Mitral Valve Surgery for Congestive Heart Failure

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KEYWORDS

• Mitral valve disease • Mitral valve repair • Congestive heart failure • Mitral regurgitation
• Transcatheter device

KEY POINTS

- Mitral valve disease is a common cause of congestive heart failure. It can be categorized from the functional standpoint in mitral regurgitation, mitral stenosis, or mixed lesions.
- Every year approximately 22,500 patients undergo surgery for mitral valve disease. More than 95% of the mitral repairs and 75% of the replacements are performed to correct mitral regurgitation.
- An increased number of patients with mitral regurgitation who are considered either inoperable or at high risk for surgery are treated with transcatheter devices. More than 5000 patients received a transcatheter mitral procedure in 2016.
- Transcatheter mitral valve procedures is an evolving treatment modality that will likely expand the number of mitral valve procedures performed.
- Mitral valve disease can be categorized from the functional standpoint in regurgitant lesions, stenosis, or both.

INTRODUCTION

Mitral valve disease is a common cause of congestive heart failure.[1,2] It can be categorized from the functional standpoint in mitral regurgitation, mitral stenosis, or mixed lesions.

Every year approximately 22,500 patients undergo surgery for mitral valve disease.[3] More than 95% of the mitral repairs and 75% of the replacements are performed to correct mitral regurgitation. In addition, an increased number of patients with mitral regurgitation who are considered either inoperable or at high risk for surgery are treated with transcatheter devices.[3] More than 5000 patients received a transcatheter mitral procedure in 2016 (Society of Thoracic Surgery [STS]/American College of Cardiology [ACC] Transcatheter Valve Therapy Registry, personal communication, 2017). This is an evolving treatment modality that will likely expand the number of mitral valve procedures performed.

MITRAL REGURGITATION

Mitral valve regurgitation can be categorized based on its etiology as either primary (organic) or secondary (functional). This discussion is limited to chronic mitral regurgitation.

PRIMARY OR ORGANIC MITRAL VALVE REGURGITATION

In primary mitral valve disease, the regurgitation occurs as a consequence of a structural defect on the valvular apparatus (leaflets, chordae, or papillary muscles).[2] The most common etiology for primary mitral regurgitation is mitral valve prolapse secondary to either myxomatous degeneration or fibro-elastic deficiency[4] (**Fig. 1**). Other less common etiologies include rheumatic heart disease, infective endocarditis, connective tissue disorders, radiation, and congenital heart disease.

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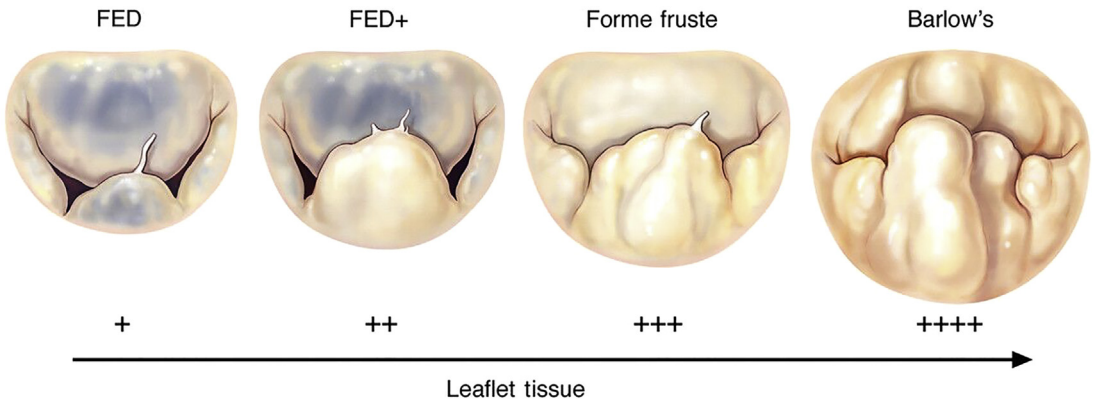

Fig. 1. Degenerative mitral valve disease ranges from fibroelastic deficiency (FED) to full myxomatous valve disease (Barlow disease). In FED, there is a deficiency of collagen with thin and almost transparent leaflets and 1 or more ruptured chordae. In myxomatous valve disease, the leaflets are diffusely thickened, redundant, with excess tissue with elongation or rupture of 1 or several chordae tendinea leading to leaflet prolapse or flail. +, increased amount of leaflet tissue. (*From* Adams DH, Rosenhek R, Falk V. Degenerative mitral valve regurgitation: best practice revolution. Eur Heart J 2010;31(16):1959; with permission.)

SECONDARY OR FUNCTIONAL MITRAL VALVE REGURGITATION

Secondary or functional mitral regurgitation is a ventricular disease in which there are no abnormalities of the mitral valve leaflet or subvalvular apparatus. The mitral regurgitation is secondary to remodeling and global or regional dysfunction of the left ventricle. Remodeling of the left ventricle leads to apical and lateral papillary muscle displacement with leaflet tethering that prevents coaptation and leads to mitral regurgitation (**Fig. 2**).[5–7] Annular dilatation plays a small role as a mechanism for the mitral regurgitation. Ischemic and nonischemic cardiomyopathy are the most common causes of functional mitral regurgitation.[8]

The presence of functional mitral regurgitation after a myocardial infarction and in patients with heart failure is a marker of poor prognosis.[9–12] It is associated with increased mortality, increased severity of heart failure symptoms, and increased rate of readmissions to the hospital. The severity of the regurgitation also affects the prognosis. Patients with mild to moderate functional (effective regurgitant orifice [ERO] 1–19 mm^2) had a 5-year survival of 49%, whereas patients with severe functional mitral regurgitation (ERO $\geq$20 mm^2) had a 5-year survival of 29%.[9–11] In functional mitral regurgitation, lesser regurgitant volumes have significantly more impact in prognosis than in patients with primary mitral regurgitation.

The pattern of annular dilation, leaflet tethering, and the direction of the mitral regurgitant jet differ with the etiology and severity of functional mitral regurgitation[13–16] (see **Fig. 2**). In ischemic cardiomyopathy, the initial ventricular remodeling occurs in the posterior-medial papillary muscle. Thus, the posterior-medial portion of the posterior leaflet (P3) is tethered and lower than the anterior, leading to a posteriorly directed mitral regurgitation jet (see **Fig. 2**, parts 1 and 2). This pattern is called "asymmetric tethering." Ischemia of the anterior wall of the left ventricle leads to functional mitral regurgitation in more advanced stages of ventricular remodeling than in patients with inferior infarction (more spherical ventricles with more tenting and lower left ventricular ejection fraction [LVEF]). Both papillary muscles are displaced laterally and apically, and therefore, both leaflets are tethered. The regurgitant jet is central. This pattern is called "symmetric tethering" (see **Fig. 2**, parts 3 and 4). Ventricular remodeling in nonischemic cardiomyopathy is also "symmetric," involving both papillary muscles and leading to a central regurgitation jet[13–16] (see **Fig. 2**, parts 3 and 4).

Because functional mitral regurgitation is a ventricular problem, reestablishing the competency of the mitral valve is not curative. In addition, there is no conclusive evidence that correcting functional mitral regurgitation improves survival.[17,18]

TREATMENT OF PRIMARY OR ORGANIC MITRAL VALVE REGURGITATION

The surgical treatment of organic mitral regurgitation is well established. Mitral valve repair is the preferred treatment for patients with mitral valve

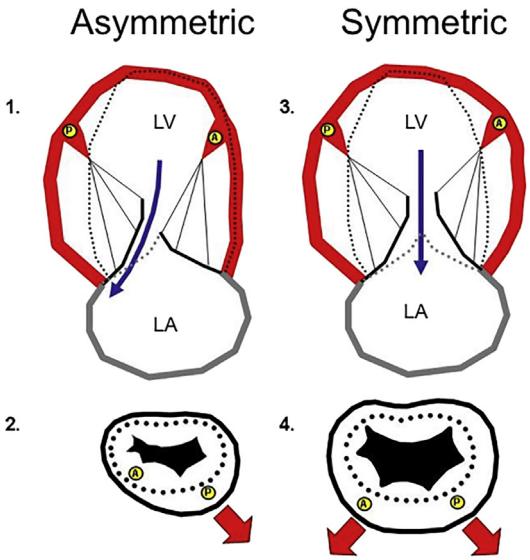

Fig. 2. Secondary or functional mitral valve regurgitation. LV remodeling with displacement of the papillary muscles leads to leaflet tethering and mitral regurgitation. The most common type is asymmetric (1, 2) with displacement of the inferior wall and postero-medial papillary muscle (P) with tethering of the posterior leaflet, dilatation of the postero-medial annulus, and posteriorly directed regurgitant jet. Symmetric tethering is seen in advanced ischemic cardiomyopathy or in nonischemic cardiomyopathy (3, 4). Both papillary muscles are involved and the jet is central. A, anterolateral papillary muscle; LA, left atrium. Dotted lines represent the normal status of the LV, the mitral leaflet in systole, and the mitral valve annulus. Blue arrow demonstrates the direction of the mitral regurgitation jet. *Red arrows* demonstrate the pattern of dilatation of the mitral annulus.

prolapse. Mitral valve repair can be achieved by several techniques, including leaflet resection, plication, neochordae insertion, and chord transposition reinforced with either a partial or complete annuloplasty ring.[19–21]

Mitral valve repair in organic mitral regurgitation is associated with a very low operative mortality and excellent long-term results.[19–21] Mitral valve repair cures primary mitral regurgitation and restores survival to the expected survival of a gender-matched and age-matched population[22,23] (**Fig. 3**). Compared with replacement, mitral valve repair is associated with lower operative mortality, improved left ventricular function, and improved long-term survival.[24] The long-term survival benefit of valve repair is seen in posterior and bileaflet prolapse, whereas the survival benefit in the less common isolated anterior leaflet prolapse repair is less clear[24] (**Fig. 4**). Mitral valve repair is a durable procedure. It is at least as durable as mitral valve replacement with a mechanical valve and far exceeds the durability of a biological valve. The annualized risk of reoperation varies by the leaflet subset: for posterior leaflet repair the risk is 0.5% per year, for bileaflet repair the risk is 0.9% per year, and for anterior leaflet repair the risk is 1.6% per year. All of them compare very favorably to the risk of reoperation with a mechanical valve: 0.66% per year (**Fig. 5**).[24]

The functional results are also good with freedom from +2 mitral regurgitation greater than 90% at 8 years (**Fig. 6**).[25,26]

Mitral valve replacement for organic mitral regurgitation is reserved for patients with complex sessions that cannot be reliably repaired and

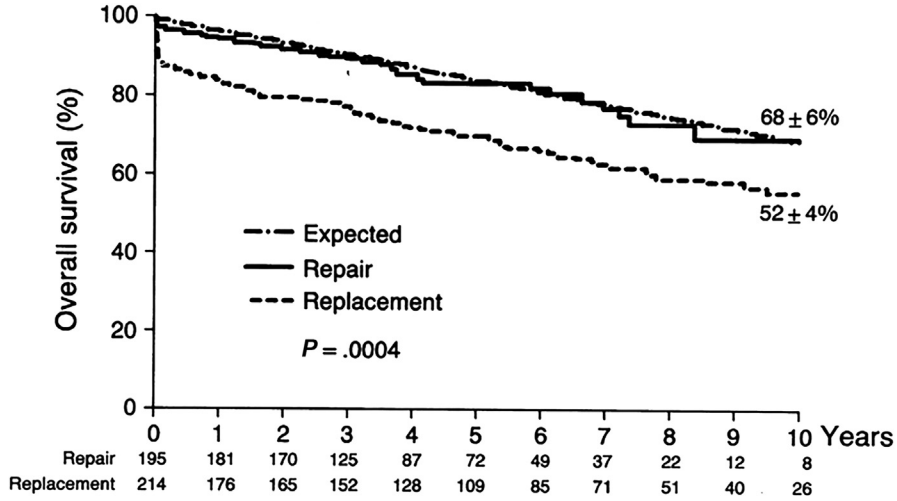

Fig. 3. Late survival following mitral valve repair (*solid lines*) or replacement (*dashed lines*) for degenerative mitral valve disease compared with expected survival (*dotted lines*). (*From* Enriquez-Sarano M, Schaff HV, Orszulak TA, et al. Valve repair improves the outcome of surgery for mitral regurgitation. A multivariate analysis. Circulation 1995;91(4):1023; with permission.)

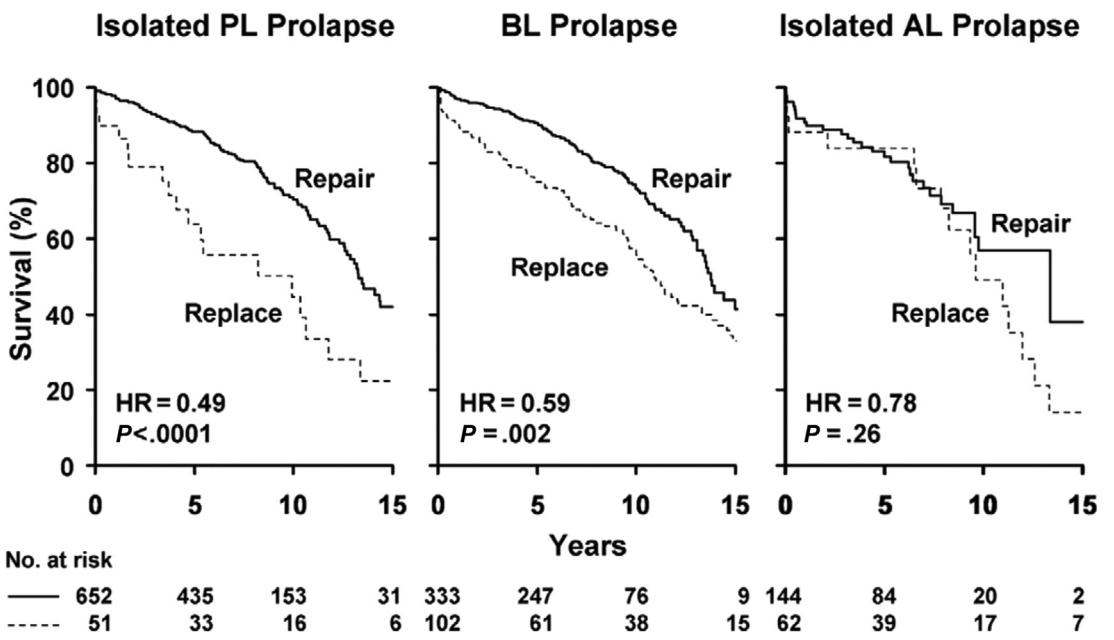

Fig. 4. Late survival among patients having mitral valve repair versus replacement for anterior (AL), posterior (PL), or bileaflet prolapse (BL). Solid line: valve repair; dashed line: valve replacement. HR, hazard ratio for survival of replacement group compared with repair group. (*From* Suri RM, Schaff HV, Dearani JA, et al. Survival advantage and improved durability of mitral repair for leaflet prolapse subsets in the current era. Ann Thorac Surg 2006;82(3):822; with permission.)

for failed repairs. Regardless of the reason, it is essential to maintain the mitral to left ventricular (LV) continuity by completely preserving the subvalvular apparatus that better preserves LV function, dimensions, and survival.[27,28]

Indications for mitral valve surgery in organic mitral regurgitation are well established in the American Heart Association (AHA)/ACC guidelines.[18] Severe mitral regurgitation is defined as (1) central jet of mitral regurgitation that occupies more than 40% of the left atrium or holosystolic eccentric jet mitral regurgitation, (2) vena contracta $\geq$0.7 cm, (3) regurgitant volume $\geq$60 mL, (4) regurgitant fraction $\geq$50%, (5) ERO $\geq$0.40 cm^2, (6) angiographic grade +3 to 4.[18]

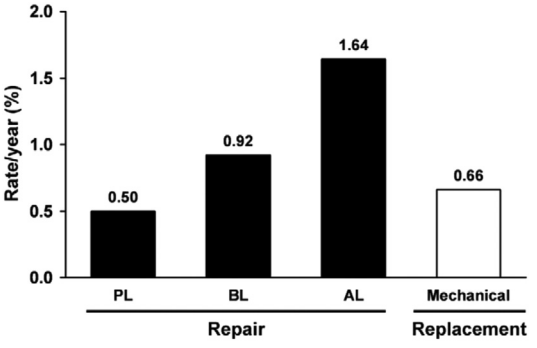

Fig. 5. Annual risk of reoperation for patients undergoing surgical correction of organic mitral regurgitation. Posterior leaflet repair (PL) has the lowest risk of reoperation, followed by mechanical valve replacement, bileaflet repair (BL), and anterior leaflet repair (AL). (*From* Suri RM, Schaff HV, Dearani JA, et al. Survival advantage and improved durability of mitral repair for leaflet prolapse subsets in the current era. Ann Thorac Surg 2006;82(3):825; with permission.)

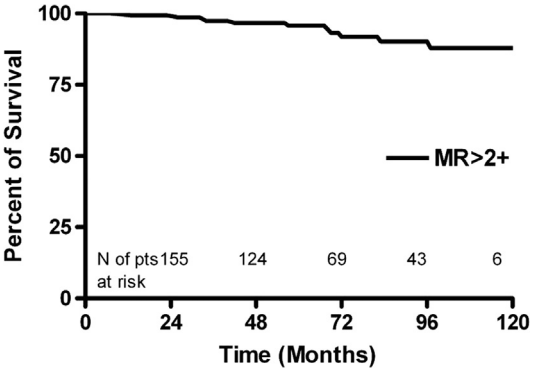

Fig. 6. Freedom from recurrent moderate (>2+) mitral regurgitation after mitral valve repair for organic mitral regurgitation. (*From* David TE. Outcomes of mitral valve repair for mitral regurgitation due to degenerative disease. Semin Thorac Cardiovasc Surg 2007;19:118; with permission.)

For patients with severe mitral regurgitation, mitral surgery is indicated when they became symptomatic (New York Heart Association [NYHA] functional class ≥2), or for asymptomatic patients when they develop LV dysfunction (LVEF ≤60%), LV dilation (LV end-systolic diameter ≥40 mm) atrial fibrillation, or pulmonary hypertension (systolic pulmonary artery pressure >50 mm Hg).[18] Mitral valve repair is also reasonable in asymptomatic patients with preserved ventricular function and dimensions when a successful and durable repair can be achieved with greater than 95% certainty and with an operative mortality less than 1% or when there has been a progressive increase in LV size or decrease in ejection fraction (EF) on serial imaging studies.[18] Concomitant mitral valve repair should be consider in patients with moderate or severe organic mitral regurgitation who are undergoing cardiac surgery for other indications.[18] Mitral valve repair in patients with less than severe mitral regurgitation is an area of ongoing research.[29]

TREATMENT OF SECONDARY OR FUNCTIONAL MITRAL VALVE REGURGITATION

Medical Management for Functional Mitral Valve Regurgitation

The severity of functional mitral regurgitation and clinical presentation are dynamic and are significantly influenced by the ventricular loading conditions. Optimizing the preload and afterload with guideline-directed medical therapy, including diuretics, beta blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, aldosterone antagonist, and cardiac resynchronization therapy (if indicated) is essential before deciding on surgical intervention.[5,6,17,18] Medical optimization decreases mitral regurgitation, pulmonary congestion, fluid overload, and myocardial ischemia.[5,6,17,18] Cardiac resynchronization therapy with biventricular pacing is indicated in patients with wall motion abnormalities and left bundle branch block resulting in improved LV function and wall motion abnormalities, increasing mitral closing force reducing or eliminating mitral regurgitation. The benefit of cardiac resynchronization therapy is more pronounced in patients with nonischemic cardiomyopathy.[5,6,17,18] It is reasonable to consider placing an epicardial pacing lead on the lateral wall of the LV in all patients at the time of mitral valve surgery.

Surgery for Functional Mitral Valve Regurgitation

The ideal goals of treatment in functional mitral regurgitation would be to restore competency of the valve and to stop or reverse the LV remodeling and dysfunction. Addressing the ventricular problem is as important as restoring the competency of the mitral valve. Although we have effective treatments to address the mitral regurgitation, an effective and predictable treatment for the LV remodeling and dysfunction is not yet available. Coronary revascularization to the ischemic myocardium should be undertaken when technically feasible. Although coronary revascularization with coronary artery bypass grafting (CABG) restores blood supply to the ischemic myocardium, improves long-term survival compared with medical therapy alone, and improves LV function, and reverse remodels the LV, the effect on mitral regurgitation is uncertain.[30–33] In many cases, revascularization alone improves moderate and mild mitral regurgitation.[33] However, there are no well-established predictors that allow for the identification of those patents in advance. Because of our inability to address the ventricular problem, it has never been demonstrated that reducing or eliminating mitral regurgitation alters the natural history of the underlying LV disease or that it improves survival.[17,18]

Mitral Valve Repair for Functional Mitral Valve Regurgitation

Mitral valve repair with a restrictive annuloplasty has been the treatment of choice to address functional mitral regurgitation for many years.[34–36] Mitral annuloplasty restores leaflet coaptation by reducing the anteroposterior distance and the valve area. The annuloplasty should be performed with a complete and rigid ring at least 1 or 2 sizes smaller than the size necessary to improve leaflet coaptation.[17,34–36] If the LV remodeling continues, further displacement of the papillary muscles will lead to further teetering and recurrent mitral regurgitation. The rate of mitral regurgitation recurrence after mitral valve repair with a restrictive annuloplasty is a very large rate (**Fig. 7**) with 10% to 20% rates of persistent mitral regurgitation early after operation and with 50% to 70% rates of recurrent mitral regurgitation at 5 years[5,37]

Multiple annuloplasty rings have been designed to address the changes in annular shape associated with functional mitral regurgitation. However, there are no studies that prove their superiority.[38] Other adjuvant techniques, like division of secondary chordae,[39] placement of edge-to-edge stitches,[40,41] and reposition of papillary muscles,[42,43] have been advocated to improve coaptation and decrease the rate of recurrence. Long-term results and precise indications for those techniques are lacking.

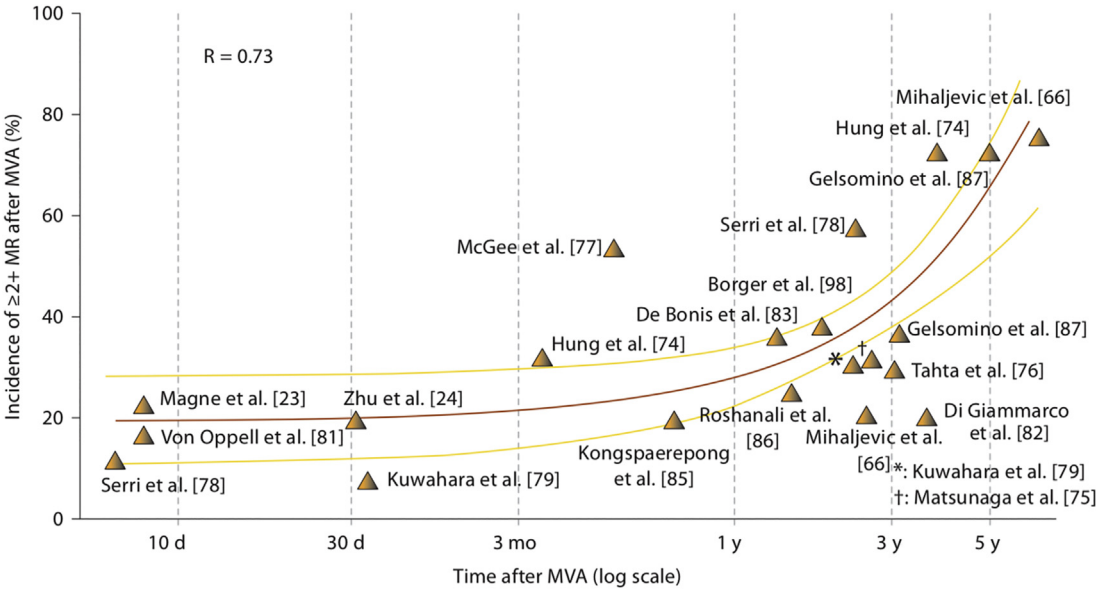

Fig. 7. Recurrence of greater than +2 mitral regurgitation after mitral valve annuloplasty (MVA) for ischemic mitral regurgitation. MR, mitral regurgitation. (*From* Magne J, Sénéchal M, Dumesnil JG, et al. Ischemic mitral regurgitation: a complex multifaceted disease. Cardiology 2009;112(4):244–59; with permission.)

Mitral Valve Replacement for Functional Mitral Valve Regurgitation

Mitral valve replacement provides a more durable correction of mitral regurgitation.[44] To prevent further deterioration of LV function, mitral valve replacement should be performed with preservation of the subvalvular apparatus of both the anterior and posterior leaflet.[27,28] Preservation of the subvalvular apparatus reduces LV systolic size and improves LV function compared with partial or no preservation.[27,28] Mitral valve replacement has been perceived for many years as detrimental to the short-term and long-term outcomes of patients with functional mitral regurgitation. Perceived disadvantages were longer operative times, increased operative mortality and morbidity, and worsened ventricular function secondary to the elimination of the continuity between the mitral annulus and the LV wall with the consequent decreased long-term survival. Many of these concerns were not supported by prospective randomized trials but by observational retrospective studies and metanalysis.[23,45,46] They were also encouraged by the demonstrated superiority of mitral valve repair over replacement for organic mitral regurgitation.[24] Other concerns associated with mitral valve repair were the need for anticoagulation to prevent thromboembolic complications, risk of endocarditis, and the durability of the valve prosthesis. In terms of durability, the median survival of patients with ischemic cardiomyopathy ranges from 6 to 7 years and more than 60% of the patients dead at 10 years.[30] Therefore, it is unlikely that these patients outlive a mitral bioprosthesis.

Repair or Replacement for Severe Functional Mitral Valve Regurgitation

The current ACC/AHA and the European guidelines recommend mitral valve surgery for symptomatic patients with severe ischemic mitral regurgitation who do not respond to medical therapy.[18,47] However, they do not specify how to select repair over replacement or whether one is superior to the other. There was no clear conclusive evidence in the literature that proved the superiority of one over the other until the Cardiothoracic Surgical Trials Network (CTSN) trial. The CTSN conducted a prospective randomized trial that examined mitral valve repair versus replacement for severe ischemic mitral regurgitation.[44] This is a landmark study that has changed the way we approach ischemic mitral regurgitation. The study randomized 251 patients with severe ischemic mitral regurgitation, LVEF of 40% and dilated LV (LV end-systolic volume index >60 mL/m^2) to mitral valve repair with a complete undersized ring or to chordal sparing valve replacement. The study showed that operative mortality was similar in repair and in replacement (4.0% in replacement vs 1.6% in repair P = .26). The 1-year and 2-year mortality, LV function, and degree of ventricular remodeling

was similar among the groups (Fig. 8).[44,48] However, the proportion of patients with recurrence of moderate to severe mitral regurgitation at 2 years was 12 times higher on the repair group (59% vs 3.9%, $P<.001$) as well as the rate of heart-failure–related adverse events and readmissions for heart failure.[44] Factors associated with the recurrence of moderate or severe mitral regurgitation in the repair group were (1) less reverse remodeling after surgery and (2) the presence of preoperative basal aneurysm or dyskinesis.[37,44] This study did not identify any other preoperative criteria that would predict the recurrence of mitral regurgitation and help discriminate between mitral valve replacement (MVR) and repair in patients with severe mitral regurgitation. Previous studies have identified severe tethering or significant LV dilatation (LV end diastolic size >6.5 cm) as predictors of recurrent mitral regurgitation.[5,8,17] Several retrospective studies had confirmed the findings that the nature of mitral valve surgery (repair or replacement) had no influence on long-term survival in ischemic mitral regurgitation.[45,49]

Management of Functional Mitral Valve Regurgitation in the Patient Who Needs Coronary Artery Bypass Surgery

The most common situation that the surgeon or cardiologist encounters is patients with coronary artery disease who need CABG and have functional mitral regurgitation. The severity of the mitral regurgitation and the decision to address it at the time of the surgery should be made with data obtained from the preoperative transthoracic echocardiogram.[8,17] The intraoperative transesophageal echocardiogram performed under general anesthesia downgrades the severity of the mitral regurgitation given the reduction in afterload induced by general anesthesia. Because ischemic mitral regurgitation is functional and depends on the loading conditions, a trial of guideline-directed optimal medical therapy should be attempted and the mitral regurgitation severity reevaluated before surgery. This medical therapy usually positively affects mitral regurgitation severity.[8,17]

The decision to perform concomitant mitral valve surgery during the CABG procedure rests on several factors, including the severity of the mitral regurgitation, the surgical risk, and the experience of the surgeon.

The addition of a mitral valve procedure to CABG is associated with increased operative mortality. Even though trial data showed that in centers of excellence, CABG with mitral valve repair or replacement can be performed with low operative mortality,[48] the mortality in the real world is much higher. The STS database shows that although the unadjusted operative mortality for CABG is a little more than 2%, the addition of mitral valve repair increases the mortality to 5% and the addition of MVR increases the mortality to 9.5%.[3] In addition, the experience of the surgeon counts. The median number of mitral valve procedures performed annually by surgeons in the United States is only 5 (range 1–166), and the probability of repairing the mitral valve increases with the number of mitral valve procedures performed by the surgeon and is associated with improved freedom from reoperation and long-term survival.[50,51]

The most important factor in deciding whether to address or not the mitral valve is the mitral regurgitation severity determined by the preoperative transthoracic echocardiogram.

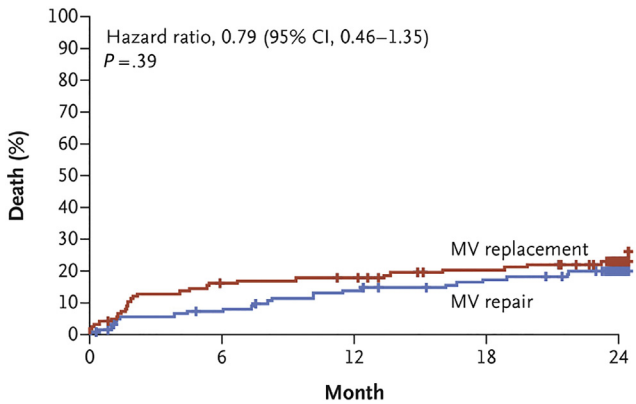

Fig. 8. Long-term survival of mitral valve repair versus replacement for severe ischemic mitral valve regurgitation: 2-year results of the CTSN trial. CI, confidence interval; MV, mitral valve. (*From* Goldstein D, Moskowitz AJ, Gelijns AC, et al. Two-year outcomes of surgical treatment of severe ischemic mitral regurgitation. N Engl J Med 2016;374(4):344–53; with permission.)

Although patients with severe mitral regurgitation will benefit from a mitral valve procedure to alleviate their symptoms and the benefit of the additional procedure will justify the risk, patients with mild mitral regurgitation should undergo CABG alone.

The management of patients with moderate mitral regurgitation is still controversial. Several questions arise in this group of patients: Is the risk of adding a mitral valve procedure justified? Are there clinical benefits associated with mitral valve repair? Does adding mitral valve repair improve symptoms, survival, and freedom from mitral regurgitation compared with CABG alone? Is there a role for MVR in this group? Does mitral valve repair prevent progression of mitral regurgitation and LV remodeling? Several of these questions were addressed in another landmark trial from the CTSN that was recently published.[52,53] In this trial, 301 patients with moderate ischemic mitral regurgitation were randomly assigned to CABG and mitral valve repair or CABG alone. Preoperatively, the mean LVEF was 40% and the LV end-systolic volume index was 55 mL/m^2. Mitral valve repair was performed with a complete annuloplasty ring and prolonged operative time and length of hospital stay. Mitral valve repair did not increase operative mortality but was associated with an increased rate of neurologic events and supraventricular arrhythmias. At 2 years, the prevalence of moderate or severe mitral regurgitation was higher in the CABG-alone group than in the combined-procedure group (32.3% vs 11.2%, $P<.001$); only 2% of patients in the CABG-alone group and none in the combined-procedure group had severe mitral regurgitation. CABG alone or with mitral valve repair resulted in reverse remodeling of the LV and in improved LV function. Mitral valve repair did not lead to significant differences in heart failure symptoms, degree of LV reverse remodeling, changes in LV function, or survival at 2 years (Fig. 9). Patients without mitral regurgitation recurrence had large reverse remodeling and more improvement in the inferior posterior lateral wall motion. Patients with combined CABG-mitral valve repair had improved exercise tolerance.[52,53]

THE GUIDELINES: HOW TO APPROACH THE PATIENT WITH FUNCTIONAL MITRAL VALVE REGURGITATION

So how do we make sense of these data? There are several guidelines that address the indications for surgery in functional mitral regurgitation. They include the 2014 AHA/ACC guidelines and the European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines[18,47] and the recently published American Association for Thoracic Surgery (AATS) guidelines.[17] The AATS guidelines provide the most comprehensive recommendations that take into account the results of the most recent clinical trials. All guidelines recommendations are summarized in Table 1.

Severe Mitral Regurgitation

Severe mitral regurgitation will not improve with coronary revascularization alone. Therefore patients with severe mitral regurgitation undergoing CABG should have their mitral valve repaired or replaced. For patients with (1) severe ischemic mitral regurgitation with no targets for revascularization (or when revascularization is not indicated) or (2) severe nonischemic functional mitral regurgitation who remain symptomatic despite guideline-directed medical therapy, isolated mitral valve surgery can be considered. Isolated mitral valve

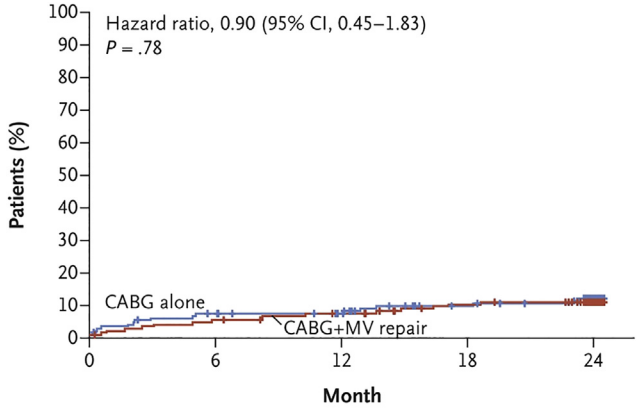

Fig. 9. Rate of death among patients undergoing either CABG or CABG plus mitral valve (MV) repair for moderate ischemic mitral regurgitation: 2-year results of the CTSN trial. CI, confidence interval. (*From* Michler RE, Smith PK, Parides MK, et al. Two-year outcomes of surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med 2016;374(20):1932–41; with permission.)

Table 1
Summary of the European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS), American Heart Association (AHA)/ American College of Cardiology (ACC), and American Association for Thoracic Surgery (AATS) guidelines for the management of patients with functional mitral regurgitation

Severity of Mitral Regurgitation	Type of Surgery Considered	2012 ESC/EACTS Guidelines (47)	2014 AHA/ACC Guidelines (18)	2017 AATS Guidelines (17)
Mild	CABG ± mitral valve surgery or isolated mitral valve surgery	There are no data to support surgical correction of mild mitral regurgitation.	Not addressed (*)	Not addressed (*)
Moderate	CABG ± mitral valve surgery	Surgery should be considered in patients with moderate MR undergoing CABG. *Class IIb, Level of Evidence C*	*Mitral valve repair* may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery *Class IIb, Level of Evidence* C	In patients with moderate ischemic mitral regurgitation undergoing CABG, mitral valve repair with an undersized complete rigid annuloplasty ring may be considered *Class IIb, Level of Evidence B*
	Isolated mitral valve surgery	Not addressed	Not addressed	Not addressed

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Table 1 (*continued*)

Severity of Mitral Regurgitation	Type of Surgery Considered	2012 ESC/EACTS Guidelines (47)	2014 AHA/ACC Guidelines (18)	2017 AATS Guidelines (17)
Severe	CABG ± mitral valve surgery	Surgery is indicated in patients with severe MR undergoing CABG, and LVEF >30%. *Class I, Level of Evidence C*	*Mitral valve surgery* is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR *Class IIa, Level of Evidence C*	*Mitral valve replacement* is reasonable in patients with severe ischemic mitral regurgitation who remain symptomatic despite guideline-directed medial and cardiac device therapy, and who have a basal aneurysm/dyskinesis, significant leaflet tethering, and/or severe LV dilatation (end diastolic diameter >6.5 cm) *Class IIa, Level of Evidence B*
		Surgery should be considered in symptomatic patients with severe MR, LVEF <30% option for revascularization and evidence of viability *Class IIa, Level of Evidence C*		*Mitral valve repair* with an undersized complete rigid annuloplasty ring may be considered in patient with severe IMR who remain symptomatic despite guideline-directed medical and cardiac device therapy and who do not have a basal aneurysm/dyskinesis, significant leaflet tethering, or severe LV enlargement *Class IIb, Level of Evidence B*
	Isolated mitral valve surgery	Surgery may be considered in patients with severe MR, LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated. *Class IIb, Level of Evidence C*	*Mitral valve surgery* may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D) *Class IIb, Level of Evidence B*	Not addressed

Repair vs. replacement	Not addressed	Not addressed	*Mitral valve replacement* for ischemic mitral regurgitation is performed with complete preservation of both anterior and posterior leaflet *Class I, Level of Evidence B* *Mitral valve repair* for ischemic mitral regurgitation is performed with small, undersized complete rigid annuloplasty ring *Class IIa, Level of Evidence B*

(*) It is not indicated.

Abbreviations: AVR, aortic valve replacement; CABG, coronary artery bypass surgery; CRT, cardiac resynchronization therapy; IMR, ischemic mitral regurgitation; LV, left ventricle; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NYHA, New York Heart Association.

Data from Refs.[17,18,47]

surgery should be considered cautiously on patients with very low LVEF (<30%), no targets for revascularization, or no viability because their operative risk is very high and the benefits may be limited. Those patients should be considered for mechanical circulatory support or heart transplantation.[54] In terms of the type of mitral valve surgery, the decision to repair or replace remains controversial given the high rate of recurrence with repair (32% at 1 year and 59% at 2 years). It appears that the patients at higher risk of mitral regurgitation recurrence are those who have larger degree of LV remodeling as evidenced by significant leaflet tethering, severe LV dilatation (LV end diastolic diameter >6.5 cm), aneurysm, or dyskinesis of the basal inferior wall, or no targets for revascularization on that region. Those patients would benefit from replacement rather than repair. In addition, the experience of the surgeon and the presence of technical issues that would require the performance of more complex, prolonged, or less reliable repairs should also weigh into replacing the valve. Even though the 2-year results of the CTSN trial did not show any difference in survival or LV function or remodeling between mitral valve repair or replacement in spite of the high rate of mitral regurgitation recurrence, the study showed a higher rate of heart failure events and readmissions.[44,48] The lack of significant demonstrable clinical adverse effect of recurrent or persistent mitral regurgitation at 2 years is likely the result of the short follow-up. It is reasonable to expect that the persistence or recurrence of mitral regurgitation will have adverse long-term consequences that may manifest beyond 2 years.

Moderate Mitral Regurgitation

For patients with moderate ischemic mitral regurgitation undergoing CABG, the addition of mitral valve repair is associated with an increased rate of perioperative stroke and supraventricular arrhythmias with no significant differences in heart failure symptoms, degree of LV reverse remodeling, LV function, or survival at 2 years.[52,53] The AATS guidelines recommend the consideration of mitral valve repair on these patients (see **Table 1**) but it does not provide conclusive recommendations on when to perform it.[17] The investigators also recommend the consideration of other clinical aspects that, although unsupported by evidence, make clinical sense: (1) Is the patient complaining mostly of heart failure symptoms, dyspnea rather than angina? Are the left-sided filling pressures elevated or the left atrium dilated? If the answer is yes to any of these questions, the addition of an annuloplasty may be reasonable. (2) To how much additional risk would this patient be subjected? Risk considerations include, for example, technical issues, left atrial size, presence of calcification of the mitral annulus, length of the surgical procedure, frailty, or need to convert to an on-pump approach. (c) The viability and presence of targets for bypass in the inferior wall is also important to consider. If the inferior wall is ischemic but viable with good revascularization targets, it is possible that the mitral regurgitation will improve after CABG alone.

There are no data to support mitral valve replacement in patients with moderate mitral regurgitation undergoing CABG. There are also no data to support the performance of isolated mitral valve surgery in these patients.

Mild Mitral Regurgitation

There are no data to support the surgical correction of mild mitral regurgitation.

MANAGEMENT OF FUNCTIONAL MITRAL VALVE REGURGITATION IN NONISCHEMIC CARDIOMYOPATHY

The treatment of functional mitral regurgitation in nonischemic cardiomyopathy follows the same principles and guidelines as in ischemic cardiomyopathy: both the mitral valve and ventricular remodeling should be addressed.[55] Surgery is indicated in patients with severe mitral regurgitation with persistent symptoms in spite of optimal medical therapy.[17,18] The uncertainties in terms of mitral valve repair versus replacement are similar to those in ischemic mitral regurgitation. However, restrictive mitral valve annuloplasty appears more effective in resolving mitral regurgitation than ischemic cardiomyopathy.[56–58] The rate of mitral regurgitation recurrence and survival are also better. Patients with very low EF, severely remodeled ventricles, and severe leaflet tethering also should be considered for chordal sparing valve replacement rather than repair.

The addition of ventricular restraint devices (CorCap; Acorn Cardiovascular Inc, St Paul, MN) to mitral valve repair has been associated with greater LV reverse remodeling and lower rate of mitral regurgitation recurrence.[59]

TRANSCATHETER MITRAL VALVE PROCEDURES

Transcatheter procedures to address mitral regurgitation can be grouped in annuloplasty procedures, leaflet procedures, chordal procedures, and mitral valve replacement.

Many of these procedures are in early stages of development or in clinical trials, but promise to revolutionize the treatment of mitral valve disease and expand the treatment to patients who are not candidates for open surgical procedures.[60,61]

The most studied device has been the MitraClip (Abbott Vascular; Santa Clara, CA), which creates an edge-to-edge repair similar to the Alfieri stitch. It has been approved by the Food and Drug Administration (FDA) for organic mitral regurgitation in symptomatic patients who are not surgical candidates and is being studied for functional mitral regurgitation. MitraClip is also approved in Europe for functional mitral regurgitation. The EVEREST II (Endovascular Valve Edge-to-Edge Repair) trial randomized patients with either organic (73%) or functional (27%) mitral regurgitation to mitral valve repair (n = 95) or MitraClip (n = 184). At 4 years, there was no difference in survival, or in the degree of improvement in LV dimensions, or in NYHA functional class between surgery and MitraClip. Both groups showed significant improvement in mitral regurgitation. However, at 4 years, the proportion of patients with grade +3 or +4 mitral regurgitation was higher in the MitraClip group (20.6% vs 9.1%). Patients who received the MitraClip required surgery for valve dysfunction more often (24.8% vs 5.5%, $P<.001$). Interestingly in the functional subgroup, +3 or +4 mitral regurgitation recurrence was more common in the surgical arm.[62,63] The results of this trial supported the FDA approval of MitraClip for the treatment of organic mitral regurgitation. The COAPT trial (Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy for Extremely High-Surgical-Risk Patients) trial randomized nonsurgical candidates with functional $\geq$ +3 mitral regurgitation to (1) optimal medical therapy and MitraClip procedure, or (2) optimal medical therapy alone. The primary effectiveness endpoint of the trial was survival and heart failure hospitalizations.

MITRAL VALVE STENOSIS

Mitral stenosis is commonly associated with rheumatic heart disease and senile calcific stenosis. The incidence of rheumatic heart disease has decreased in the developed world but continues to increase in third-world countries, in immigrant populations, and in underserved areas.[1] There is also senile calcific mitral stenosis characterized by calcification of the leaflets extending into the annulus without fusion of the commissures. This is increasingly prevalent in the elderly.[18]

Severe mitral stenosis leads to congestive heart failure by increasing left atrial pressure and pulmonary venous pressure. It is usually associated with atrial fibrillation that exacerbates the hemodynamic impairment and symptoms. Rheumatic and calcific mitral stenosis can be associated with variable degrees of mitral regurgitation.[18]

The indications for intervention in mitral stenosis are well stabilized in the AHA/ACC Guidelines. Percutaneous mitral balloon commissurotomy is the preferred treatment for symptomatic patents with severe rheumatic mitral stenosis, favorable anatomy, and no contraindications.[18] Percutaneous mitral balloon commissurotomy is not an option for patients with senile calcific stenosis. Mitral valve replacement is indicated in symptomatic patients with severe mitral stenosis who have failed or who are not candidates for percutaneous mitral balloon commissurotomy. Several centers outside the United States have developed extensive experience with mitral valve repair for rheumatic mitral valve disease achieving excellent long-term results.[64] Mitral annular calcification possesses a formidable technical challenge during mitral valve surgery and is associated with atrioventricular dissociation and perivalvular leak. The excision or exclusion of the left atrial appendage and the management of atrial fibrillation during mitral valve surgery is important to decrease the risk of thromboembolic complications.

SUMMARY

Mitral valve diseases are common causes of congestive heart failure. Chronic primary and secondary (functional) mitral valve regurgitation are the most common reasons. Valve repair for primary mitral regurgitation cures mitral valve disease, whereas in functional regurgitation, mitral valve repair is associated with high failure rates secondary to persistent/progressive ventricular dysfunction and remodeling. Most patients can be managed with strict adherence to the valve guidelines. Mitral valve replacement has an increased role in the management of functional mitral regurgitation. Surgery for mitral valve disease is indicated in symptomatic patients with severe valve disease and in asymptotic patients before irreversible ventricular damage occurs.

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