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SCIENTIFIC EDITORIAL

Right ventricle impairment: Are we changing the paradigm in organic mitral regurgitation?

Dysfonction du ventricule droit : allons nous changer de paradigme dans l'insuffisance mitrale organique ?

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Pathophysiological determinants of right ventricular function in organic mitral regurgitation

The classical determinants of right ventricular (RV) systolic function are RV load, myocardial contractility and ventricular interaction. Functional and morphological changes to the right ventricle (RV) owing to mitral valve disease have been poorly explored [1—4]. While mitral valve stenosis has mainly upstream consequences and is thought to impair RV function directly through pulmonary pressure rise, mitral regurgitation (MR) has both upstream and downstream effects. As demonstrated in our recent paper in *Circulation* [5], RV impairment, a frequent finding in organic MR (30% at the time of surgery), results from both the downstream and the upstream consequences of volume overload (Fig. 1). Downstream, MR elicits left ventricular (LV) volume overload with subsequent LV remodelling. Chronic organic MR triggers an eccentric hypertrophy with geometric changes of the LV cavity. The left ventricle (LV) enlarges and its shape evolves into a more spherical pattern, increasing the constraint on and the interaction with the RV. In dogs with congestive heart failure related to severe MR, LV enlargement compresses and flattens the RV, thereby, impairing RV function [6]. In addition, interventricular septal function is impaired in organic MR, and this alteration is even the main determinant of RV ejection fraction (EF) before surgery in our study [5]. As suggested by Carabello in the associated editorial [7], it

Abbreviations: EF, Ejection fraction; LA, Left atrial; LV, Left ventricle/ventricular; MR, Mitral regurgitation; PASP, Pulmonary artery systolic pressure; RV, Right ventricle/ventricular; TAPSE, Tricuspid annular plane systolic excursion.

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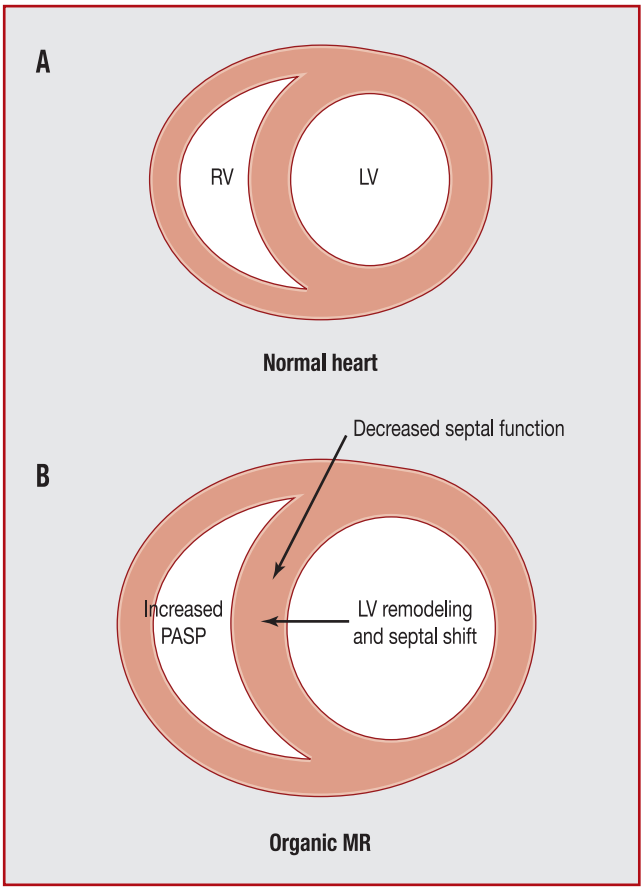

Figure 1. Pathophysiological determinants of right ventricular function in chronic organic mitral regurgitation (MR). A. Normal heart. B. Chronic organic MR results in remodelling of the left ventricle (LV) and septal shift toward the right ventricle (RV). In addition, septal systolic function is impaired. Upstream, MR elicits a backward rise in pulmonary pressure and an increase in RV afterload. In a multivariable analysis carried out in 208 patients, LV enlargement ($\beta = -0.22$, $P = 0.002$), LV septal function ($\beta = 0.42$, $P < 0.0001$) and pulmonary artery systolic pressure (PASP) ($\beta = -0.14$, $P = 0.047$) were independent contributors to RV systolic function [5].

is likely that impingement on the RV septum by the enlarged LV reduced preload in septal fibres and thus, septal function. This hypothesis is reinforced by the prompt improvement in RV function after elimination of volume overload with mitral valve surgery [5].

Upstream, organic MR elicits left atrial (LA) volume and pressure overload leading to LA enlargement, proportionate to the magnitude of MR. Increase in LA pressure induces a backward rise in pulmonary capillary wedge and artery pressure. Pulmonary artery systolic pressure (PASP) is usually proportionate to LA pressure and pulmonary capillary wedge pressure [8]. In patients with longstanding MR, pulmonary vascular remodelling or abnormal vasoconstriction contributes also to the elevation of PASP. The RV is a thin-walled structure accustomed to low afterload owing to low pulmonary resistance level, and the RV is more sensitive to pressure overload than to volume overload. RV performance alteration was thus perceived as secondary to increased afterload in organic MR, with an inverse relation between RV EF and the level of PASP [1,2]. Acute pharmacological PASP reduction with nitroglycerin in patients with organic MR reduced RV afterload and improved RV function [1]. However, PASP is barely related to RV function in our study ($\beta = -0.14$), clearly demonstrating that RV afterload is not the main determinant of RV function in chronic organic MR [7]. Recent data in patients with pulmonary hypertension suggested that RV remodelling differs according to the cause of pulmonary hypertension, with the least adverse remodelling being in patients with chronic organic MR. Moreover, in this recent work, there was no relation overall between PASP and RV EF, suggesting again that other mechanisms are involved in RV alteration.

Hence, rather than PASP, LV remodelling and septal function are the main determinants of RV systolic function in organic MR. Other variables that are not captured by our study, such as neurohormonal activation or intrinsic myocardial contractility depression, are probably involved in RV function alteration in organic MR [3,7]. Further studies would have to refine determinants of RV function in organic MR.

Impact of right ventricular and biventricular alteration on prognosis in organic mitral regurgitation

The optimal timing of surgery is fundamental in the management of organic MR. The main indications for surgery are symptom onset, LV function and LV enlargement. In organic MR, LV EF is preserved for a long period, despite progressive LV systolic function alteration. The backward ejection in the left atrium, a low impedance pathway, masks LV myocardial contractility depression, resulting in a discrepancy between LV EF and actual LV myocardial function. Despite this limitation, LV remodelling and function have long been regarded as prominent factors for referring patients for surgery in organic MR. Also, LV end-systolic diameter and LV EF are an essential part of current European and American guidelines [9,10], particularly in asymptomatic patients with severe organic MR.

Although LV evaluation remains an essential step in the clinical workup of MR, recent studies have suggested that the upstream impact of regurgitation should be also taken into account. Indeed, recent data in asymptomatic patients have defined important factors allowing risk stratification as LA size and systolic pulmonary artery pressure at rest or during exercise. LA dilatation, a direct consequence of LA volume and pressure overload, is linked to the magnitude of regurgitation in organic MR. LA dilatation is even regarded as a crystal ball in predicting outcome of patients with severe organic MR [8]. Pulmonary hypertension, a consequence of LA and capillary wedge pressure rise, is also a predictor of poor outcome in patients managed medically or after surgery [11,12]. Moreover, exercise-induced pulmonary hypertension is a predictor of symptom onset in asymptomatic patients with organic MR [13]. Hence, LA volume and resting or exercise pulmonary hypertension have been added to recent guidelines in organic MR [10].

Besides LA and pulmonary pressure, MR is considered a disease of both ventricles due to the downstream and upstream impact of volume overload. Reduced RV EF has