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REVIEW

Advancing knowledge of right ventricular pathophysiology in chronic pressure overload: Insights from experimental studies

Physiopathologie du ventricule droit dans la surcharge de pression chronique : données expérimentales récentes

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Summary The right ventricle (RV) has to face major changes in loading conditions due to cardiovascular diseases and pulmonary vascular disorders. Clinical experience supports evidence that the RV better compensates for volume than for pressure overload, and for chronic than for acute changes. For a long time, right ventricular (RV) pathophysiology has been restricted to patterns extrapolated from left heart studies. However, the two ventricles are anatomically, haemodynamically and functionally distinct. RV metabolic properties may also result in

Abbreviations: AT, angiotensin; Ea, arterial elastance; Ees, end-systolic elastance; IVA, acceleration of the myocardium during isovolumic contraction; LV, left ventricle/ventricular; MHC, myosin heavy chain; PA, pulmonary arterial; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RAAS, renin-angiotensin-aldosterone system; RV, right ventricle/ventricular; RVF, right ventricular failure; RVFAC, right ventricular fractional area change; RVMPI, right ventricular myocardial performance index; SVI, stroke volume index; TAPSE, tricuspid annular plane systolic excursion.

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a different behaviour in response to pathological conditions compared with the left ventricle. In this review, current knowledge of RV pathophysiology is reported in the setting of chronic pressure overload, including recent experimental findings and emerging concepts. After a time-varying compensated period with preserved cardiac output despite overload conditions, RV failure finally occurs, leading to death. The underlying mechanisms involved in the transition from compensatory hypertrophy to maladaptive remodelling are not completely understood.

MOTS CLÉS
Ventricule droit ;
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Couplage ventriculo-artériel ;
Recherche expérimentale

Résumé Le ventricule droit (VD) fait face à d'importantes variations de ses conditions de charge en réponse aux maladies cardiovasculaires et pathologies vasculaires pulmonaires. Le VD supporte mieux une surcharge de volume qu'une surcharge de pression, de même il s'adapte mieux aux variations progressives qu'aux changements aigus. La physiopathologie du VD a pendant longtemps été résumée à des extrapolations de la physiopathologie du ventricule gauche. Cependant les deux ventricules sont différents, tant sur le plan anatomique, hémodynamique que fonctionnel. Les caractéristiques métaboliques singulières du VD peuvent également être à l'origine d'une adaptation différente aux conditions pathologiques. Après une longue période compensatrice avec préservation du débit cardiaque, la dysfonction du VD s'installe finalement face à la surcharge chronique persistante. Les mécanismes impliqués dans la transition depuis l'hypertrophie compensatrice jusqu'au remodelage inadapté sont méconnus. Dans cette revue, les connaissances actuelles de la physiopathologie du VD dans l'hypertension pulmonaire chronique sont reportées à partir des résultats récents issus de la recherche expérimentale.

Background

Right heart failure is commonly related to left ventricular (LV) dysfunction. Ischaemic myocardial injury or, less frequently, arrhythmogenic dysplasia of the right ventricle (RV), congenital heart disease and chronic respiratory disease, including pulmonary vascular disorders, can also result in right ventricular failure (RVF). RVF is also a current problem in the post-operative course of heart transplantation and LV assist device implantation [1,2]. In pulmonary hypertension (PH), pulmonary vascular damage will inevitably affect the whole cardiopulmonary unit [3]. It has been appreciated over the last two decades that right ventricular (RV) dysfunction is the most important determinant of long-term outcomes in PH patients. Actually, prolonged survival is related more to RV function than to pulmonary haemodynamics per se. In studies addressing haemodynamic variables and survival in PH, high mean right atrial pressures and low cardiac output are consistently associated with poorer survival [4–6]. Despite major improvements in pharmacological management over the last 15 years, PH patients still die from RVF.

RV pathophysiology has been overlooked for many years. In the past, several experiments relegated the RV to a passive conduit, suggesting that the RV pump might be neglected. For example, Starr et al. showed that electrocautery ablation of the RV free wall in dogs was not associated with significant changes in haemodynamics, and that all animals survived [7]. For a long time, the Fontan procedure also supported the clinical evidence that RV absence did not compromise overall heart function [8]. Physicians have recently shown clinical interest in the right heart, as RV function appears to be a prognostic factor in left heart failure, PH and other chronic respiratory disorders. Most of mechanisms involved in left heart diseases were first extrapolated to RV pathophysiology, despite the two ventricles differing in their embryology, geometry and physiology [9,10]. Recently, a new focus on RVF has emerged, which aims to improve both understanding and clinical management. In PH, there are different phenotypic abnormalities in the RV. Surprisingly, some patients share the same phenotype, whereas the RV is not exposed to the same degree of pressure overload [11]. Considering the central role of the RV in cardiopulmonary diseases, Mehra et al. suggested a comprehensive nomenclature of right heart failure, based on aetiology, anatomical injury, pathophysiology and functional status [12]. Experimentally, major efforts have been made to improve our understanding of RV remodelling. Several animal models of chronic RVF have thus been reported over the last decade to reproduce the main features of RV dysfunction [13].

The mechanisms of RVF as well as the clinically relevant variables for measuring RV function in PH are still being debated. In this paper, after a brief description of the normal RV, we first seek to overview the functional evaluation of RV contractility and reserve in the setting of chronic pressure overload. We then present current knowledge of RV remodelling related to PH. Based on experimental findings, the cellular mechanisms and molecular pathways involved in the transition from compensated RV hypertrophy to