Review Article

Secondary mitral regurgitation surgical management: a narrative review

Sarah R. Eapen[1], Mina H. Zaky[2]^, Megan P. Kostibas[3], Michael P. Robich[4]

[1]Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, Cleveland, OH, USA; [2]Division of Cardiac Surgery, Department of Surgery, Yale School of Medicine, New Haven, CT, USA; [3]Division of Adult Cardiothoracic Anesthesiology, Department of Anesthesiology, Johns Hopkins School of Medicine, Baltimore, MD, USA; [4]Division of Cardiac Surgery, Department of Surgery, Johns Hopkins School of Medicine, Baltimore, MD, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Michael P. Robich, MD. Division of Cardiac Surgery, Department of Surgery, Johns Hopkins School of Medicine, 1800 Orleans St., Zayed 7107, Baltimore, MD 21287, USA. Email: mrobich4@jhu.edu.

Background and Objective: The most common valvular heart disease in the US is moderate to severe mitral regurgitation (MR). Function MR or secondary MR comprises many of these cases. Moderate and severe secondary MR are independently associated with increased all-cause mortality and rehospitalization for heart failure. Both ischemic and nonischemic cardiomyopathy can cause secondary MR via similar pathophysiology that leads to inadequate valve leaflets coaptation. The management of secondary MR is complex. The optimal treatment strategy for secondary MR remains controversial, reflected in the vast array of treatment options and the complexity of therapeutic decision-making. Several surgical mitral valve repair techniques have been described in the literature. Many of these aims to facilitate adequate valve leaflet coaptation. In this review, the pathophysiology of MR is described with a focus on evaluating and managing secondary MR.

Methods: A literature review was performed using PubMed and Google Scholar. Clinical trials, meta-analyses, randomized controlled trials, reviews, and systematic reviews were considered from January 1, 1995 through December 31, 2022. Articles published in languages other than English with limited text availability were excluded.

Key Content and Findings: Optimal therapeutic approach in severe secondary MR is complex and several patient factor should be considered. We provide a framework for the surgical management of secondary MR based on echocardiographic parameters, the presence of ischemia, and myocardial viability.

Conclusions: Further study is needed to guide the selection of patients most likely to benefit from mitral valve repair or replacement in the setting of secondary MR.

Keywords: Mitral regurgitation (MR); secondary MR; mitral valve repair; mitral valve replacement

Submitted Jan 03, 2024. Accepted for publication Jul 31, 2024. Published online Sep 24, 2024.

doi: 10.21037/cdt-24-6

View this article at: https://dx.doi.org/10.21037/cdt-24-6

^ ORCID: 0000-0002-1011-2108.

Introduction

Background

In the United States, mitral regurgitation (MR) is the most common cause of moderate and severe valvular heart disease in adults over the age of 55 years (1). Its estimated prevalence is 1.7% overall and 9.3% in patients over the age of 75 years (2). MR may be classified as primary or secondary. Primary MR occurs as a result of leaflet or chordal dysfunction (3). Secondary MR results from left ventricular (LV) or left atrial dysfunction (4,5). Annular enlargement and leaflet tethering lead to regurgitation in a structurally normal mitral valve. Secondary MR comprises 65% of cases, 60% of which are related to LV dysfunction (4). In patients presenting with acute decompensated heart failure and LV systolic dysfunction, the prevalence of moderate or greater secondary MR is estimated at 53% (2).

Moderate and severe secondary MR are independently associated with increased 1-year all-cause mortality and 6-month rehospitalization for heart failure.

Rationale and knowledge gap

Despite this mortality risk many of these patients do not undergo intervention due to the complexity of the disease and the controversy regarding optimal surgical approach (1,3). Additionally, multiple comorbities often accompany the presentation of secondary MR that largely increases the operative risk for these patients (1).

Further, there remains controversy as to the optimal therapy (3). Questions remain as how to identify the appropriate patients that would benefit from mitral valve repair? And what is the optimal surgical technique to address the driver of MR?

Objective

In this review, we describe the pathophysiology of MR and present a focused update on the literature regarding the surgical management of secondary MR. We also provide a decision algorithm to create a framework and to guide the selection of the optimal surgical strategy for the appropriately selected patients. We present this article in accordance with the Narrative Review reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-6/rc).

Methods

A literature review was performed using PubMed and Google Scholar. Clinical trials, meta-analyses, randomized controlled trials, reviews, and systematic reviews were considered from January 1, 1995 to December 31, 2022. Inclusion criteria beyond article type included articles written in English with full text availability. Exclusion criteria included articles written outside of the designated time frame in languages other than English with limited text availability. Specific search terms of interest were used to guide the literature review (*Table 1*).

Ischemic secondary MR

Ischemic secondary MR occurs following myocardial injury (1). Significant MR is observed in up to 30% of patients following myocardial infarction (6). LV remodeling leads to ventricular and mitral annular dilatation, papillary muscle displacement, and leaflet tethering with poor coaptation, as opposed to viable myocardium with normal annular diameter and adequate coaptating (*Figure 1A-1D*) (1). Early reperfusion in cases of ST-elevation myocardial infarction (STEMI) improves patient outcomes (7). Time to reperfusion determines the degree of myocardial necrosis, impact on LV function, and prevention of LV remodeling (8). The severity of ischemic MR correlates with myocardial viability. Viable myocardium in the infarction territory reduces LV remodeling and progression of MR. In acute STEMI, independent predictors of ischemic MR include multivessel coronary artery disease and low ejection fraction (7).

Analysis of coronary angiography data in patients with acute ischemic MR in the setting of STEMI revealed the culprit artery to be the left anterior descending coronary artery in 45%, the left circumflex coronary artery in 11%, and the right coronary artery in 44% (7). Patients with three-vessel coronary artery disease were significantly more likely to develop early ischemic MR (7). Patients with ischemic MR secondary to STEMI are also more likely to have significantly greater LV end-diastolic diameter index (LVEDDI) and lower ejection fraction. Clinically, patients with ischemic MR are more likely to present with advanced heart failure, have longer in-hospital treatment duration,

Table 1 Summary of the literature search strategy

Items	Specification
Date of search	01/01/2023
Databases and other sources searched	PubMed, Google Scholar
Search terms used	"ACC heart failure guidelines", "ACC mitral regurgitation management", "AHA/ACC guidelines valvular heart disease", "Atrial fibrillation mitral regurgitation", "Atrial functional mitral regurgitation", "Chordal cutting", "Chordal preservation", "Chordal sparing mitral valve replacement", "Functional mitral regurgitation", "Functional mitral regurgitation acute decompensated heart failure", "Functional mitral regurgitation reduced ejection fraction", "Ischemic mitral regurgitation", "Ischemic mitral regurgitation ST elevation myocardial infarction", "Left ventricular reverse remodeling ischemic mitral regurgitation", "Mitral leaflet tethering", "Mitral regurgitation recurrence", "Mitral transcatheter interventions", "Mitral valve annuloplasty", "Mitral valve annuloplasty coronary artery bypass grafting", "Mitral valve repair cardiomyopathy", "Mitral valve repair ischemic mitral regurgitation", "Mitral valve repair reduced ejection fraction", "Mitral valve surgery heart failure", "Mitral valve surgery severe left ventricular dysfunction", "Mitral valve translocation", "Moderate ischemic mitral regurgitation", "Papillary muscle approximation", "Posterior leaflet augmentation", "Posterior leaflet tethering", "Restrictive mitral valve annuloplasty ischemic mitral regurgitation", "Ring annuloplasty functional mitral regurgitation", "Secondary functional mitral regurgitation", "Secondary mitral regurgitation", "Severe ischemic mitral regurgitation", "Severe non-ischemic mitral regurgitation", "Transcatheter mitral valve repair", "Valvular heart diseases"
Timeframe	All published articles to 12/31/2022 were considered in our basic query
Inclusion and exclusion criteria	Articles published in English with full text availability were included
	Articles published in languages other than English with limited text availability were excluded
Selection process	The queries were conducted independently by S.R.E.

ACC, American College of Cardiology; AHA, American Heart Association.

and higher incidence of in-hospital mortality.

Non-ischemic secondary MR

Non-ischemic secondary MR may occur by either a ventricular or atrial mechanism. The ventricular mechanism is characterized by ventricular remodeling with LV dilatation and increased sphericity, which results in mitral valve leaflet tethering and annular dilatation (7). Ventricular remodeling also leads to papillary muscle displacement (9). Under normal physiologic conditions, tethering forces are perpendicular to the mitral annular plane. In the setting of papillary muscle displacement, tethering forces are shifted laterally, compromising leaflet coaptation. Tethering length is defined as the distance from the papillary muscle tip to the anterior mitral annulus and is the only independent predictor of MR in the setting of ventricular dysfunction (6). Common causes of non-ischemic secondary MR include dilated non-ischemic cardiomyopathy (myocarditis, fibrosis, alcohol, and most are idiopathic), hypertrophic cardiomyopathy, left atrial dilatation, and atrial fibrillation (1).

Atrial mechanism non-ischemic secondary MR occurs in the setting of atrial fibrillation, which is associated with left atriopathy (10). Atrial fibrillation leads to left atrial enlargement, annular dilatation, and secondary MR. Atrial secondary MR occurs in the setting of heart failure with preserved LV function. In comparison, ventricular secondary MR occurs due to LV dysfunction (11).

Severe chronic MR is a volume overload state that progresses to left atrial dilation and remodeling (12). Remodeling of the posterior mitral annulus leads to annular dilatation, leaflet malcoaptation, and MR regurgitation. Left atrial remodeling also predisposes patients to atrial fibrillation, which can lead to further left atrial and mitral annular dilatation and further worsen MR. In cases of isolated atrial fibrillation, the mitral leaflets and subvalvular apparatus are structurally normal. LV dimensions and function can be normal in these cases. Every 1 mm/m^2 increase in the anteroposterior diameter of the mitral annulus is associated with an odds ratio of 1.8 (95% confidence interval: 1.35–2.40) of significant MR correcting for age, hypertension, type of atrial fibrillation, left atrial dimensions, and LV function and dimensions (12). Gertz and colleagues demonstrated that mitral annulus dimension

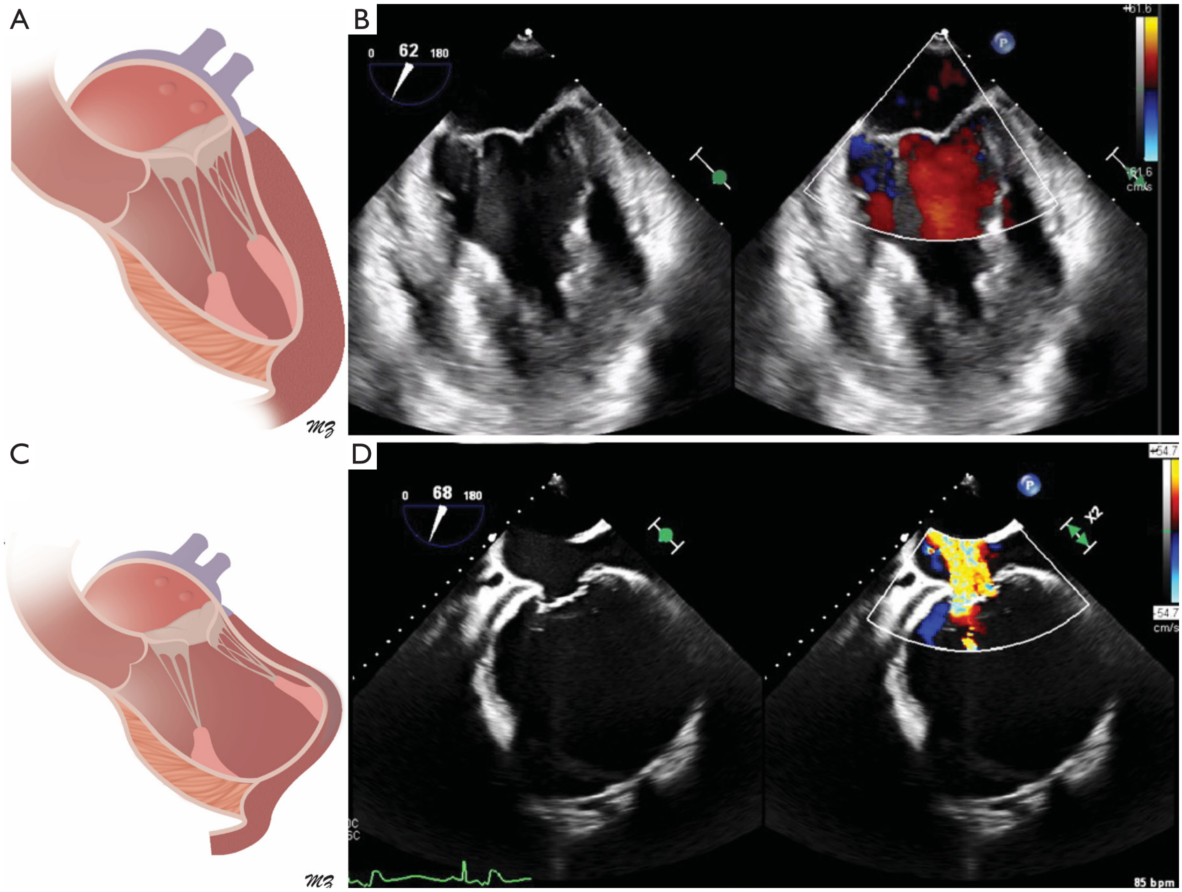

Figure 1 Normal left ventricle with appropriate mitral valve coaptation compared to a pathological dilated ventricle and annulus illustrating MR. (A) Normal mitral annulus, myocardium without ischemic disease, and adequate mitral valve coaptation. (B) TEE image of ME mitral commissural view showing normal mitral annulus, myocardium without ischemic disease, and adequate mitral valve coaptation. No regurgitation is seen in diastole. (C) Secondary MR in setting of LV disease demonstrating scaring and dilation caused by ischemic disease. This leads to ventricular and mitral annular dilatation, papillary muscle displacement, and leaflet tethering with poor coaptation. (D) TEE image of ME mitral commissural view of secondary MR in setting of LV disease demonstrating scaring and dilation caused by ischemic disease. MR, mitral regurgitation; TEE, transesophageal echocardiogram; ME, mid-esophageal; LV, left ventricular.

is the most significant determinant of MR in patients with atrial fibrillation (13). Atrial secondary MR because of progressive isolated annulus dilation can cause loss of central coaptation leading to a central jet MR (*Figure 2A,2B*) (14). These findings further support an atrial mechanism of secondary MR.

Silbiger and colleagues described the pathophysiology of atrial secondary MR as progressive left atrial and mitral annular dilatation causing displacement of the posterior mitral annulus onto the crest of the LV inlet (*Figure 3A,3B*) (15). This reduces the posterior mitral leaflet area available for coaptation and leads to an eccentric MR jet. In addition, posterior leaflet tethering results from increased distance between the posterior annulus and papillary muscle. Posterior mitral annular displacement leads to counterclockwise torque on the anterior mitral annulus along the intertrigonal axis. This causes papillary muscle tethering and tenting of the anterior mitral leaflet. The coaptation point is displaced below the annular plane into the left ventricle, which contributes to leaflet malcoaptation and MR.

Guideline-directed medical therapy (GDMT)

GDMT is often successful in reducing secondary MR and is the first step in treatment. GDMT for heart failure due to secondary MR includes beta blockers, diuretics, aldosterone

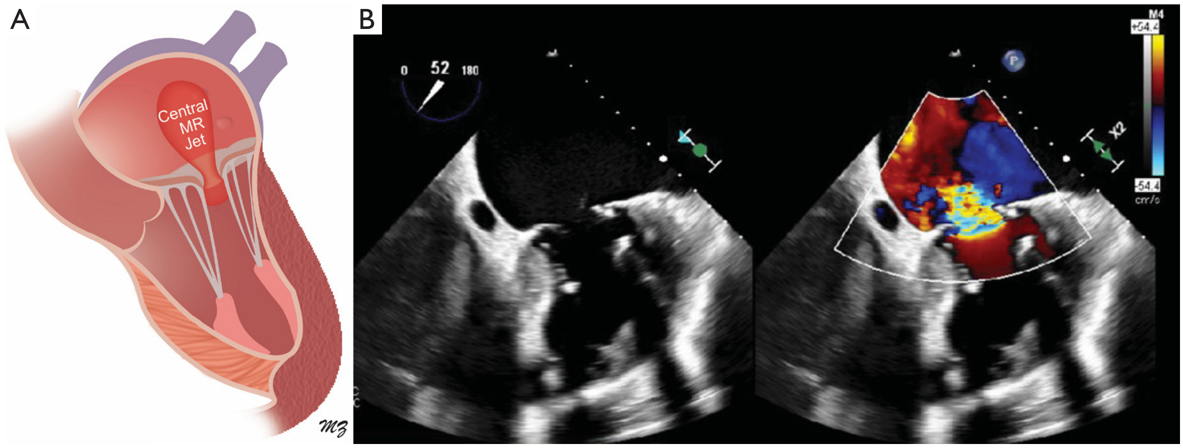

Figure 2 Left atrial dilation may be cause mitral annulus dilation loss of mitral valve coaptation leading to secondary MR. (A) Atrial secondary MR due to atrial dilation leads to mitral annulus dilation with loss of central coaptation of the leaflets causing a central MR jet. (B) TEE image of ME mitral commissural view of atrial secondary MR due to atrial dilation leads to mitral annulus dilation with loss of central coaptation of the leaflets causing a central MR jet. MR, mitral regurgitation; TEE, transesophageal echocardiogram; ME, mid-esophageal.

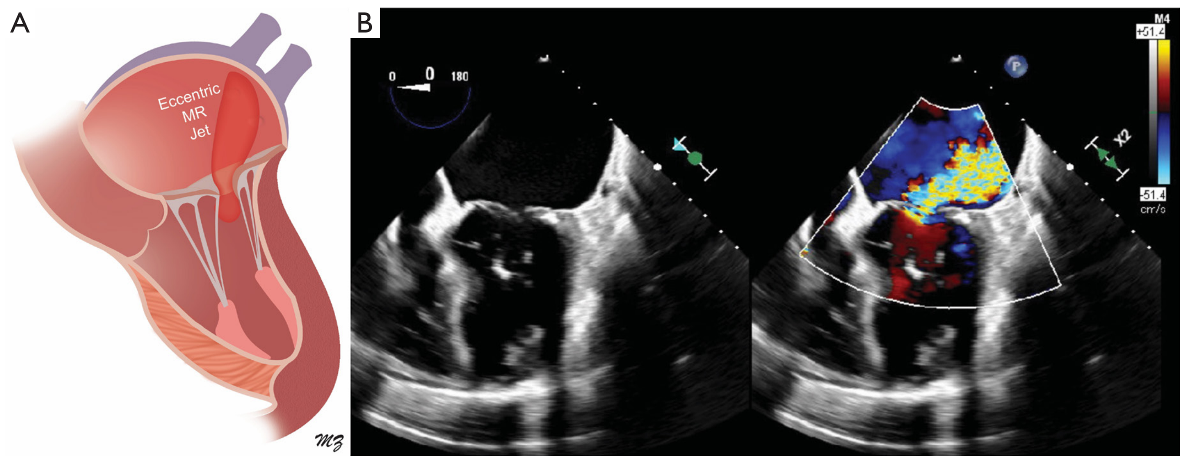

Figure 3 Left atrial dilation can lead to posterior mitral annulus displacement and loss of mitral valve coaptation leading to secondary MR with characteristic eccentric jet. (A) Atrial secondary MR due to progressive left atrial and mitral annular dilatation leading to displacement of the posterior mitral annulus onto the crest of the LV inlet. This presents with an eccentric jet. (B) TEE ME four chamber view of atrial secondary MR due to progressive left atrial and mitral annular dilatation leading to displacement of the posterior mitral annulus onto the crest of the LV inlet. This presents with an eccentric jet. MR, mitral regurgitation; TEE, transesophageal echocardiogram; LV, left ventricular; ME, mid-esophageal.

antagonists, angiotensin converting enzyme inhibitors, angiotensin receptor blocking agents, and sodium-glucose cotransporter-2 inhibitors. Nearly 40% of patients with heart failure with reduced ejection fraction and severe secondary MR can be successfully treated with medication (16). In comparison, approximately 20% of patients with non-severe secondary MR experience progression of MR despite GDMT (16). Optimization of GDMT prevents LV adverse remodeling and improves long-term prognosis (16).

Surgical management

Surgical mitral valve repair and replacement are considered if optimized GDMT does not relieve severe MR. While surgical intervention in patients with severe MR has been found to improve symptoms and quality of life, there is a complete lack of prospective data examining the value of surgical repair of secondary MR (17-19). Current guidelines have class IIb recommendation (level of evidence: B-NR) for mitral valve surgery in this setting. There is a pressing need for clinical studies comparing GDMT, surgery, and transcatheter edge-to-edge repair (TEER).

Management of ischemic MR at the time of coronary revascularization

Patients with ischemic or viable myocardium and severe ischemic MR require coronary artery bypass grafting (CABG) to reverse LV remodeling and improve ventriculo-mitral complex function and MR if they have suitable coronary anatomy (20). However, 40% to 50% of patients with severe secondary ischemic MR have persistent or worsening MR after revascularization alone. In this subset of patients, mitral valve repair or replacement is recommended in the setting of advanced New York Heart Association functional class at the time of coronary revascularization (21).

In patients with moderate secondary ischemic MR in the setting of multivessel coronary artery disease, mitral valve repair may be performed at the time of CABG (22-24). The Cardiothoracic Surgical Trials Network (CTSN) conducted a multicenter, randomized trial comparing CABG alone with combined CABG and mitral valve repair in patients with moderate ischemic MR. There was no significant difference in LV reverse remodeling, measured by LV end-systolic volume index (LVESVI), at 1- or 2-year follow-up. Mitral valve repair more durably corrected MR with a 2-year rate of recurrence (moderate or severe residual MR) of 11.2% in the combined CABG and mitral valve repair group *vs.* 32.3% in the CABG-alone group (P<0.001). However, combined CABG and mitral valve repair did not significantly improve survival or reduce overall adverse events or readmission. Combined CABG and mitral valve repair were also associated with increased risk of neurologic events and supraventricular arrhythmias (24,25).

Mitral valve repair *vs.* replacement for severe ischemic MR

The CTSN performed a multicenter, randomized controlled trial comparing mitral valve repair with an undersized restrictive complete rigid or semi-rigid annuloplasty and chordal-sparing mitral valve replacement in severe ischemic MR (26). Concomitant CABG was performed in three-quarters of enrolled patients. All patients were treated with GDMT. The primary endpoint of the trial was LV reverse remodeling at one and 2 years postoperatively, measured by LVESVI. Compared to mitral valve replacement, repair was found to be associated with higher rates of recurrent moderate or severe MR at 24 months (58.8% *vs.* 3.8%, P<0.001). However, there was no significant difference in LV reverse remodeling, major adverse cardiac or cerebrovascular events, functional status, quality of life, or survival between mitral valve repair and chordal-sparing replacement. This trial suggests that mitral valve replacement provides a more durable correction of severe ischemic MR and does not significantly impact clinical outcomes (19).

Several factors contribute to determination of the optimal therapeutic approach in severe secondary MR. Outcomes after operative intervention are related to LV dysfunction. There is some data that in patients with ejection fraction less than 30%, outcomes are substantially worse, specifically with mitral valve repair (27). Severe LV dysfunction (ejection fraction less than 30%) is observed in approximately 30% of patients with ischemic MR and contributes to surgical decision making (28). The extent of leaflet tethering and ventricular remodeling as well as the presence of concomitant coronary artery disease and atrial fibrillation are taken into consideration as well (29). One advantage of operative intervention for severe secondary MR is that it allows treatment of not only MR, but also coronary artery disease with CABG, atrial fibrillation with surgical ablation, and repair of significant tricuspid regurgitation.

Preoperative LV end-diastolic dimension (LVEDD) has been identified as the single best factor in predicting favorable LV reverse remodeling in patients with ischemic secondary MR undergoing restrictive mitral annuloplasty (29). For LVEDD, 65 mm has been identified as the optimal cut-off value to predict reverse remodeling with a sensitivity and specificity of 89%. Reverse remodeling was defined as a reduction in LVESVI of greater than 15%. In a study of patients with ischemic MR who underwent restrictive mitral annuloplasty with or without coronary revascularization, reverse remodeling occurred in the majority of patients and was predicted by preoperative LV dimensions (30). The clinical implication of this finding is that restrictive mitral annuloplasty with CABG is insufficient to ensure an adequate long-term outcome with LV reverse remodeling

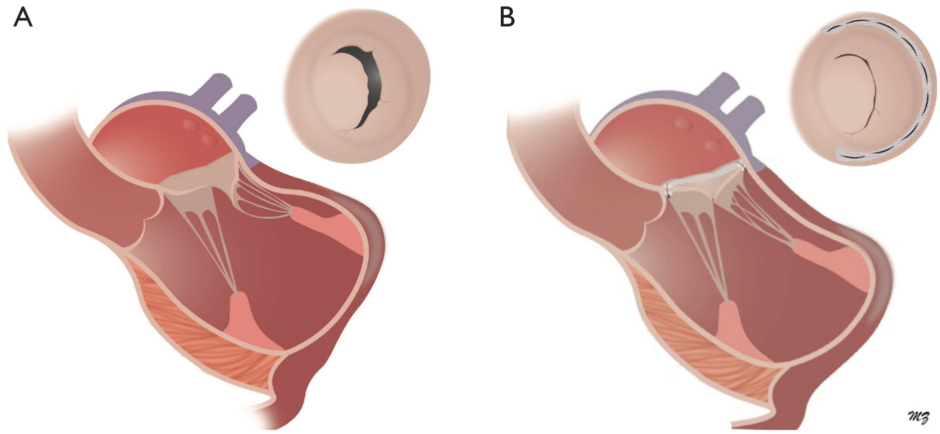

Figure 4 Restrictive annuloplasty mitral valve repair, corrects annular dilatation and flattening by reducing septolateral diameter. (A) Pre-operative annular dilation and mitral valve poor coaptation. (B) Post-operative mitral valve repair with restrictive annuloplasty resulting in adequate valve coaptation.

in patients with LVEDD greater than 65 mm. Patients with ischemic MR and dilated cardiomyopathy with LVEDD greater than 65 mm may require mitral valve replacement to address LV remodeling (31). The primary repair strategy for the treatment of secondary MR is restrictive mitral annuloplasty with an undersized, rigid complete annuloplasty ring (32).

Overview of mitral valve repair

Given the very high recurrence rate after restrictive mitral annuloplasty in patients with ischemic secondary MR, surgeons have explored adjunctive procedures. Approaches to mitral valve repair include restrictive annuloplasty, papillary muscle approximation, leaflet augmentation, mitral valve translocation, secondary chordal cutting, and TEER.

Surgical mitral valve repair techniques

Restrictive annuloplasty

In the setting of secondary MR, repair with a restrictive remodeling annuloplasty ring is an accepted approach to decrease annular dimensions, ensure coaptation, and abrogate MR (33,34). Restrictive annuloplasty corrects annular dilatation and flattening by reducing septolateral diameter (*Figure 4*). Restrictive annuloplasty is often performed by downsizing to two sizes smaller than the measured height of the anterior leaflet (20). Smaller annuloplasty ring size has been associated with greater likelihood of abolishing MR (35). Preoperative factors associated with MR recurrence after annuloplasty include lower LV ejection fraction, anterior leaflet tethering, and basal aneurysm or dyskinesis (36). In the CTSN study, only basal aneurysm was an independent predictor of recurrence. Rigid mitral annuloplasty decreases annular dimensions and enables coaptation. Although MR is usually eliminated operatively, the increase in coaptation is modest (32). If there is further ventricular adverse remodeling, further leaflet tethering leads to recurrence of MR. A subvalvular procedure at the time of restrictive annuloplasty may improve outcomes of mitral valve repair in ischemic MR (37).

Subvalvular repair

Papillary muscle approximation

Lateral and posterior papillary muscle displacement exerts tethering forces on both leaflets of the mitral valve. Papillary muscle approximation pulls papillary muscles together and thereby decreases mitral valve leaflet restriction (*Figure 5A,5B*). A randomized trial of patients with coronary artery disease and severe ischemic MR undergoing CABG compared isolated restrictive mitral annuloplasty and restrictive mitral annuloplasty with papillary muscle approximation. At 5-year follow-up, papillary muscle approximation was found to have a beneficial effect on LV remodeling and more effectively restored mitral valve geometry in ischemic MR. However, there was no significant difference in overall mortality or quality of life (38). Restrictive mitral annuloplasty is associated with similar midterm survival, but a higher rate of

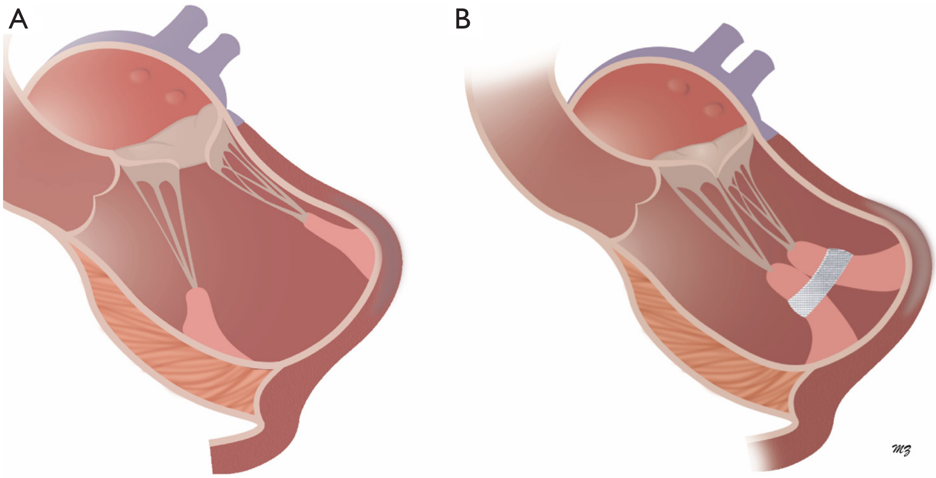

Figure 5 Papillary muscle approximation technique relieves the tethering forces on the mitral valve leaflets and reducing valve regurgitation. (A) LV and mitral annular dilatation, papillary muscle displacement, and poor coaptation. (B) Mitral valve repair using papillary muscle approximation technique, which pulls the papillary muscles together and thereby decreasing mitral valve leaflet restriction. LV, left ventricular.

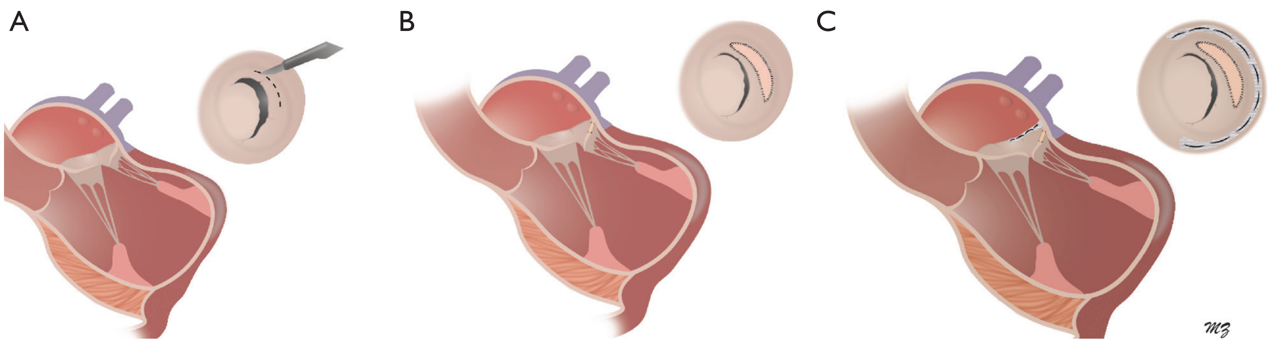

Figure 6 Mitral valve repair using the leaflet augmentation technique followed by ring annuloplasty. (A) Pre-operative annular dilation and mitral valve poor coaptation. (B) The pericardial patch is used to augment the mitral leaflet by increasing leaflet curvature thereby reducing tethering. (C) Restrictive annuloplasty further downsizes the septolateral diameter to ensure leaflet coaptation.

recurrent MR when compared with chordal-sparing mitral valve replacement (58.8% *vs.* 3.8%, P<0.001) and restrictive mitral annuloplasty with papillary muscle approximation (55.9% *vs.* 27%, P=0.01) (39). There is limited information to determine who to offer restrictive mitral annuloplasty and subvalvular repair with papillary muscle approximation.

In the REFORM-MR study, Pausch *et al.*, demonstrated that in addition to mitral annuloplasty a subannular repair option called papillary muscle relocation (PMR) in patients with ventricular secondary MR resulted in a low-rate recurrent severe MR (<5%) and a 1-year survival rate of 95.5% (40). Benefits of repair over replacement include lower perioperative morbidity, preservation of the native mitral valve apparatus, and avoidance of anticoagulation and prosthetic valve dysfunction.

Leaflet augmentation

Another approach aimed at achieving durable repair in secondary MR is posterior and/or anterior leaflet augmentation. In this approach, the mitral leaflet is augmented with a pericardial patch, followed by an undersized annuloplasty ring (*Figure 6*). Leaflet augmentation increases leaflet curvature and reduces tethering, thereby

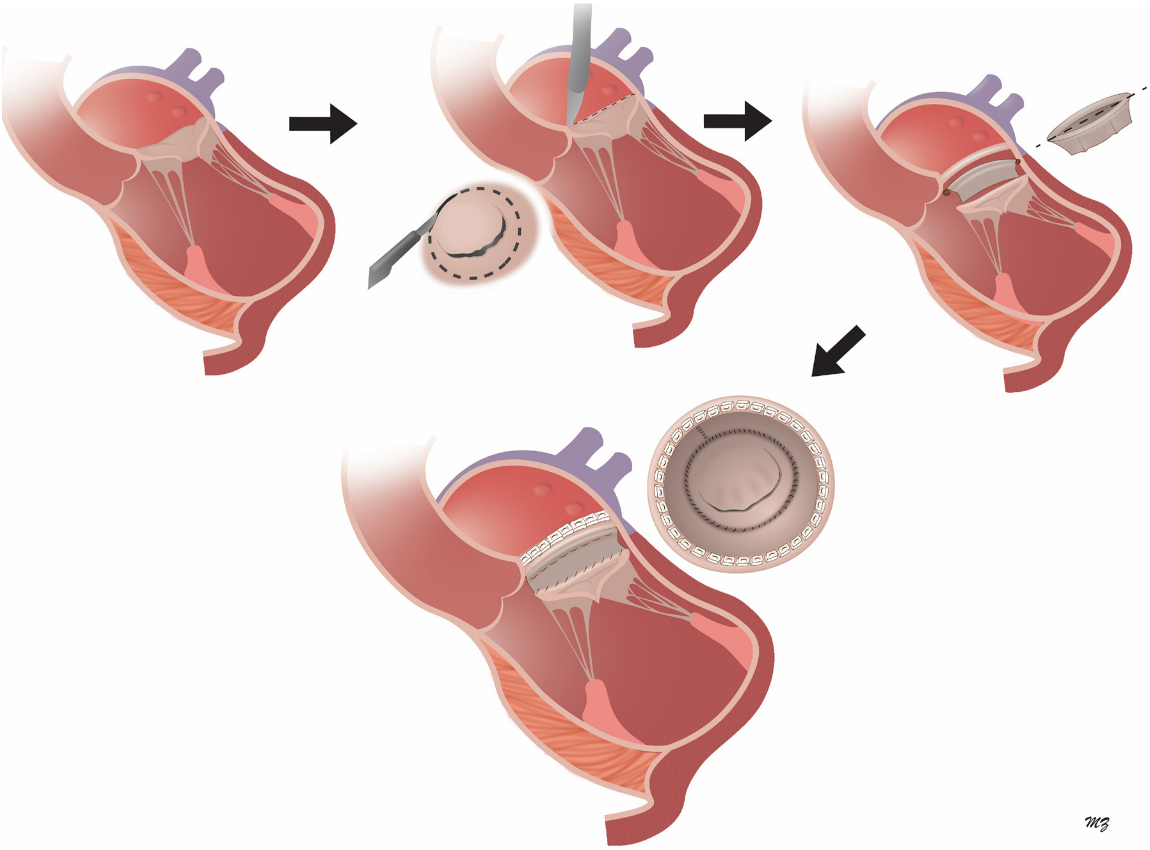

Figure 7 Mitral valve repair using the translocation technique. A frustum-shaped pericardial patch is sutured to the annulus and the native mitral valve is sutured to the ventricular end of the patch. Translocating the mitral valve leaflets apically and decreasing annular dimensions, creating supranormal coaptation, and relieving tethering.

reducing leaflet and chordal stress. In this way, leaflet geometry and bicuspid function are restored. Leaflet augmentation more completely addresses the underlying mechanism of ischemic MR and may improve mitral valve repair durability (41). In a study of 130 patients undergoing mitral valve repair with leaflet augmentation, 93% were in New York Heart Association class I or II heart failure at mean 28-month follow-up. There were 11 repair failures with a reoperation rate of 5.38% and no mortalities. Mitral leaflet augmentation allowed mitral valve leaflets to be reliably repaired with good midterm durability (42).

Mitral valve translocation

A novel technique designed to achieve durable repair of secondary MR is mitral valve translocation. This technique translocates the mitral valve leaflets apically (19,43). The mitral valve leaflets are incised *en bloc* at the annulus leaving the subvalvular apparatus intact. A frustum-shaped pericardial patch is sutured to the annulus and the native mitral valve is sutured to the ventricular end of the patch (*Figure 7*).

Mitral valve translocation works by decreasing annular dimensions, increasing effective leaflet surface area and creating supranormal coaptation, and relieving tethering. Increased coaptation with translocation may reduce risk of recurrent MR resulting from progressive adverse LV remodeling. Mitral valve translocation is more technically demanding than restrictive mitral annuloplasty and is associated with significantly longer cross-clamp time. To date, mitral valve translocation has only been reported at a single center and long-term data are lacking (43,44).

Secondary chordal cutting

Division of secondary chords, or chordal cutting, has

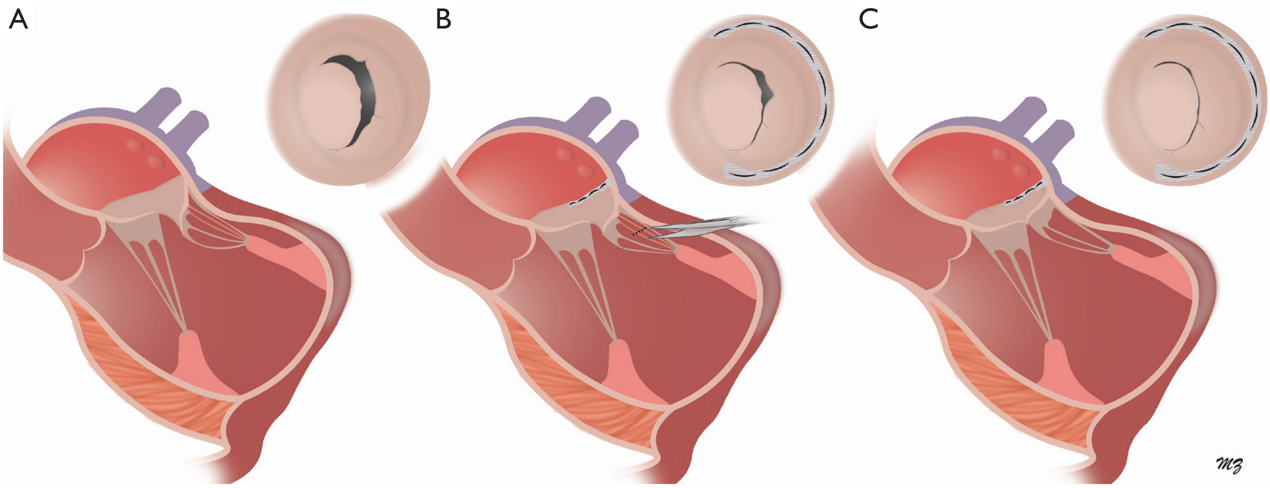

Figure 8 Division of secondary chords, or chordal cutting, may be used as a means of reducing mitral valve leaflet tethering and mitral. (A) Pre-operative annular dilation and mitral valve poor coaptation. (B) Restrictive annuloplasty further downsizes the septolateral diameter to ensure leaflet coaptation. (B,C) Division of secondary chords relieves tethering and allows for appropriate valve co-optation.

been described as a means of reducing mitral valve leaflet tethering and MR in patients with ischemic MR (45). Secondary chords to the anterior leaflet, posterior leaflet, and commissure arising from papillary muscle affected by infarcted myocardium are divided (*Figure 8*) (45). Secondary chords arising from normal papillary muscle are left intact (45). Affected papillary muscle may be identified by preoperative echocardiography or ventriculography (45). Secondary chordal cutting is performed prior to annuloplasty band insertion to optimize exposure (45). Cutting a limited number of critically positioned chordae to the leaflet that restrict closure improves coaptation and reduces ischemic MR (46).

A retrospective study comparing isolated mitral annuloplasty and secondary chordal cutting with mitral annuloplasty for ischemic MR found no significant difference in postoperative myocardial infarction, stroke, reoperation for bleeding, renal failure, or mortality. Chordal cutting was associated with greater anterior leaflet mobility (P=0.01) and lower rates of recurrent MR at 2-year follow-up (15% *vs.* 37%, P=0.03). In addition, chordal cutting did not adversely impact postoperative LV ejection fraction (10%±5% relative increase in ejection fraction in the chordal cutting group *vs.* 11%±6% in the isolated mitral annuloplasty group, P=0.9) (45).

TEER

TEER is a type of percutaneous transcatheter mitral valve repair used in the treatment of heart failure patients with secondary MR (47). It facilitates anterior-posterior edge-to-edge direct mitral leaflet approximation. The procedure is performed via femoral venous access with a steerable guide catheter under fluoroscopic and echocardiographic guidance. The guide is advanced transeptally and positioned over the mitral valve. The TEER delivery catheter is advanced until the TEER device exits the tip of the guide into the left atrium. The TEER device is oriented perpendicular to the mitral valve line of coaptation. The TEER device is opened and advanced across the mitral valve into the left ventricle. The device is then pulled back to grasp the mitral valve leaflets. Appropriate device position and residual MR are evaluated with echocardiography. Following successful placement, the device is closed and deployed. The catheters are then removed (48).

Two randomized controlled trials evaluated the safety and efficacy of edge-to-edge transcatheter mitral valve repair. The percutaneous repair with the MITRA-FR trial randomized patients to transcatheter mitral valve repair with GDMT or GDMT alone (49). There was no significant difference in all-cause mortality or heart failure hospitalization at 1 year in the MITRA-FR trial. The Cardiovascular Outcomes Assessment of the COAPT trial evaluated the safety and efficacy of transcatheter mitral valve repair in symptomatic patients with heart failure and moderate to severe secondary MR despite maximal GDMT. Interestingly, there was both a significant reduction in heart failure hospitalization and all-cause mortality at 24 months with transcatheter mitral valve repair compared to GDMT alone in the COAPT trial. Several authors have compared these two studies to understand why the outcomes were different. Durable reduction in MR, reduced rate of heart failure hospitalization, and improved functional capacity, quality of life, and survival were demonstrated with transcatheter mitral valve repair compared to GDMT alone at 36-month follow-up (50). In addition, its minimally invasive approach and limited interaction with native anatomy is associated with a high safety profile and expedited recovery (51). Based on the findings of the COAPT trial, TEER is Food and Drug Administration (FDA)-approved in moderate to severe secondary MR with a LV ejection fraction of 20% to 50%, LV end-systolic diameter less than 7 centimeters, and persistent symptoms despite optimized GDMT (52).

MR reduction with transcatheter mitral valve repair is anatomy-dependent and not always predictable. Favorable anatomy includes central mitral valve pathology between the A2/P2 scallops, mitral valve area ≥4.0 cm^2, normal leaflet thickness and mobility, no/minimal leaflet calcification, posterior leaflet mobile length ≥10 mm or classic isolated mitral valve prolapse (53). Further, this technique does not address the annular dilatation or subvalvular changes associated with secondary MR. Patient with prohibitive surgical risks with moderate to severe MR who meet the above-mentioned parameters should be evaluated by heart valve team for TEER intervention.

Chordal-sparing mitral valve replacement

In this technique, a triangular resection of the anterior leaflet is performed. Chordae tendineae attached to the ventricular surface of the remnant anterior leaflet are left intact. Inverting pledgeted sutures are passed through the mitral annulus, then passed through the sewing ring of the prosthetic valve and tied. If a mechanical valve is placed, the leaflets are oriented in an anti-anatomic position. If a bioprosthetic valve is placed, the stents must not impinge on the c or aortomitral curtain (54).

Mitral valve replacement with chordal preservation maintains LV geometry and improves early and late postoperative LV function compared to conventional mitral valve replacement (33,55,56). Chordal preservation also preserves annulo-ventricular continuity, preventing complications such as myocardial rupture (56).

Decision algorithm

The decision algorithm described in this review for the management of secondary MR begins with optimization of GDMT (*Figure 9*). Clinicians aim to achieve optimal GDMT within 3 to 6 months of the initial diagnosis of heart failure. GDMT is up-titrated to target or maximally tolerated doses. Reassessment of ventricular function with echocardiography occurs 3 to 6 months after optimized GDMT to determine the need for implantable cardioverter-defibrillator and cardiac resynchronization therapy (57). In patients with chronic severe secondary MR related to LV systolic dysfunction and persistent severe symptoms despite optimized GDMT, mitral valve surgery is considered (58). Patient with prohibitive surgical risks with moderate to severe MR who meet the above-mentioned parameters should be evaluated by heart valve team for TEER intervention.

A study of patients with MR and severe LV systolic dysfunction evaluated outcomes of isolated mitral valve surgery (59). Severe LV dysfunction was defined as an ejection fraction less than 35%. Mitral valve repair with restrictive annuloplasty was performed in 80% of patients and mitral valve replacement was performed in 20% of patients. Endpoints of the study included all-cause mortality from the time of mitral valve surgery, readmission for heart failure, and reoperation. Overall, both mitral valve repair and subvalvular apparatus preserving mitral valve replacement for MR with severe LV dysfunction groups experienced improvement in functional status and reduced admissions for heart failure. However, subgroup analysis demonstrated higher operative mortality associated with mitral valve operations for ischemic MR *vs.* other forms of MR. Higher operative mortality was particularly noted when the MR was due to restricted leaflet motion secondary to severe LV impairment (59).

In a prospective, randomized trial of mitral valve surgery in patients with New York Heart Association class II to IV heart failure with an average 23.9% LV ejection fraction, 30-day operative mortality was only 1.6%. Mitral valve surgery was found to be associated with LV reverse remodeling, evident in a significant reduction in LV end-diastolic volume, LV end-systolic volume, and LV mass index at 3, 6, 12, 18, and 24 months. The increase in LV ejection fraction was significant at 18 months (P=0.003). The increase in LV sphericity index was significant at 3, 6, 12, 18, and 24 months. The reduction in MR was significant at 6, 12, and 18 months. Recurrence of clinically

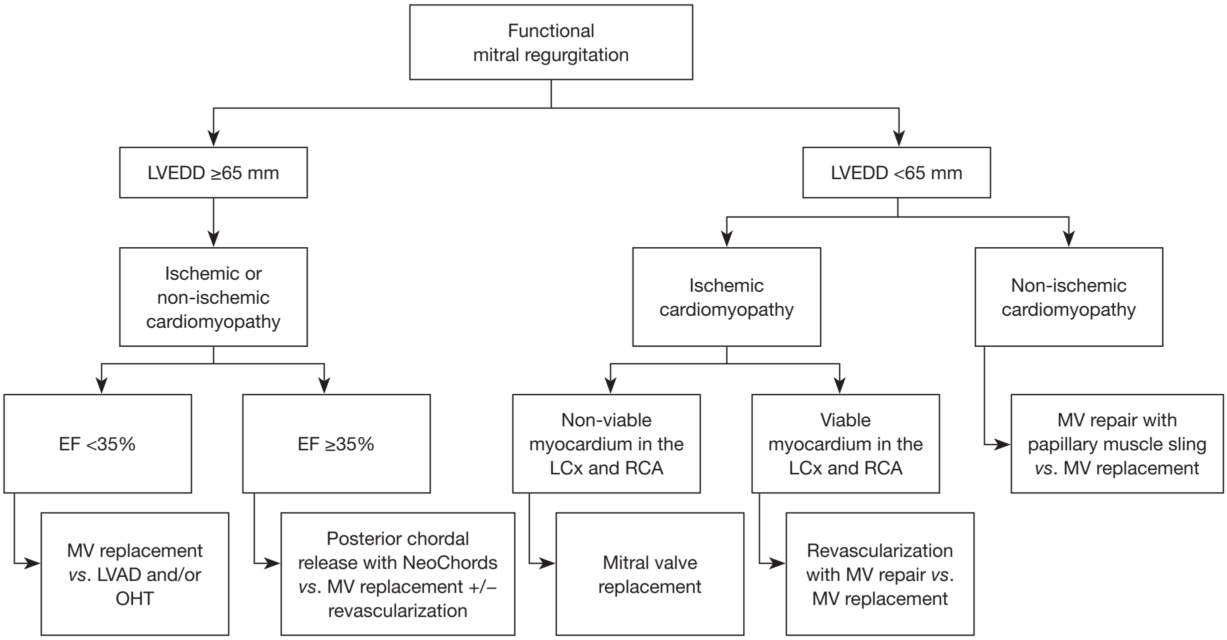

Figure 9 The decision algorithm for management of secondary MR based on echocardiographic assessment of LV function and of LVEDD in the setting of ischemic or non-ischemic cardiomyopathy. LVEDD, left ventricular end-diastolic diameter; EF, ejection fraction; LCx, left circumflex coronary artery; RCA, right coronary artery; MV, mitral valve; LVAD, left ventricular assist device; OHT, orthotopic heart transplant; MR, mitral regurgitation; LV, left ventricular.

significant MR was rare. In addition, quality of life, exercise performance, and New York Heart Association functional class were improved. Cumulative survival was 86.5% at 12 months and 85.2% at 24 months. The findings of this study support the benefit of mitral valve surgery for patients with severe secondary MR and heart failure on optimized GDMT (60).

In patients with persistent symptoms and LV dysfunction, echocardiographic assessment of LVEDD is performed. In patients with LVEDD equal to 65 mm or greater the decision is dependent on ejection fraction. If ejection fraction is greater than or equal to 35%, mitral valve repair with or without coronary revascularization is recommended. However, if ejection fraction is less than 35%, mitral valve replacement is recommended. As discussed above, LVEDD of equal to 65 mm or greater has been shown as a predictor of low likelihood of post-operative reverse remodeling occurring. Which is important in decreasing the stress on the valvular and subvalvular apparatus and crucial for a durable repair. Additionally, reduced pre-operative LV ejection fraction correlates with worse perioperative and long-term survival with mitral valve repair (27).

In young patient with severe symptomatic MR and severe LV dysfunction with LVEDD greater than 65 mm and ejection fraction of less than 35% should be appropriately worked up to determine their candidacy for heart transplantation. Destination LV assist device may be an alternative destination strategy for patients who are not transplant candidate.

In cases of LVEDD less than 65 mm, the decision-making is dependent on the whether the patient's cardiomyopathy is ischemic or non-ischemic in nature. In cases of ischemic cardiomyopathy with non-viable myocardium in the left circumflex and right coronary artery distribution, mitral valve replacement is recommended. This distribution of coronary disease results in permanent regional ischemia and dysfunction of the posterior papillary muscle causing medial sided leaflet tethering and negatively effects the durability of the repair. Additionally, as these patients usually require complex repair with restrictive annuloplasty and additional subvalvular intervention and myocardium protection can be limited. Therefore, long or multiple cardiopulmonary bypass runs during the operation in the context of this coronary disease distribution and a complex repair should be avoided. In cases of ischemic cardiomyopathy with viable myocardium in the left circumflex and right coronary artery distribution, revascularization with mitral valve repair *vs.* replacement is recommended. In the setting of non-ischemic cardiomyopathy, mitral valve repair *vs.* replacement is recommended.

While not specific to our review there is a high heterogeneity between the studies summarized throughout our review. Our aim was to present these studies in the context of our proposed algorithm that provides guidance to managing these diverse pathologies of MR. The variability in the length of follow-up in these studies complicates the assessment of durability of these procedures when compared to each other.

Conclusions

The optimal treatment strategy for secondary MR remains controversial, reflected in the vast array of treatment options and the complexity of therapeutic decision-making. An algorithm is provided to create a framework for surgical management based on echocardiographic parameters, the presence of ischemia, and myocardial viability. The decision to proceed with mitral valve operation may be considered following optimization of GDMT using a multidisciplinary team approach. Further study is needed to guide the selection of patients most likely to benefit from mitral valve repair or replacement in the setting of secondary MR. New techniques and technologies are being developed to further augment the options to manage this challenging clinical entity.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-6/rc

Peer Review File: Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-6/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-6/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: a population-based study. Lancet 2006;368:1005-11.
2. Kataria R, Castagna F, Madan S, et al. Severity of Functional Mitral Regurgitation on Admission for Acute Decompensated Heart Failure Predicts Long-Term Risk of Rehospitalization and Death. J Am Heart Assoc 2022;11:e022908.
3. Schmitto JD, Lee LS, Mokashi SA, et al. Functional mitral regurgitation. Cardiol Rev 2010;18:285-91.
4. O'Gara PT, Mack MJ. Secondary Mitral Regurgitation. N Engl J Med 2020;383:1458-67.
5. Levine RA, Schwammenthal E. Ischemic mitral regurgitation on the threshold of a solution: from paradoxes to unifying concepts. Circulation 2005;112:745-58.
6. Di Salvo TG, Acker MA, Dec GW, et al. Mitral valve surgery in advanced heart failure. J Am Coll Cardiol 2010;55:271-82.
7. Valuckiene Z, Budrys P, Jurkevicius R. Predicting ischemic mitral regurgitation in patients with acute ST-elevation myocardial infarction: Does time to reperfusion really matter and what is the role of collateral circulation? Int J Cardiol 2016;203:667-71.
8. Fu M, Chua S, Chang JP. Non-ischemic severe mitral regurgitation: When and how to operate? The role of echocardiography. J Med Ultrasound 2008;16:87-100.
9. Gertz ZM, Herrmann HC, Lim DS, et al. Implications of Atrial Fibrillation on the Mechanisms of Mitral Regurgitation and Response to MitraClip in the COAPT Trial. Circ Cardiovasc Interv 2021;14:e010300.
10. Hirji SA, Cote CL, Javadikasgari H, et al. Atrial functional

versus ventricular functional mitral regurgitation: Prognostic implications. J Thorac Cardiovasc Surg 2022;164:1808-1815.e4.
11. Lee EM, Shapiro LM, Wells FC. Importance of subvalvular preservation and early operation in mitral valve surgery. Circulation 1996;94:2117-23.
12. Delgado V, Bax JJ. Atrial Functional Mitral Regurgitation: From Mitral Annulus Dilatation to Insufficient Leaflet Remodeling. Circ Cardiovasc Imaging 2017;10:e006239.
13. Gertz ZM, Raina A, Saghy L, et al. Evidence of atrial functional mitral regurgitation due to atrial fibrillation: reversal with arrhythmia control. J Am Coll Cardiol 2011;58:1474-81.
14. Deferm S, Bertrand PB, Verbrugge FH, et al. Atrial Functional Mitral Regurgitation: JACC Review Topic of the Week. J Am Coll Cardiol 2019;73:2465-76.
15. Silbiger JJ. Does left atrial enlargement contribute to mitral leaflet tethering in patients with functional mitral regurgitation? Proposed role of atriogenic leaflet tethering. Echocardiography 2014;31:1310-1.
16. Nasser R, Van Assche L, Vorlat A, et al. Evolution of Functional Mitral Regurgitation and Prognosis in Medically Managed Heart Failure Patients With Reduced Ejection Fraction. JACC Heart Fail 2017;5:652-9.
17. Wu AH, Aaronson KD, Bolling SF, et al. Impact of mitral valve annuloplasty on mortality risk in patients with mitral regurgitation and left ventricular systolic dysfunction. J Am Coll Cardiol 2005;45:381-7.
18. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2438-88.
19. Goldstein D, Moskowitz AJ, Gelijns AC, et al. Two-Year Outcomes of Surgical Treatment of Severe Ischemic Mitral Regurgitation. N Engl J Med 2016;374:344-53.
20. Mihos CG, Santana O. Mitral valve repair for ischemic mitral regurgitation: lessons from the Cardiothoracic Surgical Trials Network randomized study. J Thorac Dis 2016;8:E94-9.
21. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2021;143:e35-e71. Erratum in: Circulation 2021;143:e228. Erratum in: Circulation. 2021;143:e784.
22. Chan KM, Punjabi PP, Flather M, et al. Coronary artery bypass surgery with or without mitral valve annuloplasty in moderate functional ischemic mitral regurgitation: final results of the Randomized Ischemic Mitral Evaluation (RIME) trial. Circulation 2012;126:2502-10.
23. Fattouch K, Guccione F, Sampognaro R, et al. POINT: Efficacy of adding mitral valve restrictive annuloplasty to coronary artery bypass grafting in patients with moderate ischemic mitral valve regurgitation: a randomized trial. J Thorac Cardiovasc Surg 2009;138:278-85.
24. Michler RE, Smith PK, Parides MK, et al. Two-Year Outcomes of Surgical Treatment of Moderate Ischemic Mitral Regurgitation. N Engl J Med 2016;374:1932-41.
25. Smith PK, Puskas JD, Ascheim DD, et al. Surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med 2014;371:2178-88.
26. Acker MA, Parides MK, Perrault LP, et al. Mitral-valve repair versus replacement for severe ischemic mitral regurgitation. N Engl J Med 2014;370:23-32.
27. Noack T, Marin Cuartas M, Kiefer P, et al. Isolated Mitral Valve Repair in Patients with Reduced Left Ventricular Ejection Fraction. Ann Thorac Cardiovasc Surg 2019;25:326-35.
28. Nappi F, Spadaccio C, Chello M, et al. Papillary muscle approximation in mitral valve repair for secondary MR. J Thorac Dis 2017;9:S635-9.
29. Badhwar V, Alkhouli M, Mack MJ, et al. A pathoanatomic approach to secondary functional mitral regurgitation: Evaluating the evidence. J Thorac Cardiovasc Surg 2019;158:76-81.
30. Braun J, Bax JJ, Versteegh MI, et al. Preoperative left ventricular dimensions predict reverse remodeling following restrictive mitral annuloplasty in ischemic mitral regurgitation. Eur J Cardiothorac Surg 2005;27:847-53.
31. Pang PYK, Huang MJ, Tan TE, et al. Restrictive mitral valve annuloplasty for chronic ischaemic mitral regurgitation: outcomes of flexible versus semi-rigid rings. J Thorac Dis 2019;11:5096-106.
32. Quinn RW, Pasrija C, Gammie JS. Secondary mitral regurgitation repair techniques and outcomes: Initial clinical experience with mitral valve translocation. JTCVS Tech 2022;13:53-7.
33. Bonow RO, O'Gara PT, Adams DH, et al. 2020 Focused Update of the 2017 ACC Expert Consensus Decision Pathway on the Management of Mitral Regurgitation: A Report of the American College of Cardiology

Solution Set Oversight Committee. J Am Coll Cardiol 2020;75:2236-70.
34. Mohebali J, Chen FY. Mitral valve repair for ischemic mitral regurgitation. Ann Cardiothorac Surg 2015;4:284-90.
35. Bolling SF, Pagani FD, Deeb GM, et al. Intermediate-term outcome of mitral reconstruction in cardiomyopathy. J Thorac Cardiovasc Surg 1998;115:381-6; discussion 387-8.
36. Kuwahara E, Otsuji Y, Iguro Y, et al. Mechanism of recurrent/persistent ischemic/functional mitral regurgitation in the chronic phase after surgical annuloplasty: importance of augmented posterior leaflet tethering. Circulation 2006;114:I529-34.
37. Mihos CG, Larrauri-Reyes M, Santana O. A Meta-Analysis of Ring Annuloplasty Versus Combined Ring Annuloplasty and Subvalvular Repair for Moderate-to-Severe Functional Mitral Regurgitation. J Card Surg 2016;31:31-7.
38. Nappi F, Lusini M, Spadaccio C, et al. Papillary Muscle Approximation Versus Restrictive Annuloplasty Alone for Severe Ischemic Mitral Regurgitation. J Am Coll Cardiol 2016;67:2334-46.
39. Nappi F, Lusini M, Avtaar Singh SS, et al. Risk of Ischemic Mitral Regurgitation Recurrence After Combined Valvular and Subvalvular Repair. Ann Thorac Surg 2019;108:536-43.
40. Pausch J, Harmel E, Reichenspurner H, et al. Subannular repair in secondary mitral regurgitation with restricted leaflet motion during systole. Heart 2023;109:1394-400.
41. Robb JD, Minakawa M, Koomalsingh KJ, et al. Posterior leaflet augmentation improves leaflet tethering in repair of ischemic mitral regurgitation. Eur J Cardiothorac Surg 2011;40:1501-7; discussion 1507.
42. Malhotra A, Majmudar S, Siddiqui S, et al. Midterm Results of Mitral Valve Repair With Pericardial Leaflet Augmentation: A Single-Center Experience. Semin Thorac Cardiovasc Surg 2020;32:433-40.
43. Gammie JS, Quinn RW, Strauss ER, et al. Initial Clinical Experience With Mitral Valve Translocation for Secondary Mitral Regurgitation. Ann Thorac Surg 2021;112:1946-53.
44. Pasrija C, Quinn RW, Bernstein D, et al. Mitral Valve Translocation: A Novel Operation for the Treatment of Secondary Mitral Regurgitation. Ann Thorac Surg 2021;112:1954-61.
45. Borger MA, Murphy PM, Alam A, et al. Initial results of the chordal-cutting operation for ischemic mitral regurgitation. J Thorac Cardiovasc Surg 2007;133:1483-92.
46. Messas E, Guerrero JL, Handschumacher MD, et al. Chordal cutting: a new therapeutic approach for ischemic mitral regurgitation. Circulation 2001;104:1958-63.
47. David TE. Ischemic mitral regurgitation: Chordal-sparing mitral valve replacement. Oper Tech Thorac Cardiovasc Surg 2012;17:194-203.
48. Abbott Cardiovascular. TEER Procedure with MitraClip Therapy. 2023 [cited 2024 Apr 30]. Available online: https://youtu.be/HdKLqTl9ZbQ?si=4O3XJLq6jxS1Biry
49. Srivastava CP, Naik RB. Mitral Valve Replacement with Total Chordal Preservation: The Eversion Technique. Cureus 2021;13:e15985.
50. Sasaki H, Ihashi K. Chordal-sparing mitral valve replacement: pitfalls and techniques to prevent complications. Eur J Cardiothorac Surg 2003;24:650-2.
51. David TE. Chordal preservation in mitral valve replacement. Oper Tech Thorac Cardiovasc Surg 1998;3:130-3.
52. Stone GW, Lindenfeld J, Abraham WT, et al. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. N Engl J Med 2018;379:2307-18.
53. Katz WE, Conrad Smith AJ, Crock FW, et al. Echocardiographic evaluation and guidance for MitraClip procedure. Cardiovasc Diagn Ther 2017;7:616-32.
54. Obadia JF, Messika-Zeitoun D, Leurent G, et al. Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation. N Engl J Med 2018;379:2297-306.
55. Mack MJ, Lindenfeld J, Abraham WT, et al. 3-Year Outcomes of Transcatheter Mitral Valve Repair in Patients With Heart Failure. J Am Coll Cardiol 2021;77:1029-40.
56. Winkel MG, Praz F, Wenaweser P. Mitral and Tricuspid Transcatheter Interventions Current Indications and Future Directions. Front Cardiovasc Med 2020;7:61.
57. Writing Committee; Maddox TM, Januzzi JL Jr, et al. 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2021;77:772-810.
58. Writing Committee Members; Otto CM, Nishimura RA, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol 2021;77:e25-e197.
59. Bishay ES, McCarthy PM, Cosgrove DM, et al. Mitral

valve surgery in patients with severe left ventricular dysfunction. Eur J Cardiothorac Surg 2000;17:213-21.
60. Acker MA, Bolling S, Shemin R, et al. Mitral valve surgery in heart failure: insights from the Acorn Clinical Trial. J Thorac Cardiovasc Surg 2006;132:568-77, 577.e1-4.

Cite this article as: Eapen SR, Zaky MH, Kostibas MP, Robich MP. Secondary mitral regurgitation surgical management: a narrative review. Cardiovasc Diagn Ther 2024;14(5):958-973. doi: 10.21037/cdt-24-6

