



# Surgical intervention for ischemic mitral regurgitation: how can we achieve better outcomes?

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Received: 1 November 2018 / Accepted: 15 April 2019 / Published online: 30 May 2019  
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## Abstract

Ischemic mitral regurgitation (MR) is a common complication of myocardial infarction. Left ventricular (LV) dysfunction and distortion of the subvalvular apparatus are the main contributors to ischemic MR. Coronary artery bypass grafting alone, mitral valve replacement, and mitral valve repair, with or without subvalvular procedures, have been performed for moderate-to-severe ischemic MR. Several randomized studies on the surgical treatment of ischemic MR have been performed; however, the optimal surgical strategy remains controversial because none have demonstrated a clear survival benefit. Since the mechanisms of ischemic MR are complex and multifactorial, comprehensive preoperative assessment of LV function and geometry (both global and regional), mitral valve configuration, viability testing, and exercise echocardiography are needed. A better understanding of this complicated disease and of the advantages and limitations of each procedure may help us devise more effective patient-specific surgical treatment strategies and achieve better outcomes.

**Keywords** Mitral valve · Functional mitral regurgitation · Mitral valve repair · Mitral valve replacement

## Introduction

Ischemic mitral regurgitation (MR) is a common complication of myocardial infarction, with a reported prevalence of 13–59%. Approximately one-third of these patients have at least moderate MR [1, 2]. Ischemic MR is an independent predictor of mortality in heart failure patients, with a reported survival rate of 50–60% at 5 years [3, 4].

The mechanism of ischemic MR is complex and multifactorial. Ischemic MR results from the distortion and remodeling of the left ventricle after myocardial infarction, where the papillary muscles are displaced away from the annular plane. Coupled with annular flattening, enlargement, and decreased contraction, this spatial deformation exerts traction on the chordae tendineae, leading to malcoaptation of the structurally normal mitral valve and subsequently to secondary MR. Furthermore, the MR-related left ventricular (LV) volume overload promotes LV remodeling, resulting in exacerbation of the MR (MR begets more MR) [1,

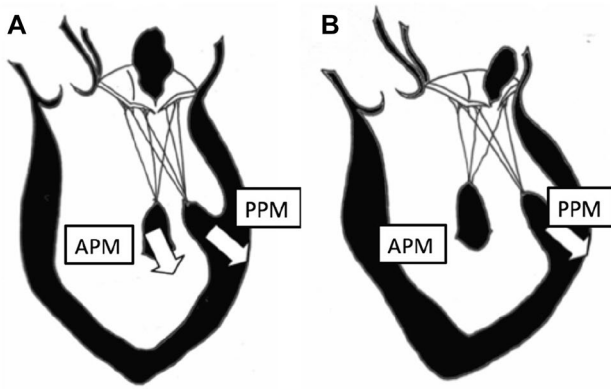
5–7]. Two patterns of leaflet tethering have been reported in secondary MR: asymmetric tethering and symmetric tethering [1] (Fig. 1). Asymmetric tethering occurs with regional LV remodeling, resulting in displacement of the posterior papillary muscle in a lateral direction. Symmetric tethering generally results from global LV remodeling, resulting in apical tethering of both the anterior and posterior papillary muscles.

Patients with ischemic MR often have multivessel coronary artery disease and need revascularization, including coronary artery bypass grafting (CABG). CABG alone may induce LV reverse remodeling and improve LV function by relieving ischemia. However, revascularization alone reduces ischemic MR only in certain patients [8–11]; therefore, concomitant mitral valve (MV) procedures have been performed in patients with ischemic MR to interrupt the vicious circle that would exacerbate the MR.

In 2016, the Cardiothoracic Surgical Trials Network (CTSN) performed two randomized control studies: one for patients with severe ischemic MR [12] and one for patients with moderate ischemic MR [13]. Neither of these studies found a clear superiority of MV repair over MV replacement for severe ischemic MR. Moreover, they found no evidence proving a better long-term prognosis for patients with moderate ischemic MR undergoing concomitant MV repair with

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**Fig. 1** The two patterns of leaflet tethering: asymmetric tethering (a) and symmetric tethering (b). *APM* anterior papillary muscle, *PPM* posterior papillary muscle

CABG. The 2017 American Heart Association/American College of Cardiology (AHA/ACC) guidelines recommend chordal-sparing MV replacement for severely symptomatic patients with severe chronic ischemic MR at the time of CABG (class of recommendation, IIa) [14]. MV repair is recommended as a class IIb recommendation regardless of MR grade because of the lack of evidence that supports the benefit of this procedure.

This review summarizes the recent studies on surgical intervention for ischemic MR, considering their interpretation and the issues and limitations associated with each procedure.

## Definition and evaluation of ischemic MR

The optimal criteria for defining severe secondary MR are controversial. Grigioni et al. [3] reported that ischemic MR is associated with a higher mortality risk, independent of baseline characteristics and degree of ventricular dysfunction, and that the mortality risk is related directly to the degree of ischemic MR, as defined by the effective regurgitant orifice area (EROA) and regurgitant volume (RVol). They suggested that total and cardiac mortality is proportionally associated with the degree of ischemic MR, defined as  $RVol \geq 30$  mL and  $EROA \geq 0.2$  cm<sup>2</sup>. They found that the magnitude of valve dysfunction worsening prognosis differs between primary and secondary MR. The 2014 AHA/ACC guidelines [15] distinguished primary and secondary MR, defining severe secondary MR as an EROA of 0.2 cm<sup>2</sup> and an RVol of 30 mL. However, in recent randomized trials, the CTSN [12, 13] used the grade of primary MR as their indicator of ischemic MR severity, and the new guidelines changed the definition of severe secondary MR from an EROA of 0.2 to 0.4 cm<sup>2</sup> and from an RVol of 30 to 60 mL based on the criteria used in CTSN randomized trials. A

regurgitant fraction (RF) > 50%, meaning that more than one-half the total LV stroke volume is lost backward into the left atrium, is assumed to be severe MR [16]. We should consider that the complex shape of EROA in secondary MR is often underestimated in its severity. Moreover, because the EROA and RVol values associated with secondary MR are dependent on LV volume and LVEF, severe secondary MR with RF > 50% at lower levels of EROA and RVol is possible. For this reason, a lesser degree of MR could have an important hemodynamic effect in ischemic MR patients whose LV is already damaged.

## Surgical intervention for ischemic MR

### MV repair vs. MV replacement for severe ischemic MR

Most studies show that severe ischemic MR is not usually improved by revascularization alone and that residual MR is associated with an increased mortality risk [11]. It is generally accepted that severe ischemic MR should be corrected at the time of CABG. MV repair using a downsized annuloplasty ring is the preferred surgical procedure for ischemic MR [17, 18]. Several observational studies have demonstrated the better efficacy of ring annuloplasty than MV replacement for improving perioperative mortality and mid- and long-term survival [19–21]. On the other hand, higher long-term mortality and a greater need for valve-related reoperations [22, 23] have also been reported. However, these were matched cohort studies rather than randomized studies, and bias undeniably affected their results. Wang et al. [24] reported in their meta-analysis of 13 studies that perioperative mortality was lower after MV repair; however, the long-term survival and reoperation rates did not differ between the groups, and recurrence of hemodynamically significant MR was more frequent in the MV repair group.

In 2016, the CTSN published the results of multicenter randomized trials on the surgical treatment of severe ischemic MR [12]. They reported no differences after 2 years, in the primary endpoint of reverse LV remodeling (change in LV end-systolic volume index from baseline) between patients who underwent MV repair vs. those who underwent MV replacement (mean changes from baseline,  $-9.0$  mL/m<sup>2</sup> and  $-6.5$  mL/m<sup>2</sup>, respectively). Furthermore, they found no significant differences in 2-year mortality (19.0% after MV repair and 23.2% after MV replacement), rates of serious adverse events, and overall readmissions. Patients in the MV repair group had more heart failure-related serious adverse events and cardiovascular readmissions. Patients who underwent MV repair had a significantly higher rate of recurrence of moderate or severe MR

at 2 years than patients who underwent MV replacement (58.8% vs. 3.8%).

As these studies suggest, the high rate of recurrent ischemic MR after MV repair may explain the lack of benefit of this procedure in terms of mid- and long-term survival, since recurrence confers a predisposition to heart failure, atrial fibrillation, and readmission. In contrast, replacement provides better long-term results in terms of freedom from reoperation and a lower risk of recurrence.

In ischemic MR, the coaptation of the leaflets is displaced apically due to tethering of the papillary muscle tips. Although the undersized annuloplasty ring reduces the lateral–septal diameter of the mitral annulus, it worsens posterior leaflet tethering because an undersized annuloplasty may shift the posterior annulus anteriorly without changing the distance between the papillary muscle tip and the posterior annulus. In addition to continuous LV remodeling after surgery, this augmented posterior tethering causes recurrent ischemic MR [1, 5, 7, 25].

Several echocardiographic risk factors for the recurrence of ischemic MR have been reported. Kron et al. [26] performed a subgroup analysis of the 116 patients

randomized to undergo MV repair in the CTSN trial and concluded that the mechanism for recurrence was largely MV leaflet tethering and that basal aneurysms and dyskinesias were strongly associated with moderate or severe recurrent MR. They concluded that patients who are at high risk of recurrent ischemic MR after MV repair can be treated more appropriately with MV replacement or more complex repair techniques that address leaflet tethering directly.

Capoulade et al. [27] reported that LV end-systolic diameter (LVESD)-ring size mismatch, which is a measure of the deviation of the normal spatial relationship between the LV and the MV apparatus, is associated with an increased risk of MR recurrence. Table 1 shows the representative risk factors associated with recurrent ischemic MR and their cutoff values. These factors reflect the degree of LV remodeling and the extent of tethering [26, 28–40]. Notably, in contrast to the poor performance of MV repair in terms of recurrence, the CTSN trial concluded that successful repair was associated with a greater degree of LV reverse remodeling than MV replacement. This may emphasize the importance of appropriate patient selection for a durable repair.

**Table 1** Risk factors associated with recurrent ischemic mitral regurgitation and their cutoff values

Echocardiographic parameters	Cutoff value
Transthoracic echocardiography	
Tenting area [29]	$\geq 2.5 \text{ cm}^2$
Tenting height [29]	$\geq 1 \text{ cm}$
Posterior tethering angle [29]	$\geq 45^\circ$
P3 tethering angle [30]	$\geq 29.9^\circ$
Anterior tethering angle [31]	$\geq 39.5^\circ$
Anterior/posterior tethering angle ratio [31]	$\geq 0.76$
Anterior leaflet excursion angle [31]	$\geq 35^\circ$
Distal anterior leaflet angle [31]	$> 25^\circ$
Interpapillary muscle distance [32]	$> 20 \text{ mm}$
MR grade [34]	Higher MR grade
LV end-diastolic diameter/body surface area [35]	$> 3.5 \text{ cm/m}^2$
LV end-systolic volume [35]	$\geq 145 \text{ ml}$
Systolic sphere index [36]	$\geq 0.7$
Myocardial performance index [36]	$\geq 0.9$
Wall motion score index [36]	$\geq 1.5$
Papillary muscle dyssynchrony [37]	$\geq 58 \text{ ms}$
LV basal wall [26]	Aneurysm/dyskinesias
Deceleration time [38]	$< 140 \text{ ms}$
Diastolic LV function [39]	Restrictive diastolic filling
Transesophageal echocardiography	
Mitral annular diameter [39]	$\geq 37 \text{ mm}$
Tenting area [40]	$\geq 1.6 \text{ cm}^2$
MR grade [40]	$\geq 3.5$

MR mitral regurgitation, LV left ventricular

## The role of MV repair for moderate ischemic MR

The indication for MV repair for moderate ischemic MR at the time of CABG is still controversial. Indications for the surgical treatment of moderate chronic ischemic MR were not highlighted in the recent European Society of Cardiology (ESC) guidelines [41], while only a class IIb recommendation of adding MV repair to CABG was included in the AHA/ACC guidelines [14] because there is no proven survival benefit. The presence of even mild-to-moderate chronic secondary MR in patients with ischemic heart disease is associated with a worse prognosis [3]. CABG alone may improve LV function and reduce ischemic MR in selected patients; however, an early persistent MR rate of 40% to 60% has been reported after isolated CABG in patients with mild-to-moderate ischemic MR [8–11]. Some observational studies indicate that ring annuloplasty is efficacious for moderate ischemic MR [42] and that it is associated with decreased residual MR and improved heart failure symptoms at follow-up.

Four randomized studies of surgery for moderate ischemic MR have been conducted [13, 43–45], three of which were designed to evaluate the long- and mid-term prognostic effect of CABG alone vs. CABG with concomitant MV repair. All failed to demonstrate any significant advantage of CABG plus MV repair in terms of short- or long-term survival; however, they did reveal some superiority to CABG alone. Since the patient populations varied among the three studies, the effect of adding MV repair may differ. We compared the differences in these studies below.

### Randomized studies of moderate ischemic MR

#### **Fattouch et al. [44]**

In 2009, Fattouch et al. reported the first randomized study comparing CABG alone and CABG plus MV repair for patients with moderate ischemic MR. The mean LV ejection fraction (EF) and LV end-diastolic diameter (LVEDD) were 43% and 58 mm in CABG patients and 42% and 59 mm in CABG + MV repair patients, respectively. Although there was no significant difference in 5-year survival, the MR grade improved in all of the CABG plus MV repair group patients vs. in only 40% of the CABG alone group patients. They reported improvement in New York Heart Association (NYHA) functional class, MR grade, LVEDD, LVESD, pulmonary artery pressure,

and left atrial size. They also performed exercise testing, which suggested that exercise exacerbated MR in patients undergoing CABG alone, as no patient who underwent concomitant MV repair experienced MR grade worsening while exercising.

#### **Randomized Ischemic Mitral Evaluation (RIME) trial [45]**

Chan et al. reported the relatively short-term results of patients with moderate ischemic MR. The mean LVEF and LVEDD were 40% and 57 mm in both the CABG and CABG + MV repair group patients, respectively, although they found no significant difference in 1-year survival, with improved MR grade in all but one patient (96%) in the CABG plus MV repair group vs. only 50% of the CABG alone group patients. They reported improved peak oxygen consumption, MR grade, LVESD, and plasma B-type natriuretic peptide levels in patients undergoing MV repair.

#### **CTSN randomized trial [13]**

Most recently, the CTSN randomized trial of 301 patients with moderate ischemic MR demonstrated no difference at 2 years in the primary endpoint of reverse LV remodeling between patients who underwent CABG alone and those who underwent CABG plus MV repair. Moreover, no difference was found between the groups in 2-year survival, overall adverse events, and readmissions, although MR grade was more frequently improved in the CABG plus MV repair group (89% of patients) than in the CABG alone group (68% of patients). They also reported that neurologic events and supraventricular arrhythmias were more frequent in the CABG plus MV repair group. The mean LVEF and LVEDD were 41% and 54 mm in the CABG group patients and 39% and 54 mm in the CABG + MV repair group patients, with the mean LV diameter being the smallest among the three randomized trials. It is notable that the percentage improvement in the infero-lateral wall motion and global wall motion scores was greater in patients who were free of moderate or severe MR after 2 years than in those with residual MR.

The Fattouch et al. and RIME studies suggested that the lack of LV reverse remodeling was closely associated with residual MR at follow-up. However, the CTSN trial suggested that a lack of LV reverse remodeling occurs not only from residual MR but also from a lack of improvement in LV wall motion after revascularization. Penicka [9] et al. reported that improved moderate ischemic MR was achieved by isolated CABG only in patients with viable myocardium and an absence of dyssynchrony between the papillary muscles. LV dilatation after myocardial infarction is associated with the degree of injury, and several studies have reported the value of myocardial viability for predicting LV

remodeling. The mean LVEDD in the CTSN randomized trial was the smallest among the three studies, which indicates a milder degree of LV damage. The study showed that neurologic events and supraventricular arrhythmias were more frequent after MV repair, suggesting that some patients are negatively affected by the procedure.

CABG alone may be a sufficient and perhaps better option for patients with moderate ischemic MR and viable myocardium, especially in the infero-lateral wall. Concomitant MV repair may be effective for patients with moderate ischemic MR, minimal viable myocardium, a larger LV, and less probability of reverse LV remodeling after revascularization. The three randomized studies we reviewed reflect the importance of patient evaluation and selection, rather than completely invalidating this procedure for moderate ischemic MR.

### Functional mitral stenosis after ring annuloplasty

The annuloplasty ring is usually downsized by one or two sizes, and several authors have mentioned functional mitral stenosis after stringent ring annuloplasty. Magne et al. [46] reported that this restriction of the anteroposterior annulus distance creates a functional mitral stenosis and that a higher stress peak mitral gradient is correlated with higher systolic pulmonary artery pressure. These hemodynamic sequelae are associated with worse functional capacity. Kubota et al. [47] suggested that the MV area is significantly smaller than the calculated area of the implanted ring. They found that annuloplasty for ischemic MR causes frequent and significant mitral stenosis due to subvalvular diastolic tethering (Fig. 2). They concluded that this functional mitral stenosis after annuloplasty may be related to heart failure symptoms and that exercise exacerbated this phenomenon. Bertrand et al. [48] found that the transmitral gradient did not correlate with exercise capacity or pulmonary artery pressure because the transmitral gradient and functional capacity

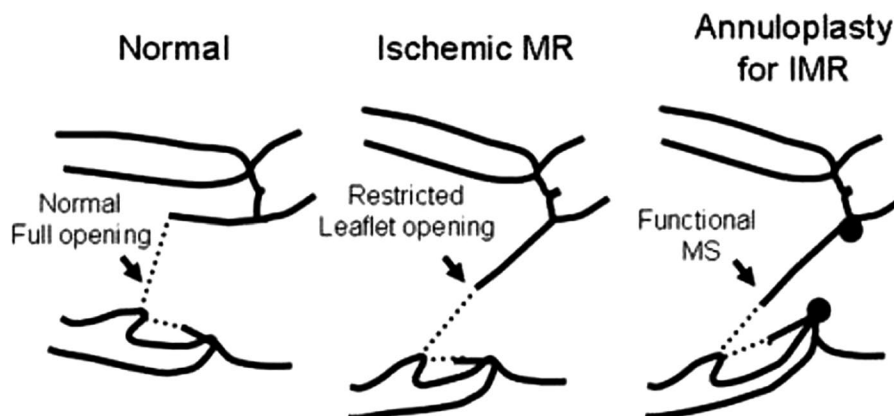
were calculated not only by the severity of mitral stenosis but also by hemodynamic factors, such as LVEF and cardiac output. They reported [49] that increased anterior leaflet opening during exercise is associated with a higher exercise-effective orifice area and that the indexed EOA (iEOA) at peak exercise is a strong predictor of exercise capacity and clinical outcomes.

As these reports suggest, restricted leaflet opening resulting from a reduced annular size and subvalvular diastolic tethering cause functional mitral stenosis. Therefore, exercise iEOA was significantly lower in patients who underwent restrictive annuloplasty than in those who underwent MV replacement, since iEOA depends on the transvalvular flow and is not influenced by the subvalvular tethering after MV replacement. Fino et al. [50] reported poorer exercise mitral hemodynamic performance and markedly elevated postoperative exercise systolic pulmonary arterial pressure after MV repair than after MV replacement. The CSTN trial also showed a trend toward greater improvement in the MV replacement group ( $p=0.07$ ) based on the Minnesota Living with Heart Failure Questionnaire, which may be due not only to the higher rate of recurrent MR, but also to functional mitral stenosis after MV repair.

### Subvalvular procedures

Although an undersized annuloplasty ring reduces the lateral–septal diameter of the mitral annulus, it does not relieve tethering of the mitral valve directly. As already mentioned, subvalvular tethering, both diastolic and systolic, impairs hemodynamic performance after stringent mitral annuloplasty. Since correction of the tethering during annuloplasty is an important issue that needs to be resolved, there is increasing interest in surgical techniques targeting the subvalvular apparatus, aimed to correct tethering and improve MV repair durability. Concomitant subvalvular procedures have the potential to achieve a less restrictive

**Fig. 2** Potential mechanism of functional mitral stenosis after surgical ring annuloplasty. Diastolic tethering reduces leaflet opening and results in functional mitral stenosis. *MS* mitral stenosis, *IMR* ischemic mitral regurgitation. Reproduced with permission from Kubota et al. [47]





ring annuloplasty and to limit subvalvular tethering, thereby limiting the reduction in posterior leaflet mobility and preventing functional mitral stenosis. The main procedures that are performed with ring annuloplasty are described in this section.

### Approximation of the papillary muscles

Anterior and posterior papillary muscle heads are approximated using a U-shaped stitch reinforced by two pledgets or an expanded polytetrafluoroethylene tube encircling the bodies of each papillary muscle and keeping them tightened together. In 2016, Nappi et al. [51] published the results of multicenter randomized trials examining the effect of papillary muscle approximation (PMA) on the long-term clinical outcomes of patients with ischemic MR. They reported a beneficial effect on the primary endpoint of reverse LV remodeling (change in LVEDD from baseline) vs. ring annuloplasty alone (mean changes from baseline,  $-5.8$  mm and  $-0.2$  mm,  $p < 0.001$ ). They also reported that the PMA group had a more effectively restored MV configuration and a lower moderate-to-severe MR recurrence rate at 5 years (27% in the PMA group vs. 56% in the annuloplasty alone group,  $p = 0.01$ ). However, they did not find significant differences in 5-year mortality or quality of life. Mihos et al. [52] also reported favorable changes in the subvalvular geometry and less MR recurrence in patients with secondary MR (including non-ischemic MR) undergoing an additional papillary muscle sling (approximation) than in those undergoing ring annuloplasty alone.

### Relocation of the papillary muscles

Kron et al. [53] reported 18 cases of ischemic MR complicated by inferior myocardial infarction, treated by posterior papillary muscle relocation with concomitant CABG and ring annuloplasty. This approach was performed with the heart arrested, and the posterior papillary muscle was relocated to just posterior to the right fibrous trigone. They concluded that direct relocation of the papillary muscles may be useful for patients with a minimally dilated LV or regional LV geometric changes. Fattouch et al. [54] performed a propensity score-matched cohort study comparing 55 patients who underwent bilateral papillary muscle relocation in conjunction with mitral annuloplasty with a true size annuloplasty ring, to patients who underwent an isolated annuloplasty with a ring downsized by two sizes. Papillary muscle relocation was accomplished by relocating the head of the anterior papillary muscle and both heads of the posterior papillary muscle to the corresponding mitral annulus. Their results showed reduced tethering in the relocation group, leading to a significant reduction in the incidence of recurrent MR (relocation group: 3.7%,

isolated annuloplasty group: 11.5%), 5-year cardiac-related deaths, and cardiac-related events. They suggest that mitral annuloplasty, with or without papillary muscle relocation, is indicated for patients with MR and an effective regurgitant orifice area  $\geq 20$  mm<sup>2</sup>. Langer et al. [55] relocated the posterior papillary muscle under transesophageal echocardiography guidance in loaded, beating hearts, through an aorto-mitral connection via the aortic wall, followed by repositioning of the posterior papillary muscle toward the mid-septal fibrous annulus. Their technique resulted in reduced tenting height and area, more freedom from MR  $>$  grade 2 at the 2-year follow-up (relocation group: 94%, isolated annuloplasty group: 71%), and reverse LV remodeling.

### Chordal cutting

Messas et al. [56] introduced the concept of chordal cutting in 2001. Remodeling after infarction distorts the base of the anterior leaflet, which is tethered by the secondary chordae. Cutting the secondary chordae of the anterior leaflet relieves the tethering and increases mobility of the anterior leaflet, leading to reduced MR. Calafiore et al. [57] performed a propensity-matched analysis of patients with ischemic MR whose coaptation depth was  $\leq 10$  mm and anterior leaflet bending angle was  $< 145^\circ$  and who underwent annuloplasty alone or annuloplasty plus a secondary chordal cutting procedure. They concluded that chordal cutting was associated with lower rates of MR recurrence and improved LVEF and NYHA functional class at mid-term follow-up. However, since the secondary chordae are attached to the ventricular side of the leaflet and enhance LV systolic pump function [58], whether this procedure, which interrupts the mitral–papillary annular continuity, affects long-term LV systolic performance is unclear.

### Surgical ventricular reconstruction

Surgical ventricular reconstruction (SVR) can restore the LV's shape and directly address tethering directly. Concomitant relocation or approximation of the papillary muscles can be performed with SVR when needed. SVR of the lateral wall excludes non-viable muscle between the anterior and posterior papillary muscles and reduces the distance between the papillary muscles, with similar effects to papillary muscle approximation [59]. Menicanti et al. [60] performed concomitant SVR and MV repair without an annuloplasty ring. They placed the purse-string suture in the transitional zone, close to the base of the papillary muscles, which imbricated the bases of the anterior and posterior papillary muscles when it was snared.

Mihos et al. [61] performed a meta-analysis of five studies covering 397 patients, including those mentioned above.

Compared with ring annuloplasty alone, ring annuloplasty plus subvalvular repair was associated with a lower MR grade at follow-up and a reduced risk of moderate-to-severe recurrent MR, greater reverse LV remodeling and LVEF, and improved MV apparatus geometry. Subvalvular procedures can be performed safely without increasing operative mortality or postoperative morbidity. However, there was no difference in survival during follow-up between the surgical approaches. The fact that a recurrence rate of 27% was observed even after the addition of PMA, as Nappi et al. [51] reported, underscores the complex nature of the disease and the difficulty in effectively preventing its recurrence. Although both Kron et al. [53] and Calafiore [57] et al. showed the effectiveness of subvalvular procedures, Kron et al. [53] concluded that relocation may be useful for patients with a minimally dilated LV, while Calafiore [57] considered chordal cutting procedures to be indicated for patients whose coaptation depth is < 10 mm, which they consider as the threshold for MV repair. More precise patient selection will help demonstrate the beneficial effects of these additional procedures.

### Importance of viability testing and stress testing

Ischemic MR is an LV disease, and evaluating LV status before surgery is critically important. As noted above, recurrence of MR after MV repair is associated with postoperative LV remodeling, and LV remodeling after revascularization is closely related to myocardial viability. Estimation of myocardial viability is most likely a key factor in predicting LV reverse remodeling after revascularization. Lund et al. [62] reported previously that an infarct size  $\geq 24\%$  of the LV area is an important threshold for predicting remodeling in patients with first reperfused myocardial infarction. Kim et al. [63] reported that the transmural extent of hyperenhancement by gadolinium using magnetic resonance imaging was significantly related to improvement in contractility, both global and regional, after revascularization.

Kalra et al. [64] reported that scar transmural extent in the region between the anterior and posterior papillary muscles was positively correlated with ischemic MR fraction (regurgitant flow divided by stroke volume). They also found that it is impairment of lateral shortening between the papillary muscles rather than passive ventricular size that determines the severity of MR. Chinitz et al. [65] also assessed the relationship between LV wall and papillary muscle infarction and ischemic MR and concluded that papillary muscle infarction extending in parallel to the adjacent LV wall injury, lateral wall injury, and greater MR are associated with lateral wall infarction.

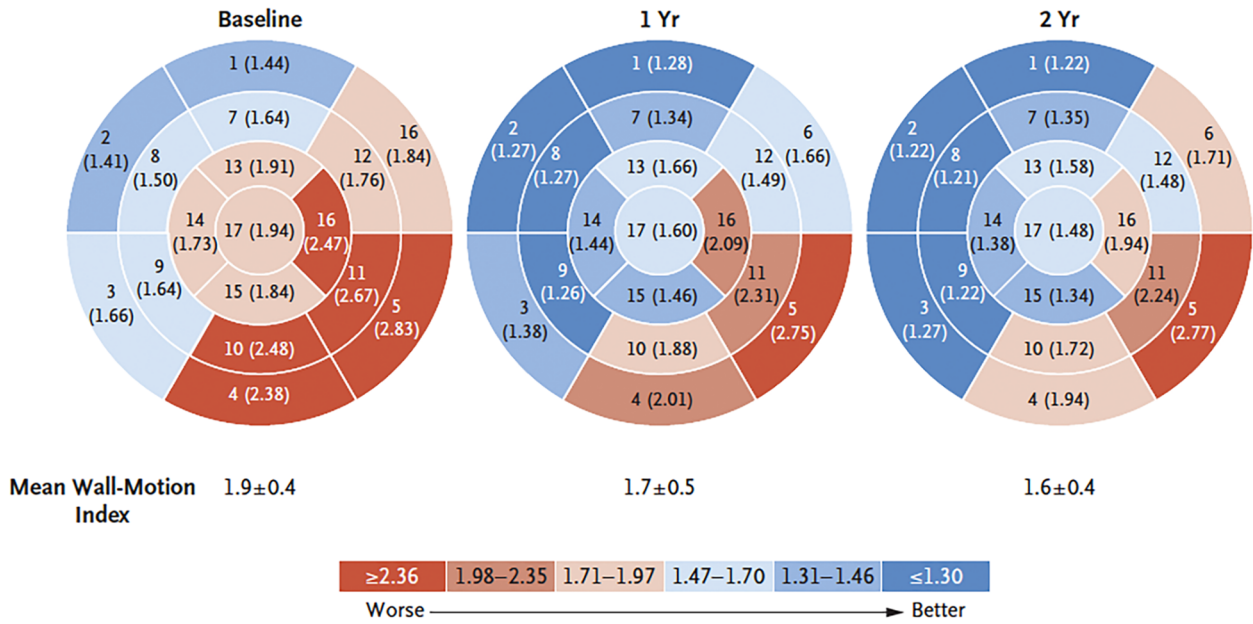
The CTSN randomized study of moderate ischemic MR [13] found that the percentage improvement in the infero-posterior lateral regional wall motion score was greater in patients who were free of moderate or severe MR, irrespective of concomitant MV repair. Their results suggest the prognostic importance not only of global viability, which predicts LV remodeling and functional recovery, but also of the regional viability of the infero-posterior wall where the papillary muscles function (Fig. 3). Viability testing also provides mortality risk stratification after MV surgery. Kusunose et al. [66] emphasized the importance of viable myocardium and complete revascularization in patients with significant ischemic MR undergoing MV intervention (including both MV repair and MV replacement) for better prognosis. They did not mention the relationship between prognosis and recurrence after MV intervention or comparison to sole CABG, but concluded that a preoperative total scar % < 25% improved survival if complete revascularization was achieved at the time of MV intervention. They also suggested that patients with total scar %  $\geq 25\%$  and significant ischemic MR were not likely to benefit from MV intervention and should be considered for advanced therapy, such as an LV assist device or heart transplant.

Stress testing is also useful for predicting the prognosis of patients with ischemic cardiomyopathy. The 2012 ESC guidelines [41] suggested that combined MV repair at the time of CABG for moderate ischemic MR be considered. When exercise echocardiography (ESE) is feasible, the development of dyspnea and increased severity of MR associated with pulmonary hypertension highlight the need for surgery. As ischemic MR is a dynamic condition, ESE may play an important role in its evaluation. The severity of ischemic MR at rest is unrelated to the magnitude of MR changes during ESE. Lancelotti et al. found [67, 68] that approximately one-third of patients with ischemic MR have a large increase in MR during exercise and that an elevation in the EROA by  $13 \text{ mm}^2$  during exercise is associated with an increased relative risk of death and heart failure. However, the value of ESE in predicting the results of surgery for ischemic MR needs to be investigated.

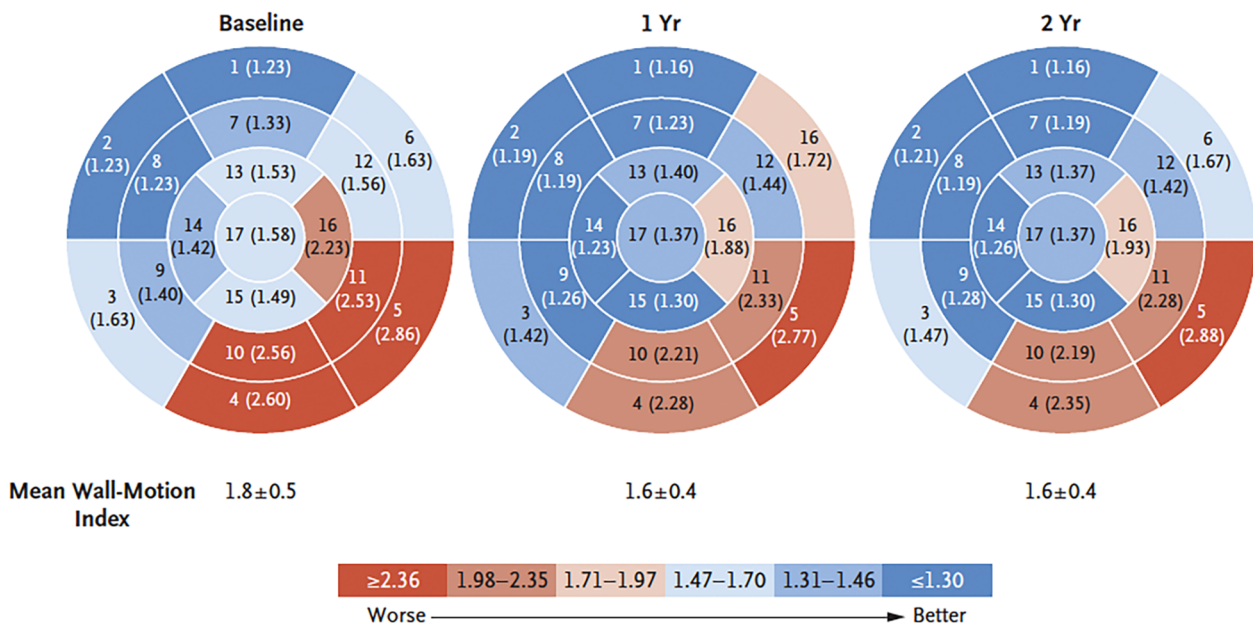
### Conclusion

Previous observational and randomized studies underscore the importance of a better understanding of the specific characteristics of LV disease in each patient, as well as the advantages and limitations of each procedure. Relieving ischemic MR does not resolve the problem of this complex LV disease completely, so it is important to identify which patients will benefit most from each surgical intervention,

**A No Moderate or Severe Regurgitation**



**B Moderate or Severe Regurgitation**



**Fig. 3** Wall motion score for patients without moderate or severe mitral regurgitation (MR) (upper panel) and those with moderate or severe MR (lower panel) after 2 years. The relative percent improvement in the global wall motion index, as well as in the infero-pos-

terior-lateral wall motion index, was greater for patients free of moderate or severe MR than for those with MR. Reproduced with permission from Michler et al. [13]

MV repair, with or without a subvalvular procedure, MV replacement, sole CABG, or more advanced therapy. Preoperative assessment of the LV status may help risk

stratification and assist with selecting the appropriate surgical procedure for each patient. A subanalysis of these randomized studies may also be helpful.



## Compliance with ethical standards

**Conflict of interest** All authors declare that they have no conflict of interest.

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