vitamin D3, Alizarin red and calcium were performed to test VC. Cell proliferation, invasion were detected by CCK-8 assay and transwell assays, and the cell apoptosis was examined by flow cytometry analysis. Western blot was employed to analyze the expression of proteins associated with IL-29, VSMCs osteoblastic transformation and JAK2/STAT3/BMP2 signaling.

RESULTS The mRNA expression of IL-29 was significantly increased and positively associated with an increased BMP2 mRNA level in calcified carotid arteries from patients with CAD or CKD. IL-29 and BMP2 proteins were co-localized from patients with CAD or CKD. IL-29 and BMP2 proteins were co-localized in the human calcified arteries. IL-29 binding to its specific receptor IL-28Rα/β (IL-29/IL-28Rα) inhibited the proliferation of rat VSMCs without changes in cell apoptosis or migration. IL-29 promoted the calcification of rat VSMCs and their osteogenic transdifferentiation in vitro as well as the rat aortic ring calcification ex vivo, induced by the CaP or osteogenic medium. The pro-calcification effect of IL-29 was reduced by pharmacological inhibition of the binding of IL-29/IL-28Rα as well as suppressing JAK2/STAT3 pathway activation that were accompanied by the decreased expression of BMP2 in the cultured rat VSMCs.

CONCLUSIONS These results suggest an important role for IL-29 in the development of VC, at least partly, via activating the JAK2/STAT3/BMP2 signaling.

GW33-e0690 PCSK9 up regulates T lymphocyte subsets TNF-α aggravating hepatic steatosis in mice
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OBJECTIVES To investigate the mechanism of proprotein convertase subtili- sin 9 (PCSK9) on hepatic steatosis in mice.

METHODS C57BL / 6 mice were recruited, transplanted with PCSK9 transgenic mice as an experimental group, GFP as a control group, and fed with a high
RESULTS (1) In the GFP group, liver oil red O showed the total amount of lipid droplets, and H&E staining showed that steatosis and vacuolization were significantly lower than in the PCSK9 group; (2) Flow cytometry showed that GFP group vs PCSK9 group, CD4+IL-2% (3.32±0.12 vs. 13.72±2.09, P<0.05); CD8+IL-2% (1.38±0.37 vs. 4.54±0.09, P<0.05); NK-IL-2% (1.45±0.34 vs 0.92±0.13, P<0.05); CD4+TNF-α% (0.95±2.77 vs 24.78±4.66, P<0.05); CD8+TNF-α% (7.62±1.85 vs 21.18±3.82, P<0.01), NK-TNF-α% (0.65±0.09 VS 1.63±0.35, P<0.05).

CONCLUSIONS PCSK9 accelerates hepatic steatosis by upgrading TNF-α in hepatic lymphocyte subsets in mice.

GW33-e0699
Recipient circulating non-bone marrow CD34+ fibroblast progenitor cells promote fibrosis in cardiac allograft
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OBJECTIVES Fibrosis is one of the major causes leading to cardiac allograft malfunction, and is mainly characterized by excessive extracellular matrix deposition secreted by activated fibroblasts. Extracellular cells play a critical role in repopulating most cellular components in cardiac allografts. However, the role of recipient-derived cells in generating activated fibrocytes is not yet clear. Thus, this process remain to be studied.

METHODS Heterotopic cervical heart transplantation was performed by transplanting hearts from female BALB/c mice to male C57BL/6J mice. Single-cell RNA sequencing (scRNA-seq) were introduced to delineate the allograft cell atlas. Y chromosomes analyses and genetic lineage tracing technique were applied to identify cells from different origins. The contribution of recipient CD34+ cells in allograft fibrosis were investigated using CD34-CreERT2: Rosa26-tdTomato mice. The exact source of recipient fibrogenic CD34+ cells were confirmed by constructing the bone marrow transplantation and parabiotic models. The CD34+ fibroblast progenitor cells were also isolated from human peripheral blood to verify its potential to differentiate into activated fibroblasts both in vivo and in vitro.

RESULTS In our study, the allograft fibroblasts expanded and exhibited a diverse activated phenotype. The majority of activated fibroblasts comes from recipient and showed high expression of CD146. Recipient CD34+ cells were proved to prefer to generate activated fibroblasts after transplantation. In addition, recipient CD34+ cells, which possessed fibrogenic potential, mainly originated from non-bone marrow circulation. The circulating CD34+ fibroblast progenitor cells were recruited to the allograft via CXCL12-AxlR1 interaction. Once located in the allograft tissue, CD34+ fibroblast progenitor cells differentiated into mature fibroblasts in response to various pro-fibrotic pathways, including TGFβ and TNFα signaling pathway.

CONCLUSIONS These results show that recipient-derived FCS were crucial contributors to allograft fibrosis, in which circulating non-BM CD34+ cells play a vital role in generating activated FCS both in vivo and in vitro. Thus, targeting recipient CD34+ cells would be a novel therapy for cardiac allograft fibrosis.

GW33-e0715
Endothelial GATA5 positively regulates angiogenesis via cathepsin S-mediated Angpt2/Flk1 and MMP2/9 signaling pathways
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OBJECTIVES Although GATA5 is vital in maintaining the function of endothelial cells, the relationship between GATA5 and angiogenesis, however, remains unclear. Our study aims to determine how endothelial GATA5 mediates angiogenesis.

METHODS 1. C57BL/6 mice were injected with endothelial cell-specific GATA5-overexpressing adeno-associated virus. One week after virus infection, the hindlimb ischemia model was established by ligating the femoral artery of mice, and the blood perfusion ratio of the operated limb/healthy limb was detected by a blood perfusion imager. CD31 staining of mouse gastrocnemius muscle showed the number of new capillaries per unit area. Western Blot and qPCR were used to detect the expression of GATA5 and related angiogenesis factors. 2. On human umbilical vein endothelial cells, transfected lentivirus to knock down the expression of GATA5 and/or administered vascular endothelial growth factor-165 intervention, through CCK-8 experiments were used to detect cell proliferation, scratch experiments to detect cell migration, and endothelial tube formation experiments to detect the ability of cells to form tubes. Western blot and qPCR assays were used to detect the protein and mRNA levels of GATA5, GATA3, Angpt2, Angpt1, Flk1, and MMP2/MMP9. The direct binding of GATA5 to cathespin S was verified by co-immunoprecipitation experiments. 3. GATA5 knockdown human umbilical vein endothelial cells were transfected with plasmids overexpressing GATA5 or cathespin S or siRNA, the expression levels of GATA5 or cathespin S, Cell function and expression of related factors were detected.

RESULTS 1. The blood perfusion ratio and CD31 immunofluorescence expression of the mice in the endothelium-specific overexpression GATA5 group were significantly higher than those of the negative control mice, and the blood perfusion ratio and protein levels of angiogenesis factors Angt2, Flk1 were increased as well. 2. Cell experiments showed that the knockdown of GATA5 could inhibit cell proliferation, migration and endothelial tube formation stimulated by VEGF-165, and at the same time, reducing the expression of cathespin S, Angpt2, Flk1 and DRP1. The results showed that GATA5 had a direct binding relationship with cathespin S. 3. Overexpression of GATA5 or cathespin S reversed the decline in cell migration and tube formation caused by GATA5 knockdown, and up-regulated the expressions of Angpt2/Flk1 and MMP2/MMP9 signaling pathways.

CONCLUSIONS Endothelial GATA5 regulates angiogenesis by regulating endothelial cell proliferation, migration tube formation through the cathespin S-Angpt2/Flk1 and MMP2/MMP9 signaling pathways.
and mitochondrial dysfunction. Finally, WY14643 pre-treatment for activating PPARα ameliorated LC3-II/I protein level and mitochondrial dysfunction-induced cardiomyopathy in septic heart.

CONCLUSIONS Cardiomyocytes PPARα but not myocard PPARα could protect against septic cardiac dysfunction by ameliorating mitochondrial dysfunction. Our study highlights that cardiomyocytes PPARα could be a preventive and therapeutic targeted to mitochondrial function in septic cardiac dysfunction.

GW33-e0730
The association of genetic polymorphism of DAB2 gene with type 2 diabetes mellitus in Chinese Uygur population
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OBJECTIVES Human Disabled-2 (DAB2) plays an indispensable role in clathrin-mediated endocytosis of selected cargo proteins including LDLR. As hyperlipidemia is a major risk factor for Type 2 diabetes mellitus (T2DM), in the present study, we focused on exploring whether genetic variants of the Dab2 gene were associated with T2DM and the risk factors for T2DM in Uygur population in Xinjiang, China.

METHODS A total of 2157 subjects were recruited in this case–control study, involved 457 T2DM patients and 1690 age- and sex-matched individuals. Four SNPs (rs1050903, rs2255280, rs2855512 and rs11959928) were genotyped using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method.

RESULTS In Uygur people, for rs2255280, the distribution of genotypes, recessive model (CC vs AA+CA), additive model (AC vs CC+AA) showed significant differences between the T2DM patients and the controls (P=0.003, P=0.005 and P=0.026, respectively). For rs2855512, meanwhile, the distribution of genotypes, recessive model (CC vs CA+AA), additive model (CA vs CC+AA) also showed significant differences between the T2DM patients and the controls (P=0.005, P=0.007 and P=0.033, respectively). The recessive model (CC vs CA+AA) of rs2255280 and rs2855512 remain significantly associated with the T2DM after adjustment for confounders (OR=1.241, 95% CI=1.047–1.496, P=0.002; OR=1.245, 95% CI=1.059–1.453, P=0.003).

CONCLUSIONS Rs2255280 and rs2855512 of Dab2 gene are associated with T2DM in Uygur subjects. Subjects with CA/CC genotype or C allele of Rs2255280 and rs2855512 were associated with a significantly increased risk of the T2DM.

GW33-e0745
Whole-exome sequencing of 41K CAD cases and 217K controls identifies perturbation in nitric oxide signaling as a non-lipid molecular subtype of coronary artery disease
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OBJECTIVES A key goal of precision medicine is to disaggregate common, complex diseases into discrete molecular subtypes. Rare coding variants in the low-density lipoprotein receptor gene (LDLR) are identified in 1–2% of coronary artery disease (CAD) patients, defining a molecular subtype with risk driven by hypercholesterolemia.

METHODS To search for additional subtypes, we compared the frequency of rare, predicted loss-of-function and damaging missense variants aggregated within a given gene in 41,081 CAD cases versus 217,115 controls.

RESULTS Rare variants in LDLR were most strongly associated with CAD, present in 1% of cases and associated with 4.4-fold increased CAD risk. A second subtype was characterized by variants in endothelial nitric oxide synthase gene (NOS3), a key enzyme regulating vascular tone, endothelial function, and platelet aggregation. A rare predicted loss-of-function or damaging missense variants in NOS3 was present in 0.6% of cases and associated with 2.42-fold increased risk of CAD (95% CI 1.80 to 3.26; P=5.5×10−10). These variants were associated with higher systolic blood pressure (+3.25 mmHg; 95% CI 1.86 to 4.65; P=5.0×10−10) and increased risk of hypertension (adjusted odds ratio 1.31; 95% CI 1.14 to 1.51; P=0.0002) but not circulating cholesterol concentrations, suggesting that – beyond lipid pathways – nitric oxide synthesis is a key non-lipid driver of CAD risk.

CONCLUSIONS Beyond LDLR, we identified an additional nonlipid molecular subtype of CAD characterized by rare variants in the NOS3 gene.

GW33-e0747
Assessment of intestinal microbiota metabolome in patients with metabolic syndrome
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OBJECTIVES Accumulated data on participation of intestinal microbiota (IM) in metabolic processes of human body suggest the existence of changes in IM and its metabolome linked to changes in IM and development of pathological conditions, including metabolic syndrome (MS). The objective was to study the relationship of IM functional activity and factors of cardiovascular risk in patients with MS.

METHODS Eighty-four patients with MS were examined (mean age 49.7±5.62 years). Examination included a questionnaire on actual nutrition (method of general semi-quantitative assessment of food groups, nutrients and energy intake) and anthropometric analysis. Explanation of carbohydrate, lipid metabolism and severity of inflammation were carried out in compliance with plasma glucose concentration, total cholesterol, LDL cholesterol, CRP. Assessment of intestinal microbial metabolites was performed by photometric analysis of short-chain fatty acids (SCFA) level in coprofitrate. Control group (CG) consisted of 20 apparently healthy individuals aged 18–62 years old. Statistical analysis of results was carried out using SPSS software package.

RESULTS Daily intake of dietary fibers (DF) was lower in all groups with MS (5.4±6.1 g) than the reference range (31.6±4.9 g), with detection of maximal differences in individuals with MS and class III obesity (P<0.001). It was revealed reduced daily DF intake as part of the diet increased BMI (r=−0.283; P<0.05), dietary energy supply (r=−0.188; P<0.05) and consumption of simple carbohydrates (r=−0.228; P<0.05) in MS individuals. CRP level in individuals with MS was significantly different from CG, regardless of BMI level, at the same time moderate positive correlation was registered between BMI and CRP levels (r=0.486, P<0.001). Glycemic levels reasonably increased with elevation of BMI (r=0.418, P<0.001), reaching 6.3 [5.8–6.8] mmol/l in the cohort with MS. Lipid parameters in MS (BMI>30 kg/m²) individuals were manifested by increase in TC, HDL, LDL, TG (P<0.05). Significant correlation of BMI values could be found only with LDL (r=−0.198, P<0.05), triglycerides (TG) (r=0.255, P<0.01) and atherogenic index (AI) (r=0.259, P<0.01). In the course of chromatographic analysis of microbial metabolites in feces, it was possible to register significant differences in the profile and concentration of SCFAs in individuals with MS in comparison with CG and groups with different BMI values. Analysis of relative concentrations of individual SCFAs (C2, C3, C4) showed changes in acid profile of CG and MS individuals with class III obesity (P<0.05) and class II obesity (P<0.001). Reductive-oxidative potential of intraluminal intestinal milieu in MS individuals with class II obesity (−0.02, −0.11 U) and with class III obesity (−0.426±0.10 U) was shifted towards slightly negative values. Those changes in concentration of both total and individual SCFAs were associated with combined changes in IM.

CONCLUSIONS Investigation of persistent metabolites of microorganisms, among which SCF as had a special place, provided new opportunities for quantitative and qualitative assessment of IM. Early detection of IM metabolome disorders in patients with MS and enrichment of the diet with dietary fibers, including nutraceuticals, offered new opportunities of non-drug correction for functional activity of IM and over and above for MS components. Managing IM represented new approach to reduce the risk of CVD and obesity.

GW33-e0752
Inhibition of the P2X7 receptor prevents atrial proarrhythmic remodeling in experimental depression
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OBJECTIVES Atrial fibrillation (AF) is the most common sustained arrhythmia; fibrosis and inflammation are critical factors in the pathogenesis of atrial fibrillation (AF). Depression is associated with chronic inflammation, and can also promote cardiac arrhythmias, but the mechanisms has not been fully elucidated. The purinergic receptor P2X7 (P2X7R), a ligand-gated cation channel, predominately mediates inflammation and cellular death, whereas its effect on atrial fibrillation is unknown. Thus, this study aimed to assess the effect of the P2X7R antagonist Brilliant Blue G (BBG) on atrial arrhythmogenic remodeling in experimental depression model and explore its potential mechanisms.

METHODS Myocardial infarction (MI) was induced by permanent ligation of LAD, and Depression (DEP) was established by chronic unpredictable mild stress (CUMS). In vitro, fibroblasts separated from LA in adult rats were subjected to IL-1β in the presence or absence of BBG and A740033,
two selective P2X7R antagonists, Atrial electrophysiology, Masson staining, Immunofluorescence, Immunohistochemistry, Western blot, RNA sequencing, RT-qPCR were conducted.

RESULTS The P2X7R was significantly upregulated in LA both in the MI and DEP rats, along with the increased risk of AF. Burst pacing induced atrial tachyarrhythmias in 10% CTL rats vs. 80% DEP-only rats, and only 20% BBG-treated DEP rats. Activation latency (LA) was significantly prolonged by DEP, whereas atrial effective refractory period (ERP) and ERP/APD90 ratio were reduced (all P<0.01). The above-mentioned electrophysiological parameters were attenuated by BBG. DEP caused atrial fibrosis. BBG strongly attenuated atrial fibrosis. DEP increased atrium expression of inflammation- and fibrosis-related mRNA and protein expression; however, BBG-treatment suppressed all these DEP-induced alterations. IL-1β induced inflammation in atrial fibroblasts, which was inhibited by BBG and A740003.

CONCLUSIONS The P2X7R antagonist BBG prevents DEP-induced atrial proarrhythmic remodeling, while suppressing inflammatory changes and fibrotic/electrical remodeling, thus providing new insights into the relationship between P2X7R and atrial arrhythmias.

GW33-e0757

Loss of BTK ameliorates the pathological cardiac fibrosis and dysfunction

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OBJECTIVES Cardiac fibrosis is a common irreversible pathological feature of diverse heart disorders. Uncontrolled cardiac fibrosis contributes to maladaptive cardiac remodeling and eventually heart failure. However, the molecular determinants of ischemic and non-ischemic cardiac fibrosis remain largely unknown. Here, we investigated the role of Bruton’s tyrosine kinase (BTK) in cardiac fibrosis and remodeling of mice under various pathological conditions.

METHODS BTK-deficient mice following myocardial infarction (MI) or pressure overload model were used to investigate the role of BTK in pathological cardiac fibrosis and heart dysfunction. We further utilized primary cardiac fibroblasts with BTK deficiency or inhibitor treatment to explore potential mechanism.

RESULTS BTK expression was increased in myocardium of mice after pressure overload or MI. BTK was mainly located in cardiac fibroblasts of myocardium, and its expression in isolated cardiac fibroblasts was upregulated following TGF-β treatment. BTK-deficient mice or the small molecule inhibitor of BTK were introduced to explore BTK function. The deficiency or pharmacological inhibition of BTK attenuated cardiac fibrosis, preserved cardiac function, prevented adverse cardiac remodeling and protected against heart failure in mice subjected to pressure overload or MI. BTK deficiency or inhibitor treatment significantly decreased the expression of fibrosis-related molecules in isolated cardiac fibroblasts and inhibited the transition of fibroblasts to myofibroblasts in response to diverse pathological stresses. BTK directly bound and phosphorylated TGF-β receptor 1 (TβR1), and then promoted the activation of downstream SMAD-dependent or -independent TGF-β signaling, leading to the enhanced transition of fibroblasts toward pro-fibrotic myofibroblasts and the excessive extracellular matrix gene expression.

CONCLUSIONS Our finding uncovers a driving role of BTK in cardiac fibrosis and dysfunction following pressure overload and MI stress conditions, and highlights novel pathogenic mechanisms in ischemic and non-ischemic maladaptive cardiac remodeling, which presents as a promising target for the development of anti-fibrotic therapy.

GW33-e0788

Effect of rapamycin on the expression of origin recognition complex 1 on vascular smooth muscle cells of rats

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OBJECTIVES To explore the effect of rapamycin on the expression of origin recognition complex 1 (ORC1) on vascular smooth muscle cells (VSMCs) of rats in vitro.

METHODS Growth curves of VSMCs were drawn by methyl-thiazolyl-tetrazo-lium (MTT) colorimetric assay. VSMCs were divided randomly into two groups. Control group (CG) cells were cultured in DMEM with 10% FBS, and experimental group (EG) cells were cultured in DMEM with 10% FBS plus different concentrations of rapamycin (0.1 μmol/L, 1 μmol/L, 10 μmol/L and 100 μmol/L) to find the optimal concentration. Expression of ORC1 at transcriptional and protein levels were displayed respectively by RT-qPCR and Western Blot during VSMCs were cultured with the optimal concentration of rapamycin at 0, 1, 2, 4, 6, and 8 h.

RESULTS MTT showed that VSMCs were proliferative and in the exponential growth phase during cultured for 1–3 d. The optimal concentration of rapamycin was 10 μmol/L. The expression levels of ORC1mRNA in EG decreased gradually from 0 h to 12 h and reduced significantly from 24 h to 48 h compared with those of CG. The expression changes of ORC1 protein by Western Blot were similar to those of ORC1mRNA.

CONCLUSIONS Rapamycin inhibits the expression of ORC1, indicating that the target of rapamycin (mTOR) is on the upstream of ORC1 in cell cycle, which shed light on novel strategies that can be used to prevent and treat vascular proliferative disease.

GW33-e0013

Efficacy and safety of a polytetrafluoroethylene membrane wrapped a single layer of sirolimus-eluting stent in a porcine coronary perforation model

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OBJECTIVES Covered stents are effective in treating coronary artery perforation (CAP), however, the high rate of immediate device deployment failure and in-stent restenosis have limited the application of the currently covered stents.

METHODS We designed a balloon-expandable covered stent system consist of a single layer of drug-eluting stent and a layer of polytetrafluoroethylene (PTFE) membrane wrapped at the outer layer of the stent. The immediate sealing effect of our novel covered stent was observed by using an Ellis type III CAP model. The device’s success was assessed based on its ability to seal the perforation, assessed by visual estimation and final thrombolysis in myocardial infarction (TIMI) 3 flow. The antiproliferative effect was evaluated in 12 swine, which were randomly assigned to treatment (sirolimus-eluting covered stents) and control (bare metal covered stents) groups. Coronary angiography and optical coherence tomography (OCT) were performed at index procedure, and 1- and 6-month after stent implantation. All swine were sacrificed for histopathological analyses at 6-month.

RESULTS The device success rate was 100%. All swine were alive at 6-month follow-up. At 1-month, the treatment group had a larger minimal lumen diameter (MLD) (1.89±0.29 vs. 0.63±0.25, P=0.004) and lower late lumen loss (LLL) (0.47±0.15 vs. 1.85±0.34, P<0.001) compared with control group. At 6-month, the treatment group had a numerically higher MLD (0.94±0.34 vs 0.63±0.25 mm; P=0.215) compared with control group. Histological analyses revealed the mean plaque area was lower in the treatment group (2.99±0.81 mm2 vs 4.29±0.77 mm2, P=0.035) than in the control group. No in-stent thrombosis was observed in either group.

CONCLUSIONS In the porcine model of coronary perforation, the PTFE membrane mixed with sirolimus-eluting stent showed a high device success rate in sealing the perforation. The drug-eluting covered stent demonstrated a relatively sustained antiproliferative effect up to 6 months post-implantation.

GW33-e0057

Identification and characterization of novel loss-of-function mutations in the PCSK9 gene associated with low-density lipoprotein cholesterol in a Uygur population in Xinjiang, China

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OBJECTIVES Dyslipidemia, represented by elevated serum LDL-C, is an important risk factor for ASCVD and reducing serum LDL-C levels can significantly reduce the risk of ASCVD morbidity and mortality. A loss-of-function mutation in the PCSK9 gene associated with low serum LDL-C levels reduces the risk of ASCVD morbidity and mortality.

METHODS We screened for non-synonymous mutations in the PCSK9 gene by whole-exome sequencing of subjects with very low LDL-C levels and normal in a healthy population of young Uyghurs in the Xinjiang region of China. The effects of mutations on PCSK9 maturation and secretion, and on LDLR degradation were determined. Functional validation was performed at the cellular,
animal and expanded population levels, respectively, to explore the molecular mechanisms by which novel mutations in the PCSK9 gene affect cholesterol metabolism.

RESULTS By whole-exome sequencing, we identified two PCSK9 nonsynonymous mutations in a healthy population of young Chinese Uyghurs. Expanded population validation revealed that PCSK9 E144K and C378W carriers displayed lower LDL-C levels. PCSK9 E144K and C378W mutations are loss-of-function mutations that are unable to perform self-catalytic splicing and translocation out of the endoplasmic reticulum, respectively. PCSK9 E144K and C378W mutations have a reduced ability to degrade hepatic LDLR. Adeno-asssociated virus-mediated expression of PCSK9 E144K and C378W in mouse liver reduced hepatic LDLR degradation and lowered serum LDL-C, total cholesterol and triglycerides.

CONCLUSIONS Our study shows that PCSK9 E144K and C378W are loss-of-function mutations. They have an effect on serum LDL-C levels in both humans and mice.

GW33-e0058 Serum SELENBP1 and VCL are effective biomarkers for clinical and forensic diagnosis of coronary artery spasms

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OBJECTIVES Coronary artery spasm (CAS) plays an important role in the pathogenesis of ischemic heart diseases, including stable angina, unstable angina, myocardial infarction, and sudden death. Currently, there are no established diagnostic biomarkers for CAS in clinical and forensic settings. The present study aimed to identify biomarkers using serum quantitative proteome and machine learning methods, and validate their effectiveness in both clinical and forensic serum samples.

METHODS A rabbit CAS provocation model was established to screen potential diagnostic biomarkers using quantitative serum proteomics, followed by parallel reaction monitoring/mass spectrometry (PRM/MS)-based targeted proteomics and machine learning analysis. Clinical and forensic serum samples were used for validation studies. Logistic regression analysis and receiver operating characteristic (ROC) curves were used to assess the diagnostic efficacy.

RESULTS A total of 67 (18.3%) serum proteins were identified as differentially expressed proteins from the rabbit CAS model. Cross-analysis of PRM/MS-based targeted proteome and machine learning results suggested that SELENBP1 and VCL were the potential candidate biomarkers for CAS. Genome-wide association study and phenome-wide association study indicated that a variation in the SELENBP1 or VCL was significantly associated with blood monocyte aggregates and left-ventricle contractility, respectively. SELENBP1 and VCL were more concentrated in extracellular vesicles (EVs)-free serum samples. In the clinical samples, serum SELENBP1 and VCL levels were significantly higher in CAS patients than in controls. The areas under curve were 0.9064 for SELENBP1 and 0.8679 for VCL when diagnosing CAS. Logistic regression analysis showed the CAS risk decreased by 30.4% and 54.8% for every 10 units increase of serum SELENBP1 and VCL, respectively. In collected forensic serum samples, postmortem serum SELENBP1 level alone diagnosed the CAS-induced deaths at a sensitivity of 100.0% and specificity of 72.73%, which was superior to traditional biomarkers cTnI and CK-MB. A combination of serum SELENBP1 and VCL yielded a diagnostic specificity of 100.0%.

CONCLUSIONS Serum SELENBP1 and VCL are effective biomarkers for both clinical and forensic diagnosis of CAS.

GW33-e0073 Plasma small extracellular vesicle-carried miRNA-501-5p promotes vascular smooth muscle cell phenotypic modulation-mediated in-stent restenosis

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OBJECTIVES Vascular smooth muscle cell (VSMC) phenotypic modulation plays an important role in the occurrence and development of in-stent restenosis (ISR). The underlying mechanism of which remains a key issue needing to be urgently addressed. This study is designed to investigate the role of plasma small extracellular vesicles (sEV) in VSMC phenotypic modulation.

METHODS sEV were isolated from the plasma of patients with ISR (ISR-sEV) or not (Ctrl-sEV) 1 year after coronary stent implantation using differential ultracentrifugation. Plasma sEV in ISR patients are elevated markedly and decrease the expression of VSMC contractile markers α-SMA and calponin and increase VSMC proliferation. miRNA sequencing and qRT-PCR validation identified that miRNA-501-5p was the highest expressed miRNA in the plasma ISR-sEV compared with Ctrl-sEV.

RESULTS We found that sEV-carried miRNA-501-5p level was significantly higher in ISR patients, and the level of plasma sEV-carried miRNA-501-5p linearly correlated with the degree of restenosis (R2=0.62). Moreover, miRNA-501-5p inhibition significantly increased the expression of VSMC contractile markers α-SMA and calponin and suppressed VSMC proliferation and migration; in vivo inhibition of miRNA-501-5p could also blunt carotid artery balloon injury induced VSMC phenotypic modulation in rats. Mechanically, miRNA-501-5p promoted plasma sEV-induced VSMC proliferation by targeting Smad3.

CONCLUSIONS Notably, endothelial cells might be the major origins of miRNA-501-5p. Collectively, these findings showed that plasma sEV-carried miRNA-501-5p promotes VSMC phenotypic modulation-mediated ISR through targeting Smad3.

GW33-e0094 Adeno-associated viral gene therapy targeting cardiomyocyte with ubiquitin-specific protease 28 prevents diabetes-induced cardiac dysfunction

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OBJECTIVES Diabetic heart failure is a leading complication and the cause of high mortality in type 2 diabetes mellitus (T2DM) patients. Most diabetes with genetic expression defects are susceptible to cardiac dysfunction, and conventional drug therapy cannot correct progression of diabetic cardiomyopathy.

METHODS We first profiled the expression of ubiquitin-proteasome system (UPS) in db/db mice, and identified ubiquitin-specific protease 28 (USP28) as the gene most associated with diabetic heart phenotype. We next established the clinical relevance of this finding by showing the down-regulation of USP28 in the failing heart of diabetes patients. We used db/db mice (a mouse model of spontaneous type 2 diabetes) and mice with high-fat diet (HFD)/streptozotocin (STZ) induced type 2 diabetes to model our diabetes model. Cardiac-specific USP28 deficient, cardiac-specific USP28 transgenic, wild type (WT) mice were fed HFD/STZ diet or standard diet. Subsequently, heart characteristics, cardiometabolic profile, transcriptomics and mitochondrial morphology and function were evaluated. Adeno-associated viral vector serotype 9 encoding Usp28 (AAV9-USP28) and AAV9-USP28 (C171S) in cardiomyocytes, and CRISPR-Cas9 gene edited pluripotent stem cells (iPSCs) was used to investigate the role of USP28. Transmission electron microscopy (TEM), oxygen consumption rate (OCR), extracellular acidification rate (ECAR) and protein truncation test were used to explore the effect of USP28 upon mitochondrial homeostasis and the underlying mechanism.

RESULTS USP28 level was substantial reduction in diabetic myocardium from patients and in spontaneously T2DM mice and mice fed with HFD/STZ diet. The level of USP28 also increased in high glucose plus palmitic acid (HG+PA)-treated iPSCs. Firstly, USP28 presented limited influence upon blood glucose, gain of body weight, insulin resistance and glucose tolerance in the myocardium. Cardiac-specific USP28 deficient mice presented deteriorated cardiac dysfunction following T2DM. Conversely, cardiac-specific USP28 transgenic mice showed improved diabetic heart phenotype. Importantly, Treatment of db/db mice with adeno-associated viral vector serotype 9 encoding Usp28 (AAV9-USP28) in cardiomyocytes counteracted T2DM induced systolic and diastolic dysfunction, cardiac hypertrophy, cardiac fibrosis and mitochondrial defect. Mechanistically, USP28 ablated free-bound, deubiquitinated and stabilized pro-sescomer activators receptor α (pPARRα), and led to PPARα-mediated Mitofusin2 (Mfn2) transcription and improved mitochondrial fission in IPS induced diabetic cardiomyocytes. Further investigation uncovered that the UCH domain of USP28 directly interacted with the DBD domain of PPARα, while inactivation of USP28 (G171S) abolished the deubiquitination of PPARα. In addition, cardiac-specific knockdown of PPARα abolished AAV9-USP28 induced cardioprotection in db/db mice. Consistently, AAV9-USP28 (C171S) showed no impact on diabetic heart.

CONCLUSIONS We demonstrated the potential of AAV-mediated-USP28 gene therapy to correct the diabetic heart pathology, providing strong rationale for future clinical translation.

GW33-e0132 Mechanism of differential response to propranolol and metoprolol in LQTS patients with hERG_G604C mutation

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OBJECTIVES β-blockers have been recommended as first-line therapy in long QT syndrome (LQTS) patients. In our center, a LQT2 patient with hERG—G604C mutation showed prolonged QTc and increased cardiac events (CEs) with propranolol treatment, while QTc was shortened and CEs were controlled after switching to metoprolol, but the mechanism remains unclear.

METHODS hERG—WT (WT), hERG—G604C (G604C) and heterozygous (WT/M) monodonal stable cells were constructed in HEK293 cells. Western Blot and RT-qPCR were used to confirm the levels of hERG protein and mRNA.
membrane protein Western Blot and immunofluorescence to evaluate protein trafficking, whole cell patch-clamp to detect I\(_{Kr}\) current, and molecular docking to predict interaction between propanolol/mexiletine and hERG channel.

RESULTS The expression of hERG mRNA and protein were comparable in WT and G604C group. G604C group presented with hERG trafficking deficiency. WT group induced strong I\(_{Kr}\) current, I\(_{Kr}\) current were disappeared in G604C group, and I\(_{Kr}\) current decreased over 50% in WT/M group. hERG mRNA and protein didn’t change significantly with increased concentration of propanolol, while propanolol inhibited I\(_{Kr}\) current with a concentration-dependent manner. Mexiletine rescued hERG protein trafficking deficiency, while transient effect of mexiletine on I\(_{Kr}\) current was a concentration-dependent inhibition. Chronic effect of mexiletine on G604C mutant hERG channel was promotion. G604C mutation enhanced the interaction between hERG channel and propanolol, while not in mexiletine.

CONCLUSIONS The combined effect of propanolol and mexiletine in LQT2 patients depends on the composite effect of rescuing mutant hERG protein trafficking deficiency, inhibition of J-transporter, I\(_{Kr}\) current, and I\(_{Kr}\) current.

GW33-e0265 Sonodynamic therapy reduces inflammation and fibrosis of epicardial adipose tissue in paced inducing atrial fibrillation rabbit model

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OBJECTIVES Epicardial adipose tissue (EAT) is an important risk factor for the occurrence and development of atrial fibrillation. There are active proinflammatory macrophages in EAT. The previous research of our research group found that sonodynamic therapy (SDT) could make macrophages died in atherosclerotic plaque and reduce inflammation of EAT. But the effect of SDT in EAT in AF is not clear. We plan to use pacing atrial fibrillation rabbits as a model to explore the effect and mechanism of SDT intervention in EAT. Then we may provide a new theoretical basis for the treatment of AF.

METHODS The experiment was divided into sham operation group (Sham group), paced +SDT treatment group (+SDT group). (1) New Zealand white rabbits were installed pacemaker, pacing 600 times/min for 4 weeks to establish the rabbit model of atrial fibrillation. The +SDT group was given 4 hours of light avoidance and SDT intervention after intravenous injection of sinoporphyrin sodium (DVDMS). The three experimental groups were taken after 2 weeks. (2) The number of macrophages in EAT insham group, paced group and +SDT group were detected by immunohistochemistry. (3) The level of EAT fibrosis in three groups were detected by Masson staining. (4) The differentially expressed genes and enrichment pathways in EAT were analyzed by transcriptional sequencing. (5) The mRNA level of inflammation and fibrosis related genes were detected by Real-time PCR. (6) The level of inflammation and fibrosis related proteins were detected by Western blot.

RESULTS (1) Immunohistochemical results showed that the number of macrophages in EAT in paced group were higher than that in Sham group. The number of macrophages in EAT decreased after SDT. (2) Masson staining showed that the collagen content in EAT in paced group were higher than that in Sham group. The collagen content decreased after SDT. (3) Enrichment analysis of differentially expressed gene KEGGs showed NF-kappa-B p50, Toll like receptor signaling pathway, and NF-kappa-B p50, Toll like receptor signaling pathway significantly.

CONCLUSIONS SDT reduces inflammation and fibrosis in EAT of atrial fibrillation rabbits through inhibiting the expression of macrophage inflammatory factors and MMP2.

GW33-e0347 HIF-1q overexpression in mesenchymal stem cell-derived exosome-encapsulated arginine-glycine-aspartate (RGD) hydrogels boost therapeutic efficacy of cardiac repair after myocardial infarction

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OBJECTIVES Naturally secreted extracellular vesicles (EVs) play important roles in stem-mediated cardioprotection. This study aimed to investigate the cardioprotective function and underlying mechanisms of EVs derived from HIF-1e engineered mesenchymal stem cells (MSCs) in a rat model of AMI.

METHODS EVs isolated from HIF-1e engineered MSCs (HIF-1e-EVs) and control MSCs (MSCs-EVs) were prepared. In vitro experiments, the EVs were incubated with cardiomyocytes and endothelial cells exposed to hypoxia and serum deprivation (H/SD). In vitro experiments, the EVs were injected in the acutely infarcted hearts of Sprague-Dawley rats.

RESULTS Compared with MSCs-EVs, HIF-1e-EVs significantly inhibited the apoptosis of cardiomyocytes and enhanced angiogenesis of endothelial cells; meanwhile, HIF-1e-EVs also significantly shrank fibrotic area and strengthened cardiac function in infarcted rats. After treatment with EVs/RGD-biotin hydrogels, we observed longer retention, higher stability in HIF-1e-EVs, and stronger cardiac function in the rats. Quantitative real-time PCR (RT-PCR) displayed that miRNA-221-3p was highly expressed in HIF-1e-EVs. After miR-221-3p was inhibited in HIF-1e-EVs, the biological effects of HIF-1e EVs on apoptosis and angiogenesis were attenuated.

CONCLUSIONS EVs released by MSCs with HIF-1e overexpression can promote the angiogenesis of endothelial cells and the apoptosis of cardiomyocytes via upregulating the expression of miR-221-3p. RGD hydrogels can enhance the therapeutic efficacy of HIF-1e engineered MSCs-derived EVs.

GW33-e0348 Predicting acute kidney injury in acute myocardial infarction patients: an artificial intelligence model using MIMIC databases

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OBJECTIVES Accurate estimation of the risk of acute kidney injury (AKI) is critical and essential for acute myocardial infarction (AMI). The aim of this study was to develop a machine learning model for improving the estimation of AKI risk in patients with AMI.

METHODS Patients data in the training group were extracted from Medical Information Mart for Intensive Care-III (MIMIC-III) database, and adult patients diagnosed with AMI were selected. Several common machine learning algorithms were conducted to select the best prediction model. Recursive feature elimination was used to select the best prediction features. The final model was validated using an external validation set from AKI patients in Medical Information Mart for Intensive Care-IV (MIMIC-IV) database database. The area under the receiver operating characteristic curve (AUC) and calibration curve were used to evaluate the performance of each prediction model. Finally, an online predictive program was developed on WeChat (a mobile messaging App commonly used in China), which could evaluate the probability of AKI in AMI patients timely.

RESULTS A total of 3882 patients with AMI were included, and among whom 192 patients were diagnosed with AKI. The random forest model showed the best prediction performance (AUROC=0.912) among five machine learning models. Creatinine, urea nitrogen, platelet count, creatinine kinase isoenzyme (CK-MB) and arterial blood systolic pressure were considered as the top five important features for developing the model. The enrolled patients were divided into low-risk and high-risk group for AKI, survival analysis showed an significant higher short-term mortality in high-risk group patients (P<0.001).

CONCLUSIONS The results revealed that the prediction performance of random forest was superior to other machine models. Random forest classifier displayed a reliable performance in assessing AKI risk in AMI patients.

GW33-e0406 PCSK9 inhibition protects against myocardial ischemia-reperfusion injury via suppressing autophagy

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OBJECTIVES Autophagy is critical for myocardial ischemia-reperfusion (I/R) injury. However, there is still considerable debate over its protective and deleterious effects. The purpose of this study was to determine the involvement of the proprotein convertase subtilisin/kexin type 9 (PCSK9) and its inhibitor in myocardial ischemia-reperfusion injury autophagy (MI).

METHODS Nine groups of eighty rats were used: sham, I/R, I/R+sham, I/R+bis, I/R+sham, I/R+bis, I/R, I/R+bis, I/R+sham, I/R+bis, I/R+sham, I/R+bis, I/R+sham, I/R+bis. A 30-minute coronary artery blockage was used to produce myocardial IR. The time required for reperfusion rose linearly with the time gradient, from 2 hours to 2 days. Following the determination of the best reperfusion period, three groups were formed: sham, I/R, and I/R+P (PCSK9...
inhibitor (evolocumab) 10 mg/kg diluted in 2 ml sterile injection water was administered subcutaneously 1 week and half an hour before each surgery. Each group’s infarction area was determined by electrocardiography (ECG), cardiac function, and 2,3,5-triphenyltetrazolium chloride (TTC)/Evan Blue (EB) staining. To detect morphological alterations in myocardial cells in each group, hematoxylin and eosin staining and Masson staining were utilized to quantify myocardial fibrosis and PSCSK9 and autophagy protein expression.

RESULTS
The results indicated that PSCSK9 expression levels increased significantly in MIRI, as indicated by increased levels of the autophagy regulatory protein light chain 3 (LC3) and Beclin-1, which activated autophagy in cardiomyocytes, exacerbated myocardial injury, and increased the size of myocardial infarcts. Meanwhile, PSCSK9 regulates mitophagy via the Bcl-2/adenosine E1B 19-kDa interacting protein (BNIP3) pathway, which controls myocardial infarction. MIRI throughout. Additionally, the PSCSK9 inhibitor significantly decreased autophagy, enhanced cardiac function, and reduced the extent of reperfusion injury, consequently reducing myocardial infarct size expansion.

CONCLUSIONS
PSCSK9 is upregulated in the myocardial ischemia-reperfusion injury hearts and regulates mitophagy via the BNIP3 pathway, which in turn contributes to reperfusion injury after myocardial infarction. PSCSK9 inhibition protects against myocardial ischemia-reperfusion injury via suppressing autophagy.

GW33-e0433
Rare-variant based linkage analysis and nanopore sequencing enable diagnosis of familial facioscapulohumeral dystrophy 1
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OBJECTIVES
Facioscapulohumeral muscular dystrophy (FSHD) is one of the most common muscular dystrophies. Over 95% of FSHD cases are caused by deletion of the subtelomereric macrosatellite repeats (D4Z4) on human chromosome 4q35. Directly sequencing these repetitive regions is difficult owing to the high similarity among repeat units and high GC content. We aim to develop an efficient and accurate procedure for the diagnosis of FSHD.

METHODS
Whole genome sequencing was performed for ten individuals from a large FSHD family. Parametric linkage analysis was performed via Merlin (v.11.2) with the following parameters: dominant model, an estimated population allele frequency of 1E-5, and penetrance of 90%. 4q and 10q haplotypes were characterized by alignment to the chromosome 4 reference genome. A BLAT of the pLAM sequence was performed to identify the A/B haplotypes. Nanopore sequencing was used to obtain the whole D4Z4 repeat sequence and the methylation status, including the DUX4 in the last D4Z4 repeat.

RESULTS
Rare variants-based linkage analysis identified one single 1.7 MB haplotype on chromosome 4q35.2, presenting in affected individuals and absent in unaffected family members. Parametric linkage analysis resulted in a LOD score of 3.228 for the region. All pedigree samples contained 4q-pLAM sequence suggesting at least one copy of a 4qA permissive haplotype. Normalized counts of reads containing 4q-specific pLAM sequence were comparable between the FSHD patients, while 4q-specific D4Z4 repeat sequence demonstrated fewer reads in pedigree samples. Nanopore obtained the whole D4Z4 repeat sequence and the methylation status, including the DUX4 in the last D4Z4 repeat.

CONCLUSIONS
Family WGS and rare variants-based linkage analyses, combined with read depth analysis, provide the possibility of detecting the D4Z4 repeat contraction for FSHD1 patients. 4q pLAM specific sequence could be detected by matching to T2T-CHM13 reference. We verified Nanopore-based ultra-long read sequencer could obtain the whole D4Z4 repeat sequence and the methylation status in real cases for the first time in the world.

GW33-e0457
Mesenchymal stromal cells overexpressing farnesoid X receptor exert cardioprotective effects against acute ischemic heart injury by binding endogenous bile acids
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OBJECTIVES
Bile acid metabolites have been increasingly recognized as pleiotropic signaling molecules that regulate multiple cardiovascular functions, but their role in mesenchymal cells (MSC)-based therapy has never been investigated. This study clarifies whether and how farnesoid X receptor (FXR), a main receptor for bile acids, improves the retention and cardioprotection of MSC against myocardial infarction (MI) injury.

METHODS
The targeted metabolomics was determined to detect the types and levels of bile acids in myocardial tissue after MI. Adenosine FXR was used to modify adipose-tissue-derived MSC (ADSC-FXR). Eight-week-old male C57BL/6J mice were used for in vivo study. CM-DH1- or tdTomato-labeled ADSC were intramyocardially injected into the peri-infarct area at 3 sites immediately after MI surgery. The ADS diameter was detected by using BWA-MEM and then measured the read count for reads containing 4q-specific pLAM sequence were comparable between the FSHD patients, while 4q-specific D4Z4 repeat sequence demonstrated fewer reads in pedigree samples. Nanopore obtained the whole D4Z4 repeat sequence and the methylation status, including the DUX4 in the last D4Z4 repeat.

RESULTS
In vivo, FXR overexpression significantly increased the ADS diameter at 3 and 7 days after intramyocardial injection compared to ADSC-ctrl. Moreover, ADSC-FXR significantly improved cardiac remodeling and function of MI mice, and increased the capillary density and ameliorated the cardiomyocyte apoptosis in the peri-infarct area. In vitro, FXR overexpression promoted ADSC paracrine angiogenesis via angiopterin-like protein 4 (Angptl4), but failed to improve ADS survival. By performing bile acid-targeted metabolomics, we found that there was a bile acid pool in the myocardial microenvironment. ADSC-FXR showed significantly lower apoptosis by upregulating NADPH quinone oxidoreductase-1 (Nqo-1) expression in the presence of FXR ligands. In addition, knockdown of retinoid X receptor (RXRα), a coactivator of FXR, largely reduced ADSC-FXR retention in the ischemic heart and their cardioprotection.

CONCLUSIONS
We first demonstrate that there is a bile acid pool in the myocardial microenvironment. Bile acid-FXR signaling enhances the cardioprotection of MSC against IHD via Nqo-1-mediated survival/rescue and Angptl4-mediated paracrine angiogenesis directly.
of ischemia reperfusion, which could be a potential obstacle for clinical transformation. Here, we explored the underlying mechanisms of SPION induced myocardial toxicity and whether MTP-131 modification could reverse the cardiotoxicity.

**METHODS** MTP-131 was physically adsorbed on SPION in order to construct mitochondrial targeted antioxidant peptides modifying SPION (SPION@MTP-131). H9c2 cells following hypoxia/reoxygenation (H/R) procedure were treated with SPION or SPION@MTP-131 to evaluate the dose- and time-dependent toxic potential, as well as investigate the effect of MTP-131 on improving SPION induced cytotoxicity. The mitochondrial ROS levels and MMP were respectively measured by Mitrosox and JC-1. The lipid peroxidation product (MDA), ATP, GSH and GPx4 were tested by ELISA. The mitochondrial structure was observed by TEM. Cellular iron metabolic homeostasis was detected by WB or ELISA. The ferroptosis markers were detected by WB analysis. RT-PCR. To explore the main form of SPION-induced cell death, cardiomyocytes were exposed to SPION combined with Fer-1, 3-mA, Nee-1 or zVAD for 24 h, respectively.

**RESULTS** SPION induced time- and concentration-dependent cardiotoxicity, evidence by significant loss of cell viability and elevated the level of LDH, whereas SPION@MTP-131 demonstrated similar results relative to the H/R group, suggesting that MTP-131 can significantly alleviate SPION induced cell damage. SPION seriously disturbed cellular iron homeostasis, characterized by increased expression of FTH and level of Ftm, and decreased expression of FPN1 and ABC8, leading to mitochondrial iron overload. The mitochondrial apoptosis and ferroptosis were evaluated by up-regulated protein expression of NRF2 and ACO3 and the increase of mRNA levels of ACSL4 and PGSS. MTP-131 significantly mitigated SPION-induced ferroptosis through reducing production of mitochondrial MDA and preserving concentrations of GSH and GPx4, indicating that MTP-131 holds a potential to reverse SPION-induced cytotoxicity by exerting mitochondrial targeted antioxidant effect. Compared with the H/R cardiomyocytes, there was no significant difference in cell viability of H9c2 cells co-incubated with SPION and Fer-1. Conversely, co-incubation of H9c2 cells with SPION by inhibitors of 3-MA, ZVAD or Nee-1 respectively, these three inhibitors caused remarkable loss of H9c2 cell viability, indicating that ferroptosis could be main mechanism of SPION induced myocardial cytotoxicity.

**CONCLUSIONS** SPION promote mitochondrial lipid peroxidation by inducing mitochondrial iron overload, thereby leading to ferroptosis of H/R cardiomyocytes. MTP-131 may inhibit SPION-induced ferroptosis of H/R cardiomyocytes, suggesting the modification of mitochondrial targeted antioxidant peptide could be a promising strategy.

**GW33-e0648**

**RESULTS** Exosomes derived from Sparc high Tregs can effectively promote myocardial infarction (AMI) repair. Under the guidance of CXCR2 based on the inflammatory microenvironment, single-cell sequencing data found that sox17 may be an important factor to reconstruct coronary microcirculation in myocardial infarction tissue. We assessed the hypothesis that sox17 can form a positive feedback loop with ME complex to improve SPION induced cytotoxicity.

**CONCLUSIONS** In conclusion, ME complex activates SOX17/VEGFR of AMI cardiomyocytes to improve the repair of AMI. Under the guidance of CXCR2 based on the inflammatory microenvironment, single-cell sequencing data found that sox17 can form a positive feedback loop with ME complex to improve SPION induced cytotoxicity.
GW33-e0038
Long term prognosis and risk factors of intravascular imaging guided intervention for in-stent restenosis of coronary artery
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OBJECTIVES To analyze the clinical characteristics, compare the differences in long-term prognosis, and clarify the predictors of the occurrence of long-term adverse events in patients who underwent coronary in-stent restenosis intervention guided by optical coherence tomography (OCT), intravascular ultrasound (IVUS), and coronary angiography (CAG).

METHODS A total of 79 patients with ISR underwent drug-eluting stent (DES) intervention guided by OCT in Chinese Academy of Medical Sciences Fuwai Hospital from January 2015 to December 2019 were retrospectively enrolled and matched by age, sex and admission date in a 1:1 ratio to the patients guided by IVUS and CAG guidance. The data on patient demographics, cardiovascular risk factors, ancillary tests, and other medical history were collected, patients were followed up by telephone or outpatient clinic, and the primary outcome (MACE) and secondary outcomes were used as study endpoints to compare the differences in long-term prognosis among the three groups and to analyze their predictive factors.

RESULTS During a mean follow-up of 3.2±1.4 years, the primary endpoint (log rank P=0.033) and secondary endpoint (log rank P=0.027) were significantly more frequent in the CAG group than in the other 2 groups, the difference in the incidence of primary endpoint (log rank P=0.493) and secondary endpoint (log rank P=0.313) between OCT and IVUS groups were not statistically significant. Cox hazard proportional model analysis showed that intravascular imaging guided intervention remained an independent protective factor for reducing the occurrence of long-term MACE (hazard ratio=0.467, 95% confidence interval: 0.200–0.998, P=0.049).

CONCLUSIONS The intravascular imaging guided PCI in patients with ISR is an independent protective factor for the occurrence of long-term MACE, and the long-term prognosis of PCI guided by OCT and IVUS is similar.

GW33-e0043
Compared sacubitril/valsartan with benalapril on left ventricular remodeling of AMI after PPCI: a case-control study
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OBJECTIVES To compare the effect of sacubitril/valsartan with benalapril on left ventricular remodeling in patients with acute myocardial infarction.

METHODS Eighty-five patients with acute ST segment elevation myocardial infarction who were treated with PCI in the Second Affiliated Hospital of Tianjin Medical University. The patients were randomly divided into two groups: the experimental group (sacubitril/valsartan, 25–100 mg/d, BID) and the control group (benalapril, 5–10 mg, QD).

RESULTS One month after the treatment of sacubitril/valsartan or benalapril, only the left ventricular end systolic diameter was statistically different between the two groups (P=0.06), and the other indexes were not statistically different three months after treatment with sacubitril/valsartan or benalapril, there were no statistical differences in the indexes related to myocardial remodeling between the two groups (P=0.05). The results of multivariate logistic analysis showed that the index of left ventricular end systolic diameter was statistically significant (odds ratio=0.006, 95% CI: 0.713–0.981, acute myocardial infarction whose LVEF is less than 50%, show sacubitril/valsartan is better than traditional ACEI.

CONCLUSIONS Sacubitril/valsartan compared with benalapril is better on left ventricular remodeling in patients with ST segment elevation acute myocardial infarction.

GW33-e0074
3-Year outcomes of the ULTIMATE trial comparing intravascular ultrasound versus angiography-guided drug-eluting stent implantation
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OBJECTIVES The multicenter randomized ULTIMATE (Intravascular Ultrasound Guided Drug Eluting Stents Implantation in “All-Comers” Coronary Lesions) trial showed a lower incidence of 1-year TVF after IVUS-guided DES implantation among all comers compared with angiographic guidance. However, the 3-year clinical outcomes of the ULTIMATE trial remain unknown.

METHODS A total of 1,448 all comers undergoing DES implantation who were randomly assigned to either IVUS guidance or angiographic guidance in the ULTIMATE trial were followed for 3 years. The primary endpoint was the risk...
for TVF at 3 years. The safety endpoint was definite or probable stent thrombosis (ST).

RESULTS At 3 years, TVF occurred in 47 patients (6.6%) in the IVUS-guided group and in 76 patients (10.7%) in the angiography-guided group (P=0.01), driven mainly by the decrease in clinically driven target vessel revascularization (4.5 vs. 6.9%; P=0.05). The rate of definite or probable ST was 0.1% in the IVUS-guided group and 1.1% in the angiography-guided group (P=0.02). Notably, the IVUS-defined optimal procedure was associated with a significant reduction in 3-year TVF relative to that with the suboptimal procedure.

CONCLUSIONS IVUS-guided DES implantation was associated with significantly lower rates of TVF and ST during 3-year follow-up among all comers, particularly those who underwent the IVUS-defined optimal procedure compared with those with angiographic guidance. (Intravascular Ultrasound Guided Drug Eluting Stents Implantation in “All-Comers” Coronary Lesions; NCT0215915).

GW33-e0100 Bivalirudin versus heparin on a background of ticagrelor and aspirin in ST-segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention: a multicenter prospective cohort study

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OBJECTIVES Current guidelines recommend potent P2Y12 inhibitors such as ticagrelor and aspirin in patients undergoing primary percutaneous coronary intervention (PPCI). We aimed to evaluate the efficacy and safety of bivalirudin with background ticagrelor and aspirin therapy in STEMI patients undergoing primary percutaneous coronary intervention compared with heparin.

METHODS A total of 800 STEMI patients who were undergoing PPCI and receiving treatment with aspirin and ticagrelor from 3 Hospitals between April 2019 and September 2021 were included in this study. The patients were assigned, according to the perioperative antiplatelet, to the bivalirudin group (n=456) or the heparin group (n=344). In this study, the primary endpoint was 30-day net adverse clinical events (NACE), a composite of major adverse cardiac or cerebral events (MACCE, a composite of cardiac death, recurrent myocardial infarction, ischemia-driven target vessel revascularization, or any bleeding as defined by the Bleeding Academic Research Consortium (BARC) definition (grades 1–5).

RESULTS The patients were followed up for 30 days after PPCI. The incidence of NACE was significantly lower in the bivalirudin group than in the heparin group (11.2 vs 16.0%, P=0.042), and this significance was mainly a consequence of the reduction in clinical bleeding events in the bivalirudin group compared with the heparin group (3.2 vs 7.1%, P=0.042). Results from multivariate Cox regression analysis showed that bivalirudin significantly reduced 30-day NACE (HR: 0.657, 95% CI: 0.462–0.990, P=0.042) and BARC1 bleeding events (HR: 0.64, 95% CI: 0.222–0.830, P=0.010). No significant between-group differences were observed for MACCE, all-cause mortality, cardiac death, recurrent myocardial infarction, stroke, target vessel revascularization, stent thrombosis, and BARC2–5 bleeding events at 30 days.

CONCLUSION In patients with STEMI who were undergoing primary PCI and receiving treatment with aspirin and ticagrelor, bivalirudin was associated with decreased rates in NACE and minimal bleeding events without significant differences in the rates of MACCE or stent thrombosis when compared with heparin. Nevertheless, large randomized trials are warranted to confirm these observations.


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OBJECTIVES Obesity is a significant risk factor of cardiovascular diseases (CVD), posing a serious threat to global health. The study regarding sagittal abdominal diameter (SAD), a proxy for visceral fat, and CVD is scarce and its association remains uncertain. The aim of current study was to evaluate the association between SAD and CVD in adults.

METHODS We included 11,477 adults from the National Health and Nutrition Examination Survey (NHANES) (2011–2016). The NHANES data allows for systematic and restricted cubic spline were used to assess the relationship between SAD and CVD. Then, the receiver operating characteristic (ROC) curve was established and the area under the curve (AUC) was calculated to compare the predictive ability of SAD, body mass index (BMI) and waist circumference (WC) on CVD.

RESULTS The weighted mean (95% CI) of SAD was 22.6 (22.4, 22.8) cm, and prevalence of CVD was 6.8%. Higher SAD levels were significantly with higher levels of glucose, insulin, HOMA of insulin resistance, HbA1c, and triglyceride, and lower levels of high-density lipoprotein cholesterol (P trend<0.001). After multivariate adjustment, higher SAD levels were significantly and linearly associated with higher prevalence of CVD, congestive heart failure (CHF), coronary heart disease (CHD), and myocardial infarction (MI): increase of risk were 10, 16, 11, and 7%, respectively, per one-unit increment of SAD (all P<0.05). Compared with participants with SAD<19.2 cm, the multivariate-adjusted ORs (95% CI) for participants with SAD≥25 cm were 1.26 (1.17, 1.36) for CVD, 3.94 (1.51, 10.29) for CHF, 6.31 (2.59, 15.37) for CHD, and 5.21 (1.62, 16.76) for MI (all P trend<0.05). The area under the ROC curve of SAD [0.69] (95% CI, 0.62–0.75) was more than BMI [0.56] (95% CI, 0.47–0.68) and WC [0.56] (95% CI, 0.50–0.68).
CONCLUSIONS Higher level of SAD were closely related to the risk of cardiovascu-
dlar disease. With the increase of SAD, the incidence of CVD increased
gradually. SAD is better than BMI and WC in predicting CVD. These findings
suggest that SAD should be evaluated to assess visceral fat and CVD risk during
physical examination.

GW33-e0133 Impact of subclinical hypothyroidism on prognosis after percutaneous coronary intervention for chronic total occlusion
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OBJECTIVES The influence of subclinical hypothyroidism (SCH) on clinical outcomes following percutaneous coronary intervention (PCI) for Chronic Total Occlusion (CTO) remains unclear. To investigate the effect of SCH on the prognosis of patients with chronic total coronary artery occlusion after Interventional therapy.

METHODS From August 2018 to October 2019, a total of 120 patients who were diagnosed with CTO and successfully treated with PCI in the Cardiac Catheterization Room of the first affiliated Hospital of Anhui Medical University were included. According to the level of (TSH), the patients were divided into two groups: euthyroid group (ET group, n=98) and subclinical hypothyroidism group (SCH group, n=22). The clinical and angiographic con-
ditions of the two groups were compared, and multivariate Cox survival analy-
sis was used to compare the differences of major adverse cardiovascular and cerebrovascular events (MACCE) between the two groups during follow-up, and multivariate Cox regression analysis was used to evaluate the independent correlation between SCH and adverse clinical outcomes.

RESULTS The average follow-up was 18 months. The incidence of MACCE in the SCH group was higher than that in the ET group (22.7% vs 15.1%). Multivariate Cox regression analysis showed that SCH was independently associated with the risk of MACCE (HR=4.56, 95% CI: 1.32–15.77, P=0.017).

CONCLUSIONS SCH negatively impacted clinical outcomes following CTO-PCI. Therefore, patients with SCH should be carefully observed after CTO-PCI.

GW33-e0140 Correlation between bilirubin levels and PCI-related death after surgery in diabetic patients with coronary heart disease
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BACKGROUND Bilirubin is a natural endogenous antioxidant, which has important physiological functions, including anti-inflammatory, anti-immunological, anti-complement, anti-immune and anti-vascular smooth muscle proliferation, can protect vascular endothelial function, and can inhibit plate-
et activation. Recent studies have found that bilirubin levels may be closely related to coronary heart disease. This study mainly explores the relationship between serum bilirubin levels and long-term cardioprotective death after ephe-
trial coronary artery intervention therapy (PCI) in diabetic patients with coro-
nary heart disease.

METHODS Retrospective analysis of 1952 patients receiving PCI coronary heart disease combined diabetes. Patients were divided into four groups according to serum bilirubin (BIL) levels: <6.10 (group 1, n=485), 6.11–8.70 (group 2, n=471), 8.71–12.00 (group 3, n=458) and >12.01 (group 4, n=445). Follow-up of patients after PCI surgery, Cox regression model was used to ana-
yze whether bilirubin levels were an independent risk factor for PCI-derived death or the survival surgery in patients with coronary heart disease combined diabetes.

RESULTS Of the 1952 patients followed, 93 (4.76%), had a heart-derived death. There were 18, 19, 19 and 37 patients with heart-derived deaths at different bilirubin levels. Lower or higher bilirubin levels were significantly associated with an increased risk of heart-derived death after PCI, independent of mixed factors. Kaplan-Meier shows survival in patients with different serum bilirubin levels, suggesting that lower or higher bilirubin levels may be higher in patients with a higher risk of cardiogenic death, the difference in incidence between groups is statistically significant (P<0.005). According to Cox regres-
sion analysis, it is suggested that age, AMI history, stroke history, LVEF, right coronary lesions, CTO, ST segment elevation are risk factors for survival in patients with high bilirubin levels; Revascularization may be a protective fac-
tor for heart-derived death after PCI.

CONCLUSIONS There is a correlation between higher or lower bilirubin levels and the occurrence of heart-derived death in patients with coronary heart dis-
ease. Too low or too high bilirubin may be an independent risk factor for clinical heart-derived death in patients with coronary heart disease combined diabetes treated with PCI.

GW33-e0156 High sensitivity C-reactive protein, body mass index and long-term outcomes in patients percutaneous coronary intervention: a large cohort study from China
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OBJECTIVES Residual inflammatory risk contributes to the occurrence of cardiovascular (CV) events. As obesity is considered as a state of chronic low-
graded inflammation, we hypothesized that body mass index (BMI) might modify the prognostic value of elevated high-sensitivity C-reactive protein (hsCRP) for CV risk in patients with coronary artery disease.

METHODS This study included 7396 patients undergoing percutaneous coro-
nary intervention (PCI) from January to December 2013. Patients were divided into three groups according to the BMI criteria for Chinese adults: normal weight (18.5 to <24 kg/m², n=1870), overweight (24 to <28 kg/m², n=3762) or obese (≥28 kg/m², n=1764). Elevated hsCRP was defined as ≥3 mg/L. The pri-
mary endpoint was major adverse cardiac and cerebrovascular events (MACCE), a composite of all-cause mortality, myocardial infarction, revascularization, and stroke. The secondary endpoint was all-cause mortality.

RESULTS During a mean follow-up of 5.1 years, 1620 (21.9%) and 276 (3.7%) patients experienced MACCE and mortality, respectively. After multivariable adjustment, elevated hsCRP was significantly associated with an increased risk of MACCE (HR: 1.19, 95% CI: 1.05–1.34, P=0.006). Significant association between hsCRP and risk of MACCE and all-cause mortality was only observed in non-obese (BMI <24 kg/m², 1.07–1.75, P=0.01; OR=1.19, 95% CI: 1.34–2.60, P<0.002) and diminished in the obese group. There was a significant interaction for all-cause mortality between BMI categories and hsCRP (P=0.04).

CONCLUSIONS In patients undergoing PCI, hsCRP-associated cardiovascular risk may be modified by BMI levels, which could help identify specific individuals who may benefit the most from further anti-inflammation treatment.
**GW33-e0178**

**P2Y12 inhibitor reloading for patients with Non-ST-segment Elevation Acute Coronary Syndrome already on chronic P2Y12 inhibitor therapy in China: findings from the CCC-ACS (Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome) project**

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**OBJECTIVES** The safety and efficacy of an additional clopidogrel load in non-ST-segment elevation acute coronary syndrome (NSTEACS) patients whilst on chronic maintenance clopidogrel therapy have not yet been well characterized in China. This study was designed to evaluate whether P2Y12 receptor inhibitor reloading is associated with in-hospital major adverse cardiac events and major bleeding for these patients.

**METHODS** The Improving Care for Cardiovascular Disease in China–Acute Coronary Syndrome (CCC-ACS project) is a novel national quality enhancement registry of the Chinese Society of Cardiology. A total of 4790 patients with a definitive diagnosis of NSTEACS on chronic P2Y12 receptor inhibitor therapy were included at 104 hospitals in China from November 2014 to December 2019. Univariable and multivariable Cox proportional hazard models were performed to compare the effect between patients with and without reloading. In Kaplan–Meier curves, the lower cumulative hazard of MACE could be identified (Log-rank test, P=0.007) in reloading group patients. In the unadjusted Cox regression model, reloading P2Y12 receptor inhibitors was associated with a decreased risk of all-cause mortality (HR, 0.37; 95% CI, 0.14–0.94; P=0.036). Reloading of P2Y12 receptor inhibitors was associated with a decreased risk of MACE in most of the subgroups.

**RESULTS** Among the NSTEACS patients on long-term P2Y12 receptor inhibitor therapy who were received P2Y12 receptor inhibitor reloading were younger and had fewer comorbid conditions. Reloading P2Y12 receptor inhibitors had lower risk of MACE (0.51 vs. 1.42%, P=0.007), as well as all-cause death (0.36 vs. 0.99%, P=0.028) and myocardial infarction (0.15 vs. 0.50%, P=0.028), however the risks of major bleeding (0.15 vs. 0.35%, P=0.234) were not significantly different between patients with and without reloading. In Kaplan–Meier curves, the lower cumulative hazard of MACE could be identified (Log-rank test, P=0.007) in reloading group patients. In the unadjusted Cox regression model, reloading P2Y12 receptor inhibitors was associated with a decreased risk of all-cause mortality (HR, 0.37; 95% CI, 0.14–0.94; P=0.036). Reloading of P2Y12 receptor inhibitors was associated with a decreased risk of MACE in most of the subgroups.

**CONCLUSIONS** The NSTEACS patients receiving long-term P2Y12 receptor inhibitors therapy was associated with decreased risk of in-hospital major adverse cardiac events or all-cause mortality, and did not increase the risk of major bleeding. In the absence of ischemia between reloading of P2Y12 inhibitor and in-hospital outcomes. Survival curves of MACE and major bleeding were illustrated using Kaplan–Meier curves and compared employing log-rank tests.  

**GW33-e0183**

**The staged revascularization for chronic total occlusion in the non-IRA in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention (p-PCI).**

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**OBJECTIVES** Patients with ST-segment elevation myocardial infarction (STEMI) concomitant with chronic total occlusion (CTO) in the non-infarct-related artery (non-IRA) were associated with an increased mortality. Successful revascularization for CTO lesion in the non-IRA could improve clinical outcomes. The meta-analysis was performed to evaluate the effect of the staged revascularization for the CTO in the non-IRA of patients with STEMI treated with primary percutaneous coronary intervention (p-PCI).

**METHODS** Studies were searched in electronic databases from inception to June, 2021. The primary endpoint was the all-cause death, and the secondary endpoint was a composite of major adverse cardiac events (MACEs). Odds ratio (OR) was pooled with 95% confidence interval (CI) for dichotomous data. Kyoto Encyclopedia of Genes and Genomes (KEGG) was used to identify the MSSD and MCA L. By comparing FFR p with FFR d, the effect of MB on FFR was analyzed. “FFR=0.8” (i.e. ΔFFR=0.2) was selected as the cut-off point of FFR. There is a significant positive correlation between MB and myocardial ischemia. In addition, we further observed the influence of MCA L and MCA A on ΔFFR and the correlation between MCA L and MSSD.

**RESULTS** A total of 3324 enrolled patients, in-hospital all-cause mortality occurred in 150 patients (3.9%) and in-hospital MACES in 181 patients (5.4%). Patients with higher RAR value had higher incidences of in-hospital all-cause mortality and in-hospital MACES (P=0.001). Multivariate logistic regression showed that the higher RAR was associated with a higher risk of in-hospital all-cause mortality [adjusted odds ratio (OR) 2.72, 95% confidence interval (CI) 1.47–5.03, P=0.001] and in-hospital MACES (adjusted OR 1.91, 95% CI 1.18–3.10, P=0.009). Receiver operating characteristic curve analysis indicated that RAR could accurately predict in-hospital all-cause mortality [area under the curve (AUC)=0.718, 95% CI 0.637–0.791] and the in-hospital MACES (AUC=0.672, 95% CI 0.631–0.712). The optimal statistical cutoff point of RAR was 4.429 by using the Youden index.

**CONCLUSIONS** RAR, as a novel and convenient predictor, was an independent predictor of in-hospital all-cause mortality and in-hospital MACES in patients with STEMI undergoing PCI.

**GW33-e0235**

**A novel predictor of the outcomes in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: random blood glucose to albumin ratio.**

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**OBJECTIVES** Random blood glucose and albumin are easily accessible, both of which are indicators of diabetes mellitus and malnutrition, respectively. However, the predictive value of random blood glucose to albumin ratio (RAR) for clinical adverse outcomes in patients with ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI) remains unclear.

**METHODS** Patients with STEMI undergoing PCI were enrolled from 2010 to 2019. These patients were categorized into 3 groups according to the RAR value quantiles (Q1, Q2 and Q3). The primary outcome was in-hospital all-cause mortality. The secondary outcomes were in-hospital major adverse cardiac events (MACES).  

**RESULTS** Of the 3324 enrolled patients, in-hospital all-cause mortality occurred in 150 patients (3.9%) and in-hospital MACES in 181 patients (5.4%). Patients with higher RAR value had higher incidences of in-hospital all-cause mortality and in-hospital MACES (P=0.001). Multivariate logistic regression showed that the higher RAR was associated with a higher risk of in-hospital all-cause mortality [adjusted odds ratio (OR) 2.72, 95% confidence interval (CI) 1.47–5.03, P=0.001] and in-hospital MACES (adjusted OR 1.91, 95% CI 1.18–3.10, P=0.009). Receiver operating characteristic curve analysis indicated that RAR could accurately predict in-hospital all-cause mortality [area under the curve (AUC)=0.718, 95% CI 0.637–0.791] and the in-hospital MACES (AUC=0.672, 95% CI 0.631–0.712). The optimal statistical cutoff point of RAR was 4.429 by using the Youden index.

**CONCLUSIONS** RAR, as a novel and convenient predictor, was an independent predictor of in-hospital all-cause mortality and in-hospital MACES in patients with STEMI undergoing PCI.

**GW33-e0236**

**No myocardic ischemia induced by myocardic bridge in resting-state confirmed by fractional flow reserve.**

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**OBJECTIVES** Studies have found that myocardic bridge (MB) is associated with atherosclerosis and myocardic ischemia. However, the vast majority of patients may have no symptom.

**METHODS** Thirty-nine patients with MB in the left anterior descending coronary artery confirmed by coronary computed tomography angiography were recruited. Hyperemic proximal FFR (FFR p) and distal FFR (FFR d) of MCA were measured by pressure wire, and then the degree of FFR (FFR p−FFR d)/ΔFFR was calculated. Quantitative coronary angiography (QCA) was used to identify the MSSD and MCA L. By comparing FFR p with FFR d, the effect of MB on FFR was analyzed. “FFR=0.8” (i.e. ΔFFR=0.2 (1−0.8)) was taken as the cutoff of myocardic ischemia to explore the correlation between MB and myocardic ischemia. In addition, we further observed the influence of MCA A and MSA D on ΔFFR and the correlation between MCA L and MSSD.

**RESULTS** FFR p was significantly lower than FFR d (P<0.01). However, ΔFFR was distinctly lower than 0.20 (P<0.01). Neither MCA A nor MSA D has correlation with ΔFFR. There is a significant positive correlation between MSSD and MCA L.

**CONCLUSIONS** Although MB causes a significant decrease in FFR, no ischemia is induced. ΔFFR is independent of both MCA L and MSSD. So it can be got the conclusion that maybe no treatment is necessary for MB itself.
CONCLUSIONS Segmental niMW is correlated with segmental MVP in STEMI patients who underwent primary PCI. Furthermore, sMWE and MVP have independent prognostic value in predicting segmental recovery, and sMWEs provide incremental prognostic value over MVP. These noninvasive echocardiographic parameters may improve the evaluation of myocardial viability and prognosis in these patients.

GW33-e0263
Construction and verification of the nomogram model for major adverse cardiovascular events risk after PCI in patients with NSTEMI
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OBJECTIVES Clinically, patients with NSTEMI have a higher risk of major adverse cardiovascular events (MACE) after PCI. Therefore, we construct a nomogram model for MACE risk after PCI in patients with NSTEMI, and evaluate its discrimination and consistency.

METHODS This study involved 653 patients with NSTEMI who underwent PCI in the First Affiliated Hospital of Xinjiang Medical University from June 2017 to April 2021. MACE was defined as cardiovascular death, cardiovascular readmission, heart failure, acute myocardial infarction, stroke and all-cause death. According to the occurrence of MACE after PCI, the patients were divided into the MACE patients (21 patients) and non-MACE patients (632 patients). The clinical data of patients were collected, and univariate analysis and multivariate Logistic regression analysis were used to explore the related influencing factors of MACE in NSTEMI patients. The determined influencing factors were introduced into R 4.1.3 software to build a nomogram model to predict the risk of postoperative MACE in NSTEMI patients. Receiver operating character curve (ROC) was used to analyze the discrimination of the nomogram model, and the calibration curve and the Hosmer-Lemeshow goodness-of-fit test were used to evaluate the consistency.

RESULTS Multivariate Logistic regression analysis showed that age [OR=4.432, 95% CI (3.661, 5.131)], Killip score [OR=3.894, 95% CI (3.366, 5.131)], Gensini score [OR=6.014, 95% CI (6.010, 6.019)], Timi score [OR=3.894, 95% CI (3.366, 5.131)] were the influencing factors of MACE after PCI in patients with NSTEMI (P<0.05). Based on the results of multivariate Logistic regression analysis, a nomogram model was constructed to predict the risk of MACE after PCI in patients with NSTEMI. The area under curve of nomogram model in predicting the MACE after PCI in patients with NSTEMI was 0.896 [95% CI (0.837, 0.934)]. The calibration curve of the nomogram model for predicting the risk of MACE after PCI in patients with NSTEMI was basically consistent with the actual curve, and the Hosmer-Lemeshow goodness of fit showed that x²=5.778, P=0.336.

CONCLUSIONS Age, Killip score, Gensini score, Grade score and Timi score are the influencing factors of MACE after PCI in patients with NSTEMI. In this study, the nomogram model for MACE risk after PCI in patients with NSTEMI was constructed based on the above 5 factors and has good discrimination and consistency.

GW33-e0271
Observation of acute and chronic injury of radial artery after transradial intervention
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OBJECTIVES Used OCT to observe acute and chronic injury of radial artery after first and repeat transradial intervention in the same patient.

METHODS A total of 51 patients who underwent repeat OCT guided transradial intervention from January 2016 to 2021 were divided into a first-time group and a repeat group according to the number of treatments. The differences of acute injuries (intimal tear, dissection, perforation, thrombosis and spasm) and chronic injuries (LN, IER, ITI) between the two groups and the differences between each segment after two operations were compared.

RESULTS There was no statistically significant difference in the incidence of acute injuries between the first and repeated group (21.2% vs 21.1%, 7 vs 10.5%, 6.4 vs 4.3%, 80.7 vs 75.4%), and there is no significant difference between the paragraphs. The repeated group LN, IER, ITI were higher than the first group. Moreover, the luminal stenosis in the sheath free area was significantly higher than that in the sheath area.

CONCLUSIONS Repeat transradial interventions had no significant effect on the occurrence of acute damage, and there was no significant difference in the incidence of acute injury between segments transradial intervention leads to intimal thickening and luminal narrowing of the radial artery with a more prominent sheath free zone.
GWS3-e0276
Digital therapy for rest heart rate control in coronary artery disease: a parallel-group, single-blind, randomised controlled trial
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OBJECTIVES The mobility and mortality of coronary artery disease (CAD) is rapidly increasing in China but access to secondary prevention remains low. Rest heart rate (RHT) is closely related to mortality in patients with CAD. In this study, we aimed to assess the digital therapy for rest heart rate in CAD patients (DIRECT-CAD) from a smartphone-based secondary prevention mini-program delivered via the social media platform WeChat.

METHODS In this parallel-group, single-blind, randomised controlled trial, we recruited patients aged 18 years or older with coronary artery disease who had received percutaneous coronary interventions from Beijing Tsinghua Changgung Hospital in Beijing, China. Participants were randomly assigned (1:1) by block randomisation to either a digital therapy programme or to usual care. In the DIRECT-CAD group, participants received comprehensive secondary prevention via WeChat. The usual care group received standard outpatient cardiology follow-up but without formal secondary prevention. Assessments were done at baseline, 1 month, 3 months, and 6 months. The primary outcome was a change in rest heart rate baseline, measured by office and family rest heart rate at 6 months.

RESULTS Between October 1, 2020, and Feb 1, 2021, 302 patients (mean age 60 ± 10 years, of whom 52 (17.2%) were female and 250 (82.8%) were male, were recruited and subsequently randomly assigned to DIRECT-CAD (n=151) or usual care (n=151). The improvement in rest heart rate at 6 months was significantly greater in the DIRECT-CAD group (from 72 ± 4 bpm at baseline to 64 ± 4 bpm than in the control group (from 72.4 ± 8 bpm at baseline to 70.8 ± 8 bpm).

CONCLUSIONS DIRECT-CAD was found to be a secondary prevention service model with high efficacy and accessibility and to be easy to use. These results justify the implementation of similar models of care on a broader scale.

GWS3-e0278
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
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OBJECTIVES The pandemic of COVID-19 has affected millions of patients and changed management strategies of various diseases. There is no large-scale data reporting clinical characteristics and outcomes of STEMI patients in low risk area during COVID-19 pandemic. To determine whether the pandemic of coronavirus disease 2019 (COVID-19) may affect clinical outcome of STEMI patients in North of 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 (PCI) 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 our study. Of note, group 2020 tended to have longer door-to-wire crossing time (206.5 ± 118 vs. 92 ± 73, P=0.003) and total delay time (from symptoms to wire crossing time) (223 ± 133 vs. 173 ± 150, P=0.003), vs. group 2019. There was 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 (33.3%) vs. 21 (41.1%), P=0.60). However, the rate of left ventricular aneurysm was significantly increased in group 2020 (27.45 ± 5.1%, P=0.006) compared with 2019.

CONCLUSIONS COVID-19 may delay the treatment time of PCI for STEMI patients, but no significant difference was observed on clinical outcome.

GWS3-e0295
Prognostic impact of stress hyperglycemia ratio in acute myocardial infarction patients with and without diabetes mellitus: insights from the NOAFCAMI-SH registry
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OBJECTIVES Stress hyperglycemia ratio (SHR) is associated with increased in-hospital morbidity and mortality in patients with acute myocardial infarction (AMI). We aimed to investigate the impact of stress hyperglycemia on long-term mortality after AMI in patients with and without diabetes mellitus (DM).

METHODS We included 2089 patients with AMI between February 2014 and March 2018. SHR was measured with the fasting glucose divided by the estimated average glucose derived from glycosylated hemoglobin (HbA1c). The primary endpoint was all-cause death.

RESULTS Of 2089 patients (mean age: 65±7.14 ± 4.76%, 76.7% were men), 796 (38.1%) had DM. Over a median follow-up of 2.7 years, 141 (6.7%) and 152 (7.2%) all-cause deaths occurred in the diabetic and non-diabetic cohorts, respectively. Compared with patients with low SHR (<1.24 in DM; <1.14 in non-DM), the hazard ratios and 95% confidence intervals for those with high SHR (2.14 in DM; 2.14 in non-DM) for all-cause mortality were 2.23 (1.34–3.68) and 1.79 (1.15–2.87); for cardiovascular mortality were 2.42 (1.63–3.51) and 2.10 (1.32–3.35) in DM and non-DM subjects, respectively. The mortality prediction was improved in the diabetic individuals with the incorporation of SHR into the Global Registry of Acute Coronary Events (GRACE) score, showing an increase in a continuous net reclassification index of 0.184 (95% CI: 0.003–0.356) and an absolute integrated discrimination improvement of 0.014 (95% CI: 0.002–0.026).

CONCLUSIONS The improvement in the prediction of long-term mortality beyond the GRACE score indicates the potential of SHR as a biomarker for post-MI risk stratification among patients with DM.

GWS3-e0303
Smoking and outcomes following personalized antiplatelet therapy in stable coronary artery disease patients: a substudy from the randomized PATH-PCI trial
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OBJECTIVES Prior studies have suggested better outcomes in stable coronary artery disease (SCAD) patients undergoing PCI who received personalized...
antiplater therapy (PAT). Smoking is a high-risk factor for poor prognosis in CAD. However, it is unknown whether smoking affects the safety and efficacy of PAT.

METHODS The PATH-PCI was a prospective, randomized, open-label trial. SCAD patients after PCI were randomized to either a standard group or a personalized group guided by a novel platelet function test. We evaluated net benefit, and adverse events of NSTEMI 180 days after the primary endpoint.

RESULTS Of 2.285 randomized SCAD patients, 1,170 (51.2%) patients were smokers. For NACES and major bleeding, we found no difference between the groups in smokers or non-smokers (P=0.05). Compared with SAT, PAT reduced the percentage of MACCEs in smokers (HR=0.513, P=0.012) and nonsmokers (HR=0.495, P=0.011). We only find PAT reduced the percentage of MACCEs in nonsmokers (HR=0.565, P=0.006). The Cox hazard model suggested that PAT was an independent protective factor against MACCEs.

CONCLUSIONS PAT is effective in SCAD patients who have undergone PCI, regardless of smoking status. PAT may be an independent protective factor against MACCEs. Smoking weakens the efficacy of PAT and has no impact on the safety of PAT.

GW33-e0333 Polymorphisms of rs55796564 in the CD74 gene are associated with myocardial infarction

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OBJECTIVES CD74 is involved in innate immunity, and it is a receptor of macrophage migration inhibition factor. Basic studies show that CD74 participates in myocardial infarction (MI) in mice. However, whether the CD74 gene is associated with MI in clinics is still unclear.

METHODS A case-control study was designed to investigate the relationships between the tag single nucleotide polymorphisms (tagSNPs) of the CD74 gene and MI in the Xinjiang population, China. Two tag SNPs (rs55796564, rs55796563) of the CD74 gene were genotyped in 996 MI patients and 998 healthy controls by an improved multiplex ligation detection reaction (iMLDR) technique.

RESULTS Comparing the differences in baseline characteristics between the MI and control groups, no significant differences were observed in age, sex, waist circumference, and systolic blood pressure (all P>0.05). And blood glucose, diastolic blood pressure, and body mass index (BMI) had differences between the two groups (all P=0.05). The distributions of rs55796564 genotype in each phenotype and dominant model were significantly different between the groups (all P=0.05). The CT+TT genotype of rs55796564 was associated with MI (odds ratio (OR) 1.29, confidence interval (CI) 1.06–1.57, P=0.011). Further, the CT+TT genotype of rs55796564 was still an independent risk factor for MI after adjusting for age, BMI, hypertension, and diabetes (odds ratio (OR) 1.30, confidence interval (CI) 1.01–1.67, P=0.045). In addition, we observed that the number of monocytes in blood was higher in the CT+TT genotype than the CC genotype (p=0.020, 1.40 (10^11)L vs. 0.47±0.32 (10^11)L, P=0.05).

CONCLUSIONS The CT+TT genotype of rs55796564 in the CD74 gene was a novel independent risk factor for MI.

GW33-e0337 Prognostic value of malnutrition using geriatric nutritional risk index in patients with NSTEMI after percutaneous coronary intervention

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METHODS Baseline malnutrition risk was determined in 756 patients with NSTEMI after PCI in this study. All patients were divided into three groups according to 3 categories of the geriatric nutritional risk index (GNRI): moderate to severe, GNRI of <92 (n=179); low, GNRI of 92–98 (n=83); and absence of risk, GNRI of ≥98 (n=494). The primary endpoint was target lesion failure (TLF), including cardiac death, stent failure, nonfatal myocardial infarction, and stroke. Long-term MACE were cardiac death, stent restenosis, and target vessel revascularization during the 1-year follow-up period.

RESULTS Average age in this study was 64.25±14.80 years old. More than half of patients were at risk of malnutrition (moderate to severe: 23.71; low: 30.8; and absence of risk: 45.49%). Compared to those with absent risk for malnutrition, moderate to severe risk was associated with significantly increased risk for in-hospital MACE [hazard ratio (HR): 2.70, 95% confidence interval (CI): 1.78 to 4.97, P=0.0020] after adjustment for baseline variables. Moreover, over a median follow-up of 1 year, addition of the GNRI score significantly raised the predictive value for the all-cause death (0.313, P=0.003 and 0.0042, P=0.011, NRI and IDI respectively). Long-term MACE (0.478, P=0.001 and 0.004, NRI and IDI respectively) as compared to traditional factors.

CONCLUSIONS Malnutrition assessed by the GNRI score on admission was an independent predictor for MACE in NSTEMI patients after PCI during the hospitalization. Addition of the GNRI score to the existing risk prediction model significantly increased the predictive ability for long-term MACE in NSTEMI patients after PCI.

GW33-e0350 Geriatric nutritional risk index: a new index for predicting the clinical outcomes in patients with non-ST-elevation myocardial infarction after percutaneous coronary intervention

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OBJECTIVES Malnutrition is associated with poor prognosis in a wide range of chronic illnesses, however, the impact of malnutrition on long-term outcomes of patients with non-ST-elevation myocardial infarction (NSTEMI) after percutaneous coronary intervention, is not known. The purpose of the study was to assess the geriatric nutritional risk index in predicting clinical outcomes in NSTEMI patients after percutaneous coronary intervention (PCI).

METHODS Baseline malnutrition risk was determined in 655 patients with NSTEMI after PCI in this study. All patients were divided into 3 groups according to 3 categories of the GNRI: moderate to severe, GNRI of <92 (n=83); low, GNRI of 92–98 (n=167); and absence of risk, GNRI of ≥98 (n=405). The primary endpoint was all-cause mortality and the secondary endpoint was major adverse cardiovascular events (MACE).

RESULTS Average age in this study was 65.32±9.97 years old. More than one-third of patients were at risk of malnutrition (moderate to severe: 12.7%; low: 25.5%; and absence of risk: 61.8%). Over a median follow-up of 1.2 years, compared to those with absent risk for malnutrition, moderate to severe risk was associated with significantly increased risk for the all-cause death (HR: 2.79, 95% CI 1.43–4.87, P=0.005), cardiovascular death (HR: 3.99, 95% CI 2.42–6.77, P<0.01) and MACE (HR: 1.46, 95% CI 1.09–2.93, P=0.05) after adjustment for baseline variables.

CONCLUSIONS Malnutrition assessed by the GNRI score on admission was an independent predictor for adverse cardiovascular events in NSTEMI patients after PCI.

GW33-e0356 Predictive value of SYNTAX score II and triglyceride glucose index for long-term prognosis in patients with acute ST segment elevation myocardial infarction with multivessel disease

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OBJECTIVES The purpose of this study is to explore the predictive value of SYNTAX-II score combined with TyG index for adverse cardiovascular events in patients with acute ST segment elevation myocardial infarction with multi vessel disease after percutaneous coronary intervention (PCI).

METHODS A retrospective cohort study was conducted on 3145 patients who underwent coronary intervention in the heart center of the First Affiliated Hospital of Xinjiang Medical University from January 2014 to January 2020. The primary endpoint was target vessel lesion failure (TVL), including cardiac death, target vessel myocardial infarction, and ischemia driven target lesion revascularization. Secondary endpoints included stent thrombosis and major adverse cardiac events (MACE), defined as all-cause death, myocardial infarction, and all revascularization.

RESULTS During the 24-month follow-up period, the incidence of primary endpoint events increased significantly with the increase of SYNTAX-II score and TyG index (P<0.05). Kaplan Meier analysis showed that patients with high TyG index had the lowest survival rate of events (P<0.001). Multivariate analysis showed that age, male, target vessel disease after percutaneous coronary intervention, DM and diabetes, low ejection fraction, creatinine clearance, TyG index and SYNTAX score were independent predictors of all-cause mortality, and TyG index and SYNTAX-II score were independent predictors of TVL (HR=1.616 and 1.165, 95% CI 1.201–2.176 and 1.020–1.046, P<0.05). The predictive value of TyG index combined with SYNTAX-II score was significantly higher than that of SYNTAX-II score alone (AUC 0.513 vs. 0.519, P=0.729, P<0.001). Hosmer lemeshow goodness of fit test was used to show that χ²=5.364, P=0.718. After TyG index was included, the net reclassification
GW33-e0357 Stress hyperglycemia ratio combined with plaque characteristics as a novel biomarker for cardiovascular outcomes after percutaneous coronary intervention in ST-elevated myocardial infarction patients: an intravascular optical coherence tomography study
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OBJECTIVES Stress hyperglycemia is a powerful predictor of adverse outcomes in patients with acute myocardial infarction (AMI). However, the relationship between SHR and the morphology and characteristics of vulnerable plaques in patients with acute myocardial infarction (AMI) has not been fully studied.

METHODS Nine hundred forty-six patients with acute myocardial infarction diagnosed in the First Affiliated Hospital of Xinjiang Medical University from January 2017 to January 2019 were included in the retrospective study. Optical coherence tomography was performed before intervention. All patients were divided into three groups according to the third quartile of SHR (below, medium, and high SHR). Patients with plaque rupture (PR) and plaque erosion (PE) were divided into three groups across the SHR tertiles. Baseline clinical data and culprit plaque characteristics were compared between the three groups, and all patients were followed up for major adverse cardiovascular events (MACE) and all-cause mortality. MACEs were defined as a composite of all-cause death, myocardial infarction (MI) recurrence, and ischemic stroke.

RESULTS In fully adjusted analyses, the middle tertile of SHR was significantly associated with greater rates of MACEs in patients with PR but not in those with PE (HR: 2.01, 95% CI: 1.25–3.88, P=0.015). Comparisons indicated a significantly higher HR for MACEs in patients in the middle tertile of SHR than in those in the lowest tertile of SHR after full additional adjustment (HR: 2.31, 95% CI: 1.10–4.67, P=0.016). However, being in the high tertile of SHR independently and significantly increased the risk of major bleeding events among patients with PE (HR: 1.65, 95% CI: 1.21–2.26, P=0.016). The area under the receiver operating characteristic curve for predicting MACEs to evaluate the diagnostic value of the SHR index combined with the morphologic characteristics of plaque after full adjustment was 0.881 (sensitivity=81.74%, specificity=78.04%, cut-off level=0.70). Kaplan–Meier curves were generated for the cumulative incidence of MACEs for up to a median of 2 years stratified by tertiles of SHR among the PR and PE subgroups. Among patients with PR, there were significant differences among the tertiles of SHR (P=0.015). The area under the receiver operating characteristic curve for predicting MACEs was significantly higher for the SHR group compared with the PR group (P=0.016).

CONCLUSIONS Microstructural OCT features of culprit lesions in combination with the SHR can be used in clinical practice to support risk stratification and predict adverse events in patients with STEMI.

GW33-e0358 IVUS combined with SYNTAX score to guide revascularization of multivessel coronary artery lesions
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OBJECTIVES This study applied IVUS calculated by machine learning algorithm to explore the predictive effect of functional SYNTAX score calculated based on IVUS algorithm on the clinical prognosis of patients with three branches of disease.

METHODS Nine hundred forty-six patients with coronary heart disease diagnosed by invasive coronary angiography (defined as three vessel stenosis >50%) from a single center were included retrospectively, excluding patients with previous revascularization, previous coronary occlusion and left main artery disease. Two independent clinicians calculated the SYNTAX score of the above patients, and according to the SYNTAX score, the patients were divided into low SY group (<22), medium SY group (22–40) and high SY group (>40). SYNTAX score was calculated only for patients with lesions with minimum lumen area <4.0 mm². The primary clinical endpoint was defined as a composite endpoint composed of all-cause death, nonfatal myocardial infarction and emergency revascularization.

RESULTS After calculating the IVUS threshold by machine learning, 8.4% (79/946) of the patients were reclassified to the low-risk group. During the median follow-up period of 24 months, the overall MACE rate of the study patients was 30.3%. Compared with the low SY group, the incidence of MACE in the medium and high SY groups was significantly higher (18.0% [88/490] vs. 6.2% [31/515] and 6.9% [95/1385], respectively, P<0.001). Meanwhile, ROC analysis showed that the SYNTAX score included in IVUS could better predict mACE than that based on a single SYNTAX score (IVUS+SS: AUC=0.72 vs. SS:AUC=0.61, P=0.01).

CONCLUSIONS Using machine learning algorithm to calculate IVUS and apply it to SYNTAX score calculation is a better predictor of mACE incidence in patients with three vessel lesions. It was found that compared with the traditional SYNTAX score, it can better predict the occurrence of MACE events, and may change the revascularization strategy of these patients.

GW33-e0393 Feasibility exploration of different antiangina regimens using electronic Patient Reported Outcomes (ePRO) tool: a multicenter, prospective study (GREAT)
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OBJECTIVES Angina pectoris (AP) is typically associated with myocardial ischemia. Patients with AP present with chest discomfort, or discomfort in the neck, shoulders or arms after physical activities or emotional stress. Insufficient reporting of angina symptoms is common in clinical practice, which may lead to under treatment and decreased quality of life for patients with AP. The registry study (GREAT) is an ongoing study that aims to evaluate the feasibility of using the electronic Patient-Reported Outcome (ePRO) tool via Wexin to monitor the efficacy and safety of different antianginal regimens in patients with AP in real-world clinical practice.

METHODS GREAT is a multicenter, prospective, observational study to explore the Chinese angina disease cohort and compare the efficacy of different antiangina regimens in patients with AP. Two natural cohorts, the nico-randil group and non-nicorandil group, will be formed based on the data of Chinese patients with AP registered in 10 hospitals. The baseline information of patients will be recorded and patients will be followed up every 3 months during the 12 months after enrollment. The visits at 3, 6 and 9 months will be conducted in the form of ePRO and telephone, and the visit at 12 months will be conducted on site. Patients are required to fill in the patient diary records (weekly) during the course of the study. Statistical analysis of efficacy and safety is based on the full analysis set and safety analysis set. Other statistical analyses, quality control and bias control are also to be conducted. Trial registration number: NCT05050773.

RESULTS Our study has enrolled 628 patients between September 2021 and February 2022 in 10 hospitals and the enrollment is ongoing at the time. The baseline data at present showed that the average Seattle Angina Questionnaire wouldn’t be gathered through the ePRO tool. The primary endpoint is the changes of SAQ at 3, 6, and 9 months, changes in the retest results of vascular stenosis indicating at 12 months, and medication compliance evaluated by proportion of days covered.

CONCLUSIONS This will be the first research exploring the efficacy and safety of AP regimen in real-world settings via ePRO in China. The results from this study may provide new perspective and potential of ePRO in clinical practice.

GW33-e0413 The predictive value of D-dimer for hospital death in patients with acute myocardial infarction
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OBJECTIVES To evaluate the predictive value of D-dimer for hospital death in patients admitted with acute myocardial infarction (AMI).

METHODS We summarized 167 cases admitted to the Department of Cardiology of our hospital from January 2012 to April 2018, who were diagnosed and died due to AMI. Six hundred seventy-four patients discharged with similar ages and gender ratios at the same time were selected as the control group. Basic characteristics were collected, including age, gender, grade of cardiac function (Killip classification), the application of aortic balloon counter pulsation, and the results of the examination at baseline, which included white blood cell count, fasting blood glucose, D-dimer, creatinine, uric acid, blood lipid, high-sensitivity C-reactive protein, creatine kinase isoenzyme and myocardial troponin, peak value of N terminal brain natriuretic peptide precursor, left
ventricular ejection fraction (2-D), and other indicators. The receiver operating characteristic (ROC) curves were plotted according to the results of multivariate logistic regression analyses, and the correlation between D-dimer and hospital death of AMI was analyzed.

RESULTS Creatine kinase isoenzyme, D-dimer, white blood cells, fasting blood glucose, creatinine, uric acid, myocardial troponin and N terminal brain natriuretic peptide or cardiac were all significantly higher in the death group than the control group (P<0.01). Yet left ventricular ejection fraction (2-D) decreased significantly in the death group (P<0.01). The level of D-dimer was predictive for hospital death with higher accuracy (AUC=0.811) in AMI than the level of creatine kinase isoenzyme (AUC=0.644).

CONCLUSIONS The level of D-dimer can predict in-hospital mortality among patients admitted with AMI.

GW33-e0418 Predictive value of the fibrinogen to γ-glutamine transferase ratio in long-term prognosis in patients with coronary heart disease: a retrospective cohort study
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OBJECTIVES The ratio of fibrinogen to γ-glutamine transferase (FGR) was used to predict long-term prognoses in patients with coronary heart disease (CHD).

METHODS A total of 5638 patients with CHD who were hospitalized from January 2008 to December 2016 were retrospectively enrolled as the study subjects. With a mean follow-up time of 35.92±2.5 months, the follow-up endpoints was the major cardiac and cerebrovascular adverse events (MACCEs). According to the ROC curve, the optimal FGR cut-off value was determined and divided into high- and low-FGR groups. Statistical methods were used to compare the differences between the two groups and their prognoses to determine whether FGR can be used as a predictor of prognosis in patients with CHD.

RESULTS The optimal cut-off value was determined via a ROC analysis (FGR=1.12, AUC=0.554, P=0.002, 95% CI [0.520–0.588]), and subjects were divided into high- and low-FGR groups. Statistical methods were used to compare the differences between the two groups and their prognoses to determine whether FGR can be used as a predictor of prognosis in patients with CHD.

RESULTS The optimal cut-off value was determined via a ROC analysis (FGR=1.12, AUC=0.554, P=0.002, 95% CI [0.520–0.588]), and subjects were divided into high- and low-FGR groups. Statistical methods were used to compare the differences between the two groups and their prognoses to determine whether FGR can be used as a predictor of prognosis in patients with CHD.

CONCLUSIONS High FGR can increase the risk of MACCEs in patients with CHD; additionally, it can be used as a new biomarker for long-term prognosis in CHD patients.

GW33-e0465 Left atrial function index predicts poor outcome in STEMI patients treated with percutaneous coronary intervention
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OBJECTIVES The prognostic value of left atrial function index (LAFI) in acute ST segment elevation myocardial infarction (STEMI) patients treated with percutaneous coronary intervention (PCI) is unknown. This study sought to determine whether LAFI predicts cardiovascular events in STEMI patients treated with PCI.

METHODS Patients with newly diagnosed STEMI and treated with PCI in Hunan Provincial People's Hospital from March 2020 to October 2020 were prospectively enrolled. All patients underwent transthoracic echocardiography at baseline and follow-up. The endpoint cardiovascular events include re-hospitalization due to unstable angina, non-fatal myocardial infarction, re-hospitalization due to heart failure and cardiovascular death.

RESULTS A total of 156 STEMI patients treated with PCI were studied with a median follow-up of 14 months. Forty-eight patients had endpoint cardiovascular events. The univariate analysis revealed that Type 2 diabetes mellitus (T2DM), White Blood Cells (WBC), N-terminal prohormone brain natriuretic peptide (NT-proBNP), Killip Classification, and variables obtained from echocardiography were significant predictors of events (all P<0.05). However, Multivariate Cox analysis demonstrated that only LAFI (HR, 0.90, 95% CI, 0.88–0.95, P<0.001) was independently predictive of cardiovascular events in patients with STEMI. Furthermore, LAFI owned the highest area under the receiver operating characteristic curve (AUC) predicting the end point cardiovascular events, with AUC of 0.90 (95% CI 0.84 to 0.94).

CONCLUSIONS LAFI is a strong and independent predictor of cardiovascular events in STEMI patients treated with PCI.

GW33-e0509 A novel simply calculated nutritional index for adverse outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention
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OBJECTIVES Malnutrition is a well-known risk factor for adverse outcomes in patients with cardiovascular disease. Few studies have applied the triglycerides, cholesterol, and body weight index (TCBI) in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary balloon angioplasty (pPCI). This study aimed to assess the association between admission TCBI and long-term adverse outcomes in patients with STEMI undergoing pPCI.

METHODS Six hundred fifty-seven patients with STEMI undergoing pPCI at the China-Japan Friendship Hospital from January 2015 to December 2018 were enrolled. The TCBI was calculated using serum total cholesterol (TC), triacylglycerides (TG), and body weight (BW) using the following formula: TCBI=TC (mg/dL)/BW (kg)/TC (mg/dL)=TC (mg/dL)/BW (kg). Subjects were divided into four groups according to quartile levels of the admission TCBI: TCBI<969.8 (quartile 1), 966.5–1566.3 (quartile 2), 1566.3–2650.2 (quartile 3), and TCBI>2650.2 (quartile 4). The primary outcome was long-term major clinical adverse events (MACE), including cardiac death, non-fatal myocardial infarction, non-fatal ischemic stroke, and peripheral artery revascularization. Multivariable Cox regression analyses were conducted to assess the relationship between admission TCBI and MACE.

RESULTS Among 657 enrolled patients, the mean age was 60.1±13.2 years, and 514 (78.1%) were male. During a median follow-up of 4.5 years, 105 (16.0%) MACES were recorded. The incidence of MACE increased from the highest quartile of TCBI to the lowest quartile of TCBI (3.6 vs. 14.5 vs. 20.1 vs. 25.6%, P<0.001). The receiver operating characteristic curve analysis revealed that TCBI possessed excellent discrimination for predicting MACE (AUC 0.675, 95% confidence interval [CI] 0.624–0.726, P<0.001). Multivariable Cox analyses revealed that the lowest quartile of TCBI (compared with the highest quartile of TCBI) was independently associated with a significantly increased risk of MACE (hazard ratio 1.284, 95% CI 1.041–1.585, P=0.020).

CONCLUSIONS Our results demonstrated that TCBI might be useful for predicting adverse outcomes in patients with STEMI undergoing pPCI.

GW33-e0511 The prognostic value of admission mean platelet volume/platelet count ratio in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention
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2Graduate School of Peking Union Medical College, Chinese Academy of Medical Sciences and Peking University Medical College, Beijing 100029, China

OBJECTIVES Elevated mean platelet volume/platelet count ratio (MPR) has been demonstrated to be associated with short-term outcomes in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI). This study aimed to assess the association between admission MPR and long-term adverse outcomes in patients with STEMI undergoing pPCI.

METHODS We retrospectively evaluated 683 patients with STEMI undergoing pPCI at the China-Japan Friendship Hospital from January 2015 to December 2018. Patients were divided into two groups according to the admission MPR values with the optimal cutoff evaluated by receiver operator characteristic curve: MPR<0.048 (n=339) and MPR≥0.048 (n=344). The primary outcome was long-term major clinical adverse events (MACE) consisting of cardiac death, non-fatal myocardial infarction, and non-fatal ischemic stroke. Patients were further categorized into three groups by the tertile of admission MPR and divided into high- and low-MPR groups. Statistical methods were used to assess the association between admission MPR and long-term adverse outcomes in patients with STEMI undergoing pPCI.

RESULTS Among 683 enrolled patients, the mean age was 60.2±13.3 years, and 514 (78.1%) were male. During a median follow-up of 4.5 years, 195 (28.9%) MACEs were recorded. The univariate analysis revealed that Type 2 diabetes mellitus (P<0.048), Killip Classifi cation, and variables obtained from echo-cardiography were signifi  cant predictors of events (all P<0.05). However, Multivariate Cox analysis demonstrated that only MPR≥0.048 (n=339) and MPR<0.048 (n=344). The primary outcome was long-term major clinical adverse events (MACE) consisting of cardiac death, non-fatal myocardial infarction, and non-fatal ischemic stroke. Patients were further categorized into three groups by the tertile of admission MPR and divided into high- and low-MPR groups. Statistical methods were used to assess the association between admission MPR and long-term adverse outcomes in patients with STEMI undergoing pPCI.

RESULTS Among 683 enrolled patients, the mean age was 60.2±13.3 years, and 514 (78.1%) were male. During a median follow-up of 4.5 years, 94 (13.8%) MACEs were recorded. The receiver operating characteristic curve analysis revealed that admission MPR≥0.048 (n=339) and MPR<0.048 (n=344). The primary outcome was long-term major clinical adverse events (MACE) consisting of cardiac death, non-fatal myocardial infarction, and non-fatal ischemic stroke. Patients were further categorized into three groups by the tertile of admission MPR and divided into high- and low-MPR groups. Statistical methods were used to assess the association between admission MPR and long-term adverse outcomes in patients with STEMI undergoing pPCI.
CONCLUSIONS While MPR is found to increase the risk of long-term MACE and non-fatal re-infarction, it is not related to long-term cardiac mortality nor non-fatal ischemic stroke in patients with STEMI undergoing PCI.

RESULTS We found that CoQ10 level was significantly lower in MI patients than healthy volunteers. CoQ10 treatment significantly improve heart function and attenuated myocardial infarction injury and cardiac remodeling, consequently, patients with MI treated with CoQ10 significantly improved ejection fraction compared with control group post PCI, and the survival rate of CoQ10-treated mice was significantly higher than that of control mice post-MI. Mechanistically, flow cytometrical analysis showed that CoQ10 treatment suppressed recruitment of inflammatory neutrophils and macrophages into infarct myocardium post MI. Specifically, bone marrow derived inflammatory macrophage subtype (MHCI High/CCR2 +) was significantly suppressed by CoQ10. Additionally, we observed the level of IL-1β and ROS positive macrophages were remarkably decreased in the myocardium of CoQ10-treated mice. In vitro, CoQ10 significantly reduced the levels of IL-1β and ROS in PMACs after inflammatory stimulated. RNA sequence on PMACs stimulated by LPS and INF-γ showed that inflammatory response related genes and oxidative stress related genes were downregulated by CoQ10 treatment. Moreover, Western blotting and qRT-PCR shown the expression levels of NLRP3/IL-1β inflammasome pathway was significantly suppressed by CoQ10.

CONCLUSIONS CoQ10 could significantly improve cardiac function and survival rate and attenuate cardiac remodeling after MI partially by regulating oxidative stress response in macrophages and its downstream inflammatory response.

RESULTS Patients with acute coronary syndrome who were hospitalized in the Department of Cardiology of our hospital from October 2006 to September 2019 and underwent percutaneous coronary stent implantation were included in the study. They were divided into 1010 cases in the modeling group and 316 cases in the validation group. The incidence of composite end points was followed up. Univariate analysis, Pearson correlation analysis and Cox proportional hazards regression model were used to screen the independent predictors of poor prognosis of ACS patients after PCI, and the nomogram was established according to these factors.

CONCLUSIONS The nomogram of ACS patients with PCI constructed in this study can individually predict the risk of MACE, ACM, and provides an effective tool for predicting the long-term prognosis of ACS patients with PCI.

RESULTS After telephone follow-up, 164 ACS patients with PCI had adverse event (MACE) and 74 ACS patients with PCI had all cause mortality (ACM). The results of multivariate Cox regression analysis with MACE as the endpoint showed that age, Creatine Kinase-MB (CKMB), left ventricular ejection fraction (LVEF) and neutrophil to lymphocyte ratio (NLR) were independent predictors of MACE in ACS patients with PCI (P<0.05). The nomogram model had high predictive value for MACE in ACS patients with PCI (C-Index:0.78). The results of multivariate Cox regression analysis with ACM as the endpoint showed that age, CKMB, LVEF, NLR and monocyte count were independent predictors of ACM in ACS patients with PCI (P<0.05). The nomogram is established with these five variables. The nomogram model had high predictive value for ACM in ACS patients with PCI (C-Index:0.81).

CONCLUSIONS The nomogram of ACS patients with PCI constructed in this study can individually predict the risk of MACE, ACM, and provides an effective tool for predicting the long-term prognosis of ACS patients with PCI.

RESULTS We found that CoQ10 level was significantly lower in MI patients than healthy volunteers. CoQ10 treatment significantly improve heart function and attenuated myocardial infarction injury and cardiac remodeling, consequently, patients with MI treated with CoQ10 significantly improved ejection fraction compared with control group post PCI, and the survival rate of CoQ10-treated mice was significantly higher than that of control mice post-MI. Mechanically, flow cytometrical analysis showed that CoQ10 treatment suppressed recruitment of inflammatory neutrophils and macrophages into infarct myocardium post MI. Specifically, bone marrow derived inflammatory macrophage subtype (MHCI High/CCR2 +) was significantly suppressed by CoQ10. Additionally, we observed the level of IL-1β and ROS positive macrophages were remarkably decreased in the myocardium of CoQ10-treated mice. In vitro, CoQ10 significantly reduced the levels of IL-1β and ROS in PMACs after inflammatory stimulated. RNA sequence on PMACs stimulated by LPS and INF-γ showed that inflammatory response related genes and oxidative stress related genes were downregulated by CoQ10 treatment. Moreover, Western blotting and qRT-PCR shown the expression levels of NLRP3/IL-1β inflammasome pathway was significantly suppressed by CoQ10.

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CONCLUSIONS CoQ10 could significantly improve cardiac function and survival rate and attenuate cardiac remodeling after MI partially by regulating oxidative stress response in macrophages and its downstream inflammatory response.
patients was 67.6%. Being female and coronary microcirculation disorder may contribute to the development of supra-normal ejection fraction.

GW33-e0548
Real-world observational study of nicorandil combined with beta-blocker in Chinese patients with coronary heart disease
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OBJECTIVES Although coronary heart disease (CHD) remains the leading cause of mortality in China, the treatment strategies are still far from satisfactory. This study was aimed to evaluate the long-term potential of nicorandil combined with beta-blocker in Chinese patients with CHD.

METHODS The data of the CHD patients from three tertiary hospitals in central China was retrospectively reviewed between October 2009 and March 2020. The primary outcome was the rate of major adverse cardiovascular event (MACE) at 2.5 years, which was a composite outcome of stroke, myocardial infarction (MI) and all-cause mortality. The secondary outcomes were the rate of the separate events at 2.5 years. Inverse probability of treatment weighting (IPTW) method based on the propensity score was used to balance intergroup differences and the relationship between the treatment and events was further assessed by Cox proportional-hazards regression analysis.

RESULTS A total of 4669 patients treated with the combination of nicorandil and beta-blocker and 12,243 patients treated with beta-blocker alone were included in the study, respectively. The median follow-up time was 0.87 and 0.81 year for the combination and beta-blocker alone group, respectively. After IPTW for propensity score, the primary outcome showed that the cumulative MACE-free survival rate at 2.5 years was higher in the nicorandil and beta-blocker combination groups compared to beta-blocker alone group (77 vs. 68%). Cox regression analysis showed that the combination group was associated with a higher MACE-free survival (HR=0.86, 95% CI: 0.73–0.98; P<0.0001). The secondary outcome showed a higher stroke-free survival rates in the combination group (89 vs. 77%) at 2.5 years, while the other two events (MI and all-cause mortality) showed no difference between the two groups. Cox regression analysis also showed that the combination group was significantly associated with higher stroke-free survival (HR=0.49, 95% CI: 0.43–0.56; P<0.0001). Interaction analyses were performed for the following subgroups: age (<85 or ≥85 years), gender (male vs. female), coronary syndrome (ACS), smoking, drinking, revascularization, diabetes and hypertension, and showed a favorable consistency with the primary outcome.

CONCLUSIONS Treatment of nicorandil combined with beta-blocker is associated with less MACE and stroke in patients with CHD in the Chinese population.

GW33-e0569
Obstructive sleep apnea affects heart rate variability in patients with coronary artery disease: a cross-sectional study
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OBJECTIVES It is unknown how obstructive sleep apnea (OSA) affect coronary artery disease (CAD) in dynamic electrocardiogram, especially heart rate variability (HRV). We aimed to determine the association of OSA and HRV in patients with CAD.

METHODS Consecutive CAD patients from the Third Xiangya Hospital of Central South University were recruited. Patients were divided into two groups according to apnea-hypopnea index (AHI): OSA group (AHI≥15) and control group (AHI<15). Parameters of HRV from dynamic electrocardiogram including SDNN, rMSSD, pNN50, VLF, LF, HF/HF were analysed in different types of CAD and different period of time like wakefulness and sleep.

RESULTS Sixty-three eligible participants were enrolled finally, including forty-three in OSA and twenty in control. There were no significant differences between OSA and control group in parameters of HRV. While taking period of time into consideration, we found all parameters on OSA group were higher at night than in the daytime (SDNN 104.6 ± 60.3, P=0.031; rMSSD 60.2 ± 57.1, P=0.066; pNN50 121.2±9.8, P=0.157; TF 3544.5±2262.0, P=0.082; VLF 2692.1±1475.4, P=0.001; LF 575.7±384.5, P=0.005; HF 259.9±175.9, P=0.006; respectively) while in control group, the results were some kind of different even opposite. In different type of CAD, parameters of HRV were showed opposite trend. In angina type patients, HRV decreased in OSA group in most parameters (SDNN 130.8±80.3 vs. 123.17; rMSSD 65.40±55.29; pNN50 13.90 vs. 9.29; VLF 1509.96 vs. 1841.50; LF 484.87 vs. 353.26; HF 329.77 vs. 131.92; while in myocardial infarction patients, HRV was increased in OSA group in all parameters (SDNN 104.40 vs. 110.79; rMSSD 45.20 vs. 46.53; pNN50 6.80 vs. 12.26; VLF 1793.25 vs. 2553.27; LF 753.65 vs. 557.91; HF 168.99 vs. 302.55), even though there were no statistic significance.

CONCLUSIONS In CAD patients, OSA would influence the change of HRV from daytime to night and different types of CAD would be different in HRV when OSA happened.

GW33-e0597
Short-term exposure to traffic-related air pollution and STEMI events: insights into STEMI onset and related cardiac impairment
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OBJECTIVES Evidence on the impacts of traffic-related air pollution (TRAPE) on ST-segment elevation myocardial infarction (STEMI) events is limited. We aimed to assess the acute effects of TRAF exposure on the clinical onset of STEMI and related cardiac impairments.

METHODS We recruited patients who were admitted for STEMI and underwent primary percutaneous coronary intervention at Peking University Third Hospital between 2014 and 2018. Air pollutants indicators relevant to traffic-related air pollution were measured. Concomitantly, hourly concentrations of traffic pollutants were monitored throughout the study period, including fine particulate matter, black carbon (BC), particles in size ranges of 5–560 nm, oxides of nitrogen (NOX), nitrogen dioxide, and carbon monoxide.

RESULTS The mean (SD) age of participants was 62.4 (12.5) years. Daily average real-world observational study of nicotine and beta-blocker in Chinese patients with coronary heart disease
Yanping Guo, Zhaoshi Gao, Ruifeng Yang
Department of Cardiology, Peking University Third Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

OBJECTIVES Despite the WHO guidelines recommending the use of nicotine and beta-blocker in Chinese patients with CHD, Real-world observational study of nicorandil combined with beta-blocker in Chinese patients with CHD.

GW33-e0607
Reverse J-shaped association between estimated glomerular filtration rate and contrast-associated acute kidney injury in patients undergoing elective percutaneous coronary intervention
Man-Qing Luo, Li-Wei Zhang, Li-Chuan Chen, Kai-Yang Lin, Yan-Song Guo1
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OBJECTIVES Estimated glomerular filtration rate (eGFR) remains to be used routinely to assess glomerular filtration function in clinical practice. A decline in eGFR is confirmed as a significantly independent risk factor with contrast-associated acute kidney injury (CA-AKI), and closely associated with chronic kidney disease (CKD) progression and poor prognosis. Recent evidence has indicated that glomerular hyperfiltration increased the risk of kidney disease, however, the association between glomerular hyperfiltration and the risk of CA-AKI as well as long-term prognosis in patients undergoing elective percutaneous coronary intervention (PCI) remains unclear.

METHODS We retrospectively observed 6227 consenting patients undergoing elective PCI from January 2012 to December 2018 in a tertiary center. Serum creatinine was measured at admission and within 48 to 72 hours after contrast exposure. The GFR was calculated by 2011 CKD Epidemiology Collaboration (CKD-EPI) equation. CA-AKI was defined as an increase in serum creatinine ≥25% or 0.3 mg/dL within 48 h after contrast medium exposure. The relationships between eGFR levels and CA-AKI as well as long-term prognosis in patients undergoing elective percutaneous coronary intervention (PCI) remains unclear.

RESULTS Our findings extend current understanding that short-term exposure to higher levels of traffic pollution was associated with increased STEMI risks and exacerbated cardiac impairments, and provide evidence on traffic pollution control priority for protecting vulnerable populations who are at greater risks of cardiovascular events.
increased risk of CA-AKI as compared to normal eGFR (OR=2.57, 95% CI: 1.92–3.40, P<0.001; OR=2.66, 95% CI: 1.82–3.78, P<0.001, respectively). After adjustment of potential confounding factors, the significant difference was still observed (OR (95% CI): 1.89 (1.37–2.59), P<0.001; OR (95% CI): 3.19 (2.13–4.68), P<0.001, respectively). Furthermore, the patients with high eGFR had a greater risk of CA-AKI than those with low eGFR (OR=1.085, 95% CI: 1.012–1.27, P<0.05). Nevertheless, the restricted cubic spline in a Cox proportional hazards model showed that the lower eGFR, the higher the long-term mortality. In multivariable Cox analysis, there was no statistically significant difference between high and normal eGFR in long-term mortality.

CONCLUSIONS Glomerular hyperfiltration was independently associated with CA-AKI in patients undergoing elective PCI, and the risk was higher than low eGFR level. Whereas the adverse effect cannot directly reflect on the long-term prognosis. The definition of CA-AKI may need to be optimized further to recognize the patients developing CA-AKI associated with poor prognosis.

**GW33-e0641**  
Association of between arterial-ventricular coupling and left ventricular remodeling in patients with acute myocardial infarction undergoing percutaneous coronary intervention

Man-Qing Luo, Li-Wei Zhang, Li-Chuan Chen, Kai-Yang Lin, Yan-Song Guo  
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OBJECTIVES The ventricle after acute myocardial infarction (AMI) will undergo a process of remodeling characterized by continuous changes in ventricular size, shape, structure and function. However, onset of cardiac remodeling can delay after the initial 3 months and has a detrimental impact on long-term outcomes. Therefore, it is pivotal to recognize the potential change of cardiac remodeling at an early stage. Arterial-ventricular coupling (AVC) is an important determinant of cardiovascular function, which can well reflect arterial stiffness and cardiac function and their relation. Moreover, alterations in AVC may be more sensitive than ejection fraction. In previous studies, the association between AVC and late ventricular (LV) remodeling has not been explored. The present study aims to investigate the relationship between AVC and late LV remodeling and the impact of LV remodeling on long-term prognosis in patients with AMI undergoing percutaneous coronary intervention (PCI).

METHODS We prospectively observed 767 consenting new-onset AMI patients without early LV remodeling after PCI from January 2010 to December 2020. The patients received echocardiography during admission and 3 to 12 months after admission. Late LV remodeling is defined as a >15% increase in left ventricular end-systolic volume (LVESV). AVC was calculated as the ratio of effective arterial elastance (Ea) to LV end-systolic elasticance (Ees). The association of AVC with late LV remodeling was investigated by logistic regression analysis. Cox proportional hazards models were used to estimate the risk of incident HF and mortality in those with late LV remodeling.

RESULTS The incidence of LVLR was 27.5% (211/767). The best cutoff value of baseline AVC for predicting late LV remodeling was 0.6966 (AUC=0.630, 95% CI: 0.572–0.701). After multivariable adjustment of clinical laboratory variables, AVC<0.696 remained a significant independent risk predictor of late LV remodeling in AMI patients undergoing PCI (OR: 3.32, 95% CI: 2.24–4.95, P<0.001). In the multivariable cox analysis, after adjusting for the potential confounders, late LV remodeling can increase the risk rate of long-term mortality, rehospitalization or an urgent visit for heart failure (HR: 2.56, 95% CI: 1.63, 4.02, P<0.001) during the median follow-up of 2 years.

CONCLUSIONS In patients with AMI treated with PCI, baseline AVC assessed by the non-invasive measurement of the Ea/Ees ratio has a significant role in late ventricular remodeling in patients with acute myocardial infarction undergoing percutaneous coronary intervention (PCI). The increasing sUAR was significantly associated with a higher risk of CA-AKI in STEMI patients undergoing PCI, and had a good predictive value for CA-AKI after PCI in STEMI patients. Future studies are needed to confirm the predictive value of sUAR in PCI-AKI.

**GW33-e0637**  
Estimation of predicted 10-year survival and risk of cardiovascular complications in an unorganized population of men and women

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OBJECTIVES Estimation of the predicted 10-year survival rate and the risk of cardiovascular complications in an unorganized population of men and women of working age in the cities of the Golden Ring.

METHODS The cross-sectional population study included 1200 men and women aged 30–69 years from 5 cities of the Vladimir region (Vladimir, Kovrov, Murom, Yuryev-Polsky and Vyszniki). The response to the study was at least 80%. Overall, 1004 people completed the study. Of these, 346 men (34.5%) and 658 women (65.5%). Respondents were interviewed according to a standard questionnaire, including information on socio-demographic indicators, behavioral risk factors, the presence of somatic diseases, records of medications taken, and an assessment of psychosomatic status. Instrumental and laboratory studies included in the standard dispensary examination were performed. The European SCORE scale was used to assess the risk of cardiovascular complications. To assess the long-term survival of individuals, the Charlesson comorbidity index was used.

RESULTS Hypertension was detected in 38% of men and 43% of women. IHD among men was registered three times more often than in women: 15 and 50%, respectively. Other NCDS, such as diabetes mellitus, COPD and malignant tumors, were detected separately in no more than 5% of cases. 67% of women had low to moderate cardiovascular risk. Among men was registered three times more often than in women: 15 and 40%, respectively. Other NCDS, such as diabetes mellitus, COPD and malignant tumors, were detected separately in no more than 5% of cases. 67% of women had low to moderate cardiovascular risk. Among men this figure is 36.7%, while among women it is 10% less. Among men this figure is 36.7%, while among women it is 10% less. It was found in every fourth participant in the study (27%) (P<0.002). The combination of the two diseases was 32.6%. Among men, this figure is 36.7%, while among women it is 10% less. It was found in every fourth participant in the study (27%) (P<0.002). The combination of the three diseases among men was detected in 12%, and among women it was detected in 5.6% of cases (P<0.001). Short-term survival (21 and <5%) by Charlesson index was determined in less than 10% of men and women. The largest number of respondents had 90 and 77% 10-year survival.

CONCLUSIONS In an unorganized population of adults, high and very high cardiovascular risk is found in one in four men and only one in 16 women. A short 10-year survival rate according to the Charlson index was found in every tenth respondent, while at the same time, every second participant had an average 10-year survival rate. Thus, the comorbidity of somatic diseases with low and average 10-year survival requires complex preventive interventions.

**GW33-e0638**  
Comprehensive analysis of clinical and instrumental parameters and coronary blood flow in patients with acute forms of coronary artery disease on the background of type 2 diabetes mellitus

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OBJECTIVES To study the features of clinical and instrumental parameters and lesions of the coronary bed in patients with acute forms of coronary artery disease on the background of type 2 diabetes mellitus (DM).
GW33-e0662
Prognostic analysis of medical interventional therapy and surgical bypass grafting in patients with chronic total occlusion
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OBJECTIVES To compare the prognosis between interventional therapy and coronary artery bypass grafting in patients with chronic total occlusion.

METHODS This study was a single center retrospective cohort study. From July 2015 to June 2020, 409 patients with CTO revascularization were continuously enrolled in the first affiliated Hospital of Xinjiang Medical University through stent therapy or surgical bypass graft. According to the inclusion criteria and exclusion criteria, 320 patients were enrolled in the study. According to the different ways of revascularization, the patients were divided into two groups: interventional therapy group (PCI group, n=153) and surgical bypass transplantation group (CABG group, n=167). The clinical baseline data and coronary artery lesion characteristics of the patients in the study group were collected. The main end point of the study was all-cause death, and the secondary end point was major coronary events (MACEs) including all-cause death, acute myocardial infarction, repeated revascularization, stroke and CTO target vessel reocclusion. All the patients were followed up. The mortality and cumulative incidence of end-point events between the two groups were described by Kaplan-Meier survival curve, and the differences between the two groups were compared by log-rank test. COX proportional hazard model and propensity score matching method were used to analyze the difference between interventional therapy and surgical bypass transplantation on the long-term prognosis of patients.

RESULTS The median follow-up period was 35 months. There was no significant difference in the risk ratio of all-cause death (HR=0.94, 95% CI 0.70–1.28, P=0.71) between the PCI group and the CABG group. After the tendency scores were matched, there was no significant difference in the risk ratio of all-cause death (HR=0.85, 95% CI 0.67–1.08, P=0.172) and the risk ratio of MACE (HR=0.95, 95% CI 0.74–1.23, P=0.896) between the two groups. According to the characteristics of age, complications and vascular lesions, it was found that there was no significant difference in the risk ratio of all-cause death and the risk ratio of MACE between PCI treatment and CABG treatment.

CONCLUSIONS There is no significant difference in long-term prognosis between PCI and CABG revascularization of CTO target vessels in patients with CTO.

GW33-e0667
Timing of angiography and outcomes in patients with non-ST-segment elevation myocardial infarction
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OBJECTIVES Although guidelines have been recommended the invasive strategy for non-ST-segment elevation myocardial infarction (NSTEMI) patients within 24 hours, the optimal timing of the invasive strategy remains controversial. We sought to investigate the association between the timing of different invasive strategies and clinical outcomes in patients with NSTEMI.

METHODS Using data from the Evaluation and Management of Patients with Acute Chest pain in China (EMPACT) database, we retrospectively analyzed 969 patients. They were stratified into 3 groups according to timing of coronary angiography (CAG): from admission; no early (≤24 hours), or delayed (>24 hours) CAG. The primary outcomes were major adverse cardiac events (MACEs) within 30 days.

RESULTS Nine hundred sixty-nine patients with NSTEMI from the EMPACT database were eligible for this study. Five hundred one NSTEMI patients (51.7%) underwent CAG within 24 hours. Among them 152 (33.3%) had early CAG and 571 (44.4%) had delayed CAG. The rate of MACEs at 30 days in overall patients was 9.2, including 15 (5.6%) deaths. Patients who underwent CAG had a lower rate of 30-day MACEs and mortality than those who did not receive CAG (MACEs: 5.6 versus 13.3, P=0.001; mortality: 1.6 versus 9.8, P=0.001). Nonetheless, there was no statistically significant difference in the rates of MACEs and mortality between the early and delayed CAG groups. Independent predictors of the rate of MACEs included whether to undergo CAG (OR=0.385, 95% CI: 0.200, 0.744, P=0.004) or PCI (OR=2.910, 95% CI: 1.273, 6.561, P=0.011), age (OR=1.043, 95% CI: 1.015, 1.017, P=0.002), acute HF (OR=2.962, 95% CI: 1.612, 5.442, P=0.001), and systolic blood pressure (OR=0.976, 95% CI: 0.907, 0.96, P=0.001). The independent predictors of whether to underwent CAG revealed the age (OR=0.947, 95% CI: 0.933, 0.96, P<0.001), cardiogenic shock (OR=0.154, 95% CI: 0.05, 0.534, P=0.003), pulmonary moist rales (OR=0.901, 95% CI: 0.213, 0.756, P=0.005), and CKD (OR=0.064, 95% CI: 0.016, 0.251, P=0.001).

CONCLUSIONS This real-world cohort of NSTEMI patients confirmed that early invasive strategies did not reduce the incidence of MACEs and mortality within 30 days compared with delayed invasive strategies in patients with NSTEMI.

GW33-e0671
Neutrophil-to-lymphocyte ratio (NLR) and mean platelet volume-to-lymphocyte ratio (MPVLR) are diagnostic and predictive indicators of functionally significant coronary artery stenosis
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OBJECTIVES For borderline coronary lesions, due to the limited information provided by coronary angiography, the severity of coronary stenosis cannot be correctly evaluated, let alone the coronary ischemia. At present, the results of a number of studies have confirmed that Fractional Flow Reserve (FFR) is the gold standard for evaluating coronary function. FFR is a useful functional index for judging whether the stenosis of the coronary artery does cause the ischemia of the distal myocardial tissue. There are many reasons for patients with insufficient coronary blood flow reserve, and inflammation may have an important influence on the coronary blood flow reserve. Neutrophil-to-lymphocyte ratio (NLR) and Mean platelet volume to lymphocyte ratio (MPVLR) are used as indicators to reflect the level of inflammation and physiological stress. Numerous studies have clarified its relationship with cardiovascular disease. The purpose of this study is to clarify the diagnostic and predictive effects of NLR and MPVLR indicators on insufficient blood flow reserve in patients with stable angina.

METHODS This study was continuously selected from August 2017 to October 2020 in the First Affiliated Hospital of Xinjiang Medical University. Coronary angiography was performed to indicate coronary artery borderline disease (coronary artery stenosis diameter 50–70%) and the reference diameter of the diseased vessel is greater than 2.5 mm. There were 395 patients with chronic stable angina. Collect subjects’ venous blood samples for blood routine, biochemical, cardiac ultrasound and other related examinations.

RESULTS In 395 patients with stable angina, FFR≤0.8 group had higher levels of NLR, MPVLR and other inflammatory markers than FFR>0.8 group (P<0.05). After adjusting for confounders, NLR (OR=1.435, 95% CI 1.205–1.718, P<0.001) MPVLR (OR=1.312, 95% CI 1.163–1.480, P<0.001) was independently associated with functional significant coronary artery stenosis. After a follow-up of 12 months for patients with FFR or less than 0.8 groups, COX regression results showed that NLR and MPVLR were independent predictors of adverse cardiovascular events in patients with FFR≤0.8. When NLR was greater than 2.44 and MPVLR was greater than 5.59, the survival rate of patients with hemodynamically significant stable angina decreased significantly.

CONCLUSIONS NLR and MPVLR have an independent predictive effect on whether patients with stable angina are associated with insufficient blood flow reserve, and can be further used to evaluate the prognosis of patients with insufficient blood flow reserve.
Shrunken pore syndrome: a new and more powerful phenotype of renal dysfunction than chronic kidney disease for predicting contrast-associated acute kidney injury

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OBJECTIVES Shrunken pore syndrome (SPS) as a novel phenotype of renal dysfunction is characterized by a difference in renal filtration between creatinine and creatinine. The manifestation of SPS was defined as creatinine C-based eGFR (eGFRcys) less than 60% of creatinine-based eGFR (eGFRCr). SPS has been shown to be associated with the progression and adverse prognosis of various cardiovascular diseases, and with an increased risk of short-term and long-term mortality in patients undergoing elective PCI.

RESULTS Overall, 649 (12.85%) patients had Shrunken pore syndrome and mortality compared to those without both (HR=5.546, 95% CI: 3.375–8.849, P=0.001). Notably, Patients with CKD only had higher all-cause mortality risk than those with SPS but without CKD (HR: 2.007, 95% CI: 1.469–2.743, P<0.001). Patients with both SPS and CKD appeared to present the highest risk of long-term mortality compared to those without both (HR=5.746, 95% CI: 3.775–8.849, P<0.001).

CONCLUSIONS SPS is a new and more powerful phenotype of renal dysfunction for predicting CA-AKI than CKD, while CKD shows a more prognostic related clinical predictive value.

Machine learning algorithms for acute kidney injury prediction in patients with acute myocardial infarction

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OBJECTIVES Predictive models based on machine learning have been widely used in clinical practice. Patients with acute myocardial infarction (AMI) are prone to the risk of acute kidney injury (AKI), which results in a poor prognosis for the patient. The aim of this study was to develop a machine learning predictive model for the identification of AKI in AMI patients.

METHODS Patients with AMI who had been registered in the Medical Information Mart for Intensive Care (MIMIC) III and IV database were enrolled. The primary outcome was the occurrence of AKI during hospitalization. We developed Random Forests (RF) model, Naïve Bayes (NB) model, Support Vector Machine (SVM) model, eXtreme Gradient Boosting (xGBoost) model, Decision Trees (DT) model and Logistic Regression (LR) models with AMI patients in MIMIC-IV database. The importance ranking of all variables was obtained by the SHapley Additive exPlanations (SHAP) method. AMI patients in MIMIC-III databases were used for model evaluation. The area under the receiver operating characteristic curve (AUC) was used to compare the performance of each model.

RESULTS A total of 3882 subjects with AMI were enrolled through screening of the MIMIC database, of which 1098 patients (28.2%) developed AKI. We randomly assigned 70% of the patients in the MIMIC-IV data to the training cohort, which is used to develop models in the training cohort. The remaining 30% were allocated to the testing cohort. Meanwhile, MIMIC-III patient data performed the external validation function of the model. Three thousand eight hundred eighty-two patients and 37 predictors were included in the analysis for model construction. The top 5 predictors were serum creatinine, blood urea nitrogen, atrial fibrillation, blood glucose concentration, and hemoglobin concentration (SHAP values are 0.730, 0.348, 0.310, 0.306 and 0.287, respectively). In the testing cohort, using top 20 important features, the models of RF, NB, SVM, xGBoost, DT model and LR obtained AUC of 0.961, 0.709, 0.775, 0.780, 0.784 and 0.787, respectively. Placing RF models of number of different variables on the external validation cohort yielded their AUC of 0.725, 0.779, 0.777, 0.781 and 0.788, respectively.

CONCLUSIONS Machine learning algorithms, particularly the random forest algorithm, have improved the accuracy of risk stratification for AKI in AMI patients and are applied to accurately identify the risk of AKI in AMI patients.

The relation between urinary 8-iso-prostaglandin F2α level and culprit plaque rupture in the diabetic patients with acute coronary syndrome

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OBJECTIVES Enhanced isoprostanes-related oxidative stress was reported to play a key role in cardiovascular complications in patients with type 2 diabetes mellitus (T2DM). The spontaneous plaque rupture and subsequent thrombosis is the most common cause of ischemic cardiovascular events. The relationship...
between urinary 8-iso-prostaglandin F$_2$α (8-iso-PGF$_2$α) and coronary plaque rupture has not been fully elucidated. The aim of this study was to evaluate the assessment of rupture of culprit lesions in diabetic patients with acute coronary syndrome (ACS) by the use of urinary 8-iso-PGF$_2$α.

**METHODS** A total of 136 diabetic patients with ACS were included in this observational and case-control study. Sixty-eight patients with plaque rupture were matched by age and gender with other 68 patients without plaque rupture. The characteristics of ruptured culprit plaque were identified by intra-vascular ultrasound. Urinary 8-iso-PGF$_2$α level was measured before coronary angiography and corrected by creatinine clearance.

**RESULTS** Under the same age and gender conditions, patients with ruptured plaque had greater plasma hemoglobin A1c (HbA1c, 7.6±1.2 vs. 7.2±1.0, P=0.038), higher sensitive C reactive protein (CRP, 3.9 (1.1, 5.9) vs. 2.3 (0.6, 4.4) mg/dL, P=0.043), urinary 8-iso-PGF$_2$α levels (147.5 (68.6, 217.9) vs. 108.9 (59.5, 182.3) pmol/mmolCr, P=0.009), and more positive remodeling plaques (remodeling index, 1.0±0.15 vs. 0.97±0.17, P=0.018) than patients with non-ruptured plaque. In multivariate analysis, high urinary 8-iso-PGF$_2$α and plasma CRP and positive remodeling index were significantly associated with incidence of plaque rupture, but HbA1c was not. Urinary 8-iso-PGF$_2$α also displayed a significant value in predicting ruptured plaques in diabetic patients with ACS by constructing the receiver-operating characteristic (ROC) curve (Area under the ROC curve: 0.803, P=0.001).

**CONCLUSIONS** High urinary 8-iso-PGF$_2$α levels appeared to be correlated with plaque rupture in diabetic patients with ACS, which indicated that urinary 8-iso-PGF$_2$α may be an important predictor for the cardiovascular outcomes in diabetic patients with coronary heart disease. The study suggests therapies aimed at reducing oxidative stress would benefit diabetic patients at risk of developing adverse cardiac events.

**GW33-e0688**

Prognostic value of malnutrition using geriatric nutritional risk index in patients with non-ST-elevation myocardial infarction after percutaneous coronary intervention

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**OBJECTIVES** Malnutrition is associated with poor prognosis in a wide range of chronic illnesses, however, the impact of malnutrition on long-term outcomes of patients at advanced stages of atherosclerosis, non-ST-elevation myocardial infarction (NSTEMI), is not known. This study aims to investigate the relationship between malnutrition and adverse cardiovascular events in patients with NSTEMI after percutaneous coronary intervention (PCI).

**METHODS** Baseline malnutrition risk was determined in 754 patients with NSTEMI after PCI in this study. All patients were divided into 3 groups according to the level of dietary risk: moderate, severe, GNRI of 92–98 (n=222); and absence of risk, GNRI ≥98 (n=430). The primary endpoint was all-cause mortality and the secondary endpoint was major adverse cardiovascular events (MACE).

**RESULTS** Average age in this study was 60.37±10.92 years old. More than two-fifth of patients were at risk of malnutrition (moderate to severe: 13.5%; low: 29.4%) and absence of risk: 57.1%. Over a median follow-up of 40 months, compared to those with absent risk for malnutrition, moderate to severe risk was associated with significantly increased risk for the all-cause death, cardiovascular death and MACE (HR: 2.92, 95% CI: 1.42–7.35, P=0.016; HR: 1.46, 95% CI: 1.02–2.09, P=0.040; respectively) after adjustment for baseline variables. Moreover, addition of the GNRI score significantly raised the predictive value for the all-cause death (adjusted HR: 2.33; 95% CI: 1.49–3.69, P=0.002), cardiovascular death (adjusted HR: 1.39; 95% CI: 1.00–1.95, P=0.049), and MACE (adjusted HR: 1.37; 95% CI: 1.00–1.95, P=0.049) respectively compared to traditional factors.

**CONCLUSIONS** Malnutrition assessed by the NSTEMI score on admission was an independent predictor for adverse cardiovascular events in NSTEMI patients after PCI. Addition of the GNRI score to the existing risk prediction model significantly increased the predictive ability for cardiovascular events in NSTEMI patients after PCI.

**GW33-e0693**

Optical coherence tomography findings of the braid-like coronary artery: case series

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**OBJECTIVES** In coronary angiography (CAG), woven coronary artery and thrombus recanalization both show the braided hair like coronary arteries, which is difficult to distinguish. We aimed to analyze the characteristics of woven coronary artery and thrombus recanalization by optical coherence tomography (OCT), and make a detailed differential diagnosis between these two diseases.

**METHODS** Six patients with braided hair like coronary arteries in CAG underwent OCT tests including two-dimensional (2D) images and three-dimensional (3D) reconstruction. Detailed clinical and imaging characteristics were analyzed.

**RESULTS** Through the implementation of OCT, three patients were diagnosed as woven coronary artery, three patients were diagnosed as thrombus recanalization. The lesion of woven coronary artery was characterized by multiple, separate small vessels, which do not communicate with each other, showed by OCT. These separated channels had a complete arterial wall structure of intima and media, indicating that they were intact and independent. However, the lesion of thrombus recanalization displayed many microchannels without layer-structured arterial wall. These microchannels communicated with each other showing a typical lobulate/structure protruding to the lumen, and the larger one passed through the whole lesion.

**CONCLUSIONS** OCT makes a better differential diagnosis between woven coronary artery and thrombus recanalization than CAG. Using OCT after CAG can improve the accuracy of woven coronary artery diagnosis. In addition, OCT could accurately locate the lesion segments and helps to describe the morphological characteristics.

**GW33-e0694**

Coronary artery calcium and cystatin C for risk stratification of MACCEs and all-cause death in symptomatic patients

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**OBJECTIVES** The risk stratification and event prediction capabilities of coronary artery calcium score (CACS) and Cystatin C (Cys-C) alone for major adverse cardiovascular and cerebrovascular events (MACCEs) and all-cause death have been well described, but the combination has not been studied. The aim of this study was to examine the independent and joint associations of baseline CACS and Cys-C with the risk of MACCEs and all-cause death in symptomatic populations.

**METHODS** The study included 7140 patients with symptoms of chest pain who underwent cardiac CT examinations to measure CACS. All of them had serum Cys-C results. Endpoints were set for MACCEs and all-cause death events.

**RESULTS** Seven thousand one hundred forty four patients were followed for 2 median of 1106 days. At the end of the follow-up period, 305 patients had experienced MACCEs and 191 patients had experienced all-cause death. CACS≥200 and Cys-C≥0.995 mg/L were independently associated with an increased risk of MACCEs (adjusted hazard ratio [HR]: 1.46; 95% confidence interval [CI]: 1.15 to 1.85; P=0.002 and adjusted HR: 1.57; 95% CI: 1.24 to 2.00; P=0.001, respectively), Cys-C≥0.995 mg/L was independently associated with an increased risk of MACCEs and all-cause death (adjusted HR: 2.26; 95% CI: 1.64 to 3.13; P=0.001), but CACS≥200 was only nominally associated with an increased risk of all-cause death (adjusted HR: 1.31; 95% CI: 0.97 to 1.78; P=0.077). Compared with CACS<100 and Cys-C<0.995 mg/L patients, CACS≥100 and Cys-C≥0.995 mg/L patients had the highest risk of MACCEs and all-cause death (adjusted HR: 1.33; 95% CI: 1.27 to 1.45; P=0.001), respectively. Even in patients with CACS<100, Cys-C≥0.995 mg/L was also associated with a higher risk of MACCEs and all-cause death than Cys-C<0.995 mg/L (adjusted HR: 1.76; 95% CI: 1.21 to 2.56; P=0.003 and adjusted HR: 2.01; 95% CI: 1.21 to 3.37; P=0.007, respectively).

**CONCLUSIONS** The combined stratification of CACS and Cys-C showed an incremental risk of MACCEs and all-cause death, reflecting complementary prognostic value. Our results support the combination of the two indicators for risk stratification and event prediction.

**GW33-e0700**

Prognostic impacts of the dynamic evolution of renal function in patients undergoing elective percutaneous coronary intervention

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**OBJECTIVES** Previous studies have shown that chronic kidney disease (CKD) affected the long-term prognosis of patients who underwent the elective percutaneous coronary intervention (PCI). However, the prognostic impact in patients with the development of the contrast-associated acute kidney injury (CASI) is unclear. The purpose of this study was to investigate the prognostic impact of the dynamic evolution of renal function in patients undergoing elective PCI.
(CA-AKI) or the onset of the acute kidney disease (AKD) were controversial. For the moment, little attention has been paid to the relationship between the dynamic evolution of renal function and its prognosis.

**METHODS** We used three stages to characterize the dynamic evolution of renal function, namely the occurrence of CKD at baseline, the occurrence of CA-AKI in the postoperative period and the occurrence of AKD at 3 months postoperatively. All-cause mortality was used as the primary endpoint of the study. The five-year survival rate of each group was analyzed using Kaplan-Meier curve. The relationships between each group and long-term prognosis were analysed by multivariable Cox regression analysis.

**RESULTS** We prospectively enrolled 2951 patients who underwent EPCI from April to December 2018. They were divided into three groups according to baseline CKD and CA-AKI: STAGE I (Unimpaired renal function group, CKD(-)/CA-AKI(-) (n=1247)), STAGE II [Partially impaired renal function group, IIa: CKD(-)/CA-AKI(+), (n=91) and IIb: CKD(+)/CA-AKI(-) (n=1472)] and STAGE III [severely impaired renal function group, CKD(+)/CA-AKI(+), (n=1435)]. Subsequently, based on the occurrence of AKD, they were divided into six groups: STAGE I/AKD(-) (n=1121), STAGE I/AKD(+) (n=353), STAGE II/AKD(-) (n=1508), STAGE II/AKD(+) (n=55), STAGE III/AKD(-) (n=108), STAGE III/AKD(+) (n=33). In a mean follow-up period of 3.3±2.39 years, we found that the occurrence of both CKD and CA-AKI affected the long-term prognosis of patients. The occurrence of AKD did not affect the prognosis of patients in the STAGE I group (hazard ratio [HR]=1.10, 95% CI: 0.15–8.11, P=0.928) and the STAGE III group (hazard ratio [HR]=1.12, 95% CI: 0.46–2.68, P=0.806). However, for the STAGE II group, the development of AKD would lead to a poor prognosis for patients.

**CONCLUSIONS** In patients undergoing EPCI, the occurrence of CKD and CA-AKI affected the long-term prognosis of patients. The prognostic impact of the occurrence of AKD depended on the renal function of patients. In patients with unimpaired renal function and severely impaired renal function, the prognostic impact of AKD was negligible. However, in patients with partial abnormal avoidance of AKD could benefit the patient.

**GW33-e0705**

Malnutrition increases the risk of left ventricular remodeling

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**OBJECTIVES** Malnutrition is associated with increased incidence of heart failure (HF). Left ventricular (LV) remodelling is one of the most important processes in the aetiology and evolution of HF. However, the relationship between nutritional status and LV remodelling is not well known. The study aims to investigate the association between malnutrition and LV remodelling.

**METHODS** We enrolled 16,149 patients from January 2007 to December 2018 at Guangdong Provincial People’s Hospital (NCT04407936). The primary endpoint was LV remodeling, defined as an absolute decrease in LV ejection fraction ≥ 10% after discharge compared with baseline. Nutritional status was assessed by the Controlling Nutritional Status (CONUT) score. Eligible patients were divided into absent-mild malnutrition group (CONUT score ≤ 5) and moderate-severe malnutrition group (CONUT score > 5). Univariable and multivariable logistic regression was performed to verify the association between malnutrition and LV remodeling.

**RESULTS** A total of 7217 patients (mean age 61.3±10.5 years, 71.7% male) were included in the final analysis, among which 712 (9.9%) had LV remodeling. The independent remodeling in moderate-severe malnutrition group was significantly higher than that in absent-mild malnutrition group (12.9 vs. 9.5%, P=0.002). In multivariable logistic regression, moderate-severe malnutrition group was significantly associated with 1.69-fold increased risk of LV remodeling after adjusting confounders (OR: 1.69, CI: 1.32–2.16). Similar results were observed in subgroup stratified by age, gender, and coronary artery disease.

**CONCLUSIONS** Nearly one eighth of patients were classified as moderate-severe malnutrition, 12% of whom had LV remodeling. Moderate-severe malnutrition was associated with 6% increased risk of LV remodeling. Further studies are needed to prospectively evaluate the nutrition-oriented management outcomes on LV remodeling.
such as Takayasu arteritis (n=2). Therefore, heterogeneity of ACS causes, clinical and angiographic features determined the treatment strategy.

CONCLUSIONS ST-segment elevation, low ejection fraction, history of MI and complex coronary lesions were predictors of in-hospital adverse outcomes. Identification of the ACS causes was necessary for personalized treatment and sometimes led to the choice of an invasive strategy.

GW33-e0726 Benefits of successful percutaneous coronary intervention in chronic total occlusion patients with diabetes
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OBJECTIVES Diabetes was commonly seen in chronic total occlusion (CTO) patients but data regarding the impact of successful percutaneous coronary intervention (PCI) on clinical outcome of CTO patients with diabetes is controversial. And importantly, no studies have compared quality of life (QOL) after CTO-PCI in patients with and without diabetes.

METHODS Consecutive patients undergoing elective CTO-PCI were prospectively enrolled at XiJing Hospital from Apr 2018 to Apr 2021. Patients were subdivided into 2 groups: Diabetes and No Diabetes. Detailed baseline characteristics, assessment of symptom and QOL, angiographic and procedural details, in-hospital complications, and 1 month and 1 year follow-up data were collected. Accordingly, data were analyzed for risk predictors of clinical outcome in patients with diabetes underwent successful revascularization.

RESULTS A total of 995 patients underwent CTO-PCI attempts. Diabetes was present in 346 (36.23%) patients, who had more hypertension, previous stroke, chronic kidney disease, multi-CTO lesion and higher J-CTO score (P<0.05), and their procedural success rate did not significantly reduce compared to without diabetes (91.33 vs. 91.68%, respectively; P=0.850). In-hospital major adverse cardiac cerebrovascular event (MACCE) (3.76 vs. 3.39%, P=0.764) was similar in the two groups. At 1 month and 1 year follow-up after successful CTO-PCI, major adverse cardiac event (MACE) and all-cause mortality were also similar in the two groups (P=0.05). LV EF<40% was an independent risk factor of MACE (OR=6.212, 95% CI 3.170–12.174; P<0.001) and all-cause mortality (OR=12.657, 95% CI 3.992–40.041; P<0.001) 1 year after successful revascularization. Symptoms and QOL were markedly improved regardless of diabetes both at 1 month and 1 year follow-up, and importantly, the improvement degree of patients with diabetes was similar with those without diabetes (P=0.05).

CONCLUSIONS Successful CTO-PCI could represent an effective strategy improving clinical outcome, symptoms and QOL in CTO patients with diabetes.

GW33-e0727 Benefits of successful percutaneous coronary intervention in Chinese CTO patients with low LVEF
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OBJECTIVES Low LVEF was commonly seen in CTO patients and was considered as an independent risk factor of poor prognosis of those patients. Yet, data regarding the clinical outcome, symptom and QOL of successful revascularization of CTO in low LVEF patients were scarcely reported. This study set out to assess the clinical outcome, symptoms and quality of life (QOL) of chronic total occlusion treated with percutaneous coronary intervention (CTO-PCI) in Chinese patients with low left ventricular ejection fraction (LVEF)<40%.

METHODS Patients consecutively undergoing elective CTO-PCI at XiJing Hospital from Apr. 2018 to Apr. 2021 were included in this study. Patients were subdivided into 3 groups: LVEF≥50%, 40%<LVEF<50% and LVEF<40%. Detailed baseline characteristics, assessment of symptoms and QOL, angiographic and procedural details, in-hospital complications, and 1 month and 1 year follow-up data were collected. Accordingly, data were analyzed for its risk predictors of procedural success and clinical outcome in patients with low LVEF.

RESULTS Of 995 CTO patients, LVEF<40% was present in 172 (17.29%), who had more previous MI, multi-CTO lesion, LCX-CTO lesion, application of MCS and higher SYNTAX score (P<0.001), and their procedural success rate did not drop significantly compared with the other two groups (92.91 vs. 92.31 vs. 91.33 vs. 91.96 vs. 91.96 vs. 89.86%; P=0.078). In-hospital major adverse cardiac and cerebrovascular event (MACCE) (2.55 vs. 2.56 vs. 8.14%; P<0.001) and other complications (6.05 vs. 5.13 vs. 19.76%; P<0.001) were the highest in patients with LVEF<40%. At 1 month and 1 year follow-up, major adverse cardiac event (MACE) and all-cause mortality were also the highest in patients with LVEF<40% after successful CTO-PCI (P<0.001), while they were markedly lower than those with failed CTO-PCI (P<0.001). LVEF<40% was an independent risk factor of MACCE (OR=2.905, 95% CI 1.930–4.372; P<0.001) and all-cause mortality (OR=5.833, 95% CI 3.420–10.501; P<0.001) 1 year after successful revascularization. Symptoms and QOL were markedly improved regardless of LVEF both at 1 month and 1 year follow-up, notably at a similar degree between patients with LVEF<40% and the other two groups (P>0.05).

CONCLUSIONS CTO-PCI could represent an effective revascularization strategy improving clinical outcome, symptoms and QOL in CTO patients with low LVEF.

GW33-e0728 Predictive value of the TC/HDL-C for chronic total occlusion of coronary heart disease
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OBJECTIVES Dyslipidemia has been well-recognized as critical risk factor of coronary heart disease (CHD). Recently, studies reported that the ratio of total cholesterol and high-density lipoprotein cholesterol (TC/HDL-C) was associated with cardiovascular diseases, but its association with chronic total occlusion (CTO), the most severe coronary lesion of CHD, requires elucidation.

METHODS A total of 6260 CHD inpatients were consecutively enrolled between November 2012 and July 2020 at XiJing Hospital. Data on baseline and coronary angiography characteristics were collected and Gensini score (GS) was calculated by coronary artery stenosis. TC/HDL-C value was evaluated by the ratio of TC and HDL-C levels. The prognostic ability of several blood lipid indicators including total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) or TC/HDL-C to discriminate CTO from non-CTO was investigated using binary logistic regression and receiver operating characteristic (ROC) curve analysis. Additionally, the discrimination value of TC/HDL-C for multi-CTO or GS was also investigated.

RESULTS Among the 6260 CHD patients, CTO and non-CTO were evaluated in 2437 and 3823 patients, respectively. CTO patient showed higher levels of baseline TC, TG, LDL-C, while baseline HDL-C was higher in non-CTO patients, and TC/HDL-C was significantly higher in CTO patient. Additionally, the discrimination value of TC/HDL-C (0.703) than for TC (0.578), TG (0.542), LDL-C (0.520), and...
We performed preoperative echocardiography and lung ultrasound combined with ACEF score to predict the risk of CTO patients, thus providing evidence for the earlier clinical decisions and intervention.

**RESULTS** Eighty-five patients were enrolled, and the average hospital stay was 9.05±7.35 days. The ACEF score during hospitalization was positively correlated with the number of B-lines (r=0.427, P<0.001) and NT-proBNP (r=0.282, P=0.009). In the multivariate logistic regression analysis, B-lines number (OR 1.1495% CI: 1.00–1.305, P=0.035) and ACEF Score (OR 65.3995% CI: 1.68–2580.693, P=0.035) were independent predictors of adverse events during hospitalization in AMI patients. The area under the receiver operating characteristic curves (AUCs) were 0.753 (P<0.001), 0.818 (P<0.001) and 0.862 (P<0.001) for ACEF Score, LUS and their combination, respectively.

**CONCLUSIONS** Both the number of B-lines and the ACEF Score can be used as independent predictors of adverse events in AMI patients during hospitalization. The number of B-lines combined with ACEF Score provides incremental value in predicting the risk of adverse events and is important for risk stratification during hospitalization.

**GW33-e0732**

**CAC for risk stratification among hypertriglyceridemia patients with extreme atherosclerotic cardiovascular disease**

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**OBJECTIVES** It is extremely important to identify those at extreme ASCVD risk and intervene effectively. In this study, we sought to evaluate whether the coronary artery calcium (CAC) score can enhance current paradigms for risk stratification among hypertriglyceridemia in primary prevention of patients with extreme atherosclerotic cardiovascular disease risk.

**METHODS** We conducted 1478 participants with extreme ASCVD risk from the affiliated hospital of Xinjiang Medical University from June 2017 to April 2021. We evaluated the incidence of MACE overall and further stratified by CAC scores (0, >100 to >100) and triglycerides level (>2.6 mmol/L, 2.6–5.54 mmol/L, >5.54 mmol/L). The number needed to treat for 5 years (NNT5) to prevent 1 event was estimated among patients with extreme ASCVD risk. We used Kaplan-Meier survival functions to generate cumulative incidence estimates of MACE. Cox proportional hazards regression models were used to evaluate the independent associations between CAC>0 to 100 and CAC>100 (compared with CAC=0) and MACE, adjusting for demographics, traditional cardiovascular risk factors, statin use and level of triglycerides.

**RESULTS** The study population comprised 1478 patients with extreme ASCVD risk. Median age was 57 years, and 45% of patients were women. There was marked heterogeneity in CAC burden overall and different triglycerides level. Overall, the incidence of MACE was 60.0% and there was a marked increase with higher CAC scores. 69% of patients were hypertensive and 39% had MACE within 40 months. Among participants with hypertriglyceridemia, 62% had CAC=100, and their event rates were markedly higher (38.4 vs 21.2%) and the NNT5 lower (14 vs 54) than those of the 5% of patients with CAC=0. The incidence of MACE of severe hypertriglyceridemia was higher than that of mild to moderate hypertriglyceridemia. Among the 31% patients without hyperlipidemia, 39% had CAC=100, their 40-months incidence of MACE (15.9%) was lower than the overall incidence among patients with hypertriglyceridemia.

**CONCLUSIONS** CAC can improve current risk stratification and therapy allocation paradigms among individuals with hypertriglyceridemia with extreme ASCVD risk. Future trials of risk-reduction therapies in hypertriglyceridemia could use CAC>100 to enroll a high-risk study sample, with implications for a larger target population.
METHODS A total of 1,263 patients from the derivation cohort were included in the current analysis of nomogram development. LASSO regression analysis was employed for the development of the prediction model. The model was internally validated using bootstrap resampling and externally validated in two independent and large real-world cohorts, including validation cohort 1 (containing 2,612 consecutive subjects from a multicenter cohort) and validation cohort 2 (containing 1,461 consecutive subjects with long-term follow-up). The model performance was assessed by Harrell’s C-index, calibration curves and clinical usefulness analysis.

RESULTS The proposed nomogram finally included 9 variables. The 1-, 2-, 5- and 10-year area under the receiver operating characteristic curve (AUC) of the nomogram were 0.70, 0.71, 0.73 and 0.73, respectively, showing the good discrimination of the model. The calibration was acceptable considering that optimism-corrected slopes of 1-, 2-, 5- and 10-year calibration plots were 0.93, 0.94, 0.93 and 0.94, respectively. Application of the nomogram in two validation cohorts still revealed good discrimination (1-, 2- and 5-year AUC were 0.80, 0.79 and 0.73, respectively) and good calibration (1-, 2- and 5-year optimism-corrected slopes were 1.01, 1.01 and 1.02, respectively). Decision curve analysis demonstrated that the prediction nomogram was clinically useful.

CONCLUSIONS The individualized prediction nomogram was a useful risk stratification tool that could help identify high-risk patients with cardiovascular diseases where more precise treatment should be performed.

GW33-e0771 Higher HbA1c variability is associated with higher risk of cardiovascular diseases: insights from pooled results among patients with diabetes mellitus
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OBJECTIVES HbA1c variability is a key parameter of glucose fluctuation. The relationship between glucose fluctuation and cardiovascular diseases (CVDs) in patients with diabetes mellitus (DM) remains elusive.

METHODS PubMed, Cochrane Library, Web of Science and Embase were searched up to 1 July 2022. Studies reporting the association of HbA1c variability [standard deviation of HbA1c (HbA1c-SD), coefficient of variation of HbA1c (HbA1c-CV), and HbA1c variability score (HVS)] and the CVDs risk in DM patients were included. We used three different insights (a high-low dose meta-analysis, a study-specific meta-analysis, and a non-linear dose-response meta-analysis) to explore the relationship of HbA1c variability and the CVDs risk. Subgroup analysis was also performed to screen the potential confounding factors.

RESULTS A total of 14 studies with 2,541,017 DM patients were eligible. The highest HbA1c variability was significantly associated with the increased CVDs risk (HbA1c-SD, RR 1.45; HbA1c-CV, RR 1.74; HVS, RR 2.46; all P=0.000) compared to the lowest HbA1c variability. The RR of CVDs for per HbA1c variability were significantly more than 1 (P=0.000). Subgroup analysis for per HbA1c-SD showed that a significant exposure-covariate interaction was identified in the lowest tertile group (P=0.009 for interaction). Dose-response analysis showed a positive association between HbA1c-CV and the CVDs risk (P for non-linearity-co.001).

CONCLUSIONS Our study suggests that the higher HbA1c variability might be significantly associated with the higher CVD risk among T2DM patients. The CVDs risk might be higher among T1DM patients than T2DM patients.

GW33-e0009 Integrating waist circumference and body mass index to predict all-cause death for patients with hypertension: a population-based cohort study
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OBJECTIVES This study aims to investigate the integration of both waist circumference and body mass index (BMI) to predict all-cause death and cardiovascular-specific death in patients with hypertension.

METHODS This prospective cohort study included 12,386 participants with a median follow-up of 6.2 years. Waist circumference-to-BMI ratio (WtBR) was used to integrate waist circumference and BMI, defined as a ratio of waist circumference to BMI. We applied adjusted Cox regression models, restricted cubic spline, Kaplan-Meier curves, random forest analysis, and sensitivity analysis to evaluate the association between WtBR and all-cause mortality. Then, to assess the discriminative ability of WtBR for cardiovascular-specific death, we used Fine-Gray competing risk regression models setting non-cardiovascular death as a competing risk. Additionally, a prediction model was created based on WtBR to evaluate the risk of all-cause mortality in patients with hypertension.

RESULTS The adjusted model showed a significant association of waist circumference and BMI with all-cause death with hazard ratios (95% confidence interval) of 1.44 (1.33–1.57) and 0.42 (0.34–0.51), respectively. When analyzed as a continuous variable, WtBR was consistently associated with an increased risk of death in a linear pattern with an adjusted HR of 2.42 (2.06–2.85). Patients in the highest quintile showed the highest risk of death than the lowest quintile. Sensitivities analysis demonstrated the robustness of the association. However, no significant association was observed between WtBR and cardiovascular-specific death. In the testing set, the predictive model showed a reliable performance with an area under the curve of 0.803, specificity of 0.72, and negative predictive value of 0.84. The visualized nomogram can be easily accessed at https://data15651725761.shinyapps.io/ACM-for-HP/.

CONCLUSIONS WtBR provides an additional opportunity to predict all-cause death in patients with hypertension. Waist circumference should be routinely examined in patients with hypertension regardless of BMI to better manage obesity-related health risks.
GW33-e0049

High waist circumference is a risk factor for hypertension in normal-weight or overweight individuals with normal cardiometabolic profiles

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OBJECTIVES This study aims to investigate the relationship between waist circumference and hypertension risk in normal-weight and overweight individuals with normal cardiometabolic profiles.

METHODS This study included 7,177 normal-weight and overweight individuals with normal cardiometabolic profiles from the 2001-2014 US National Health and Nutrition Examination Survey. We first summed up their demographic characteristics, cardiometabolic profiles, and behavioral factors across waist circumference quartiles. Then, we analyzed the relationship between waist circumference and hypertension prevalence using multivariate logistic regression models and restricted cubic spline. Finally, we applied multivariate Cox regression analysis and Kaplan-Meier curve analysis to explore the association of waist circumference with all-cause mortality in individuals with hypertension.

RESULTS In multivariate logistic regression analysis, we observed a positive and significant association of waist circumference (as a continuous variable) with hypertension prevalence in all three models (non-adjusted, minimally-adjusted, and fully-adjusted), with odds ratios (95% confidence intervals) of 1.76 (1.65-1.86), 1.28 (1.19-1.38), and 1.12 (1.08-1.38), respectively. And when analyzed as a categorical variable, individuals in the highest waist circumference group had a 1.44-fold increased risk of hypertension than those in the lowest group in the fully-adjusted model. In multivariate Cox regression analysis, waist circumference had a positive and significant association with all-cause mortality in individuals with hypertension in the non-adjusted model (HR: 1.27; 95% CI: 1.10-1.47) and the fully-adjusted model (HR: 1.59; 95% CI: 1.22-2.06), with no significant difference observed in the minimally-adjusted model.

CONCLUSIONS We found waist circumference had a positive and significant association with hypertension prevalence in normal-weight/overweight individuals with normal cardiometabolic profiles and all-cause mortality once cardiometabolic factors were adjusted, and fully-adjusted, with odds ratios (95% confidence intervals) of 1.76 (1.65-1.86), 1.28 (1.19-1.38), and 1.12 (1.08-1.38), respectively. And when analyzed as a categorical variable, individuals in the highest waist circumference group had a 1.44-fold increased risk of hypertension than those in the lowest group in the fully-adjusted model. In multivariate Cox regression analysis, waist circumference had a positive and significant association with all-cause mortality in individuals with hypertension in the non-adjusted model (HR: 1.27; 95% CI: 1.10-1.47) and the fully-adjusted model (HR: 1.59; 95% CI: 1.22-2.06), with no significant difference observed in the minimally-adjusted model.

GW33-e0360

Application of roy adaptation model in treatment adherence of patients with hypertension

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OBJECTIVES To explore the effect of Roy adaptation model in predicting treatment adherence of hypertensive patients.

METHODS A total of 182 hospitalized hypertensive patients in the cardiovascular department of a level A tertiary hospital in Chongqing from May to November 2021 were selected by convenience sampling method. The personal information questionnaire, Therapeutic adherence scale for hypertensive patients, Coping and Adaptation Processing Scale-Short Form, Beijing Scale-Short Form was 0.785 and 0.698, respectively. The sensitivity was 70.49% of Logistic regression prediction model and Coping and Adaptation Processing Scale-Short Form was 0.785 and 0.698, respectively. The sensitivity was 70.49% of Logistic regression prediction model and Coping and Adaptation Processing Scale-Short Form was 0.785 and 0.698, respectively.

RESULTS The proportion of low treatment adherence in 182 hypertensive patients was 67%, and the score of daily life management dimension was the lowest 3.20 (2.80, 3.60). Logistic regression analysis showed that the ability of coping and adaptation, age, residence and economic stress were predictors of treatment adherence in hypertensive patients. The area under the ROC curve of Logistic regression prediction model and Coping and Adaptation Processing Scale-Short Form was 0.785 and 0.698, respectively. The sensitivity was 70.49% and 85.00%, respectively. The cut-off value of Coping and Adaptation Processing Scale-Short Form was 39 points.

CONCLUSIONS Roy adaptation model can be used to understand and predict the treatment adherence of hypertensive patients. Coping and Adaptation Processing Scale-Short Form can effectively and efficiently screen hypertensive patients with poor treatment adherence, and provide the basis for intervention framework.
associated with a specificity of 74.60% and a sensitivity of 84.3% for hypertensive early renal damage (area under the curve [AUC]: 0.819, 95% CI: 0.768, 0.870; P<0.0001).

CONCLUSIONS MHR is associated with eGFR and has a high screening value in early renal damage in young and middle-aged Chinese Participants with essential hypertension.

GW33-e0414 Obstructive sleep apnea in middle-aged and elderly patients with hypertension
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OBJECTIVES This paper intended to explore the prevalence of obstructive sleep apnea (OSA) in middle-aged and elderly hypertension patients and the relationship between OSA and nocturnal blood pressure.

METHODS Middle-aged and elderly hypertension patients were enrolled consecutively. All patients underwent portable overnight cardiopulmonary polygraphy and 24-hour ambulatory blood pressure monitor measurement on the same day. According to whether the nocturnal blood pressure drop rate was normal, the patients were divided into dippers and nondippers, and the clinical data of the two groups were compared.

RESULTS The prevalence of OSA in middle-aged and elderly hypertension patients was 78.8%, and the prevalence of moderate-to-severe OSA was 43.8%. The proportion of moderate-to-severe OSA in nondippers was significantly higher than that in dippers (5.0% vs 32.3%, P=0.021). The 24-hour mean systolic blood pressure, nighttime mean systolic blood pressure, nighttime mean diastolic blood pressure, morning systolic blood pressure and morning diastolic blood pressure in nondippers were significantly higher than those in dippers (P<0.05). Logistic regression analysis showed that apnea-hypopnea index (AHI) was a risk factor for nondipping nocturnal blood pressure. The ROC curve showed that AHI had certain predictive value for the occurrence of nondipping nocturnal blood pressure, with AUC=0.620 (95% CI: 0.533–0.706, P=0.011).

CONCLUSIONS Middle-aged and elderly hypertension patients have a high prevalence of OSA, especially moderate-to-severe OSA, which more likely to lead to abnormal nocturnal blood pressure drop rate, nocturnal hypertension and morning hypertension. AHI is a risk factor for nondipping nocturnal blood pressure and can predict the occurrence of nondipping nocturnal blood pressure to some extent.

GW33-e0441 Relationship between vascular ageing and left ventricular geometry in newly diagnosed primary aldosteronism
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OBJECTIVES Changes in left ventricular (LV) geometry are early manifestations of cardiac damage. The relationship between vascular ageing and LV geometry has been reported. However, in primary aldosteronism (PA), with more severe target organ damage than essential hypertension, the relationship between vascular ageing and LV geometry is unclear. The aim of our study was to investigate the association of vascular ageing parameter and LV geometry in newly diagnosed PA.

METHODS We conducted a retrospective study among patients with newly diagnosed PA from January 1st 2017 to September 30th 2021 at the Third Xiangya Hospital. The data of vascular ageing parameters were collected, including ankle-brachial index (ABI), brachial-ankle pulse wave velocity (baPWV) and carotid intima-media thickness (cIMT). Echocardiography including ankle-brachial index (ABI), brachial-ankle pulse wave velocity (baPWV) and carotid intima-media thickness (cIMT). Echocardiography data were collected to assess LV geometry patterns.

RESULTS A total of 146 patients with newly diagnosed PA were included. Mean age was 44.77±9.79 years and 46.8% participants were female. Linear regression analysis adjusting all potential confounders showed cIMT was significantly associated with LV mass index (LVMI) (β=4.4420, P=0.001) and baPWV was significantly associated with relative wall thickness (BWT) (β=0.0065, P=0.025). Multifactorial adjusted logistic regression analysis demonstrated that cIMT was significantly associated with LV hypertrophy (LVH) (OR=7.421, 95% CI: 1.717–81.688, P=0.021) and baPWV was significantly associated with relative wall thickness (BWT) (β=0.0065, P=0.025).

CONCLUSIONS baPWV was significantly associated with LVCG and cIMT was significantly associated with LVH in newly diagnosed PA. This study provides insights on the importance of baPWV measurement and cIMT measurement in early assessment of cardiac damage in newly diagnosed PA.

GW33-e0622 Association between hypertension and metabolic associated fatty liver disease among U.S. adults
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OBJECTIVES Data are limited on the association between hypertension and metabolic associated fatty liver disease (MAFLD). The aim of current study was to evaluate the association between hypertension and MAFLD in adults.

METHODS This population-based cross-sectional study used data on U.S. adults aged 20 to 80 years from the National Health and Nutrition Examination Survey 2017–2018. Multivariable logistic regression analyses were performed to assess the relationship between hypertension and MAFLD.

RESULTS Among 4658 (weighted N=209,971,629) adults included in this study (mean age, 46.6 years [95% CI, 45.3–47.6 years]; 1376,507 [50.7%] female), 1,100 (58.0%) had hypertension and 1,558 (62.0%) did not have hypertension. A total of 2013 participants (42.2%) were classified as having MAFLD. Compared with participants without hypertension, those with hypertension had a higher prevalence of MAFLD (5.8% [310/5312] vs 4.1% [393/9629]). In a multivariable logistic regression model adjusted for age, sex, BMI category, presence of hypertension or diabetes, smoking status, alcohol consumption, leisure time physical activity, education level, family income to poverty, smoking status, alcohol consumption, leisure time physical activity, eGFR, BMI category, the history of metabolic syndrome, cardiovascular disease and diabetes, and current drug (anti-diabetes, anti-hypertensive, anti-platelet), hypertension was associated with MAFLD (OR=1.47, 95% CI, 1.16–1.87). In subgroup analyses, hypertension was associated with MAFLD among male (OR, 2.10; 95% CI, 1.52–2.89), among those aged 20 to 59 years (OR, 1.68; 95% CI, 1.32–2.14), and among Non-Hispanic White (1.92; 95% CI, 1.47–2.51).

CONCLUSIONS In this cross-sectional study, hypertension was associated with MAFLD in U.S. adult and the associations remained robust after adjusted for a variety of potential confounding.
GW33-e0682
High waist circumference increases the risk of new-onset hypertension: an integrated study
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OBJECTIVES This study aims to investigate whether high waist circumference increases the risk of hypertension based on the nationwide US and China population.

METHODS Multiple data sources were analyzed in this study, including the National Health and Nutrition Examination Survey (NHANES), China Health and Nutrition Longitudinal Study (CHARLS), China Health and Nutrition Survey (CHNS), and Gene Expression Omnibus (GEO), and UK Biobank databases. This study used the TwoSampleMR package to estimate the causal link of waist circumference and BMI with the development of hypertension. GWAS summary data were acquired from the EEU GWAS database (https://gwas.mrcieu.ac.uk/), which integrates a curated database including a summary catalog originated from thousands of GWAS summary datasets. Waist circumference (ukb-b-9405) was used as exposure, whereas hypertension (ukb-b-12469) was used as outcomes. The expression profile of GSE703532 and GSE155903 were acquired from the GEO database. GSE703532 collected abdominal subcutaneous adipose tissue gene expression by the Affymetrix Human Genome U19 Array. We performed weighted gene co-expression network analysis (WGCNA) to identify the top 50 genes of interest/network. GW155903 recorded single-cell RNA sequencing on stromal vascular fraction. We analyzed single-cell RNA-seq data by the ‘Seurat’ package.

RESULTS After a mean follow-up of 3.8 years, 2564 individuals (38.1%) developed hypertension. When analyzed as a continuous variable, waist circumference contributed significantly to hypertension in all three models with HRs of 1.18 (1.13–1.24), 1.29 (1.23–1.34), and 1.45 (1.39–1.52), respectively. Consistently, when analyzed as categories, the risk of new-onset hypertension increased with the elevated categories from Q1 to Q4. In the fully adjusted model, individuals in the highest waist circumference quartile (Q4) showed a 1.52 (1.39–1.65) risk of hypertension compared with the lowest quartile (Q1). The results remained stable in the sensitivity analysis. The restricted cubic spline showed that the risk of hypertension increased with waist circumference.

Mendelian randomization analysis found that the increased waist circumference could potentially cause the risk of hypertension. The enriched biological processes of the key module identified by the WGCNA were involved in Neutrophil activation, T cell activation, Lymphocyte proliferation, and so forth. A higher percentage of macrophage was observed in the obese group and the lean group. The top 20 biological processes were identified by the GO enrichment on the DEGs, including positive regulation of cell adhesion, extracellular matrix organization, regulation of cell-cell adhesion, and so forth. Among the many enriched KEGG pathways, PI3K-Akt signaling pathway showed the highest enrichment, followed by those of cell organization, regulation of cell-cell adhesion, and so forth. Among the many enriched pathways, pathways, F3K-Akt signaling pathway showed the highest enrichment, followed by those of cell organization, regulation of cell-cell adhesion, and so forth. Among the many enrichment-related pathways, T cell pathways were enriched.

CONCLUSIONS This study demonstrated high waist circumference is a risk factor for hypertension. We provided the expression profiles of abdominal subcutaneous adipose tissue based on array and single cell sequence.

GW33-e0734
Differences in risk factors for cardiovascular diseases in men and women in rotational shift work in the Arctic
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OBJECTIVES To study factors associated with the risk of heart failure (HF) in asymptomatic patients with arterial hypertension (AH) in the conditions of rotational shift work in the Arctic.

METHODS In Yamburg polar settlement (68 N) 100 males (M) and 80 females (F) with grade 1–2 AH and normotensive individuals were examined. EchoCG and Fick’s method (Heavy; Hypertensive; Atrial Fibrillation; Pulmonary Hypertension; Elder; Filling Pressure) scale was used to calculate the probability of HF. Treadmill test was carried out according to the Bruce method.

RESULTS Group 1 (gr.1) included 95 M and F patients with zero HF probability (the sum of H2EPEF scores from 0 to 1 points), group 2 (gr.2) - 85 persons of both sexes with an intermediate HF probability (the sum of H2EPEF points from 2 to 5). Patients of gr.2 were older (P=0.038), worked longer in rotational shifts (P=0.0143), had higher ambulatory SBP (P=0.001) and DBP (P=0.0013) associated with greater body mass index (BMI) (P=0.0001). Based on odds ratio (OR) analysis, the factors that most influenced on intermediate HF probability in patients was the Quetelet index (OR=1.261, 95% CI 1.140; 1.393), in the logistic regression model, the appearance of dyspnea during the treadmill test occupied a leading position (OR 0.113, 95% CI 0.044; 0.292, P=0.001). The value of the inotropic reserve (OR 1.020, 95% CI 1.006; 1.035, P=0.005). Analysis of EchoCG revealed in gr.2 significant differences in LVMV and LVMII (P=0.0002 and 0.072, respectively), LV internal area (P=0.0002), isovolumic relaxation time (P=0.003) and E/Em lat. ratio (P=0.0001) indicating signs of LV diastolic dysfunction.

CONCLUSIONS The factors associated with the risk of HF at an early stage with an intermediate HF probability included the H2EPEF scale in asymptomatic patients with AH are BMI, duration of rotational shift work, dyspnea and increased inotropic reserve during physical activity, decreased adaptive potential and impaired LV diastolic dysfunction. Identified factors associated with the risk of HF, including asymptomatic LV diastolic dysfunction, can be included in the definition of the initial stage of HF, which refers to individuals at risk of developing symptomatic HF. Initiation of management strategies targeting identified risk factors in patients with asymptomatic HF may slow symptomatic disease progression in rotational shift workers in the Arctic region.

GW33-e0730
Factors associated with the risk of heart failure in asymptomatic patients with arterial hypertension in the conditions of rotational shift work in the Arctic
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2Medical Unit “Gazprom dobycha Yamburg” LLC

OBJECTIVES To study factors associated with the risk of heart failure (HF) in asymptomatic patients with arterial hypertension (AH) in the conditions of rotational shift work in the Arctic.

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RESULTS Group 1 (gr.1) included 95 M and F patients with zero HF probability (the sum of H2EPEF scores from 0 to 1 points), group 2 (gr.2) - 85 persons of both sexes with an intermediate HF probability (the sum of H2EPEF points from 2 to 5). Patients of gr.2 were older (P=0.038), worked longer in rotational shifts (P=0.0143), had higher ambulatory SBP (P=0.001) and DBP (P=0.0013) associated with greater body mass index (BMI) (P=0.0001). Based on odds ratio (OR) analysis, the factors that most influenced on intermediate HF probability in patients was the Quetelet index (OR=1.261, 95% CI 1.140; 1.393), in the logistic regression model, the appearance of dyspnea during the treadmill test occupied a leading position (OR 0.113, 95% CI 0.044; 0.292, P=0.001). The value of the inotropic reserve (OR 1.020, 95% CI 1.006; 1.035, P=0.005). Analysis of EchoCG revealed in gr.2 significant differences in LVMV and LVMII (P=0.0002 and 0.072, respectively), LV internal area (P=0.0002), isovolumic relaxation time (P=0.003) and E/Em lat. ratio (P=0.0001) indicating signs of LV diastolic dysfunction.

CONCLUSIONS The factors associated with the risk of HF at an early stage with an intermediate HF probability included the H2EPEF scale in asymptomatic patients with AH are BMI, duration of rotational shift work, dyspnea and increased inotropic reserve during physical activity, decreased adaptive potential and impaired LV diastolic dysfunction. Identified factors associated with the risk of HF, including asymptomatic LV diastolic dysfunction, can be included in the definition of the initial stage of HF, which refers to individuals at risk of developing symptomatic HF. Initiation of management strategies targeting identified risk factors in patients with asymptomatic HF may slow symptomatic disease progression in rotational shift workers in the Arctic region.

GW33-e0780
Insight on efficacy of renal artery denervation for refractory hypertension with chronic renal failure: a long-term study
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OBJECTIVES To explore the long-term safety and efficacy of renal denervation in patients with RHT and CVD, a post hoc analysis of eGFR subgroup results was completed.

METHODS Fifty-four patients with uncontrolled hypertension associated with sympathetic nervous system activation underwent RDN and were included in the study. The patients were divided into three groups according to eGFR: eGFR 46–90 mL/min group, eGFR 15–45 mL/min group and eGFR<15 mL/min group. The planned follow-up period is 48 months to assess office blood pressure, renal function, type of antihypertensive medication, and RDN complications.

RESULTS The ablation sites of GFR 46–90 mL/min group and GFR 15–45 mL/min group were 32,572.99 mmHg and 29,532.47, respectively. No complications occurred in the GFR 46–90 mL/min group. The GFR<15 mL/min group lower HDL-C (OR=0.115; 95% CI [0.029; 0.392] P=0.001); hs-CRP (OR=0.894; 95% CI [0.815; 0.958], P=0.005); NT-proBNP (OR=0.989; 95% CI [0.982; 0.995], P=0.001). M and W did not differ significantly (P=0.003) in the risk of HREFP development assessed by HZPEFE scale, which does not exclude differences in the mechanisms of LV remodeling and functional changes in M and F.
was treated with 27.07±5.59 mmHg ablation. Renal artery dissection occurred in each group of GFR 15–45 mL/min and GFR=15 mL/min. And renal stent implantation artery was performed on these two patients. No severe renal artery stenosis occurred. There were no significant differences in SCR and eGFR between the three groups at each follow-up point. Compared with baseline, the SBP was significantly of each group decreased to varying degrees at each follow-up point. SBP decreased most in GFR 46–90 mL/min group. Compared with baseline, the type of antihypertensive drugs used in GFR 46–90 mL/min group decreased significantly except for 36 and 48 months. The type of antihypertensive drugs was significantly decreased after RDN. This was especially pronounced in patients with GFR 15–45 mL/min.

ARRHYTHMIAS

GW33-e0011 Assessing the mC HEST score as a pragmatic risk prediction model for incident atrial fibrillation: Insights from the Multi-Ethnic Study of Atherosclerosis (MESA)

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Conflicts of interests
None directly related to this paper.

BACKGROUND The comparative performance of the mC HEST (Coronary artery disease/Chronic obstructive pulmonary disease, Hypertension, Elderly [65–74: 1 point; over 75: 2 points], Systolic and diastolic heart failure [2 points], Artery disease/Chronic obstructive pulmonary disease, Hypertension, Elderly [2 points], MI [2 points], Stroke/transient ischemic attack (TIA), and all-cause death. Subgroup analysis identified two significant mitral isthmus (MI) block (RR 1.52; 95% CI, 1.16–1.99; P=0.00); decreased to varying degrees at each follow-up point. SBP decreased most in GFR 46–90 mL/min group. Compared with baseline, the type of antihypertensive drugs used in GFR 46–90 mL/min group decreased significantly except for 36 and 48 months. The type of antihypertensive drugs was significantly decreased after RDN. This was especially pronounced in patients with GFR 15–45 mL/min.

CONCLUSIONS RDN can safely reduce SBP in CKD patients combined with RHT for 48 months, with the most significant reduction in GFR 15–45 mL/min group. The type of antihypertensive drugs was significantly decreased after RDN. This was especially pronounced in patients with GFR 15–45 mL/min.

GW33-e0052 The long-term outcomes of ablation with vein of Marshall ethanol infusion versus ablation alone in patients with atrial fibrillation: a meta-analysis

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OBJECTIVES The long-term outcomes of ablation with vein of Marshall ethanol infusion (VOM-ABL) compared with ablation alone in patients with atrial fibrillation (AF) remains elusive. We aimed to explore whether VOM-ABL showed better long-term benefits and screen the potential determinants of outcome impact of VOM-ABL procedure.

METHODS PubMed, Cochrane Library, Web of Science, and Embase were searched up to 1 September 2021. Studies comparing the long-term (one-year or longer) outcomes between VOM-ABL and ablation alone were included. Subgroup analysis identified potential determinants for VOM-ABL procedure.

RESULTS Compared with ablation alone, VOM-ABL was associated with a significantly higher rate of long-term freedom from AF/atrial tachycardia (AT) (risk ratio [RR], 1.28; 95% confidence interval [CI], 1.12–1.47; P=0.00), and successful mitral insufficiency (MI) block (RR 1.52; 95% CI, 1.16–1.99; P=0.00) whereas, no significant difference in pericardial effusion, stroke/transient ischemic attack (TIA), and all-cause death. Subgroup analysis identified two success treatment–covariate interactions: one was ablation strategy subgroup (RR, 1.41; 95% CI, 1.27–1.56 vs PVI; RR, 1.04; 95% CI, 0.82–1.30; P=0.00 for interaction) for freedom from AF/AT, while the other was VOM-ABL group size subgroup (2100; RR 1.98; 95% CI, 1.24–3.17 vs <110; RR 1.20; 95% CI, 1.10–1.30, P=0.04 for interaction) for MI block.

CONCLUSIONS This meta-analysis demonstrates that VOM-ABL has superior efficacy and comparability compared with ablation alone in AF patients with long-term follow-up. Moreover, PVI+ and VOM-ABL group size subgroup ≥2100 may be associated with a great impact on freedom from AF/AT and MI block, respectively.

GW33-e0036 Influence of obesity on atrial fibrillation incident in patients with heart failure with preserved ejection fraction: obesity paradox remained?

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OBJECTIVES There exists argument for “obesity paradox” in heart failure with preserved ejection fraction (HFpEF). However, the influence of obesity on atrial fibrillation (AF) incident in patients with HFpEF is unclear.

METHODS We included 2138 subjects with HFpEF from the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial. Kaplan-Meier curves and Cox regression with hazard ratios (HRs) and confidence intervals (CIs) were used to assess the incidence of AF with and without obesity. Obesity is defined as body mass index (BMI) ≥30 kg/m². We also performed a sensitive analysis by using competing risk regression (one-to-one converger) outcomes between different BMI groups and AF, de-sex and de-age defined as competing events. Obesity (BMI from 25.0 to 29.9 kg/m²) had the lowest BMI incidence, thus we set the overweight group as the reference.

RESULTS Of 2138 patients with HFpEF without baseline AF, there are 1165 obese, 708 overweight and 165 normal weight. With a median follow up of 3.3±1.7 years, 103 patients developed new-onset AF. The incident rate of AF in patients with obesity, overweight and normal weight were 1.04 per 100 person-years, respectively. Group with obesity experienced the higher new-onset AF incidence than those with overweight (log-rank test=0.035) compared with the overweight in HFpEF, with no significant association with normal BMI (1.8–2.49 kg/m²). In the cox regression analysis, the positive association remained in HFpEF with obesity (adjusted HR: 1.68; 95% CI: 1.04–2.71, P=0.034) after adjustment for age, sex, current smoking, cGFR, ethnicity, alcohol intake, NYHA class, spironolactone randomization, history of DM, PCI, hypertension, thyroid diseases and usage of aspirin. When BMI was defined as a continuous variable, the occurrence of AF increases by 3% every kg/m² increase (HR: 1.03; 95% CI: 1.00–1.06, P=0.04) after adjustments. Sensitivity analysis by competing risk model and subgroups analysis generated consistent results, either BMI was analyzed as category or continuous variable.

CONCLUSIONS Obesity increases the risk of new-onset AF in patients with HFpEF. “Obesity Paradox” for AF did not remain in patients with HFpEF.
**GW33-e0106**

Utility of provocative tests in the diagnosis and genotyping of congenital long QT syndrome: a systematic review and meta-analysis

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**OBJECTIVES** Diagnosis is particularly challenging in concealed or asymptomatic long QT syndrome (LQTS). Provocative testing, unmasking the characterization of LQTS, is a promising alternative method for the diagnosis of LQTS, but without uniform standards.

**METHODS** A comprehensive search was conducted in PubMed, Embase and the Cochrane Library through Oct. 14, 2021. Review Manager 5.3 (Cochrane Collaboration, Oxford, UK) was used for all data analyses. A fixed-effects model was used to pool data and differences of QTC between groups were expressed as mean difference (MD) with a 95% confidence interval (CI).

**RESULTS** A total of 22 studies with 1137 LQTS patients were included in our study. At baseline, QTc interval was 40 ms longer in LQTS patients than in control (MD 40.54, 95% CI 37.43–43.65, P<0.001). Compared to control group, LQTS patients had 28 ms longer QTc upon standing (MD 28.82, 95% CI 21.05–36.59, P<0.001), nearly 30 ms longer both at peak exercise (MD 27.51, 95% CI 21.51–33.11, P<0.001) and recovery 4–5 min (MD 29.85, 95% CI 24.36–35.35, P<0.001). With epinephrine infusion, QTc interval was prolonged both in control and LQTS patients, most obviously in LQT1 (MD 68.26, 95% CI 58.91–77.61, P<0.001) and LQT2 (MD 60.17, 95% CI 50.18–70.16, P<0.001). Subgroup analysis showed QTc interval response to abrupt stand test and exercise testing varied between LQT1, LQT2 and LQT3, named Type I, Type II and Type III.

**CONCLUSIONS** QTc trend Type I and Type III during abrupt stand test and exercise test can be used to propose a prospective evaluation of LQT1 and LQTS, respectively. QTc trend combined epinephrine infusion test could distinguish LQT3 from control. A preliminary diagnostic workflow was proposed but deserves further evaluation.

**GW33-e0117**

Repeated stellate ganglion blockade for the treatment of ventricular tachycardia storm in patients with nonischemic cardiomyopathy

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**OBJECTIVES** The sympathetic nervous system plays a key role in both initiation and persistence of ventricular arrhythmias (VA). This study sought to describe our institutional experience with providing repeated percutaneous stellate ganglion blockade (R-SGB) as a treatment for drug-refractory electrical storm in patients with nonischemic cardiomyopathy (NICM).

**METHODS** This study included 8 consecutive patients who had drug-refractory electrical storm and underwent R-SGB between June 1, 2021, and January 31, 2022. Lidocaine (10 mL, 1%) was injected in the vicinity of the left stellate ganglion under the guidance of ultrasound, once per day for 7 days. Data were collected for patient clinical characteristics, immediate and long-term outcomes, and procedure related complications.

**RESULTS** Totally, five patients with dilated cardiomyopathy, two patients with arhythmogenic right ventricular cardiomyopathy and one patient with hypertrophic cardiomyopathy were enrolled. Clinical characteristics included age, 51±12.6 years; men, 100%; and left ventricular ejection fraction, 37.8±6.6%. After the treatment of R-SGB, 75% of patients were free of electrical storm. Twenty-four hour Holter monitoring showed a significant 97% reduction in ventricular arrhythmogenic VT episodes from 43±17.75 vs. 1.50±25.95 after R-SGB (P<0.001). There were no procedure-related major complications. The mean follow-up was 4.7±2.1 months, and the median time to recurrent VT was 60 days.

**CONCLUSIONS** Minimally invasive R-SGB was a safe and effective method to attenuate electrical storm in patients with NICM. Half of patients were free of VT episode in 2 months. Hence R-SGB could serve as bridge therapy to stabilize ventricular rhythm in patients with VT storm.

**GW33-e0131**

The effect of mexiletine in patients with type 2 long QT syndrome

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**OBJECTIVES** Long QT syndrome (LQTS) is caused by gene mutations encoding cardiac ion channels or ion channel regulatory proteins, resulting in prolonged cardiac repolarization and prolonged QT/QTc interval on electrocardiogram. Currently, β-blockers are recommended as first-line therapy for LQTS. As a gene-specific therapy, mexiletine has been proven efficacy in LQT3 patients, but its role in LQT2 patients remains controversial.

**METHODS** Patients admitted to the Department of Cardiology of Beijing Tsinghua Changgung Hospital, which met the diagnostic criteria of LQTS, and were treated with mexiletine. Genetic testing has been completed, and The American College of Medical Genetics and Genomics (ACMG) has been assessed. The pathogenicity as pathogenic or possibly pathogenic mutation. Exclude acquired LQTS due to electrolyte disturbances, medications, and other causes.

**RESULTS** In our center, 14 patients from 12 families have been treated with mexiletine. All 14 patients had a history of syncope, and 1 patient was complicated with deafness. 11 patients were female, with mean age of 23.5±17.2 years and a mean QTc of 551 (509–659) ms. The baseline QTc interval of 1 patient was not available, and the baseline QTc interval of the other 13 patients was greater than 500 ms, with an average of 551 (509–566) ms. Of the 14 patients, 9 had a family history of QTs and 11 had a family history of sudden death. LQTS classification showed 9 cases with LQT2, 2 cases with LQT3, LQT5, LQT7 and JLSN with both 1 case. β-blockers were used in 10 patients. In 9 LQT2 patients, the QTc intervals was 551 (524–600) ms before mexiletine, and shortened to 503 (474–520) ms after mexiletine, with an average shortening of 62.45±2.4 ms (P<0.05).

**CONCLUSIONS** Although, in current guidelines, mexiletine has been recommended as a gene-specific therapy in LQT3 patients, our experience showed that mexiletine also shortens the QTc significantly in most LQT2 patients.

**GW33-e0163**

Heart rate variability as a predictor of sustained ventricular tachycardia in patients with arrhythmogenic cardiomyopathy

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**OBJECTIVES** Arrhythmogenic cardiomyopathy (ACM) is an inherent cardiomyopathy with high risk of ventricular arrhythmias (VAs). Cardiac sympathetic nervous system (SNS) might play important roles in arrhythmogenesis of ACM. This study aims to assess the activity of cardiac ANS in ACM patients by heart rate variability (HRV), and to investigate its value in risk stratification for VAs.

**METHODS** A total of 88 ACM patients and 65 sex- and age-matched healthy participants were enrolled. The time domain measures, which were calculated based on statistical and mathematical analysis on RR intervals, were used to assess heart rate variability (HRV).

**RESULTS** Patients in the ACM group had comparable age (41.8±12.9 vs 42.0±15.1 years old) and proportion of male (76.1% vs 64.6%) to those in the HC group. In addition, there were similar comorbidities between ACM and HC groups. As variables reflected greater sympathetic nervous contribution to HRV, the levels of SDNN and SDANN were significantly lower in ACM group compared with those in HC group (115.97±32.83 vs 155.03±35.57 ms, P<0.001 for SDNN; 98.08±31.28 vs 139.92±35.47 ms, P<0.001 for SDANN). There were also decreased levels of rMSSD (32.90±14.72 vs 36.63±13.10 ms, P=0.02) and pNN50 (10.42±9.64 vs 14.62±10.63%, P=0.004) in the ACM group. To investigate the role of HRV in risk stratification of VT in patients with ACM, patients with ACM were divided into sVT group (52 patients) and non-sVT group (36 patients) according to the presence of sVT in their history. Comparing the HRV variables between sVT group and non-sVT group showed that the levels of SDNN and SDANN in patients with sVT were lower than those in patients without sVT (105.02±28.11 vs 131.83±31.31 ms, P<0.001 for SDNN; 88.42±25.7 vs 112.13±32.36 ms, P<0.001 for SDANN). However, the difference of neither rMSSD nor pNN50 was significant between the two groups (31.52±11.74 vs 34.9±8.14, P=0.17 for rMSSD; 8.15±3 vs 12.31±1.52%, P=0.11 for pNN50). Multivariate logistic regression analysis showed SDNN was independently associated with sVT in ACM patients (odds ratio [OR] 0.59, 95% confidence interval [CI] 0.45–0.78, P<0.001). Receiver operating characteristics curve demonstrated SDNN had clinical values in distinguishing ACM patients with sVT from those without sVT. The area under the curve (AUC=0.73, 95% CI 0.63–0.84, P<0.001). The cutoff value of the SDNN level for predicting sVT in ACM patients was 126.5 ms based on the optimal balance between sensitivity and specificity. The level of SDNN<126.5 ms indicated sVT with 78.6% sensitivity and 66.7% specificity. The positive and negative predictive value of sVT for ACM patients were also 76.9 and 66.7%, respectively.

**CONCLUSIONS** The present study suggests that HRV is impaired in patients with ACM, and the impaired HRV is independently associated with the ventricular arrhythmogenesis. In addition, the SDNN level has a moderate value in risk stratification for VAs in ACM patients.
GW33-e0252
Left bundle branch area pacing combined with atrioventricular node ablation in persistent atrial fibrillation patients with heart failure
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OBJECTIVES Biventricular pacing (BVP) combined with atrioventricular node ablation (AVNA) is the physiological pacing methods proposed in recent years; Studies have shown that it is similar to biventricular pacing and can also achieve cardiac resynchronization.

METHODS Six patients with heart failure and persistent atrial fibrillation were included in this study, and the duration of atrial fibrillation was greater than 12 months. The average age of the patients was 69.4 ± 10.5 years, 66.9% man) with a history of CAD and hypertension. SKNA at the onset of PSVT is higher than that in non-PSVT group and healthy people. SKNA at the onset of PSVT is higher than that in non-PSVT group and healthy people. SKNA was still higher than baseline of SKNA in PSVT group and healthy people.

RESULTS A total of 278 patients (mean age: 74.2 ± 10.5 years, 66.6% man) with post-MI NOAF were included. MACEs occurred in 146 patients (52.1%) during a median follow-up of 10.6 (IQR: 8.4–14.2) months. Multivariable Cox regression analyses showed that it was the NOAF proportion (hazard ratio for 1% increase was 1.07, 95% confidence intervals (CI): 1.06–1.09, P = 0.001), a history of cardiac diseases (HR: 3.21, 95% CI: 2.33–4.14, P < 0.001), and 6-minute walking distance were compared before and after operation. The average follow-up was 3 months after operation. The changes of left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter, NYHA class, and 6-minute walking distance were compared before and after operation.

RESULTS The results showed that the LVEF of 6 patients at 3 months after operation was significantly improved compared with the baseline (24.6 ± 5.4% vs. 47.8 ± 12.6%, P < 0.05); the NYHA classification was significantly improved (baseline 3.8 ± post operation 2.6 ±, P < 0.05); the 6-minute walking distance was significantly increased (baseline 138.8 ± 56.6 ± mm vs post operation 67.0 ± 56.6 ± mm, P < 0.05). SKNA was still higher than baseline of SKNA in PSVT group and healthy people. SKNA was significantly enhanced and heart rate was accelerated by atropine administration.

CONCLUSIONS For long-term persistent atrial fibrillation patients with heart failure, LBBAP combined with AVNA can improve left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter, NYHA class, and 6-minute walking distance compared before and after operation.

GW33-e0293
Identifying optimal metrics of atrial fibrillation burden for the risk stratification in acute myocardial infarction patients developing new-onset atrial fibrillation
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OBJECTIVES The objective metrics of new-onset atrial fibrillation (NOAF) burden in acute myocardial infarction (AMI) individuals have not been evaluated. We aimed to assess the relation between post-MI NOAF burden metrics and major adverse cardiac events (MACES) and to determine which one added most to the predictive power of the Global Registry of Acute Coronary Events (GRACE) score.

METHODS The post-MI NOAF burden metrics including longest NOAF duration, total NOAF duration, and NOAF proportion (percentage of time in NOAF) were collected from the NOAFCAMI-SH registry. All-cause death and heart failure hospitalization were recorded as MACES. Time-dependent ROC analyses were used to explore the discriminative ability of prediction models. The continuous net reclassification index (cNRI) and integrated discrimination improvement (IDI) were also calculated to evaluate the added value of NOAF burden metric on top of the GRACE score.

RESULTS A total of 278 patients (mean age: 74.2 ± 10.5 years, 66.6% man) with post-MI NOAF were included. MACEs occurred in 146 patients (52.1%) during a median follow-up of 10.6 (IQR: 8.4–14.2) months. Multivariable Cox regression analyses showed that it was the NOAF proportion (hazard ratio for per 1 SD increment: 1.306, 95% confidence interval [CI]: 1.115–1.528, P = 0.001) rather than the longest and total NOAF durations that was an independent predictor of MACES. Comparison of predictive performance demonstrated that adding NOAF proportion, but not NOAF durations, to the GRACE score significantly improve its reclassification ability, as evidenced by continuous net reclassification indexes and 95% CI of 0.202 (0.069–0.394), 0.223 (0.086–0.360), and 0.058 (0.020–0.195) for integrated discrimination improvements and 95% CI of 0.09 (0.006–0.098), 0.074 (0.008–0.060), and 0.032 (0.004–0.066) at 1-, 2-, and 3-year follow-up, respectively.

CONCLUSIONS Post-MI NOAF burden measured by NOAF proportion has the greatest prognostic impact and may add to risk stratification beyond the GRACE score.
CONCLUSIONS The present incidence of AF was 5.2/1000 person-years in the studied population aged over 60 years in China. Among various ECG abnormalities, only APC, atrial flutter, JPC, junctional rhythm, short PR interval, second-degree AVB Mobitz type I, second-degree AVB Mobitz type II, VPC, right atrial enlargement and pacing rhythm were independently associated with AF incidence.

GW33-e0420 Contemporary survival and anticoagulation of patients with atrial fibrillation: a community based cohort study in China
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Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine

OBJECTIVES The understanding of death in patients with atrial fibrillation (AF) in China is limited. This study aimed to assess the contemporary survival of AF patients in China and to explore risk factors for deaths.

METHODS This was a prospective community-based cohort study including 559 AF patients who were followed-up from July 2015 to December 2020.

RESULTS During 66-month follow-up, there were 200 deaths (56.5% cardiovascular, 40.0% non-cardiovascular, and 3.5% unknown causes) among 559 AF patients with the median age of 76 years. The top three causes of death were heart failure (33.0%), ischemic stroke (17.0%) and cancer (16.5%). Multivariate Cox regression analysis indicated baseline variables positively associated with all-cause death were age (HR: 1.10, 95% CI: 1.08–1.13), AF subtype (HR: 1.37, 95% CI: 1.08–1.73), prior myocardial infarction (HR: 3.40, 95% CI: 1.48–7.78), previous tumor (HR: 2.61, 95% CI: 1.37–4.98), hypoglycemic therapy at baseline (HR: 1.81, 95% CI: 1.13–2.91), but body weight (HR: 0.98, 95% CI: 0.97–1.00) and use of calcium channel blocker (CCB) (HR: 0.62, 95% CI: 0.41–0.96) played a protective role to all-cause death. Of patients who were alive at the end of follow-up, 24.0% were on oral anticoagulants (OAC) alone, 4.5% on dual antithrombotic therapy, 33.1% on antiplatelet agents alone and 38.4% weren’t on any antithrombotic medication.

CONCLUSIONS Ischemic stroke still remains one of the leading causes of death and OAC is seriously underused in AF patients in China. Independent risk factors for death are age, AF subtype, previous tumor, prior myocardial infarction, hypoglycemic therapy, low body weight and no CCB use.

GW33-e0421 Pattern of atrial fibrillation is associated with cancer death
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OBJECTIVES Limited data are available on the association between atrial fibrillation (AF) and cancer. This study aimed to investigate the association between pattern of AF and cancer mortality.

METHODS This is a community-based cohort study including 559 AF patients aged over 60 years old with a 66-month follow-up.

RESULTS AF was paroxysmal in 18.4% (n=103), persistent in 61.2% (n=342) and permanent in 20.4% (n=114) of the 559 AF patients with the median age of 76 years. A total of 33 cancer deaths were adjudicated. The majority of cancer deaths were attributed to digestive tumors (accounting for 54.5%) and respiratory tumors (accounting for 24.4%). With the follow-up of 2562 patient-years, cancer mortality was 1.29 per 100 person-years (%/P-Y) regardless of AF patterns. The rates of cancer mortality were 0.79%/P-Y for paroxysmal AF, 0.96%/P-Y for persistent AF and 2.68%/P-Y for persistent AF, showing permanent AF was associated with higher risk of cancer mortality compared with paroxysmal AF and persistent AF (P=0.004). Multivariate Cox regression analysis indicated baseline variables independently associated with cancer death were AF pattern (HR: 1.62, 95% CI: 1.10–2.38), age (HR: 1.12, 95% CI: 1.08–1.16), diabetes mellitus (HR: 2.26, 95% CI: 1.15–4.57), symptom pattern of AF (HR: 1.41, 95% CI: 1.01–1.99), previous tumor (HR: 5.04, 95% CI: 2.28–11.15), and liver disease (HR: 5.57, 95% CI: 1.99–15.58).

CONCLUSIONS Permanent AF conferred higher risk of cancer death than paroxysmal AF and persistent AF. AF pattern was independently associated with cancer mortality.

GW33-e0426 Characteristics and ablation outcomes of atrial tachycardias in patients with prior cardiac surgery or with spontaneous scars: where are the differences?
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General Hospital of Northern Theater Command

OBJECTIVES Myocardial scar is usually found in patients after invasive procedure, such as cardiac surgery and catheter ablation, while it is also observed in some patients without prior invasive procedure, which is thought spontaneous scar. Atrial scars can be related to atrial tachycardia (AT), but whether the incisinal scars caused by prior cardiac surgery (PCS) and spontaneous scars (SS) play the same roles in arrhythmia mechanisms has not been clearly clarified. This study was to analyze the characteristics, mechanisms and ablation outcomes of ATs in patients with PCS and patients with SS.

METHODS Forty-six patients with PCS and 18 patients with SS who underwent catheter ablation for right atrial AT from September 2013 to April 2019 in General Hospital of Northern Theater Command were retrospectively reviewed. Baseline information, recordings of electrophysiological study and radiofrequency ablation, and acute and long-term ablation outcomes were collected and analyzed.

RESULTS There were average 1.52 ATs in patients with PCS and 2.33 ATs in patient with SS (P<0.01). In PCS group, cavo-tricuspid isthmus (CTI)-dependent atrial flutter (AFL) was the most common, found in 43 (93.9%) patients, and the scar-mediated intra-atrial reentrant AT (IART) was presented in 18 (39.1%) patients; in SS group, AFL and IART were both presented in high proportion of patients (77.8 and 88.9%, separately), and the focal AT was found in 22.2% patients. Incidence of IART and FAT in patients with SS were significantly higher than those with PCS (86.9 vs. 39.1%, P<0.01; 22.2 vs. 2.2%, 73.7%). Patients with non-surgery related scar had older surgical age (69.1 vs. 77.8%, P=0.44), while the scar-related ablation was more frequently performed in patients with SS (39.1 vs. 83.3%, P<0.01). There were no significant differences on acute success rate between two groups (93.9 vs. 83.3%; P=0.44). While the long-term success rate was lower in the SS group after the follow-up of average 66.8 months (87.0 vs. 61.1%; P<0.05). Patients with SS had significantly higher occurrence of bradyarrhythmias (8.7 vs. 33.3%, P<0.05), mainly the SS.

CONCLUSIONS CTI-dependent AFL is prevalent in both patients with PCS and patients with SS. Routine CTI ablation was recommended in these two conditions. Compared with patients with PCS, patients with SS have more frequently with higher incidence of IART and FAT, and more ablation is needed. Patients with SS have lower long-term success rate and higher incidence of bradyarrhythmias, mainly the SS.

GW33-e0429 Radiofrequency catheter ablation of ventricular tachycardia after repaired congenital heart disease
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General Hospital of Northern Theater Command

OBJECTIVES Though surgical repair of congenital heart disease has improved the prognosis and prolonged the longevity greatly, arrhythmia after cardiac surgical repair is common in the long term. This study aims to clarify the clinical characteristics and long-term ablation outcomes of ventricular tachycardia (VT) in patients with surgical repaired congenital heart disease.

METHODS Nineteen patients with surgical repaired congenital heart disease who underwent radiofrequency catheter ablation for VT were enrolled. The baseline characteristics, recordings of electrophysiological study and catheter ablation, and the outcomes of long-term follow-up of each patient were collected and analyzed.

RESULTS There were 17 patients with tetrology of Fallot (TOF), one patient with trilogy of Fallot and 1 with congenital pulmonary stenosis in this research. Scars in right ventricular outflow tract (RVOT) and ventricular septum were mapped in all patients, consistent with RVOT incision and ventricular septal defect patch, while non-surgery related scars were found in three patients (two patients in RV apex and one patient in RV anterior wall). The acute success rate of the first ablation was 94.7% (18/19), and nine patients had VT recurrence during follow-up. After one or more ablation, the long-term success rate was 84.2%. Patients with non-surgery related scar had older surgical age, larger RA and LA dimension, more VT, and lower long-term success rate (P<0.05).

CONCLUSIONS The scar of RVOT incision and ventricular septal defect patch can be found in patients with TOF, trilogy of Fallot or congenital pulmonar stenosis, but some patients may also present non-surgery related scar, who often undergo surgery at older age. Those patients with older age of surgery have lower long-term success rate of VT ablation.

GW33-e0440 Impact of pericoronary adipose tissue attenuation on recurrence after radiofrequency catheter ablation in patients with atrial fibrillation
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OBJECTIVES Posterior left atrial (LA) adipose tissue attenuation is an independent predictor for AF patients recurrence. Pericoronary adipose tissue...
(PCAT) inflammation may be directly related to coronary inflammation and play an important role in the pathophysiology of AF. This study aimed to evaluate the association between pericoronary adipose tissue attenuation (PCATA), as a marker of inflammation, and atrial fibrillation (AF) recurrence after radiofrequency catheter ablation (RFCA).

**METHODS** This was a retrospective study of 299 AF patients with coronary computed tomography angiography (CCTA) before ablation who underwent the first RFCA were included between 2018 and 2021 in the First Affiliated Hospital of Zhengzhou University. We investigated the association between the risk of AF recurrence and PCATA. Multivariate Cox regression analysis and restricted cubic splines of each PV as a routine approach were performed to explore the relationship between PCATA and AF recurrence. The area under the receiver operating characteristic curve (AUC), relative integrated discrimination improvement (IDI) and categorical free net reclassification (NRI) were used to assess the discrimination ability of the models.

**RESULTS** Overall, 299 patients were enrolled with a mean age of 60.5±11.0 years. Our analysis showed excellent intra-reader and inter-reader reliability in PCATA measurement performed by 50 random AF patients. During 1 year follow up, 34.1% of patients experienced recurrence. All patients were divided into two groups according to with AF recurrence (102/299) and without AF recurrence (197/299). In multivariable analysis, RCA-PCATA (HR: 1.04, 95% CI: 1.02–1.06, P=0.001) remained an independent factor for AF recurrence. The association between higher RCA-PCATA levels and AF recurrence remained consistent using the cut-off value of ROC (77.45 HU). The risk of AF recurrence was significantly improved by adding RCA-PCATA (AUC, 0.731 vs. 0.690, P=0.023; relative EDI, 0.047, P=0.022; categorical NRI, 0.154, P=0.004).

**CONCLUSIONS** RCA-PCATA was independently associated with the recurrence of AF after ablation. The PCATA is a novel marker to quantify the degree of inflammation and to identify optimal candidates and guide the treatment after catheter ablation. PCATA in standard CCTA reporting could be more meaningful for assessing AF patients’ risk classification.

**GW33-e0477** Advancing the second-generation 28-mm cryoballoon in different bifurcations of pulmonary vein as a conventional approach during atrial fibrillation cryoblation

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**OBJECTIVES** Cryoballoon (CB) based ablation for pulmonary vein isolation (PVI) has demonstrated high procedural success rates and a promising clinical outcome for patients with paroxysmal and persistent AF. How to expand the ablation area of antrum and lead to better outcomes is still a challenging topic.

**METHODS** A total of 89 consecutive patients who underwent CB ablation in different bifurcations of each PV as a routine approach were consecutively and enrolled. The nadir temperatures were all moderately correlated with the bifurcation diameters and the temperature difference was positively correlated with the diameter difference in various bifurcations of each PV.

**RESULTS** The CB catheter advanced in different bifurcations of each PV could achieve different force directions to the antrum and the orientation difference was negatively correlated with the ostium-bifurcation distance. After the first application in one bifurcation of each PV, PV potentials could still be recorded in the other bifurcation in 13 patients, and the PV foci could trigger AF in 2 of them. The total isolated antral surface areas after the application in a second bifurcation were larger than those after the first application whether in left PVs [(40.88±15.10) cm² vs (26.73±12.61) cm², P=0.001] or in right PVs [(43.26±18.5) cm² vs (29.06±13.95) cm², P=0.001].

**CONCLUSIONS** Applications performed in different bifurcations of each PV might create a wide area antral ablation lesion especially in those with small diameter or early branching. CB catheter advanced in different bifurcations would contribute to eliminate PV foci adequately.

**GW33-e0537** The three-dimensional spatial relationship among the coronary artery, pulmonary sinus and right ventricular outflow tract: shadowed by the trivial

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**OBJECTIVES** Coronary artery (CA) injury during radiofrequency ablation (RFA) is a fatal complication, and ablation catheter and CA distances are not routinely evaluated during routine right ventricular outflow tract (RVOT) ablation. CA injury has been increasingly reported during RVOT ablation in recent years. Recently, ablation on the pulmonary valve is considered to be at greater risk of CA injury. The aim of this study was to investigate the anatomical relationship between the catheter and coronary artery during ablation of RVOT-originated arrhythmias.

**METHODS** The right ventricular, pulmonary and coronary arteries were reconstructed using CartoSegmentation in cardiac enhanced CT segmentation and fused with the electroanatomical model to measure the distance from the effective ablation target to the nearest CA and from the nearest ablation target to the CA, respectively.

**RESULTS** Twenty-four patients each with ventricular arrhythmias ablated in the RVOT supravalvular and subvalvular were retrospectively enrolled consecutively. There was no significant difference in the minimum distance from the effective ablation target to the CA between the supra- and subvalvular groups (10.29±6.79 vs. 13.85±7.35, P=0.114), with a total of three patients (8.3%) in the supravalvular group and 2 (12.5%) in the subvalvular group having an ablation site to CA distance of less than 5 mm (P=1.00). There was no significant difference in the distance from the nearest ablation target to the CA (8.9±3.62±6.2 vs. 10.59±6.87, P=0.396), and the distance from the ablation point to the CA was less than 5 mm in seven patients (29.2%) in the suprapulmonary group and 5 (20.8%) in the subpulmonary group (P=0.505).

**CONCLUSIONS** There was no significant difference in the distance from the ablation point to the CA between the suprapulmonary and subvalvular ablation points, but the distance to the CA needs to be evaluated at the time of ablation in both cases.
quality of the included literature. The Review manage 5.4 software was used for meta-analysis.

RESULTS A total of four studies were included, with a total of 9205 patients. The meta-analysis showed that compared with the ACEI/ARB group, the incidence of atrial arrhythmia was reduced in the ARNI treatment group, and the incidence of atrial arrhythmia was reduced in the ARNI treatment group, and the incidence of bradycardia. Similarly, patients with higher waist circumference had increased risk of atrial fibrillation (HR 1.05[95% CI 1.04, 1.06]), but not ventricular arrhythmias. In analyses of sex-specific incident AF was examined using Cox regression. The potential dose-response were fitted by restricted cubic spline curve.

CONCLUSIONS A U-shaped association between TyG index and risk of AF was observed in Americans people without known cardiovascular disease. Sex may a modifier in the association between TyG index and AF incidence.

GW33-e0628
Temporary pacemaker reference for left bundle branch pacing
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OBJECTIVES In 2017, Huang et al. proposed the left bundle branch pacing, which attracted much attention because of its relatively easy implantation technology and more stable pacing parameters. At present, there are two difficult problems in left bundle branch pacing: choosing the proper implantation site and determining the proper implantation depth. This study is to explore the effectiveness of left bundle branch pacing with temporary pacemaker as reference.

METHODS A total of 30 patients with pacing indications will be selected for left bundle branch pacing in Shijiazhuang People’s Hospital from August 2021 to August 2022. The radian of the temporary pacemaker across the tricuspid ring and the apex of the heart was used to confirm the implantation site of the left bundle branch. DSA was used to measure the depth of electrode wire implantation. Compared with traditional positioning of left bundle branch pacing, the success rate of surgery, operation time, X-ray exposure time, times of electrode implantation, pacing parameters of left bundle branch during operation and follow-up, pacing characteristics, and surgery-related complications were evaluated.

RESULTS As of May 27, 2022, a total of 30 cases of left bundle branch pacing were successfully completed, with a total success rate of 93.3% (28/30). The comparison of the number of patients in the two groups (120 min: 75 min), and the X-ray exposure time of the two groups (17 min: 12 min), the number of electrode implantation (5 times: 2.5 times), the intraoperative operation parameters were stable, and the postoperative follow-up parameters were stable.

CONCLUSIONS Temporary pacemakers for targeting area reference can improve surgical success, reduce surgical time, reduce X-ray exposure time, and shorten the learning curve for beginners. Intraoperative full use of the inherent measurement means of DSA can provide the position of the electrode into the interval, which helps to judge the depth of the left bundle branch electrode.
control on cognitive outcomes in patients with OH is unclear. We evaluated the association between OH and cognitive outcomes and the effects of intensive BP control on cognitive outcomes in patients with OH.

**METHODS** We analyzed 8547 participants from the Systolic Blood Pressure Intervention Trial (SPRINT) who had completed at least one follow-up cognitive assessment. OH was defined as a drop in systolic BP of at least 20 mmHg or diastolic BP of at least 10 mmHg from sitting to standing. The cognitive outcomes, including probable dementia (PD), mild cognitive impairment (MCI), and the composite outcomes of PD or MCI, were evaluated biennially. The multivariable Cox proportional hazards regression was applied to assess the relationship between the baseline OH and incident cognitive outcomes. We also performed sensitivity analyses. The analyses stratified by severity of OH.

**RESULTS** Among 8547 participants, 615 (7.2%) participants had baseline OH (OH vs. No OH 69.7±9.5 years vs. 67.8±9.3 years). Baseline Montreal Cognitive Assessment scores for participants with and without OH did not show significant differences. Baseline OH was not significantly associated with cognitive dysfunction, as adjusted hazard ratios (HR) was 0.98 for PD (95% CI 0.66–1.47, P=0.93), 1.12 for MCI (95% CI 0.83–1.51, P=0.46), and 1.09 for the composite outcomes of PD or MCI (95% CI 0.85–1.41, P=0.49). The presence of OH did not significantly modify the effect of intensive BP control on cognitive outcomes. OH should not be a barrier to adopting a strict BP control strategy considering the cognitive outcomes among hypertensive patients.

**CONCLUSIONS** In this post-hoc analysis of the SPRINT trial, OH was not independently associated with an increased risk of cognitive impairment. The presence of OH did not modify the effects of intensive BP control on cognitive outcomes. OH should not be a barrier to adopting a strict BP control strategy considering the cognitive outcomes among hypertensive patients.

**GW33-e0640**

**Dose elderly patients with atrial fibrillation have a comparable ablation outcome with younger ones? Evidence from the pooled clinical studies**

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**OBJECTIVES** Age is an independent risk factor for the progress and prognosis of atrial fibrillation (AF). However, the ablation outcomes between elderly and younger patients with AF remain elusive.

**METHODS** Cochrane Library, Embase, PubMed, and Web of Science were systematically searched up to 1 April 2022. Studies comparing the AF ablation outcomes between elderly and younger patients and comprising the outcomes of AF ablation for elderly patients were included. Trial sequential analysis (TSA) was performed to adjust the random error and lower statistical power in our meta-analysis. Subgroup analysis identified possible determinants of outcome impact for elderly patients after ablation. Moreover, linear and quadratic prediction fit plots with confidence interval were performed, as appropriate.

**RESULTS** A total of 27 studies with 113,106 AF patients were eligible. Compared with younger group, elderly group was significantly associated with a lower rate of freedom from AF (risk ratio [RR], 0.93; 95% CI 0.90–0.95) as well as a higher incidence of safety outcomes (cerebrovascular events: RR, 1.64; P=0.001; serious hemorrhage complications: RR, 1.60; P=0.019; all-cause death: RR, 2.61; P=0.003). Subgroup analysis and quadratic prediction fit analysis revealed the follow-up time was the potential determinant on freedom from AF for elderly patients after AF ablation.

**CONCLUSIONS** Our meta-analysis suggests that elderly patients may have inferior efficacy and safety outcomes to younger patients with AF ablation. Moreover, the follow-up time may be a potential determinant of outcome impact on freedom from AF for elderly patients after AF ablation.

**GW33-e0663**

**Clinical analysis of delayed cardiac tamponade in atrial fibrillation patients with left atrial appendage closure**

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**OBJECTIVES** To investigate the relationship of delayed cardiac tamponade (CT) after left atrial appendage closure (LAAC) in atrial fibrillation (AF) patients and the effects of implanted ocluders and adjacent anatomical structures.

**METHODS** This study is a retrospective and cross-sectional study. AF patients with LAA closure complicated with delayed CT and with concurrent emergent pericardiocentesis drainage in Zhoupu Hospital Affiliated to Shanghai University of Medicine & Health Sciences from August 2016 to June 2021 were selected, the mean follow-up time was 16±1.2 months. The clinical data including the relationship between the left atrial appendage and pulmonary artery, vein anatomy by left atrium computed tomography angiography (CTA) before and after LAAC were retrospectively analyzed.

**RESULTS** Thirteen patients whom delayed CT treated by pericardiocentesis and drainage after LAAC, of whom 7 males, average 72±18.3 years, including 11 delayed CT patients, and 6 patients LAAC with simultaneous cryoablation, the classification of types of left atrial appendage including cauliflower and chicken wing types. The incidence of CT-LAAbes 6.6% (6/91 cases), Watchman 0.71% (4/562 cases), LAmbre 0.93% (2/216 cases) and Laeger 6.25% (1/16 cases) respectively. The average diameter of the seal plate was 29.3±2.8 mm; 10 patients have cardiac CTA reviewed, 8 of whom the ocluder were attached to pulmonary artery, 1 patient attached to left superior pulmonary vein only, and 1 patient attached to pulmonary artery and left superior pulmonary vein, except one patient died 2 days after LAAC, other patients have a good prognosis.

**CONCLUSIONS** Anatomic relationship of the left atrial appendage, pulmonary artery and left superior pulmonary vein related to delayed CT after LAAC, and which more closely related to larger ocluder and anchor hook.

**GW33-e0686**

**Length of hospitalization-related differences and associated long-term prognosis of patients with cardiac resynchronization therapy: a propensity score matched cohort**

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**OBJECTIVES** Previous studies indicated that prolonged lengths of hospitalization (LOH) during cardiac resynchronization therapy (CRT) implantation are associated with poorer physical status and higher in-hospital mortality. However, evidence on the impact of LOH on the long-term prognosis of CRT patients is limited. The purpose of this study was to assess LOH-related prognostic differences in CRT patients.

**METHODS** In the propensity score-matched cohort, patients with standard LOH (57 days, n=172) were compared with those with prolonged LOH (>7 days, n=172) for cardiac function and study outcomes during follow-up. The study outcomes were all-cause death and heart failure (HF) hospitalization. In addition, cardiac function and changes in cardiac function at the follow-up period were used for comparison.

**RESULTS** At a mean follow-up of 3.36 years, patients with prolonged LOH, as compared with those with standard LOH, were associated with a significantly higher risk of all-cause death (hazard ratio [HR] 1.87, 95% confidence interval [CI] 1.18–2.66, P=0.007), and a higher risk of HF hospitalization (HR 1.68, 95% CI 1.08–2.63, P=0.023). Moreover, patients with standard LOH had a more significant improvement in QRS duration in follow-up than those with prolonged LOH.

**CONCLUSIONS** LOH-associated differences were found in the long-term prognosis of CRT patients. Patients with prolonged LOH had a worse prognosis than those with standard LOH.

**GW33-e0711**

**Serum biomarkers of fibrosis as predictors of left atrial appendage thrombosis in patients with non-valvular atrial fibrillation**


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**BACKGROUND** Left atrial appendage (LAA) thrombosis is known to occur in approximately 10% of patients (pts) with atrial fibrillation (AF) and is associated with a 3.5-fold increased risk of stroke/systemic embolism. Since LA fibrosis increases the development and maintenance of AF, and is associated with an increased risk of stroke, we hypothesized that levels of circulating fibrosis biomarkers may be predictors of LAA thrombosis in pts with non-valvular AF (NVAF). The objective was to conduct a comparative analysis of clinical, echocardiographic (EchoCG) imaging and serum biomarker levels in pts with NVAF, depending on the presence of LAA thrombus, followed by the identification of independent predictors of LAA thrombosis.

**METHODS** The study included 142 pts (90 men and 52 women) with NVAF hospitalized for catheter ablation or cardioversion, aged 34–72 years, divided into 2 groups comparable in gender and age: gr. 1 (n=49) – with LAA thrombosis, gr. 2 (n=97) – without LAA thrombosis. Patients underwent transthoracic and transesophageal EchoCG, determination of biomarkers in the blood: NT-proBNP (pg/mL), GDF-15 (pg/mL), TGF-β1 (pg/mL), PiNP (ng/mL), ST2 (ng/mL), highly sensitive (hs) CRP (mg/L), cystatin C (mg/L).
RESULTS The groups did not differ in the mean CHA2DS2-VASc score (2.2±1.0 in gr. 1 and 1.9±1.0 in gr. 2), as well as in the proportion of low-risk pts (0–1 point): 29 and 37% respectively (P=0.15). In gr. 1, persistent AF, coronary artery disease, congestive heart failure f. 2–3 were more common, higher volumes of both atria, left ventricular myocardial mass index and systolic pressure in the pulmonary artery were noted, lower left ventricular ejection fraction and blood flow rate in LAA. There were no differences in the proportion of pts taking oral anticoagulants (OAC), as well as in the spectrum of OAC taken. Pts in gr. 1 showed higher levels of NT-proBNP (28.10 ± 25.60 vs. 67.40 ± 97.64 [44.4–208.5], respectively, P=0.0001), GDF-15 (1039.5 ± 853.0 ± 1461.0 and 810.6 ± 650.0: 988.0), P=0.0001 and PIINP (8.00 ± 6.40: 104.0 and 64.9 ± 59.6: 68.6, P=0.0002), while the levels of TGF-b1, h CRP, ST2 and cystatin C did not differ. The cut-off values of biomarkers calculated using ROC analysis, clinical data and EchoCG indicators that differ between groups are included in the stepwise multivariate regression analysis. The following independent predictors of LAA thrombosis were identified: LA volume index (ml/m2) – odds ratio (OR) =1.084, (95% confidence interval (CI) 1.028–1.143, P=0.003), GDF-15 (1.0±2.933 mg/mL – OR=3.054, 95% CI 1.260–7.403, P=0.013, PIIINP (95% confidence interval (CI) 6.0±2.933 mg/mL – OR=5.865, 95% CI 1.34–26.4, P=0.018, P=0.0001). When evaluating the model using ROC analysis, the area of the curve AUC=0.815 (P<0.001). The higher preoperative leukocyte count is an independent predictor of LAA thrombosis.

HEART FAILURE

GW33-e0006 Preoperative leukocyte count as a useful predictor for unplanned heart failure readmission in elderly diabetic patients with newly implanted cardiac pacemakers: a 5-year cohort study

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OBJECTIVES Long-term incidence of heart failure (HF) remained higher in diabetic patients with right ventricular pacing. Early high leukocyte count plays an essential role in the development processes of HF. However, studies exploring associations between early leukocyte count and the incidence of HF in elderly diabetic patients with newly implanted pacemakers are lacking. This study examined whether higher leukocyte count is a risk factor for HF in elderly diabetic patients with newly implanted pacemakers.

METHODS From January 2017 to January 2018, 233 consecutive diabetic patients were older than 65 years undergoing newly implanted cardiac pacemakers were enrolled in this study, and information on demographic characteristics, disease and medication history, and laboratory test were collected. The study endpoint was the first readmission for HF.

RESULTS The mean leukocyte count was 6.73±1.77 (109/L), and 47 (20.17%) incident HF readmission occurred during the 5-year follow up. Multivariate cox regression models were used to reveal the positive association between preoperative leukocyte count and incidence of HF readmission (hazard ratio [HR] 1.34, 95% confidence interval [CI] 1.06, 1.64). The HR (95% CI) for HF readmission in the high-level leukocyte group (tertile 3) was 3.21 (1.17, 8.79) compared with the lower leukocyte group (tertile1). Further subgroup analyses showed that the relationship between leukocyte count and HF readmission was more robust in the presence of hypertension (P for interaction ≤0.001).

CONCLUSIONS The higher preoperative leukocyte count is an independent risk factor for HF readmission in elderly diabetic patients with newly implanted pacemakers, especially in the presence of hypertension.

GW33-e0026 Expression of serum endoplasmic reticulum stress protein XBP-1S in patients with acute myocardial infarction in different cardiac function grades

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OBJECTIVES Expression of serum endoplasmic reticulum stress protein XBP-1S in peripheral venous blood of patients with different levels of cardiac function caused by acute myocardial infarction (AMI) within 24 hours.

METHODS 168 patients with normal physical examination were selected as the control group. AMI patients in the 230 case group were divided into the acute cardiac function classification (Killip classification) method after the onset: 122 cases were included in the cardiac function classification 1 group; the cardiac function classification 2 group was included 36 cases; 14 cases were included in the cardiac function classification 3 group; 58 cases were included in the 4-level cardiac function group. ELISA method was used to detect the XBP-1S and BNP content in the patient’s serum within 24 hours.

RESULTS 1. Analysis by non-parametric rank sum test: the concentration of XBP-1S in the control group is 142.26 (125.62–155.4) ng/mL; the level 1 group of cardiac function classification is 151.79 (131.01–178.84) ng/mL; the level of cardiac function 2 is 158.09 (152–161.15); the 3-level cardiac function group is 171.5 (148.72–195.9); the 4-level cardiac function group is 295.13 (263.64–367.76); P<0.05, the difference is statistically significant. Serum BNP content is analyzed by non-parametric rank sum test: the BNP content of the control group is 40 (32–65) ng/mL; the cardiac function grade 1 group is 144.6 (130.2–349) ng/mL; the cardiac function grade 2 The group is 61.12 (161.1–1192) ng/mL; the cardiac function grade 3 group is 158.45 (57–14569) ng/mL; the cardiac function grade 4 group is 1599 (1019–3212) ng/mL; P<0.05.

CONCLUSION The response in UPR’s IRE1’s XBP-1 signaling pathway is one of the three classic pathways that participate in the ER response. Under normal circumstances, the expression of XBP-1S is very low, but patients with IRI and heart failure caused by AMI may be significantly induced.

GW33-e0051 Insulin resistance is associated with heart failure with recovered ejection fraction in non-diabetic patients

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OBJECTIVES Due to advances in medical treatments, a substantial proportion of heart failure (HF) patients have experienced recovery of ejection fraction (HFrecEF). Insulin resistance (IR) is prevalent in HF and tightly related with prognosis. This study investigates the relationship between IR and the incidence of HFrecEF in non-diabetic patients.

METHODS A total of 262 non-diabetic HF patients with reduced EF (HFrEF) were consecutively enrolled. Patients were classified into HFrecEF (follow-up EF>40% and ≥10% absolute increase) or otherwise persistent HFrEF based on repeat echocardiogram after 12 months. IR was estimated by an updated homeostasis model assessment (HOMA-IR).

RESULTS The median HOMA2-IR level was 1.05 (IQR 0.67–1.63) in our cohort of non-diabetic HF patients. During follow-up, 121 (46.18% [95% CI 40.15%–52.22%]) patients developed HFrecEF. Compared with HFrEF patients, HFrecEF patients had significantly lower HOMA2-IR levels (0.92 [IQR 0.61–1.37] vs. 1.14 [IQR 0.75–1.78], P<0.007), especially in non-ischemic etiology. Log-transformed HOMA2-IR was inversely correlated to improvements in EF (Pearson’s r=0.25, P<0.001). After multivariate adjustment, the OR associating HOMA2-IR was associated with a 4.12% decreased likelihood of HFrecEF (OR=0.98 [95% CI 0.902–0.987]).

CONCLUSIONS This study reveals that IR is independently associated with compromised development of HFrecEF in non-diabetic patients.

GW33-e0124 Characteristics of patients undergoing pericardiocentesis and safety of pericardiocentesis under anticoagulation or antiplatelet therapy

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OBJECTIVES Pericardial effusions can be caused by a variety of diseases. The safety of urgent pericardiocentesis for large pericardial effusion in some patients without the cessation of anticoagulants or antiplatelet agents is uncertain. This study aimed to analyze the characteristics of patients undergoing pericardiocentesis, and the safety of pericardiocentesis under anticoagulants or antiplatelet agents at a regional medical center in southwest China.

METHODS We performed a retrospective observational study of 347 consecutive patients undergoing pericardiocentesis at our hospital between 2012 and 2022. The baseline characteristics, medications and procedural details were collected through the electronic medical records. Patients were divided into Groups of Antithrombotic (use of any antithrombotic agents or antiplatelets at the day of procedure) or Non-antithrombotic. Comparisons between groups were performed using Mann-Whitney U-test for non-parametric data. All procedures were performed by experienced cardiologists. Bleeding events were defined using the National Institutes of Health scale of adverse events (CTCAE).

RESULTS Among the 347 patients included, 52 patients (14.7%) were under usage of antithrombotic agents. They were older, had more comorbidities of hypertension, diabetes, chronic kidney disease, coronary artery
GW33-e0177
Pulmonary hemodynamic and prognostic value of cardiopulmonary exercise score in patients with left heart failure
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OBJECTIVES Secondary pulmonary hypertension in left heart failure (PH-LHF) was 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 (RHC). 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. Patients were prospectively followed for composited clinical events (all-cause death and rehospitalization for HF) for at least 1 years.

RESULTS The high HFCE score group of 26 (25%) patients had a higher prevalence of NYHA class III-IV, higher NT-proBNP level, lower 6-minute-walk-distance (6-MWD), the high HFCE score group had worsening hemodynamic parameters including higher prevalence of combined post- and pre-capillary PH (Cpc-PH), higher mean pulmonary artery pressure (mPAP), higher pulmonary artery wedge pressure (PAWP), higher pulmonary vascular resistance (PVR) and lower cardiac output (CO). The high HFCE score correlated well with the high level of PVR, PAWP and mPAP, and the low level of CO. There were 54 composed clinical events (12 all-cause death, 43 HF rehospitalization) in 46 (45%) patients during the mean follow-up period of 477 days, which were increased corresponded with the HFCE score. In the multivariate model, the HFCE Score was an independent predictor of composed clinical events (P=0.007). Kaplan-Meier analysis showed a significantly higher probability of composed clinical events in the patients with a higher HFCE score (8–14 points) (P=0.004).

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.

GW33-e0291
HbA1c variability is associated with long term outcome of heart failure patients with and without diabetes
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OBJECTIVES Glycemic control is an important clinical issue in the management of patients with heart failure (HF), but the effect of long-term glycemic variability on clinical outcomes in HF patients remains unclear. This study aims to evaluate the association of HbA1c variability and clinical outcomes for patients with HF.

METHODS Using a previously validated territory-wide clinical information resource, HF patients who had more than 3 times HbA1c measurements after the diagnose of HF were included (N=77,006) from 2004–2018. Average success variability (ASV) (average absolute difference between successive values), standard deviation (SD) and mean of HbA1c were calculated. Competing risk analysis using Cox proportional-hazard models was performed to estimate the risk of rehospitalization and all-cause mortality associated with HbA1c variability.

RESULTS Of all eligible patients, the mean age was 67.5±12.2 years and 39,409 (51.2%) were male. During a mean follow-up of 7,725.2 years, 61,032 (81.9%) patients had an incidence of HF rehospitalization, while 40,743 (52.3%) experienced the endpoint of death. Greater long-term HbA1c variability was significantly associated with higher risk of HF rehospitalization (HR=1.25, 95% CI, 1.23 to 1.27, P<0.001) and all-cause mortality (HR=1.53, 95% CI, 1.507 to 1.570, P<0.001). Interestingly, for patients without DM, higher HbA1c variability had an even stronger impact on HF rehospitalization than DM patients (DM patients: HR: 1.22, 95% CI, 1.20 to 1.25; Non-DM patients: HR: 1.86, 95% CI, 1.70 to 2.04). High HbA1c mean was associated with higher risk of HF rehospitalization in DM patients while in Non-DM patients the effect was opposite (DM patients: HR: 1.64, 95% CI: 1.60 to 1.66; Non-DM patients: HR: 0.88, 95% CI: 0.83 to 0.92).

CONCLUSIONS This study suggests that for patients with HF, substantial variability was associated with a higher risk of HF rehospitalization, this effect existed in both patients with and without diabetes.
GW33-e0585

Association between triglyceride and all-cause and cause-specific mortality in heart failure patients: a territory-wide study in Hong Kong

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BACKGROUND To determine the association between levels of triglyceride (TG) and all-cause mortality, cardiovascular death (CVD) or non-cardiovascular death (non-CVD), and the concentration of TG associated with the lowest risk of adverse outcomes in heart failure (HF) patients.

METHODS Using a previously validated territory-wide clinical information registry, all eligible patients with HF (N=1,473,996) from 1996 to 2020 were enrolled. Baseline levels of time-weighted TG associated with risk of mortality were evaluated on a continuous scale using restricted cubic splines and by categories with Cox proportional hazards regression models. The main outcomes were all-cause mortality, CVD and non-CVD. Secondary outcomes were cause-specific mortality (cardiac death, myocardial infarction-related death, pneumonia-related death and other mortality).

RESULTS Among 147,996 individuals, the mean age was 70.0±12.5 years and 73.571 (49.9%) were male. The association between levels of weight-weighted TG and the risk of all-cause mortality was J shaped, with low and high levels associated with an increased risk of all-cause mortality, CVD and non-CVD. Compared with individuals with concentrations of TG of 1.14–2.85 mmol/L, the multivariable-adjusted hazard ratio for all-cause mortality was 1.39 (95% confidence interval 1.35 to 1.44) for individuals with TG concentrations of less than 0.71 mmol/L and 1.97 (1.67 to 2.32) for TG concentrations of more than 5.70 mmol/L. The concentration of TG associated with the lowest risk of all-cause mortality was 1.84 mmol/L. Similar results were seen in men and women, in patients with or without lipid-lowering treatment, and for cause-specific mortality.

CONCLUSION In the HF population, low and high levels of TG were associated with an increased risk of all-cause mortality, CVD and non-CVD. The lowest risk of all-cause mortality was found at a TG concentration of 1.84 mmol/L.

GW33-e0587

Hemodynamic monitoring improved the clinical outcomes of the patients with acute myocardial infarction complicated by cardiogenic shock

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OBJECTIVES Acute myocardial infarction with cardiogenic shock (AMICS) often leads to a poor prognosis. Prompt and accurate monitoring of hemodynamic changes is crucial to the condition. Pulse index continuous cardiac output (PiCCO) provides precise hemodynamic parameters. However, there is scanty utilization of PiCCO in the management of AMICS. In this study, PiCCO is evaluated for its potential utility in improving management and clinical outcomes among AMICS patients.

METHODS A total of 100 patients with AMICS were prospectively assigned to the PiCCO group and the control group by a 1:1 ratio in Shanghai East hospital from 2018 to 2021. The major adverse cardiovascular and cerebrovascular events (MACCEs) and parameters related to cardiac function were compared during follow-up.

RESULTS PiCCO-guided intensive care reduced MACCEs and all-cause death 8 weeks after admission (P<0.05). The duration of hospitalization was appreciably shortened in the PiCCO group (P<0.05). The levels of hs-TnT, NT-proBNP, LVEF and Scr were improved more immediately and significantly in the PiCCO group accompanied by optimizing hemodynamic parameters (P<0.05).

CONCLUSIONS Hemodynamic monitoring optimized the therapy for AMICS patients and improved their clinical outcomes.

GW33-e0590

Statin associated lower risk of incident dementia in heart failure patients: a territory-wide cohort study in Hong Kong

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OBJECTIVES The number of heart failure (HF) patients who develop dementia has grown rapidly due to improved treatment and aging populations. Data relating to the association of statin use on the risk of dementia incidence among patients with HF are sparse.

METHODS Using a previously validated territory-wide clinical information registry, statin use was ascertained among all eligible patients with HF (N=104,295) from 2004 to 2018. Inverse probability of treatment weighting (IPTW) was used to balance baseline covariates between statin users (N=5,400) and statin non-users (N=50,591). Competing risk regression with Cox proportional-hazard models was performed to estimate the risk of incident dementia associated with statin use.

RESULTS Of all eligible subjects, the mean age was 74.4±12.6 years and 52,511 (50.3%) were male. Over a median follow-up of 9.9 years (interquartile range [IQR]: 6.4–13.0), 10,051 (9.8%) patients were diagnosed with dementia. In adjusted analysis, all-Alzheimer’s disease (N=2,250), vascular dementia (N=1,812), and unspecified dementia (N=5,590). After IPTW, statin use was associated with a 20% lower risk of incident dementia compared with non-use (multivariable-adjusted sub-distribution hazard ratio [SHR]=0.80; 95% Confidence Interval [CI], 0.76–0.84). Furthermore, statin use was associated with a 27% lower risk of Alzheimer’s disease (SHR=0.72; 95% CI, 0.63–0.82), 18% lower risk of vascular dementia (SHR=0.82; 95% CI, 0.70–0.95), 20% lower risk of unspecified dementia (SHR=0.80; 95% CI, 0.75–0.85).

CONCLUSIONS Our study suggests that in patients with HF, statin use was associated with a significantly lower risk of incident dementia, including Alzheimer’s disease, vascular dementia, and unspecified dementia.

GW33-e0591

Efficacy of cardiac contractility modulation in patients with heart failure: a meta-analysis

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OBJECTIVES To investigate the effectiveness of cardiac contractility modulation (CCM) in patients with heart failure.

METHODS We searched Wanfang, CNKI, VIP, Cochrane Trial Center, MEDLINE, and EMBASE from January 2001 to March 2022 to identify eligible clinical studies, which were systematically reviewed and meta-analysed. The primary endpoints were all-cause mortality, all-cause hospitalizations, heart failure hospitalizations, peak oxygen consumption, 6-minute walk test distance, quality of life scores, and incidence of arrhythmias.

RESULTS A total of six trials were included, four of which were randomised controlled studies, recruiting a total of 935 patients. The analysis showed that CCM failed to improve all-cause mortality, all-cause hospitalizations, and heart failure hospitalizations, but significantly improved peak oxygen consumption (Mean Difference=0.91, 95% CI 0.44–1.307, P<0.0001), 6-minute walk test distance (Mean Difference=20.36 m, 95% CI 16.48–24.24, P<0.0001) and quality of life as measured by MLWHFQ (Mean Difference=−7.85, 95% CI 10.76 to 4.94, P<0.0001).

CONCLUSIONS CCM failed to improve mortality and hospitalization in heart failure patients with short-term follow-up, but it had a statistically significant effect on patients’ quality of life. Larger randomized controlled trials may be needed to determine whether CCM treatment is beneficial in long-term follow-up.
GW33-e0595 Clinical characteristics of elderly chronic heart failure inpatients complicated with atrial fibrillation and its relationship with left atrial enlargement
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OBJECTIVES To analyze the clinical characteristics and risk factors of elderly patients hospitalized with chronic heart failure (CHF) combined with atrial fibrillation (AF) and their relationship with left atrial enlargement (LAE).

METHODS Through the hospital information system and inpatient electronic medical record system, the gender, age, past medical history, discharge diagnosis and echocardiographic indexes of elderly patients (260 years old) hospitalized with CHF in our hospital from 2008 to 2020 were collected. The CHF patients were divided into two groups according to whether they were combined with AF. The differences in clinical characteristics, risk factors for AF, and the correlation between AF, CHF, and LAE were analyzed.

RESULTS Among the 4650 elderly CHF inpatients, 1411 (30.34%) were complicated with atrial fibrillation and its relationship with LAE. Compared with the CHF/AF− group (n=3239), patients in the CHF/AF+ group were older (71.79±7.90 years vs 72.12±7.64 years, P<0.05), women predominated (44.15 vs 39.12%, P<0.001), with more severe heart failure symptoms, a higher proportion of patients in New York Heart Association (NYHA) class III and above (74.69 vs. 68.42%, higher prevalence of valvular heart disease (348 cases, 24.66%) and primary cardiomyopathy (164 cases, 11.62%). Parameters reflecting left atrial size in cardiac ultrasound [left atrial anterior–posterior diameter (LAD–AP), medio–lateral diameter, supero–inferior diameter and left atrial volume index (LAVI)] and relative wall thickness in the CHF/AF+ group were significantly higher than those in the CHF/AF− group. The incidence of LAE was also significantly higher in the CHF/AF+ group than in the CHF/AF− group when LAVI and LAD–AP were used for the definition of LAE. Multifactorial logistic regression analysis showed that LAVI (OR=1.06) and high left ventricular mass index (defined as 35±15g/m² in men and 29±15g/m² in women, OR=2.08) were independent risk factors for the development of AF in the elderly CHF patients.

CONCLUSIONS Elderly patients with CHF have a higher comorbidity prevalence of AF, and those with AF may have more severe heart failure symptoms, more significant LAE, and worse left ventricular diastolic function. LAE is an independent risk factor for the development of AF in the elderly patients with CHF.

GW33-e0600 Clinical characteristics of different types of elderly patients hospitalized with chronic heart failure
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OBJECTIVES To investigate and compare the clinical characteristics of elderly patients hospitalized with different types of chronic heart failure (CHF) in our hospital.

METHODS Through the hospital information system and inpatient electronic medical record system, the gender, age, past medical history, discharge diagnosis and echocardiographic indexes of elderly patients (260 years old) hospitalized with CHF in our hospital from 2008 to 2020 were collected. Then the study population were divided into three groups according to left ventricular ejection fraction (LVEF) in CHF inpatients: patients with an ejection fraction of 50% or less (HFpEF), patients with mildly reduced ejection fraction (HFrEF) and patients with reduced ejection fraction (HFrEF). Clinical characteristics were compared among the above three CHF categories.

RESULTS A total of 4650 valid data were included in the analysis, of which 595 cases (12.9%, average age 71.6±7.76 years) were HFpEF, 1915 cases (41.2%, average age 72.63±7.86 years) were HFrEF, and the oldest in all elderly CHF inpatients, with an average age of 73.66±7.86 years. The top 5 underlying causes of CHF were ischemic heart disease (3375 cases, 72.58%), primary hypertension (2945 cases, 63.33%), arrhythmia (1986 cases, 42.71%), valvular heart disease (724 cases, 15.57%), and primary cardiomyopathy (497 cases, 9.83%). Among these, the prevalence of primary cardiomyopathy (354 cases, 21.76%) and ischemic heart disease (580 cases, 80.22%) was the highest in HFrEF and HFrEF group, respectively. However, the prevalence of primary hypertension (1592 cases, 69.22%) and arrhythmia (1012 cases, 44.00%) were the highest in HFrEF group. The top 5 co-morbidities of CHF were dyslipidemia (3946 cases, 84.86%), chronic kidney disease (2190 cases, 47.10%), type 2 diabetes mellitus (1693 cases, 36.41%), anemia (1606 cases, 34.54%) and ischemic cerebrovascular disease (840 cases, 18.06%). The prevalence of dyslipidemia (653 cases, 87.81%) and type 2 diabetes mellitus (405 cases, 41.26%) and ischemic cerebrovascular disease (470 cases, 20.46%) were more common in HFrEF group. There were significant differences in cardiac structural and functional ultrasound indices among the three types of CHF. Among them, left ventricular diastolic dimension, left ventricular mass index, left atrial anterior–posterior diameter, and left atrial volume index were the highest in HFrEF group, while the relative wall thickness, LVEF, and fractional shortening were the highest in HFrEF group (all P<0.05).

CONCLUSIONS There are significant differences in the underlying etiology, co-morbidities and ultrasound indices among different types of elderly CHF inpatients. It is of great importance to carry out targeted comprehensive management and conduct clinical studies according to clinical characteristics.

GW33-e0606 Autonomic nervous system in hypertension and heart failure
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OBJECTIVES Left ventricular hypertrophy (LVH) is a clinically relevant sequel of elevated blood pressure (BP), then essential hypertension (EH) acts as a chief risk factor of congestive heart failure (CHF). Autonomic nervous system (ANS) plays a pivotal role in EH and LHV. Heart rate variability (HRV) is currently used as a noninvasive evaluation of ANS. Blood pressure and its variability (BPV) is also considered to be a marker of ANS in some reports. To explore the difference of autonomic nerve in patients with normal blood pressure, hypertension and heart failure and its correlation with left ventricular hypertrophy.

METHODS One hundred ninety-two patients with essential hypertension, 40 patients with hypertension and heart failure, and 72 patients without hypertension or heart failure were enrolled. The general data of three groups were collected, 24-hour holter, ambulatory blood pressure measurement and echocardiography were performed. Heart rate variability (HRV), blood pressure variability (BPV) and left ventricular mass index (LVMI) calculated.

RESULTS Gender distribution, history of diabetes, smoking and drinking, body mass index, triglyceride and glycosylated hemoglobin were similar among the groups. The age, cholesterol, BNP, albumin, LVM, standard deviation of all normal sinus R–R intervals over 24 h (SDNN), high-frequency normal units (HFnu), 24 h, day and night mean systolic blood pressure, diastolic blood pressure, pulse pressure, standard deviation of systolic blood pressure and systolic blood pressure decline rate among the three groups were statistically significant (P<0.05, P<0.01). In each pairwise comparison between groups, pulse pressure was significantly different (4.95±5.8, 5.8±4.1, 7.86±3.4, 6.68±1.4±4.8, all P<0.01). There was a poor correlation between pulse pressure and LVMI (r=0.2, P=0.01).

CONCLUSIONS Pulse pressure may be a more sensitive index for left ventricular hypertrophy.

GW33-e0632 Analysis of cardiac structure and function in 2281 elderly patients with ejection fraction preserved heart failure complicated with anemia
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OBJECTIVES To analyze the characteristics of cardiac structure and function in elderly patients with ejection fraction preserved heart failure (HFpEF) complicated with anemia.

METHODS A total of 2281 elderly HFpEF patients (260 years old) hospitalized in our hospital from February 2008 to December 2019 were enrolled and divided into anemia group or control group according to whether they had anemia or not. The clinical data of the patients were collected and the differences of cardiac ultrasound structure and function between the two groups were compared and analyzed.
RESULTS There were 949 elderly HFpEF inpatients complicated with anemia, accounting for 41.6%. Compared with the control group, the anemia group had a higher proportion of male (54.69 vs 45.31%), older age (74.79±9.79 vs 73.40±7.27 years old), lower body mass index (24.34±4.10 vs 24.87±4.05 kg/m²), higher systolic and diastolic blood pressure (140.08±70.58 vs 136.77±74.89 mmHg), and more heart failure symptoms. Among them, the proportion of of New York Heart function above grade III was higher (27.75 vs 13.44%). The renal function was worse in the anemia group and the proportion of chronic kidney disease above grade 4 (55.11 vs 16.26%) was much higher than that of the control group. The all-cause mortality in hospital (3.58 vs 1.50%) was also higher (P<0.05) in the anemia group. Echocardiographic results showed that left heart enlargement was more obvious in the anemia group, including left atrial anteroposterior diameter (57.53±8.62 mm), left atrial volume index (57.4±27.29 vs 32.2±21.79 ml/m²), left ventricular end-systolic volume (49.48±23.97 vs 41.15±15.75 mm), left ventricular end-diastolic volume (103.69±30.07 vs 97.36±31.03 mm), left ventricular end-systolic diameter (32.6±24.48 vs 31.6±4.69 mm), and left ventricular end-diastolic diameter (46.87±7.57 vs 45.76±7.47 mm), when compared with the control group. Moreover, the indexes of left ventricular hypertrophy, such as left ventricular posterior wall thickness (10.68±1.47 vs 10.47±2.52 mm) and left ventricular mass index (120.24±39.99 vs 110.14±26.91 g/m²) were also significantly higher than the control group. The CRP, HDL and IL-6 levels were also larger than those in the control group. Moreover, the heart and renal function and prognosis are poor.

GW33-e0664 Prognostic value of high-sensitivity modified Glasgow prognostic score in patients hospitalized for heart failure
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OBJECTIVES Inflammation plays a key role in the progression of heart failure (HF). High-sensitivity modified Glasgow prognostic score (HS-mGPS) is a sensitive inflammation biomarker that has been validated in HF. It is unknown whether HS-mGPS can assess the prognosis in patients hospitalized for HF. We sought to determine whether HS-mGPS is independently associated with long-term mortality in patients hospitalized for HF.

METHODS We enrolled patients hospitalized for HF from 52 hospitals in China. HS-mGPS according to previously published literature: pro-inflammatory, high-sensitivity C-reactive protein (hsCRP) ≤3 mg/L were defined as 0 score, those with hsCRP>3 mg/L and albumin 235 g/L as 1 score, and those with hsCRP>3 mg/L and albumin<235 g/L as 2 scores. The level of hsCRP were centrally analyzed with blood samples, and the level of albumin at admission were obtained from medical charts of the hospital indexation. The outcome was all-cause death after discharge. Unadjusted death rates were displayed with Kaplan–Meier plots and tested. Multi-variable Cox proportional regression models were performed to assess the association of HS-mGPS with mortality, and the full multivariable model was based on literature review and clinical knowledge. We evaluated the incremental prognostic value of HS-mGPS and established risk scores by C-index, net reclassification improvement (NRI), and integrated discrimination improvement (IDI) when adding it to Get With the Flow (GWTG) HF score.

RESULTS Of the 4486 patients included in this analysis, the median (interquartile range, IQR) age was 67 (57, 75) years old and 37.5% were female. The median (IQR) levels of hsCRP and albumin at admission were 4.3 (1.7, 13.5) mg/L and 38.8 (35.7, 41.9) g/L. There were 1770 (39.5%) patients with 0 HS-mGPS score, 2012 (44.9%) with 1 score, and 704 (15.7%) with 2 scores. Within 2-year of discharge, 131 patients died. Patients with increasing HS-mGPS had significantly higher risk of mortality in unadjusted analysis (P for log-rank=0.0001). Using multi-variable Cox models, compared with 0 HS-mGPS score, the adjusted hazard ratios (HRs) were 1.22 (95% confidential interval [CI], 1.06–1.39) for 1 score and 1.78 (95% CI, 1.52–2.00) for 2 scores. When adding HS-mGPS to GWTG HF score, the C-index was 0.66 (95% CI, 0.64–0.67), the NRI was 0.04 (95% CI, 0.00–0.09), and the IDI was 0.02 (95% CI, 0.01–0.03).

Conclusions In this first report of HS-mGPS among patients with HF, HS-mGPS is a strong predictor for long-term mortality, and it could serve as a convenient inflammation-based tool for rapid risk stratification.
CONCLUSIONS

The systolic blood pressure and pulse pressure might be mediators of VFA-induced arterial stiffening in HFpEF patients.

BLOOD LIPIDS AND ATHEROSCLEROSIS

GW33-e0105

The associations among carotid plaque progression, cerebrovascular/cardiovascular diseases and LDL-C/non-HDL-C goal achievement in diabetic patients: a retrospective cohort study

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OBJECTIVES

Impaired glycolipid metabolism can induce vascular injury and plaque formation. Carotid ultrasonography is an important examination to assess carotid plaque progression and lipid-lowering goal achievement. Current recommendations provide no instruction for repeated carotid ultrasound examinations to guide lipid-lowering therapeutic decisions. It is important to investigate the associations between carotid plaque progression and lipid-lowering goal achievement and cardiovascular disease.

METHODS

Diabetic patients who underwent at least 2 carotid ultrasound scans with intervals ≥30.5 years and were hospitalized in the Department of Endocrinology at Sun Yat-sen Memorial Hospital were included. Patients were divided into 3 groups based on carotid plaque progression: the persistent low-risk plaque/spring pre-existence, newly-onset plaque and persisting SE. Age, smoking, BMI and VFA were significantly associated with higher mortality in HFpEF by cox univariable analysis. However, pericardial adipose tissue (PAT) thickness, epicardial adipose tissue (EAT) thickness, abdominal obesity, waist/hip ratio and body fat mass failed to predicting outcomes of HFpEF. After adjusting for confounders of other underlying risk factors, VFA could independently predict all-cause mortality in patients with HFpEF.

CONCLUSIONS

VFA might be an independent prognostic risk factor for all-cause mortality in patients with HFpEF.
GW33-e0224
Identification and validation of candidate gene module along with immune cells infiltration patterns in atherosclerosis progression to plaque rupture via transcriptome analysis
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OBJECTIVES
Atherosclerosis is the major cause of a global cardiovascular disease, ischemic stroke, as well as peripheral arterial disease. The inflammatory nature of atherosclerosis remains a predominant reason for plaque vulnerability. The interplay between immune cells and genetic markers in atherosclerosis formation, progression, and plaque rupture is still vastly under-investigated.

METHODS
In this study, three atherosclerosis-related microarray datasets were downloaded from the NCBI-GEO database. Gene set enrichment analysis (GSEA) was performed for interpreting the biological insights of gene expression data. CIBERSORTx algorithm was applied to infer the relative proportion of infiltrating immune cells of the atherosclerotic samples. DEGs of the datasets were screened using R. The protein interaction network was constructed using STRING. The cluster genes were analyzed by Cytoscape software. Gene Ontology (GO) enrichment was performed via geneontology.org. The least absolute shrinkage and selection operator (LASSO) logistic regression algorithm and receiver operating characteristics (ROC) analyses were performed to build machine learning models for differentiating atherosclerosis status. The Pearson correlation analysis was carried out to illustrate the relationship between cluster genes and immune cells. The expression levels of the cluster genes were validated in two external cohorts. Transcriptional factors and drug-gene interaction analysis were performed to investigate the promising targets for atherosclerosis immunotherapy.

RESULTS
Pathways related to immunoinflammatory responses were identified according to GSEA analysis, and the detailed fractions infiltrating immune cells were compared between the early and advanced atherosclerosis. Additionally, we identified 170 DEGs in atherosclerosis progression (log2FC>1 and adjusted q-value<0.05). They were mainly enriched in GO terms relating to inflammatory response and innate immune response. A cluster of nine genes including ITGB2, C1QC, LY86, CTSS, C1QA, CSF1R, LAPTM5, VEGFA, and CD163 was found to be significant, and their correlations with infiltrating immune cells were calculated. The cluster genes were also validated to be upregulated in two external cohorts. Moreover, C1QA and ITGB2 may exert pathogenic functions in the entire process of atherogenesis.

CONCLUSIONS
We reanalyzed the transcriptomic signature of atherosclerosis development from onset to plaque rupture along with immune cells landscape, as well as revealed new insights and specific prospective DEGs for the investigation of disease-associated dynamic molecular processes and their regulations with immune cells.

GW33-e0365
Remnant cholesterol and joint arteriosclerosis and atherosclerosis progression beyond LDL cholesterol in the general population
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OBJECTIVES
Remnant cholesterol could predict cardiovascular events, while its effect on joint arteriosclerosis and atherosclerosis progression remains unclear. This study aims to evaluate the association of remnant cholesterol with arteriosclerosis and atherosclerosis progression trajectories in the general population, and evaluate its effect beyond low density lipoprotein (LDL) cholesterol.

METHODS
This longitudinal study collected data across five biennial surveys of the Beijing Health Management Cohort from 2010 to 2019. We used the multi-trajectory model to cluster the joint arteriosclerosis and atherosclerosis progression groups measured by brachial-ankle pulse wave velocity (baPWV) and ankle brachial index (ABI). Remnant cholesterol was both calculated by Martin-Hopkins method and Friedewald equation. Then, the ordinal logistic model was performed to assess the effect of baseline lipid profiles on progression trajectories. We also performed discordance analyses for remnant cholesterol vs. LDL cholesterol according to the percentile distance (ten percentiles) and clinical cut-off points.

RESULTS
A total of 3,186 participants were included, with three clusters following distinct arteriosclerosis and atherosclerosis progression patterns identified using a multi-trajectory model. In the multivariable-adjusted ordinal logistic model, remnant cholesterol was significantly associated with baPWV and ABI progression (OR: 1.20; 95% CI: 1.13–1.28, per 10 mg/dL). We also performed discordance analyses for remnant cholesterol vs. LDL cholesterol, and the discordant low remnant cholesterol group was associated with decreased risk compared to the concordant group (OR: 0.73; 95% CI: 0.60–0.89). People with a high remnant cholesterol level were at an increased risk of joint arteriosclerosis and atherosclerosis progression, even with optimal LDL cholesterol.

CONCLUSIONS
Remnant cholesterol is independently associated with joint arteriosclerosis and atherosclerosis progression beyond LDL cholesterol. Remnant cholesterol could be an earlier risk factor than LDL cholesterol of arteriosclerosis and atherosclerosis in the general population. Future studies are needed to assess whether remnant cholesterol is a potential intervention target for arteriosclerosis and atherosclerosis, and cardiovascular events, even in people with an optimal LDL cholesterol level.

GW33-e0460
Liver damage of xuezhikang compared with statin in patients with hypercholesterolemia: results from a multicenter, retrospective real-world study in China
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OBJECTIVES
Both Xuezhikang and statins could effectively decrease cholesterol levels. However, the potential harmful effect of statin therapy on liver has become a concern in clinical practice. Thus, we conducted a large multicenter, retrospective cohort study to investigate the safety of xuezhikang compared with statin in patients with hypercholesterolemia, especially liver damage.

METHODS
A total of 1,746 patients with hypercholesterolemia were enrolled from 3 centers in China. Five hundred eighty-three patients received 1,200 mg/d of Xuezhikang while 1,163 patients received moderate statin. The primary outcome was defined as the changes of liver transaminase from baseline to the study end-point (90 days from the baseline). Secondary outcomes included the incidences of liver transaminase > 3 upper limit of normal (ULN), the absolute value of liver transaminases, creatine kinase (CK), HbA1c, fasting glucose at the study end-point, the changes of low-density lipoprotein cholesterol (LDL-C), cholesterol and non-high-density lipoprotein cholesterol (non-HDL-C) from baseline to end-point.

RESULTS
Mean baseline aspartate transaminase (AST) for the two treatment groups were 22.27 and 21.93 U/L, while the mean alanine transaminase (ALT) was 21.07 and 20.39 U/L for the xuezhikang and statin groups respectively. After a follow-up duration of 90 days, the changes of AST/ALT from baseline to end-point were lower in xuezhikang group than in statin group (xuezhikang vs. statin for AST: 1.34±5.77 vs. 3.86±11.61, P=0.001; xuezhikang vs. statin for ALT: 5.42±16.19 vs. 2.9±3.7, P=0.002). After adjusted for age and gender, the changes of AST/ALT were still lower in xuezhikang group than in statin group (ALT P=0.001, ALT P=0.004, respectively). Similar effects were observed on the absolute value of AST (xuezhikang vs. statin: 23.61±8.3 vs. 23.70±11.9, P=0.001). The incidences of ALT/AST > 3 ULN were low in both groups and no difference was observed (xuezhikang vs. statin: 0.2 vs. 0.3%, P=0.670). No significant difference was observed in terms of the CK, HbA1c, and fasting glucose at the end-point between the groups (P>0.05). In addition, both treatments produced significant efficacy on LDL-C (xuezhikang: 3.26±2.44 mmol/L, P=0.001; statin: 3.34±2.10 mmol/L, P=0.001), cholesterol (xuezhikang: 5.72±4.58 mmol/L, P=0.001; statin: 5.69±4.18 mmol/L, P=0.001) and non-HDL-C (xuezhikang: 4.41±2.91 mmol/L, P=0.001; statin: 4.36±3.29 mmol/L, P=0.001) from baseline to end-point. However, significantly lower proportions of patients achieved LDL-C levels < 2.6 mmol/L (80 vs. 60%), < 1.8 mmol/L (41 vs. 22%) and < 1.4 mmol/L (71 vs. 53%) with statin than xuezhikang (all P<0.001).

CONCLUSIONS
In patients with hypercholesterolemia, xuezhikang treatment was much safer on liver function compared with moderate statin, but also produced significant efficacy on lipid reduction compared with baseline.

GW33-e0552
Effects of rosuvastatin for delaying progression of atherosclerosis in people living with HIV
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OBJECTIVES
People with HIV are more susceptible to atherosclerosis due to immune disorder, chronic inflammatory state, and highly active antiretroviral therapy. Present research are design to evaluate the efficacy and safety of rosuvastatin for delaying progression of atherosclerosis in people living with HIV.

METHODS
Randomized controlled trials (RCTs) were searched from MEDLINE (1980–July 2021), the Cochrane Controlled Trials Register, EMBASE (1985–July 2021), Science Citation Index and PUBMED (updated through July 2021). We included RCTs of unilateral or bilateral carotid intimomedia-thickness from baseline as defined as the primary outcome while the variation of LDL-C, IL-6 and hsCRP as the second. Statistical analyses were performed using Review Manager software (version 5.4; The Cochrane Collaboration). The analysis was
stratified by the difference of control group: placebo or rosuvastatin therapy. The weighted mean difference (WMD) of continuous variables was calculated with 95% confidence interval (CI). Heterogeneity was assessed by the I2 measure of inconsistency, statistically significant if I2 >50%. For all the outcomes a P value of less than 0.05 was considered statistically significant.

**RESULTS**

Three eligible trials of rosuvastatin therapy involving a total of 273 participants were included after reviewing by two independent reviewers. (137 subjects received rosuvastatin, while 136 subjects were in the placebo) All of three studies showed that the change of mean carotid IMT progression from baseline were significantly different between rosuvastatin and placebo, the Z score for overall effect of IMT was 6.03 (P=0.0001). Total 95% CI of weighted mean difference (WMD) between two groups were −0.01 [−0.01, −0.01]. Three studies provided information regarding variation of hsCRP and IL-6. There was a significant difference between two groups in hsCRP [Z score 4.03 (P=0.0001)] 95% CI [−3.55, −0.50] and IL-6 [Z score 3.51 (P=0.0001)] 95% CI [−1.16, −0.86]. A significant difference was also found in the change of LDL-C from baseline. [Z score 3.43 (P=0.0006)] 95% CI (−3.65) (−2.9, 13)]. Rosuvastatin was not significantly different of serious adverse events and withdrawal than placebo (P>0.05).

**CONCLUSIONS**

Rosuvastatin is an accessible, safe and effective drug that could be utilized for delayed progression of atherosclerosis in people living with HIV. The tolerability, benefits, and safety should be confirmed in in-depth clinical trials.

**GW33-e0636**

**Aerobic exercise ameliorates dysfunctional high-density lipoprotein sub-fractions via protein composition alteration in youth with obesity**

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**OBJECTIVES**

Obesity becomes an emerging cardio-metabolic problem globally. High-density lipoprotein (HDL) might be compromised in obesity. The mechanisms for the beneficial effects of aerobic exercise on HDL have not been investigated comprehensively. This study was designed to investigate whether aerobic exercise without restricted diet ameliorates dysfunctional HDL by altering protein composition in youth with obesity.

**METHODS**

This was a single centre and self-control study. All youth participants with body mass index > 28 kg/m² received a personalized 12-week moderately aerobic exercise program according to the result of cardioregulatory fitness test. Fasting plasma samples of each participant were collected before and after exercise intervention. HDL from each sample was isolated by fast protein liquid chromatography and further evenly divided into three sub-fractions: large-HDL, medium-HDL, and small-HDL fraction. The protein composition of three HDL sub-fractions were analyzed by mass spectrometry using label-free protein quantification. We detected HDL-cholesterol, HDL2-cholesterol and HDL3-cholesterol concentrations from samples before and after exercise intervention. We also measured the functional characteristics in each HDL sub-fraction: cholesterol efflux capacity, anti-oxidative capacity (by HDL inflammatory index), and HDL-related endothelial protection capacity.

**RESULTS**

Though the levels of plasma HDL-cholesterol levels were similar before and after the 12-week exercise training, HDL-cholesterol level was significantly increased. One hundred sixteen HDL-bound proteins were detected in HDL-subfractions and further grouped into 4 functional categories (lipid metabolism, immune response, coagulation, and others). The composition of HDL-bound proteins was significantly altered after 12-week exercise intervention. In medium-HDL fraction, the levels of apoA1 and apoE were increased. Meanwhile, the aerobic exercise induced a significant improvement in cholesterol efflux capacity of medium-HDL. We also found that the function, inhibiting the tumor necrosis factor-α-induced monocyte adhesion to endothelial cells, were improved in large-HDL fraction along with the significant elevation of apoM level. However, HDL inflammatory index in all three sub-fractions were not changed after exercise intervention.

**CONCLUSIONS**

A 12-week aerobic exercise program might lead to an efficient cardio-protective improvement on HDL via protein composition alterations.

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**STRUCTURAL HEART DISEASE**

**GW33-e0007**

**Current treatment and future prospect of LVHT**

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**OBJECTIVES**

Left ventricular hypertrophy (LVHT) is a rare myocardial hypertrophy associated with indistinct etiology and significant mortality. Although LVHT has been increasingly recognized among cardiologists nowadays, few advances have been achieved to conquer this disease up to now, particularly its treatment. Therefore, in this investigation we aimed to analyze and summarize current clinical treatment of LVHT and come up with novel therapeutic strategies for lower mortality, combined to updating therapeutic technologies in cardiology.

**METHODS**

Five patients were selected (two females, three males) from Shanghai General Hospital on the basis of suspicious CMRI (cardiac magnetic resonance imaging) manifestations and typical clinical presentations for diagnosing LVHT. The average age of those five patients were 56.60±3.1 years, ranging from 46 to 62 years.

**RESULTS**

Through analyzing five patients’ therapeutic protocols, we discover that clinical treatment of LVHT is mainly focus on the symptoms or the complications of LVHT, such as heart failure, arrhythmia and thromboembolism. For patients who suffered from heart failure, tablets like β-blockers, angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), mineralocorticoid receptor antagonists, and diuretics were used to manage cardiac dysfunction. For patients who were undergoing arrhythmia such as atrial fibrillation (AF), radiofrequency catheter ablation (RFCA) and oral anticoagulation were applied. Implantable cardioverter defibrillator (ICD) implantation were executed when ventricular tachycardias were recorded for the prevention of sudden cardiac death (SCD). β-blockers were also used for heart rate stabilization and long-term cardiac benefit. For patients who had the history of thromboembolism, antiplatelet therapy was utilized.

**CONCLUSIONS**

Currently, clinical therapy of LVHT is symptomatic treatment. Complications such as heart failure, arrhythmia and thromboembolism in LVHT patients are treated in the same way as those diseases caused by other etiologies. Lack of specific therapeutic strategies for treating LVHT is an intractable obstacle for reducing the mortality of this disorder.

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**GW33-e0436**

**A nomogram for predicting patent foramen ovale-related stroke recurrence**

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**OBJECTIVES**

The high prevalence of patent foramen ovale (PFO) in cryptogenic stroke suggested a stroke-causing role for PFO. As risk factors for recurrent stroke are not recognized, clinicians cannot sufficiently identify, treat, and follow-up high-risk patients. Therefore, this study aimed to establish a prediction model for PFO-related stroke recurrence.

**METHODS**

This study included 392 patients with PFO-related stroke in a training set and 164 patients with PFO-related stroke in an independent validation set. In the training set, independent risk factors for recurrence were identified using forward stepwise Cox regression were included in nomogram1, and those identified using least absolute shrinkage and selection operator (LASSO) regression were included in nomogram2. Nomogram performance and discrimination were assessed using the concordance index (C-index), area under
Cardiovascular Innovations and Applications, Vol. 7, Suppl 1, 2022

C65

This observational cohort study evaluated 117 adult patients (age

Methods
Concurrent presence of mitral stenosis (MS) and mitral regurgitation for tricuspid annuloplasty.

Conclusions
Patients with mixed mitral valve disease compared to isolated MS. The existing THV could not meet the anatomical characteristics of the patients with AR, whereas the newly designed THV based on the dual-anchoring multiplanar measurement, type-1 transcatheter heart valve (THV) anchoring at the annulus, left ventricular outflow tract (LVOT), and ascending aorta (AA); type-2 anchoring at the annulus and AA; type-3 anchoring at the annulus and LVOT; and type-4 anchoring at only one level or not anchoring at all. Among them, types 1–3 were considered as candidates for TAVR, while type 4 was not.

Results
Patients (n=136) with AR (mean age, 68.7 years ± 10.7; 98 men) were included, with 117 (86.0%) tricuspid, 14 bicuspid, and 5 quadricuspid valves. Dual-anchoring multiplanar measurements showed the annulus shorter than LVOT, 2.2, 6.8, and 10 mm on annulus (27.233 vs. 27.533; 27.653; 28.752; 28.752, 27.9122, 30.1, 31.715 mm, respectively); AA 40 mm was wider than AA 30 and 35 mm, but narrower than AA 45 and 50 mm (39.956 vs. 38.3169, 39.1565, 40.7265, and 41.4264 mm, respectively). For 10% oversize of THV, the proportions of the annulus, LVOT, and AA unable to meet the diameter were 22.8, 37.5, and 56%, and proportions of anatomical classification types 1–4 were 32.4, 5.9, 30.1, and 31.6%, respectively. Moreover, for 20% oversize, the proportion of type 4 was 59.5%. However, the newly designed THV could significantly improve the type 1 proportion (88.2%).

Conclusions
The existing THV could not meet the anatomical characteristics of the patients with AR, whereas the newly designed THV based on the anatomical characteristics could theoretically facilitate TAVR.

GW33-e0683
Evolution of cardiac damage and clinical outcome after transcatheter aortic valve replacement
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Objectives
The impact of transcatheter aortic valve replacement (TAVR) on extra-valvular cardiac damage stage of aortic stenosis (AS) patients in the short term and its association with subsequent long-term prognosis is unknown.

Results
Isolated MS was present in 39 (33%) patients, while concomitant MS and MR was present in 78 (67%). Compared to patients with isolated MS, those with mixed mitral valve disease more frequently had HF and more prevalent use of diuretics. Left ventricular end-diastolic and end-systolic volumes, left atrial volume, and right ventricular systolic pressure were higher in patients with mixed mitral valve disease than their counterparts. Over a median follow-up of 5.7 years (interquartile range: 4.4 to 9.0 years), 50 adverse events (35 HF hospitalizations, 10 strokes, and 5 deaths) occurred. In multivariable Cox regression analysis, left ventricular end-diastolic volume was the only independent echocardiographic predictor for adverse events (adjusted hazard ratio 1.05, 95% confidential interval 1.01–1.09, P=0.043), after adjusting for baseline HF, use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, and estimated glomerular filtration rate. There was no difference in event rates between patients with mixed mitral valve disease and isolated MS (38 vs. 51%, P=0.790).

Conclusions
Mixed mitral valve disease confers a high risk of adverse events.左心室端-心房和端-心房体积，左心房体积，和右心室收缩压在混和性二尖瓣疾病患者与对应的对照组中更高。在中位5.7年（四分位范围4.4至9.0年）随访期间，共有50例不良事件（35例心衰住院，10例卒中，5例死亡）发生。在多变量Cox回归分析中，左心室舒张末期体积是唯一的独立的超声心动图预测因素（调整后危险比1.05，95%置信区间1.01–1.09，P=0.043），在调整了基线心衰，使用血管紧张素转换酶抑制剂/血管紧张素II受体阻断剂后。与混和性二尖瓣疾病的患者相比，混合性二尖瓣疾病和孤立性二尖瓣疾病患者的心衰住院率没有差异（38 vs. 51%）。
This study aims to shed light on the evolution of extra-valvular cardiac damage after TAVR and its association with clinical outcomes in TAVR recipients.

**METHODS**

As patients undergoing TAVR were consecutively enrolled following additional exclusion criteria. Based on the echocardiographic parameters at baseline, within 30 days and 1-year post-TAVR, patients were classified into five cardiac damage stages (0–4), respectively. Data collection included baseline demographics, clinical data, and predischarge outcomes. The concordance characteristics consisted of clinical, laboratory, and echocardiographic data. Pre-discharge outcomes were obtained from the local hospital database and were rigorously assessed for quality. The primary clinical outcome was all-cause mortality, defined according to the Valve Academic Research Consortium-3 criteria.

**RESULTS**

Among 644 included patients, 18 (2.8%) were Stage 0, 74 (11.5%) Stage 1, 427 (66.3%) Stage 2, 72 (11.2%) Stage 3, and 53 (8.2%) Stage 4 at baseline. In general, the baseline cardiac damage stage changed in 22.2% of TAVR recipients (mostly regressed), accompanied by improvement of dyspnea degree and left ventricular ejection fraction (LVEF) within 30 days post-TAVR. Afterward, no further significant changes in the proportion of respective stage groups were observed in the whole cohort during one-year post-TAVR. During a median follow-up period of 2 years after TAVR, a total of 43 (6.7%) deaths occurred. Two-year mortality was associated with both baseline stage (HR 1.59, 95% CI 1.10–2.20; P=0.014, for linear trend) and residual cardiac damage within 30 days post-TAVR (HR 2.97, 95% CI 2.07–4.25; P<0.001, for linear trend). In a multivariate-adjusted Cox proportional hazards regression model, both baseline stage and 30 days post-TAVR residual cardiac damage were independent risk factors for 2-year mortality (P<0.001).

**CONCLUSIONS**

This investigation provided insight into the evolution of the cardiac damage stage in AS subpopulation after TAVR and confirmed the superior predictive value of post-TAVR cardiac damage over its baseline counterpart. These findings suggest the significance of echocardiographic reassessment models for prediction of post-TAVR cardiac damage. Thirty days post-TAVR cardiac damage could act as a straw in the wind to hint at long-term outcomes for TAVR recipients.

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**GW33-e0695**

Development and validation of a risk score to predict mortality for elder patients with mitral regurgitation

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**OBJECTIVES**

Risk stratification for elder patients with mitral regurgitation (MR) is crucial in the context of an increasing number of patients accepting transcatheter aortic valve replacement (TAVR). The aim of this study was to develop a simple risk score to predict mortality for elder MR patients (≥60 years).

**METHODS**

Two thousand seven hundred thirty-eight patients with moderate or severe MR from the China Valvular Heart Disease Study (China-VHD) were used to externally validate the Elder-MR score, and the model was internally verified using the Development cohort. The primary outcome was 1-year mortality. Cox’s proportional hazards model and the stepwise selection with Akaike’s information criterion (AIC) were used to select potential predictors. The discrimination was assessed using Harrell’s c-statistic and the calibration was evaluated with the calibration plot. The overall performance of the Elder-MR score was measured by the Brier score.

**RESULTS**

Eight predictors were selected to build the Elder-MR score: age ≥75 years, BMI ≥20 kg/m², NYHA class III/IV, functional MR, anemia, eGFR <60 mL/min/1.73 m², albumin<25 g/L, and LVEF<60%. The Elder-MR score ranges from 0 to 15 points according to the sum of the weights of these factors. The score exhibited good performance both in the development cohort (c-statistic 0.73, 95% CI: 0.69–0.77; Brier Score 0.06) and the validation cohort (c-statistic 0.73, 95% CI: 0.69–0.77; Brier Score 0.06). One-year mortality of patients under medical management with low risk (0–4 points), moderate risk (5–9 points), or high risk (10–15 points) was 2.7, 9, and 20% in the development cohort (P<0.001), and 2.9%, 8.8%, and 17.7% in the validation cohort (P<0.001). Each point increase in the Elder-MR score was associated with a 2.27-fold risk of death (HR 2.27, 95% CI: 1.79–2.84; P<0.001, in the validation cohort). When compared to the EuroScore II, the Elder-MR score exhibited better predictive accuracy in predicting 1-year mortality (Net reclassification improvement, NRI 0.266, P<0.01; Integrated discrimination improvement, IDI 0.026, P<0.01) in the validation cohort.

**CONCLUSIONS**

The Elder-MR score showed good performance in predicting 1-year mortality both in the development cohort and the validation cohort. It may serve as a useful risk stratification tool to help clinical decision-making in elder MR patients.

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**GW33-e0718**

Pressure related parameters derived from patient-specific computer simulation technology for prediction of new-onset conduction disturbances in transcatheter aortic valve replacement

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**OBJECTIVES**

Transcatheter aortic valve replacement (TAVR) is an effective treatment for aortic valve disease, and the correct selection of prosthetic valve size plays a crucial role in the operation, which directly affects the success rate of operation and the incidence of major complications, such as peri-valvular leakage and permanent pacemaker implantation. The objective of this study is to evaluate the consistency and reproducibility of Anythink for aortic root measurements by comparing the measurement data of Anythink, models of semi-automatic preoperative CT analysis software, with those of 3mensio.

**METHODS**

Sixty-seven patients who underwent TAVR in the First Medical Center of the Chinese PLA General Hospital from December 2016 to February 2018 were retrospectively included. The new semi-automated software Anythink and the 3mensio “gold standard” measurement software were used to analyze the aortic annulus and surrounding structures. The relation and consistency of the measurement results of two softwares were analyzed. Two independent doctors applied Anythink software to repeat the measurements to assess the reproducibility of Anythink measurements for the same subjects. The valve models were selected based on the measurements of Anythink and 3mensio software and the similarities and differences between the two softwares were assessed for practical use in guiding clinical valve selection.

**RESULTS**

There was no statistical difference in the t-test for the measured parameters of the aortic root between Anythink and 3mensio. Annulus average diameter: 24.0±2.2 vs. 23.9±2.3 (P=0.321); annulus area: 450.6±88.3 vs. 447.5±90.0 mm² (P=0.69); annulus perimeter: 76.5±7.2 vs. 76.6±7.6 mm (P=0.75); distance from annulus plane to left coronary ostium (LCO): 13.3±7.3 vs. 13.1±7.3 mm (P=0.268); distance from annulus plane to right coronary ostium (RCO): 15.4±2.9 vs. 15.4±2.9 mm (P=0.97); angle between annulus and horizontal plane: 53.5±10.0 vs. 51.1±9.7° (P=0.647). The Pearson correlation analysis between software showed a positive correlation (r=0.884 vs. 0.981 and all P values less than 0.01). The kappa-test values of valve models selected by Anythink and 3mensio based on average diameter, area diameter and perimeter diameter were 0.886, 0.796 and 0.775. In patients with postoperative paravalvular leakage, the recommendations from area diameter measured by Anythink had a larger trend compared with 3mensio, while in patients with postoperative paravalvular new conduction block, the recommendations from Anythink had a smaller trend.

**CONCLUSIONS**

Anythink, the domestic semi-automatic TAVR preoperative CT analysis software, has excellent measurement consistency and high reproducibility for aortic root measurements.
postoperative new-onset CDs has been assessed and diagnosed by postoperative echocardiogram data.

**RESULTS**

There was no significant difference between FEops and 3mensio for the measured parameters of aortic annulus (perimeter: 74.00 mm, P = 0.087; area: 423.62 ± 85.4 mm², P = 0.004 and LVOT (perimeter: 77.42 ± 1.06 mm, P = 0.001 and 11.06 ± 7.39 mm, P = 0.000; area: 423.81 ± 11.06 mm², P = 0.000 and 438.00 ± 15.67 mm², P = 0.000). The Pearson correlation analysis between FEops and 3mensio measurements showed a positive correlation (r = 0.878–0.974 and all P values less than 0.01). Of the 30 patients completed the finite element simulation, 8 (27%) patients developed new complete left bundle branch or a highly hyperexcitable left ventricular block after TAPVC repair which could be considered as postoperative new-onset CDs. The CPI and MCP in new-onset CDs were significantly higher [30 (24–57)] vs. [9 (2–12)] mm 2, P = 0.001 (38–77) vs. [28 (0.05–0.047) MAP] compared with that of patients without new-onset CDs. Other parameters between the two groups showed no statistical difference. The AUC of receiver of operating characteristic curve for CPI and MCP for discrimination of postprocedural new-onset CDs was 0.937 (95% CI [0.785–0.993], P = 0.001 and 0.750 (95% CI [0.559–0.889], P = 0.039), respectively. The CPI represented better prediction power for adverse prognosis than MCP (P = 0.044).

**CONCLUSIONS**

The patient-specific computer simulation technology FEops can reconstruct a model with high consistency with standard 3mensio. Pressure related parameters derived from FEops, especially CPI, can precisely predict the risk of postprocedural new-onset CDs, which means they reflect a clinical predictive value for identifying patients with adverse prognosis.

GW33-e0743

The 100 most-cited articles on total anomalous pulmonary venous connection

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**OBJECTIVES**

The number of times an article is cited reflects its impact on the research community. The aim of this study was to explore the characteristics of the most frequently cited articles published on total anomalous pulmonary venous connection (TAPVC).

**METHODS**

The database of the Clarivate Analytics’ Web of Science Core Collection Expanded Science Citation Index (1900 to present) was searched using the topic words ‘total anomalous pulmonary venous connection’, ‘total anomalous pulmonary venous drainage’ or ‘total anomalous pulmonary venous return’ on 21 May 2022. This database indexed more than 53 million records from over 9500 impact high journals across 178 scientific disciplines. The ‘document type’ was activated to limit the document type to ‘Article’ or ‘Review’. Two authors read the abstract or full text if need to identify the 100 most-cited articles dedicated to TAPVC. The following information were recorded: title, corresponding author, number of citations, publication year, country origin, institution, journal, funding source, and article type. The institution and country origin were defined by the address of the corresponding author. Data analysis was performed using statistical software SPSS version 19.0 (SPSS Inc., Chicago, IL, USA).

**RESULTS**

A total of 1352 papers were retrieved after the initial search, with 984 as ‘Article’ and 36 as ‘Review’. The top 100 cited articles were published between 1952 and 2018 with a mean number of citations of 52 (range 26 to 148). The 1990s was the most productive decade. The 100 top-cited articles were published in 24 journals, led by Journal of Thoracic and Cardiovascular Surgery (21 articles), followed by Annals of Thoracic Surgery (20 articles), and Circulation (16 articles). Hospital for Sick Children, Toronto led the list of classics with six papers. All articles except one were written in English. The United States of America contributed most of the top 100 cited articles (60 articles). Christopher A. Caldarone, John W. Kirklin, and P. E. F. Daubeny were the most productive authors with 3 articles each. The majority of the top 100 list were clinical articles, among which cohort study (n = 51) was the most common type, and only 1 reported a clinical trial. Among these articles, 31 were funded by public foundations, none received support from commercial companies, for the remaining 69 the funding source was not specified. Specifically, 15 studies received grants from the National Institutes of Health.

**CONCLUSIONS**

The bibliometric analysis gives a historical perspective on the scientific progress in the field of TAPVC and informs people of important advances in the study of this disease.

GW33-e0744

Review of surgical experience in 61 patients with mixed total anomalous pulmonary venous connection

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**OBJECTIVES**

Prior studies have reported a high mortality and incidence of post-repair pulmonary venous obstruction (PVO) in mixed total anomalous pulmonary venous connection (APVC). This study sought to review the surgical outcomes in this entity.

**METHODS**

A review of 61 patients undergoing surgical repair of mixed TAPVC was conducted. Patients with a single ventricle were excluded. Patients were subdivided into 3 groups according to Chowdhury’s classification. Predictors for death and postoperative PVO were explored by Cox regression model.

**RESULTS**

This study trended towards an older cohort with a median age of 88 years (2–114 years), 66% were male. There were no early death and 7 late deaths. Follow-up was available in 96.7% of the patients after discharge with a median duration of 53 months (range, 1–177). Nineteen patients developed new-onset PVO among whom 2 required reintervention. Patients with preoperative PVO had a 4-fold higher risk (95% confidence interval, 1.36–12.38) of postoperative PVO than those without and were more likely to die (P = 0.009). No statistical difference was observed among the 3 subgroups in terms of mortality (P = 0.075) and postoperative PVO (P = 0.16).

**CONCLUSIONS**

Preoperative PVO was significantly associated with postoperative PVO. There was no statistical difference in terms of death and postoperative PVO among the 3 subtypes of mixed TAPVC. Mid-term results favoured a complete rechanneling of pulmonary veins in ‘3+1’ type.
GW33-e0370
Modulation of activated microglia in the hypothalamic paraventricular nucleus to prevent ventricular arrhythmia in stress-induced cardiomyopathy rat model
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OBJECTIVES
Life-threatening ventricular arrhythmias have been reported in patients with stress-induced cardiomyopathy (SICMP). Growing evidence suggests a major role of the brain, particularly during stress. Paraventricular nucleus (PVN) of the hypothalamus may play an important role on this context, however, the mechanisms remain unknown. In this study, we investigated whether inhibition of activated microglia in the PVN could reduce ventricular arrhythmia (VA) in rats with SICMP.

METHODS
Male SD rats were selected to immobilization stress for 6 h last ing 7 days to establish SICMP model. The anesthetized rats were randomly divided into three groups of normal control, SICMP, and SICMP-minocycline. Electrocardiogram was continuously recorded. RNA sequencing, sympathetic nerve activity (heart rate variability and noradrenaline levels) and ventricular electrical instability (ventricular effective refractory period and ventricular fibrillation inducibility) were measured. Furthermore, brain hilar tissues were extracted to detect expression of inflammatory cytokines, microglia and neuro activation.

RESULTS
RNA sequencing analysis showed that functions of differentially expressed genes in the PVN of SICMP rats were significantly enriched in neuro-inflammation-related pathways. Microglia were activated and sympathetic activity increased in PVN in SICMP rats. The induction of ventricular fibrillation rate was significantly increased in rats with SICMP. Inhibiting microglia activation could significantly reduce the induction of ventricular fibrillation rate and maintain cardiac electrical stability.

CONCLUSIONS
Activated in the hypothalamic paraventricular nucleus in stress-induced cardiomyopathy, to prevent ventricular arrhythmia complication, inhibiting activation of activated Microglia in the PVN could reduce VA occurrence and improve ventricular electrical instability in SICMP rats by central neuro-inflammatory-related pathways. These findings suggest that Microglia are a potential target for prevention and treatment of VA complicating SICMP.

GW33-e0402
The prognostic value of serum calcium levels in elderly patients with non-ischemic dilated cardiomyopathy
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OBJECTIVES
Dilated cardiomyopathy (DCM) is the most commonly diagnosed type of systolic heart failure, at present, there are no clear clinical risk factors for elderly patients with non-ischemic dilated cardiomyopathy (NIDCM). Thus, we conducted a retrospective study with a relatively large sample size to investigate the prognostic value of baseline serum calcium in elderly patients with NIDCM.

METHODS
A total of 1089 elderly patients (age ≥ 60 years) diagnosed with non-ischemic dilated cardiomyopathy (DCM) were retrospectively enrolled from January 2010 to December 2019. Serum calcium level produced more prognostic value in elderly patients with NIDCM, which might be considered as a new prognostic indicator to reduce the future risk of death. Hypocalcemia in patients should be noted.

GW33-e0514
Analysis of changing trends in the clinical features and treatment of dilated cardiomyopathy
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OBJECTIVES
To explore the trends of the disease clinical features and treatment of DCM (Dilated Cardiomyopathy) patients in the First Affiliated Hospital of Xinjiang Medical University from 2011 to 2020.

METHODS
DCM patients (n=1080) from the hospitalized patient were divided into five calendar periods of inclusion, 2011–2012 (Period 1, n=690), 2013–2014 (Period 2, n=765), 2015–2016 (Period 3, n=770) T, 2017–2018 (Period 4, n=838), 2019–2020 (Period 5, n=871). The demographic information and clinical data including medical past history, diagnosis, investigations, current treatment and comorbidities were collected.

RESULTS
The total number of inpatient with DCM showed an increasing trend over the five calendar periods, The Han, Uyghur, Kazakh, Hui and others nationalities accounted for 54.3% (145), 29.9% (142), 6.6% (260), 6.2% (44), 4.1% (161), respectively. Over the periods, patients were older (P<0.05), the symptoms by New York Heart association were more severe (P<0.05), and left ventricular ejection fraction was higher (P<0.05), thus, the hospital stay was longer (P<0.05). Multivariate Cox proportional hazard analysis showed that patients with a serum calcium ≤ 8.62 mg/dL had a higher proportion of comorbid conditions, including atrial fibrillation, cerebral infarction, gallstone, comparing with the former period. With the passage of time, the proportion of DCM patients with complete left bundle branch block, unstable ventricular tachycardia/cardioid grade II and above atrioventricular block were increased (P<0.05). The drug treatment regimen was achieved, such as the proportion of ACEI/ARB, beta-blocker and aldosterone antagonists usage rate gradually increased (P<0.05), and the proportion of digoxin usage decreased by 24.3% (mean 46.1%, 49.2%, 40.1%, 26.3%, 21.8%, P<0.05). Device (implantable cardioverter defibrillator and/or cardiac resynchroniza tion) therapy increased by 12.3% over the time (mean 0.43%, 3.27%, 5.22%, 8.59%, 12.74%, P<0.05). The overall treatment outcome was valid, and the average length of stay was gradually shortened (P<0.05).

CONCLUSIONS
From 2011 to 2020, the number of DCM visits has been gradually on the rise, paralleled by a continuous change in both clinical characters and phenotypes in the DCM population in Xinjiang, towards a more complex phenotype. Although the treatment plan has been optimized and proved to be effective, the diagnosis and treatment of DCM still has a long way to go.

GW33-e0521
The clinical value of MHR in chronic heart failure with dilated cardiomyopathy
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OBJECTIVES
To explore the clinical value of monoocyte count and high-density lipoprotein cholesterol ratio (MHR) in the diagnosis and treatment of chronic heart failure (CHF) in patients with dilated cardiomyopathy (DCM).

METHODS
A total of DCM 300 patients with chronic heart failure treated in the first affiliated Hospital of Xinjiang Medical University in the past four years were selected and divided into NYHA II, NYHA III and NYHA IV group (100 patients), according to the cardiac function classification of New York Heart Association. In the same period, 100 patients with organic heart disease and chronic heart failure were selected as the control group. The level of MHR, the relationship between MHR and N-terminal precursor B-type natriuretic peptide (NT-proBNP), and the relationship between MHR and echocardiographic indexes related to cardiac remodeling and cardiac function were observed and analyzed in DCM and chronic heart failure.

RESULTS
The MHR of DCM patients with chronic heart failure was significantly higher than that of the control group (P<0.001), and there were differences among different grades of heart failure in the case group (P<0.05). After controlling the influence of gender, it was found that MHR was positively correlated with left atrial diameter (LAD), left ventricular end-diastolic diameter (LVESD), left ventricular end-systolic diameter (LVESD) and NT-proBNP. It was negatively correlated with LVEF. Correlation analysis showed that MHR was positively correlated with left atrial diameter (LAD), left ventricular end-diastolic diameter (LVESD), left ventricular end-systolic diameter (LVESD) and NT-proBNP. It was negatively correlated with LVEF. Correlation analysis showed that MHR was positively correlated with NT-proBNP alone (AUC=0.974) (P<0.05). These results suggest that MHR may be associated with cardiac remodeling and cardiac function in DCM. The higher the MHR, the more pronounced the cardiac remodeling and cardiac function the better prognosis the patient had. With the passage of time, the average length of stay was gradually shortened (P<0.05).

CONCLUSIONS
From 2011 to 2020, the number of DCM visits has been gradually on the rise, paralleled by a continuous change in both clinical characteristics and phenotypes in the DCM population in Xinjiang, towards a more complex phenotype. Although the treatment plan has been optimized and proved to be effective, the diagnosis and treatment of DCM still has a long way to go.
CONCLUSIONS: Clinically, doctors can try to use MHR as an indicator of the presence of chronic heart failure and the severity of heart failure in DCM patients. In particular, the combined determination of MHR and NT-proBNP may be more helpful to improve the sensitivity and specificity of clinical diagnosis of chronic heart failure in DCM. As a result, doctors can have more early identification and accurate implementation of the standardized treatment of chronic heart failure in DCM patients.

GW33-e0659
A novel cardiac MRI based nomogram for risk stratification in dilated cardiomyopathy with reduced ejection fraction
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OBJECTIVES: Dilated cardiomyopathy (DCM) patients with reduced ejection fraction (EF) are at high risk of adverse consequences, but effective and specific risk evaluation remains challenging. This study aimed to develop and validate a new nomogram score to predict outcomes in DCM patients with reduced EF.

METHODS: A total of 335 consecutive DCM patients with reduced EF who underwent cardiac magnetic resonance feature-tracking (CMR-FT) were retrospectively enrolled. The major adverse cardiac events (MACEs) included all-cause mortality and heart transplantation. These patients were randomly divided into training and validation cohort (7:3). In the training cohort, LASSO regression analysis and non-multiplicative Cox regression analysis were utilized to identify prognostic factors. A nomogram based on the selected predictive variables was built to predict MACEs. AUC, Harrell’s C-index, and calibration curves were used to evaluate the efficiency of the nomogram in both training and validation cohorts.

RESULTS: MACEs occurred in 93 (39.7%) out of 234 patients in the training cohort, and in 41 (40.6%) out of 101 patients in the validation cohort. Six variables including hypertension, NT-proBNP, LA diameter, LVESVI, LGE presence, and LVGLS were found to be significantly associated with MACEs and were used for constructing the nomogram. The nomogram achieved good discrimination with C-indexes of 0.86 (95% CI: 0.72 to 0.93; P < 0.001) and 0.85 (95% CI: 0.77 to 0.96; P < 0.001) in the training and validation cohorts respectively. The calibration curve for 1-, 3-, and 5-year survival also showed high coherence between the predicted and actual probability of MACEs. Decision curve analysis identified our model was clinically useful in predicting MACEs.

CONCLUSIONS: This study presents a predictive model and constructs a nomogram that incorporates the cardiac MRI parameters and clinical risk factors, which can be conveniently used to facilitate the risk stratification in DCM patients with reduced EF.

GW33-e0660
Incremental prognostic value of left atrial and biventricular feature-tracking in dilated cardiomyopathy
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OBJECTIVES: Although cardiac magnetic resonance feature-tracking (CMR-FT) has been used to detect myocardial deformation, the association between atrial and ventricular strain with outcomes is unclear in dilated cardiomyopathy (DCM) patients. To investigate the value of five new inflammatory markers in predicting unplanned ICU admission in DCM. ROC cure analysis result showed that in modeling group and validation group, the area under curve (AUC) of the model were 0.77 (95% CI: 0.73–0.82) and 0.76 (95% CI: 0.68–0.83), with good discrimination. The Hosmer-Lemeshow test showed that the nomogram prediction model had good correction ability (χ?2 = 3.48, P = 0.529), with good goodness of fit.

CONCLUSIONS: This study identified the PLR, NLR, SII and SIRI all associated with unplanned ICU admission and the combination of SIRI with the MAGGIC risk score could predict unplanned ICU admission more accurately.
**OBJECTIVES** The SYNTAXES study, repeat revascularization within 5 years and randomized treatment. The association between repeat revascularization within 5 years and 10-year mortality was assessed.

**RESULTS** A total of 330 (250 repeat revascularization after initial PCI and 110 repeat revascularization after initial CABG) out of 1800 patients (18.3%) underwent repeat revascularization within 5 years, with a trend toward lower mortality compared to patients who did not undergo repeat revascularization (13.2% vs 17.6%, adjusted HR: 0.8, 95% CI: 0.74–1.2, P=0.08). Among patients requiring repeat revascularization, those who underwent PCI as initial revascularization had a higher risk of 10-year mortality compared to initial CABG (13.5% vs 17.6%, adjusted HR: 0.8, 95% CI: 0.5–1.5, P=0.08).

**CONCLUSIONS** In the SYNTAXES study, repeat revascularization within 5 years had no impact on 10-year all-cause death in the population overall. Among patients requiring any repeat procedures, mortality was higher after initial treatment with PCI than after CABG. These exploratory findings should be investigated with larger populations in future studies.

**GW33-e0120**

**Circulating exosomal miRNAs as novel biomarkers for acute aortic dissection**

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**OBJECTIVES** Objective: Acute aortic dissection (AAD) is a serious and life-threatening cardiovascular emergency. The aim of this study was to investigate whether exosomal miRNAs in circulating exosomes could serve as novel diagnostic biomarkers for AAD.

**METHODS** Using miRNA microarray sequencing, the differentially expressed exosomal miRNAs between AAD group and healthy control (HC) were found. In this study, we investigated 8 exosomal miRNAs (miR-499a-5p/miR-143-3p/miR-143-3p/miR-4433b-3p/miR-744-5p/miR-4488/miR-202-3p/miR-206), 4 genes (MMMP-9/MMMP-12/TGF-β/D-Dimer) in AAD (n=30) and HC (n=30) expression levels between the two groups. The combined diagnosis of exosomal miRNA and gene expression was performed (AUC=0.8, 0.04=0.05). The ROC curve was drawn to evaluate the diagnostic efficiency. Predict the gene targets of differentially expressed exosomal miRNAs and analyze the functions and signaling pathways of these targets using online databases.

**RESULTS** The exosomes isolated from the two groups of serum were bilayer membranes with a diameter of about 100 nm. Stably expressed in CD9, CD63 and TSG101. Compared with the healthy control group, 8 exosomal miRNAs (miR-499a-5p/miR-143-3p/miR-143-3p/miR-4433b-3p/miR-744-5p/miR-4488/miR-202-3p/miR-206) were regulated to varying degrees (P<0.05).

**CONCLUSIONS** Circulating exosomal miR-499a-5p, miR-143-3p and miR-202-3p can be used as potential diagnostic biomarkers for AAD, and the combination of various markers can coordinate and complement each other, and can significantly improve the diagnosis of aortic dissection sensitivity and specificity.

**GW33-e0167**

**Implication of pulmonary artery systolic pressure for prolonged cardiopulmonary bypass duration in patients undergoing re-repair for degenerative mitral regurgitation**

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**OBJECTIVES** Emerging evidence revealed that the longer duration of cardiopulmonary bypass (CPB) during cardiac surgery renders patients at higher risk of adverse outcomes. However, little is known regarding the risk factor of prolonged CPB in patients undergoing re-repair of degenerative mitral regurgitation (DMR). We aimed to explore the prognostic significance of pulmonary artery systolic pressure (PASP) on CPB duration (PASP) and DMR patients undergoing re-repair of DMR.

**METHODS** Patients with DMR undergoing re-repair in our center were consecutively enrolled from Jan 2009 to Dec 2021. Patients were stratified into the prolonged CPB group (CPB time≥132 min, n=61) and the shorter CPB (CPB time<132, n=59). Proportional Univariable and multivariable logistic regression analyses were used to evaluate the impact of PASP on the risk of prolonged CPB duration.

**RESULTS** There was no significant difference between group A and group B in terms of red blood cell reduction, postoperative ventilator using time, postoperative drainage volume, postoperative drainage days, Postoperative hospital days and postoperative complications.

**CONCLUSIONS** Prolonged CPB duration in patients with degenerative mitral regurgitation can be predicted by preoperative PASP. Patients with PASP > 60 mmHg during CPB have a 4.2-fold increased risk for prolonged CPB duration.
GW33-e0556

Long-term prognostic implications of concomitant inflammation and malnutrition in valvular heart surgery

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OBJECTIVES Novel strategies to improve the long-term risk stratification of valvular heart surgery are urgently needed as a result of the increasing prevalence of valvular heart diseases globally. This study aimed to evaluate the long-term prognostic implications of inflammatory and nutritional status in predicting survival and adverse outcomes in patients undergoing valvular heart surgery.

METHODS One thousand forty-six patients who underwent valvular heart surgery were stratified into three groups according to their inflammatory and nutritional status: without inflammation and malnutrition (normal), inflammation or malnutrition alone (mild), and concomitant inflammation and malnutrition (severe). Inflammatory and nutritional status were defined using neutrophil-to-lymphocyte ratio (NLR) and prognostic nutritional index (PNI) respectively. Optimal NLR and PNI thresholds for predicting all-cause mortality were determined using receiver-operating characteristic analysis. Any discrimination improvement of NLR and PNI to EuroSCORE II and STS score was assessed by C-statistics, continuous net reclassification (cNRI) and integrated discrimination improvement (IDI) indices. The endpoints of interest included all-cause mortality, cardiovascular death and adverse events (composite of death and heart failure [HF] hospitalization).

RESULTS Over a median follow-up of 4.3 years (IQR: 2.6 to 6.4 years), 139 (13.3%) deaths and 148 (14.1%) HF hospitalizations occurred. Based on the optimal cut-offs of NLR (13.3%) and PNI (45.8%), 714 (68.3%), 214 (20.5%) and 18 (11.3%) patients were categorized into normal, mild and severe groups respectively. Compared with patients without inflammation and malnutrition, those with concomitant inflammation and malnutrition before surgery had the highest risk of all-cause mortality (hazard ratio [HR] 3.14, 95% confidence interval [CI] 1.36–8.57), cardiovascular death (subdistribution HR [SHR] 5.19, 95% CI 2.33–11.60) and adverse events (HR 3.14, 95% CI 2.25–4.38; P<0.001 for all), adjusted for demographics, cardiovascular risk factors and diseases, medications, valvular surgeries and concomitant risk scores. Discriminatory improvement for predicting all-cause mortality was observed when baseline NLR and PNI were added to EuroSCORE II (C-statistic 0.77 vs 0.73, P=0.04; cNRI 0.24, 95% CI 0.12–0.36, P=0.004; IDI 0.04, 95% CI 0.01–0.08, P=0.004) and STS score (C-statistic 0.78 vs 0.73, P=0.03; cNRI 0.16, 95% CI 0.06–0.32, P=0.002; IDI 0.02, 95% CI 0.00–0.049, P=0.048) respectively. One year following surgery (n=740), those with persistent concomitant inflammation and malnutrition before surgery had the highest risk of all-cause mortality (HR 8.82, 95% CI 4.21–18.49), cardiovascular death (SHR 5.83, 95% CI 3.16–10.76) and adverse events (HR 5.83, 95% CI 3.16–10.76) than those without (P<0.001 for all).

CONCLUSIONS Concomitant inflammation and malnutrition is common and is strongly associated with mortality and HF in patients undergoing valvular surgery. Beyond conventional risk scores, assessments of inflammatory and nutritional status of patients before and after surgery using NLR and PNI may provide additional prognostic and discriminatory value for long-term outcomes following valvular surgery.

GW33-e0559

Low serum albumin level is associated with higher long-term mortality in patients with acute aortic syndrome

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OBJECTIVES Previous studies found that low serum albumin (SA) is independently associated with increased in-hospital mortality in both type A and B acute aortic dissections (AD). However, few studies have reported the long-term outcomes of patients admitted with hypalbuminemia. This study aimed to evaluate the association between admission SA levels and long-term all-cause mortality in patients with acute aortic syndrome (AAS).

METHODS Demographic and clinical data were collected from 1072 patients diagnosed with AAS (intramural haematoma or aortic dissection) from 2015 to 2020 in the First Affiliated Hospital of Shantou University Medical College. Patients were divided into low-albumin group and high-albumin group. The association between long-term all-cause mortality of AAS patients and SA levels on admission was analyzed using Cox proportional hazard regression models.

RESULTS A total of 1072 patients with AAS were enrolled, of whom 304 patients (28.4%) died during the follow-up period. The long-term mortality rate of AAS patients in the low albumin group is higher than that in the high albumin group, regardless of AAS type (type A: 50.2 vs 30.6%, P=0.001; type B: 24.8 vs 12.6%, P=0.001). The survival curve showed that the mortality rate of the high albumin group was significantly lower in the low albumin group (P=0.001). Multivariate Cox regression analysis further showed that SA is an independent predictor of long-term mortality in AAS patients (HR, 0.498; 95% CI, 0.394–0.628; P=0.000).

CONCLUSIONS SA is independently associated with increased long-term all-cause mortality in both type A and B AAS. We should pay enough attention to AAS patients whose serum albumin level is reduced at the time of admission, and give appropriate treatment when necessary.

GW33-e0676

Risk factors for radial expansion rate of stent after carotid artery stenting: a high-resolution magnetic resonance vessel wall imaging research

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OBJECTIVES No studies have investigated risk factors affecting radial expansion rate of stent after carotid artery stenting (CAS). This study aimed to investigate risk factors influencing radial expansion rate of stent after CAS.

METHODS Eighty-nine patients with CAS for carotid atheroscleroticstenosis who had high-resolution magnetic resonance vessel wall imaging (HR-VWI) prior to stenting were included in this analysis. Carotid plaque burden and component were evaluated by HR-VWI. The plaque calcification circumference and site were evaluated on the 5-point and 4-point grading scale respectively. The radial expansion rate of stent (%preoperative stentosis rate)–(post-stenting stenosis rate). The low radial expansion rate of stent was defined as radial expansion rate of stent (%)<50. The baseline and clinical characteristics, plaque burden and component were compared between the patients with low radial expansion rate of stent and high radial expansion rate of stent. Univariate and multivariate logistic analysis were used to explore risk factors influencing radial expansion rate of stent.

RESULTS Among the 89 patients, 46 patients (51.7%) developed low radial expansion rate of stent after CAS. The logistic regression analysis showed that coronary artery disease (OR, 0.12; 95% CI, 0.02 to 0.63, P=0.01), higher Max wall thickness (OR, 0.58; 95% CI, 0.38–0.88, P=0.01), higher circumference total scores of calcification (OR, 1.19; 95% CI, 1.04–1.36, P=0.01), higher Maximum circumference score of calcification in single slice (OR, 0.16; 95% CI, 0.05–0.50, P=0.00) and higher Maximum area percentage of calcification (OR, 0.84; 95% CI, 0.71–0.99, P=0.04) were independently associated with low radial expansion rate of stent.

CONCLUSIONS Coronary artery disease, Max wall thickness, circumference degree of calcification and Maximum area percentage of calcification influenced radial expansion rate of stent after CAS.

GW33-e0701

Candida tropicalis bioprosthetic valve endocarditis inducing mitral valve stenosis: case report and pathological analysis

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OBJECTIVES Candida tropicalis (C. tropicalis) is a general non-albicans Candida species often causes superficial and localized mucosal Infections, vaginal infections, urinary tract infections, invasive infections and disseminated infections. C. tropicalis seldom cause endocarditis in the bioprosthetic valve.
In the reports of infective endocarditis in prosthesis valves, most occurred in aortic valves. As a less frequent clinical case, we report a case of mitral bioprosthetic valve stenosis due to Candida tropicalis infection.

**METHODS** A 72-year-old woman suffered from diabetes and obesity. She developed fever six months after a bioprosthetic mitral valve replacement, and blood cultures showed C. tropicalis infection. The damaged valve was removed and redo valve replacement was performed. Vegetations were found on both sides of the damaged valve. Pathological examination was also consistent with C. tropicalis infection.

**RESULTS** The patient recovered well and continued to receive antifungal treatment with caspofungin until blood culture was negative. At six months follow-up, the patient was afibrile and the valve function was acceptable.

**CONCLUSIONS** Bioprosthetic valve endocarditis should be comprehensive treated to avoid serious infections and complication. Active control of risk factors will contribute to the prevention of fungal infections. Comprehensive treatment is required including drug therapy and active surgical treatment.

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**C L I N I C A L   D R U G   R E S E A R C H   A N D   D E V I C E   D E V E L O P M E N T**

GW33-e0062

**Characteristics of new and old anticoagulants in the ventricular mural thrombus**

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**OBJECTIVES** To describe the characteristics, treatment practices, and thrombus outcomes of patients with ventricular mural thrombus (VMT), with emphasis on the comparison of non-vitamin K antagonist oral anticoagulants (NOACs) and vitamin K antagonists (VKAs).

**METHODS** We performed a retrospective cohort study in National Center of Cardiovascular Diseases of China between 2010 and 2019. Patients with VMT newly treated with either NOACs or VKAs were included. The primary outcome was the rate of thrombus resolution within 3 months.

**RESULTS** We included a total of 196 patients-68.9% (n=135) were treated with NOACs. Patients with a medical history of heart failure (OR 2.10, 95% CI 1.17 to 3.77, P=0.003) or low LVEF (OR 0.36, 95% CI 0.20 to 0.65, P=0.001) at baseline might have a higher thrombus resolution. At 3 months follow-up, a significant difference was observed in the thrombus resolution between the NOACs and VKAs group with or without adjustment (OR 2.61, 95% CI 1.39 to 4.89, P=0.003; adjusted OR 3.21, 95% CI 1.58 to 6.52, P=0.001) with a similar time to resolution. Further analysis showed when patients were male, more than 50 years old, LVEF≥30%, or had a medical history with heart failure, thrombus resolution was greater in NOACs group.

**CONCLUSIONS** Patients with a medical history of heart failure or low LVEF had a greater thrombus resolution. And with or without adjusting for baseline covariates, the resolution of VMT after NOACs treatment was significantly higher than the result obtained with VKAs therapy at 3 months.

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GW33-e0161

**Acute high-risk chest pain diseases during pregnancy and puerperium**

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**OBJECTIVES** Acute high-risk chest pain diseases, including acute myocardial infarction (AMI), aortic dissection (AD), and pulmonary embolism (PE) during pregnancy and puerperium are devastating, yet data regarding contemporary incidence and outcomes are limited. We aimed to investigate the incidence and outcomes of these diseases during pregnancy and puerperium.

**METHODS** The National Inpatient Sample was queried to identify women aged ≥18 years with pregnancy-related hospitalizations from 2008 to 2017. Temporal trends in the incidence and outcomes of these diseases were extracted.

**RESULTS** Among 41,174,101 hospitalizations, acute high-risk chest pain diseases were diagnosed in 40,235 (0.098%), the incidence increased from 79.82/100,000 in 2008 to 114.79/100,000 in 2017 (P trend <0.0001). The mortality slightly decreased from 2.24% in 2008 to 2.21% in 2017 (P trend=0.0240). The most frequent disease was PE (86.3%), followed by AMI (9.6%) and AD (3.3%). In pregnancy, the incidence of PE decreased significantly after 2014 and was lower than that of AMI and AD in 2016 and 2017. In puerperium, the incidence of PE was markedly higher than that of AMI and AD from 2008 to 2017. Subgroup analysis showed the incidence of these diseases was higher in black women, lowest-income households, and elderly parturients (P trend<0.0001). The mortality slightly decreased from 2.24% in 2008 to 2.21% in 2017 (P trend=0.0240). Exhibiting 100-fold higher than patients without these diseases. The mortality of AMI decreased from 5.52% in 2008 to 2.56% in 2017 (P trend=0.0240). No such trend was found in AD and PE patients. The following factors were significantly associated with these diseases: over 45 years old (OR, 9.75; 95% CI, 7.78–12.22).

**CONCLUSIONS** The incidence of acute high-risk chest pain diseases, especially PE in puerperium, increased consistently. Although mortality has shown a downward trend, it is still at a high level. Monitoring and management of these diseases in pregnancy and puerperium, especially for those over 45 years old, with valvular disease or metastatic cancer, should be strengthened in the future.
GW33-e0450
Suspected facioscapulohumeral muscular myodystrophy with cardiac symptom
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OBJECTIVES
Facioscapulohumeral muscular myodystrophy (FSHD) is a hereditary myodystrophy typically affecting skeletal muscles of the facial muscles, shoulder girdles, and upper arms. The clinical course of FSHD is highly variable and the heart is rarely involved. We aim to describe the detailed clinical characteristics of an unusual FSHD case.

METHODS
We collected data on ten family members from a Chinese FSHD family with their ages, gender, physical examination, investigations, and clinical manifestation details. Radiology, electromyography (EMG), 24-hour Holter monitor, echocardiography, cardiopulmonary exercise test (CPET), audiometry, and muscle biopsy were only performed for the proband.

RESULTS
We report the case of a 32-year-old man with recurrent chest pain, elevated myocardial injury markers, and incomplete right bundle branch block (RBBB). Coronary angiography, echocardiography, and cardiac magnetic resonance (CMR) did not identify any structural or functional abnormality. Medical and family history of muscle weakness suggested the diagnosis of dystrophy with cardiac involvement. Electromyography (EMG), muscle MRI, and muscle biopsy did not provide any indicative evidence for definitive diagnosis. Whole exome sequencing (WES) did not find pathogenic variant. Clinical diagnosis was made according to clinical criteria depending on the presence of typical clinical findings and the absence of other explanations. Cardiac-pulmonary exercise test (CPET) revealed reduced exercise capacity with maximal exercise 383 watts under RAMP protocol with peak oxygen uptake (Peak VO2) was 53% predicted and anaerobic threshold (AT) 43% predicted.

CONCLUSIONS
Our study provided detailed information of an unusual FSHD case with cardiac presentation mimicking coronary artery disease. Persistent elevated cardiac enzymes, family history of myopathy could be the prelude of FSHD.

GW33-e0631
Comorbid diseases in patients after COVID-19
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OBJECTIVES
Objective the study was to study the features of comorbid conditions in patients who underwent COVID-19 and the features of the course of the postcovid period.

METHODS
We analyzed the dynamics in 220 patients who underwent COVID-19. The mean age of the patients was 54.61±11.4 years. Of these, men accounted for 107 (48.6%) and women - 113 (51.4%).

RESULTS
Analysis of the obtained data showed that 121 (55%) patients had arterial hypertension (AH), 1/3 of patients had 74 (33.6%) obesity, 39 (17.7%) patients had coronary heart disease (CHD) and 26 (11.8%) patients had chronic heart failure (CHF). Slightly less common diseases such as chronic kidney disease (CKD), atrial fibrillation (AF), chronic obstructive pulmonary disease (COPD). In the post-hospital period, many patients continued to present various complaints. After 3 months observation, at least 1 symptom persisted in 36% of patients, and after 6 months, observations - in 25.7%. The most common symptoms that persisted in patients up to the 3rd and 6th months were weakness - 70 (31.8%) and 51 (24.1%), as well as shortness of breath - 63 (28.6%) and 38 (17.9%). These symptoms were observed in every third patient after 3 months and every fifth in 6 months. Attention was drawn to the fact that in the first 3 months many patients - 40 (18.1%) complained of rises in blood pressure against the background of previously effective antihypertensive therapy, as well as palpitations 26 (11.6%). According to the survey, after 3 months. after COVID-19 convalescence: 14.5% of patients had shortness of breath with significant exercise, 8.2% of patients with normal exercise, 5% of patients with minor exercise, 1.4% of patients at rest. Persistence of dyspnea after 6 months most often observed in patients with cardiovascular pathology. According to data analysis after 6 months. Shortness of breath with significant physical exertion, shortness of breath persisted in 4.7% of patients, with normal physical exertion in 3.8% of patients, with slight physical exertion in 2.3% of patients, at rest in 0.5% of patients.

CONCLUSIONS
In patients after COVID-19, cardiovascular diseases were most common.

GW33-e0658
Assessment of cardiovascular risk factors in patients with COVID-19 convalescents
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OBJECTIVES
Assessment of cardiovascular risk factors in convalescent COVID-19 with chronic heart failure.

METHODS
One hundred thirty patients the average age of 60, 82±0.42 years (women 57 (43.8%), men 73 (56.16%) were divided into 3 functional classes (FC) using a six-minute walk test in convalescent COVID-19 with chronic heart failure. This included FC I-36, II FC-60, III FC-34 patients. The presence of adiposity in established groups, hereditary, hypodynamia, cigarette smoking, cholesterol, hypertension, heart ischemic disease were studied.

RESULTS
Among the total number of patients, hypertension was 122 (93.8%), hypodynamia 117 (90.0%), hereditary 110 (84.6%), coronary heart disease 109 (83.8%), and adiposity 105 (80.8%), cigarette smoking 73 (56.0%), cholesterol 72 (54.4%) observed in the patient. When gender risk factors were observed, the incidence of risk factors was higher among men than women in particular, the presence of coronary heart disease was 95 to 70%, cholesterol 60 to 40%, especially cigarette smoking 66% 5%. Distribution of risk factors in functional classes as the functional class of patients increased, the type of risk factors encountered in them and the frequency of their occurrence increased. When analyzed according to the meeting of risk factors in one patient, patients with 1 risk factor in the group account for 8.4%, patients with 2 risk factors account for 14.6%, patients with 3 risk factors account for 76.6%.

CONCLUSIONS
Studies have shown that risk factors for patients with chronic heart failure in the period after coronavirus infection COVID-19 are directly correlated with the degree of disease, and there are correlations between age, gender, and functional classes.

GW33-e0714
Influence of long-term controlled therapeutic exercises on blood pressure profile parameters, elastic properties of arterial wall, metabolic and mineral indices in females with arterial hypertension
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OBJECTIVES
To study the role of therapeutic exercises (TE) in the correction of blood pressure, stiffness of the vascular wall metabolic indices of body structure (volume, mass, area of visceral fat) and bone mineral metabolism in postmenopausal hypertensive patients.

METHODS
The study included 158 patients (mean age was 58.3±7.61 years). All patients are divided into 3 groups. The first control group is 20 women without arterial hypertension and menopause. The second group consisted of 58 patients with arterial hypertension (AH) and postmenopause who were not undergone complex of TE and the 3rd group - 60 women with AH and postmenopause who were undergone TE complex. Patients of all groups were examined in dynamics: at the starting point of the study and in 12 months after, ambulatory monitoring of blood pressure; sphygmography; densitometry and test for serum biochemistry parameters of blood samples, including sex hormones, vitamin D.

RESULTS
In the course of the study, blood pressure, vascular wall stiffness parameters, metabolic indices of body structure and disorder parameters of bone mineral metabolism were comparable in group 2 and 3 against the background of significantly reduced levels of sex hormones. Multidirectional correlation relationships between the studied parameters are revealed. The therapy in combination with therapeutic exercises led to a significant decrease in blood pressure and metabolic indices of body structure (P<0.001) and to a persistent tendency of decrease the pulse wave velocity and increase of bone mineral metabolism in g/cm².

CONCLUSIONS
The result of the study indicates that the exercise therapy complex used in the form of regular classes can be recommended for implementation in clinical practice with the aim of comprehensively affecting the patient’s body and developing personalized treatment tactics for postmenopausal women with hypertension.
GW33-e0736
Association of brachial-ankle pulse wave velocity and left ventricular longitudinal strain three months after COVID-19 pneumonia
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OBJECTIVES
Data regarding the influence of arterial stiffness on longitudinal myocardial strain has been scarce. This is especially important for those who have undergone a complicated course of COVID-19. The objective was to investigate the associations between brachial-ankle pulse wave velocity (baPWV) and left ventricular (LV) longitudinal strain 3 months after COVID-19 pneumonia.

METHODS
Three hundred sixty-nine participants (52±11 (from 19 to 84) years; 50.9% women) 3 months ±3 weeks after discharge after COVID-19 pneumonia were prospectively enrolled into the study. All participants underwent conventional echocardiography, including 2D speckle-tracking echocardiography. baPWV measurements were made at the same day as the echocardiography in 322 patients. The parameters of LV global and segmental longitudinal strain were studied in 296 patients with optimal visualization quality in echocardiography. Both baPWV and LV longitudinal strain were measured in 243 patients.

RESULTS
Three months after discharge, obesity was noted in 46.5% of patients, cardiovascular diseases were diagnosed in 73.4%. Arterial hypertension occurred in 71.5% of patients, coronary artery disease - in 22.5%. The median baPWV were 13.3 [11.8; 15.1] cm/s and 13.4 [11.9; 15.1] cm/s for the left and right sides, respectively. Mean LV ejection fraction was 67.8±5.0%, mean LV global longitudinal strain was −19.6±2.5%. The baPWV showed a weak correlation with longitudinal strain of LV basal level (r=0.289 for the right side and r=0.272 for the left side, both P<0.001) and of LV mid level (r=0.229, P<0.001 for the right side and r=0.218 for the left side, P=0.001). The baPWV showed a correlation of medium strength only with the longitudinal strain of the LV basal anterior segment (r=0.303 for the right side and r=0.299 for the left side, both P<0.001). There were no correlations between baPWV and longitudinal strain of LV apical level segments.

CONCLUSIONS
In patients 3 months after COVID-19 pneumonia baPWV increase associated with deterioration of LV longitudinal strain at basal and mid levels, more pronounced in LV basal anterior segment.

GW33-e0769
Pregnancy outcomes of women with eisenmenger syndrome: a single-center study
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OBJECTIVES
Eisenmenger syndrome (ES), first described by Victor Eisenmenger in 1897, is a congenital heart defect characterized by right-to-left or bidirectional shunting with severe pulmonary hypertension (PH). Women with ES have poor tolerance of pregnancy-related physiological changes and develop high-risk complications, including rapidly progressive cardiopulmonary decompensation, thrombotic complications, and sudden death.

METHODS
Pregnant women with ES admitted to the Beijing Anzhen Hospital between 2010 and 2019 were retrospectively analyzed and followed-up.

RESULTS
Forty-two parturient women with ES were recruited. Their average age was 26.7 years (standard deviation [SD], ±4.0 years). The average gestational age was 33.7 weeks (SD, ±2.5 weeks). The average percutaneous oxygen saturation was 84.1 (±9.2). Thirty-eight (90.5%) patients had finger clubbing. Seventeen (40.5%) women had congenital heart disease (CHD) diagnosed before age 10 years, 28 (66.7%) had ventricular septal defects, and 40 (95.2%) had experienced cesarean delivery. The average pulmonary artery systolic pressure was 107.5 mmHg (SD, ±20.3 mmHg). Twelve (28.6%) women experienced pulmonary hypertensive crisis; 11 (26.2%) of these women died. Regarding the offspring, the average fetal weight was 1778.1 g (SD, ±555.3 g) and six (14.3%) offspring died. CHD was diagnosed in three (7.1%) offspring. There were significant differences in age, gestational age, percutaneous oxygen saturation, Apgar score, and heart failure between the maternal death and non-death groups (P<0.05). Death was mainly related to pulmonary hypertensive crisis and heart failure.

CONCLUSIONS
We recommend pregnancy termination if ES occurs during early pregnancy; however, if it occurs during late pregnancy, then patients should be informed of the risks. Multidisciplinary cooperation should be strengthened to improve the prognosis of the mothers and their offspring.
GW33-e0200
Larger nocturnal hypoxemic burden due to obstructive sleep apnea predicts a higher risk of long-term adverse outcomes in patients with pulmonary hypertension
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OBJECTIVES
Despite the improvement in the prognosis of pulmonary hypertension (PH), substantial morbidity and mortality remain. We aimed to investigate the prognostic value of obstructive sleep apnea (OSA) on the risk of major adverse cardiovascular events (MACEs) in a large cohort of patients with PH, with a focus on the role of nocturnal hypoxemic burden.

METHODS
Consecutive patients diagnosed with PH by right heart catheterization who underwent overnight cardiorespiratory polygraphy for OSA assessment at our center were enrolled. Pulse oximetry was used to determine hypoxic burden (time percentage spent with oxygen saturation <90% [T90]) during the night. The primary endpoint was the incidence of MACEs defined as the composite events of all-cause mortality and clinical worsening and was recorded via medical hospital medical records or phone calls to patients. Univariable and multivariable Cox regression analyses were used to calculate the hazard ratios (HR), and Kaplan-Meier curves were used to compare the survival probability between groups.

RESULTS
Of 469 eligible Chinese patients with PH, 160 (34.1%) had OSA at baseline. Over a median follow-up of 12.1 months, 79 (16.8%) patients experienced MACEs. Logistic regression analysis revealed T90 was an independent predictor of MACEs (HR: 1.009, 95% CI 1.002–1.014, P=0.009). After adjustment for potential confounders, T90 was still an independent predictor of MACEs with an adjusted HR of 1.006 (95% CI: 1.001–1.012, P=0.033). The likelihood of MACEs increased by 8% (95% CI 1.020–1.144) per 10-unit increase in T90. One-year event-free survival probability for patients in groups of T90 longer and shorter than 25% were 22.0 and 11.4%, respectively (Log-rank P=0.003).

CONCLUSIONS
Among patients with PH, OSA-related T90 but not AHI was a robust risk predictor of long-term MACEs. Investigation of nocturnal hypoxemic burden in PH may aid in the early risk stratification in patients with PH.

GW33-e0327
The effects of choline in patients with pulmonary hypertension and monocrotaline induced pulmonary hypertension rats
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OBJECTIVES
Plasma choline might be a potential biomarker in cardiovascular diseases while its value on PH was still unknown. We aimed to examine the hypothesis that circulating choline levels serve as a biomarker in PH, and to determine the effects of elevated levels of plasma choline in monocrotaline (MCT)-induced PAH rats.

METHODS
Inpatients diagnosed with PH in Fuwai Hospital were included in this study. Fasting blood samples were obtained to assess choline levels and other laboratory values. An animal study was conducted to further explore the specific effects of choline in PH. Rats were randomly divided into four groups after a 1-week adaptation period including normal control group, choline group, monocrotaline group, and MCT+choline group. Finally, the choline levels, hemodynamic examinations, changes in organ-tissue and molecular levels were all evaluated.

RESULTS
In total, 272 inpatients with PH were included in this study. After adjusting for confounders, the high circulating choline level was still associated with poor severity. Moreover, high choline levels were associated with poor prognosis in total PH cohort. The choline levels in the rats increased in MCT + choline group, accompanied by improved hemodynamic parameters, decreased right ventricular hypertrophy, and amelioration of pulmonary vascular remodelling. The decrease in abnormal apoptosis, excessive cell proliferation, and restoration of endothelial nitric oxide synthase after choline treatment further explained the amelioration of PH.

CONCLUSIONS
Elevated choline level might be a consequence caused by disease and presumably serve as a potential biomarker in PH.

GW33-e0632
Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL): a novel biomarker for prognostic assessment and risk stratification of acute pulmonary embolism
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OBJECTIVES
Tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL) is associated with poor prognosis in cardiovascular diseases. However, the predictive value of TRAIL in acute pulmonary embolism (PE) for the short-term outcome and risk stratification remains unknown.

METHODS
This study prospectively included 151 normotensive patients with acute PE. The study outcome was a composite of 30-day adverse events, defined as PE-related death, shock, mechanical ventilation, cardiopulmonary resuscitation, and major bleeding.

RESULTS
Overall, nine of 151 (6.0%) patients experienced 30-day adverse composite events. Multivariable logistic regression showed that TRAIL was an independent predictor of study outcome (OR: 0.19 per SD; 95% CI 0.04–0.90). ROC curve revealed that TRAIL’s area under the curve (AUC) was 0.83 (95% CI 0.76–0.88). The optimal cut-off value for TRAIL was 18 pg/mL, with sensitivity, specificity, negative predictive value, positive predictive value, positive likelihood ratio and negative likelihood ratio of 89%, 69%, 99%, 15%, 2.87 and 0.16, respectively. Compared with the risk stratification algorithm outlined in the 2019 ESC guidelines, our biomarker-based risk stratification strategy (combining TRAIL, hs-cTnI) has a similar risk classification effect.

CONCLUSIONS
Reduced plasma TRAIL levels predict short-term adverse events in normotensive patients with acute PE. The combination of the 2019 ESC algorithm and TRAIL is helpful for risk stratification in normotensive patients with acute PE.
OBJECTIVES 

Several anthracyclines have been associated with cardiac side effects, such as supraventricular arrhythmia, QT prolongation and atrial fibrillation. In order to evaluate the arrhythmogenic risk of anthracyclines as a class, and the comparative risk for each individual drug, we conducted a systematic review, meta-analysis, and network meta-analysis.

METHODS 

PubMed, Web of Science, EMBASE and the Cochrane Library were searched, up to March 2022, for randomized controlled trials, cohort studies, and case-control studies that investigated the association between anthracyclines treatment and the risk of arrhythmia. We followed the PRISMA 2020 guidelines for data selection and extraction. Outcomes were pooled using fixed effects models in cohort studies and randomized controlled studies, and random effects models in single-arm studies. Direct and indirect comparisons in network meta-analysis were performed using frequentist methods.

RESULTS 

Three cohort studies, 9 RC Ts, and 18 single-arm studies were included in our analysis. Anthracyclines use was associated with a statistically significant 90% increase in the risk for arrhythmia (odds ratio [OR] 1.90; 95% confidence interval [CI] 1.62–2.24) and 114% increase in the risk for supraventricular arrhythmia (OR 2.14; 95% CI 1.91–2.38). And the single-arm study also indicated that incidence of arrhythmia rate is 20%, 95% CI is 15/100–25/100. Epirubicin ranked most likely to have the highest risk for arrhythmia compared with non-anthracycline antineoplastic drugs in the analysis (OR 43.07 [95% CI 2.80–1,109.83]) by network meta-analysis.

CONCLUSIONS 

Our findings show a significant association between anthracyclines use and an increased risk for arrhythmia, especially supraventricular arrhythmia. Epirubicin application ranked with the highest probability for arrhythmia. Further study is required to determine how to reduce the risk for anthracyclines-associated arrhythmia and add the evaluation of patients' ECG in studies with the use of anthracyclines.

CONCLUSIONS 

Primary cardiac angiosarcoma is rare disease with poor prognosis and lack of specificity in early clinical manifestations. Imaging examination has a certain hinting effect. Multimodal treatment will improve its prognosis.

OBJECTIVES 

Our previous study (JACC: CardioOncology (2020) 2(4):614–29) showed the acute administration of ibrutinib in spontaneous hypertension rats (SHRs) can lead to increased ventricular arrhythmias (VA) vulnerability. AMPK mediated calcium handling was presumed to be the underlying mechanism. The in-vivo study was designed to unveil and verify the molecular mechanisms.

METHODS 

Old Sprague-Dawley (SD) rats were selected, and ibrutinib 10 mg/kg/d was chosen as the treatment dose. After 2 weeks and 4 weeks of oral gavage (control group [DMSO] and ibrutinib group), the hearts of the SD rats were harvested, Langendorff-perfused and subjected to incremental stimulation. 1. A novel perfusion calcium mapping of the Langendorff-perfused hearts was done. Frequency and threshold of post incremental pacing VA, time duration of VF after pacing, the composition of VF after pacing were compared in two groups to validate the ibrutinib-induced VA animal model. Besides, the calcium dynamics was analyzed. Proteins related with calcium handling, PFK-Akt pathway, AMPK level were analyzed with Western blot method.

RESULTS 

10 mg/kg/d ibrutinib oral gavage for 4 weeks can establish a ibrutinib-induced VA rat model. In this model, ibrutinib can significantly increase the rate of VA after incremental pacing (15.3±8.5 vs 5.77±0.04) and lower the threshold of post pacing VA (10.75±9.2 vs 13.7±5.9 Hz, P=0.02). After burst pacing, ibrutinib significantly prolonged the total duration of VF (190.3±18.4 vs 82.5±3.9, P=0.0017) and increased sustained VF induction rate (40 vs 10%, P=0.004). Besides, the post-pacing VF composition analysis showed that, ibrutinib significantly increased the proportion VF needs defibrillation (40 vs 10%) and lowered the proportion of self-terminating (40 vs 75%). Calcium dynamics analysis showed ibrutinib prolonged CaTSD80 (P=0.01), reduced transient calcium amplitude alternans ratio (P=0.008), and shortened time to peak (P=0.046). WB showed in ibrutinib group, PFK1100 expression (P=0.01), AMPK phosphorylation level (P=0.024), and Akt phosphorylation level (P=0.05) were reduced.

CONCLUSIONS 

In-vivo study established an animal model of ibrutinib-induced VA. Besides, ibrutinib related calcium handling dysfunction include both the calcium release function by RyR2 and the calcium uptake capacity by SERCA2a in the sarcoplasmic reticulum. AMPK mediated calcium dysfunction is the underlying mechanism of ibrutinib-induced VA.
230 mg/g as abnormal albuminuria, 30–300 mg/g as microalbuminuria (MAU), and 2300 mg/g as macroalbuminuria.

RESULTS The prevalence of abnormal albuminuria was 19.09%; it was 17.24% for MAU, lower in male (13.83%) than in female (20.08%; P<0.001). Compared with those with normal albuminuria, the risk of CVD increased among subjects with MAU (OR=1.225, 95% CI 1.115–1.346) and macroalbuminuria (OR=1.864 95% CI 1.5–2.316). When MAU complicated by hypertension and diabetes mellitus, the risk of CVD increased by 1.758 times.

CONCLUSIONS The prevalence of abnormal albuminuria was high among Chinese aged 35 years and over. Those with abnormal albuminuria have higher CVD risk, especially with hypertension and diabetes mellitus.

GW33-e0489 Prognostic value of 1,5-anhydroglucitol level in patients with acute myocardial infarction
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OBJECTIVES Diabetes mellitus is an essential risk element for cardiovascular disease. 1,5-anhydroglucitol (1,5-AG), a new marker for glucose monitoring, can predict poor outcomes in acute myocardial infarction (AMI) patients is unclear.

METHODS A prospective cohort study was employed in the present study. We enrolled 270 AMI patients who underwent coronary angiography at Beijing Hospital from March 2017 to 2020. Serum 1,5-AG concentration and biochemical indicators were tested before CAG. Cox regression analysis was conducted to investigate the relationship between 1,5-AG levels and major adverse cardiovascular and cerebrovascular events (MACCEs) and all-cause mortality.

RESULTS During a median follow-up of 44 months, 49 MACCEs occurred, and 33 patients died. The levels of 1,5-AG were significantly lower in the MACCEs group than that in the non-MACCEs group (P=0.001). Kaplan-Meier analysis revealed that low 1,5-AG levels were related to MACCEs (P=0.005) and all-cause mortality (P=0.024). Multivariate analysis indicated that 1,5-AG:8.84 μg/mL (AUC=0.75, 95% CI 0.67–0.82, P=0.036). However, no predictive value of 1,5-AG was found for all-cause mortality in AMI patients (P=0.05).

CONCLUSIONS Low 1,5-AG levels can forecast MACCEs in AMI patients but not all-cause mortality.

GW33-e0668 A mouse model for metabolic-associated steatohepatitis with advanced liver fibrosis and cardiac dysfunction
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OBJECTIVES Metabolic-associated fatty liver disease (MAFLD) is frequently complicated with cardiovascular events leading to a higher mortality rate. Animal models mimicking this condition are scarce. We aim to create a mouse model for metabolic-associated steatohepatitis with advanced liver fibrosis and cardiac dysfunction.

METHODS We maintained 12-week-old male apolipoprotein E/low-density lipoprotein receptor double-knockout (AL) mice on a low-carbohydrate–high-protein-high-fat atherogenic diet (AD) and a standard chow diet (SCD) with or without ethanol treatment for 16 weeks. Age-matched male C57BL/6J mice on SCD without ethanol treatment served as controls, and C57BL/6J mice on AD served as controls. Both the reference values and those in group 2, which reflected the presence of pronounced vascular inflammatory potential for possible adverse events in this group of patients in post-COVID period. In addition, the exceeding values of NT-proBNP, IL-1b, IL-6, IL-8, TNFα and apical LV myocardial strain in group 2 patients compared to group 1 may be indicators of the occurrence and progression of adverse cardiovascular events in patients with DM2.

CONCLUSIONS Thus, in groups of patients with AH and CAD, which differ only by the presence of DM2, it is clearly seen that comorbid condition can significantly affect the development of adverse cardiovascular complications. Further studies are needed to increased inflammatory potential of blood parameters, increased stiffness of the vascular wall, and the presence of myocardial longitudinal strain of LV apical segments.

GW33-e0712 The analysis of laboratory and instrumental parameters in prediction of long-term events in patients with cardiovascular pathology in combination with type 2 diabetes mellitus who underwent COVID-19 associated pneumonia
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OBJECTIVES By given pandemic status, the viral infection has shown how SARS-CoV-2 can affect patients who involved in other noninfectious epidemics that have been gaining momentum for years. The objective was to perform a prospective analysis of blood biomarkers in patients with cardiovascular diseases (CVD) who underwent COVID-19 associated pneumonia in groups with and without type 2 diabetes mellitus (DM2); to assess the nature of their relationship with instrumental parameters and to identify indicators of long-term adverse cardiovascular events.

METHODS The study was prospective, the protocol was approved by the local ethics committee - No 159 dated July 23, 2020 and registered in the international registry of clinical trials of the US National Institute of Health (ClinicalTrials.gov Identifier: NCT04501822).

Out of 380 patients with SARS-CoV-2 associated pneumonia participating in the study, we used data from 65 patients in the present work. Patients were divided into 2 groups: group 1 included patients with CVD: arterial hypertension (AH) and/or type 2 diabetes mellitus (DM2) (n=20), mean age 62.5±15.4 years. Patients were examined at baseline in the infectious disease hospital and 3 months after discharge. During laboratory examination of blood biosamples we evaluated parameters of general blood test; biochemical parameters; concentration of highly sensitive C-reactive protein (hs-CRP), levels of interleukin (IL-1, IL-6, IL-8), homocysteine; from instrumental parameters - ABPM, pulse wave velocity in right and left arterialies, echocardiography with the study of left ventricular (LV) apical myocardial strain, computer tomography of lungs.

RESULTS The analyzed parameters of general blood test showed that leukocyte count and its components - increase in neutrophils (neutrophilia) and decrease in LYM/CRP ratio (lymphocytes/CRP) were more significantly changed in DM2 group. Patients in both groups had a significant excess of baseline max CRP concentrations with decrease in parameters after 3 months, but with persistent excess values in group 2 (P<0.001). Three months after discharge patients with DM2 had levels of hs-CRP, IL-1β and TNFα (P<0.05) that exceeded both the reference values and those in group 1, which reflected the presence of more pronounced vascular inflammatory potential for possible adverse events in this group of patients in post-COVID period. In addition, the exceeding values of NT-proBNP, IL-1β, IL-6, IL-8, TNFα and apical LV myocardial strain in group 2 patients compared to group 1 may be indicators of the occurrence and progression of adverse cardiovascular events in patients with DM2.

CONCLUSIONS Thus, in groups of patients with AH and CAD, which differ only by the presence of DM2, it is clearly seen that comorbid condition can significantly affect the development of adverse cardiovascular complications. Further studies are needed to increased inflammatory potential of blood parameters, increased stiffness of the vascular wall, and the presence of myocardial longitudinal strain of LV apical segments.
RESULTS

Compared with Con group, the body weight of DOX group was significantly decreased (21.685±0.87 g vs 19.741±1.35 g, P=0.043) and systolic arterial pressure in DOX group was significantly increased (112.67±5.60 mmHg vs 125.92±3.33 mmHg, P=0.007). Echocardiogram showed that the left ventricular ejection fraction (53.10±2.8% vs 41.83±3.4%, P=0.019), short axis shortening rate (26.97±2.3% vs 20.21±2.74%, P=0.021), left ventricular posterior wall thickness during diastolic period (1.28±0.07 mm vs 0.99±0.18 mm, P<0.001) were significantly decreased in DOX group. Compared with Con group, surface electrocardiograph showed that the PR interval (42.752±2.99 ms vs 62.23±11.59 ms, P=0.006), QT interval (19.75±2.50 ms vs 29.93±5.13 ms, P=0.004) and QTX interval (50.82±9.50 ms vs 80.24±16.38 ms, P=0.009) in DOX group were significantly prolonged. High power transmission electron microscopy (TEM) observed that cardiac cells in DOX group were extensively vacuolated and disordered, with smaller mitochondria, higher membrane density, less cristae and incomplete membrane structure. Western Blot showed that the protein expressions of α-SMA, Mfn2 and Caspase3 were significantly increased in DOX group, while the protein expressions of Sirt1 and Sirt3 were significantly reduced. Compared with DOX group, the protein expressions of Mn-SOD and Mfn2 in DOX+RES group decreased, and mitochondrial morphology tended to be stable. Caspase3 protein expression and cell apoptosis was significantly reduced. Compared with DOX group, the body weight of DOX+RES group was 19.67±1.28 g and systolic arterial pressure was 117.2±5.50 mmHg. The left ventricular ejection fraction (55.3±2.8%), short axis shortening rate (27.6±2.3%), left ventricular posterior wall thickness during diastolic period (1.2±0.07 mm), PR interval (38.5±2.99 ms), QT interval (18.75±2.50 ms), QTX interval (48.5±9.50 ms) and cell apoptosis were in the middle of Con and DOX groups. Therefore, the combined treatment of DOX and RES had better effect on myocardial injury by regulating mitochondrial function.

CONCLUSIONS

DOX induced myocardial injury might lead to abnormal mitochondrial morphology and function, induce apoptosis and promote fibrosis formation by interfering with mitochondrial fusion and division. Resveratrol, the Sirt1 agonist, ameliorates Doxorubicin-induced myocardial injury by regulating mitochondrial function.

GW33-e0762

The impact of acute myeloid leukemia subtypes on cardiovascular mortality among patients receiving chemotherapy

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OBJECTIVES

The anthracyclines are the cornerstone of acute myeloid leukemia (AML) chemotherapy. The anthracycline-induced cardiotoxicity is a common problem in clinical settings, but there are limited data concerning its cardiac-specific mortality in patients with AML, especially among different histological subtypes.

METHODS

The present study was based on the Surveillance, Epidemiology, and End Results (SEER) database. Participants with established AML from 2000 to 2019 were included in our analysis. The demographic data (age, gender, race, marital status, and economic condition), histological types of AML, and diagnosis information was collected. The patients were divided into histological groups according to the 2016 World Health Organization (WHO) classification. The subdistribution hazard ratios (SHRs) were estimated to evaluate the association of AML subtypes with cardiac-specific death using Fine and Gray competing risk-adjusted models.

RESULTS

A total of 20,177 patients diagnosed with AML and receiving chemotherapy were associated with a high risk of cardiac-specific death. The incidence of cardiovascular mortality was highest in AML patients with recurrent genetic abnormality compared to other histological subtypes. Besides, patients who were male, old age and poor economic condition were associated with a high risk of cardiac-specific death.

PERIPHERAL VASCULAR DISEASE

GW33-e0387

Relationship between physical performance and peripheral arterial diseases in different age groups of Chinese community-dwelling older adults

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BACKGROUND AND AIMS

This study aimed to examine the relationship between physical performance and peripheral artery disease (PAD) in different age groups of Chinese older adults.

METHODS

We enrolled 1,416 relatively healthy 265 years old participants of Chinese ethnicity. We classified the participants into two age categories: the pre-old group (65–74 years, n=1,015) and the old group (75 years, n=401). We assessed the cross-sectional association of the ankle-brachial index (ABI), which is used for the classification of patients with PAD (ABI<0.9). Physical performance mainly focused on muscle strength, mobility and balance, which were measured via hand grip, 4-m walking speed, and the Timed Up and Go Test (TUGT).

RESULTS

A total of 125 (8.8%) patients met the diagnostic criteria and were defined as having PAD. After multivariate adjustment, we found that grip strength and 4-metre walking speed were correlated negatively with PAD [odds ratio (OR)=0.952, 95% CI=0.918–0.998; OR=0.266, 95% confidence interval (CI)=0.083–0.843] in pre-old participants, while TUGT (OR=1.058, 95% CI=1.007–1.112) was correlated positively with PAD only in older participants.

CONCLUSIONS

Our study further confirmed the association between physical performance and PAD in community-dwelling older Chinese adults. Muscle strength and mobility correlated negatively with PAD in pre-old participants, and balance was positively associated with PAD in older participants. These findings might help with better early screening and management of PAD.

GW33-e0576

Identification of pivotal chromatin regulators in the progression from asymptomatic to symptomatic carotid plaque: a new perspective for the early diagnosis

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OBJECTIVES

Patients with symptomatic carotid plaque (SCP) are at risk of developing severe complications. Previous studies have mainly focused on plaque pathology classification, which is inconsistent with clinical manifestations. Chromatin regulators (CRs) play a critical part in epigenetic regulation. Our study aimed to identify differentially expressed CRs (DECRs) for early SCP diagnosis.

METHODS

GSE111782 was downloaded from GEO database. CRs were extracted using Perl. A series bioinformatics and machine learning approaches were used to screen the DECRs in the progression from asymptomatic carotid plaque (ASCSP) to SCP, including DECRs identification using Limma, functional enrichment analysis, protein-protein interaction (PPI) network construction, support vector machine recursive feature elimination (SVM-RFE) and random forest algorithms application. Finally, the receiver operating characteristic curve (ROC) was used to determine the diagnostic value, and the nomogram was created for clinical usage.

RESULTS

Seven hundred and forty CRs were extracted and 39 DECRs were identified from the dataset, of which seven and thirty-two were up- and down-regulated, respectively. DECRs were mainly enriched in chromatin organization and histone modification. After removing non-connection DECRs from the PPI network, a total of 30 DECRs were visualized and 19 DECRs with nodes over three were chosen for machine learning. Seven DECRs with the highest
accuracy and lowest error in SCP diagnosis were filtered using SVM-RFE. Ten DECRs were selected by random forest based on the importance score. From the intersection of SVM-RFE and random forest, three DECRs (JAK2, RBBP7, EHMT1) were selected. Finally, the area under curve (AUC) of JAK2, RBBP7, EHMT1, and nomogram calculated from the ROC curve were 0.765, 0.815, 0.790 and 0.852, respectively, indicating the optimal diagnostic value.

CONCLUSIONS We identified three DECRs (JAK2, RBBP7, EHMT1) for the early diagnosis of the progression from ASCP and SCP. The DECRs were primarily involved in regulating chromatin structure and histone modification. Meanwhile, we provided the nomogram for further clinical practice.

METHODS We included 123 consecutive in-stent restenosis patients with OCT during angiography follow-up after percutaneous coronary intervention. The enrolled patients were randomly divided into the training cohort (85 lesions) and testing cohort (41 lesions). We adopted Inception V3 as the main network, and added two convolutional layers, a pooling layer and a fully connected layer. To further promote the diagnosis performance, we fused the deep learning signature with related clinical features to construct nomogram.

RESULTS The AUC of the nomogram is 0.751. The accuracy of neothrombosis diagnosis is more balanced (sensitivity: 0.733, specificity: 0.692) compared with deep learning signature (sensitivity: 0.867, specificity: 0.462). To compare the performance of the nomogram with cardiologists, an independent dataset of 41 lesions were employed. The accuracy of the nomogram is 0.707, which is comparable to those of the two senior cardiologists (0.659, 0.634, P=0.416, P=0.316) and the three junior cardiologists (0.610, 0.561, 0.463, P=0.181, P=0.377, P=0.056). The sensitivity of nomogram is 0.731, which is comparable with both senior and junior cardiologists. The specificity of the nomogram is 0.692, which is similar to the senior cardiologists (0.692, 0.692, P=1.00, P=1.00). However, it is relatively higher than those of the junior cardiologists (0.500, 0.423, 0.269, P=0.020, P=0.059, P=0.005).

CONCLUSIONS The deep learning model using coronary angiography showed the potential to differentiate in-stent restenosis lesions with and without neothrombosis.

GW33-e0115 Dual left anterior descending artery with anomaly origin of the long left coronary artery from the right coronary sinus or right coronary artery
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OBJECTIVES Dual left anterior descending (LAD) is a rare type of coronary variant, in which the short LAD travels and terminates in the upper anterior interventricular groove (AIVG) and the long LAD travels in the middle and lower AIVG. It is rare that long LAD originates from right coronary sinus (RCS) or right coronary artery (RCA), but the special origin and course of the long LAD branch may lead to hemodynamic changes, causing myocardial ischemia. Moreover, accurate knowledge of the origin and course of the two LADs is crucial to the success of coronary artery bypass grafting.

METHODS Twenty-five patients with dual LAD anomaly with long LAD originating from RCS or RCA who underwent coronary CT angiography (CCTA) in our hospital from were retrospectively collected. According to the course of the long LAD, it was divided into pre-pulmonic (pre-LAD, 12 cases) and sub-pulmonic (sub-LAD, 13 cases), and the CCTA examination of 30 patients without coronary artery variation was collected as control group. The length and diameter of each segment were measured. And the origin, course, branching, and atherosclerotic plaques of short LAD and long LAD were evaluated.

RESULTS The LAD long branch of 16 patients originated from the RCS, and 9 originated from the proximal RCA. The total length of the long LAD and short LAD were (137.52±22.33) mm and (47.59±12.33) mm, and the difference was statistically significant (P<0.05). The diameters of the initial section were [2.10 (2.00, 2.65)] mm and [2.30 (1.90, 2.80)] mm, the difference was not statistically significant (P>0.05). There was no significant difference in the origin of pre-LAD and sub-LAD, and the presence of diagonal branches (P>0.05). Septal branches were seen in 3 pre-LAD and 11 sub-LAD, and the difference was statistically significant (P<0.05). In the pre-LAD group, the right conical branches all originated from the long LAD; in the sub-LAD group, the right conical branches all originated from the RCA or RCS. Plaques were seen in 2 pre-LADs, but no plaques were found in sub-LADs; plaques were seen in 12 short LADs. The length of the LAD in the control group was longer than that of the sub-LAD, the segment before the anterior interventricular groove of the pre-LAD was longer than those of the sub-LAD and the control group, and the distal diameter of the sub-LAD and control group LAD were larger than those of the pre-LAD, and these differences were all statistically significant (P<0.05). In conclusion, the diameter of the distal segment of the sub-LAD was larger than that of the middle segment, and the difference was statistically significant (P<0.005).

CONCLUSIONS The anatomical differences between the dual LAD anomaly with long LAD originating from the right RCS or RCA and the normal LAD are large. CCTA can comprehensively evaluate the origin, course, branches, anatomical relationships, and lumen condition of the two LADs in the dual LAD variant.
CONCLUSIONS FAPI PET-CT/MR imaging is an invasive tool to identify the area of activated cardiac fibroblasts and detect the potential gastroesophageal tumor simultaneously in AMI patients complicating GIB.

GW33-e0155
Molecular imaging of fibroblast activity in pressure overload heart failure
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OBJECTIVES Cardiac fibrosis, mediated by the activation of cardiac fibroblasts, is critical in pressure overload-induced heart failure. Fibroblast activation protein (FAP), specifically expressed by activated fibroblasts, can be visualized by radiolabeled FAP inhibitors (FAPI) PET/CT. We aimed to evaluate whether 18Ga-FAPI-04 can characterize the early stages of cardiac fibrosis in pressure overload heart failure.

METHODS Sprague-Dawley rats underwent abdominal aortic constriction (AAC) (n=12) and sham surgery (n=10). All rats were scanned with 18Ga-FAPI-04 PET/CT at 2, 4, and 8 weeks after surgery. Cardiac function was measured by echocardiography. The expression of FAP in the myocardium was detected by immunohistochemistry.

RESULTS Compared with the sham group, we observed decreased ejection fraction (EF) and fractional shortening (FS) and increased left ventricular internal dimensions in systole (LVd) and diastole (LVDd) in the AAC group at 4 and 8 weeks (all P<0.05). The AAC group showed higher 18Ga-FAPI-04 accumulation in the heart than the sham group at 2, 4, and 8 weeks (P<0.05), and FAP expression significantly changed from 2 to 8 weeks. Immunohistochemistry confirmed the higher density of the FAP+ area in the AAC group. The intensity of the 18Ga-FAPI-04 PET signal correlated with the density of the FAP+ area on histology (Pearson's correlation coefficient r=0.79, P<0.001). The expression of the 18Ga-FAPI-04 signal at 4 weeks correlated with the deteriorated cardiac function at 8 weeks (EF: r=-0.78; FS: r=-0.67; LVDd=0.8; LVIDd=0.65; all P<0.05). The AAC group also showed an increased 18Ga-FAPI-04 signal in the liver, peaking at 4 weeks and then declining after that. Cardiac and liver PET signals directly correlated at 4 weeks in the AAC group (r=0.69, P=0.001). A combination of the FAPI intensity in the heart and liver at 4 weeks better predicted the deterioration of cardiac function at 8 weeks.

CONCLUSIONS The activated fibroblasts in the heart and liver after pressure overload can be monitored by 18Ga-FAPI-04 PET/CT. This imaging technique reveals an early fibrotic link in cardio-liver interactions and could predict non-ischemic heart failure prognosis.

GW33-e0196
Ischemia-like late gadolinium enhancement related to adverse outcomes in hypertrophic cardiomyopathy patients with non-extensive fibrosis
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OBJECTIVES Late gadolinium enhancement (LGE) has been established as an independent predictor for adverse outcomes in hypertrophic cardiomyopathy (HCM). However, the prevalence and clinical significance of some LGE subtypes have not been well demonstrated. The current study aims to investigate the prognostic value of ischemia-like LGE pattern and right ventricle insertion points (RVIP) LGE location in HCM patients.

METHODS In this single-center retrospective study, 497 consecutive HCM patients with LGE confirmed by cardiac MR (CMR) were included. Ischemia-like LGE pattern was defined as LGE involving the subendocardium; RVIP LGE was defined as LGE involving the junctions of the interventricular septum and right ventricular free walls. Cases with ischemic heart disease were excluded from the study. Endpoint included a composite of heart failure events, arrhythmic events, and stroke.

RESULTS Of the 497 patients, ischemia-like LGE and RVIP LGE were observed in 184 (37.0%) and 414 (83.3%), respectively. All patients were divided into two groups based on the LGE amount of 15%. During follow-up of 57.8 months, 66 of 497 patients (13.3%) experienced composite endpoint. Spline analysis showed a non-linear association between LGE extent with hazard ratios for composite outcomes: the incidence of the 18Ga-FAPI-04 uptake in the gastrointestinal tract or prostate. They were diagnosed with gastric cancer, rectal cancer, and prostate cancer following a biopsy, respectively. Other patients with negative FAPI imaging were diagnosed with gastric ulcers and did not detect gastrointestinal tumors by the gastroenterological endoscope.
outflow tract obstruction, and maximum LV wall thickness, ischemia-like LGE was associated with composite endpoint instead of LGE extent in group with non-extensive LGE (HR=2.87; P=0.003), while LGE extent significantly related to composite endpoint instead of ischemia-like LGE in patients with extensive LGE (HR=1.45; P=0.003). RVIF LGE was not significantly associated with poor outcomes in both groups.

CONCLUSIONS In HCM patients with non-extensive LGE, ischemia-like LGE rather than LGE extent is associated with unfavorable outcomes, which is an underrecognized phenotype showing the potentiality to improve risk stratification. However, the presence of RVIF LGE did not merit a prognostic value.

RESULTS We measured the distance between the midpoint of inferior vena cava opening to the midpoint of the fossa ovalis at different heights, then we find that the fossa ovalis is not a regular membranous plane. Because there is no regularity in the distance between them, The distance between the inferior vena cava opening and the front of the midpoint of 1/2 height of the fossa ovalis (16.29 mm) is longer than the midpoint (10.02 mm) and posterior (5.85 mm). By measuring above distance, it is aimed to adjust the operator in adjusting the length and curvature of the needle, preventing damaging the atrium and leading to cardiac pressure plug. The distance from the midpoint of the inferior vena cava opening to the midpoint of 1/2 height of the fossa ovalis and distance from the middle point of 1/2 height of the coronary sinus fit the equation of y=0.385x+0.548 (The former represents y, and the latter represents x). Indicating that if we have determined the position of the coronary sinus, it can be used to determine the position of the fossa ovalis and adjust the length and curvature of the needle and catheter. The distance from the inferior vena cava to the anatomical structure of right atrium (fossa ovalis, coronary sinus, tricuspid orifice of the central fiber) increased with the right atrium diameter, and the distance from the pulmonary vein to the fossa ovalis increased with the left atrium diameter.

CONCLUSIONS In conclusion, fossa ovalis and coronary sinus exhibit significant individual anatomical variability, which could influence the process of radiofrequency ablation. With the cardiac computed tomography, we can infer the position of the fossa ovalis from the position of the coronary sinus. Furthermore, the length and flexibility of the position of the ablation catheter can be adjusted timely for patients with large atrium.

GW33-e0201 Personalizing CMR-based risk stratification for outcomes in dilated cardiomyopathy with LVEF<35%: cohort study with a long-term follow-up

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OBJECTIVES Recent studies have demonstrated that a considerable number of patients who succumbed to SCD had a LVEF<35%. The risk of adverse events have not yet been systematically studied in these DCM patients. This study aims to identify the risk factors for adverse events in DCM patients with a LVEF<35% and establish a scoring model to predict the adverse event risk.

METHODS A cohort of 466 consecutive DCM patients (358 men, 44 years) with a LVEF<35% who had undergone gadolinium-enhanced cardiac magnetic resonance (CMR) imaging were enrolled in this study. The primary endpoint was a composite of SCD or aborted SCD. The secondary endpoints were all-cause mortality, heart transplantation, and hospitalization for heart failure. The risk factors for primary and secondary endpoints were identified by multivariate cox analysis and used to create a nomogram.

RESULTS During a mean follow-up period of 79.42±9.5 months, a total of 40 patients died and 41 patients reached the primary and secondary endpoints, respectively. Multivariate stepwise analyses showed that age (hazard ratio, HR=1.024; 95% CI, 1.001–1.053), family history of SCD (HR=5.51; 95% CI, 1.178–2.95), NYHA (HR=2.04; 95% CI, 1.21–3.85), and left atrial diameter (HR=2.75; 95% CI, 1.21–5.53) had a significant prognostic association with the primary endpoints (all P<0.05). Multivariate stepwise analyses showed that NYHA (HR=1.94; 95% CI, 1.16–3.25), left atrial volume index (LAVi=47.3 mL/m² (HR=2.14; 95% CI, 1.27–3.60), LGE<6% (HR=2.96; 95% CI, 1.370–5.46, and global longitudinal strain (GLS)<−8% (HR=2.45; 95% CI, 1.467–4.105) had significant prognostic associations with the secondary endpoints (all P<0.05). Nomograms for the adverse events were created by using these factors.

CONCLUSIONS LGE and GLS are new parameters derived from CMR that can timely for patients with large atrium.

GW33-e0531 Endogenous assessment of late gadolinium enhancement gray zone in patients with non-ischemic cardiomyopathy with T1 and native T1 mapping

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OBJECTIVES Both T1 and native T1 mapping are promising tools to endogenously assess myocardial tissue characterization. However, the comparison of their abilities in characterizing LGE gray zone has not been reported yet. This study aims to validate and compare the feasibility of T1 and native T1 mapping in detection of myocardial fibrosis in patients with non-ischemic cardiomyopathy, focusing on the performance of both methods in identifying LGE gray zone.

METHODS Twenty-seven hypertrophic cardiomyopathy (HCM) patients, 16 idiopathic dilated cardiomyopathy (DCM) patients and 18 healthy volunteers were prospectively enrolled. All the CMR protocols were performed in 3.0T MR system (Ingenia 3.0T, Philips Healthcare, the Netherlands). T1 mapping, precontrast T1 (native T1) mapping, post-contrast T1 mapping and LGE imaging were performed in all the patients. T1 mapping and native T1 mapping were performed in healthy controls. Patients were divided into LGE positive group and LGE negative group for the comparison of global T1 and native T1 values. Differences in native T1 and LGE areas were divided into LGE core (0–2 SDs above remote myocardium) and gray zone (≥6 SDs above remote myocardium) according to the signal intensity of LGE. Native T1 value, T1 value and ECV were calculated at each region of interest (ROI, with a radius of ≤2 mm) according to the classification of LGE for comparison.

RESULTS LGE was detected in 17 HCM patients and 10 DCM patients respectively. Patients showed significant higher native T1 values than controls (HCM: 48.6±2.6 ms versus DCM: 46.2±1.0 ms and Control: 41.7±0.8 ms, P<0.001). No matter the presence of LGE, patients had significantly higher native T1 and T1 values than controls (native T1: 1301.5±30.97 ms for LGE+ group and 1285.47±52.38 ms for LGE− group versus 1252.1±5.1 ms, P<0.001). Meanwhile, patients also showed higher T1 values than controls and HCM patients had the highest T1 value than other two groups (HCM: 48.6±2.6 ms versus DCM: 46.2±1.0 ms and Control: 41.7±0.8 ms, P<0.001). No matter the presence of LGE, patients had significantly higher native T1 and T1 values than controls (native T1: 1301.5±30.97 ms for LGE+ group and 1285.47±52.38 ms for LGE− group versus 1252.1±5.1 ms, P<0.001). However, the T1 values of gray zone had significantly higher than control (P<0.01) while the native T1 values were not (P=0.089). T1 values were significantly associated with both native T1 values (r=0.54, P<0.001) and ECV values (r=0.54, P<0.001).

CONCLUSIONS T1 mapping is a feasible method to detect myocardial fibrosis in patients with non-ischemic cardiomyopathy no matter the presence of LGE. Furthermore, T1 mapping may serve as a better discriminator in the identification of LGE gray zone.
GW33-e0560

Coronary microvascular dysfunction in nonobstructive hypertrophic cardiomyopathy: assessment with first-pass perfusion imaging using 3.0 T cardiac magnetic resonance

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OBJECTIVES To assess coronary microvascular dysfunction in nonobstructive hypertrophic cardiomyopathy (NOHCM) patients using CMR resting first-pass perfusion (FFP) imaging to create a more robust understanding of this largely ignored HCM subgroup.

METHODS Forty-seven NOHCM patients and 28 healthy controls (HCs) were retrospectively analyzed. All subjects underwent a 3 T CMR scanning. Imaging protocols included short axis cine, FFP, and late gadolinium enhancement (LGE), TTM, SI max, and upslope in multiple groups were assessed and compared by ANOVA test. The Pearson's correlation test was used to determine the relationships between LV EDTH, LGE, left ventricular outflow tract/aortic valve diameter ratio (LVOT/AO), and FFP parameters (TTM, upslope).

RESULTS Compared with HCs, NOHCM patients had a longer TTM and lower upslope in the basal, mid-ventricular and apical myocardial segments (all P<0.01), but there were no significant differences in SI max. Compared with myocardial segments with lower upslope in NOHCM (TTM: 25.47 ± 2.30 vs. 29.71 ± 5.09; upslope: 10.23 ± 2.72 vs. 8.77 ± 2.30, P<0.001), the Pearson's correlation test was used to determine the relationships between LV EDTH, LGE, left ventricular outflow tract/aortic valve diameter ratio (LVOT/AO), and FFP parameters (TTM, upslope).

CONCLUSIONS Patients with nonobstructive HCM have coronary microvascular dysfunction, which has a consistent relationship with myocardial structure and myocardial fibrosis.

GW33-e0570

Functional evaluation of constructed pseudo-endogenous microRNA-targeted myocardial ultrasound nanobubble

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OBJECTIVES This study aimed to construct pseudo-endogenous microRNA-targeted myocardial ultrasound nanobubble pAd-AAV-g/miRNA-1 NBs and evaluate its characteristics, targeting, and function.

METHODS The pAd-AAV-g/miRNA-1 gene complex was linked to nanobubble NBs by the “avidin-biotin bridging” method to prepare cardiomyocyte-targeted nanobubble pAd-AAV-g/miRNA-1 NB. The shape, particle size, dispersion, and stability of nanobubbles and the connection of pAd-AAV-g/miRNA-1 with NBs were measured, including the coronary artery calcification score (CAC), lesion length, >3CAD-BADS 4 proportion, perivascular FAI and CT-FFR. The included vessels were divided into a nonsevere calcification group and a severe calcification group according to the quartile of CACS. FFR<0.80 represents the presence of hemodynamically significant ischemia.

RESULTS A total of 124 patients with 152 vessels were included (age 61.15±9.2 years; male 64.5%). Significant differences in lesion length (28.4±14.2 vs. 23.12±13.3 mm, P=0.021), perivascular FAI (37.0±7.5 vs. 39.0±7.4, P<0.001) and CT-FFR (0.78±0.06 vs. 0.85±0.04, P=0.001) were noted between the nonsevere calcification group and the severe calcification group (47 vessels) and the FFR<0.80 group (105 vessels). Furthermore, the perivascular FAI in the FFR<0.80 group was significantly greater than that in the FFR≥0.80 group (nonsevere calcification: -73.2±7.5 vs. -78.2±7.4, P=0.002; severe calcification: -72.5±7.7 vs. -82.6±8.3, P<0.001). In discriminating hemodynamically significant ischemia, the specificity and accuracy of CT-FFR were significantly affected by severe calcification, which demonstrated a significantly declining trend (P=0.033 and P=0.010, respectively). The diagnostic performance of CT-FFR in the severe calcification group was lower than that in the nonsevere calcification group and perivascular FAI. However, perivascular FAI showed good discriminative performance in the severe calcification group. In combination with perivascular FAI, the predictive value of CT-FFR in identifying hemodynamically significant ischemia with severe calcification increased from an AUC of 0.740 to 0.919.

CONCLUSIONS A coronary artery with severe calcification, the diagnostic performance of CT-FFR in discriminating flow-limiting lesions could be greatly impaired. Perivascular FAI represents a potential reliable imaging marker to provide incremental diagnostic value over CT-FFR for identifying hemodynamically significant ischemia with severe calcification.

GW33-e0668

Incremental diagnostic value of perivascular fat attenuation index for identifying hemodynamically significant ischemia with severe calcification

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OBJECTIVES To explore the incremental value of perivascular fat attenuation index (FAI) to identify hemodynamically significant ischemia in severe calcified vessels.

METHODS Patients who underwent coronary computed tomography angiography (CCTA) examination at Chinese PLA General Hospital from 2017 to 2020 and subsequently underwent fractional flow reserve (FFR) examination within 1 month were consecutively included. Several CCTA-derived indices were measured, including the coronary artery calcification score (CACS), lesion length, >3CAD-BADS 4 proportion, perivascular FAI and CT-FFR. The included vessels were divided into a nonsevere calcification group and a severe calcification group according to the quartile of CACS. FFR<0.80 represents the presence of hemodynamically significant ischemia.

RESULTS A total of 124 patients with 152 vessels were included (age 61.15±9.2 years; male 64.5%). Significant differences in lesion length (28.4±14.2 vs. 23.12±13.3 mm, P=0.021), perivascular FAI (37.0±7.5 vs. 39.0±7.4, P<0.001) and CT-FFR (0.78±0.06 vs. 0.85±0.04, P=0.001) were noted between the nonsevere calcification group and the severe calcification group (47 vessels) and the FFR<0.80 group (105 vessels). Furthermore, the perivascular FAI in the FFR<0.80 group was significantly greater than that in the FFR≥0.80 group (nonsevere calcification: -73.2±7.5 vs. -78.2±7.4, P=0.002; severe calcification: -72.5±7.7 vs. -82.6±8.3, P<0.001). In discriminating hemodynamically significant ischemia, the specificity and accuracy of CT-FFR were significantly affected by severe calcification, which demonstrated a significantly declining trend (P=0.033 and P=0.010, respectively). The diagnostic performance of CT-FFR in the severe calcification group was lower than that in the nonsevere calcification group and perivascular FAI. However, perivascular FAI showed good discriminative performance in the severe calcification group. In combination with perivascular FAI, the predictive value of CT-FFR in identifying hemodynamically significant ischemia with severe calcification increased from an AUC of 0.740 to 0.919.

CONCLUSIONS A coronary artery with severe calcification, the diagnostic performance of CT-FFR in discriminating flow-limiting lesions could be greatly impaired. Perivascular FAI represents a potential reliable imaging marker to provide incremental diagnostic value over CT-FFR for identifying hemodynamically significant ischemia with severe calcification.

GW33-e0681

Validation of hemodynamic stress calculation in coronary CTA versus intravascular ultrasound

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OBJECTIVES Development in computational fluid dynamics and 3D construction could facilitate the calculation of hemodynamic stresses in coronary computed tomography angiography (CCTA). However, the agreement between CCTA derived stresses and intravascular ultrasound/intracoronary angiography (IVUS/ICA)-derived stresses remains undetermined. Thus, the purpose of this study is to investigate if CCTA can serve as alternative to IVUS/ICA for hemodynamic evaluation.

MATERIALS AND METHODS In this retrospective study, 13 patients (14 arteries) with coronary angiography who underwent CCTA and IVUS/ICA were included in this study. Slices-level minimal lumen area (MLA), percent area stenosis (AS), velocity, pressure, Reynolds number, wall shear stress (WSS) and axial plaque stress (APS) were determined by both modalities. The agreement between CCTA and IVUS/ICA was assessed using the intra-class correlation coefficient, Pearson’s correlation coefficient and Bland–Altman analysis.

RESULTS Excellent intraobserver agreement and interobserver agreement were found for WSS with ICCs of 0.926 and 0.928 (P<0.001 for both) and for APS with ICCs of 0.884 and 0.910, respectively. CCTA overestimated the degree of area stenosis (50.22±16.15% vs. 36.41±23.37%, P=0.004) with a smaller MLA (5.81±2.44 mm2 vs. 6.7±2.04 mm2, P<0.01). No statistical difference was observed in WSS (6.5±7.26 vs. 5.8±5.55 mmHg, P=0.420) and APS (16.0±11.59 vs. 1.27±8.90 mmHg, P=0.691) between CCTA and IVUS. Good correlation was found in velocity (0.796), Reynolds number (0.810) and WSS (0.720), while the ICC of APS was 0.339, indicating a relatively poor correlation. In the mildly calcified vessels, good or moderate agreement was found between CCTA and IVUS/ICA in WSS and APS, with an ICC of 0.800 and 0.415, while a significantly lower agreement was found in severely calcified vessels, with an ICC of 0.479 (WSS) and 0.230 (APS).

CONCLUSION CCTA can serve as a satisfactory alternative to the reference standard, IVUS/ICA in morphology simulation and hemodynamic stress calculation, especially in the calculation of wall shear stress.
GW33-e0692
Perivascular fat attenuation index provides incremental prognostic value for 5-year major adverse cardiovascular events in patients with type 2 diabetes mellitus
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OBJECTIVES Perivascular fat attenuation index (FAI) has been introduced as a marker to quantify the coronary artery inflammation and showed independent prognostic importance of all-cause and cardiac mortality over traditional risk factors. However, it remains to be determined if fat attenuation index can provide an increased value of MACEs in Type 2 diabetes mellitus (T2DM) patients over the current coronary computed tomography angiography (CCTA) parameters.

METHODS We prospectively included 1030 DM patients who underwent CCTA because of suspected CAD between January 2015 and December 2017 and examined their CCTA findings, including coronary artery calcium score (CACS), obstructive lesion (>50% diameter stenosis), presence of high-risk plaque (HRP), lesion-specific ischemia, and presence of HRP, and lesion-specific ischemia. The composite endpoint, major adverse cardiovascular events (MACEs), were defined as cardiovascular death, nonfatal myocardial infarction, and stroke, and obstructive lesion requiring hospitalization. The incremental predictive abilities for MACEs were compared among 3 models (model 1: clinical characteristics, model 2: model-adverse CCTA findings, and model 3: model 2+FAI).

RESULTS During a median follow-up of 5.6 years (interquartile range, 3.1–8.0), 534 DM patients developed a major adverse cardiovascular event (MACE). The mean perivascular fat attenuation index (FAI) in 5-year MACEs was 1.86 (95% CI: 1.52–2.30, P<0.001) and a marker to quantify the coronary artery inflammation and showed independent incremental prognostic value for 5-year major adverse cardiovascular events. Nonetheless, RCA FAI was of incremental prognostic value for 5-year MACEs. Model 2 had a significantly higher predictive ability than model 1 (area under the curve [AUC] for model 1: 0.763, 95% CI: 0.716–0.809, P=0.02; for model 2: 0.779, 95% CI: 0.734–0.825, P=0.001).

CONCLUSIONS In euthyroid INOCA patients, increased FT4/FT3 ratio levels demonstrate a poor prognosis, yet the risk factors for CMD remain unclear. Subtle changes in thyroid hormone levels within the normal range, especially the free thyroxine (FT4)/free triiodothyronine (FT3) ratio, have been shown to regulate the cardiovascular system. This prospective study investigated the correlation between FT4/FT3 ratio and CMD in euthyroid patients with INOCA.

GW33-e0748
Effect of myocardial function as measured by the strain technique and molecular changes in the myocardium of obese mice
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BACKGROUND Obesity is a major independent risk factor for cardiovascular diseases, such as coronary heart disease. Patients with obesity have altered cardiac structure and function before the development of coronary atherosclerosis. Obesity-induced myocardial remodeling refers to alterations in myocardial structure, function, and phenotype, including changes in ventricular mass, volume or morphology, increased fibrotic content, cellular hypertrophy, and apoptosis. Patients with obesity often have a normal left ventricular ejection fraction in routine echocardiography. However, myocardial strain technology can identify subclinical changes in myocardial function. Therefore, this study assessed myocardial function in obese mice by strain technique and differential expression of myocardial molecular mechanism between obese and normal mice was analyzed by pathology, immunofluorescence detection and exosome miRNA sequencing reveal changes of molecular of obese myocardium.

METHODS Eight-week-old C57BL/6J mice (n=32) were equally divided into the control (control diet for 12 weeks) and obese (high-fat diet for 12 weeks) groups. The characteristics of mice were evaluated using metabolic tests, two-dimensional strain analysis with echocardiography, Pathology, immunofluorescence detection, and miRNA sequencing of exosomes were used to determine molecular changes in the obese myocardium.

RESULTS The ventricular septum of obese mice was significantly thickened, and the cardiomyocytes in obese mice were increased. Nucleotide oligomerization domain-like receptor protein 3 expression was increased in obese mice as shown by immunofluorescence (P<0.001). Left ventricular remodeling was more marked in the obese group than in the control group (P<0.001).
RESULTS The prevalence of CVD risk factors did not differ significantly among the 3 groups (P>0.05). There were significant increases in troponin-I and C-reactive protein from the CSA group to the PMI group (P<0.05). Nevertheless, white blood cell, neutrophils counts and BNP did not differ significantly among groups.

Scar was larger in the SMI group than the CSA group [25.0 (16.0) vs. 7.5% (10.0), P<0.001]. Scar was larger in the SMI group than the CSA group [25.0 (16.0) vs. 7.5% (10.0), P<0.001]. In contrast, there was no significant difference in TPD and HM among groups (P>0.05). The SMI group exhibited significantly deteriorated cardiac function compared to the PMI and CSA groups, respectively (P<0.001). Besides, the SMI and PMI groups had adverse cardiac remodeling compared with CSA group. PMI vs. CSA group, P=0.005; PMI vs. CSA group, P=0.012. While the cardiac function and LV remodeling didn’t differ between the PMI and SMI groups (P>0.05).

The TBR of BM activity was highest in the PMI group, intermediate in the SMI group, and lowest in the CSA group [2.82±0.34 vs. 1.97±0.27 vs. 1.41±0.21, P<0.001]. The spleen TBR did not differ significantly among the three groups (P>0.05). Aortic arch TBR in both PMI [1.46±0.30] and CSA and PMI groups [1.31±0.30 vs. 1.04±0.19, P=0.002] were higher than the CSA group. BM and spleen metabolic activity were significantly correlated with the aorta TBR (P<0.001).

CONCLUSIONS In summary, prolonged hematopoiesis is upregulated following acute MI in comparison to chronic stable angina. Patients with PMI presented subsequent enlarged scar and worsened cardiac dysfunction than PMI. Further studies of this diminished hematopoiesis, including the hemopoietic-cardiovascular immune axis in recurrent MI patients, are warranted.

GW33-e0713 Prospective analysis of hematological parameters as a basis for prevention of post-COVID complications in patients with cardiovascular diseases

Tatiana Petelina, Natalia Muskhina, Valerya Garanova, Ksenia Avdeeva, Liana Valeeva, Anastasia Shcherbinina, Lyudmila Gapon

OBJECTIVES The study of the characteristics and dynamics of laboratory biomarkers in patients with cardiovascular diseases (CVD) undergoing COVID-19-associated pneumonia may be of great importance for the development of patient monitoring algorithms for the prevention of long-term complications. The objective was to study prospectively the dynamics of hematological parameters in patients with CVD to identify predictors of disease severity and potential indicators of post-COVID vascular complications 3 months after discharge from a COVID isolation hospital.

METHODS The study was prospective, the protocol was approved by the local ethics committee - No 159 dated July 23, 2020 and registered in the international clinical trials of the US National Institute of Health (https://clinicaltrials.gov Identifier number NCT0451822). The study included 16 patients who underwent COVID-19-associated pneumonia. The patients were divided into 2 groups. The first group – 49 patients without CVD, the second group – 67 patients with CVD. A blood sample was performed in all patients at the time of hospitalization and 3 months after discharge from the hospital. The parameters of general blood count, biochemistry, hemostasis, and biomarkers of inflammation were assessed - concentration of C-reactive protein (CRP), highly sensitive CRP (hs-CRP), homocysteine and IL-6. All patients initially underwent computed tomography of the chest organs.

RESULTS We found that erythrocyte sedimentation rate (ESR), WBC (leukocytes), neutrophils/lymphocytes ratio, fibrinogen, lactate dehydrogenase (LDH), lymphocytes/CRP ratio were parameters that significantly distinguished patients in the 1st and 2nd groups. Three months after discharge from the hospital in patients of both groups the increased indicators approached the reference values, however, some parameters such as CRP, ESR, WBC, fibrino-

GW33-e0761 Declined hematopoiesis-inflammation response in patients with recurrent myocardial infarction

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OBJECTIVES Recurrent myocardial infarction (MI) after an acute coronary syndrome portends an unfavorable outcome, which might be induced by a diminished hematopoiesis-inflammatory activation after recurrent MI. FDG PET in hematopoietic tissues provides a non-invasive measurement of proliferative activity. We analyzed the FDG activity of bone marrow (BM), as a surrogate biomarker for prolonged hematopoiesis-inflammation activation in categorized patients after the primary (PMI) and secondary myocardial infarction (SMI). Further, in comparison with chronic stable angina (CSA) patients.

METHODS We retrospectively recruited 97 patients who experienced acute MI (PMI=43 (38 males) vs. SMI=24 (20 males) and CSA patients (24 males). All patients underwent 18F-FDG cardiac PET and gated myocardial perfusion imaging. PMI and SMI were determined by clinical criteria. BM and splenic 18F-FDG activity were quantified as standardized uptake activity (SUVmax).

RESULTS The TBR of BM activity was highest in the PMI group, intermediate in the SMI group, and lowest in the CSA group [2.82±0.34 vs. 1.97±0.27 vs. 1.41±0.21, P<0.001]. The spleen TBR did not differ significantly among the three groups (P>0.05). Aortic arch TBR in both PMI [1.46±0.30] and CSA and PMI groups [1.31±0.30 vs. 1.04±0.19, P=0.002] were higher than the CSA group. BM and spleen metabolic activity were significantly correlated with the aorta TBR (P<0.001).

CONCLUSIONS In summary, prolonged hematopoiesis is upregulated after acute phase of MI in comparison to chronic stable angina. Patients with PMI presented subsequent enlarged scar and worsened cardiac dysfunction than PMI. Further studies of this diminished hematopoiesis, including the hemopoietic-cardiovascular immune axis in recurrent MI patients, are warranted.

CARDIOVASCULAR LAB MED

GW33-e0713 Prospective analysis of hematological parameters as a basis for prevention of post-COVID complications in patients with cardiovascular diseases

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OBJECTIVES The study of the characteristics and dynamics of laboratory biomarkers in patients with cardiovascular diseases (CVD) undergoing COVID-19-associated pneumonia may be of great importance for the development of patient monitoring algorithms for the prevention of long-term complications. The objective was to study prospectively the dynamics of hematological parameters in patients with CVD to identify predictors of disease severity and potential indicators of post-COVID vascular complications 3 months after discharge from a COVID isolation hospital.

METHODS The study was prospective, the protocol was approved by the local ethics committee - No 159 dated July 23, 2020 and registered in the international clinical trials of the US National Institute of Health (https://clinicaltrials.gov Identifier number NCT0451822). The study included 16 patients who underwent COVID-19-associated pneumonia. The patients were divided into 2 groups. The first group – 49 patients without CVD, the second group – 67 patients with CVD. A blood sample was performed in all patients at the time of hospitalization and 3 months after discharge from the hospital. The parameters of general blood count, biochemistry, hemostasis, and biomarkers of inflammation were assessed - concentration of C-reactive protein (CRP), highly sensitive CRP (hs-CRP), homocysteine and IL-6. All patients initially underwent computed tomography of the chest organs.

RESULTS We found that erythrocyte sedimentation rate (ESR), WBC (leukocytes), neutrophils/lymphocytes ratio, fibrinogen, lactate dehydrogenase (LDH), lymphocytes/CRP ratio were parameters that significantly distinguished patients in the 1st and 2nd groups. Three months after discharge from the hospital in patients of both groups the increased indicators approached the reference values, however, some parameters such as CRP, ESR, WBC, fibrinogen remained at a higher level in group 2. Correlation analysis revealed the relationship between parameters of inflammation and hemostasis in the 2nd group of patients, which confirms the presence of latent vascular inflammatory potential in this group. It was revealed that such indicators as lymphocytes, neutrophils and LDH were associated with the initial volume of lung lesion more than 50%. Increase of these parameters by 1 unit contributes to increase in the volume of lung tissue damage by 6.5, 6.4, 11 and 0.6% respectively.

CONCLUSIONS Thus, dynamic control of laboratory parameters has prognostic value in assessing the nature of the course of COVID-19-associated pneumonia in patients with CVD and developing an algorithm for personalized monitoring of patients in the post-COVID period with the aim of timely correction of therapy to prevent unwanted vascular complications.
Salvianolic acid B protects cardiomyocyte injury through Nrf2/HO-1-ANT signaling pathway
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OBJECTIVES In recent years, lipid accumulation has been proved to play an important role in the pathological process after myocardial infarction and is considered to be one of the important causes of ferroptosis. However, whether salvianolic acid B (SAB) plays a protective role in myocardium by inhibiting ferroptosis of myocardium by inhibiting lipid accumulation after myocardial infarction remains unclear. Therefore, we decided to determine whether SAB plays an important role in myocardial protection by inhibiting lipid accumulation.

METHODS The protective effect of SAB on myocardium was studied in vitro. Male C57BL/6 mice were treated with SAB (50 mg/kg/d, gavage) for 14 days after permanent myocardial infarction caused by coronary artery ligation, and echocardiography was performed to assess cardiac function. H9c2 was divided into control group, model group (PA), SAB treatment group (20 μM) and SAB + NAC (5 μmol/L, ROS inhibitor) group. CCK8 staining was used to detect cell viability. Lipid accumulation was used to detect intracellular lipid accumulation by lipid accumulation detection. Electron microscopy was used to observe cell morphology, and Iron Assay Kit was used to detect intracellular Iron levels. The expressions of Nrf2, HO-1, ANT1, GPX4, SLC7A11, Ferritin and Ferritin Light Chain were detected by Western blot.

RESULTS Compared with model group, the area of myocardial infarction was significantly reduced and cardiac function was significantly improved in SAB treatment group. In addition, we found that ferroptosis caused by myocardial infarction mainly manifested as mitochondrial outer membrane rupture, increased density of bilayer membrane rupture, release of inflammatory mediators such as arachidonic acid, and decreased expression of ferroptosis related proteins GPX4, SLC7A11, Ferritin and Ferritin Light Chain. All of these changes can be prevented by SAB intervention, which is as effective as the ROS inhibitor NAC. In vitro, SAB was found to reduce elevated intracellular ferroptosis levels.

CONCLUSIONS We believe that SAB can prevent cardiac injury and dysfunction caused by myocardial infarction to a certain extent by reducing lipid accumulation, and provide a new approach for clinical treatment of heart failure.

A randomized, placebo-controlled, double-blind trial to evaluate efficacy and safety of Shen-Yuan-Dan capsules, a traditional Chinese medicine, for treatment of peri-procedure myocardial injury following percutaneous coronary intervention
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OBJECTIVES Peri-procedural myocardial injury (PMI) is a common complication of percutaneous coronary intervention (PCI), which cannot be entirely avoided using available treatments. The findings of earlier research have shown that Shen-Yuan-Dan (SYD) capsules, a traditional Chinese medicine, can potentially alleviating PMI. This study aimed to confirm further this hypothesis in a rigorous, well-designed randomized controlled study.

METHODS Our clinical trial was randomized, double-blind, and placebo-controlled. A total of 181 patients with unstable angina (UA) undergoing elective PCI were randomized to pretreatment with SYD or a placebo under the basis of conventional treatment; 87 patients were pretreated with SYD (four capsules, 3 times a day, with a further four capsules 2 hours before PCI) 3 days before the procedure, and 94 patients were given a placebo. No patients received reloading statins before PCI, and SYD or placebo was maintained for 1 month after PCI. The primary endpoint was the incidence of PMI. The secondary endpoint was the incidence rate caused by myocardial infarction to a certain extent by reducing lipid accumulation to a certain extent by reducing lipid accumulation.

RESULTS The levels of creatine kinase-myocardial band (CK-MB) in both the SYD and placebo groups were increased at 4 hours and 24 hours after PCI compared with before the procedure (P<0.05). The incidence rate of PMI in the SYD group (10.3%) was lower than that in the placebo group (34%) (absolute difference, 23.7% [95% CI, 11.7–34.8%], P=0.01). After taking SYD, the relative risk reduction (RRR) and absolute risk reduction (ARR) were 69.7% and 24.3%, respectively; further, number needed to treat (NNT) was 4.2. The 30-day major adverse cardiovascular event (MACE) rate was not statistically different between the SYD and placebo groups (6.9 vs. 6.0%, P=0.352). There were no abnormalities during the trial.

CONCLUSIONS These findings showed that pretreatment with SYD could safely reduce the incidence rate of PMI in patients with UA undergoing elective PCI. Further study on the effects of SYD and how it can improve adverse cardiovascular events outcomes is needed.
GW33-e0008

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OBJECTIVES This study investigates the prevalence trends of obesity and abdominal obesity in US adults from 2001 to 2018.

METHODS We included 44,184 adults from the nine cycles of the continuous NHANES (2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, 2013-2014, 2015-2016, 2017-2018). The weighted mean body mass index and waist circumference were calculated, and the sex-specific annual change was illustrated by the survey cycle. We used the weighted sex-specific logistic regression models to analyze the prevalence of obesity and abdominal obesity from 2001 to 2018. The weighted adjusted odds ratio (OR) with 95% confidence interval (CI) was calculated.

RESULTS In the obese population, the prevalence of class I obesity ranked first (20.17%), followed by class II obesity (8.98%) and class III obesity (6.32%). Abdominal obesity was observed in 53.13% of all populations, with a significantly higher prevalence in females (62.92 vs. 43.15%; P<0.001). Females showed a significantly lower waist circumference (85.45 vs. 100.66 cm; mean difference, -5.20 cm; P<0.001), whereas BMI (28.78 vs. 28.54 kg/m²; mean difference, 0.24 kg/m²; P=0.005) was slightly higher in females than males. Consistently, the sex-specific smoothed density distribution curve showed a lower and right-shifted curve of BMI and waist circumference stratified by sex. A rightward shift change was observed in BMI and waist circumference distribution over the past three intervals. The weighted mean BMI (β-coefficient, 0.10; 95% CI: 0.001 and waist circumference (β-coefficient, 0.28; P<0.001) significantly increased over the 18-year survey. The mean BMI has increased from 27.83 to 29.55 kg/m², whereas the mean waist circumference increased from 95.28 to 101.18 cm. We observed the significant association of survey year with BMI and waist circumference. Mosaic plot and bar plot were used to present the distribution of each BMI category by age, gender and residence group. Restricted cubic spline and survival curve were generated to identify the relationship between CVH score and all-cause mortality primarily. Cox proportion regression was conducted to estimate HRs and 95% CIs for the association with gradual adjustment. Subgroup and sensitivity analysis was applied to test the robustness of results.

RESULTS A total of 4,999 subjects were included in this study, the average age of whom was 70.49±SD (6.77) years old, with 40.3% male and 59.7% female. Only 8% study participants had high-normal fat, high-normal muscle and high-fat mass were at greater risk of abnormal glucose and lipid metabolism.

CONCLUSIONS This study provides evidence for the benefits of CVH metrics in reducing risk of all-cause mortality among Chinese older population. Obtaining ideal CVH would definitely be a long-term goal, the immediate action or short-term goal is to encourage the attainment of per point of CVH score at a time progressively. Public health policies and strategies should be implemented especially focusing on behavior interventions among Chinese older adults.

GW33-e0040
Impact of muscle on glucose and lipid metabolism depends on body fat accumulation in children

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OBJECTIVES The limitations associated with the use of body mass index in assessing obesity make it impossible to study the influence of muscle-fat composition on cardiometabolic risk. The aim of the present study was to investigate the associations of muscle-fat composition, especially the muscle mass, with glucose and lipids metabolism in children and adolescents.

METHODS This nationwide cross-sectional study included 8905 children and adolescents (50.1% boys) aged 6 to 18 years. All participants underwent dual-energy x-ray absorptiometry for body composition, and their glucose and lipids were measured. Multivariable-adjusted linear regression coefficients and odds ratios were calculated to assess the associations between muscle mass and glucose and lipids metabolism. Hierarchical analysis and piecewise regression model were used to study the effect of muscle-fat composition on glucose and lipid metabolism.

RESULTS The proportion of high total cholesterol (TC, 6.9 and 6.8%) and high triglyceride (TG, 22.3 and 6.6%) was found in both female and male participants with high muscle and high fat, while girls with high muscle and high fat also had the highest proportion of hyperglycemia (7.1%). After fat stratification, higher muscle mass was associated with lower odds of having hyperglycemia (OR=0.95; 95% CI: 0.94-0.96; P<0.001) and hypertriglyceridemia (OR=0.84; 95% CI: 0.80-0.88; P<0.001). Muscle mass was inversely associated with TC (β=-0.07; 95% CI: -0.12, -0.03; P<0.001) in boys with normal fat. Muscle mass was not associated with hyperglycemia (OR=0.83; 95% CI: 0.53-1.25; P=0.368) and TC (OR=0.94; 95% CI: -0.05, 0.98; P=0.59) in high fat boys. Children with high-muscle and high-fat had higher risks of having insulin resistance, high TC, high TG, high low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), and high non-HDL-C than those with different body fat compositions.

CONCLUSIONS Fat modifies the effect of muscle on glucose and lipid metabolism. Higher muscle mass was only associated with a lower risk of hyperglycemia and TC levels in individuals with normal weight. Children with high-muscle and high-fat mass were at greater risk of abnormal glucose and lipid metabolism.
GW33-e0118
A bibliometric study and visualization analysis of chronotherapy
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OBJECTIVES This study aimed to review the research status and to demonstrate the hotspots and frontiers of chronotherapy.

METHODS Literature regarding chronotherapy from inception to 2021 were retrieved from the Web of Science Core Collection database. CiteSpace 5.8. R1 was used to generate network maps about the collaborations between authors, countries, and institutions and reveal hot spots and frontiers of chronotherapy.

RESULTS A total of 829 studies related to chronotherapy were included. The number of literature regarding chronotherapy was generally increased with some fluctuations. Hermida RC was the most prolific author (79 articles, 9.53%). The USA and Universidad de Vigo were the leading country and institution in this field with 221 and 85 publications, respectively. Chronobiol Int was the most commonly cited journal (514 articles). The first co-referenced report described the MAFEC trial which analyzed the effect of circadian rhythm time of hypertension treatment on cardiovascular risk. Hot topics focused on the circadian rhythm, hypertension, melatonin, sleep deprivation, cancer and rheumatoid arthritis.

CONCLUSIONS This study suggested the prosperous research trends and close connections in the field. Major ongoing research trends include the timing of antihypertensive medication dosing, melatonin, sleep deprivation, cancer and rheumatoid arthritis.

GW33-e0135
Causal association between vitamins and atrial fibrillation risk: a Mendelian randomization study
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OBJECTIVES Dietary intake and high blood concentration of vitamins have been associated with low atrial fibrillation (AF) risk. However, the causal relationship between vitamins and AF have not been fully elucidated. Here, we investigated the relationship between genetically determined vitamin levels and AF by conducting a Mendelian randomization (MR) study.

METHODS Single-nucleotide polymorphisms for circulating vitamin levels, including vitamin A, B, C, D, E, and whether determined either as absolute levels or metabolites were obtained from public genome-wide association studies (GWAS) and were used as genetic instrumental variables. Summary statistics for gene-AF associations were retrieved from the largest GWAS of AF mainly based on European population, which included 65,446 AF cases and 522,744 controls. Two-sample Mendelian randomization analysis was implemented to investigate the causality between vitamin levels and AF.

RESULTS Our MR study found that genetically predicted circulating vitamin levels were not causally associated with AF risk. For absolute vitamins, the odds ratio for AF ranged from 0.97 (95% confidence interval [CI]: 0.92–1.01, P=0.76) for vitamin B9 to 1.43 (95% CI 0.95–2.15, P=0.09) for vitamin E. For vitamin metabolites, the odds ratio ranged between 0.97 (95% CI: 0.64–1.47, P=0.21) for epidermal and 1.11 (95% CI: 0.90–1.36, P=0.34) for vitamin B6.

CONCLUSIONS Our study did not find convincing evidence to support genetically determined circulating vitamin levels were associated with AF. Therefore, there may be no direct beneficial effects of vitamin intake on prevention of primary AF.

GW33-e0228
Cardiovascular outcomes of SGLT2 inhibitors in patients with CHF, with or without diabetes mellitus: a network meta-analysis of randomized controlled trials
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OBJECTIVES A network meta-analysis of randomized controlled trials (RCTs) was conducted to evaluate the cardiovascular protective effect of prophylactic use of SGLT2 inhibitors in patients with CHF, without diabetes mellitus.

METHODS We will search, with no time restrictions, the following databases for relevant English language literature: PubMed, Cochrane Library, Embase and Web of Science. All the English publications until 6 March 2022 will be searched without any restriction of countries or article type. Reference list of all selected articles will independently screened to identify additional studies left out in the initial search. We included RCTs comparing any SGLT2 inhibitor with placebo or other standard treatment without SGLT2 inhibitor in patients with CHF, reporting desired cardiovascular outcomes and with a follow-up duration of at least 6 months. Cardiovascular outcomes was defined as major adverse cardiovascular event, cardiovascular death, cardiovascular readmission, patient readmission, acute myocardial infarction and all-cause mortality.

RESULTS Our network meta-analysis included 11 articles, comprising a combined cohort of 20,392 patients with CHF. Frequentist network meta-analysis demonstrated that application of SGLT2 inhibitors (dapagliflozin, empagliflozin, canagliflozin, atoglipiflozin) in patients with CHF reduced the risk of MACE (HR 0.52; 95% CI 0.36–0.68), cardiovascular death (HR 0.66; 95% CI 0.58–0.75), cardiovascular readmission (HR 0.62; 95% CI 0.55–0.71), cardiovascular death (HR 0.81; 95% CI 0.70–0.95), acute myocardial infarction (HR 0.73; 95% CI 0.53–0.90), and all-cause death (HR 0.86; 95% CI 0.72–0.90), with no significant heterogeneity detected.

CONCLUSIONS In patients with CHF, SGLT2 inhibitors were associated with reduced risks of MACE, cardiovascular death, cardiovascular readmission, acute myocardial infarction, all-cause mortality. Therapy with SGLT2 inhibitors in patients with CHF, without diabetes mellitus results in a sustained reduction of the cardiovascular outcomes.

GW33-e0258
Association between extreme temperature and myocardial infarction hospitalizations in Beijing, China from 2007 to 2019: a time series study
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OBJECTIVES The increasingly frequent and intense extreme temperatures have raised concerns regarding their deleterious impacts on public health. We aimed to assess the association between extreme temperature and daily myocardial infarction (MI) hospitalizations in Beijing, China from 2007 to 2019.

METHODS This study enrolled 918 participants aged 45 to 74 years who were free of cardiovascular disease at baseline and completed carotid ultrasound measurements twice in 2002 and 2007 over a 5-year interval from the Chinese Multi-Provincial Cohort Study-Beijing Project. Metabolic health was defined as having 0–1 metabolic abnormality from the following criteria: elevated blood pressure (≥130/85 mmHg); elevated fasting blood glucose (≥5.6 mmol/L); decreased level of high-density lipoprotein cholesterol (<1.04 mmol/L for male and <1.29 mmol/L for female), and elevated level of triglyceride (≥2.07 mmol/L). Participants were cross-classified by change in metabolic health status from 1992 to 2002 and body mass index (BMI) categories (normal weight: BMI<24 kg/m²; overweight: BMI=24–28 kg/m²; obesity: BMI≥28 kg/m²) in 1992. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using multivariate logistic regression adjusting for age, sex, current smoking status, low density lipoprotein cholesterol and high-sensitivity C-reactive protein.

RESULTS The mean age of the participants was 59.6±7.9 years at baseline and 45.2% were men. There were 445 (48.3%) participants maintaining metabolic health from 1992 to 2002. During 5-year follow-up period, a total of 422 (62.7%) participants had had MI plaque progression. Transitions from metabolically healthy to unhealthy or initial metabolically unhealthy was associated with a higher risk of plaque progression (OR=1.5; 95% CI: 1.14, 2.00; P=0.004). Compared with sustaining metabolically healthy participants with normal weight, stable metabolically healthy overweight participants had 72% increased risk of plaque progression (OR=1.72; 95% CI: 1.09, 2.70; P=0.020).

CONCLUSIONS Metabolic unhealth, either initially unhealthy or transition from healthy to unhealth, is a risk factor of carotid atherosclerosis progression. Even when metabolic health is maintained during long periods of time, overweight individuals have a higher risk of carotid atherosclerosis progression.
METHODS From 2007 to 2019, all MI hospitalizations among permanent Beijing residents aged ≥35 years old were collected from the Beijing Cardiovascular Disease Surveillance System. The associations between ambient temperature and MI hospitalizations were estimated by a combination of Poisson generalized additive models and distributed lag nonlinear models controlling for relative humidity, PM₂.₅ long-term trends, and day of the week. For the single-lag association, we depicted the overall lag structure figure for the extreme cold (at 29.6°C, the 97.5th percentile) and heat (at −2.5°C, the 2.5th percentile) temperatures. For the cumulative association over 0–21 lag days, we depicted the cumulative exposure-response curve and defined the heat and cold effect as cumulative-lag risks at the extreme heat and cold temperatures relative to the minimum estimated, respectively. The Z test was used to compare the difference in the two effect estimates among subgroups in gender and age groups.

RESULTS Between 2007 and 2019, 216,883 events of MI hospitalizations were recorded. On average, there were 46 cases per day. The daily mean temperature ranged from −14.3°C to 34.5°C, with an average of 1.56°C. For the single-lag association, the effects in extreme cold occurred on lag day 1, increased up to lag day 3, and decreased with mild effects on subsequent days. By contrast, the effects of extreme heat were the most pronounced on the present day and followed by mild effects on the subsequent days. For the cumulative association over 0–21 lag days, the exposure-response curve between daily mean temperatures and MI hospitalizations was inverse J-shaped and the impact of low temperature was greater. The cold and heat effects were 1.95 (95% CI: 1.89–2.00) and 1.09, respectively. Subgroup analysis showed that older individuals (aged ≥65 years) had a greater risk of cold than younger individuals (aged 35–64 years) (RR, 1.97 vs. 1.55 to 2.50; 91 vs. 1.14; 95% CI, 1.02 to 1.75; P < 0.006). There were no significant gender differences for both cold and heat effects.

CONCLUSIONS Extreme temperatures were associated with increased MI hospitalizations. The single-lag effects lasted longer for extreme cold than heat, and the cumulative-lag effects showed a significant cold effect, but not the heat effect. The elderly was more sensitive to cold. The evidence has important implications for public health practices to minimize the adverse health effects of temperatures, especially low temperatures.

GW33-e0368 Joint effect of homocysteine and uric acid on arterial stiffness in the general population
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OBJECTIVES Homocysteine (Hcy), serum uric acid (UA) and arterial stiffness are closely associated with cardiovascular diseases. Both serum Hcy and UA could affect the arterial stiffness level. In this study, we evaluated the joint effect of Hcy and UA on arterial stiffness in the general population.

METHODS The study consisted of 17,697 participants from Beijing Health Management Cohort, who underwent health examination between January 2012 and December 2019. Brachial-ankle pulse wave velocity (baPWV) was used as an index of arterial stiffness. Unadjusted and adjusted linear regression models were used to estimate the sex-specific association of Hcy and UA concentrations with baPWV level.

RESULTS On multivariable linear regression analysis, one-standard deviation (SD) rise of Hcy (7.6 μmol/L) and UA (7.8 μmol/L) were associated with an 7.38 and 7.65 increased baPWV (cm/s) in male. Similarly, one-SD rise of Hcy (4.0 μmol/L) and UA (4.9 μmol/L) were associated with an 1.00 and 1.60 increased baPWV in female. Individuals with both high Hcy and UA had the highest baPWV, compared with those with low Hcy and low UA (β; 30.76, 95% CI: 18.36–43.16 in male; β; 53.53, 95% CI: 38.46–68.60 in female).

CONCLUSIONS This study indicated the joint effect of elevated Hcy and UA on arterial stiffness. People with simultaneously high Hcy and UA should be aware of the risk of arteriosclerosis and cardiovascular events.

GW33-e0404 Cardiovascular disease and all-cause mortality attributable to individual and combined cardiometabolic risk factors among Chinese
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OBJECTIVES Few have systematically clarified cardiovascular disease (CVD) and all-cause mortality attributable to individual and combined cardiometabolic risk factors, especially for Chinese people. The present study was to investigate and quantify the individual and combined associations and population attributable fraction (PAF) of cardiometabolic risk factors, including hypertension, diabetes and dyslipidemia, on CVD and all-cause mortality, and calculate the reductions in CVD-free years and life expectancy in relation to cardiometabolic risk factors among Chinese population.

METHODS Twenty-two thousand six hundred sixty participants aged ≥35 without self-reported medical history of CVD at baseline were included between October 2012 and December 2019 based on a nationally representative population-based study. CVD events and mortality were followed up in study cohort from 2012 and 2019. Cox regression was applied to evaluate the proportional impact of individual and combined cardiometabolic risk factors (including hypertension, diabetes and dyslipidemia) with CVD risk and all-cause mortality. We also described the PAF for CVD and mortality, and reductions in CVD-free years and life expectancy associated with different combination of cardiometabolic conditions.

RESULTS Mean age of the participants was 56.1±13.10 years. During the 4.92 years of follow-up, we detected 438 fatal or nonfatal CVD (including 279 stroke, 126 coronary heart disease and 33 other cardiovascular events) and 1128 deaths. Hazard ratio were 1.57 (95% confidence interval (CI) 1.32–1.86, 1.71 (95% CI 1.42–2.08) and 2.34 (95% CI 1.74–3.09) for CVD and 1.54 (95% CI 1.32–1.79), 1.45 (95% CI 1.21–1.75) and 2.36 (95% CI 1.80–3.09) for all-cause mortality, respectively, in participants with one, two or three cardiometabolic risk factors compared with participants without diabetes, hypertension, and dyslipidemia. Subjects with the combination of diabetes, hypertension, and dyslipidemia had greater than 2-fold increased CVD and all-cause mortality. The cardiometabolic multi-morbidities showed a multiplicative increased CVD and all-cause mortality risk and similar results were found for CVD subtypes. The PAFs for total CVD, stroke, coronary heart disease and all-cause mortality attributable to all cardiometabolic risk factors were 24.42 (95% CI 24.11–24.94), 24.21 (95% CI 23.79–24.64), 23.58 (95% CI 23.06–24.06) and 22.11 (95% CI 21.75–22.49), respectively. For participants with only one risk factor, we found that the PAFs of CVD and mortality were mainly caused by hypertension. We estimated that participants aged between 40 and 60 years old, with three cardiometabolic disorders, had approximately 2.4 years of reduced CVD-free years and 3.3 years of reduced life expectancy compared with participants without any abnormalities of cardiometabolic disorders.

CONCLUSIONS Cardiometabolic risk factors were additively associated with a higher risk of CVD incidence and all-cause mortality. A large proportion of CVD and all-cause mortality and reduction in CVD-free years and life expectancy were significantly associated with cardiometabolic risk factors, highlighting the importance of cardiometabolic multi-morbidities in the primary prevention of CVD and comprehensive management for hypertension, diabetes and dyslipidemia.

GW33-e0405 The burden of cardiovascular disease attributable to high systolic blood pressure across China and its provinces, 2005–2018
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OBJECTIVES Temporal trends and geographical variations in cardiovascular disease (CVD) burden attributable to high systolic blood pressure (SBP) in China have not been fully elucidated in the past. The current study was performed to quantify the CVD burden attributable to high SBP at both the national and provincial level in China, assisting public policy making in promoting blood pressure control measures.

METHODS We evaluated SBP levels and estimated the number of deaths, age-standardized mortality rates, years of life lost (YLLs) for death related to CVD
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and its subcategories (including ischaemic heart disease, ischaemic stroke, haemorrhagic stroke and other cardiovascular diseases) attributable to high SBP at both national and provincial levels in China from 2005 to 2018. We pooled blood pressure data of 1350 million adults from the China Chronic Disease and Risk Factor Surveillance project, the China Health and Nutrition Survey and China Hypertension Surveillance. We applied a temporal-spatial Bayesian hierarchical model to estimate all year-specific local SBP levels, and a comparative risk assessment method to compute the health burden attributable to high SBP by age, sex, year and province.

RESULTS Nationally, age-standardised mean SBP was 128.4 mmHg (95% uncertainty interval 126.6 to 130.1) for 2005 to 2018. CVD deaths in China were attributable to elevated SBP, consisting of 1·12 million (95% UI 1·04 to 1·20) deaths from ischaemic heart disease, 0·63 million (95% UI 0·56 to 0·70) deaths from ischaemic stroke, 0·58 million (95% UI 0·57 to 0·60) deaths from haemorrhagic stroke and 0·54 million (95% UI 0·52 to 0·56) deaths from other CVD. The age-standardised CVD mortality rates associated with high SBP increased by 17·8% between 2005 and 2018 with an estimated annual percentage change was −1·50 (95% UI −1·55 to −1·45). Despite the decline in corresponding age-standardised mortality rates, the number of deaths from ischaemic heart disease and ischaemic stroke attributable to high SBP, however, increased in most provinces from 2005 to 2018, consistent with the national trend, because of the change in demographic structure in the population. YLLs for total CVD deaths attributable to high SBP increased from 40·13 million (95% UI 39·70 to 40·52) in 2005 to 48·16 million (95% UI 47·44 to 48·90) in 2018 nationally. YLL rates also varied substantially across provinces, ranging from 3·17 to 15·9 (95% UI 4977 to 43 to 3448 to 83) per 100,000 people in Fujian to 7·91 to 9·05 (95% UI 864 to 28 to 7498 to 94) per 100,000 people in Hebei in 2012. Age-standardised YLL rates for ischaemic heart disease and ischaemic stroke attributable to high SBP were particularly high in northeastern provinces, including Heilongjiang, Liaoning and Jilin.

CONCLUSIONS The deaths and YLLs for CVD attributable to high SBP increased substantially in recent years, especially among the elderly, although age-standardised CVD mortality rates decreased in China between 2005 and 2018. Effective and locally adapted preventive interventions should be implemented to lower the prevalence of high SBP to reduce the health burden of SBP-related CVD in the population.

GW33-e0408 Intermediate-density lipoprotein particle numbers are independently associated with progression of carotid atherosclerosis

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OBJECTIVES Despite lipid-lowering therapy, residual risk still exists for atherosclerotic cardiovascular disease (ASCVD). As the precursor of low-density lipoprotein particle number, intermediate-density lipoprotein [IDL] has been reported to be an important role in the pathogenesis of atherosclerosis and be a potential target for the early prevention of cardiovascular disease.

RESULTS During 5-year follow-up period, the progression of carotid plaque was observed in 45.8% of participants. The median level of baseline IDL-P was 199.0 mg/dL, which was independent associated with plaque progression and changes in TPA. Compared with the lowest quartile of IDL-P, RR in the highest quartile of IDL-P was 1.36 (95% confidence interval: 1.09 to 1.66) for progression of carotid plaque. Among participants without baseline plaque, adjusted ORs in the highest quartile of IDL-P was 1.68 (95% CI: 1.05 to 2.70). Similar results were found in participants without lipid-lowering therapy or diabetes at baseline. This relation still preserved even among participants with low-density lipoprotein cholesterol less than 130 mg/dL.

CONCLUSIONS Increased IDL-P levels are associated with an increased risk of carotid atherosclerosis progression in participants free of cardiovascular disease from a community-based population study, suggesting IDL-P exerting an important role in the pathogenesis of atherosclerosis and be a potential target for the early prevention of cardiovascular disease.

GW33-e0505 Exploring optimal exercise-based rehabilitation program for pulmonary hypertension: a systematic review and meta-analysis of randomized controlled trials

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OBJECTIVES The optimal individualized exercise training program for patients with pulmonary hypertension (PH) is unclear. In this study, we aimed to conduct a meta-analysis of randomized controlled trials (RCTs) to estimate the efficacy of exercise training and determine the optimal exercise training program characteristics.

METHODS We searched studies up to May 2022 from PubMed, MEDLINE, Embase and Cochrane. We included all RCTs analyzing the effectiveness of exercise training in PH patients. The primary outcome of this meta-analysis were changes in six-minute walk distance (6MWD) and changes in peak oxygen uptake (peak VO2). Other outcomes included changes in N-terminal pro brain natriuretic peptide (NT-pro BNP), physical summation score of short-form health survey 36 (SF-36 PCS), and mental summation score of short-form health survey 36 (SF-36 MCS). We performed subgroup analyses based on 2 factors: exercise training duration and exercise training modality. We accessed risk of publication bias and study quality of included studies.

RESULTS In total, 13 studies with 552 PH patients were included. Intervention duration ranged from 3 weeks to 6 months. Exercise modality included aerobic exercise training, inspiratory muscle training (IMT) only, combined exercise, and mixed exercise. Exercise training was associated with significant improvement of 6MWD [MD: 47.89 meters (95% CI: 34.77 to 61.01)], peak VO2 [MD: 1.77 mL/kg/min (95% CI: 0.75 to 2.79)], SF-36 PCS [MD: 4.13 (95% CI: 1.93 to 6.33)] and SF-36 MCS [MD: 1.70 (95% CI: 1.71 to 5.60)]. Exercise training did not reduce NT-pro BNP levels. Long duration exercise training subgroup [MD: 60.03 meters (95% CI: 37.17 to 74.89) in 6MWD, MD: 2.04 mL/kg/min (95% CI: 0.63 to 3.45) in peak VO2] had better improvement compared with the other subgroups. In a subgroup analysis using exercise training modality as a grouping factor, the aerobic exercise only subgroup did not improve 6MWD [MD: 48.42 meters (95% CI: 13.03 to 108.87)] and only the mixed exercise subgroup was associated with a significant improvement in peak VO2 [MD: 2.25 mL/kg/min (95% CI: 0.58 to 3.92)].

CONCLUSIONS Long duration exercise training with mixed exercise form of modality is probably an effective supplementary treatment for stable and well-compensated PH patients.

GW33-e0525 Effect of a web-based platform on hypertension control in community: a randomized clinical trial

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OBJECTIVES We aimed to assess the effect of a web-based platform improving the blood pressure (BP) control.

METHODS A cluster randomized clinical trial of a hypertension management program was conducted in 66 communities, which were randomized to either the intervention group (n=44) or control group (n=22). The intervention programme included self-monitoring, self-treatment and treatment. A web-based-platform was established to support the implementation of intervention. The primary outcome was the change in BP control rate from baseline to 12 months among hypertensive patients in the intervention and control group. The analysis was by intention to treat. The trial has registered in the Chinese Clinical Trial Registry, number ChiCTR180001779.

RESULTS BP control rate at baseline was 23.5% in the intervention group and 22.7% in the control group. After 12 months of the intervention, the BP control rate for the intervention group compared with the control group was significantly higher (48.2 vs 31.1%; odds ratio 1.18; 95% CI: 1.13 to 1.23; P<0.001). At 12 months, the mean systolic BP fell by 11.8 mmHg in the intervention group and by 2.0 mmHg in the control group; the mean reduction was 6.8 mmHg (95% CI: −11.4 to −8.2; P<0.001) greater with the intervention. The mean reduction in diastolic BP was 1.7 mmHg (95% CI: −2.8 to −0.7; P<0.001) greater in the intervention group than the control group.

CONCLUSIONS Interventions program supported by a web-based platform appeared to be more effective than usual care, resulting in improved hypertension control, and lower BP level. A suitable designed web-based platform may provide a new way to improve the unsatisfactory status of BP control faced in many countries.
GW33-e0553  
Association of access to urban parks with incident cardiovascular disease: findings from the Chinese multi-provincial cohort study  
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OBJECTIVES  Living in neighborhoods with better accessibility of parks may be related to lower risk for cardiovascular disease (CVD). However, limited findings are available among older adults from Asian countries. We aimed to estimate the association between neighborhood accessibility of parks and incident CVD in China.

METHODS  A total of 4505 participants aged 51 to 80 years from the Chinese Multi-provincial Cohort Study without CVD at baseline were included. Outcomes were defined as incident CVD, coronary heart disease (CHD), and stroke. Neighborhood accessibility of parks was defined as the presence of parks (yes or no) and the count of parks within 1000 m buffer around residential addresses with points of interest data based on Geographic Information Systems. Shared frailty models were used to estimate the association between neighborhood accessibility of parks with the risk for incident CVD, CHD, and stroke, adjusting for potential confounders. Hazard ratios (HRs) between subgroups were compared using Z-test.

RESULTS  The mean age of the participants was 62.4 (±7.5) years at baseline and 2298 (51.0%) participants were women. A total of 1985 individuals (44.1%) reported the presence of parks within 1000 m buffer around residents’ addresses and 1723 (38.2%) had two or more parks. For participants with the presence of parks compared with those without any parks in 1000 m buffer, but not CHD (HR=0.89, 95% CI 0.71–1.11) and CHD (HR=1.10, 95% CI 0.81–1.51) in fully adjusted models. Further analysis with count indicator indicated living within 1000 m of one park was associated with a decreased risk of stroke (HR=0.84, 95% CI 0.44–0.93), but no significant association was found for two or more parks (HR=0.79, 95% CI 0.52–1.19) compared with those without. The relationships were not significant for CVD and CHD incidence. Subgroup analyses showed a significant interaction between the presence of parks and history of hypertension on incident CVD (P for interaction=0.021).

CONCLUSIONS  Residing in neighborhoods with better accessibility of parks is associated with a lower risk of incident CVD. Urban planning into park policies that increase the accessibility of urban parks could contribute to CVD prevention.

GW33-e0589  
Preserved ratio impaired spirometry in relation to cardiovascular outcomes  
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OBJECTIVES  Preserved ratio impaired spirometry (PRISm) is a heterogeneous condition characterized by a normal forced expiratory volume in 1 s (FEV1) to forced vital capacity (FVC) ratio despite underlying impairment of pulmonary function. Data relating to the association of baseline and trajectory of PRISm with diverse cardiovascular outcomes is sparse.

METHODS  Based on the UK Biobank study, this population-based prospective cohort study included 75,536 participants with spirometry (best measure FEV1 and FVC values) at baseline (2006–2010). Those with baseline spirometry and who had a follow-up spirometry at 2014+ were included in the lung function trajectory analysis. Normal spirometry was defined as a FEV1/FVC ratio >0.70. Airflow obstruction was defined as a FEV1/FVC ratio <0.70. PRISm was defined as a FEV1 <80% predicted and a FEV1/FVC ratio <0.70. PRISm was defined as a FEV1 <80% predicted and a FEV1/FVC ratio <0.70. Cox proportional hazards multivariable regression was performed to evaluate the outcomes of major adverse cardiovascular events (MACE), incident myocardial infarction (MI), stroke, heart failure (HF), and mortality in association with lung function. Linear associations of relative FEV1 and FVC predicted percentage change with diverse cardiovascular outcomes were also evaluated by cubic spline model.

RESULTS  Among 329,954 adults with spirometry data available at baseline, 242,555 (73.5%) had normal spirometry, 37,897 (11.5%) had PRISm and 49,504 (15.0%) had airflow obstruction. For baseline analysis, the median follow-up time was 9.0 years (interquartile range: 8.4–9.8 years). The multi-variable adjusted hazard ratios for participants had PRISm (vs. normal spirometry) were 1.26 (95% confidence interval 1.17 to 1.35) for MACE, 1.12 (1.01 to 1.25) for MI, 1.88 (1.72 to 2.05) for HF, 1.26 (1.13–1.40) for stroke, and 1.55 (1.37–1.76) for CVD mortality, respectively. A total of 22,781 participants had a follow-up spirometry after 6.4 years. Longitudinal analysis showed that persistent PRISm and airflow obstruction was associated with a higher incidence of MACE (1.96 (1.24 to 3.09) and 1.43 (1.00 to 2.04)) versus consistently normal lung function, respectively. Compared with persistent PRISm, changing from PRISm to normal spirometry was associated with a lower incidence of MACE (0.41 (0.17 to 0.96). Each five unit increase in relative FEV1s or FVCs predicted percentage change was associated with a lower risk of MACE (FEV1: 0.091 (0.88–0.95); FVC: 0.09 (0.90–0.97)) and MI (FEV1: 0.092 (0.86–0.97); FVC: 0.09 (0.90–0.99)).

CONCLUSIONS  Individuals with baseline or persistent PRISm were at a higher risk of diverse cardiovascular outcomes even after adjusting for a wide range of confounding factors. Early detection and interventions for lung pathology may reduce subsequent MACE inflicted by lung diseases.

GW33-e0652  
Trends in incidence, long-term all-cause and cardiovascular and cerebrovascular mortality of metabolic syndrome in U.S. adults from 1999–2014: an observational study  
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OBJECTIVES  Metabolic syndrome (MetS) is very prevalent and related to severe diseases and death. This study aimed to investigate the incidence and mortality trends of MetS in recent decades. The gender and age differences of mortality had a yearly decline trend, while the cardio-cerebrovascular death experienced a short period of rise then declined and stabilized. Similarly, the temporal mortality trends in MetS patients of different ages and gender had the same results. Specifically, the incidence of MetS in female was higher than that in male (Adjusted P<0.001; OR, 1.14; 95% CI, 1.05–1.24), but the mortality was much lower after an average of 7.7 years’ follow-up (All-cause mortality, Adjusted P<0.001; HR, 0.68; 95% CI, 0.57–0.81; Cardiovascular mortality, Adjusted P<0.001; HR, 0.53; 95% CI, 0.37–0.83).

CONCLUSIONS  From 1999–2014, the incidence of MetS in U.S. adults was significantly increased overall, while the mortality rate of MetS had a significantly downward trend. Both trends showed marked gender differences, being more prevalent and at lower risk in female compared with male. It is important to identify the factors to curb the incidence of MetS and decrease the mortality especially in male.

GW33-e0657  
Associations of high triglyceride-glucose index onset age with cardiovascular disease and mortality: the Kuilian Study  
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GW33-e0021
The improvement effect of resistance training on cardiovascular health of middle-aged and elderly women
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OBJECTIVES “Report on Cardiovascular Health and Diseases in China 2020” shows that the incidence of cardiovascular disease in China continues to rise. Some studies have demonstrated that elderly women have a higher mortality rate from cardiovascular disease than men. Therefore, it is more important for middle-aged and elderly women (MEW) to prevent cardiovascular disease. The American College of Sports Medicine recommends resistance training (RT) to prevent the functional decline of the body brought by aging and to improve muscle strength and physical function. Therefore, this study will focus on the effects of RT on cardiovascular health in MEW so as to prevent cardiovascular disease.

METHODS In this study, the latest research results of “RT”, “MEW”, “cardiovascular health” and other related research fields were searched in databases such as CNKI, Wanfang Data, VIP, PubMed, Web of Science. Finally, the articles with low relevance to the topic were excluded, 59 targeted articles were identified. A further analysis was carried out to explore the effects of RT on cardiovascular health of MEW.

RESULTS (1) RT promotes cardiovascular protection by inducing post-exercise hypotension; improves endothelial cell function, regulates blood pressure (BP); causes hemodynamic and neurohumoral factors such as plasma catecholamines and vascular tone to interact to induce BP changes, promote cardiovascular health in MEW. (2) RT can raise the activity of lipolytic enzymes in muscles, significantly improve local muscle metabolism, enhance cholesterol catabolism in peripheral tissues, reduce LDL-C deposition in the vascular endothelium, lessen visceral and subcutaneous fat, and improve lipid metabolism. (3) RT can increase nitric oxide bioavailability, increase the expression and activity of nitric oxide synthase; improve vaso regulation and promote sympathetic-vascular balance, reduce heart rate variability, decrease the risk of cardiovascular disease. (4) RT improves arterial stiffness by activating muscles, increasing glycolysis, causing hemodynamic and neurohumoral factors such as plasma catecholamines and vascular tone to interact to induce BP changes, promote cardiovascular health in MEW. (5) RT can improve the total antioxidant capacity of the brain and increase the expression and activity of antioxidant enzymes, improve the antioxidant capacity and reduce the oxidative stress response, decrease the inflammatory response associated with increasing age. (6) It is suggested that MEW should perform RT at least twice a week. Further studies may focus on appropriate frequency and intensity of RT for MEW.

CONCLUSIONS RT can improve dyslipidemia, heart rate variability, arterial stiffness, lower blood pressure and reduce oxidative stress. In MEW, RT can counteract the effects of menopause and changes in hormone levels on the cardiovascular system to a certain extent and reduce the risk of cardiovascular disease. Therefore, it is recommended that MEW perform appropriate RT in daily life to delay the adverse effects of aging.

GW33-e0067
The prevention and control effect of exercise on abnormal lipid metabolism induced by changes in postmenopausal hormone secretion
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OBJECTIVES Due to the insidious form of the disease, abnormal lipid metabolism in postmenopausal women leads to develop further due to delayed intervention, which can lead to obesity, cardiovascular disease and non-alcoholic fatty liver, etc. Studies show that this is related to the change of hormone secretion in the body after menopause. Regular exercise can effectively improve blood lipid indexes in postmenopausal women by promoting hormone secretion and activating estrogen receptor. This study summarized the changes of hormone secretion related to lipid metabolism after menopause and its effects on lipid metabolism, and explored the intervention effects and regulatory mechanisms of different exercise modes on abnormal lipid metabolism in postmenopausal women, so as to provide theoretical support and practical guidance for the prevention and treatment of postmenopausal abnormal lipid metabolism.

METHODS Using the method of literature review, the related articles were searched in CNKI and PubMed databases by computer, and the key words were “menopause”, “hormones”, “lipid metabolism”, “exercise” and “training”. The research included postmenopausal hormone secretion change patterns, effects and mechanisms on lipid metabolism, and results and mechanisms of exercise.
interventions. The articles with low relevance to the topic were excluded, and 64 targeted articles were selected for further analysis.

**RESULTS** (1) The abnormalities of lipid metabolism in postmenopausal women are due to hormonal changes. Previous studies have suggested that this is mainly related to estrogen deficiency, but more and more studies in recent years have found that follicle stimulating hormone is also related. (2) Changes in E and FSH level in women during the menopausal transition and postmenopause do not follow a single pattern, but are related to multiple factors such as race/ethnicity, weight, age and health status. (3) Abnormalities in postmenopausal lipid metabolism are formed by E through increased energy intake, involved in lipid metabolism in multiple tissues, and reduced energy expenditure, suggesting that the mechanism of the problem is not unique and unilateral, but may be the result of multiple mechanisms acting together. (4) Compared with E, the mechanism of the effect of FSH on lipid metabolism in postmenopausal women is less clear. (5) It is proven that bile duct cells and lipid synthesis in adipose tissue, or the regulation of fat accumulation and distribution during aging. (6) Different types of exercise such as aerobic exercise, resistance training, combined aerobic and resistance training, high-intensity interval training, handball exercise and water exercise all have positive effects on lipid metabolism in postmenopausal women. (6) Exercise promotes improved lipid metabolism by improving the secretion of E and FSH in plasma, skeletal muscle and other tissues, activating estrogen receptors and ERE and other mechanisms.

**CONCLUSIONS** Abnormal lipid metabolism caused by changes in hormone levels leads to a series of problems such as obesity and cardiovascular diseases, which plague many postmenopausal women, endangering their life and health, and seriously affecting the quality of life. Exercise can improve abnormal lipid indicators in postmenopausal women and should be promoted as soon as possible to reduce the medical burden on families and the country.

**GW33-e0098**

**Effect of HIIE and MICE on vascular function of recessive obese women with family history of hypertension**

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**OBJECTIVES** To reveal features of changes in vascular function among recessive obese women with family history of hypertension after different types of exercise with same energy expenditure, instruct them to do exercise scientifically and prevent hypertension and atherosclerotic cardiovascular disease (ASCVD).

**METHODS** Forty-five recessive obese women (20.5±1.7 yrs) with family history of hypertension participated in the study. They were evenly randomized to moderate intensity continuous exercise (MICE) group, high intensity intermittent exercise (HIIE) group and control (CONT) group. The exercise began after 2 hours of the meal. The HIIE group performed an interval running session consisting of 4.4 min bouts (running at the intensity of 85–95% HRmax for 4 min, interspersed by 3-min rest). The MICE group did exercise 40 min at the intensity of 65–75% HRmax. The energy expenditure was similar between those two groups. The PWV and ankle brachial index were determined at the time points of pre-exercise, immediately after exercise, then every 5 minutes ± 10 min.

**RESULTS** (1) Immediately after exercise, participants in the MICE group had a significant reduction in the PWV level (12.5%, P<0.01). Forty min after exercise, PWV level in MICE group returned to the baseline. (2) The HIIE group demonstrated significantly decreased level of PWV (867.00±84.33 vs 972.50±93.05 cm/s, P<0.01) immediately after exercise. Forty min after exercise, participants in HIIE group still had a significant lower PWV level compared with the baseline (4.4%, P<0.01). (3) During recovery period, compared with CONT group, participants in HIIE and MICE groups had significant lower PWV level from 5 min to 25 min (P<0.05). There were no significant differences in PWV level between HIIE group and MICE group at all time.

**CONCLUSIONS** Both HIIE and MICE could reduce arterial stiffness and ameliorate vascular elasticity of recessive obese women with family history of hypertension which were beneficial to prevent hypertension and ASCVD in early life. It was suggested that HIIE may result in a greater stimulus for vascular adaptations when compared to MICE.

**GW33-e0103**

**Canagliflozin and atrial fibrillation in type 2 diabetes mellitus: a secondary analysis from the CANVAS program and CREDENCE trials and meta-analysis**

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**OBJECTIVES** The effect of sodium-glucose co-transporter 2 inhibitors on atrial fibrillation/flutter (AF/AFL) is unclear. We assessed the effects of canagliflozin on the incidence of AF/AFL and other key cardiorenal outcomes in a pooled analysis of the CANVAS and CREDENCE trials.

**METHODS** Participants with T2D and high risk of cardiovascular disease or chronic kidney disease participated in the CANVAS and CREDENCE trials and meta-analysis. The studies compared canagliflozin with placebo. The explored the effects of canagliflozin on the incidence of first AF/AFL events and AF/AFL related complications (ischemic stroke/transient ischemic attack/hospitalisation for heart failure), Major adverse cardiovascular events (MACE), and a renal-specific outcome by baseline AF/AFL status were analysed using Cox regression models.

**RESULTS** Overall 354 participants experienced a first AF/AFL event. Canagliflozin had no detectable effect on AF/AFL (HR 0.82; 95% CI, 0.67, 1.02) compared with placebo. Subgroup analysis, however, suggested a possible reduction in AF/AFL in those with no AF/AFL history (HR 0.78; 95% CI, 0.62, 0.96). Canagliflozin was also associated with a reduction in AF/AFL related complications (HR 0.74; 95% CI, 0.65, 0.86). There was no evidence of treatment heterogeneity by baseline AF/AFL history for other key cardiorenal outcomes (all P(interaction)=0.14). Meta-analysis of five SGLT2 inhibitor trials demonstrated a 19% reduction in AF/AFL events with active treatment (HR 0.81; 95% CI 0.72, 0.92).

**CONCLUSIONS** Overall, a significant effect of canagliflozin on the incidence of AF/AFL events could not be shown, however, a possible reduction in AF/AFL events in those with no prior history requires further investigation. Meta-analysis suggests SGLT2 inhibition reduces AF/AFL incidence.
indicators in young people improved after SIT for 2 to 4 weeks, but no changes were found after HIT. (4) For lipid profile, both acute SIT and HIIT reduced lipid levels at 24 h after exercise, but the effects of SIT and HIIT beyond 2 weeks or more on blood lipids are controversial and need further study.

CONCLUSIONS SIT and HIT are time-efficient and effective exercise modalities for improving CRF and cardiovascular risk factors (blood pressure, blood glucose, lipid profile) in young people who “lack the time” to exercise, while SIT is a more efficient alternative to HIT for those who can tolerate the intensity of SIT.

GW33-e0237
Effect of exercise and CRF improvement on CV risk in postmenopausal women
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OBJECTIVES Cardiovascular disease (CVD) is one of the major threats to the health of postmenopausal women. The decrease in cardiorespiratory fitness (CRF) may be related to the increased CVD risk caused by the reduction of estrogen levels. Exercise and physical activity (PA) can improve CRF and reduce the risk of CVD. Most of postmenopausal women have low CRF, lack of sufficient exercise time, and high-intensity exercise may expose them to adverse cardiovascular events. Therefore, it is very important to explore suitable exercise prescription for them. This study started from the level of PA, exercise intensity and type of exercise, trying to summarize and provide a reference for improving CRF and quality of life for them.

METHODS The literature method was used to retrieve relevant articles in databases such as PubMed and CNKI by computer. The search terms were: “postmenopausal women”, “cardiorespiratory fitness”, “cardiovascular risk”, “exercise” and “physical activities”. Articles related to CVD risk factors, exercise, PA level, and improvement of CRF were included; repeated studies and low correlation studies were excluded, and finally 38 articles with strong pertinence were selected for further analysis.

RESULTS (1) Obesity, hypertension, hyperlipidemia, type 2 diabetes, sedentary lifestyle and insufficient PA are the main cardiovascular risk factors in postmenopausal women. Among them, changing sedentary lifestyle and increasing PA levels are the key to intervene. Substituting low-intensity or moderate-intensity PA for sedentary time was associated with a significantly lower risk of death from CVD through the “isochronous substitution model”. (2) Compared with aerobic exercise alone, aerobic combined with resistance exercise can significantly reduce SBP, DBP, IAPP and HR, especially in overweight postmenopausal women over 60 years. In addition, SBP and DBP can be more effectively reduced when combined aerobic and resistance exercise frequency <3 times per week, total weekly exercise time ≥150 min, and exercise duration is 12 weeks. (3) Nordic walking (NW) at lipid metabolism intensity for 6 weeks significantly reduced body mass, body fat mass, resting BP, and HR, significantly increased VO2max in sedentary postmenopausal women, showing its effectiveness in improving CRF, body composition, and etc.

CONCLUSIONS Substituting PA for sedentary time, performing aerobic combined with resistance exercise and NW with lipid metabolism intensity can effectively improve CRF and cardiovascular function of postmenopausal women, and reduce the risk of CVD.

GW33-e0442
Chinese doctors’ awareness and practice on the medication adherence in hypertensive patients: a questionnaire-based study
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OBJECTIVES Medication adherence refers to the patient’s medication behavior, which is consistent with the doctor’s requirements. Poor medication compliance is one of the main influencing factors to achieve the goal of blood pressure. There are few studies about medication adherence in hypertensive patients in China, and most of the researchers focused on exploring the status and influencing factors of patients’ medication adherence such as gender, age, type of medications, number of medications, and so on, but seldom on doctors’ awareness and practice in this regard. We aimed to investigate the current situation and influencing factors of Chinese doctors’ awareness and practice on medication adherence in hypertensive patients.

METHODS We formulated a questionnaire and used an online platform to conduct a questionnaire survey on Chinese doctors. Through the analysis, we obtained an overall cognitive or practical score from 0 to 50 and explored the influencing factors of Chinese doctors’ awareness and practice on medication adherence through univariate analysis and multivariate analysis. Spearman correlation coefficient method was used to analyze the correlation between cognitive scores and practical scores.

RESULTS A total of 236 valid questionnaires were collected. The average cognitive scores of the total study population, 186 physicians and 122 cardiologists were 29.79±8.78, 31.04±8.43, and 34.25±7.29, respectively. The average practical scores of the total study population, 186 physicians and 122 cardiologists were 39.42±7.13, 40.46±6.16, and 41.55±6.01, respectively. Doctors with more professionalism, higher professional titles, and higher education tended to have better awareness and practice (P<0.05). And there was a significant correlation between doctors’ awareness and practice of medication adherence (R=0.682, P<0.000). Chinese doctors have many misunderstandings and deficiencies on awareness and practice of medication adherence.

CONCLUSIONS Chinese doctors have insufficient awareness and practice of medication compliance in hypertensive patients, related to doctor’s education, professional title, and major.

CARDIAC REHABILITATION

GW33-e0055
Effects of continuous management on anxiety and depression after pacemaker implantation: thoughts in the post-epidemic era
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OBJECTIVES Pacemaker implantation is the main treatment for bradycardia but perioperative anxiety and depression might affect the prognosis, especially in the post-pandemic era. There are few reports on the clinical application of continuous management mode. We investigated the effect of continuous management on postoperative mental improvement in patients with pacemaker implantation.

METHODS In this prospective, single-center, single-blind randomized clinical trial, a total of 140 patients with dual chamber permanent pacemaker implantation were included, and randomly divided into conventional management group (control group) and continuous management group (study group). The mental status were evaluated by self-rating depression scale (SDS) and self-rating anxiety scale (SAS) before the operation, 4 weeks and 12 weeks after the operation respectively.

RESULTS A total of 137 patients finished the whole follow-up, including 67 in the control group and 70 in the study group. Of these, 72 (52.6%) were female, and the mean age was 66.0 (IQR: 62.0–72.0) years. In terms of preoperative mental status, there were 87 (63.5%) cases with mild to moderate depression, while 63 (46.0%) with mild to moderate anxiety. Compared with the control group, among those in the study group, SDS standard scores of 55 (IQR: 47.2–59.0) before operation decreased to 45 (IQR: 38.0–50.0) at 4 weeks and 36.5 (IQR: 32.0–43.5) at 12 weeks after operation. Meanwhile, SAS standard score of 48 (IQR: 38.0–58.0) before operation decreased to 42 (IQR: 36.0–53.0) at 4 weeks and 36 (IQR: 31.0–40.0) at 12 weeks after operation. Additionally, at 4 weeks after operation, the SDS standard scores scored 8 (IQR: 4.2–13.0) points lower than baseline and the SAS standard scores scored 6 (IQR: 3.0–9.0) points lower in the study group. At 12 weeks after operation, the SDS standard scores scored 15 (IQR: 11.0–18.0) points lower than baseline and the SAS standard scores scored 13 (IQR: 9.0–26.0) points lower in the study group. Compared with the control group, the postoperative SDS and SAS standard scores decreased more significantly from baseline in the study group (all P<0.005).

CONCLUSIONS Anxiety and depression are common in patients with pacemaker implantation, which needs more attention especially in the post-epidemic era. The continuous management is a feasible and promising management mode, which is worth recommending in improving patients’ mental status after operation.

GW33-e0411
Study on current status and influencing factors of exercise adherence in home-based cardiac rehabilitation in patients with coronary artery disease
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OBJECTIVES Applying the theory of planned behavior to investigate the exercise adherence behavior and factors influencing home-based cardiac rehabilitation in patients with coronary artery disease.
METHODS From April 2021 to October 2021, 303 patients with coronary artery disease who visited and followed up at the Peking University Third Hospital were recruited by convenience sampling. The Physical Activity Rating Scale (PARS-3) was used to measure the physical activity level of patients. Patients’ adherence was evaluated by comparing it with the recommended physical activity level of guidelines. A questionnaire based on the theory of planned behavior with exercise planning and self-regulation added was used to investigate the factors influencing exercise adherence. Logistic regression was used to analyze the influence of each factor on exercise adherence.

RESULTS 36% (109/303) of patients had poor exercise adherence. Logistic regression analysis found that attitude (OR=6.271, 95% CI 2.055–13.773, P<0.05), subjective norm (OR=4.492, 95% CI 2.277–8.865, P<0.05), self-regulation (OR=1.678, 95% CI 1.778–7.606, P<0.05), and exercise planning (OR=1.280, 95% CI 1.026–3.821, P<0.05) had a statistically significant effect on promoting home exercise adherence.

CONCLUSIONS The overall exercise adherence of home-based cardiac rehabilitation needs to be improved in patients with coronary artery disease. Enhancing the attitude, subjective norm, exercise planning, and self-regulation of patients can promote home exercise adherence.

GW33-e0513 Effect of enhanced external counterpulsation therapy on left ventricular strains: a prospective cohort study
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OBJECTIVES Enhanced external counterpulsation (EECP) is currently a safe, effective treatment for coronary heart disease (CHD). However, its effect on cardiac systolic function has not been elucidated yet. Three-dimensional speckle tracking echocardiography (3D-STE) is more sensitive and comprehensive to evaluate cardiac function. However, there is currently no study to evaluate the effect of EECP on systolic function through 3D-STE. Here, we aimed to evaluate the effect of EECP on the cardiac systolic function through 3D-STE.

METHODS Totally, forty patients with CHD after incomplete revascularization (IR) participated in the study. Twenty subjects chose the treatment protocol of standard course of EECP combined with drug therapy (EECP group) and the other twenty chose drug therapy (control group). All subjects underwent 3D-STE, transthoracic echocardiography (TTE) examinations at baseline, after 18 hours of treatment (at 3–4 weeks of follow-up for control group) and 35 hours of treatment (at 7 weeks of follow-up for control group).

RESULTS After 35 hours of EECP treatment, the myocardial strain parameters, including twist (6.2 (3.9, 11.9) vs. 3.0 (1.4, 5.9), P=0.013) and torsion (1.2 (1.0, 1.9)/cm vs. 0.7 (0.6, 1.0)/cm, P=0.002) improved significantly, and were significantly better than those in the control group. There were no significant differences in any of the indicators from baseline at the 18-hour follow-up point.

CONCLUSIONS For patients with CHD after IR, the EECP can significantly increase twist and torsion values, suggesting that EECP can effectively improve cardiac systolic function in such patients, which might be helpful for clinical application of EECP.

GW33-e0551 Cardiac rehabilitation for heart failure with preserved ejection fraction exercise capability, ventilation efficiency, quality of life, systolic and diastolic function: a systematic review and meta-analysis
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OBJECTIVES Cardiac rehabilitation can significantly improve physical function and prognosis in heart failure with reduced ejection fraction (HFREF), but there is little evidence of its effect on heart failure with preserved ejection fraction (HFpEF). Therefore, this study conducted a meta-analysis on randomized controlled trial (RCT) to evaluate the effects of cardiac rehabilitation on the exercise capacity, ventilation efficiency, and quality of life, cardiac systolic and diastolic function of HFpEF.

METHODS Cochrane library, PubMed, Embase and Web of Science were searched for published RCT researches on cardiac rehabilitation on HFpEF, forming a database dating till May 2021. Based on inclusion and exclusion criteria, 566 patients were included in the meta-analysis.

RESULTS Compared with the control group, meta-analysis showed improvement in exercise capability after treatment in the cardiac rehabilitation group [6-minute walk distance (6MWD): weight mean difference (WMD): 35.42, 95% CI 12.34 to 58.50, P<0.003, I2=0%; peak oxygen uptake (peakVO2); WMD: 2.80, 95% CI 2.09 to 3.51, P<0.00001, I2=0%]. There was a statistically insignificant trend to improve anaerobic threshold oxygen uptake (VOAT): WMD: 1.93, 95% CI 0.66 to 3.20, P=0.003, I2=72%; exercise test duration: standard weight mean difference (SWMD): 0.62, 95% CI 0.34 to 0.91, P<0.0001, I2=0%, improvement in quality of life [Minnesota living heart failure questionnaire (MLHFQ)]; WMD: −11.76, 95% CI −16.64 to −6.88, P<0.0001, I2=0%, improvement in systolic function (left ventricular ejection fraction (LVEF)): WMD: −1.79, 95% CI −6.3 to 2.94, P=0.002, I2=47%, partial improvement in diastolic function [E/E’ ratio: WMD: −2.33, 95% CI −2.96 to −1.70, P<0.00001, I2=62%, while E/A ratio: WMD: −0.04, 95% CI −0.11 to 0.03, P=0.25, I2=19%], and no improvement in ventilation efficiency [minute ventilation to carbon dioxide production slope (VE/VO2)]: WMD: −1.12, 95% CI −2.74 to 0.50, P=0.18, I2=70%].

CONCLUSIONS Cardiac rehabilitation had a positive effect on HFpEF, improving exercise capability, quality of life and cardiac systolic function, but there was no evidence of its effect on diastolic function. As for the diastolic function, improvement was obvious in E/E’ ratio, while not in E/A ratio, thus entailing more relevant researches to assess the effect of cardiac rehabilitation on the diastolic function.

GW33-e0554 Ratio of minute ventilation to carbon dioxide production slope to peak oxygen uptake in the prognostic assessment of chronic heart failure patients with diabetes
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OBJECTIVES To analyze the value of the ratio of carbon dioxide ventilation equivalent slope to peak oxygen uptake (VE/VO2 slope/peakVO2) in predicting prognosis for chronic heart failure (CHF) patients with diabetes.

METHODS A total of 158 CHF patients with diabetes who visited the Cardiac Rehabilitation Center of Tongji Hospital Affiliated to Tongji University and completed cardiopulmonary exercise test from March 2007 to December 2018 were enrolled in the study. The clinical data, cardiopulmonary exercise test results and follow-up information of patients were collected to explore the predictors of all-cause mortality in CHF patients with diabetes.

RESULTS The median follow-up time was 394 (153–950) days. All-cause death occurred in 28 patients. Compared with the surviving patients, the peakVO2 of all-cause death patients were lower [12.95 (11.05–14.66) mL.min⁻¹.kg⁻¹ vs. 14.66 (12.90–16.40) mL.min⁻¹.kg⁻¹, P<0.001], the VE/VO2 slope [36.48 (34.65–44.80) vs. 34.70 (30.72–37.50), P=0.001] and VE/VO2 slope/peakVO2 ratio [3.01 (2.44–4.10) vs. 2.44 (1.80–3.01), P=0.001] were higher, and the proportion of digoxin [12 (42.9%) vs. 23 (17%), P=0.004], diuretic [19 (67.9%) vs. 49 (37.9%), P<0.001] and spironolactone [17 (60.7%) vs 45 (34.6%), P=0.01] were higher. The areas under the receiver operating characteristic curve (AUC) of VE/VO2 slope, peakVO2 and VE/VO2 slope/peakVO2 ratio in predicting all-cause mortality in CHF patients with diabetes were 0.697 (P=0.001), 0.682 (P=0.003) and 0.711 (P=0.001) respectively; the optimal thresholds were >34.10 (HR=3.50, 95% CI 1.21 to 10.16, P=0.021), >13.55 mL.min⁻¹.kg⁻¹ (HR=0.39, 95% CI 0.18 to 0.87, P=0.021) and >2.79 min.kg⁻¹ (HR=2.37, 95% CI 1.10 to 5.08, P=0.027) respectively; the sensitivities were 0.857, 0.679 and 0.607, and the specificity were 0.485, 0.631 and 0.715, respectively. Multivariate Cox regression analysis showed that after adjusting related risk factors, VE/VO2 slope/peakVO2 ratio was independent risk factor for all-cause mortality in CHF patients with diabetes (HR=3.21, 95% CI 1.38 to 7.45, P=0.007).

CONCLUSIONS VE/VO2 slope/peakVO2 ratio could provide a predictive value for all-cause mortality of CHF patients with diabetes.
GW33-e0063
A meta-analysis comparing different oral anticoagulation for the treatment of ventricular thrombus
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OBJECTIVES Patients with ventricular thrombus (VT) often require anticoagulation therapy and it remains unknown that whether non-vitamin K antagonists (NOACs) or vitamin K antagonists (VKAs) is more effective. We aimed to compare the effectiveness and safety of NOACs and VKAs on the rate of thrombus resolution and clinical outcomes.

METHODS MEDLINE, PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure Database and Wanfang Database, were searched up to November 22, 2021. Observational studies comparing the two agents in patients with VT were included. The primary outcome was the rate of thrombus resolution, and the secondary outcomes were bleeding, systemic embolism, stroke and all-cause death. Odds ratio (OR) and 95% confidence intervals (CI) were used for the pooled results.

RESULTS Eighteen studies with 1755 participants (NOACs, n=607; VKAs, n=1148) were included. NOACs compared to VKAs had no significant difference in thrombus resolution (OR 0.92, 95% CI 0.68–1.23, P=0.558, I²=0%), bleeding (OR 0.85, 95% CI 0.54–1.35, P=0.496), systemic embolism (OR 0.77, 95% CI 0.41–1.43, P=0.401), stroke (OR 0.65, 95% CI 0.29–1.49, P=0.312) and all-cause death (OR 1.02, 95% CI 0.65–1.67, P=0.925). Subgroup analyses showed an insignificance in thrombus resolution between NOACs and VKAs according to baseline characteristics.

CONCLUSIONS Our findings showed that NOACs were comparable to VKAs in thrombus resolution, as well as systemic embolism, stroke, bleeding events and all-cause death. And in different proportion of baseline LVEF, history of ischemic cardiomyopathy and combination with antiplatelet agents, the thrombus resolution among the two groups remained similar.

GW33-e0109
Discovery of novel desmoplakin mutations in caravajal syndrome: two case reports and literature review
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OBJECTIVES Caravajal syndrome (CS) is an autosomal dominant (AD) or autosomal recessive (AR) genetic cardiocutaneous syndrome that associates with mutations in desmoplakin (DSP) gene and characterized by woolly hair, palmoplantar keratoderma (PPK) as well as left ventricular dilated cardiomyopathy (DCM).

METHODS In this report, whole exome sequencing (WES) was conducted to examine the mutations of patients and the Sanger sequencing was applied to identify suspicious variants in their parents.

RESULTS A 7 years old female patient was admitted to our center due to heart failure. She had curvy hair at birth, developed palmoplantar keratosis at the age of 4 years, and heart failure at the age of 6 years. WES result suggested she carried a novel homozygous variant c.4597C>T(p.H618P) in DSP gene, whereas her parents carried the same variant in heterozygous state. Patient 2 presented with similar symptoms and carried a de novo heterozygous variants c.1853A>C(p.H618P) in DSP gene.

CONCLUSIONS This report extended the spectrum of CS associated DSP gene mutations and provided important clinical references.

GW33-e0251
Predictive value of visceral fat-related and lipid-related indicators for metabolic syndrome in a Chinese population over 60 years of age: a cross-sectional study
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OBJECTIVES To explore the predictive power of metabolic syndrome (Mes) for lipid-related parameters, including visceral adiposity index (VAI), lipid accumulation product (LAP), ambulatory arterial stiffness index (AAI), plasma arteriosclerosis (AI), plasma arteriosclerotic index (API), and lipid composite index (LCI) in identifying Mes in the Chinese population over 60 years old.

METHODS A total of 10,588 elderly Chinese subjects (aged ≥60 years) were enrolled in the community-based cross-sectional study from January 2018 to December 2020. Gender, age, height, body mass index and waist circumference were measured, serum samples were retained, and relevant metabolic indicators such as blood glucose and lipid levels were measured.

RESULTS All seven parameters had a predictive value in identifying Mes based on the subject receiver operating characteristic curve (ROC) analysis. The statistical significance of the differences in the area under the curve (AUC) indicated that the AUC for LAP was the largest in both sexes (0.881 in men and 0.887 in women). The optimal critical value of LAP was 38.44 in men and 43.00 in women.

CONCLUSIONS Visceral fat-related and lipid-related indicators in people over 60 years old have a predictive value for metabolic syndrome, and the predictive value of LAP is higher than that of VAI, TC/HDL-C, non-HDL-C, A1P, and LCI by sex.

GW33-e0378
Impairment of left ventricular function in the depressed Chinese miniaturized mouse model by cardiovascular magnetic resonance feature-tracking
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2Siemens Shenzhen Magnetic Resonance, MR Collaboration NE Asia

OBJECTIVES Depression increases the risk of cardiovascular disease and an independent predictor of worse cardiovascular outcomes. Few studies have examined the relationship between depression and left ventricular (LV) alterations using cardiovascular magnetic resonance feature-tracking (CMR-FT). So, the aim of this study was to investigate the effect of depression on LV systolic function by CMR-FT.

METHODS Seven anesthetized, healthy Chinese Miniature mice were completed basic data and CMR scan baseline and after 14 days of depression modeling. The behavioral tests, including open-Field Test (OFT), sucrose Preference Test (SPT), the time to intake a certain amount of food and sugar was carried out to test the depression models. CMR cine images were acquired and CVI software was utilized to analyze global longitudinal strain (GLS), global circumferential strain (GCS) and global radial strain (GRS). Besides, late gadolinium enhancement (LGE) imaging detected myocardial infarction and/or scar.

RESULTS The decrease of Open-Field Test, sucrose Preference Test, extension of time to intake a certain amount of food and sugar compared with baseline indicated a successful modeling of depressed swine. There was no statistical trend in GRS (25.35±14.78 vs 22.86±16.71, P=0.043), GLS (17.66±6.9% vs 22.3%±12.3%, P=0.256) and GRS. GRS were significantly reduced after modeling compared with baseline.

CONCLUSIONS Depression has a tendency to lead to LV early systolic dysfunction in special LV global circumferential strain and global radial strain.
GW33-e0620
Characterization of an aging-based diagnostic gene signature and molecular subtypes with diverse immune infiltrations in HF
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OBJECTIVES Aging is a major risk factor for heart failure (HF). At present, the relationship between aging and heart failure is not completely clear. There is an urgent need to explore new diagnostic biomarkers, as well as molecular subtypes and therapeutic targets.

METHODS Gene expression data of HF and normal samples were collected from GEO database. Differential expression analysis was used to screen for HF-specific aging-related genes. Logistic regression analysis was proposed to construct a diagnostic model and ROC curves were used to assess the discriminatory ability. Consensus cluster analysis was used to classify the molecular subtypes based on aging. Immunity levels were estimated based on immune cell infiltration, immune checkpoints, and immune reaction gene-set. Aging molecular phenotype-relevant genes were then identified by Weighted gene co-expression network (WGCNA). The Connectivity Map (CMAP) database were used to predict small-molecule drugs.

RESULTS We obtained six HF-specific aging-related genes based on differentially expressed genes between HF and normal samples. In addition, we identified 2 distinct subtypes of HF characterized by markedly different immune infiltration. A yellow-green module containing 321 genes that were highly correlated with the subtypes in WGCNA was subsequently identified. On the basis of the differentially expressed genes between HF and normal samples, we used the CMAP database to explore small molecule drugs that could be used as therapeutic agents.

CONCLUSIONS Our study evaluated different immune cell infiltrations in HF and normal samples and identified different aging-related subtypes, which provide more individualized treatment options and prognostic predictions for HF patients. Small molecule drugs were discovered that may be potentially useful in treating patients with HF.

GW33-e0635
Relationship of altmetric metrics to science communication for high-impact clinical and cardiovascular publications: the era of social media
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OBJECTIVES The relationship between science communication on social media and impact on citation is controversial. The Altmetric attention score (AAS) is a qualitative metric that is complementary to traditional metrics, such as impact factors or citation counts. We would explore the association between AAS and traditional bibliometric metrics among high-impact clinical and cardiovascular publications in 2018.

METHODS The most-cited articles published in the top 10 highest Web of Science (WOS) Impact Factor journals (according to Journal Citation Reports 2020: category “Medicine, General & Internal” and “Cardiac & Cardiovascular systems”) in 2018 were included. The 3-year citations, AAS, and associated social media impact for each article were collected using WOS and AAS calculator. Descriptive statistics and Spearman rank correlation analyses were determined using the SPSS software. Bibliometric data from total articles were analyzed using the VOS viewer.

RESULTS A total of 100 articles were published in this study period, including 34 (34%) original research, 31 (31%) reviews, and 23 (23%) guidelines or scientific statements. AAS (r=0.353, P<0.01) and Tweets (r=0.305, P<0.01) were significantly positively correlated with citation number. News outlets, Twitter, and blogs were the most weighted variables correlated with AAS. Research hot keywords focused on myocardial infarction, guidelines/scientific statements, sudden cardiac death, hypertension, and open-label/randomized controlled

CONCLUSIONS Results of this cross-sectional study showed moderate correlation between AAS and citation rates. Further science dissemination strategy on social media and online platform may beneficial for impact and citations.

GW33-e0770
Analysis of differentially expressed genes between paroxysmal and persistent atrial fibrillation
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OBJECTIVES Comparative studies of differentially expressed genes (DEGs) between paroxysmal and persistent atrial fibrillation (PAF and PsAF) patients are scarce. This study aimed to analyze the differentially expressed long non-coding RNAs and messenger RNAs (DELncRNAs and DEMRNAs) in PAF and PsAF patients and explored the novel AF-related molecular mechanisms.

METHODS Two target datasets about paroxysmal and persistent atrial fibrillation patients (GSE75092 and GSE113013) were downloaded and further analyzed from the Gene Expression Omnibus database by R software. Upregulated and downregulated differentially expressed genes (DEGs) and the co-expressed differentially expressed genes (co-DEGs) of the two datasets were identified, of which enrichment analyses and protein-protein interaction network construction were performed.

RESULTS A total of 127 DELncRNAs and 321 DEMRNAs were screened in GSE75092; while 46 DELncRNAs and 64 DEMRNAs were screened in GSE113013. We further identified 8 co-DEGs in the overlap between the two datasets on Venn Diagram, which comprised 3 LncRNAs and 5 mRNAs. The GO analysis of GSE75092-DEGs showed that the top 5 biological processes were mainly enriched in response to virus (P<0.001), defense response to virus (P<0.001), nuclear transport (P=0.004) and nucleocytoplasmic transport (P=0.009). The cellular component category was mainly enriched in focal adhesion (P=0.042) and cell-substrate junction (P=0.042). The GO analysis of GSE113013-DEGs showed that no significant functions were enriched in any category. And two identical pathways, influenza A and adrenergic signaling in cardiomyocytes, were found in the KEGG analysis of the DEGs between the two datasets. In addition, the protein-protein interaction network of DEGs was constructed while no common hub genes were found between the PPI modules of the two datasets.

CONCLUSIONS Multiple DEGs were found in patients with either paroxysmal or persistent AF, and their functions were mainly enriched in metabolism and inflammation-related signaling pathways. The antiviral defense mechanism of PAF was an exciting difference we found.
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