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 ?

Thierry le Tournneau

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],
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...
beeen reported in patients with MR with or without LV failure [3] and is most commonly observed in patients with large regurgitation, even in those with normal LV systolic function. Although small studies raised the question of the prognostic influence of RV alteration in organic MR, these studies were not fully conclusive [2]. Thus, in our study [5], we aimed to assess the long-term influence of RV function alteration on postoperative prognosis in patients referred to surgery for chronic organic MR. RV function alteration was defined as an isotropic RV EF less or equal to 35% according to previous publications. Surprisingly, patients without ventricular dysfunction (LV EF ≥ 60% and RV EF > 35%) or with isolated RV dysfunction have a similar cardiovascular survival rate 10 years after surgery (≈ 92%). Patients with isolated LV dysfunction (LV EF < 60% and RV EF > 35%) have an excellent postoperative outcome, with a low rate of cardiovascular death 10 years after surgery. By contrast, combined LV and RV impairment (LV EF < 60% and RV EF ≤ 35%) is associated with a poor outcome after surgery, with a cardiovascular survival rate of only 52% at 10 years. These results therefore strongly favour RV systolic function assessment in the clinical workup of patients with organic MR, to improve the clinical decision-making process.

**Echocardiographical variables to assess right ventricular function in organic mitral regurgitation**

The usefulness of echocardiographical variables in assessing RV function in chronic organic MR is questionable. Although numerous echocardiographical variables have been proposed to assess RV function, only a few studies focused on RV assessment in mitral valve regurgitation at rest [5,14] or during exercise [14]. Our data raise the question of the diagnostic value of echocardiographic variables in predicting RV EF in patients with organic MR [5]. Indeed, we provide insight on the limited usefulness of variables assessing longitudinal function of the RV free wall for predicting RV EF in organic MR. First, tricuspid S wave velocity is poorly correlated to RV EF (r = 0.28); and second, RV free wall function is not related to RV EF by isotropic evaluation. By contrast, RV septal function is tightly related to global RV EF, supporting the hypothesis that RV function should be addressed overall in organic MR or at least by taking into account septal function. In the same way, it has been demonstrated that tricuspid annular plane systolic excursion (TAPSE) and tricuspid S wave velocity change significantly after mitral valve surgery whereas RV EF does not, supporting the hypothesis of geometrical rather than functional changes to the RV. Indeed, the RV undergoes geometrical modifications after cardiac surgery related to cardiac translation [15] and to volume overload elimination with acute LV reverse remodelling [5]. Thus, these results raise suspicion about the reliability of TAPSE or tricuspid S wave velocity in organic MR. Although further studies would have to evaluate new two-dimensional echocardiographical variables, such as RV strain, nowadays, RV systolic function should be assessed by EF measurement based on cardiac magnetic resonance imaging, gamma-angiocardiography or three-dimensional echocardiography in the setting of severe organic MR.

**Conclusion**

RV EF impairment is a frequent finding in patients with organic MR referred for surgery. Although RV EF alteration was previously perceived as a consequence of pulmonary pressure rise in organic MR, our findings demonstrate that RV systolic alteration is mainly related to LV remodelling and septal function impairment owing to volume overload. Isolated RV dysfunction (RV EF ≤ 35%) before surgery is not a harmful condition per se in chronic organic MR, whereas biventricular impairment is a strong predictor of poor postoperative outcome. It is noteworthy that biventricular impairment did not influence early postoperative outcome in our study, but only mid- or long-term outcome. Thus, preoperative RV dysfunction might prompt the proposal of a close follow-up after surgery. Finally, RV EF should be assessed by using three-dimensional echocardiography, cardiac magnetic resonance imaging or gamma-angiocardiography as a part of the clinical workup of organic MR.

**Disclosure of interest**

The author declares that he has no conflicts of interest concerning this article.

**References**


