

## Surgical management of moderate ischemic mitral valve regurgitation: Where do we stand?

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surgical approach for the treatment of IMR remains debated. Some authors demonstrated that coronary artery bypass graft (CABG) alone is beneficial in patients with IMR. Conversely, in most patients, moderate IMR will persist or worsen after CABG alone which translate in higher long-term mortality as a function of residual mitral regurgitation severity. A probable reason for this unclear surgical management of functional MR is due to the contemporary suboptimal results of reparative techniques. The standard surgical treatment of chronic IMR is CABG associated with undersized annuloplasty using complete ring. Though, the recurrence of mitral regurgitation remains high (> 30%) because of continuous left ventricle remodeling. To get better long term results, in the last decade, several subvalvular procedures in adjunct to mitral anuloplasty have been developed. Among them, surgical papillary muscle relocation represents the most appreciated option capable to restore normal left ventricle geometry. In the next future new preoperative predictors of increased mitral regurgitation recurrence are certainly needed to find an individual time period of treatment in each patient with moderate IMR.

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### Abstract

Ischemic mitral regurgitation (IMR) represents a common complication after myocardial infarction. The valve is anatomically normal and the incompetence is the result of papillary muscles displacement and annular dilatation, causing leaflets tethering. Functionally the leaflets present a restricted systolic motion due to tethering forces that displaces the coaptation surface toward the left ventricle apex. The patients present poor left ventricular function at the time of surgery and the severity of the mitral regurgitation increases the risk of mortality. Currently there is general agreement to treat surgically severe IMR nevertheless strong evidences for patient with moderate insufficiency remains poor and proper treatment debated. The most effective

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**Core tip:** Moderate ischemic mitral regurgitation should always be considered in patients undergoing other cardiac surgery. Restrictive anuloplasty alone fails as valid treatment because often associated with persistence and high recurrence rate of mitral regurgitation due to continuous ventricular remodeling. Probably more aggressive repair procedures addressing the subvalvular mitral apparatus would help to find more durable results for this complex disease. In the next future new preoperative predictors of increased MR recurrence are certainly needed to find an individual time period of treatment in each patients with moderate ischemic mi-

tral regurgitation.

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## INTRODUCTION

Ischemic mitral regurgitation (IMR) occur in up to 40% of patients affected by myocardial infarction<sup>[1]</sup>. IMR affects the myocardium rather than the valve itself and valve incompetence is the result of papillary muscles (PPMs) displacement, leaflet tethering, and annular dilatation. Functionally the leaflets present a restricted systolic motion due to tethering forces that displaces the coaptation surface toward the left ventricle (LV) apex<sup>[2]</sup>. The patients present poor left ventricular function at the time of surgery and the severity of the mitral regurgitation increases the risk of mortality (lower among patients with mild IMR). Currently there is general agreement to treat severe IMR surgically, nevertheless evidences for patient with moderate insufficiency remain poor and proper treatment is debated.

## ECHOCARDIOGRAPHIC CONSIDERATIONS

To define the severity of mitral regurgitation by Doppler echocardiography, the effective regurgitant orifice (ERO) area and the regurgitant volume (RV) are used. Organic MR is usually characterized by an ERO area > 0.4 cm<sup>2</sup> and RV > 60 mL/beat; these cut points are significantly lower for patients with functional MR (ERO area > 0.2 cm<sup>2</sup> and RV > 30 mL/beat, respectively)<sup>[3,4]</sup>.

MR severity in any individual patient should not be defined exclusively on the basis of few quantitative parameters but on an integrative evaluation that assess supplementary helpful findings, such as the pulmonary vein flow pattern, the size of left atrial and LV chambers. Lastly, since functional MR is an essentially dynamic lesion, the severity of regurgitation varies as a function of LV loading conditions and heart rhythm. For that reason, stress echocardiography is an important adjunct to the noninvasive evaluation of appropriate patients<sup>[5]</sup>.

## OPEN CONTROVERSIAL ON SURGICAL MANAGEMENT

The most effective approach for the management of IMR remains discussed. Some authors demonstrated that coronary artery bypass graft (CABG) alone is beneficial in patients with IMR<sup>[6,7]</sup>. Conversely, in most patients moderate IMR will persist or worsen after CABG

alone which translate in higher long-term mortality as a function of residual MR severity<sup>[8]</sup>. A probable reason for this unclear surgical management of functional MR is due to the contemporary suboptimal results of reparative techniques<sup>[9,10]</sup>. Undersized annuloplasty with complete ring, associated with CABG, presently is the most frequently performed surgical procedure to treat chronic IMR. However, recurrent MR can be expected in 1/3 of patients because of continued LV remodeling<sup>[11,12]</sup>. There are many reviews about of adding subvalvular procedures to mitral annuloplasty to reduce the tenting forces and improve the long-term repair results<sup>[13-15]</sup>. Recent experimental and clinical studies reported that displacement of the PPMs, due to LV remodeling, represents a key characteristic in the development of IMR; surgical papillary muscles relocation may represent a new precious instrument for surgeons<sup>[15-18]</sup>. On the other hand, some authors reported very good results after mitral valve replacement<sup>[19,20]</sup>. In a recent randomized trial<sup>[21]</sup>. The Cardiothoracic Surgical Trials Network evaluate the relative risks and benefits of replacement versus repair, with or without CABG, in patients with severe IMR. As regard left ventricular reverse remodeling and 12-mo survival the authors observed no significant difference between mitral valve annuloplasty and replacement. However, in more than 30% of the patients in the repair group, a significant recurrent IMR developed. These data suggest a large potential benefit of valve repair if the effects of recurrent IMR can be limited. Therefore, the timing of valve repair in IMR needs to be assessed and patients with moderate regurgitation could benefit from early mitral surgery in morbidity though prolonged survival has to be demonstrated<sup>[22]</sup>.

## FUTURE PERSPECTIVES

Currently there is general agreement to treat only severe IMR at the time of CABG. Conversely, according recent guidelines<sup>[23,24]</sup>, mitral valve repair should be considered for patients with chronic moderate secondary MR who are undergoing other cardiac surgery (class of recommendation II b and II a respectively for American heart association/American college of cardiology and ESC guidelines). Consensus opinions regarding best practices rely on studies that are retrospective, observational, and most often single centered<sup>[25]</sup>. In 2009, the first trial on efficacy of adding mitral valves plasty to CABG for moderate IMR have been published by our group<sup>[26]</sup>. We demonstrated that the effectiveness of adding mitral valve plasty to CABG was well demonstrated by the improvement of NYHA class and percentage of LVEF and by the decrease of MR, left ventricular end-diastolic and end-systolic diameters, left atrial size and pulmonary artery pressure. In the same direction the Randomized Ischemic Mitral Evaluation Trial support the addition of MVR to CABG in patients with moderate ischemic MR undergoing CABG<sup>[27]</sup>. In this study, 73 patients referred for CABG with moderate IMR and an ejection fraction

> 30% were randomized to receive CABG plus mitral valve plasty (34 patients) or CABG only (39 patients). Moderate IMR was defined by an effective regurgitant orifice area of 0.20 to 0.39 cm<sup>2</sup>, RV of 30 to 59 mL/beat, and vena contracta width of 0.30 to 0.69 cm. Mitral valve plasty was performed with insertion of a Carpentier-McCarthy-Adams ETlogix Ring (Edwards Lifesciences) in 85% of patients and a Carpentier-Edwards Physio Ring (Edwards Lifesciences) in 15% of patients. Mean mitral leaflet coaptation length was  $7.1 \pm 1.2$  mm, and technical success was defined as no or trivial MR intra-operatively. The authors demonstrated that the addition of mitral valve repair by anuloplasty to CABG reduced MR severity, LV volumes, and BNP levels, with an improvement in functional capacity and symptoms at 1 year. Longer-term follow-up of MR severity in both treatment groups would be of interest because LV reverse remodeling continue for up to 2 years after coronary artery revascularization, and it is possible that patients in the CABG-only group may demonstrate greater reverse remodeling with time. Unfortunately, in both trials<sup>[26,27]</sup> there are no data on the use of cardiac resynchronization therapy when appropriate, strongly encouraged in guidelines. Another randomized, controlled multicenter trial in patients with moderate IMR is ongoing (ClinicalTrials.gov NCT00806988) designed to assess the effect of mitral valve repair added to CABG surgery on the combined end point of survival and re-hospitalization for heart failure in patients with moderate IMR followed for 5 years<sup>[28]</sup>. Moreover, the Cardiothoracic Surgery Network will shortly complete enrollment of 300 patients in a companion study of CABG plus mitral valve repair versus CABG alone in patients with moderate IMR<sup>[29]</sup>. Results from these trials will further elucidate the optimal treatment algorithm for patients with IMR; however, discrepancies in trial design, echocardiographic inclusion/exclusion criteria, and surgical technique suggest a continued role for large observational studies to facilitate a valid management of these patients. A key point could be to improve patient selection to identify more precisely which individuals will benefit from surgical intervention. In particular, stress tests could be very helpful to determine the precise time of intervention in this clinical setting. In particular, recent research efforts concentrated on exercise echocardiography<sup>[5,30]</sup>. Hung *et al.*<sup>[11]</sup>, for example, demonstrated as CABG alone left more patients with heart failure symptoms at rest and during exercise. This diagnostic tool should always be considered pre-operatively because induced dyspnea, increased in MR severity and systolic pulmonary artery pressure are often disguised in patients with moderate IMR at rest. Only a proper preoperative evaluation would not leave patients un-correctly treated. Therefore, this new clinical strategy would maximize the beneficial effects of repair and neutralize the effects of recurrent IMR. In the next future, the research for preoperative predictors of increasing MR recurrence and for alternative reparative approaches are probably the two key points to find an individual treat-

ment in each patients with this complex post-ischemic complication.

## CONCLUSION

Moderate IMR should always be considered in patients undergoing other cardiac surgery. Restrictive anuloplasty alone fails as valid treatment because often associated with persistence and high recurrence rate of MR due to continuous ventricular remodeling. Probably more aggressive repair procedures addressing the subvalvular mitral apparatus would help to find more durable results for this complex disease. In the next future new preoperative predictors of increased MR recurrence are certainly needed to find an individual time period of treatment in each patient with moderate IMR.

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