2015 The American Association for Thoracic Surgery Consensus Guidelines: Ischemic mitral valve regurgitation

The American Association for Thoracic Surgery Ischemic Mitral Regurgitation Consensus Guidelines Writing Committee:

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Mechanism of ischemic mitral regurgitation: apical displacement of leaflet coaptation with restricted leaflet closure and resultant regurgitation.

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Abbreviations and Acronyms

3D	= three-dimensional
AATS	= American Association for Thoracic Surgery
ACE-I	= angiotensin-converting enzyme inhibitor
AHA	= American Heart Association
AVR	= aortic valve replacement
CABG	= coronary artery bypass grafting
CAD	= coronary artery disease
COAPT	= Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy for Extremely High-Surgical-Risk Patients
COR	= Class of recommendation
CRT	= cardiac resynchronization therapy
CTSN	= Cardiothoracic Surgical Trials Network
EF	= ejection fraction
EROA	= effective regurgitant orifice area
FMR	= functional mitral regurgitation
GDMT	= guideline-directed medical therapy
HF	= heart failure
IMR	= ischemic mitral regurgitation
LBBS	= left bundle branch block
LOE	= level of evidence
LV	= left ventricle
LVEDD	= left ventricular end-diastolic diameter
LVEF	= left ventricular ejection fraction
MR	= mitral regurgitation
MV	= mitral valve
NYHA	= New York Heart Association
PISA	= proximal isovelocity surface area
RR	= relative risk
RV	= right ventricle
TEE	= transesophageal echocardiography
TTE	= transthoracic echocardiography
VC	= vena contracta

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METHODS OF REVIEW

The AATS Guidelines Committee identified the management of IMR as a key topic in cardiothoracic surgery suitable for the establishment of clinical guidelines. The Guidelines Committee selected Irving Kron, MD, as chair of the IMR Working Group and asked him to appoint an IMR Guidelines Writing Committee to create evidence-based guidelines for the AATS Guidelines Committee. The chair assembled a multidisciplinary group of experts including both adult cardiac surgeons and cardiologists. Members

were tasked with performing comprehensive literature searches, and making recommendations based on a review of the literature. Members also graded the quality of the evidence supporting the recommendations and with assessing the risk-benefit profile for each recommendation. The level of evidence was graded by the work force panel according to standards published by the Institute of Medicine (Figure 1). For the development of the guidelines, we followed the recommendations of the Institute of Medicine's 2011 *Clinical Practice Guidelines We Can Trust: Standards for Developing Trustworthy Clinical Practice Guidelines* (www.iom.edu/cpgstandards).

Scheduled teleconferences were used to organize the topics to be covered by the guidelines, review the literature review summaries, and propose recommendations. For all meetings, agendas were circulated beforehand and minutes were circulated afterward. All of the conference calls were recorded by the AATS staff to improve transcription of notes. The final recommendations were voted on by the Writing Committee to present to the Councilors of the AATS and review the final manuscript. All recommendations were subjected to a vote. Acceptance for the final document required >75% approval of each recommendation. Therefore, the process followed the recommendations of the Institute of Medicine, but an extensive consultation with all other stakeholders including patients was not performed. Instead, the AATS guidelines attempt to provide a rapid response to the rapid changing medical literature and provide clinicians with the recommendations of senior content experts based on the best available information. The expert consensus provides important guidance to clinicians particularly when the quality of the evidence is limited or contradictory. These consensus guidelines provide the best opinion of a group of content experts.

The following recommendations are based on expert consensus opinion as well as on the best available evidence. When high-quality evidence was lacking, we present expert opinion based on best practices. The guidelines were prepared for publication in *The Journal of Thoracic and Cardiovascular Surgery*.

SECTION I: INTRODUCTION TO IMR GUIDELINES

Significant recent advances have been made in the treatment of ischemic cardiomyopathy, although controversy remains regarding the best management strategy for IMR in this population. North American and European guidelines for the management of patients with valvular heart disease have touched on treatment strategies for IMR but lack surgical clarity, because that was not the primary focus of these efforts.^{1,2} In an effort to better define surgical definitions and strategies, the AATS appointed a Writing Committee to create this complementary guideline document, which outlines the optimal surgical management of patients with IMR.

The AATS Writing Committee for the Consensus Guidelines for Ischemic Mitral Valve Regurgitation realized that establishing set guidelines for the treatment of IMR would be difficult. At one time, it was felt that this would be an easy problem to define and treat; however, as more knowledge becomes available, treatment choices and timing have become more complex. Several recent clinical trials that have investigated these subjects have led to conclusions that contradicted the groups' initial beliefs.

It must be remembered that IMR is a disease of the ventricle. The valve, by definition, is normal but leaks

Applying Classification of Recommendations and Level of Evidence			
<u>Class I</u> Benefit >>> Risk	<u>Class IIa</u> Benefit >> Risk	<u>Class IIb</u> Benefit ≥ Risk	<u>Class III</u> Risk ≥ Benefit
Procedure/Treatment SHOULD be performed / administered	Additional studies with focused objectives needed IT IS REASONABLE to perform procedure/administer treatment	Additional studies with broad objectives needed; Additional registry data would be helpful. Procedure/Treatment MAY BE CONSIDERED	No additional studies needed. Procedure/Treatment should NOT be performed/administered SINCE IT NOT HELPFUL AND MAY BE HARMFUL
Level A: Recommendation based on evidence from multiple randomized trials or meta-analyses. Multiple (3-5) population risk strata evaluated. General consistency of direction and magnitude of effect.			
Level B: Recommendation based on evidence from a single randomized trial or non-randomized studies. Limited (2-3) population risk strata evaluated.			
Level C: Recommendation based on expert opinion, case studies, or standard-of-care. Very limited (1-2) population risk strata evaluated.			

FIGURE 1. Schema used to guide the grading of available published evidence and the expected effect of the intervention for their impact on patient outcomes.

owing to ventricular mechanisms. The regurgitation is quite dynamic. All of us have witnessed patients who progressed from minimal to severe regurgitation during the same hospitalization. This is related mostly to loading conditions, but often related to ongoing ischemia as well. Treatment options are often difficult, because these are often-fragile patients who suffer many of the complications related to atherosclerotic vascular disease. In addition, traditional repair methods are somewhat limited; they work in only a single plane, and often fail to address issues with the sub-valvular apparatus. Finally, most of the studies examining this issue are limited by reports of short-term outcomes, including many of those cited in this particular set of guidelines. We have 2-year results in some studies, but do not have 5- or 10-year results. These patients have exhibited high mortality at 5 to 10 years; however, as surgical and medical therapy have improved, many of these patients are surviving longer. These guidelines reflect the efforts of a panel of experts, drawing on expert opinion among other modalities, and are based on what we know at this time. There is no doubt that the guidelines will continue to evolve as reports of longer-term follow-up emerge in the future.

SECTION II: DEFINITIONS AND MECHANISMS OF IMR

Definition of IMR

Using the construct of Carpentier's pathophysiological triad,³ it is possible to strictly define IMR on the basis of

etiology, lesion, and dysfunction. The etiology in this process is ischemic heart disease, and by definition patients must have evidence of coronary artery disease (CAD) and previous myocardial infarction, with either regional or global dysfunction or dilatation (remodeling) of the left ventricle (LV). The primary lesion in IMR is leaflet tethering, which results from ventricular remodeling associated with an ischemic insult. Posteromedial and apical displacement of the papillary muscles, which correlates with a measurable "tethering distance,"^{4,5} leads to apical tenting and restriction of the free margin of the leaflets and poor leaflet coaptation. Tethering of secondary chordae can lead to a "seagull" deformation of the anterior leaflet, which has been targeted in certain repair series.⁶ Although both papillary muscles are typically displaced, the posterior papillary muscle group usually predominates, which leads to more aggressive tethering of the P3 leaflet segment. This is particularly true in posterior infarction related to the posterior descending artery distribution. In such circumstances, the MR jet is usually eccentric and posteriorly directed along the P3 area, which is selectively restricted.^{7,8} In contrast, left anterior descending infarction tends to lead to more global remodeling involving both papillary muscles, and more diffuse leaflet tethering involving all segments leads to large central jets of MR.^{7,8}

Although annular dilatation and distortion often accompany ventricular remodeling, papillary muscle displacement, and leaflet tethering, it is usually an associated lesion as opposed to a primary lesion in IMR. The degree

of annular dilatation is much less in IMR than in degenerative MR,⁹ which is one reason that “downsizing” of the annuloplasty is recommended to address leaflet tethering in IMR. The posteriomedial portion of the annulus is most often affected, although the anterior annulus is now recognized to flatten and elongate in IMR as well.^{10,11} Posterior infarction tends to lead to septal lateral dilatation along the A1-P3 axis, whereas anterior infarction leads to more global septal lateral dilatation, leading to symmetric and circular enlargement of the annulus.¹²

Although the majority of patients with IMR present with remote infarction and ventricular remodeling with leaflet tethering, acute ischemia with regional wall motion abnormalities can lead to similar findings of leaflet tethering in selected patients. In this setting, revascularization alone may lead to resolution of wall motion abnormalities and IMR. Papillary muscle elongation with leaflet prolapse is a rare cause of MR related to myocardial infarction, and generally should not be distinguished from more typical IMR with restricted leaflet motion. Isolated basilar infarction can lead to annular dilatation without leaflet tethering, and this is perhaps the most favorable dysfunction associated with IMR.

SECTION III: IMAGING OF IMR

Imaging Features of IMR

Posterolateral displacement of the papillary muscles leads to stretching of the chordae tendineae and increased tethering forces on the mitral valve (MV) leaflets.¹³⁻¹⁵ This results in apically displaced leaflet coaptation with restricted leaflet closure and resultant regurgitation (Figure 2). A key imaging feature of IMR is the presence of mitral leaflet apical tethering, in which the coaptation point is apically displaced. Because of tethering from the chords, leaflets are unable to coapt normally to the annular plane, resulting in incomplete closure (Figure 3). Leaflet morphology is normal, and it is important to exclude structural abnormalities of the leaflets such as ruptured chord or flail portion. Owing to the decreased surface area of the posterior leaflet relative to the anterior leaflet, tethering of the posterior leaflet is often greater, resulting in asymmetric tethering and coaptation and an eccentrically directed MR jet (Figure 4). Tethering of the basal or strut chordae can lead to a bend in the body of the anterior leaflet, contributing to tethering and impaired coaptation (Figure 5). There are various methods for quantifying the degree of tethering. The most common is a simple area measurement from the leaflets to the annular plane (tenting area), typically performed at mid-systole, when the area is at a minimum. Another measure is coaptation height or depth, which measures the maximal distance from the leaflet tips to the annular plane and appears to correlate with the presence and severity of IMR.¹⁶ More recently, 3-dimensional (3D)

FIGURE 2. Illustrated mechanism of IMR. Apically displaced leaflet coaptation with restricted leaflet closure results in MR. MR, Mitral regurgitation; AoV, aortic valve.

echocardiography has been applied to quantify leaflet tethering by measuring the tethering distance from the papillary muscle tip to the mitral annulus and measurement of tenting volume (ie, volume from leaflets to annular plane) and may provide additional data for assessing tethering (Figure 6).¹⁷

LV remodeling can be relatively focal, with ventricular distortion limited to the inferior-posterior segment such as occurs in a basal inferior aneurysm (Figure 7), or the remodeling can be diffuse, with global LV dilation and a spherically shaped LV.¹⁸

Grading of MR: How to Do It

General considerations. Echocardiography is the primary imaging modality used to grade MR. It is a noninvasive, accessible, and cost-effective imaging tool. Grading of MR should not rely on a single parameter but rather an integrative approach incorporating multiple quantitative and qualitative echocardiographic measures should be included in the quantitation of MR.

The grading of MR is based on Doppler techniques and supportive echocardiographic data.

Doppler Techniques

Doppler techniques are based on evaluation of the flow dynamic pattern of the MR jet. The MR jet has 3 parts: (1) the proximal isovelocity surface area (PISA), the zone of flow convergence as it approaches the mitral regurgitant orifice; (2) the vena contracta (VC), the MR jet as it goes through the regurgitant orifice; and (3) the distal jet, the MR flow as it exits the leaflet level (Figure 7).

FIGURE 3. TTE demonstrating reduced mitral leaflet coaptation in the annular plane, resulting in incomplete leaflet closure and MR. LV, Left ventricle; LA, left atrium; MR, mitral regurgitation.

Distal jet area method. The distal jet area method involves measuring the maximal MR jet as it exits the leaflet level and enters the left atrium. The maximal jet area is traced in the apical 4- and 2-chamber views, and an average of the areas is calculated. The jet area is commonly normalized to the left atrial area and expressed as a ratio or percentage of the maximal left area measured in same frame (Figure 8).^{19,20} An MR jet area/left atrial appendage ratio of <20% corresponds to mild MR; a ratio of >40%, to severe MR (Figure 1). The distal jet area method is a simple semiquantitative assessment of MR; however, this method is influenced by both technical and physiological factors. Common technical factors involve ultrasound machine settings, such as gain and Nyquist limits, which affect the size of the distal jet. Physiologic factors that affect the distal jet are loading conditions (eg, blood pressure, volume status).

Eccentric MR jets can be “absorbed” by the left atrial wall, leading to underestimation of the degree of MR. Eccentric jets in which the MR jet travels out of the plane

of the ultrasound beam will be missed or underestimated as well. Owing to the limitations with eccentric jets, the jet area method is best applied to centrally directed jets.²¹

VC width. The VC, the narrowest portion of the MR jet, provides a simple linear measurement of the proximal MR jet.²² The VC width is measured along the anteroposterior plane of the mitral orifice and ideally should be measured in the parasternal long-axis view, because this view provides optimal resolution of the VC in the anteroposterior plane (Figure 9). If the parasternal long-axis view is technically poor, then an apical long-axis view can be used. Measurement of VC width should be avoided in the 2-chamber view (mediolateral dimension), because this view images the MR proximal jet along the coaptation line.

VC measurements of <3 mm correspond to mild MR; 0.3 to 0.69 mm, to moderate MR; and ≥0.7 mm, to severe MR (Table 1). VC width is a simple, direct, clinically useful semiquantitative measure of MR. In addition, the VC is less influenced by physiological loading conditions and

FIGURE 4. TTE demonstrating decreased surface area of the posterior leaflet relative to the anterior leaflet and tethering of the posterior leaflet, resulting in asymmetric tethering and coaptation with an eccentrically directed mitral regurgitant jet.

FIGURE 5. TTE demonstrating tethering of the basal or strut chordae that can result in a bend in the body of the anterior leaflet, further contributing to mitral leaflet tethering and impaired coaptation. LV, Left ventricle; LA, left atrium.

easier to measure in eccentric jets compared with distal jet area, and thus may be more reproducible.²¹ The reference range of VC width is narrow, and thus small differences in width can have a large impact on MR grading. Therefore, it is important to maximize the sector (zoom) and depth for optimal color Doppler resolution.

PISA method. This quantitative Doppler method measures the effective regurgitant orifice area (EROA) of the MR flow and MR regurgitant volume. The PISA method is based on the fluid dynamics principle that as flow approaches a circular finite orifice, it forms concentric hemispherical shells with gradually decreasing surface area and increasing velocity.²³⁻²⁵ This principle is applied

to mitral regurgitant flow, where the PISA region is the hemispherical shell that forms proximal to the mitral leaflets on the LV side, and the finite orifice is the mitral regurgitant orifice at the level of the leaflets. The flow rate of the hemispherical shell equals the rate at the orifice by the conservation of mass principle. Assuming a hemispherical shape for the isovelocity shells, then flow rate = surface area of a hemisphere = $2\pi r^2 \times$ aliasing velocity, where r is the radius of the hemispherical shell.

EROA and mitral regurgitant volume can be derived from the flow rate using the following formulas:

EROA = MR flow rate/peak MR velocity by continuous wave (Figure 10)

and

Regurgitant volume = EROA $\times$ time-velocity integral (MR jet).

The accuracy and reproducibility of the PISA method are highly dependent on attention to technique of acquisition and measurements. The PISA region should be magnified with sector and depth optimized for color Doppler resolution. Measurement of the PISA should be aligned parallel to flow rate direction to optimize Doppler resolution. To optimize measurement of the radius, r , the baseline of the Nyquist limit is shifted toward the direction of the MR flow. Nyquist limit ranges of 30 to 40 cm/second are optimal for PISA radius measurement.

Factors influencing the PISA method. In theory, the PISA method provides an accurate quantitative measure of MR; however, there are technical and practical aspects to the PISA method that limit its clinical applicability. Eccentric MR jets can distort the PISA region owing to constraint from the left atrial wall or mitral leaflet, resulting in a falsely increased radius and overestimation of EROA.²⁶

An angle correction factor can be applied to the surface area calculation, but this is not widely used because of the difficulty in measuring the angle and that additional complexity that this adds to PISA calculation. Importantly, although eccentric jets do occur with IMR because of asymmetric tethering of the leaflets, the eccentricity of the jet is typically insufficient where distortion of the PISA zone occurs.

An important limitation of the PISA method for calculating EROA is that the contour of the PISA region is not always hemispherical, but is often hemielliptical,^{27,28} especially in cases of IMR, where the mitral orifice shape is often noncircular. This has the effect of underestimating the EROA using the standard hemispherical assumption used in PISA. 3D echo-guided measurement of the VC area, which is a direct measure of the effective orifice area, avoids the inherent underestimation of EROA by the 2D PISA method.^{29,30} Several previous studies that examined and validated 3D-measured VC area against other methods of MR quantitation, including cardiac magnetic resonance, found that 3D-measured VC area can provide an important

FIGURE 6. Measurement of tenting volume used in 3D echocardiography. AO, Aorta; AL, anterolateral; PMs, papillary muscles.

FIGURE 7. TTE demonstrating LV remodeling as a result of IMR with segmental LV remodeling and inferior wall basal aneurysm formation as well as diffuse LV remodeling. LV, Left ventricle.

alternative method of quantitating MR, especially in cases with discrepant data.³¹⁻³³ The bias for PISA to underestimate MR severity in functional MR (FMR) may partly explain the finding that lower thresholds for EROA are associated with worse prognosis in IMR.²⁹

Reference values for EROA based on etiology of MR. Recent valvular guidelines have proposed different cutoff values of EROA and MR right ventricle (RV) for severe MR depending on the etiology of MR, with severe IMR having cutoffs of 0.2 cm² for EROA and >30 mL for RV in severe IMR, and higher cutoffs of 0.4 cm² for EROA and >60 mL for RV in primary MR.^{2,34} The lower cutoff

value for IMR is based on poor outcomes in patients with an EROA of ≥ 0.2 cm². Some important limitations of a lower EROA cutoff value for IMR should be kept in mind. First, prognostic data are based on retrospective analyses, with their potential selection bias. Second, EROA and RV values are dependent on LV volumes, which can account for lower EROA values in IMR. Third, a hemispherical assumption will underestimate EROA and MR RV in IMR. Finally, measurement of EROA and RV

FIGURE 8. Measurement of distal jet area by Doppler echocardiography. PISA, Proximal isovelocity surface area; VC, vena contracta.

FIGURE 9. Measurement of the VC in an apical long-axis view by TTE. LV, Left ventricle.

TABLE 1. Integrative method of IMR grading

Doppler measures (semiquantitative and quantitative)			
Parameter	Mild	Moderate	Severe
EROA, cm ²		<0.2	≥0.2 vs 0.4≥*
VC width, cm	<0.3	0.3-0.69	≥0.7
Jet/LAA area, %	<20	20-39	≥40
MR regurgitant volume, mL	<30	30-59	≥30 vs 60*
Supportive criteria			
E-wave velocity			
Pulmonary vein flow reversal			
Density of continuous-wave MR jet			
Chamber size			

EROA, Effective regurgitant orifice area; VC, vena contracta; LAA, left atrial appendage; MR, mitral regurgitation. *Recent valvular guidelines have adopted a lower EROA cutoff value of 0.2 cm²,^{21,22} compared with the traditional cutoff value of 0.4 cm² for severe IMR.⁸ See the text for details.

by the PISA method remains a challenging technique to reliably reproduce across laboratories.²⁹

Supportive criteria. A tall E-wave peak velocity from the mitral inflow pattern is supportive of severe MR. A peak E wave velocity of >1.2 m/s is suggestive of severe MR. A dense continuous-wave Doppler profile provides important complementary data for severe MR. It is important that the transducer be aligned parallel to the MR flow profile to provide an accurate continuous-wave Doppler profile. Systolic blunting of the systolic wave is consistent with at least moderate MR. Systolic pulmonary vein flow reversal is a specific sign of severe MR, although not a sensitive sign.²¹

An assessment of LV function, including LVEF, LV dimensions, wall motion abnormalities, and structural abnormalities of the MV chordae and papillary muscles, should be incorporated when grading MR.

Transesophageal echocardiography assessment of MR degree. MR is impacted by loading conditions, which is

important to consider when assessing MR in the intraoperative setting. Clinical decision making based on MR degree assessed in the operating room is best avoided, given that MR grade is often lower than that in ambulatory conditions owing to the unloading that occurs with anesthesia.³⁵ Grading of MR ideally should be done with the patient awake, alert, and medically stable. In addition, grading MR using transesophageal echocardiography (TEE) is less well validated than doing so using transthoracic echocardiography (TTE). In cases where preoperative assessment of MR is not available, intraoperative volume loading or increasing afterload to mimic standard ambulatory loading conditions may be performed to better assess the degree of MR.³⁶

Putting it All Together: Importance of an Integrative Method

It is important to emphasize that an integrative approach as currently recommended by guidelines should be used to grade MR.^{2,29,34} Grading of IMR should incorporate multiple Doppler parameters and supportive criteria. This has the advantage of drawing on the strengths of each Doppler technique while avoiding reliance on a single parameter, thereby minimizing the limitations inherent in each.

SECTION IV: INDICATIONS FOR SURGERY AND SECONDARY PREVENTION OF MR
Secondary MR

Secondary MR can be categorized into 4 stages that can be used to define prognosis and guide therapy: at risk of secondary MR, progressive secondary MR, asymptomatic severe secondary MR, and symptomatic severe secondary MR.¹ There is a strong association between IMR severity and both all-cause mortality and heart failure (HF)-related hospitalizations. In one study, IMR was present in 194 of 303 patients with myocardial infarction (64.0%), and

FIGURE 10. Calculation of MV EROA using the PISA method. EROA, Effective regurgitant orifice area; MR, mitral regurgitation.

was a significant independent predictor of long-term mortality (relative risk, 1.88; 95% confidence interval, 1.23-2.86; $P = .003$).³⁷ In a study from the Duke Cardiovascular Databank, angiographic 3+ to 4+ MR was present in 29.8% of 2057 HF patients with a left ventricular ejection fraction (LVEF) <40%, and was an independent predictor of 5-year mortality (adjusted hazard ratio, 1.23; 95% confidence interval, 1.13-1.34).³⁸ So whereas the presence of severe IMR predicts a poor prognosis in patients with LV dysfunction and HF, whether correction of the MR improves prognosis remains unknown.

Therapy for Secondary MR

In the opinion of this expert panel, the goals of therapy in patients with secondary MR should be to improve symptoms and quality of life, reduce HF-related hospitalization, and improve survival. The therapies shown to be most effective for secondary MR are those directed at the underlying LV dysfunction, including guideline-directed medical therapy (GDMT) for HF and biventricular pacing when appropriate. Coronary revascularization therapy (CRT) should be considered in patients with ischemia and myocardial viability. The role of surgical MV repair or replacement is to interrupt the vicious cycle of LV volume overload, causing LV dilatation leading to IMR, which further increases LV volume overload and dilatation, leading to further increased MR.

Medical therapy. All patients with IMR should receive GDMT for long-term management of CAD and, when present, LV systolic dysfunction and HF. Interventions include the following:

- Aspirin
- A P2Y12 inhibitor if percutaneous coronary intervention has been performed
- High-intensity statin therapy
- Beta-blockers for at least 3 years after myocardial infarction or indefinitely in the presence of residual angina, HF, hypertension, arrhythmia, or other indications
- An angiotensin-converting enzyme inhibitor (ACE-I), or an angiotensin receptor blocker if unable to tolerate an ACE-I
- Eplerenone or spironolactone, as dictated by LVEF, HF status, and the presence of diabetes
- CRT, with or without a defibrillator, if other indications are met (eg, wide QRS left bundle branch block [LBBB], reduced ejection fraction [EF], HF).

GDMT for HF is first-line treatment for patients with secondary MR.¹ Unfortunately, morbidity and mortality in patients with LV dysfunction and secondary MR remain high despite GDMT. Among 404 patients with secondary MR treated with GDMT, 4-year cardiac mortality was 43% in the patients with moderate MR and 45% in those with severe MR, compared with only 6% in those with mild MR

($P = .003$).³⁹ Moderate or severe MR was also an independent predictor of new-onset HF in patients with ischemic LV dysfunction (relative risk, 3.2; 95% confidence interval, 1.9-5.2; $P = .0001$).

Beta-blockers and ACE-Is are recommended for all patients with LV dysfunction and IMR. By reversing LV remodeling, maximal GDMT will sometimes secondarily reduce severe MR to at least moderate MR. In several small nonrandomized studies, carvedilol use in patients with HF and IMR was associated with improved LV systolic function with reduced MR severity lasting for 6 to 12 months.^{40,41}

CRT for IMR. CRT is a well-established treatment for HF in selected patients with LV dyssynchrony. CRT is recommended with class I level of evidence for patients in sinus rhythm with New York Heart Association (NYHA) class II to IV symptoms on GDMT with LVEF $\leq 35\%$, LBBB, and a QRS duration ≥ 150 msec. CRT also may be useful in patients with LVEF $\leq 35\%$, sinus rhythm, and a non-LBBB pattern with a QRS duration ≥ 150 msec, and in those with LBBB and a QRS duration 120-149 msec (class IIa indications).⁴² Previous randomized trials have shown improvements in both survival and HF rehospitalization rates in patients treated with CRT with or without defibrillation,⁴³ along with reductions in LV end-diastolic and end-systolic dimensions and improved LVEF.

The effect of CRT on secondary MR is inconsistent, although most studies have shown reductions in overall MR severity with restoration of synchronous ventricular contractions and LV remodeling. In the sham-controlled MIRACLE trial of 450 NYHA class III/IV HF patients with LVEF $\leq 35\%$ and QRS duration ≥ 130 msec, CRT resulted in marked reductions in LV end-diastolic and systolic volumes, improved LVEF, and sustained reductions in MR (as assessed by the relative size of the mitral jet area in the left atrial appendage).⁴³

Unfortunately, severe IMR improves in no more than one-half of patients after CRT, although such improvement does identify a cohort with an improved prognosis. In a study of 85 HF patients with 3+/4+ secondary MR, MR grade at 6 months was reduced after CRT in 42 (49%). Two-year survival was 92% in MR responders versus 67% in nonresponders ($P < .001$).^{44,45}

Revascularization for IMR. The need for coronary revascularization should be assessed with the usual clinical and noninvasive diagnostic testing to demonstrate ischemia, including myocardial perfusion imaging, stress echocardiography, and cardiac magnetic resonance imaging. A heart team approach is considered essential for appropriate decision making regarding the optimal revascularization strategy in patients with multivessel disease. Many patients with moderate IMR will experience a sustained reduction in MR severity with revascularization alone. Identification of these patients preoperatively has not

been standardized, however. Guidelines for surgical myocardial revascularization for IMR are discussed in more detail in the next section.

Indications for surgery in IMR. Surgical options for IMR include surgical MV repair and replacement, implantation of a mechanical LV assist device, and orthotopic heart transplantation. Although secondary MR can acutely be corrected by MV surgery, it has never clearly been demonstrated that reducing or eliminating the MR alters the natural history of the primary disease (dilated cardiomyopathy) or improves survival.^{13,45-47} Moreover, whether the response to surgery differs in secondary MR due to ischemic versus nonischemic cardiomyopathy has not been established.

Thus, the indications for surgery for IMR are more reserved than those pertaining to patients with primary, degenerative MR, owing in large measure to the recognition that intermediate- and long-term outcomes are inextricably linked to the underlying LV dysfunction and adverse remodeling. One-year mortality after MV surgery for severe IMR (with or without coronary artery bypass grafting [CABG]) is approximately 17%. Rates of postoperative moderate or severe MR at 1 year after MV repair of severe IMR are higher than previously appreciated. Although MV repair with CABG is significantly more effective than CABG alone in reducing or eliminating moderate IMR, there are no between-group differences at 1 year in LV end-systolic volume index or rates of major adverse cardiac and cerebrovascular events.⁴⁸ Longer follow-up of postoperative patients following treatment of IMR is needed to determine whether differences will emerge in hard clinical endpoints, such as death and hospitalization for HF.

In the most recent European guidelines (2012), MV repair for isolated severe secondary MR is afforded a class IIb (level of evidence [LOE] C) recommendation, but only for patients at low surgical risk with an LVEF $\geq 30\%$.² The 2014 American Heart Association (AHA)/American College of Cardiology guideline for the management of patients with valvular heart disease¹ contains the following recommendations for surgery in secondary MR:

1. Moderate MR
 - a. MV repair can be considered at the time of CABG (class of recommendation [COR] IIb, LOE B)
 - b. MV surgery can be considered at time of other cardiac surgery (eg, aortic valve replacement [AVR]) (COR IIb, LOE C)
2. Severe MR
 - a. MV surgery is reasonable at time of CABG or other cardiac surgery (eg, AVR) (COR IIa, LOE C)
 - b. MV surgery can be considered an isolated procedure for treating significant HF symptoms that persist despite GDMT (COR IIb, LOE C)

SECTION V: SURGICAL GUIDELINES FOR THE TREATMENT OF IMR

Repair versus Replacement for Severe IMR

For patients with severe IMR that remains symptomatic despite optimal medical treatment (including biventricular pacing if indicated), MV surgery is recommended by the present guidelines: AHA/American College of Cardiology—COR IIb, LOE C and European Society of Cardiology/European Association for Cardiothoracic Surgery—COR I, LOE C if undergoing CABG with LVEF $>30\%$; receiver operating characteristics IIa, LOE C, LVEF $<30\%$; COR IIb, LOE C if not undergoing CAB. Despite these recommendations, the guidelines provide no guidance in selecting MV replacement versus MV repair. This treatment choice is controversial, given the perception that MV repair is associated with lower short- and intermediate-term morbidity and mortality,⁴⁹ whereas MV replacement of IMR is associated with high recurrence rates of moderate/severe MR.⁵⁰⁻⁵² This perception rests on an imperfect evidence base; the meta-analysis by Vassileva and colleagues⁴⁹ is limited, in that it is a compilation of retrospective and single-center studies. Moreover, very few patients in the studies reviewed underwent MV replacement with complete retention of both anterior and posterior chords, which we now know is important for the preservation of LV function.⁴⁹ Table 2 summarizes existing society guidelines as well as the guidelines promulgated by this Writing Committee for the surgical treatment of IMR.

Recently, the level of evidence for the decision between MV replacement and repair for severe IMR has been better informed by a large retrospective multicenter propensity-matched study and a multicenter randomized trial.^{53,54} In the former, Lorusso and colleagues⁵⁴ reported no difference in short- or long-term mortality between patients treated with MV replacement and those treated with MV repair. They also found no differences found between groups in late LV function, cardiac- and valve-related death, or patients' functional capacity. The landmark National Institutes of Health–sponsored Cardiothoracic Surgical Trials Network (CTSN) randomized study showed no difference between groups in the primary endpoint of reverse LV remodeling (change from baseline in LV end-systolic volume index) at 1 year, along with no differences with respect to early or 1-year mortality, major adverse cardiac and cerebrovascular events, or patients' quality of life.⁵³ In contrast, both studies demonstrated that MV repair was associated with a significant recurrence of moderate/severe MR. In the propensity-matched study, MV repair was the strongest predictor of the need for a valve-related reoperation. In the randomized study, recurrence of MR in surviving patients was 32.6% at 1 year and 46% at 2 years.⁵⁴ Interestingly, in a subgroup

TABLE 2. Summary comparison of existing society guidelines and AATS guidelines for surgical treatment of IMR

Existing society guidelines	AATS guidelines
Moderate IMR	Moderate IMR
A. MV repair can be considered at time of CABG (COR IIb, LOE B)	A. Patients with moderate IMR undergoing CABG should undergo concomitant MV repair with an undersized complete rigid annuloplasty ring to mitigate recurrence of MR in patients who have heart failure symptoms, those with significant mitral annular dilation and those in whom bypassable, hibernating, viable myocardium supporting the papillary muscle(s) is thought to be minimal (COR IIb, LOC A).
B. MV surgery can be considered at time of other cardiac surgery (eg, AVR) (COR IIb, LOE C)	
Severe IMR	Severe IMR
A. MV surgery is reasonable at time of CABG or other cardiac surgery (eg, AVR) (COR IIa, LOE C)	A. In the presence of basal aneurysm/dyskinesis, significant echocardiographic evidence of leaflet tethering, or moderate to severe LV remodeling (LVEDD >65), patients should consider MV replacement (COR IIa, LOE A)
B. MV surgery can be considered as an isolated procedure for treatment of significant heart failure symptoms that persist despite guideline directed medical therapy (COR IIb, LOE C)	B. In the absence of basal aneurysm/dyskinesis, echocardiographic evidence of significant leaflet tethering, or moderate to severe LV remodeling (LVEDD < 65), patients should consider MV repair with an undersized complete rigid ring (COR IIb, LOE B).
MV replacement vs repair	MV replacement vs repair
Not available	A. MV replacement for IMR is performed with complete preservation of both anterior and posterior leaflet chords (COR I, LOE B)
	B. MV repair for IMR is performed with a small undersized complete rigid annuloplasty ring (COR IIa, LOE B)

AATS, The American Association for Thoracic Surgery; IMR, ischemic mitral regurgitation; MV, mitral valve; CABG, coronary artery bypass grafting; COR, class of recommendation; LOE, level of evidence; AVR, aortic valve replacement; LV, left ventricle; LVEDD, left ventricular end-diastolic diameter.

analysis, patients who underwent MV repair without recurrent MR had greater LV reverse remodeling compared with the patients who underwent MV replacement.⁵⁴ In the CTSN randomized trial, the strongest predictor of recurrent/residual MR in the MV repair group was the presence of a basal aneurysm/dyskinesis.⁵³

Multiple single-center studies have demonstrated independent predictors of recurrent IMR. These predictors fall into 2 categories: echo parameters of leaflet tethering and degree of LV remodeling. Studies have demonstrated that echo measures of increased tethering, such as anterior and posterior leaflet angle, tethering length, and tenting area and height, are predictive of recurrent MR. These studies point to the angle between the tip of the anterior leaflet and the annular plane as the most important predictor of recurrence. An anterior leaflet angle of >25 to 39.5 degrees was identified as an independent predictor of recurrence more important than any other measurement of tethering (eg, postleaflet angle, coaptation depth, tenting) or measurements of LV size (left ventricular end-diastolic diameter [LVEDD] >65 mm) or sphericity.⁵⁵⁻⁶⁰ Other groups have posited LV size, LV function, or degree of MR as key independent determinants of recurrent MR,^{55,61-68} whereas others have emphasized the importance of both LV size and tethering as independent predictors.^{61,64}

MV replacement is indicated for patients identified as high risk for postoperative MR recurrence after simple annuloplasty repair alone and patients undergoing surgery in less-experienced centers where annuloplasty alone is the sole repair option offered. More complex MV repair operations that specifically address leaflet tethering through leaflet augmentation and/or papillary muscle repositioning have shown promising results, but remain investigational and incompletely validated by randomized clinical trials.^{6,59,69,70}

In the presence of basal aneurysm/dyskinesis, significant echo evidence of leaflet tethering and/or moderate to severe LV remodeling (LVEDD >65), MV replacement should be considered (COR IIa, LOE A). In the absence of basal aneurysm/dyskinesis, echo evidence of significant leaflet tethering, or moderate to severe LV remodeling (LVEDD <65), MV repair with an undersized, complete, rigid ring should be considered (COR IIb, LOE B).

Long-term follow-up of the randomized MV repair and MV replacement patients in the CTSN Severe IMR trial will be important to better understand the clinical consequences of recurrent MR, as well as prosthetic valve deterioration/complications. Current recommendations will be updated to reflect this new evidence as it becomes available.

Surgical Decision Making in Patients With Moderate IMR Undergoing CABG

As mentioned above, present AHA/American College of Cardiology Foundation guidelines include recommendations for surgery for moderate IMR that are relatively conservative, stating that MV repair can be considered at the time of CABG (COR IIb, LOE B) and that MV surgery can be considered at the time of other cardiac surgery (eg, AVR) (COR IIb, LOE C).

Although MV repair with CABG is significantly more effective than CABG alone in reducing or eliminating moderate IMR, there were no between-group differences at 1 year in LV end-systolic volume index or in rates of major adverse cardiac and cerebrovascular events in a recent CSTN study.⁵³ Longer follow-up of postoperative patients following treatment of IMR will reveal whether differences in residual/recurrent MR will become manifest in hard clinical endpoints such as death and rehospitalization for HF. Two previous randomized trials from Europe found a significant benefit of combined CABG/MV repair for patients with CAD and moderate IMR, including better reduction of MR, improved LVEF and LVESD, and improved NYHA functional class.^{71,72} There were no between-group differences in early mortality or longer-term survival.

Thus, although present guidelines support the heart team in choosing to perform either CABG alone or CABG plus MV repair for patients with moderate IMR who have a clinical indication for surgical coronary revascularization, they do not provide strong guidance as to which patients will benefit most from either procedure. This decision can be challenging and typically falls to the responsible surgeon. When weighing CABG alone against CABG plus MV repair, surgeons should consider many variables, including the predominant symptom(s) and incremental risk.

What symptoms are predominant? Angina, shortness of breath/dyspnea on exertion/HF, or both? Might the presence of diabetes complicate interpretation of these symptoms? Patients, families, and referring physicians generally want these presenting symptoms to be addressed; when dyspnea is an important symptom in the setting of documented moderate IMR, the surgeon may logically feel that MV repair should be added to planned CABG. Conversely, if angina without dyspnea is the presentation, then CABG alone may be warranted. Although not supported by a robust evidence base, this approach remains compelling to many surgeons and cardiologists.

What incremental risk would the addition of MV repair to CABG impose on the particular patient? This question must include consideration of surgeon/center-specific outcomes with mitral and coronary surgery and patient-specific comorbidities that might significantly increase the risk of adverse events with prolonged cardiopulmonary

bypass/cross-clamping. In centers where MV repair is expertly practiced, the incremental risk may be low. Conversely, for a surgical team inexperienced in MV repair, CABG alone may be a more reliable alternative. Indeed, the complexity of the planned CABG itself may reasonably influence the decision to add MV repair to the procedure. If numerous difficult or precarious coronary arteries must be bypassed, then the operating team may reasonably seek to limit the duration and cumulative difficulty of the procedure by not adding MV repair. Similarly, the overall condition of the patient may be an important consideration as well. Very elderly, frail patients and those with severe comorbidities (eg, chronic obstructive pulmonary disease, peripheral vascular disease, previous stroke, renal failure) may benefit from a “less is more” approach to treating CAD in the setting of moderate IMR, unless HF is problematic. For some patients, the addition of MV repair to CABG may be inappropriate if ascending aortic calcification or other risk factors mandate an off-pump approach.

Although the foregoing general considerations are valid, thoughtful heart team members may seek to more specifically identify preoperatively which patients will experience a reduction of moderate IMR with CABG alone and which patients will require MV repair to enjoy the presumed benefits of reduced MR.

The mechanism of IMR typically relates to ischemia or infarction of the posterolateral LV in the region that supports the posterior papillary muscle. Ventricular dilation and dysfunction result, causing lateral displacement of the posterior papillary muscle and tethering of the posterior mitral leaflet, resulting in secondary/functional regurgitation due to failure of coaptation of morphologically normal mitral leaflets (Carpentier type IIIb dysfunction). It is intuitive to believe that CABG alone will improve this pathophysiological situation only if the posterolateral LV is viable, ischemic, and bypassable. If the posterolateral LV supporting the posterior papillary muscle is grossly infarcted, thinned, or aneurysmal, then revascularization of this regional myocardium is unlikely to improve regional wall motion or secondary MR. Similarly, if no suitable coronary artery target exists in this region, then significant improvement in regional wall motion and, subsequently, in secondary MR is unlikely with CABG alone.

Annular dilatation (type I dysfunction) of >38 to 40 mm in diameter also may play a role in IMR when significant ventricular dilatation is present, and may reasonably push surgical decision making toward adding MV repair to planned CABG. Significant enlargement of the left atrium to >4 cm in diameter suggests longstanding significant MR and similarly may guide the surgeon toward adding MV repair to CABG alone.

Patients with moderate IMR undergoing CABG should undergo concomitant MV repair with an undersized complete

rigid annuloplasty ring to mitigate the recurrence of MR. These patients included those with HF symptoms or significant mitral annular dilation, and those in whom bypassable, hibernating, viable myocardium supporting the papillary muscles is thought to be minimal (COR IIb, LOC A).

Technical Aspects of MV Repair for IMR

In operations for IMR, meticulous attention should be paid to myocardial preservation and cardiopulmonary perfusion. At the time of exposure of the MV, the MV may appear “normal.” The surgical reduction in AP diameter and orifice area of the MV is an overcorrection and overcompensation for a disease of the ventricle. This undersizing of the mitral ring was first proposed by Bolling in 1995,⁷³ and has become a standard technical approach for IMR repair. When undersizing a mitral ring, the use of a large number of annular sutures compared with the number used in degenerative MR repair is recommended, to distribute the workload of annular reductive force. These sutures may be placed very closely together, or even on a diagonal. Some advocate the use of pledgetted sutures or the placement of an extra row of sutures or a few pledgetted reinforcement sutures posteriorly once the ring is tied in place.

The vast majority of patients may be well served with a small (26 or 28) ring. Although initially there were concerns regarding systolic anterior motion of the anterior leaflet and mitral stenosis from such downsizing, these mechanisms have not resulted in adverse clinical sequelae in any long-term follow-up series. The type of ring used for MV repair is an important technical consideration. In a landmark paper, Hueb and colleagues¹⁰ noted that the fibrous portion of the mitral annulus anteriorly between the 2 mitral trigones dilated proportionally and to a similar degree as the posterior muscular annulus. This mechanism directs the technical approach to MV repair and hints at why some previous approaches to MV repair using incomplete and/or flexible bands had a very high failure rate. Magne and colleagues⁷⁴ reported failure rates of up to 80% at 6 months postoperatively, with recurrence of at least 2+ MR with large flexible and/or partial bands in IMR patients. Other studies have shown that partial bands result in unacceptable rates of recurrent MR, and that this residual IMR leads to little effective reverse LV remodeling and poor outcomes.^{63,75-77} In a comparison trial of patients treated with MV repair for IMR, Spoor and colleagues⁷⁸ reported a 5-fold greater incidence of recurrent IMR with the use of flexible rings as opposed to small complete rigid rings. Finally, Silberman and colleagues,⁷⁹ in a multivariate analysis of predictors of residual and recurrent MR in IMR, identified LV size and the type of ring as the 2 most significant predictors. In fact, the type of ring was a better predictor than LV size.⁷⁹ That study showed that small rigid and complete rings were best for IMR. In this specific disease state of IMR, large partial or incomplete rings likely do

not provide a durable repair for IMR and are not favored technically. Numerous specific small rigid and complete IMR rings with a disproportionate AP diameter dimension reduction are available. Although none of these rings has been associated with significant differences in clinical outcomes, these rings are likely most favored for the technical repair of FMR.

When coming off cardiopulmonary bypass, no MR should be detected on intraoperative or postoperative TEE. Moreover, the zone of coaptation should be at least 8 to 10 mm long (ie, deep). If this is not the case under anesthesia, then the patient certainly is at much greater risk for recurrent MR when awakened and removed from the vascular unloading effects of general anesthesia.

Other adjunct therapies have been used for repair of IMR. There are often deep clefts between P1 and P2, and between P2 and P3, which should be closed. Borger and colleagues⁶ have advocated dividing secondary chords to both the anterior and posterior leaflets, to allow for a longer zone of coaptation. Although this method has proven technically successful, there has been no long-term follow-up, and there concerns have been expressed about the effect on ventricular function of disrupting any chordal structures in these already compromised ventricles.

MV Replacement in IMR

There is a clear consensus on the technical aspects of MV replacement for IMR. MV replacement should be a total valve-sparing replacement. A randomized trial comparing partial and complete chordal-sparing MV replacement demonstrated much better-preserved LV volume and function with complete-sparing versus posterior leaflet-sparing techniques. For IMR, non–valve-sparing MV replacement should be completely abandoned.

There are numerous techniques for total valve-sparing MV replacement in IMR. One technique is the anterior flip-over, in which a C-shaped incision is made in the anterior leaflet and the entire anterior apparatus is moved posteriorly. Following appropriate valve sizing, pledgetted stitches of the MV replacement are placed through the posterior annulus, the edge of the posterior leaflet, and the anterior leaflet, placing both the chordal apparatus and leaflets behind the MV prosthesis. A second approach to achieving this is to remove the center of the anterior leaflet and then rotate the remaining portions of the anterior leaflet to the left and right commissures. Valve sizing for IMR should be prudent, avoiding oversized valves. With modern MV prostheses, there should be no concern about stenosis, and overly large, bulky valves may impair LV dynamics and interventricular conduction in these already poor LVs.

- MV replacement for IMR is performed with complete preservation of both anterior and posterior leaflet chords (COR I, LOE B).

- MV repair for IMR is performed with a small undersized complete rigid annuloplasty ring (COR IIa, LOE B).

SECTION VI: PERCUTANEOUS TRANSCATHETER MV REPAIR: GUIDELINES FOR TREATMENT OF IMR

IMR is a marker for significant morbidity and mortality. Although some patients are treated with mitral surgery, many of these patients are not referred for mitral surgery, often owing to the presence of comorbidities. The MitraClip system (Abbott Vascular, Santa Clara, Calif) is used for percutaneous transcatheter mitral repair using on the Alfieri technique. Based on the EVEREST II trial,⁸⁰ and its use in high-risk patients,⁸¹ it is currently approved by the US Food and Drug Administration for use in symptomatic patients with primary (degenerative) MR who are at prohibitive risk for surgery as determined by the heart team. For FMR, the MitraClip device has received a class IIB recommendation by the European Society of Cardiology, similar to the recommendations for open mitral surgery. In the United States, the device is under investigation for functional MR through the COAPT (Clinical Outcomes Assessment of MitraClip Percutaneous Therapy for Extremely High-Surgical-Risk Patients) trial (ClinicalTrials.gov; NCT01626079).

MitraClip Procedure

The MitraClip procedure is described in detail elsewhere.⁸² The procedure is typically performed in a cardiac catheterization suite or hybrid operating room, under general anesthesia and with TEE guidance. An arterial line is not necessary but can be helpful. Pulmonary artery pressures are measured before and after the procedure; continuous monitoring is not necessary. Femoral venous access is typically obtained in the right groin. A transeptal puncture is performed; unlike in standard techniques, here the particular location of this puncture is critical, to allow optimal navigation in the left atrium for accurate device placement. The patient is systemically heparinized, the venous access is dilated, and the 24F guide sheath is advanced from the femoral vein into the right atrium, and then across the atrial septum. The MitraClip device is guided into optimal position and orientation under TEE. The clip arms are opened to orient them perpendicular to the line of MV coaptation, and then advanced into the LV. The device is then retracted underneath the mitral leaflets, the frictional gripper arms are dropped onto the atrial side of the leaflets, and the device itself is closed to pull more of the leaflet tissue into the device. Adequate insertion of the leaflets in the device and reduction in MR are then assessed by TEE. If insufficient, the device can be opened and leaflets released, and as many attempts as necessary can be made. Once leaflet insertion and MR

reduction are adequate, the device can be released. Additional devices can be placed in a similar manner to optimize MR reduction while avoiding creation of mitral stenosis. On the completion of mitral repair, the steerable guide is removed and heparin reversed. A purse string subcutaneous suture is placed at the femoral venous access site to achieve hemostasis.

MitraClip Data in FMR

Although data have not been well stratified specifically by IMR and nonischemic MR, there are available data on the MitraClip procedure in FMR, particularly outside the United States.⁸³ The MitraClip received CE marking in 2008. Since 2009, the ACCESS-EU registry has been enrolling patients. Of the 567 patients treated, 77% had functional MR. These patients had a logistic EUROSCORE of 24.8%, with the majority in NYHA class 3 to 4 congestive heart failure.⁸⁴ The operative and 1-year mortality were 2.8% and 17%, respectively. Reduction of MR to $\leq 2+$ was achieved in 91.6% at discharge, and 78.5% still had an MR of $\leq 2+$ at the 1-year follow-up. This resulted in an improvement in the 6-minute walk from 274.7 feet to 334.2 feet at 2-year follow-up.⁸⁴

The European SENTINEL registry includes 25 centers in 8 European countries. In 2011 to 2012, a total of 628 patients were treated with the MitraClip, including 72% with FMR.⁸⁵ The procedural mortality was 2.9%, and estimated 1-year mortality was 15.3%. The rehospitalization rate was 25.8% in the patients with FMR.⁸⁵

At Alfieri's own center, 109 consecutive high-risk surgical cases were treated with the MitraClip. Investigators reported treating a challenging cohort of patients with a mean EF of 28%, chronic renal failure in 47%, and a mean Euroscore of 22%.⁸⁶ The 30-day mortality was a remarkable 1.8%. At 12 months, 87% had MR $\leq 2+$, and the mean EF improved to 34.7% ($P = .002$).⁸⁶

In the United States, published data on the MitraClip procedure in FMR is limited. In the recently completed Endovascular Valve Edge-to-Edge Repair (EVEREST II) High-Risk Study, 46 of the 78 patients treated had FMR.⁸⁷ Successful repair was obtained in 96%. The 30-day mortality was 7.7%, which compared favorably to the Society of Thoracic Surgeons operative mortality of 14.2%. The 12-month survival was 76%. These patients were compared with a group of similar patients who had been screened for the MitraClip procedure but were not enrolled and were instead treated with medical therapy. The 12-month survival in the medically treated group was only 55%. These data suggest that the MitraClip may have a beneficial effect on survival. Moreover, 79% of these FMR patients had MR $\leq 2+$, and 80% had at least a 1 grade improvement in NYHA functional class.⁸⁷ These data provided the foundation for the COAPT trial.

COAPT Trial

The COAPT trial is currently underway at more than 80 sites in the United States to investigate the safety and effectiveness of the MitraClip compared with standard medical therapy for HF in symptomatic patients with $\geq 3+$ FMR who have been deemed not appropriate for MV surgery by the local heart team. Patients need to be on stable and optimized goal-directed medical therapy before enrollment. Once enrolled, patients are randomized to the MitraClip procedure or medical therapy for HF alone. The primary safety endpoint consists of a composite of device embolization, single leaflet detachment, development of mitral stenosis, and need for an LVAD, transplantation, or any other nonelective cardiovascular surgery related to the device or procedure at 12 months. The primary effectiveness endpoint is rehospitalization for HF at 24 months. Although the COAPT trial is not powered for mortality, this endpoint will be captured as a secondary endpoint. This trial will be one of the largest and most notable studies in FMR and is expected to shape future surgical and transcatheter trials for this disease.

Heart Team Assessment

A particular recent focus for valve therapy is patient assessment by the heart team. This focus was initially emphasized during clinical trials but has persisted owing to Food and Drug Administration labeling, and the belief that better patient selection produces superior outcomes. The heart teams at many centers have expanded to include not only the cardiac surgeon and interventional cardiologist, but also the HF cardiologist, imaging cardiologist, and geriatrician. In addition, owing to comorbidities, most centers have the option of assigning pulmonologists, nephrologists, hepatologists, and oncologists to aid in the assessment of select patients. The members of the heart team assess the patient either independently or jointly, review relevant studies, and make a uniform decision about the optimal therapy for the patient.

SECTION VII: CONCLUSIONS

IMR is a disease of the ventricle. There are specific imaging criteria, best performed with integrative results. Surgical therapy is appropriate for certain symptomatic patients. MV repair versus replacement has had equivalent results for severe MR. Moderate MR can be successfully treated with CABG alone if the primary symptom is angina. The role of percutaneous transcatheter mitral repair (ie, MitraClip) has been defined for degenerative MV disease, but not yet for IMR. This technology may play a role in high-risk patients. Further follow-up of existing clinical trials will better define appropriate interventional modalities.

Conflict of Interest Statement

A potential conflict of interest exists for Michael J. Mack (co-principal investigator of the COAPT Trial, of which Abbott Vascular is a trial sponsor; uncompensated). All other authors have nothing to disclose with regard to commercial support.

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