

EDITORIAL COMMENT

Pulmonary Pressures and Outcome in Primary Mitral Regurgitation



Paradigm Shift From Rung to Ladder*

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*Declare the past, diagnose the present,
foretell the future.*

– Hippocrates (1)

Primary mitral regurgitation (MR) is a progressive disease that is a growing health problem because of the aging population, and it leads to a need for mitral valve (MV) surgery when regurgitation is severe and symptoms develop, or significant left ventricular (LV) remodeling and/or dysfunction exists. Based on the latest U.S. and European guidelines, MV repair should also be considered in asymptomatic patients with severe MR, preserved LV ejection fraction, and resting pulmonary hypertension (PH) with systolic pulmonary arterial pressure (SPAP) ≥ 50 mm Hg (class IIa) (2,3). MV repair may also be considered in these patients when PH occurs at exercise (class IIb) (3).

According to the World Symposium classification, group 2 PH is merely a reflection of the hemodynamic effects of MR (4). The sustained elevation of left atrial volume and pressure due to chronic volume overload is passively transmitted backward into the pulmonary veins, leading to PH (4). The presence of pulmonary vasoconstriction and progressive pulmonary vascular remodeling are additional contributors to PH.

The prevalence of PH in MR varies according to symptomatic status, MR severity, and the presence of

LV systolic dysfunction (4). Significant PH (SPAP > 50 mm Hg) is present in 20% to 30% of patients with severe MR (5,6) and in up to 64% of severely symptomatic patients (New York Heart Association [NYHA] functional classes III to IV) (7). In asymptomatic patients, the prevalence of PH is lower, approximately 6% to 30% (4,8), but increases to 58% during exercise (8).

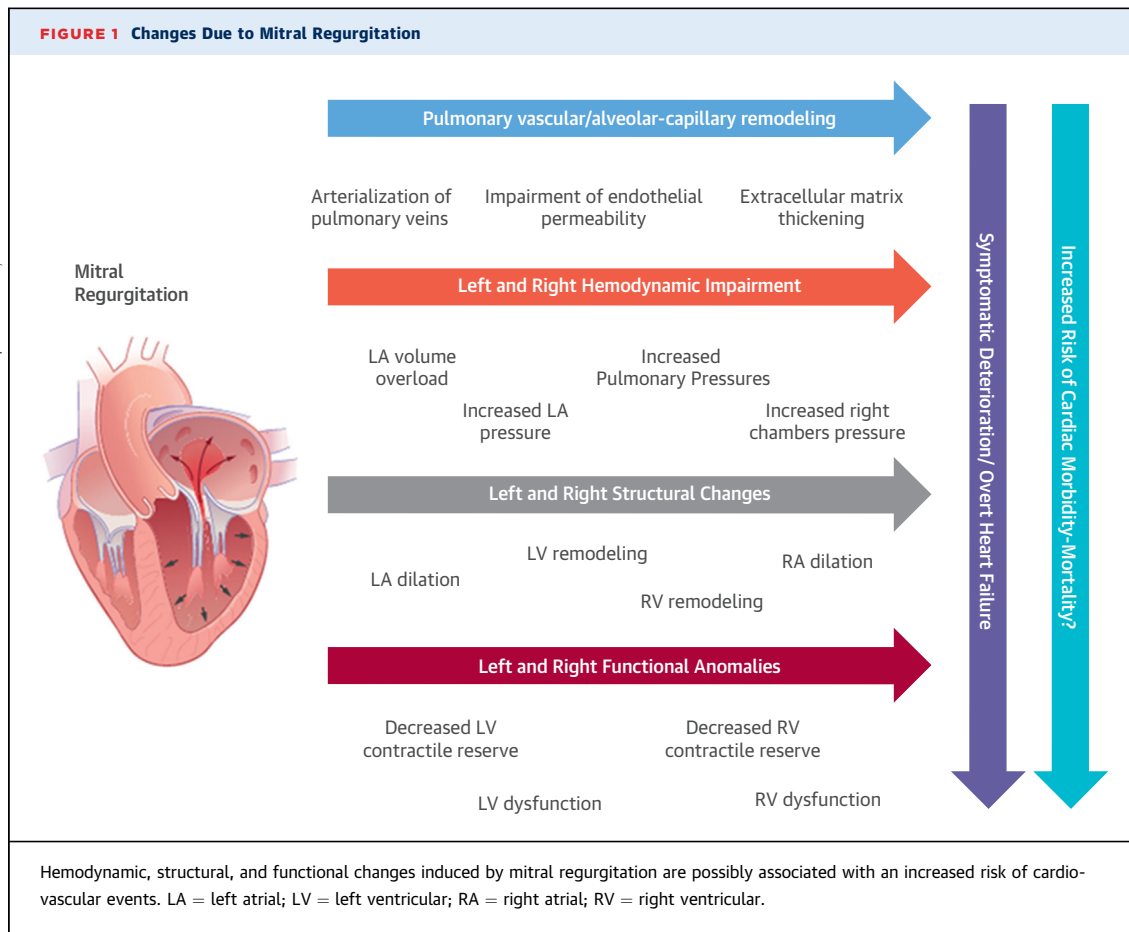
Previous small, often heterogeneous, studies have shown that the presence of PH in patients undergoing MV surgery is associated with poorer outcomes in terms of survival, LV dysfunction, limited LV reverse remodeling, symptom relief, and persistence of PH (–4–9). Significant PH is associated with > 2 -fold increased risk of post-operative death (7). Although long-term survival after MV surgery is inversely related to the severity of PH, modest increases in SPAP also adversely affect outcomes (7,9).

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In this issue of *the Journal*, these observations have been elegantly confirmed in the study by Mentias et al. (10), who evaluated the impact of baseline pulmonary pressures on long-term outcome in primary MR. This study involved mainly surgical patients (86%) at low risk (Society of Thoracic Surgeons [STS] score $3.98 \pm 1\%$) with $\geq 3+$ MR and preserved LV function. The investigators reported that age, New York Heart Association functional class, pre-operative atrial fibrillation, coronary artery disease, indexed LV end-systolic diameter, and baseline SPAP ≥ 35 mm Hg were predictors of long-term mortality, whereas MV surgery was associated with improved survival. They further showed that the impact of SPAP on outcome was progressive and not confined to patients with the highest baseline SPAP values. The use of SPAP also had an incremental prognostic value over classical

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clinical data when incorporated into the clinical model that included STS score, indexed LV end-systolic dimension, flail mitral leaflet, and MV surgery. SPAP significantly improved reclassification for mortality, even when a threshold of ≥ 35 mm Hg was used. Interestingly, the central message of the study did not change in terms of SPAP and its incremental prognostic usefulness when analysis was limited to patients in New York Heart Association functional class I without atrial fibrillation.

Intriguingly, this low SPAP threshold for better mortality prediction can be found in older adult patients without compromised outcome as an impact of age on LV diastolic properties (11). However, it was also close to the resting SPAP recently reported by our group to be more likely associated with exercise PH, which is a predictor of poor outcome in degenerative MR (12). Higher left atrial pressures, lower atrial compliance, decreased functional reserve with exercise (left atrial, pulmonary vascular, and right ventricular function reserve), subtle impairment in LV systolic and diastolic function, and the dynamic nature of MR may all contribute to the negative

impact of even mildly elevated pulmonary pressures. A higher degree of PH probably indicates more severe disease with a higher risk of post-operative morbidity (i.e., right ventricular failure) and mortality. In the study by Mentias et al. (10), most of the deaths occurred in the group of patients with SPAP ≥ 50 mm Hg.

Although retrospective, this study is 1 of the largest on the topic, with sound results and potentially significant clinical implications. However, whether post-operative mortality was related directly to progressive PH remains to be established. Because of the study's observational nature, individual progression of pulmonary pressures was not assessed, and as such, no follow-up times were pre-specified for determining this potential continuum. Also, the current study did not indicate whether surgical intervention before PH onset might have improved prognosis. Finally, the sample size of nonoperated patients was too small to generalize the findings to patients with no indication for MV surgery.

Recent evaluations of the natural history and the results of interventions have raised the question of

the optimal timing of intervention in patients with primary MR. The current study supported that surgery should not be delayed in the presence of significant PH in patients with primary MR. Nevertheless, waiting for SPAP to progress to ≥ 50 mm Hg to treat MR is likely to expose patients to a markedly compromised prognosis and persistent postoperative PH. Moreover, the impact of SPAP on mortality seems to be progressive beyond a level that is close to ≥ 35 mm Hg. In this SPAP category, the increase in mortality risk is not linear, and as such, identifying the group of patients in whom early operative strategy might optimize outcomes is highly relevant. In these patients, an enlarged left atrium, decreased global longitudinal function,

dynamic MR, exercise-induced severe PH, impaired exercise capacity, and reduced contractile reserve are all parameters that might help stratify patient individual risk (13,14) (Figure 1). Prospective studies of large cohorts using pulmonary pressure monitoring and encompassing most of these outcome variables would be needed to confirm these hypotheses.

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