Translational Cardiovascular Imaging: A New Integrated Approach to Target Myocardial Fibrosis Turnover in Different Forms of Cardiac Remodeling

Dear Sir,

In the last decade, despite the consistent refinement of the single imaging modalities, the evaluation of patients with major cardiac pathologies has become increasingly multimodal, aiming at an integrated output. Echocardiography has been recently characterized by some relevant technological developments (i.e., three-dimensional [3D] acquisitions and myocardial deformation imaging) that have consistently increased its diagnostic capabilities and fields of application. However, despite these improvements, even novel echocardiographic techniques may not directly assess the ultrastructural characteristics of the cardiac muscle.

Myocardial fibrosis (MF) is the common end-point of different cardiac pathologies, determining both diastolic and systolic left ventricular (LV) dysfunction and, ultimately, the progression toward congestive heart failure.\textsuperscript{[1,2]} However, despite being one of the main actors of any cardiac remodeling process, some intrinsic characteristics of MF deposition can typically differentiate the etiology of the underlying cardiac pathology. Accordingly, while macroscopic “substitutive fibrosis” is the hallmark of ischemic scar, the deposition of a diffuse interstitial and/or perivascular fibrosis generally takes places in nonischemic settings, such as cardiomyopathies, hypertensive, and diabetic heart disease as well as valvular heart diseases (reactive fibrosis).

Interestingly, while most of the above pathophysiological models are characterized by the deposition of MF, there are different mechanisms that regulate the turnover of myocardial extracellular matrix (ECM) and, ultimately, MF accumulation. For instance, some bioactive molecules have a profibrotic action (i.e., norepinephrine, angiotensin II, endothelin-1, and aldosterone) and other have an antifibrotic action (natriuretic peptides, nitric oxide). Other important molecules contribute to regulate ECM: Transforming growth factor-\(\beta\)1 (LV hypertrophy), insulin-like growth factor 1 (adaptive remodeling), and matrix metalloproteinases (maladaptive remodeling). The latter constantly degraded ECM proteins, predisposing to LV dilatation and systolic heart failure. According to these mechanisms, adequate ECM metabolism is determined by the subtle equilibrium between many bioactive molecules – profibrotic versus antifibrotic – that ultimately regulate the formation of MF. An inadequate ECM metabolism could determine collagen accumulation and relative increase of the stiffness of the heart (when profibrotic factors prevail) or, on the other hand, progressive collagen degradation with a progressive dilation of the heart (when antifibrotic factors are more active). In the first case, diastolic dysfunction usually takes place while in the second scenario, LV systolic dysfunction typically occurs.

In particular, modern conventional cardiac imaging techniques (i.e., backscatter, speckle tracking, and 3D-imaging at echocardiography as well as late gadolinium enhancement and T1/T2 mapping at cardiac magnetic resonance [CMR]) allow an in-depth evaluation of LV structure and function, theoretically offering the chance of an early diagnosis of subclinical stages of cardiac remodeling. However, the depiction of such a complex process represented by cardiac remodeling through conventional cardiovascular imaging techniques alone appears rather reductive.

Novel soluble biomarkers have been recently proposed to monitor MF deposition and, in general, adverse LV remodeling. Among those, some molecules have shown an ability not only in detecting MF but also as relevant prognosticators in different cardiac pathologies: “pro-collagen type 1”; the ratio between matrix metalloproteinase and tissue inhibitors of metalloproteinase; some types of noncoding microRNAs and soluble ST2.

Fully agreeing with a recent State of Art Paper, dealing with hot issues about the future of imaging and developing a roadmap to address critical challenges,\textsuperscript{[3]} we propose “translational cardiovascular imaging” as a new approach for the evaluation of cardiac remodeling processes: A comprehensive evaluation of cardiac structure and function through innovative imaging techniques (i.e., 3D-echocardiography and speckle tracking as well as \textit{in vivo} tissue characterization by CMR) together with the assessment of some specific biomarkers of cardiac remodeling. The objective is the redefinition of the role of cardiovascular imaging, oriented to an integrated (imaging and biohumoral) approach for a better assessment of cardiac pathophysiology, hopefully helping with risk stratification and clinical management. The ultimate cost-benefit ratio of this integrated approach should be carefully assessed in clinical studies; however, it is easily derivable that, thanks to their wide availability and relatively low cost, the integration of echocardiography and biomarkers represents an attractive choice.
In conclusion, a proper characterization of any form of cardiac remodeling process should integrate the standard evaluation of LV structure and function (easily obtained by echocardiography) with the evaluation of MF burden (promisingly by specific biomarkers).[4]

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Vitantonio Di Bello, Nicola Riccardo Pugliese, Riccardo Liga, Valentina Barletta, Veronica Santini, Lorenzo Conte, Iacopo Fabiani
Department of Surgery, Medical, Molecular, and Critical Area Pathology, Pisa University, Pisa, Italy

Address for correspondence:
Prof. Vitantonio Di Bello,
S. D. CardioAngiologia, Via Paradisa,
2 – Ospedale Cisanello, 56124 Pisa, Italy.
E-Mail: vitantonio.dibello@med.unipi.it

REFERENCES

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.