Editorial

The Right Ventricle Revisited

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William Harvey was the first to describe the physiology of the pulmonary circulation in 1616. Over the following four centuries, however, little emphasis was placed on the right ventricle (RV) and its role in the pathophysiology of heart disease. It was only in the past two decades that we began to witness an increase in the attention paid by researchers and clinicians to the right heart chambers. This interest has been paralleled by the evolution of invasive and noninvasive cardiac imaging methods that have improved our understanding of the anatomy, physiology and pathophysiology of the right heart and pulmonary circulation in both congenital and acquired heart disease.

The RV has a more complex shape than the left ventricle (LV), appearing triangular when viewed from the side and semilunar (crescentic) when viewed in cross section; its three-dimensional shape is more complex, unlike the ellipsoid shape of the LV.[1] The RV myocardium is thinner than the left, and the RV has approximately one sixth of the LV mass with an almost similar (slightly higher) end-diastolic volume, a fact which reflects the low resistance in the pulmonary circulation.[1] Compared to the LV, the less muscular RV is more sensitive to afterload alterations, which depend mostly on pulmonary vascular resistance.[2,3] In the normal heart, an increased RV preload improves myocardial contraction on the basis of the Frank–Starling law. However, excessive and prolonged RV volume overload reduces RV contractility and suppresses LV filling, ultimately leading to impaired global heart function.[3]

Ventricular interdependence, indicating that the size, shape, and compliance of one ventricle affects the hemodynamic properties of the other,[4] plays an essential part in the pathophysiology of RV dysfunction. Systolic ventricular interdependence is mediated mainly through the interventricular septum, while the pericardium contributes more to diastolic ventricular interdependence. In acute RV pressure- or volume-overload states, dilatation of the RV increases intrapericardial pressure and shifts the interventricular septum to the left, altering LV geometry. As a consequence, the LV diastolic pressure–volume curve shifts upward, leading to a decreased LV preload, increased LV end-diastolic pressure and consequently low cardiac output.[4]

Right heart failure is becoming increasingly frequent as the prevalence of predisposing conditions in the population increases. In the majority of cases, RV function is compromised as a result of pressure overload, volume overload, or a combination of both. Impaired RV contractility due to primary loss of RV myocardium may also underlie right heart failure; however, conditions specifically leading to RV myocardial damage are, with the exception of ischemia, rare and gen-

erally not confined to the right heart. Notably, up to 25% of critically ill patients with acute lung injury and up to 50% of those with sepsis may develop acute right heart failure in the intensive care unit as a result of multiple mechanisms.[5]

Acute pulmonary embolism (PE) is the prototype of RV failure due to acute pressure overload.[6] Increased pulmonary artery pressure occurs in up to 60-70% of patients who have acute PE and roughly correlates with the anatomic severity of thromboembolic obstruction; in addition, vasoconstrictive agents released from the thrombus and reaction to hypoxia contribute to the increase in pulmonary vascular resistance. Preexisting cardiac or pulmonary disease may enhance the hemodynamic impact of an acute thromboembolic event. RV dilatation and hypokinesis result from the interplay of these factors and may initiate a vicious circle of increased myocardial oxygen demand, myocardial ischemia or infarction, and left ventricular preload reduction. Ultimately, the inability to maintain the cardiac index and arterial pressure leads to cardiogenic shock. Thus, RV dysfunction is the critical hemodynamic event and an important determinant of the clinical presentation, course and prognosis of PE.

The pathophysiology of chronic pressure overload, which may lead to repeated episodes of acute decompensation, has been thoroughly studied in the setting of pulmonary arterial hypertension.[7,8] The increase in ventricular mass induced by an increase in afterload is predominantly the result of protein synthesis and an increase in cell size through the addition of sarcomeres in parallel. However, the RV is not capable of sustaining pressure overload over the long term. Cardiac contractile force decreases, probably due to functional and/or structural changes in cardiomyocytes. In fact, pressure-induced growth and proliferation of cardiomyocytes is accompanied by extracellular matrix synthesis, which influences diastolic and systolic function as well as ventricular morphology and provides the background for electrical instability.[9,10] The RV thus enters a vicious circle of increased wall tension, mismatch in myocardial oxygen demand and RV perfusion, leading to further impairment of contractility and dilatation. Maladaptive neurohormonal signaling, oxidative stress, and inflammation may further contribute to the development of RV failure.

Adult congenital heart disease and acquired valvular heart disease may place substantial volume loads on the RV. Such conditions include atrial septal defect, pulmonary artery regurgitation and tricuspid regurgitation. Eccentric hypertrophy is the initial adaptive response of the heart to volume overload. Prolonged hypertrophy becomes detrimental, resulting in cardiac dysfunction and heart failure via mechanisms similar to those operating under pressure overload. Overall, the RV tolerates volume overload better than pressure overload and may therefore stay well adapted for extended periods of time. For example, in volume overload associated with left-to-right shunt, the condition may remain relatively asymptomatic until pulmonary vasculopathy develops and the shunt reverses. In fact, even with established Eisenmenger's pathophysiology, the outcome of these patients is better than that of patients with idiopathic pulmonary arterial hypertension.[11]

Echocardiography remains the most widely used modality for the assessment of RV size and function in clinical practice. As the complex structure of the RV does not allow geometrical assumptions on echocardiography, chamber diameters and areas are used as surrogate parameters in the echocardiographic assessment of RV size.[12] Established and emerging tools used for the semi-quantitative assessment of global and regional RV function include the tricuspid annular plane systolic excursion (TAPSE), tissue (pulsed and color) Doppler imaging (TDI), and strain and strain rate (Doppler-based and speckle tracking-based) myocardial deformation imaging.[13-15] Three-dimensional echocardiography may facilitate the study of RV morphology and function, overcoming the complexity of the RV shape.[16] The high accuracy and reproducibility of magnetic resonance imaging (MRI) measurements, without the need for geometrical assumptions, has made cardiac MRI the current gold standard for the study of RV size and function.[17] Using magnetic resonance angiography, a detailed 3-dimensional pulmonary angiogram can be obtained with injection of gadolinium in a peripheral vein, allowing global assessment of the pulmonary circulation.

In summary, advances in imaging modalities have recently enabled us to accurately study RV physiology in health and disease. It has become apparent that the function of the RV strongly affects the function of the LV, and *vice versa*. Although the improvement in our knowledge of RV physiology has yet to result in specific advances in the clinical management of RV failure, it has become evident that RV function is an important determinant of prognosis in heart failure, irrespective of the etiological background. Therefore,

RV function has to be considered as an important variable in therapeutic decision-making and should also be assessed as a marker of response to treatment in patients with heart failure.

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