The Right Heart-Pulmonary Circulation Unit
Physiopathology

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KEYWORDS

• Right heart failure • Pulmonary hypertension • Right ventricular function adaptation
• Reduced ejection fraction • Right heart pulmonary circulation

KEY POINTS

- The most common cause of right heart failure is increased afterload caused by pulmonary hypertension.
- Right ventricular function adaptation to increased afterload is basically systolic, with secondary increase in dimensions and systemic congestion.
- Increased right ventricular dimensions and decreased ejection fraction are associated with a decreased survival in severe pulmonary hypertension.
- Targeted therapies titrated to reverse the right ventricular remodeling dimensions improve survival in severe pulmonary hypertension.

INTRODUCTION: THE (IN)DISPENSABLE RIGHT VENTRICLE

Evolution from poikilothermic ancestors of fishes to amphibians and reptiles to endothermic birds and mammals has gone along with a progressively greater oxygen consumption per unit of body weight, requiring a thinner pulmonary blood gas barrier. Preservation of the integrity of this barrier has been made possible by the complete separation of a high-flow/low-pressure pulmonary circulation with reshaping of the right ventricle (RV) as a thin-walled and crescent-shape volume generator.[1] Because there is a systemic venous return pressure gradient propelling blood flow back to the right heart and the pulmonary circulation, one could have wondered to what extent the RV as a volume pump then still contributes to the filling of the left heart.

This question was addressed by Starr and colleagues[2] who in 1943 reported that the ablation of the RV free wall in dogs by cauterization and

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ligation of the right coronary artery did not affect the systemic venous pressure. Subsequent studies showed that animals with a surgically removed RV free wall could lead a normal sedentary life and even enjoy moderate levels of exercise.[3] The notion of a "dispensable" RV inspired the introduction by Fontan and Baudet of a cavopulmonary anastomosis as a palliative intervention for single ventricle congenital heart disease in 1971.[4] We now know that patients with the so-called Fontan circulation may remain clinically stable for decades, but cannot tolerate strenuous exercise and may rapidly deteriorate in case of an increase in pulmonary artery pressure (PAP), for example, when exposed to high altitudes or when the left heart fails.[5]

In the absence of the RV, venous return to the left heart is driven entirely by mean systemic filling pressure, which is normally around 10 mm Hg.[6] The driving pressure for systemic venous return is the difference between systemic filling pressure and a right atrial pressure, which is ideally equal to zero with respect to atmospheric pressure. As long as venous resistance is very low, this small driving pressure propels the entire cardiac output (CO) to the right heart, and in case of a Fontan circulation, through the pulmonary circulation to the left heart. Only slight increases in systemic filling pressure with some fluid retention and sympathetic nervous activation may suffice to ensure sufficient preloading of the LV during moderate exercise. Exercise capacity in young patients with Fontan physiology is actually subnormal, with the stroke volume (SV) reserve being almost exclusively responsible of a 30% to 40% decrease in maximum oxygen uptake as compared with healthy controls.[7] This gives a measure of the contribution of RV ventricular pump function to maximum CO.

HOW THE RIGHT VENTRICLE ADAPTS TO INCREASED AFTERLOAD

Despite its particular structure and usual function as a low-pressure flow generator, the RV has the capacity to adapt its contractile function to increased afterload. A "homeometric" or systolic functional adaptation (ie, Anrep's law of the heart) is turned on as soon as within minutes of an increase in the PAP. Initially, there is also a minor heterometric (or dimensional) adaptation (ie, Starling's law of the heart) to preserve flow output that becomes the predominant adaptation when the homeometric adaptation cannot be maintained. Insufficient contractility, or systolic function adaptation, limits maximum CO and decrease aerobic exercise capacity. Dilatation with eventual diastolic dysfunction causes systemic congestion.[8] Dilatation of the RV is accompanied by a septal shift, which alters left ventricular (LV) filling with eventual atrophic remodeling and depressed systolic function of the LV.[9] Decreased LV diastolic compliance and underfilling contributes to RV dysfunction-related decrease in maximum CO and a diminished maximum oxygen uptake. Depressed LV systolic function has a direct negative effect on RV contractility and may contribute, therefore, to RV failure symptomatology.[9]

Increased afterload imposed on the RV is accompanied by regional myocardial contraction inhomogeneity, or dyssynchrony and delayed systole such that the RV is still ejecting blood while the LV is filling, also described as postsystolic shortening or asynchrony. Ventricular dyssynchrony and asynchrony have additional negative effect RV systolic function and combine with the mechanical effect of septal shift to further alter ventricular interdependence.[9]

By far, the most common cause of RV failure is increased afterload in pulmonary hypertension (PH). In fact, it has been better realized in recent years that the symptomatology and the prognosis of PH are essentially determined by RV function adaptation to afterload.[8] Early stage RV failure in PH is characterized by a decreased maximum CO, which results in a decreased maximum oxygen uptake or maximum average running or walking speed, or decreased running or walking distance in a given amount of time. Progression of RV failure in PH is associated with the dilatation of right heart chambers and results in further impairment of exercise capacity now accompanied by signs of systemic congestion. Because a limitation of maximum CO may be symptomatic only during exercise, but then confused with shortness of breath and fatigue in deconditioned patients, and because systemic congestion is a late occurrence, comprehensive assessment of the RV in PH requires not only a clinical examination and exercise testing, but also echocardiographic examination or MRI and right heart catheterization measurements.

A right heart catheterization allows for only limited description of RV function, including right atrial pressure to estimate the RV end-diastolic volume (EDV), or preload, PAP, or pulmonary vascular resistance (PVR) to estimate afterload, and SV to reflect contractility. Imaging offers more. By far, the most commonly used techniques are echocardiography and cardiac magnetic resonance. Both imaging modalities provide accurate though imprecise indirect estimates of PAP, left atrial pressure and CO, and derived calculations of PVR and pulmonary arterial compliance (PAC).[10] More important, both echocardiography