The Myocardium in Mitral Regurgitation
A Tale of 2 Ventricles
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Contractility in Mitral Regurgitation

In prolonged severe mitral regurgitation (MR), contractility is depressed in both experimental animals and humans. Such depression is initially reversible but becomes irreversible at some point in the natural history of the disease, as evidenced by the poor prognosis of depressed EF that implies extensive myocardial damage. Contractile dysfunction in MR accrues from the loss of myocyte contractile elements and from abnormal calcium handling that alters myocardial excitation-contraction. In the early stages of disease, contractile dysfunction is reversible, preferably by mitral valve repair but also in part by β-adrenergic receptor blockade. Recently, β-blockade has been suggested to be protective in human MR, and with this finding taken together with other data, it appears that sympathetic overactivation plays a major role in the pathogenesis of myocardial injury in MR.

The Present Study

MR obviously effects a volume overload on the LV; therefore, the LV has been the target of most studies of MR. Increased preload, together with usually normal afterload, increases LV EF in MR so that the normal EF in patients with severe MR is probably ~70%. By the time EF is reduced to 60% or even 64%, prognosis worsens, presumably because myocardial damage causing reduced contractility has ensued. The present study by Le Tourneau et al adds to our knowledge of the pathophysiology of MR in several ways. First, it confirms and emphasizes previous observations that right ventricular (RV) dysfunction plays a direct role in MR prognosis. Furthermore, it provides insight into the mechanism of RV dysfunction.

To reiterate, EF is determined by preload, afterload, wall thickness, and contractility, and all 4 factors vary from patient to patient. The increased LV filling pressure in MR, together with reflexive pulmonary vasoconstriction, often leads to pulmonary hypertension, thus afterloading the RV. It is often presumed that RV ejection performance, when impaired, is due to increased pulmonary pressure. Because the geometric vagaries of the RV make calculation of systolic wall stress (thought by many to be the gold standard of afterload) extraordinarily difficult, it is rarely measured and was not measured here. However, estimated pulmonary pressure barely correlated with RV EF, suggesting that RV afterload was not a major cause of reduced RV ejection performance. More important was the effect of MR on the interventricular septum. Reduced septal function played a major role in reduced RV function preoperatively, and its reversal helped explain improved postoperative RV function in patients in whom comparison studies were available. It is likely that impingement on the RV septum by the enlarged LV reduced preload in those fibers, reducing septal function, while a reduction in LV volume postoperatively allowed repreload of the RV septal fibers. However, in the Le Tourneau et al multivariable analysis, the combination of septal function, LV dimension, and pulmonary pressure had an R of 0.55 and thus an r² of 0.30, suggesting that much of the RV dysfunction remains unexplained by those factors. Thus, impaired contractility becomes likely to play a large role in the observed outcome, and irreversible contractile dysfunction of the LV and possibly the RV explains the poor 10-year survival of those patients with combined RV and LV dysfunction. Patients with isolated RV dysfunction probably had that finding based on the septal dysfunction and pulmonary hypertension but not contractile dysfunction because outcome was favorable in such patients. Patients with reduced LV EF had a modestly poor prognosis, almost certainly because of irreversible LV contractile dysfunction in those patients. On the other hand,
patients with reduced LV and RV EF probably had contractile dysfunction of both ventricles, a finding that again raises a neurohumoral hypothesis. Because both ventricles are bathed in the same humoral soup, if catecholamines can damage the LV, they likely could damage the RV as well, perhaps as shown in the Figure.

Mitrail regurgitation creates an intricate interplay between LV volume overload, LV remodeling, RV–LV interaction, pulmonary hypertension, neurohumoral activation, and myocardial damage that should be avoided or intercepted before the LV or both ventricles become permanently damaged, points dramatically emphasized in this work by Le Tourneau et al.15

**Disclosures**

None.

**References**


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