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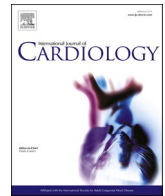
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Editorial

State of energy of ventricular flow: A cause or the first indicator of adverse remodeling?

Ventricular remodeling is characterized as a set of molecular, cellular, and interstitial changes that occur in the heart in response to a disease or insult, which clinically manifest as changes in size, mass, anatomy, and function of the heart. Overall remodeling is the culmination of a multifaceted series of transcriptional, signaling, structural, electrophysiological, and functional events occurring within the cardiac tissue. These proceedings could result in short-term benefit, but like any inflammatory processes if they remain persistent, they turn into maladaptive or adverse remodeling, and predispose to cardiovascular morbidity and mortality. Ventricular remodeling often begins as minor degradations of the heart function, which may be difficult to detect, then progressively develops, and eventually leads to full manifestations of heart failure [1]. Identifying the primary changes that triggers the sequence of events leading to remodeling is of paramount importance to establish physics-based predictive models in cardiology.

In recent years, numerous studies have highlighted the significance of ventricular blood flow dynamics to gain a deeper understanding of cardiac function [2]. Indeed, ventricular contraction's ultimate purpose is to generate and sustain pulsatile blood flow while avoid overpressure and turbulence. These phenomena mechanistically involve an interplay between kinetic energy (KE, proportional to the square of blood velocity), potential energy (proportional to pressure gradients) and work performed by the myocardium. This sequence of events is achieved through the reciprocal forces exchanged between blood and surrounding tissues. To make the picture more complex, intraventricular pulsatile blood flow forms vortices, peculiar flow features that can either preserve kinetic energy into a rotatory movement or dissipate kinetic energy by becoming unstable and transforming into turbulence. As such, identification of parameters that signify changes in the blood flow dynamics and energetics is crucial to predict the risk of future remodeling.

The last two decades have seen important advancements in imaging technologies that allow describing the mechanical cardiac function in unprecedented depth. Deformation imaging and strain analysis represent the most recent successful approach to study ventricular contraction and relaxation. Alternatively, phase-contrast magnetic resonance and echocardiography promise a further step to explore the intimate mechanical function of the cardiovascular system through characterizing intraventricular blood flow characteristics [3]. On that basis, a number of studies began to suggest a number of indicators related to blood flow that can be associated with adverse remodeling or maladaptive response to sub-clinical changes [4]. A possible relationship between blood flow and longer-term outcome can be considered after STEMI (ST-elevated myocardial infarction) where identification of

predictors of adverse left ventricular (LV) remodeling could improve the clinical management of such patients. Existing literature indicates infarct size as a prognostic indicator of clinical outcome [5]. However, the association between the infarct size and adverse LV remodeling is not consistently predictive and additional information must be considered to improve risk stratification and monitoring of such patients. A recent study analyzed the incidence of adverse LV remodeling in STEMI patients with reperfused segments and found that it was associated with alterations in intra-LV pressure gradients during diastole [6].

In the current issue of the IJC, Demirkiran et al. [7] analyzed the energetic characteristics of the diastolic blood flow in STEMI patients using 4D Flow MRI. They report initial evidence that changes in the LV blood flow KE are inversely associated with adverse LV remodeling. In particular, they found that the LV KE during late-diastole post-acute myocardial infarction is independently associated with adverse LV-remodeling and is a predictor of superior performance compared to infarct size. Although the reported results should be cautiously considered only as preliminary and non-conclusive mainly because the correlation coefficient between A-wave's KE index and volumetric remodeling is too low [7], this study provides additional evidence supporting the fact that changes in blood flow anticipate LV remodeling. However, the exact nature of such changes has yet to be learned.

The delicate process of remodeling can lead to perturbations in the ventricular blood flow. Nature optimizes the ventricular blood flow momentum and energy transfer through the heart via propulsion and vortex formation; any changes in the composition and function of the heart may lead to deviation of optimal flow energetics and momentum transfer within the heart [8]. In healthy hearts, the transmitral vortex helps effective transfer of the blood flow momentum and energy and minimizes the stroke work [9]. If adverse remodeling affects any of the above, diastolic vortex flow is disturbed, which can drastically dissipate flow kinetic energy across the right or left heart. Changes in left or right ventricular structure and function affecting diastolic vortex formation ultimately would lead to higher or lower ventricular total energy, where a higher percentage of it is dissipated due to the formation of small incoherent flow structures (turbulence).

Changes in ventricular pressure due to remodeling is directly associated with an imbalance in the ventricular state of energy. This include ventricular flow kinetic energy and myocardial work, defined as the product of pressure and volumetric change. The state of energy reflects both vortex formation, which influences ventricular fluid dynamics and energy dissipation, and optimal pressure gradients that propel intraventricular blood flow [10]. When the blood flow becomes abnormal in

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one or more of such aspects, ventricular compensation develops, which often leads to a vicious cycle where ventricular dilatation and loss of contractility negatively affect the ventricular state of energy and ultimately progresses toward adverse remodeling. Identifying early changes in heart function that are associated with the events leading to remodeling is still an unresolved challenge.

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