Mitral regurgitation of degenerative etiology: should the timing of surgery be changed in the mitral valve repair era?

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The timing of surgery in patients with chronic mitral regurgitation is a controversial issue. Left ventricular dysfunction progresses silently and is partly predictable; depressed left ventricular contractility sometimes accompanies a normal ejection fraction. Severe symptoms remain a clear recommendation for surgery. However several factors suggest that surgery should not be delayed until severe symptoms appear: impact on survival of ejection fraction < 60%, preoperative symptoms, and atrial fibrillation. Early surgery is justified in patients with degenerative mitral regurgitation independently of the type of lesion (prolapse of posterior, anterior or both the leaflets), because the addition of new techniques to the surgical armamentarium has neutralized prolapse of the anterior leaflet as an incremental risk factor for reoperation. In conclusion, early surgery is a reasonable treatment for low-risk patients with repairable valves and should be considered in asymptomatic patients with ejection fraction approaching the lower limit of normal, history of paroxysmal atrial fibrillation or pulmonary hypertension during exercise.

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The timing of operative intervention in patients with chronic mitral regurgitation (MR) is still controversial and remains a challenge for both the cardiologist and the surgeon[1]. The decision-making is difficult because of the silent progression of left ventricular (LV) dysfunction and owing to the lack of a quantitative approach during echocardiography performed for the evaluation of MR. Severe symptoms improve after surgery and remain a clear recommendation for surgery in MR[2]. However, several factors have led to the suggestion that surgery should not be delayed until the development of severe symptoms.

Masked left ventricular dysfunction

LV dysfunction progresses silently, is only partly predictable and may occur unexpectedly. Thus, the possibility of reliably monitoring patients with severe MR is limited[3-8]. The ejection fraction (EF) is an unreliable indicator of early depression of LV myocardial contractility in the presence of MR, because of systolic unloading of the left ventricle[5]. Starling et al.[3] demonstrated this phenomenon using end-systolic pressure-volume relations to assess LV chamber elasticity; these investigators showed that a depressed LV contractility was sometimes associated with severe MR in spite of the fact that the EF was within the normal range. In such patients the decreased LV contractility was shown to be reversible after surgical treatment; this improvement in LV contractility occurred late in this group of patients compared with the early recovery observed in patients with normal preoperative contractility indexes. The preservation of the annulo-ventricular continuity is crucial for an optimal postoperative LV function[9].

The preoperative EF is well-known to predict postoperative LV function and mortality, and the finding of Ling et al.[10] that an EF < 60% was predictive of higher mortality supports the view that when the EF approaches the lower limit of normal, surgical treatment is indicated, even in asymptomatic patients.

The potential for occult LV dysfunction in MR has been recognized in the past. Many previous studies[11-13] have attempted to determine a simple guide to the optimal timing for operative intervention in asymptomatic patients. Enriquez-Sarano et al.[7] suggested that, together, preoperative EF and end-systolic diameter, as determined at echocardiography, have a more predictive power than either one of them alone.

For example, a patient with EF < 50% and end-systolic diameter > 45 mm has a 70% likelihood of postoperative ventricular dysfunction. A study group[14] found a correlation between left atrial size and postoperative outcome. In addition, the evaluation of baseline or exercise-induced pulmonary hypertension at echocardiography may be useful for clinical management[15]. Assessment of LV size and function constitutes only one component of this complex clinical decision[16].

Symptoms and surgical risk

In evaluating patients with pure isolated MR who are being considered for mitral surgery we should also consider the impact of preoperative symptoms on survival after surgical correction. Sousa et al.[4] showed that the operative risk for patients in NYHA functional classes I and II is remarkably low: 0.5% for all ages and 0% for patients < 75 years. Tribouilloy et al.[17] demonstrated that the postoperative survival of NYHA classes I and II patients is not only better than that of classes III and IV patients, but also corresponds to the expected survival. The mechanism by which preoperative symptoms influence postoperative outcome is unclear. A prolonged duration of volume overload may have contributed to higher frequencies of postoperative LV dysfunction[7], left atrial alterations[14], impaired diastolic LV function or myocardial fibrosis[18,19].

Role of atrial fibrillation

Atrial fibrillation has also been identified as an independent predictor of overall survival after surgery for MR[7]. The onset of atrial fibrillation has been considered as a decisive crucial development in the course of MR[20] and is a reliable marker for the monitoring of disease progression in patients with severe MR. Tribouilloy et al.[17] showed that compared with patients in NYHA classes I and II, a higher proportion of patients with MR in NYHA classes III and IV has been found to be in atrial fibrillation despite the absence of any significant differences in EF. Kim et al.[21] confirmed, in a longitudinal echocardiographic study, that the incidence of atrial fibrillation was significantly higher in patients with progression of disease severity despite a normal EF. Lim et al.[22] reported significantly lower 3- and 5-year survival rates following mitral valve repair in patients who were in preoperative atrial fibrillation compared with patients who were in sinus rhythm. The onset of atrial fibrillation may be a useful marker of disease progression because of its association with poor LV function, and its negative impact on postoperative survival should form part of the clinical decision-making process.

An early approach for patients with MR and no or only minimal symptoms is acceptable only under rigorous conditions. First, the diagnosis of severe MR should be well documented, keeping in mind that the methods currently available for the assessment of the severity of MR are not perfect. Potential pitfalls should be avoided by an integrated approach, which should include pathophysiologic, methodological and clinical aspects; the risk associated with moderate MR does not justify surgery; the operative risk should be low and determined on the basis of the patient's age and clinical conditions. Second, the degenerative etiology of MR is to be considered; when degenerative disease is the cause of valve dysfunction, reconstructive operations are associated with a high expectation of a long-lasting competent valve. Long-term evaluation has proved that the results are less satisfactory when rheumatic disease is the cause of MR[23]. Third, the probability of valve repair should be high and determined on the basis of the surgeon's experience and of the severity of the valve lesions. Prolapse of the posterior leaflet has been for years corrected using quadrangular resection, following the techniques originally developed and systematically applied by Carpentier[24], starting in 1970. With this kind of lesion the likelihood of valve repair approaches 100% and the long-term follow-up confirms satisfactory results[25]. In the past, early surgery in case of prolapse of the anterior leaflet was not justified because this type of lesion was an incremental risk factor for reoperation. This was true even during the initial phase of our experience when triangular leaflet resection and chordal shortening were the only techniques used to repair such lesions. Since the results of triangular resection of the anterior leaflet, as well as those of chordal shortening, have proved to be unsatisfactory both in our experience as well as in that of others[25-27], we developed a new technique, the "edge-to-edge" technique or Alfieri repair, for the correction of prolapse of the anterior leaflet due to chordal rupture or elongation[28,29]. Chordal transposition from the posterior to the anterior leaflet[30] and replacement with polytetrafluoroethylene sutures[31] appeared to be equally effective although technically more demanding. Due to the high reoperation rate following correction of prolapse of the anterior leaflet, the "edge-to-edge" repair was performed mostly in the subset of patients with such a lesion. On the other hand, this technique was less commonly employed in case of prolapse of the posterior leaflet when quadrangular resection would have required extensive decalcification of the posterior annulus.

The addition of the above-mentioned techniques to the surgical armamentarium has neutralized prolapse of the anterior leaflet as an incremental risk factor for reoperation, thereby increasing the population of patients who can undergo early mitral valve reconstruction. Therefore, it is mandatory to identify before surgery, using echocardiographic examination, the feasibility of valve repair and to exclude posterior leaflet hypoplasia or those valves with extremely thin leaflets and chordae

tendinae (personal communication) suggesting fibroelastic deficiency, which are not suitable for reconstructive surgery.

Conclusions

It is generally agreed that surgical intervention is indicated if MR is severe and if symptoms that limit activity are present. In case of asymptomatic patients the relevant question is whether early surgery may improve the long-term survival by avoiding the complications of MR that may occur during the phase of medical observation. Ling et al.[10] showed that, in patients with MR due to flail leaflets, early surgery was associated with both lower long-term mortality attributable to a marked decrease in cardiac mortality as well as with very low incidences of sudden death and intractable heart failure; early surgery was also associated with a decreased late incidence of *de novo* chronic atrial fibrillation. The beneficial effects of valve repair on late survival should also be taken into consideration, since at multivariate analysis valve repair was also an independent favorable predictor of operative mortality[32]; consequently, valve repair is an incentive to consider surgery at an early stage in the course of the disease before the onset of LV dysfunction.

In conclusion, early surgery is a reasonable treatment for low-risk patients with repairable valves and should be considered in asymptomatic patients with severe MR, EF approaching the lower limit of normal and history of paroxysmal atrial fibrillation or pulmonary hypertension during exercise.

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