

EXPERT CONSENSUS DECISION PATHWAY

2020 Focused Update of the 2017 ACC Expert Consensus Decision Pathway on the Management of Mitral Regurgitation



A Report of the American College of Cardiology Solution Set Oversight Committee

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ABSTRACT

Mitral regurgitation (MR) is a complex valve lesion that can pose significant management challenges. This expert consensus decision pathway emphasizes that recognition of MR should prompt an assessment of its etiology, mechanism, and severity, as well as consideration of the indications for treatment. The document is a focused update of the 2017 ACC Expert Consensus Decision Pathway on the Management of Mitral Regurgitation, with some sections updated and others added in light of the publication of new trial data related to secondary MR, among other developments. A structured approach to evaluation based on clinical findings, accurate echocardiographic imaging, and, when necessary, adjunctive testing can help clarify decision making. Treatment goals include timely intervention by an experienced multidisciplinary heart team to prevent left ventricular dysfunction, heart failure, reduced quality of life, and premature death.

The American College of Cardiology requests that this document be cited as follows: Bonow RO, O’Gara PT, Adams DH, Badhwar V, Bavaria JE, Elmariah S, Hung JW, Lindenfeld J, Morris AA, Satpathy R, Whisenant B, Woo YJ. 2020 focused update of the 2017 ACC expert consensus decision pathway on the management of mitral regurgitation. J Am Coll Cardiol 2020;75:2236-70.

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TABLE OF CONTENTS

PREFACE	2238
1. INTRODUCTION	2238
2. METHODS	2238
Table 1. Summary of Changes in the 2020 Focused Update	2239
3. ASSUMPTIONS AND DEFINITIONS	2240
Figure 1. Pathway for Management of MR	2241
4. DESCRIPTION AND RATIONALE	2240
5. EVALUATION OF THE PATIENT	2240
5.1. History and Physical Examination	2240
5.2. Hemodynamic Effects of MR	2242
5.3. Determining the Etiology and Mechanism of MR	2243
Figure 2. Decision Tree for Distinguishing Primary From Secondary MR	2243
Table 2. Suggested Qualitative and Quantitative Parameters for Standardized Echo Reporting	2246
Figure 3. Anterior Leaflet Override in Secondary MR	2245
5.3.1. Spectrum of Secondary MR	2244
5.4. Assessment of MR Severity	2245
5.4.1. CFD Jet Size	2245
Figure 4. Effect of Driving Velocity on Size and Penetration of Color Doppler MR Jet	2247
5.4.2. Quantitative Parameters	2245
Figure 5. MR Limited to Late Systole in MV Prolapse	2248
Figure 6. Example of Underestimation of EROA by 2D PISA in a Patient With Secondary MR and a Markedly Crescentic Orifice Shape	2249
5.4.3. Integration of Multiple Parameters	2247
Figure 7. Decision Tree for Assessing Severity of Chronic MR by TTE	2250
Table 3. Strengths and Limitations of Common Echocardiographic Parameters of MR Severity	2251
Figure 8. Referral of Patients With MR	2252
5.4.4. Dynamic Nature of MR	2250
5.4.5. Differences in Assessing MR Severity in Primary Versus Secondary MR	2251
5.4.6. Prognosis in MR	2253
5.4.6.1. Primary MR	2253
Table 4. Factors Affecting Prognosis in Primary MR	2254
5.4.6.2. Secondary MR	2253

6. TREATMENT OF CHRONIC MITRAL REGURGITATION	2254
6.1. General Considerations	2254
6.2. Surgical Treatment of Mitral Regurgitation	2255
6.2.1. Primary MR (Figure 9A)	2255
6.2.2. Secondary MR (Figure 9B)	2256
6.2.3. Feasibility of Surgical Repair	2256
Figure 9A. Intervention for Primary Mitral Regurgitation	2253
Figure 9B. Intervention for Symptomatic Secondary MR	2254
Table 5. Pathoanatomically Directed Contemporary Surgical Techniques for MR	2257
Table 6. Feasibility of Surgical MV Repair	2257
Figure 10. Examples of MV Morphology Observed on TEE That Are Amenable to Surgical Repair in Patients With Primary MR	2258
6.2.4. Determination of Risk for Surgery	2257
6.3. Transcatheter Treatment of Mitral Regurgitation	2258
6.3.1. Primary MR	2258
6.3.2. Secondary MR	2259
6.3.3. Edge-to-Edge Leaflet Coaptation	2260
Figure 11. Transcatheter Edge-to-Edge MV Clip Device	2261
Figure 12. Algorithm for Determining Eligibility for Transcatheter MV Intervention	2262
Table 7. Feasibility of Transcatheter Edge-to-Edge Clip Repair	2259
6.3.3.1. Feasibility of Edge-to-Edge Leaflet Coaptation	2260
Figure 13. Mitral Anatomy in Transcatheter Edge-to-Edge MV Clip	2263
7. DISCUSSION AND INTENDED USE OF PATHWAY	2261
7.1 Key Points	2261
PRESIDENT AND STAFF	2263
REFERENCES	2263
APPENDIX 1	
Author Relationships With Industry and Other Entities (Relevant)	2267
APPENDIX 2	
Peer Reviewer Information	2269
APPENDIX 3	
Abbreviations	2270

PREFACE

The American College of Cardiology (ACC) has a long-standing history of developing documents (e.g., decision pathways, health policy statements, appropriate use criteria) to provide members with guidance on both clinical and nonclinical topics relevant to cardiovascular care. In most circumstances, these documents have been created to complement clinical practice guidelines and to inform clinicians about areas where evidence may be new and evolving or where sufficient data may be more limited. In spite of this, numerous care gaps continue to exist, highlighting the need for more streamlined and efficient processes to implement best practices in service to improved patient care.

Central to the ACC's strategic plan is the generation of "actionable knowledge"—a concept that places emphasis on making clinical information easier to consume, share, integrate, and update. To this end, the ACC has evolved from developing isolated documents to creating integrated "solution sets." These are groups of closely related activities, policy, mobile applications, decision support, and other tools necessary to transform care and/or improve heart health. Solution sets address key questions facing care teams and attempt to provide practical guidance to be applied at the point of care. They use both established and emerging methods to disseminate information for cardiovascular conditions and their related management. The success of the solution sets rests firmly on their ability to have a measurable impact on the delivery of care. Because solution sets reflect current evidence and ongoing gaps in care, the associated tools will be refined over time to best match member needs.

Expert Consensus Decision Pathways (ECDPs) represent a key component of solution sets. The methodology for ECDPs is grounded in assembling a group of clinical experts to develop content that addresses key questions facing our members across a range of high-value clinical topics (1). This content is used to inform the development of various tools that accelerate real time use of clinical policy at the point of care. They are not intended to provide a single correct answer; rather, they encourage clinicians to ask questions and consider important factors as they define a treatment plan for their patients. Whenever appropriate, EDCPs seek to provide a unified articulation of clinical practice guidelines, appropriate use criteria, and other related ACC clinical policy. In some cases, covered topics will be addressed in subsequent clinical practice guidelines as the evidence base evolves. In other cases, these will serve as standalone policy.

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1. INTRODUCTION

Improvements in multimodality imaging, surgical techniques, and clinical outcomes, as well as the introduction of transcatheter interventions into clinical practice, have transformed the care of patients with valvular heart disease. Long-term natural history studies have informed clinical decision making regarding the appropriate timing for valve interventions. Nevertheless, knowledge and performance gaps remain that may adversely affect patient outcomes and for which practice tools may provide a means of improvement.

Recent emphasis has been placed on multidisciplinary team (MDT) consensus decision making to optimize outcomes for patients with valvular heart disease, including those with aortic stenosis or mitral regurgitation (MR). The evaluation and management of patients with MR, a valve lesion prevalent among aging U.S. adults, can be very challenging for clinicians, in part because of its various causes, dynamic nature, and insidious progression. MR derives from functional impairment or anatomic derangement of any 1 or more of the components of the mitral apparatus necessary for normal valve function, including the left ventricle (LV), papillary muscles, chordae tendineae, leaflets, and annulus. A highly functioning and expanded MDT is critical for the care of patients with significant MR.

This document contains clinical expert consensus recommendations to guide the approach to patients with MR. The ECDP emphasizes:

- Clinical and echocardiographic assessment
- Establishment of MR etiology (primary, secondary, mixed) and mechanism
- Consideration of associated hemodynamic consequences
- Recognition of the indications for surgical or transcatheter intervention
- Appreciation of the increasing complexity of surgical mitral valve (MV) repair as a function of pathoanatomy
- Understanding of the current role for transcatheter MV edge-to-edge repair using a clip device

Recommendations are based on the [2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease](#) (2), its [2017 focused update](#) (3), and the results of landmark randomized controlled trials (RCTs) (4,5) published in 2018. Additional clinical context and practical advice are provided for medical and surgical decision making in complex patient scenarios.

2. METHODS

The writing committee for this updated 2020 ECDP was formed in 2018. As outlined in [Table 1](#), several revisions

TABLE 1 Summary of Changes in the 2020 Focused Update

2020 Focused Update Section	2017 ECDP	2020 Focused Update
1. Introduction	Noted limited role for transcatheter edge-to-edge repair for prohibitive-surgical-risk patients with primary MR	Acknowledges new RCT data supporting transcatheter edge-to-edge repair in selected patients with HF and secondary MR
Comment: The MITRA FR and COAPT studies were published in 2018. The U.S. FDA approved the use of transcatheter edge-to-edge repair using a clip device for selected patients with heart failure and secondary MR in March 2019.		
2. Figure 1. Pathway for Management of MR	Transcatheter treatment limited to primary MR	<ul style="list-style-type: none"> ■ Exercise echo added to list of ancillary testing that may be considered to establish severity of MR ■ Transcatheter treatment extended to secondary MR after documentation of persistent symptoms despite optimal GDMT for HF with reduced EF ■ HF expert added to list of clinicians who may provide patient follow-up
3. Section 5.2. Hemodynamic Effects of MR	Major focus on primary MR	Additional emphasis placed on pathophysiological changes with secondary MR
4. Section 5.3.1. Spectrum of Secondary MR	Included consideration of LVAD/transplant for patients with severe LV remodeling and depressed systolic function who are not candidates for conventional surgery	Includes theoretical concept of disproportionate MR as a proposed means of evaluating secondary MR and potential candidacy for valve directed therapies
5. Figure 8. Referral of Patients with MR	Major focus on primary MR	<ul style="list-style-type: none"> ■ Expansion of secondary MR considerations ■ Inclusion of consideration of rhythm control in patients with AF, especially those with atrial functional MR
6. Section 5.4.6. Prognosis in MR	Limited role for transcatheter edge-to-edge repair	Includes statement about survival benefit with edge-to-edge repair in selected patients with secondary MR
7. Figure 9A. Intervention for Primary MR Figure 9B. Intervention for Symptomatic Secondary MR	Treatment restricted to surgery	<ul style="list-style-type: none"> ■ New Figures 9A (Primary MR) and 9B (Secondary MR) ■ Expanded options for secondary MR ■ Inclusion of transcatheter MV therapy
8. Section 6.3. Transcatheter Treatment of MR	Limited to primary MR	Includes secondary MR
9. Figure 12. Algorithm for Determining Eligibility for Transcatheter MV Intervention	Limited to primary MR	Includes secondary MR
10. Table 7. Feasibility of Transcatheter Edge-to-Edge Clip Repair	Limited to primary MR	Includes secondary MR
11. Section 7. Discussion and Intended Use of Pathway and Section 7.1. Key Points	Limited role for transcatheter edge-to-edge repair in primary MR	<ul style="list-style-type: none"> ■ Expands MDT to include cardiologist with experience managing HF and MR in management of patients with secondary MR ■ Expands use of edge-to-edge repair for selected patients with secondary MR

AF = atrial fibrillation; COAPT = Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy; ECDP = expert consensus decision pathway; EF = ejection fraction; FDA = Food and Drug Administration; GDMT = guideline-directed management and therapy; HF = heart failure; LV = left ventricle; LVAD = left ventricular assist device; MDT = multidisciplinary team; MITRA-FR = Percutaneous Repair with the MitraClip Device for Severe Functional/Secondary Mitral Regurgitation; MR = mitral regurgitation; MV = mitral valve; RCT = randomized controlled trial; TTE = transthoracic echocardiography.

have been made to the 2017 ECDP in response to rapid developments in the field and the March 2019 the U.S. Food and Drug Administration (FDA) approval of an edge-to-edge transcatheter repair system for treatment of selected patients with secondary MR (6); these include changes to the master document, figures, and tables. The revised document and tools were based on the writing committee's knowledge of the evidence assembled and recommendations made in the 2014 AHA/ACC Guideline for Management of Patients With Valvular Heart Disease (2), its 2017 focused update (3), additional literature review through September 2019, and, when evidence was lacking or limited, expert consensus. The writing committee (see Appendix 1) included representatives from the following areas: general cardiology, heart valve disease,

advanced heart failure (HF)/transplantation, imaging, interventional/structural heart disease, and cardiac surgery.

The work of the writing committee was supported exclusively by the ACC without commercial support. Writing committee members volunteered their time to this effort. Conference calls of the writing committee were confidential and attended only by committee members and ACC staff. A formal peer review process was completed consistent with ACC policy and included expert reviewers nominated by the ACC (see Appendix 2). A public comment period was also held to obtain additional feedback. Following reconciliation of all comments, this document was approved for publication by the ACC Clinical Policy Approval Committee.

3. ASSUMPTIONS AND DEFINITIONS

This effort was neither conceived nor designed to rewrite or reinterpret the [2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease](#) (2) or its [2017 focused update](#) (3). Rather, it was intended to update recommendations put forth in 2017 that have since been influenced by interim developments. The writing committee did not stipulate the means by which MR may first be appreciated and did not focus on community efforts to increase the rate of accurate MR detection. Evaluation and management algorithms in this document flow from an echocardiographically validated diagnosis of MR. Primary MR is defined by principal involvement of the leaflets and/or chordae tendineae in the pathological process (e.g., myxomatous disease, endocarditis). Secondary MR is characterized by incompetence due to adverse changes in LV size, shape, or function with or without annular dilatation (e.g., ischemic cardiomyopathy). Mixed MR is due to both primary and secondary causes (e.g., MV prolapse/flail with ischemic cardiomyopathy). It is now recognized that primary and secondary MR are different diseases with different outcomes and indications for treatment. The writing committee used the American Society of Echocardiography's 2017 Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation to grade MR severity and emphasized the need for additional testing when severity could not be established with certainty (7). The 2019 AATS/ACC/SCAI/STS Expert Consensus Systems of Care Document: Operator and Institutional Recommendations and Requirements for Transcatheter Mitral Valve Intervention has been updated from its original 2014 version (8). Operator and institutional requirements for transcatheter MV interventions are the subject of this multisocietal review (8). The writing committee did not define a comprehensive valve center nor stipulate the criteria by which a MV surgeon or interventionalist is considered experienced or highly experienced. The members of the MDT and their respective roles have also been addressed in the multisocietal review. Characteristics of a comprehensive (Level I) valve center and the minimum requirements for MDT composition are addressed in the 2019 AATS/ACC/ASE/SCAI/STS Expert Consensus Systems of Care Document: A Proposal to Optimize Care for Patients With Valvular Heart Disease (9). The current document provides additional emphasis on the roles of the interventional echocardiographer and cardiologist with experience managing HF and MR.

CENTRAL ILLUSTRATION

Figure 1 provides an overview of this ECDP. See the text for more detailed considerations and guidance.

4. DESCRIPTION AND RATIONALE

MR is the most common type of moderate or severe heart valve disease among U.S. adults older than 55 years. Its prevalence increases further as a function of age (10). The [2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease](#) (2) emphasizes disease staging, wherein patients are classified as being at risk for developing MR (Stage A), having mild or moderate MR that may progress over time (Stage B), having asymptomatic severe MR (Stage C) with normal (C1) or reduced (C2) LV function, or having symptomatic severe MR (Stage D). Indications for treatment depend on disease stage, the characterization of which relies on accurate assessment of MR severity and an understanding of the efficacy and safety of any therapeutic intervention. A survey commissioned by the ACC identified multiple knowledge and practice gaps among respondents, including failure to identify clinically significant MR on physical examination, failure to recognize the difference between primary and secondary MR, poor quality and incomplete echocardiographic assessment and reporting, lack of awareness of guideline-based recommendations for treatment, and lack of awareness of the case volume and outcomes of surgical repair at their institution (11).

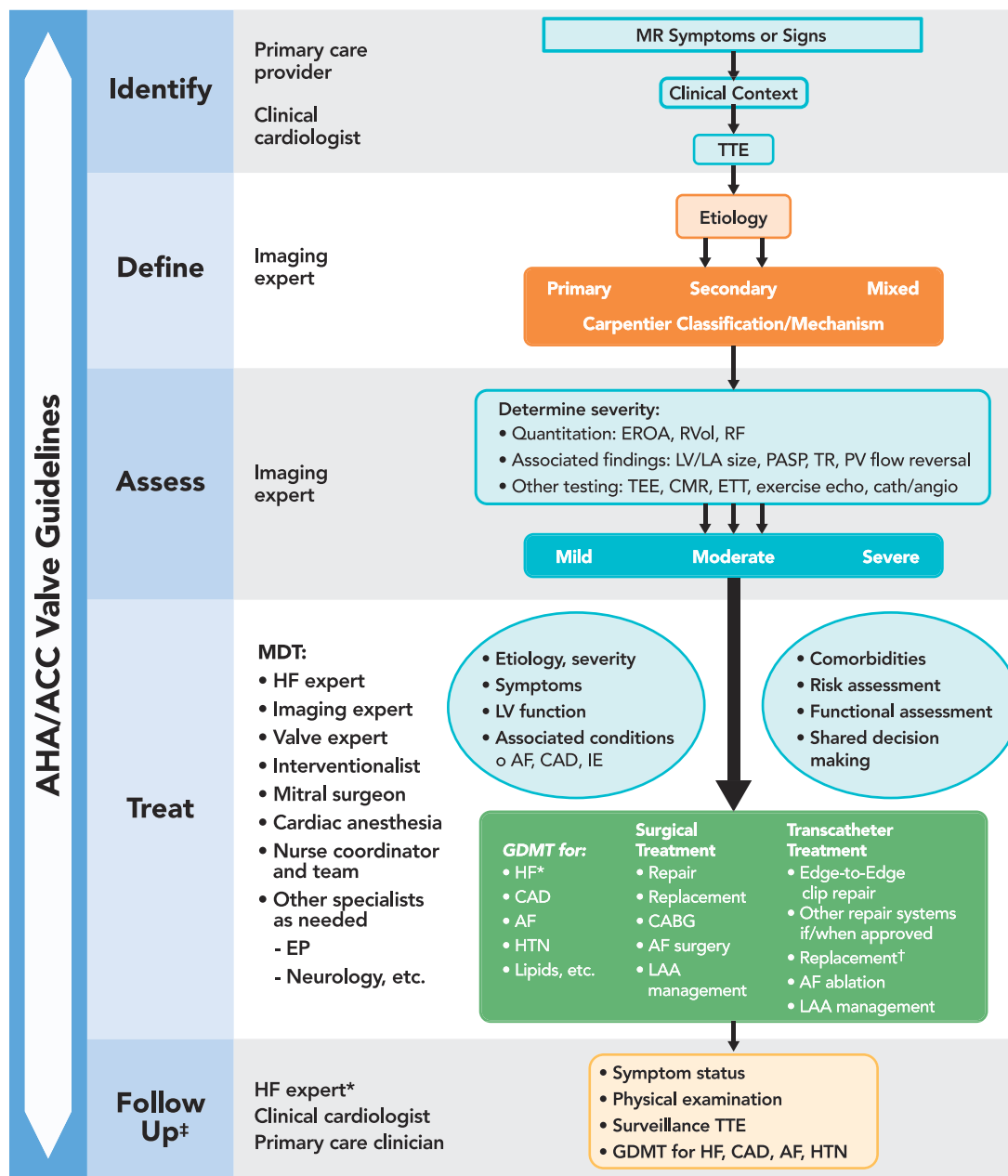
This ECDP document focuses on the evaluation and management of patients with MR, with specific emphasis on 1) clinical assessment; 2) proper identification of the etiology and mechanism of MR; 3) determination of MR severity; 4) assessment of the feasibility of surgical or transcatheter intervention in appropriate patients; and 5) indications for consideration of referral to a regional, comprehensive valve center (9). Within each section, clear and precise terminology is recommended for communicating the essential features of MR in the medical record. Because patients with acute MR typically present with hemodynamic compromise for which the need for urgent intervention is well-recognized, this document focuses on chronic MR, where gaps in knowledge and practice are more common.

5. EVALUATION OF THE PATIENT

5.1. History and Physical Examination

Assessment of the patient with chronic MR begins with a directed history and physical examination. Symptoms may be absent or subtle, even in patients with severe MR due to flail leaflet (Stage C) (12). The lack of symptoms in the chronic phase may relate to enhanced left atrial (LA) compliance, whereby a large regurgitant volume (RVol) may be accommodated within an enlarging LA without an increase in pressure sufficient to cause dyspnea. Patients may also reduce their activity levels, often subconsciously, to avoid symptoms. It is helpful to ask the

FIGURE 1 Pathway for Management of MR



Abbreviations:

AF = atrial fibrillation; Angio = angiography; CABG = coronary artery bypass graft; CAD = coronary artery disease; Cath = catheterization; CMR = cardiovascular magnetic resonance; EROA = effective regurgitant orifice area; ETT = exercise tolerance testing; GDMT = guideline-directed management and therapy; HF = heart failure; HTN = hypertension; IE = infective endocarditis; LAA = left atrial appendage; LV = left ventricle; MR = mitral regurgitation; PASP = pulmonary artery systolic pressure; PV = pulmonary vein; RF = regurgitant fraction; RVol = regurgitant volume; TEE = transesophageal echocardiogram; TR = tricuspid regurgitation; TTE = transthoracic echocardiogram

* Advanced heart failure/transplant expertise is preferred when available. Treatment for secondary MR should include CRT when indicated by wide QRS and LV dysfunction.

† Investigational replacement systems are in clinical development and not approved.

‡ Follow up of treated primary MR is most often provided by a valve expert or general cardiologist. Follow up of treated secondary MR and HF should be provided by a HF expert when available.

patient what the most vigorous activity s/he currently undertakes is and compare that with what s/he was able to do previously. Family members may often report symptoms and/or diminished activity about which the

patient is unaware. Another simple approach is to ask the patient what s/he is capable of doing on a scale of 1 to 10, with 1 being no activity at all and 10 being any activity without limitation (13). In addition to exertional dyspnea,

common symptoms include fatigue and palpitations. Incorporation into the medical record of a patient questionnaire on health status is encouraged. The STS/ACC Transcatheter Valve Therapy (TVT) Registry ([NCT01737528](#)) includes an entry for the Kansas City Cardiomyopathy Questionnaire ([14,15](#)). The Patient Reported Outcomes Measurement Information System (PROMIS) is an alternative assessment tool ([16](#)).

If the patient is asymptomatic, exercise testing may be performed safely and may elicit symptoms or demonstrate reduced exercise capacity at an earlier stage in the natural history of the disease. Echocardiographic imaging performed as part of the exercise protocol may reveal elevated pulmonary artery systolic pressures, worsening MR, or failure of LV or right ventricular systolic function to augment normally ([17–20](#)). Exercise testing can prompt reclassification of patients from Stage C to D or even from Stage B to D. The 6-minute walk test is a simple, inexpensive, and reproducible method of assessing functional capacity and may reflect normal daily activity level better than a maximal, symptom-limited exercise test in a frail or elderly patient ([21](#)).

In patients with primary MR, the presence of a diastolic filling complex (S_3 plus short diastolic murmur) is usually associated with a significant RVol and severe MR ([22](#)). In secondary MR, an S_3 gallop is harder to interpret because it may be due to the underlying LV dysfunction. If the murmur of primary MR is not audible after listening in multiple positions or with dynamic maneuvers, or limited in timing to late systole only, it is likely that the degree of MR is not severe. One or more non-ejection clicks may be audible in primary MR. Differential radiation of the murmur of primary MR provides a clue as to the underlying leaflet pathology. Murmurs associated with anterior leaflet flail are directed to the axilla and left infrascapular area, whereas murmurs associated with posterior leaflet flail radiate anteriorly and can be confused with systolic ejection murmurs. With secondary MR, the murmur is usually best heard at the apex and radiates to the axilla. Atrial fibrillation (AF) or other arrhythmias may be present in patients with MR and can render the examination more challenging, particularly when the heart rate is rapid ([22](#)).

5.2. Hemodynamic Effects of MR

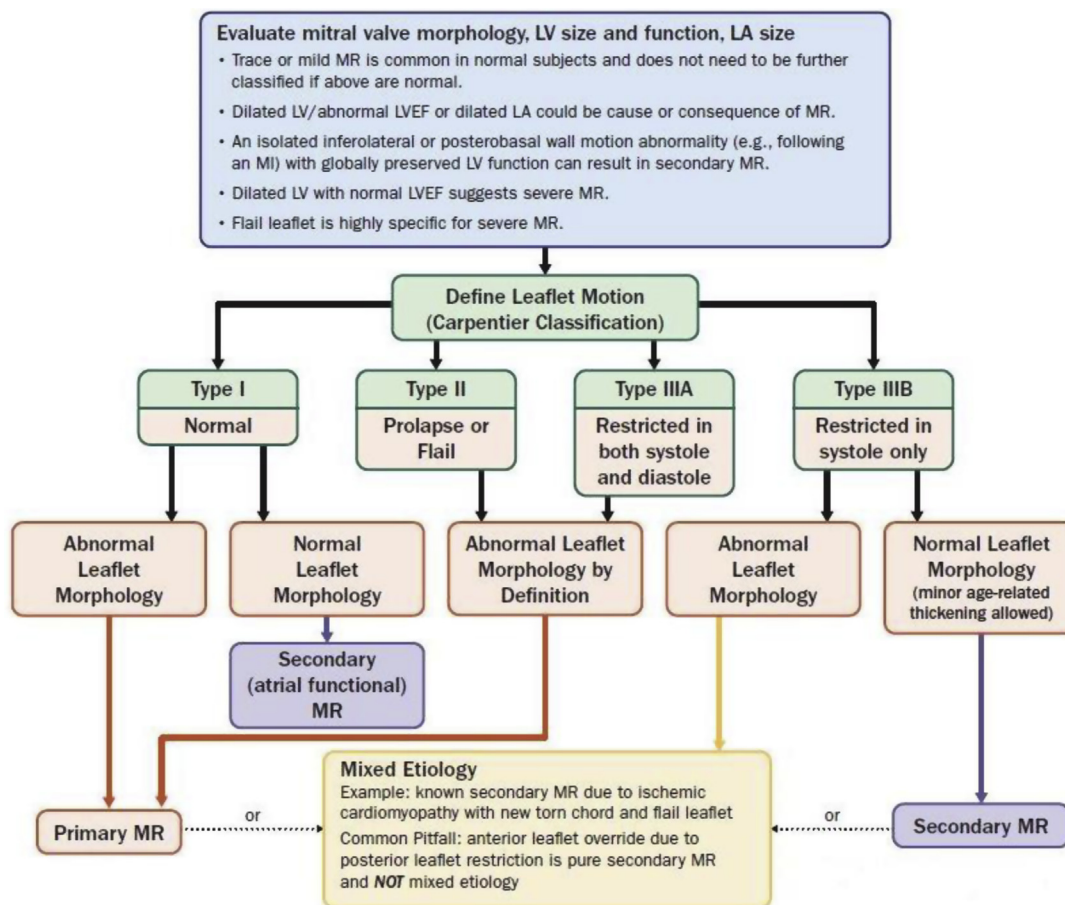
MR is considered to be primary when the mechanisms of regurgitation are related to disease of the MV leaflets or chordae tendineae. Chronic, severe, primary MR imposes a pure volume overload on the LV, resulting in eccentric hypertrophy and LV dilation. Increased preload, combined with low-to-normal afterload, augments LV ejection fraction (EF), which is typically supranormal. As the LV dilates, LV wall stress increases. Incipient and

irreversible myocardial dysfunction may occur with longstanding LV volume overload. Because EF is a load-dependent measure of LV systolic function, it can be preserved even as myocardial contractile function begins to decline. Thus, although symptoms are a strong indication for MV surgery, current clinical practice guidelines recommend surgical intervention in asymptomatic patients with primary MR and LVEF <60% or LV end-systolic dimension >40 mm ([2](#)). These thresholds, however, may already indicate LV dysfunction, and MV surgery is also reasonable for asymptomatic patients with primary severe MR when serial imaging studies demonstrate a progressive increase in LV size (i.e., an end-systolic dimension approaching 40 mm) or decrease in LVEF (approaching 60%) ([3](#)). In addition, surgery for severe primary MR is reasonable in patients with recent-onset atrial fibrillation (AF) or pulmonary hypertension (pulmonary artery systolic pressure >50 mm Hg). In patients who are candidates for MV repair, such as those with myxomatous MR, long-term outcomes are optimized with surgical valve repair *before* the onset of symptoms, LV systolic dysfunction, pulmonary hypertension, or AF. Thus, it is reasonable to refer asymptomatic patients with severe primary MR to an experienced surgeon when the likelihood of a successful and durable repair exceeds 95% and the mortality risk of surgery is <1%.

In secondary MR, the relationship between LVEF and the associated volume overload is confounded by the fact that LV dilation and decreased function are usually the cause rather than the consequence of MR. In some patients, secondary MR may simply be a marker of a diseased ventricle, whereas in others it may contribute importantly to further progression of LV remodeling and dysfunction and thus worsen outcomes independently. The latter group of patients include those with isolated atrial functional secondary MR, in whom the MR is due to annular dilation and malcoaptation of the leaflets as a consequence of the arrhythmia ([23](#)). In addition, the severity of secondary MR can be quite dynamic and can change abruptly in response to afterload (blood pressure), preload (volume), ischemia, and heart rate/rhythm. The presence of any degree of secondary MR is associated with worsened prognosis in patients with ischemic or nonischemic cardiomyopathy ([14,24–30](#)). Although a conceptual framework for relating the severity of secondary MR (as assessed by the effective regurgitant orifice areas [EROAs]) to the degree of LV dilation (represented by LV end-diastolic volume) has been proposed, further prospective validation is required before recommendations for widespread clinical adoption can be made ([31,32](#)).

In addition to its effects on LV volume and function, chronic severe MR (whether primary or secondary) results

FIGURE 2 Decision Tree for Distinguishing Primary From Secondary MR



LA = left atrial; LV = left ventricle; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MR = mitral regurgitation.

in LA dilation, increased LA pressure, and pulmonary venous hypertension. AF is a common development in chronic severe MR. As noted, in some patients, AF is the cause and not the result of MR (atrial functional MR). Thus, AF is another aspect of chronic MR in which cause and effect are not always easily delineated. The assessment of MR severity must take into account the clinical context, systemic blood pressure, heart rhythm, valve anatomy, LV size/function, LA size/volume, pulmonary artery systolic pressure, and intensity of guideline-directed management and therapy where appropriate.

5.3. Determining the Etiology and Mechanism of MR

The identification of MR etiology and mechanism is most commonly achieved by transthoracic echocardiography (TTE) (Figure 2). MV morphology should be carefully

assessed in multiple views using B-mode imaging to evaluate structure and motion; color flow Doppler (CFD) is utilized to localize the origin of MR jet(s). If image quality is poor with TTE, transesophageal echocardiography (TEE) may be needed to define anatomy and function more precisely. TEE may identify lesions such as vegetations or flail segments not detected by TTE (11,33-36). Careful measurement of LV and LA volumes and of LV dimensions should be performed according to the [American Society for Echocardiography \(ASE\) guidelines for chamber quantification](#) (37). MV morphology, LV and LA volumes, and LV size and systolic function are used together to classify the etiology and mechanism of MR (Figure 2). Abnormal mitral leaflet morphology includes thickening, calcification, redundancy, perforation, vegetations, other masses, and clefts. Such abnormalities

should be described in detail (diffuse vs. focal, size, leaflet location). Abnormal subvalvular morphology includes chordal rupture, thickening, fusion, vegetations, and masses, which should similarly be described in detail by size and location. Abnormal annular morphology includes dilation and calcification. Mitral annular calcification can be localized posteriorly or extend into the LV outflow tract or LV myocardium. When MR is due to primary MV pathology, left-sided chamber dilation should be considered a clue that the MR is both chronic and severe. Primary MR with normal LV and LA size, function, and volume is unlikely to be severe (3). If the mitral apparatus is structurally normal, significant MR is likely to be secondary. In such cases, the mechanism of MR still needs to be identified. For example, most patients with secondary MR have a dilated LV with global or regional wall motion abnormalities with systolic tethering of the leaflets, annular dilation, or both (38–42); however, isolated regional wall motion abnormalities, particularly in the inferobasal or posterobasal segments, may cause severe secondary MR despite preserved global LV function and dimensions. It is also possible to have MR secondary to pure annular dilation in patients with severe LA dilation (43). This has been termed “atrial functional MR,” and it is mostly commonly seen in persistent or long-standing persistent AF or in restrictive cardiomyopathies, such as that due to amyloid.

Once leaflet morphology is characterized, leaflet motion should be described using Carpentier’s classification system (44) (Figure 2). Normal leaflet motion (Type I) may be seen in primary MR due to endocarditis, perforation, or clefts and in primary or secondary MR due to isolated annular dilation. Excessive leaflet motion (Type II) is most commonly seen with MV prolapse or flail leaflet. Leaflet prolapse occurs when the leaflet body moves above the saddle-shaped annulus in systole, whereas leaflet flail occurs when a focal portion of the leaflet edge moves above the annulus and zone of coaptation. With flail leaflets, torn chords are usually visible and are associated with adverse prognosis (45). Restricted leaflet motion (Type III) is subclassified into restriction during both systole and diastole (IIIA) or during systole only (IIIB). The former is classic for rheumatic MV disease, radiation- or drug-induced injury, or other inflammatory conditions. The latter is typical of MR secondary to ischemic or nonischemic cardiomyopathy.

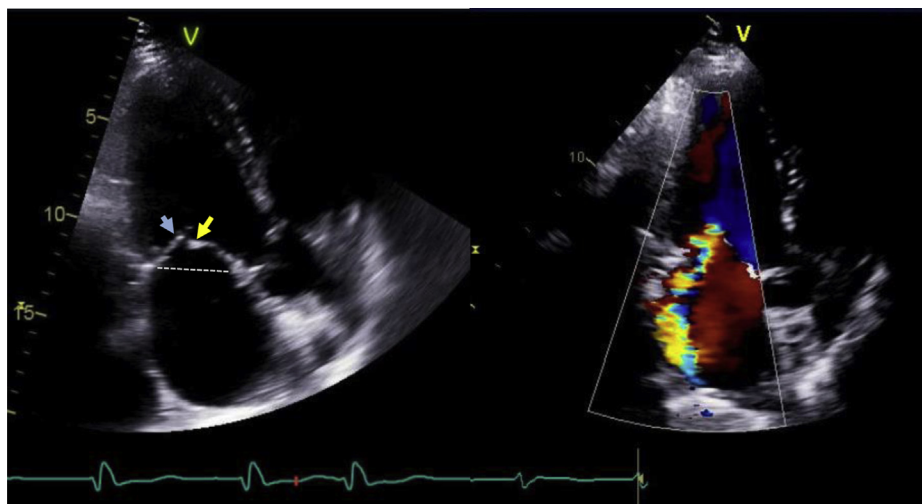
It is important to note that mixed pathology can and does occur. Untreated primary MR, for example, may eventually result in irreversible LV dilation/dysfunction in which both leaflet prolapse and tethering may coexist. Other examples include patients with long-standing

secondary MR due to ischemic heart disease or AF who subsequently rupture a chord, patients with MV prolapse who have a myocardial infarction or develop a cardiomyopathy due to an independent cause, and older patients with calcifications of the leaflets or clefts/deep folds with underlying LV disease. A common mistake in clinical practice is to misconstrue anterior leaflet override as prolapse. In Type IIIB leaflet motion, the posterior leaflet is often severely tethered and the anterior leaflet overrides it (Figure 3) but does not move above the annular plane. This finding should not be equated with anterior leaflet prolapse or with mixed-etiology MR. MR jet direction by CFD provides an important clue to the mechanism of MR. An anteriorly directed jet is most commonly due to posterior leaflet prolapse/flail or anterior leaflet restriction, whereas a posteriorly directed jet is typically due to anterior leaflet prolapse/flail or posterior leaflet restriction. If the jet direction is eccentric, but the mechanism uncertain, TEE is indicated to clarify leaflet pathology and motion. Table 2 lists the descriptors of MR mechanism and severity that should be included in standardized echocardiographic reports.

5.3.1. Spectrum of Secondary MR

Classically, secondary MR occurs as a consequence of adverse LV remodeling, papillary muscle displacement, leaflet tethering, and annular dilation. MV closing forces may also be reduced. At one end of the spectrum is a severely dilated, spherical LV with markedly depressed LV systolic function and secondary MR, which occurs along the leaflet coaptation line. At the other end of the spectrum, a patient with an isolated inferobasal myocardial infarction may develop severe secondary MR due to asymmetric posteromedial annular dilation and posterior leaflet tethering, despite normal LV size and global EF (46). As noted in the previous text, secondary MR may also emerge or worsen in the context of AF due to LA stretch and annular dilation despite preserved LV systolic function. Management considerations need to take into account the mechanism(s) of MR and the potential indications for other interventions, such as coronary revascularization and rhythm control. In patients with HF, advanced LV remodeling/chamber dilatation, and significant LV systolic dysfunction who remain symptomatic despite optimized guideline-directed management and therapy (GDMT) (including cardiac resynchronization therapy [CRT] when indicated), MV intervention may not improve HF symptoms or quality of life if the dominant problem is severe LV dysfunction (4). Heart transplantation or destination LV assist device therapy may be a more effective treatment strategy than MV intervention in this context. For patients with HF and moderate to

FIGURE 3 Anterior Leaflet Override in Secondary MR



Anterior leaflet override in secondary MR due to ischemic cardiomyopathy. Apical long-axis views (left panel) showing fixed posterior mitral leaflet (PML) (blue arrow) with an overriding anterior mitral leaflet (AML) (yellow arrow). Coaptation is absent with a large “wrap-around” color Doppler jet directed posteriorly by the fixed PML (right panel). This is commonly misdiagnosed as MV prolapse but cannot be such because the AML never moves superiorly to the mitral annulus (dotted line). AML = anterior mitral leaflet; LV = left ventricle; LA = left atrium; MR = mitral regurgitation; PML = posterior mitral leaflet.

severe or severe secondary MR with lesser degrees of LV remodeling who remain symptomatic despite GDMT, MV intervention may be beneficial (5). However, the identification of patients appropriate for such intervention is challenging.

5.4. Assessment of MR Severity

5.4.1. CFD Jet Size

Severity of MR is most commonly assessed using CFD during TTE or TEE. CFD is a misnomer because it is not actually a flow image—it is an image of the spatial distribution of velocities within the image plane and is profoundly affected by instrument settings and hemodynamic factors (7). If these are held constant, the size of a jet through a given EROA is determined by its momentum flux, $\rho A v^2$, where ρ is blood density, A is orifice area, and v^2 is velocity squared (47). Thus, a 6.0 m/s MR jet appears 44% larger than a 5.0 m/s MR jet on CFD. High-velocity MR jets, such as occur with hypertension, aortic stenosis, or LV outflow tract obstruction, will therefore make MR appear worse on CFD (Figure 4), which should be recognized by the interpreting physician. Accordingly, it is crucial to record blood pressure, estimated LV systolic pressure in the presence of aortic stenosis or LV outflow obstruction, heart rate, and rhythm at the time of TTE and to incorporate them when grading MR severity (7). The tendency for CFD to overestimate MR severity has been shown in a study comparing TTE with cardiac magnetic resonance (CMR) imaging for

quantitation (48). This also explains why healthy individuals with no heart murmur often have mild MR on CFD (49). MR can be significantly underestimated when jets have a low driving pressure or are markedly eccentric as momentum is transferred to the LA wall (50). Low-velocity jets (e.g., 4 m/s) suggest high LA pressure and low LV pressure and, therefore, indicate severe MR with hemodynamic compromise (assuming proper alignment of the continuous wave Doppler beam with the MR jet). In addition to jet driving velocity and eccentricity, CFD jet size is affected by multiple other technical and hemodynamic factors (51). Thus, both U.S. and European guidelines recommend that MR jet size assessed by CFD not be used alone to assess MR severity (7,52).

5.4.2. Quantitative Parameters

Calculation of EROA, a marker of lesion severity, as well as RVol and regurgitant fraction (RF), is strongly recommended for assessing MR severity (7). These parameters can be measured by several techniques, including the proximal isovelocity surface area (PISA) method, volumetric methods, and 3-dimensional imaging. It is crucial to recognize the technical limitations and imprecision of each method and the overlap of values obtained. Volumetric methods (including those with CMR) suffer from multiplication of the errors inherent in measuring stroke volumes at different locations, but account for the whole of MR over the duration of systole. Single-frame measurements, such as with PISA or vena contracta width or

TABLE 2

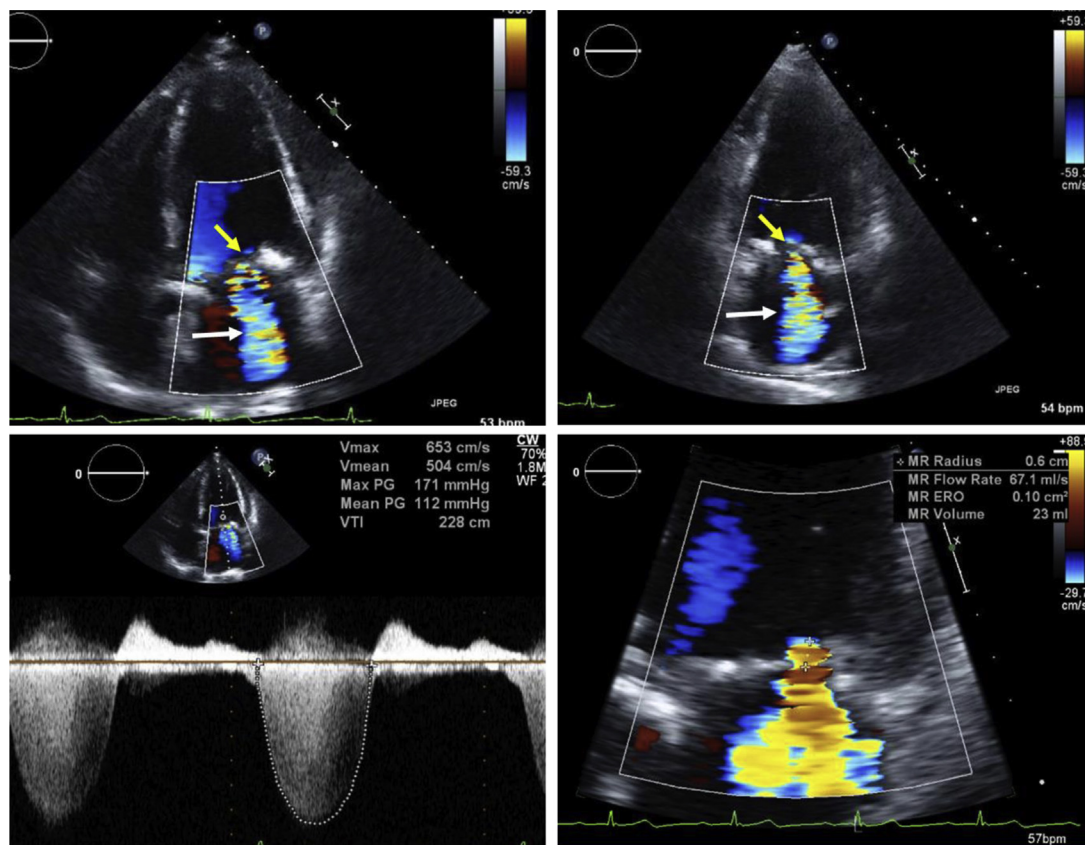
Suggested Qualitative and Quantitative Parameters for Standardized Echo Reporting

MITRAL REGURGITATION ASSESSMENT Suggested Qualitative and Quantitative Parameters for Standardized Echo Reporting*		
HEMODYNAMIC AND RHYTHM PARAMETERS	QUALITATIVE PARAMETERS (CONT.)	QUALITATIVE PARAMETERS (CONT.)
<ul style="list-style-type: none"> Blood Pressure Heart Rate Rhythm 	Mitral stenosis <ul style="list-style-type: none"> Rheumatic Degenerative Other Carpentier Classification <ul style="list-style-type: none"> Normal leaflet motion (Type I) may be seen in primary MR due to endocarditis, perforation, or clefts, or in secondary MR due to pure annular dilation. Excessive leaflet motion (Type II) is most commonly seen with mitral valve prolapse or flail leaflet. Restricted leaflet motion (Type III): subclassified into <ul style="list-style-type: none"> III A: restriction during both systole and diastole III B: restricted during systole only (e.g., ischemic etiology) 	Mitral Inflow Profile: <ul style="list-style-type: none"> E dominant pattern A dominant pattern (incompatible with severe MR)
QUALITATIVE PARAMETERS		QUANTITATIVE PARAMETERS
Leaflet Morphology: <ul style="list-style-type: none"> Structurally normal Nonspecific thickening Focal calcific or nodular thickening Diffusely calcified Myxomatous Vegetations Tumor Clefts Perforation Chordal Morphology: <ul style="list-style-type: none"> Ruptured chordae: <ul style="list-style-type: none"> AML PML Redundant chordae: <ul style="list-style-type: none"> AML PML Annulus Size and Morphology (commissure-commissure and anterior-posterior measurements) <ul style="list-style-type: none"> Normal Dilated Calcified (location and extent) Leaflet Mobility: <ul style="list-style-type: none"> Normal Redundant, no prolapse Systolic anterior motion (SAM) <ul style="list-style-type: none"> AML PML Flail <ul style="list-style-type: none"> Anatomic localization: <ul style="list-style-type: none"> A1 A2 A3 P1 P2 P3 Posteromedial commissure Anterolateral commissure Prolapse <ul style="list-style-type: none"> Anatomic localization: <ul style="list-style-type: none"> A1 A2 A3 P1 P2 P3 Posteromedial commissure Anterolateral commissure Restricted or Tethered Leaflets <ul style="list-style-type: none"> AML PML Both 	Submitral morphology: <ul style="list-style-type: none"> Thickening Calcification Retraction Tumor Vegetation MR Mechanism: <ul style="list-style-type: none"> Primary Secondary <ul style="list-style-type: none"> Dilated Cardiomyopathy Ischemic Cardiomyopathy Other Mixed MR Jet Duration (CW Doppler and frame-by-frame analysis of color flow Doppler): <ul style="list-style-type: none"> Holosystolic Early systolic Midsystolic Late systolic Bimodal CW Doppler density MR Jets: <ul style="list-style-type: none"> Single Multiple MR Jet Direction: <ul style="list-style-type: none"> Centrally directed Eccentric <ul style="list-style-type: none"> Posteriorly directed Posterolaterally directed Laterally directed Anteriorly directed Anteromedially directed Medially directed Pulmonary Vein Flow Profile: <ul style="list-style-type: none"> Normal Systolic flow blunting Systolic flow reversal Number of veins exhibiting systolic reversal 	Vena Contracta: <ul style="list-style-type: none"> Vena contracta width: mm Vena contracta area (cm²) Threshold values specific for severe MR <ul style="list-style-type: none"> EROA >0.4cm² Regurgitant volume >60 mL/beat Regurgitant fraction >50% Left Atrial Size: <ul style="list-style-type: none"> Left atrial dilation Left atrial volume index: mL/m² Mitral Valve Area: cm² <i>cm² (for patients with coexisting rheumatic or degenerative mitral stenosis or for planning edge-to-edge clip)</i> <ul style="list-style-type: none"> 2D planimetry (biplane) 3D planimetry (multiplanar Reconstruction) Pressure half-time Continuity equation PISA <ul style="list-style-type: none"> Mean transmitral Doppler gradient: mm Hg @ heart rate (input HR concurrently recorded during CW Doppler acquisition) Left Ventricular Function: <ul style="list-style-type: none"> Ejection fraction (normal > 60%) Global LV dysfunction Regional LV dysfunction (detail wall motion) Left Ventricular Size: <ul style="list-style-type: none"> End diastolic LV dimension End systolic LV dimension and/or End diastolic volume/volume index End systolic volume/volume index Right Ventricular Size (tricuspid annular and midventricular measurements) <ul style="list-style-type: none"> Normal Dilated Right Ventricular Systolic Function: <ul style="list-style-type: none"> Normal Impaired Tricuspid Annulus: <ul style="list-style-type: none"> Normal Dilated Tricuspid Valve Regurgitation: <ul style="list-style-type: none"> Mild Moderate Severe PA Systolic Pressure: mm Hg Estimated RA pressure: mm Hg

*Above criteria applicable for native mitral valve disease only and not for assessing MR post mitral valve repair (surgical or transcatheter).

Abbreviations: AML = anterior mitral leaflet; CW = continuous wave; EROA = effective regurgitant orifice area; ERO = effective regurgitant orifice; LV = left ventricular; MR = mitral regurgitation; PA = pulmonary artery; PISA = proximal isovelocity surface area; PML = posterior mitral leaflet; RA = right atrial; RF = regurgitant fraction; SAM = systolic anterior motion

FIGURE 4 Effect of Driving Velocity on Size and Penetration of Color Doppler MR Jet



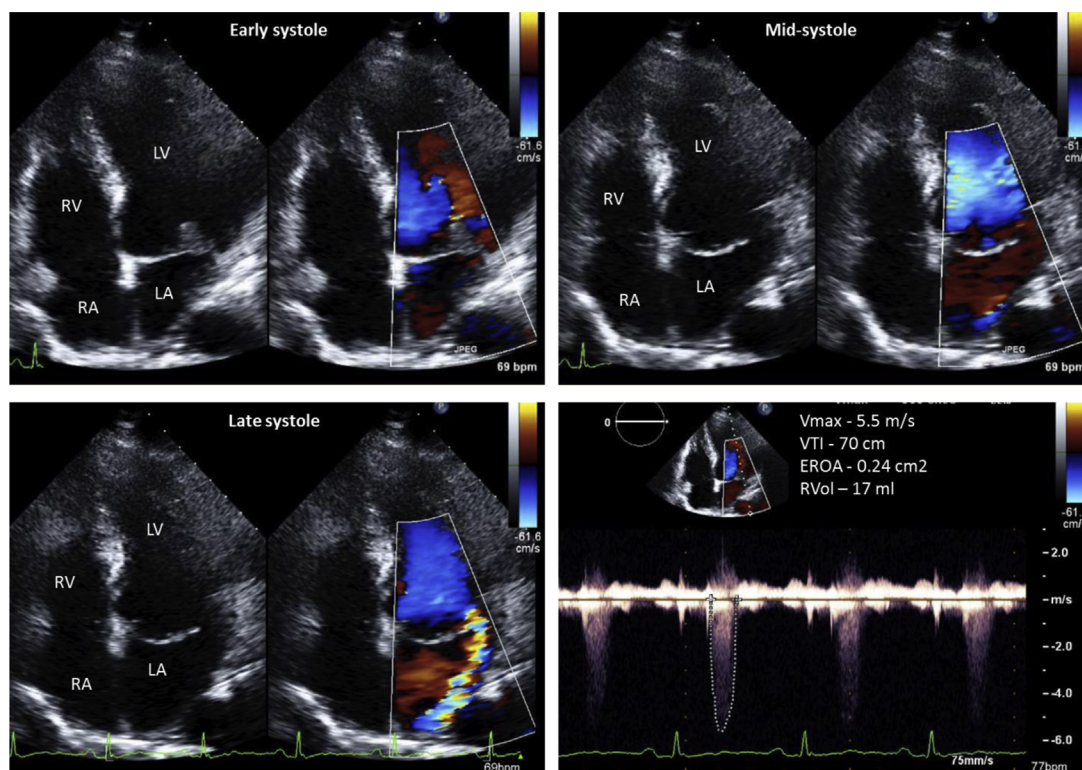
Example of the effect of driving velocity on size and penetration of MR jets. Top panels: Large MR jet (white arrows) penetrating deep into LA in apical 4- (left) and 2- (right) chamber views. In both views, the jet origin is narrow with a tiny proximal flow convergence zone (yellow arrows). Bottom left: CW Doppler of MR jet shows a very high velocity 6.5 m/s, corresponding to a LV-LA pressure gradient of 170 mm Hg. Per jet momentum flux, a 6.5 m/s jet appears 69% larger than a typical 5.0 m/s MR jet. In this patient, severe aortic stenosis was present, leading to a very high LV systolic pressure. Bottom right: PISA confirms mild MR with EROA 0.10 cm² and RVol 23 ml. CW = continuous wave; EROA = effective regurgitant orifice area; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; PISA = proximal isovelocity surface area; RVol = regurgitant volume.

area, can markedly overestimate MR severity when the jet is limited to early or late systole (Figure 5) (53). When MR is holosystolic, properly measured values of EROA ≥ 0.4 cm², RVol ≥ 60 mL or RF $\geq 50\%$ are highly specific for severe MR. Properly measured values of EROA < 0.2 cm², RVol ≤ 30 mL, or RF $< 30\%$ are highly specific for mild MR. Intermediate values can occur in severe MR but lack specificity. An example wherein lower values of EROA and RVol may underestimate lesion severity is the secondary MR associated with markedly crescentic orifice geometry, where PISA yields a falsely low value for EROA due to its inherent assumption of a round orifice (Figure 6) (54-63). Another example is when multiple MR jets are present, such that a measured EROA from a single jet does

not reflect the totality of MR. Addition of multiple EROAs or vena contracta areas is reasonably accurate but has not been well validated. It is also common to find lower quantitative values in the setting of relatively smaller LV volumes (e.g., in women). In such cases, there are usually other signs of severe MR.

5.4.3. Integration of Multiple Parameters

A comprehensive approach is recommended whereby multiple parameters are evaluated and integrated to form a final determination of MR severity (7,52,64) (Figure 7). The strengths and limitations of these parameters are listed in Table 3 and described in detail in the 2017 ASE Guidelines for Assessment of Native Valve Regurgitation

FIGURE 5 MR Limited to Late Systole in MV Prolapse

Example of nonholosystolic MR in MV prolapse. Top panels show no MR by color Doppler in early systole (top left) and mid-systole (top right). Late systolic MR is present by color Doppler (bottom left) and continuous wave Doppler (bottom right). Note that only the dense part of the MR CW profile should be traced. EROA calculated as 0.24 cm² with RVol, 17 ml. LA volume, LV size, and systolic function and pulmonary vein flow were normal in this patient with mild MR; however, relying only on the single-frame EROA would overestimate MR severity in this case.

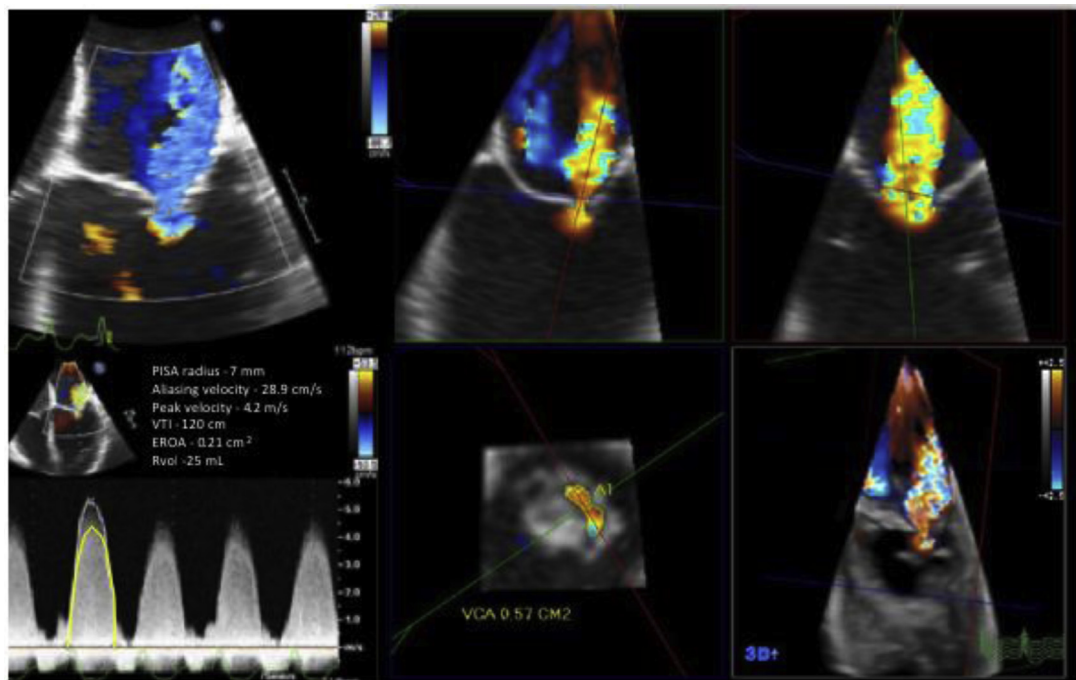
CW = continuous wave; EROA = effective regurgitant orifice area; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; MV = mitral valve; RA = right atrium; RV = right ventricle; RVol = regurgitant volume; VTI = velocity time integral.

(7). Evaluation of MR severity requires a comprehensive TTE study that includes assessment of these parameters. It is important to emphasize that no single echocardiographic parameter has the measurement precision or reproducibility to serve as the sole arbiter of MR severity. Moreover, MR severity is notoriously dynamic (65-67). Therefore, the effects of chronic MR on LV and LA volumes and on pulmonary artery pressure must be considered in an integrative fashion. Nevertheless, it is recognized that most physicians interpreting an echocardiogram look at CFD to identify the presence of MR and form an initial impression of its severity. This assessment should only be considered a starting point that requires further confirmation using a Bayesian approach that integrates multiple factors to arrive at a final determination (Figure 7). After an initial impression of MR severity is

formed, one should next consider whether LA and LV sizes are normal and whether the MR is holosystolic. For example, if one assesses MR as severe on the basis of a large CFD jet, but LA and LV sizes are normal and the MR is limited to late systole, the initial impression is most likely an overestimate. One should consider common reasons for overestimation of MR, such as high MR driving velocity (Figure 4) and MR duration limited to very early or very late systole (Figure 5).

When multiple specific parameters for mild or severe MR align with the initial impression of MR severity, MR can be correctly graded with high probability of being accurate. Fortunately, this scenario is relatively common in practice, especially with the finding of mild MR and a structurally normal MV. However, when different parameters are discordant among themselves or with

FIGURE 6 Example of Underestimation of EROA by 2D PISA in a Patient With Secondary MR and a Markedly Crescentic Orifice Shape



Underestimation of EROA and RVol by 2D PISA due to markedly crescentic orifice shape. PISA radius (top left) and CW MR jet (bottom left) with calculated EROA of 0.17 cm² and RVol of 22 mL. Note that the CW MR jet is overtraced (white line, bottom left)—a common mistake that actually underestimates EROA. Proper tracing of the dense portion of the jet (yellow line) revealed EROA 0.21 cm² and RVol 25 mL. Middle and right, upper and lower panels. 3D reconstruction of the vena contracta in the same patient showing vena contracta-derived area of 0.52 cm² (middle, lower panel), yielding a RVol of 64 mL (0.5 cm² × 128 cm). The EROA is underestimated by 2D PISA, which assumes circular orifice geometry, because of the crescent-shaped MR jet. 2D = 2-dimensional; 3D = 3-dimensional; CW = continuous wave; EROA = effective regurgitant orifice area; MR = mitral regurgitation; PISA = proximal isovelocity surface area; RVol = regurgitant volume; VTI = velocity time integral.

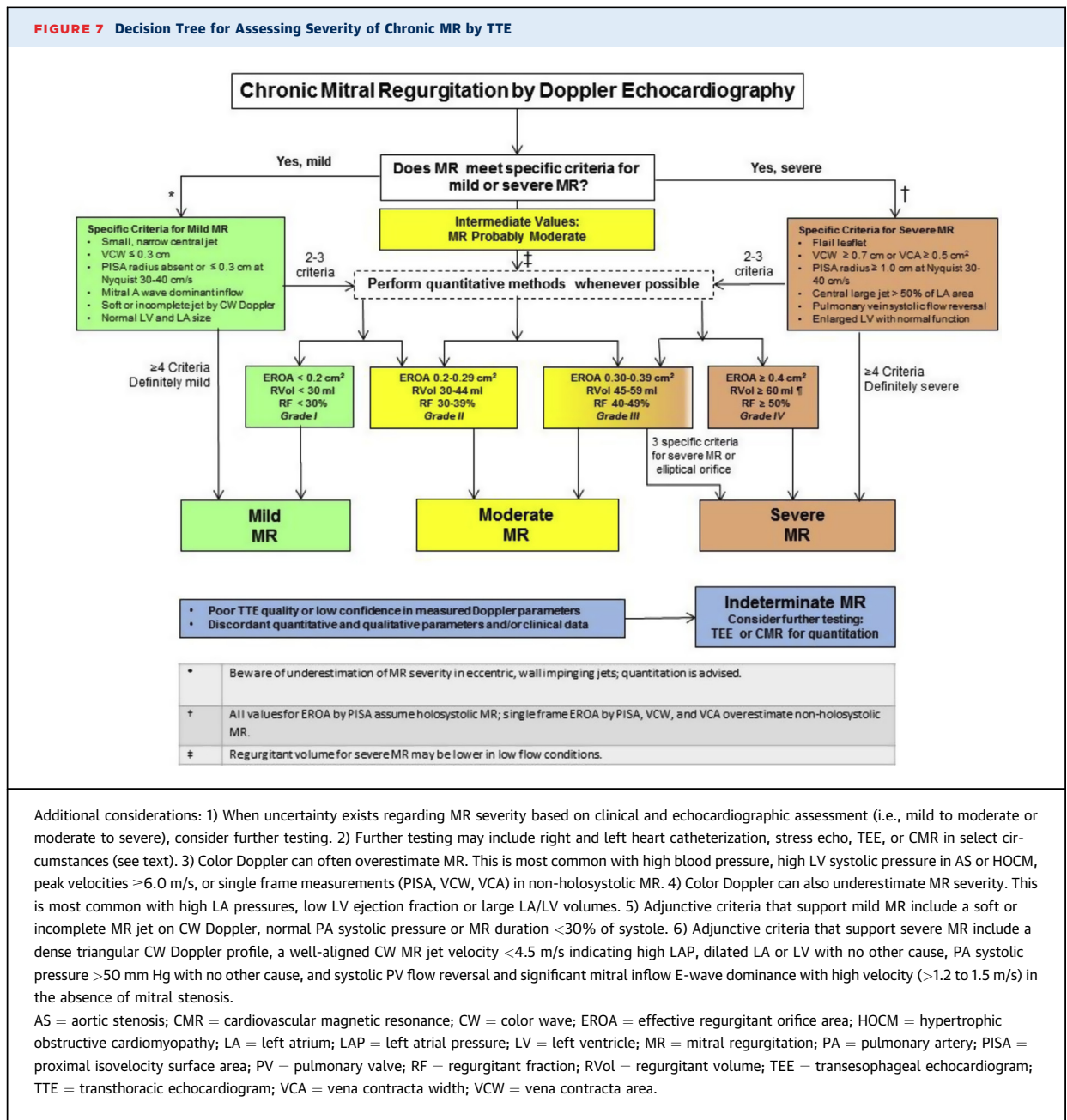
clinical findings, MR severity should be considered uncertain and further testing pursued. In such cases, TEE may be sufficient to define leaflet pathology and quantify MR severity, although it may underestimate MR severity during anesthesia due to favorable loading conditions. CMR is generally more accurate and reproducible for quantitating RVol and RF as well as LV volumes and LVEF (7,68-72).

Right and left heart catheterization may be indicated to assess hemodynamics. Despite its known limitations, a high-quality LV angiogram can also be helpful in resolving uncertainty in some cases. Invasive measurement of pressures, cardiac output, and pulmonary vascular resistance allows a comprehensive assessment, the results of which can be correlated with symptoms and response to medical therapy. Stress echocardiography can also be a valuable tool to assess any discrepancies between

noninvasive and clinical findings and to help define symptoms, exercise capacity, MR severity, pulmonary artery systolic pressure, and LV/RV responses to exercise. High-quality CMR can be very helpful in many patients in whom MR severity is unclear, although the technology is not widely available. Consideration should be given to referring such patients to a comprehensive valve center for multidisciplinary evaluation and treatment.

An evidence-based algorithm for referral of patients with MR is outlined in **Figure 8**. Based on the [2014 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease \(2\)](#) and its [2017 focused update \(3\)](#), this algorithm attempts to mitigate any potential gaps in the clinical approach to MR (11). Decisions regarding when to follow and when to refer patients with MR for further assessment or intervention can be challenging. Once the diagnosis of MR is established by TTE,

FIGURE 7 Decision Tree for Assessing Severity of Chronic MR by TTE



the next step is to establish the clinical context and symptomatology, the etiology of MR (primary vs. secondary vs. mixed), and its severity using the integrative methods previously outlined. This expert consensus algorithm provides a roadmap for the clinician to navigate decision-making for additional testing or referral for definitive treatment (see [Figures 9A and 9B](#)).

5.4.4. Dynamic Nature of MR

MR is a dynamic condition and its severity can change with LV loading parameters (65). Sedation and reduced blood

pressure during TEE may result in a significant reduction in MR severity, compared with an assessment using TTE in the awake state. Patients with hypertensive urgency/emergency can present with moderate or severe MR that can improve substantially with control of blood pressure. MR severity, however, will increase with maneuvers that decrease LV preload in patients with MV prolapse (70) as well as in patients with hypertrophic obstructive cardiomyopathy. Afterload reduction would also be expected to increase MR severity in hypertrophic obstructive cardiomyopathy. GDMT, revascularization, CRT (when

TABLE 3 Strengths and Limitations of Common Echocardiographic Parameters of MR Severity

Parameter	Strengths	Limitations
Valve Morphology	Flail leaflets or ruptured papillary muscles are specific for severe MR	Other findings are nonspecific
Regurgitant Color Flow	Easy to use, evaluates spatial orientation of MR jet, differentiates mild versus severe	Subject to technical and hemodynamic variation; can be underestimated with wall-impinging jets; image quality-dependent
Vena Contracta Width	Quick and easy to use; independent of hemodynamic and instrumentation factors; applies to eccentric jets; can differentiate mild versus severe MR	Not applicable to multiple jets; intermediate values require confirmation; small measurement errors can lead to big changes; 2D measure of a 3D structure; limited lateral resolution
Proximal Isovelocity Surface Area (PISA)	Can be applied to eccentric jets (when angle-corrected); not affected by etiology of MR; quantitative; provides both lesion severity (EROA) and volume data (RVol)	Not valid with multiple jets; provides peak flow and maximal EROA; interobserver variability; errors in radius measurement are squared; multiple potential sources of measurement error
Flow Quantitation-PW	Quantitative; valid in multiple jets and eccentric jets; provides both lesion severity (EROA, RF) and volume data (RVol)	Time consuming; measurement of flow at MV annulus less reliable with calcified MV and/or annulus; not valid with concomitant significant AR unless pulmonic site is used; requires measurement at multiple sites, which introduces errors
Jet Profile-CW	Simple, readily available Easy assessment of MR timing	Qualitative; complementary data; complete signal difficult to obtain in eccentric jet; gain dependent
Peak Mitral E Velocity	Simple, readily available, A-wave dominance excludes severe MR	Influenced by LA pressure/compliance, LV relaxation, MV area, and AF; complementary data only, does not quantify MR severity
Pulmonary Vein Flow	Simple; systolic flow reversal is specific for severe MR	Influenced by LA pressure, AF; not accurate if MR jet directed into the sampled vein; absence does not rule out severe MR
LA and LV Size	Enlargement sensitive for chronic severe MR, important for outcomes; normal size virtually excludes severe chronic MR	Enlargement seen in other conditions (nonspecific); may be normal in acute severe MR

AF = atrial fibrillation; AR = aortic regurgitation; CW = continuous wave; EROA = effective regurgitant orifice area; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; MV = mitral valve; RF = regurgitant fraction; RVol = regurgitant volume.

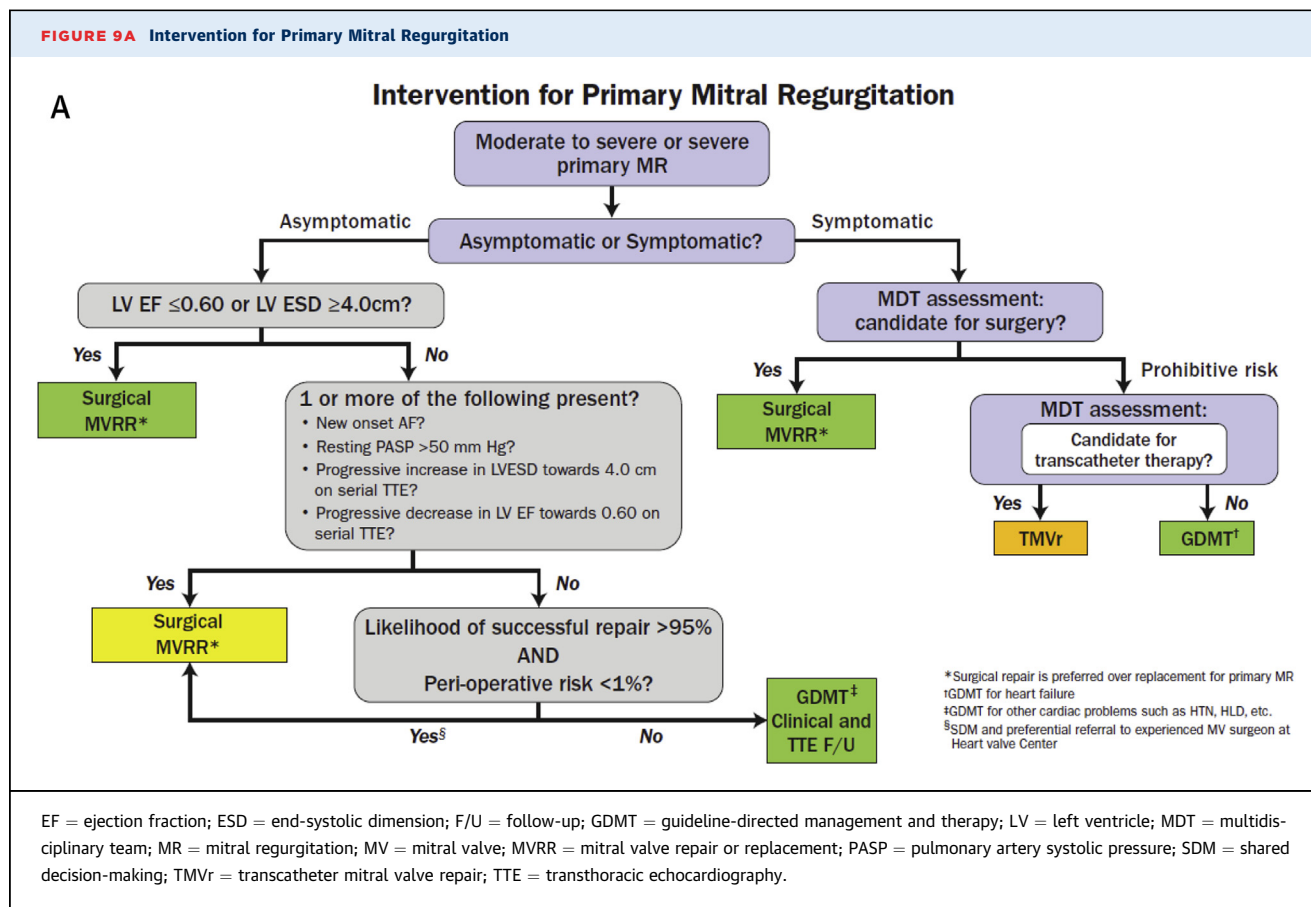
indicated), and successful management of AF may improve MR severity in secondary MR, particularly if such interventions result in reverse LV remodeling, improved regional wall motion, or LV synchrony. MR severity is also dynamic within the cardiac cycle (66,67). The classic example is late systolic MR due to leaflet prolapse. It is important to recognize this phenomenon because single-frame measurements on TTE or TEE may overestimate MR severity. In such circumstances, EROA or RVol should be measured with volumetric techniques because they account for all of systole (53). It is possible to correct EROA for duration of systole, but this method has not been validated. In secondary MR, a biphasic pattern can be seen in which MR improves during midsystole when LV pressure (i.e., closing force) is at its maximum (66). It is important for the sonographer not to “overgain” the machine to make this phenomenon disappear. It is also important to measure PISA radius and MR peak velocity at the same point in the cardiac cycle (7). CFD measures of MR severity can vary significantly during rapid AF or with large variations in the R-R interval. Likewise, caution must be used to avoid measuring MR during premature ventricular beats as well as in post-premature ventricular beats. Early systolic or late diastolic MR can occur with conduction system abnormalities, and this should be recognized as a potential source of overestimating MR severity by single-frame technique (73).

5.4.5. Differences in Assessing MR Severity in Primary Versus Secondary MR

Primary MR is generally easier to evaluate because of the morphological abnormalities of the mitral leaflets or chordae. Some morphological abnormalities, such as a flail leaflet with torn chords, leaflet destruction, and perforation due to endocarditis or severe leaflet retraction without visible coaptation, are specific markers of severe MR. LV or LA dilation in chronic primary MR is most often a consequence of the MR and a strong clue that the MR is severe. Exceptions could occur if a patient with long-standing MV prolapse and mild MR develops an ischemic or nonischemic cardiomyopathy. On the other hand, when MR is primary and LV and LA size are normal, severe MR is very unlikely. Secondary MR is more difficult to grade because morphological abnormalities of the leaflets and chords are absent. Symptoms, pulmonary congestion on examination or chest x-ray, elevated corrected brain natriuretic peptide or N-terminal pro-brain natriuretic peptide levels, and adjunctive findings on TTE or TEE, such as LV or LA dilation and systolic blunting of the pulmonary venous flow pattern, may be due to the underlying cardiomyopathy and, therefore, are less helpful in grading MR severity. Further confounding this situation is the fact that in secondary MR, the shape of the regurgitant orifice is often markedly crescentic, leading to underestimation of EROA by the PISA method

of 0.3 cm² with an MR velocity-time integral of 150 cm yields an RVol of 45 mL. Although these values are in the traditional range of moderate MR, they constitute a RF of 75% (45 mL/60 mL), consistent with severe MR and loss of three fourths of forward cardiac output into the LA. In the latter patient, the same values (EROA of 0.3 cm² and RVol of 45 mL) would yield an RF of 37.5%, consistent with moderate MR. Thus, consideration of quantitative values for MR severity should also account for LV volumes and EF. It is recognized that the accepted EROA threshold for

FIGURE 9A Intervention for Primary Mitral Regurgitation



severe MR ($\geq 0.40 \text{ cm}^2$) can be lower in patients with secondary MR and elliptical orifices, emphasizing the need for an integrative assessment of severity (7).

5.4.6. Prognosis in MR

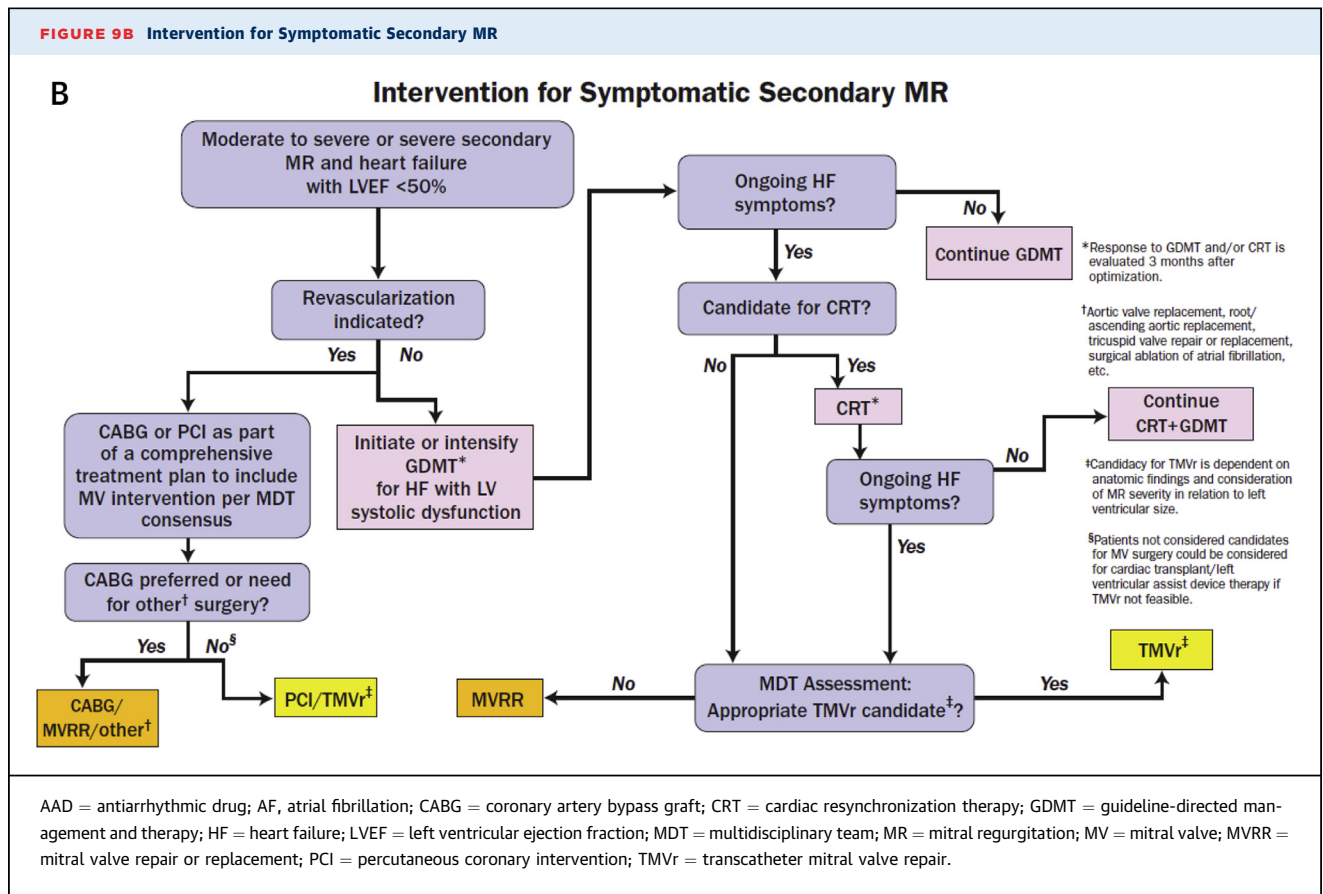
5.4.6.1. Primary MR

Table 4 lists prognostic variables important in the assessment of primary MR. Some of these are clinical (age, HF, coronary artery disease, and functional class); others relate to MR itself or the effects of MR on the LV or LA. LVEF $\leq 60\%$, LV end-systolic diameter $\geq 40 \text{ mm}$, LA systolic volume index $> 60 \text{ mL/m}^2$, EROA, recent-onset AF, and pulmonary hypertension have been associated with worse prognosis (75-78). A small subset of patients with MV prolapse has been identified in whom the risk of sudden cardiac death appears to be increased independent of the degree of MR (79). The performance of MV surgery before symptoms emerge or LV function (EF $\leq 60\%$) and size (LV end-systolic diameter $\geq 40 \text{ mm}$) thresholds are met leads to improved survival and functional outcomes (2,80,81). Flail leaflet is associated with

adverse prognosis and is usually a specific sign of severe MR (12,75,76), although occasionally patients with flail leaflets have only moderate MR by integrative assessment. Rarely, patients with flail leaflet may experience sudden cardiac death (79,82). Early surgical referral of the patient with flail leaflet can also be considered.

5.4.6.2. Secondary MR

In ischemic cardiomyopathy, the presence of MR of any grade results in worse long-term prognosis, but severe ischemic MR is also an indicator of short-term mortality. An EROA $\geq 0.2 \text{ cm}^2$ has been shown to be a predictor of adverse outcomes in some studies of patients with secondary MR (25,27,29). Importantly, secondary MR appears to be an independent marker of adverse prognosis, even when LV volumes, LVEF, renal function, and other parameters are included in multivariable analysis (25,28). Surgical correction of secondary MR may improve symptoms and quality of life but has not been shown to improve survival (83). Transcatheter edge-to-edge clip repair, however, has been shown in 1 RCT to improve both survival and quality of life in selected patients with HF



and moderate to severe or severe MR who remain symptomatic despite optimal treatment with guideline-directed management of HF, including CRT when indicated (5). Nevertheless, the 2-year rate of death or hospitalization for HF with transcatheter and optimal medical therapy in this trial was still 46% (vs. 68% in those managed medically) (5).

6. TREATMENT OF CHRONIC MITRAL REGURGITATION

6.1. General Considerations

Deciding on the optimal treatment of chronic MR is based on multiple variables, including MR type and severity, hemodynamic consequences, disease stage, patient comorbidities, and the experience/competence of the MDT and its members (84). Evidence-based referral may be aided by use of the algorithm in Figure 8. Reporting echocardiographic findings using standardized nomenclature helps to guide surgical/interventional decision-making (44) (Table 2). The anterior and posterior leaflets are divided into three anatomic sections from lateral to medial (A1, A2, and A3, and P1, P2, and P3, respectively). The two leaflets meet at the lateral and medial

commissures, where focal pathology (e.g., calcification) may occur. The chordal structures may have excess or restricted motion and are defined by their leaflet insertion

TABLE 4 Factors Affecting Prognosis in Primary MR

Factor Type	Specific Factors
1. Factors related to the LV or LA	<ul style="list-style-type: none"> Systolic dysfunction (EF <60%) LV enlargement (LVESD >4cm) LA enlargement (LA systolic volume index ≥60 ml/m²)
2. Clinical factors	<ul style="list-style-type: none"> Age Presence/absence of heart failure Functional class Presence/absence of CAD
3. Rhythm/hemodynamic factors	<ul style="list-style-type: none"> AF Arrhythmic MVP* Pulmonary hypertension
4. Factors related to MR, timing of intervention	<ul style="list-style-type: none"> Severity of regurgitation Flail leaflet Delay in MV intervention after onset of LV dysfunction

*Characteristics include inferior T-wave inversions on 12-lead ECG, complex ventricular ectopy, spiked configuration of lateral annular tissue Doppler velocity (Pickelhaube sign), and late gadolinium enhancement (myocardial fibrosis) on cardiac magnetic resonance imaging.

AF = atrial fibrillation; CAD = coronary artery disease; EF = ejection fraction; LA = left atrium; LV = left ventricle; LVESD = left ventricular end-systolic diameter; MR = mitral regurgitation; MVP = mitral valve prolapse.

as primary (leading edge insertion), secondary (mid-scallop insertion), and tertiary (basal insertion). A well-performed TTE is sufficient for treatment planning in most instances. The majority of information needed to complete surgical/interventional planning can be obtained with 4 conventional TEE views (mid-esophageal 4-chamber, long-axis 2-chamber, midcommissural 2-chamber, and basal short-axis view) and a 3-dimensional en face view (surgeon's view). Although focused use of CFD at a Nyquist of 50 to 70 cm/s may aid in mechanism confirmation, planning for intervention should be based on imaging without color in each of these views. Description of other TEE techniques used during MV operation is beyond the scope of this document.

The principal treatment modality for primary MR is surgery. At present, transcatheter mitral repair using an edge-to-edge clip device can be considered for the treatment of patients with primary MR and severe symptoms who are felt to be poor surgical candidates (2,3). Surgical or transcatheter treatment for secondary MR is undertaken only after appropriate medical and device therapies have been instituted and optimized, as judged by the MDT with input from a cardiologist with experience managing HF and MR. Transcatheter mitral valve repair (TMVr) systems other than the edge-to-edge clip, as well as transcatheter mitral valve replacement (TMVR) devices, are currently not approved for clinical use in the United States but remain the subject of intense investigation. This field is rapidly evolving and novel devices are very likely to enter into practice in the near future.

6.2. Surgical Treatment of Mitral Regurgitation

6.2.1. Primary MR (Figure 9A)

MV surgery is indicated in patients with primary severe MR and EF >30% who are symptomatic (Stage D) or asymptomatic but with LVEF 30% to 60% or LV end-systolic dimension ≥ 40 mm (Stage C2) (85). MV repair is strongly preferred over replacement for primary MR whenever anatomically feasible and as dictated by the experience and skill of the operating surgeon. MV repair is reasonable for patients with primary MR and preserved LV size and systolic function (LV end-systolic diameter <40 mm, LVEF >60%) when there is a progressive increase in LV size or decrease in LV function on serial imaging (2), when AF has recently (<3 months) intervened, or when resting pulmonary artery pressures are elevated (>50 mm Hg at rest) (3). MV repair is also reasonable for asymptomatic patients with normal LV size and function when the likelihood of a successful and durable repair without residual MR exceeds 95% and an operation can be performed with <1% mortality at a heart

valve center by an experienced surgeon (3). Short- and long-term outcomes of successful valve repair for primary MR exceed those for valve replacement across all age ranges. Successful repair at the indicated time results in long-term survival equivalent to that of the normal age-matched population (80,81). Timely surgical referral for primary MR must take into account the feasibility of repair as well as surgeon and institutional outcomes. The latter are particularly relevant when considering referral of an asymptomatic patient.

Surgeon experience has been recognized for many years as an important determinant of successful MV repair. Society for Thoracic Surgeons (STS) registry data from 2005 to 2007 estimated a nearly 3-fold greater likelihood of successful repair when surgeon experience was over 100 cases per year compared with 5 to 10 cases per year, with a threshold for frequency of successful repair being >50 mitral surgical cases per year (repair or replacement) (86). Data from New York State suggest that higher total annual surgeon volume is associated with increased repair rates for primary MR, with an improved 1-year survival and decreased reoperation risk when >25 total mitral operations are performed annually (87). In addition, repair rates among surgeons with case volumes <25 mitral operations per year increase significantly if they operate at an institution in which another surgeon performs >50 mitral cases per year, with repair rates for primary MR >70% (87). Using this observational study as a single example, an appropriate threshold for high surgical volumes predictive of improved outcomes for MV operation might be >25 per year per operator and >50 per year per institution.

The MV repair rate for primary MR was estimated at 75% among 867 centers in North America reporting more than 10 such cases to the STS Adult Cardiac Surgery database over a 3-year period between 2011 and 2014 (88). In such patients, the 30-day operative mortality rate should be <1%. To achieve these benchmarks, it is anticipated that some centers may limit some surgeons to repair of those pathologies that are most easily approached (e.g., isolated posterior leaflet prolapse or partial flail), whereas more experienced surgeons would be expected to undertake repair of more advanced pathologies. Some surgeons consider MV repair to constitute a surgical subspecialty (89,90).

Another analysis from the STS Adult Cardiac Surgery database on access to MV repair or replacement surgery in the United States by hospital referral region, as defined by the Dartmouth atlas, indicates that the proportion of the population living within a hospital referral region with a center performing ≥ 25 MV repairs or replacements per year is 92.6%, whereas 81.7% of the population lives

within a hospital referral region with a center performing ≥ 40 MV repairs or replacements per year (91). Centers performing ≥ 40 MV repairs or replacements per year of which ≥ 10 are MV repairs are in the same hospital referral region as 78.7% of the population. Outcome data as a function of center case volume above or below thresholds of 25 and 40 annual cases are not available from the STS Adult Cardiac Surgery Database.

6.2.2. Secondary MR (Figure 9B)

Guideline recommendations for MV surgery for the treatment of moderate or severe secondary MR, with or without concomitant coronary artery bypass grafting, are more conservative, in part due to the recognition that surgical intervention in this patient group may improve symptoms and quality of life, but has not been shown to improve survival (83,85,92). MV repair (usually with a downsized annuloplasty ring) may be considered at the time of coronary artery bypass grafting for patients with multivessel coronary artery disease and moderate secondary MR, although its benefit in this context is uncertain (93-95). In patients with severe secondary MR, MV surgery (either replacement or repair) is reasonable at the time of other cardiac surgery and can be considered as an isolated procedure for selected patients with advanced New York Heart Association functional class despite guideline-directed management inclusive of CRT when indicated (3). The decision to replace or repair the valve can be challenging (92) and is deferred to an experienced surgeon in consultation with the MDT; however, for severely symptomatic patients with severe ischemic, secondary MR, it is reasonable to choose chordal-sparing MV replacement over downsized annuloplasty repair (3,92). This recommendation reflects the results of an RCT of repair versus chordal-sparing replacement in patients with severe ischemic MR, which demonstrated that repair patients experienced a significantly higher rate of recurrent moderate or severe MR with more HF events and cardiovascular readmissions during follow-up (71). Whether more advanced surgical repair techniques (including chordal and/or papillary muscle interventions) or better patient selection (based on LV size parameters, regional wall motion abnormalities, and/or leaflet tethering indices) might improve outcomes with surgery remains to be determined in prospective comparative effectiveness trials. The optimal surgical approach to severe secondary MR (i.e., repair vs. replacement) depends on the specific pathoanatomic findings, degree of leaflet tethering, extent of ventricular remodeling, and the presence of coronary artery disease and/or AF (96). It is recognized that there are other clinical scenarios in which surgical MV repair or replacement in combination with

other procedures may be preferred, such as in the management of significant atrial functional MR with annular dilatation and persistent or long-standing persistent AF (97,98). A catheter-based AF ablation procedure would generally not be recommended in such patients who are deemed appropriate candidates for surgical management of their MR. There are individual patient considerations that require careful assessment and MDT consensus decision-making.

6.2.3. Feasibility of Surgical Repair

MV repair is a complex operation comprising a wide spectrum of available techniques to achieve durable success (99). The principal goals of MV repair are to restore leaflet coaptation depth to >5 mm, stabilize and remodel the annulus, restore normal leaflet motion, and eliminate MR. The major factors determining repair feasibility are pathoanatomy and surgeon experience.

The surgical spectrum of primary MR with Carpentier type II motion ranges from focal prolapse in the setting of an otherwise anatomically normal MV, known as fibroelastic deficiency, to a more diffuse process with excess, redundant, billowing tissue as noted in Barlow's syndrome (100). Alternatively, primary MR with Carpentier type II motion may take an intermediate form between these 2 extremes, a pathoanatomical variant referred to as a *forme fruste*. In primary MR with Carpentier type IIIA motion, the surgical spectrum includes focal or diffuse leaflet and subvalvular thickening and commissural fusion due to rheumatic heart disease, prior radiation, or other inflammatory conditions. Different causes of primary MR may occur in the same patient, potentially affecting repair feasibility, and highlighting the critical importance of preoperative imaging and MDT assessment.

Common techniques of MV repair are listed in Table 5 and include construction of artificial neochordae with polytetrafluoroethylene or limited triangular resection as applied in cases of focal prolapse or fibroelastic deficiency, and extensive posterior leaflet resection and remodeling in cases of diffuse myxomatous degeneration and echocardiographic predictors of postoperative systolic anterior motion of the anterior MV leaflet. A suggested approach to determine the feasibility and complexity of repair is described in Table 6. The majority of experienced MV surgeons can perform successful and durable repairs for patients with echocardiographic findings of focal posterior prolapse or flail without annular or leaflet calcium. However, once additional annular, commissural, or bileaflet pathoanatomic complexities arise, in isolation or combination, more specific experience with MV repair is often required. Other confounding factors impacting reparability that may necessitate advanced mitral surgical

TABLE 5 Pathoanatomically Directed Contemporary Surgical Techniques for MR

Primary MR

- 1. Nonresection techniques using either PTFE neochord reconstruction or ipsilateral chordal transfer from secondary to primary position, with annuloplasty ring**
 - May be used for focal leaflet flail or bileaflet prolapse
 - May be used for *forme fruste** diffuse myxomatous disease of the posterior leaflet
 - May be used for isolated anterior leaflet prolapse
- 2. Focal triangular resection with annuloplasty ring**
 - May be used for focal leaflet flail of the posterior or commissural leaflet
 - Rarely may be used for focal anterior leaflet defects
- 3. Sliding leaflet valvuloplasty with annuloplasty ring**
 - May be used for *forme fruste** diffuse posterior leaflet myxomatous disease
 - May be used in the setting of bileaflet prolapse with excess posterior leaflet
 - May be used in either of the above with significant echocardiographic predictors of systolic anterior motion of the anterior MV leaflet

Secondary MR

- 1. Restrictive remodeling rigid annuloplasty ring**
 - May be used as primary modality for annular dilatation mechanism
 - May be used in conjunction with secondary or tertiary chordal cutting
 - May be used with other adjunctive procedures (e.g., papillary muscle sling)
 - Should be avoided as sole therapy in setting of Carpentier Type IIIB mechanism with left ventricular inferobasal aneurysm
- 2. Chord-sparing MV replacement**
 - May be used as primary modality for annular dilatation with severe leaflet tethering (i.e., >10 mm tenting height) or presence of inferobasal aneurysm
 - Reasonable to consider in preference to MV repair for patients with severe ischemic MR

**Forme fruste* refers to a pathoanatomic form of primary MR intermediate between fibroelastic deficiency and Barlow's disease.

MR = mitral regurgitation; MV = mitral valve; PTFE = polytetrafluorethylene.

evaluation include reoperation, prior endocarditis, basal septal hypertrophy with echocardiographic predictors of postoperative systolic anterior motion of the anterior mitral leaflet, and congenital anomalies (35,99,100).

Patients who have a single segment flail of the posterior leaflet due to fibroelastic deficiency in the absence of calcification of the annulus or leaflets have the highest chance of technically successful and durable valve repair. These patients should not undergo valve replacement unless a repair has been attempted and was unsuccessful (85). Alternatively, patients with severe anterior, bileaflet, Barlow's, or mixed disease that may require extensive and complex reparative techniques should be preferentially referred to an experienced MV surgeon at a high-volume institution (87). The most important predictor of long-term failure is the presence of moderate or greater residual MR at the time of the index operation (101-103). There is a small subgroup of patients with primary MR in whom valve replacement may be preferred over valve repair, such as those who have had a prior cardiac operation or prior chest radiation, in whom any subsequent operation for a failed repair would be undertaken at substantially increased risk. Figure 10 shows echocardiographic examples of MV morphologies that are likely, possible, or challenging for successful surgical MV repair (see also Table 6).

Postoperative TTE is recommended either prior to discharge or by 1 to 3 months after surgical MV repair or replacement. Longitudinal TTE studies thereafter are dictated by clinical findings, as well as by the presence of a prosthetic heart valve replacement.

6.2.4. Determination of Risk for Surgery

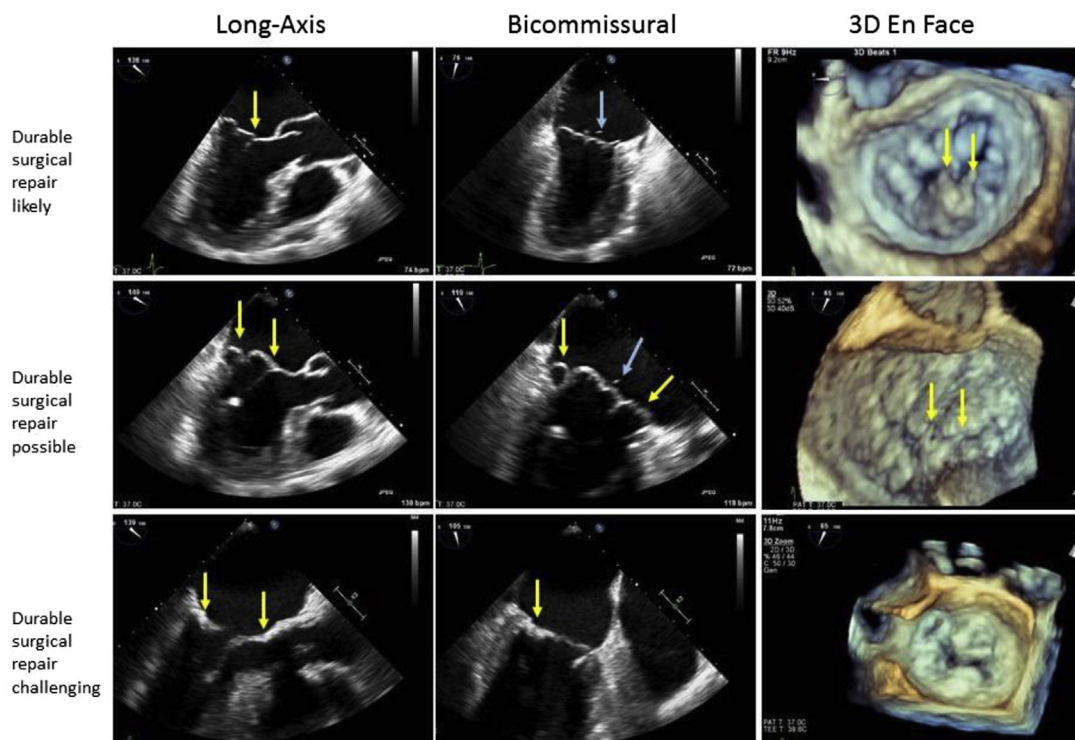
When a patient is being evaluated for treatment of MR, a key component is an assessment of the individual's risk for surgical MV repair or replacement. Evaluation includes the use of a standardized Predicted Risk of Mortality developed by The Society for Thoracic Surgeons (STS PROM), which is based on the outcomes of large numbers of patients who have undergone surgery (88,104). Additional factors not included in this risk score also contribute to

TABLE 6 Feasibility of Surgical MV Repair

	Ideal Pathoanatomy	Challenging Pathoanatomy	Relative Pathoanatomic Contraindications
Primary Lesion Location	Posterior leaflet only	Anterior leaflet or bileaflet	None
Leaflet Calcification	None	Mild	Moderate to severe
Annular Calcification	None	Mild to moderate with minimal leaflet encroachment	Severe or with significant leaflet encroachment
Subvalvular Apparatus	Thin, normal	Mild diffuse thickening or moderate focal thickening	Severe and diffuse thickening with leaflet retraction
Mechanism of MR	Type II fibroelastic deficiency or focal myxomatous prolapse or flail	Type II <i>forme fruste</i> or bileaflet myxomatous (Barlow's) disease; Type I healed or active endocarditis; Type IIIA/B with mild restriction or leaflet thickening	Type IIIB with severe tethering and inferobasal aneurysm; Type IIIA with severe bileaflet calcification; Type I active infection with severe leaflet or annular tissue destruction
Unique Anatomic Complexities	None	Redo cardiac operation or mitral re-repair; anatomic predictors of systolic anterior motion (e.g., septal hypertrophy); adult congenital anomalies; focal papillary muscle rupture	MV reoperation with paucity of leaflet tissue; diffuse radiation valvulopathy; papillary muscle rupture with shock

MR = mitral regurgitation; MV = mitral valve.

FIGURE 10 Examples of MV Morphology Observed on TEE That Are Amenable to Surgical Repair in Patients With Primary MR



TEE images showing examples of primary MV pathology with different likelihood of durable surgical repair. Long-axis views (left panels), bicommissural views (middle panels) and 3D en face views (right panels) are shown. At top, durable surgical repair is likely with thin, pliable leaflets (yellow arrow, left upper panel), and with torn chords to the posterior middle scallop (P2) seen in the upper middle (blue arrow) and right panels (yellow arrows). Durable surgical repair is also possible in the middle row of panels. Both anterior and posterior leaflets exhibit marked prolapse (yellow arrows, left middle panel) involving multiple scallops with torn chords (middle center panel, blue arrow; middle right panel, yellow arrows). The annulus is severely dilated. The bottom row of panels shows a patient for whom durable repair is challenging due to severe mitral annular and leaflet calcification (yellow arrows, bottom left and middle panels) with restricted leaflet excursion (bottom right panel). In addition to severe MR, this patient had a mean transmitral gradient 14 mm Hg at a resting heart rate of 68 beats per minute.

3D = 3-dimensional; MR = mitral regurgitation; TEE = transesophageal echocardiography; MV = mitral valve.

procedural and postprocedural risk, including liver disease, pulmonary hypertension, porcelain aorta, and post-radiation scarring, as well as reduced patient ability to recover from surgery due to frailty. Measures of frailty such as the 5-meter or 6-minute walk test and handgrip strength have become part of the MDT evaluation of elderly patients for surgical or transcatheter therapy. The [2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease](#) (2) includes a risk assessment tool that incorporates these considerations.

6.3. Transcatheter Treatment of Mitral Regurgitation

6.3.1. Primary MR

Currently, TMVr of severe primary MR using a clip device to achieve edge-to-edge coaptation can be considered in

very symptomatic (New York Heart Association functional class 3 to 4) patients who are felt to be poor candidates for surgical repair (3). This conservative recommendation reflects the demonstrated superiority of surgical repair over TMVr for reducing or eliminating primary MR. It is recognized that TMVr, compared with surgery, is associated with faster recovery times and less bleeding. Although other TMVr and novel TMVR systems are currently the subject of intense clinical investigation and are likely to be introduced into clinical practice over the near to intermediate term, use of a clip to approximate opposing segments of the anterior and posterior leaflets, in a manner analogous to the surgical edge-to-edge technique, is currently the only FDA-approved device in the U.S. for primary MR. FDA approval for this indication

TABLE 7 Feasibility of Transcatheter Edge-to-Edge Clip Repair

	Favorable Features*	Less Favorable or Unfavorable Features*
Location of Leaflet Pathology	Noncommissural pathology (medial, middle, lateral segments)	Commissural segments, leaflet perforations, or clefts
Calcification	No or minimal calcification	<ul style="list-style-type: none"> ■ Severe leaflet calcification or calcification in area of grasping zone ■ Severe annular calcification
Mean MV Gradient	Transmitral gradient <4 mm	Mitral stenosis (rheumatic or calcific; mean mitral gradient >5 mm Hg)
MVA	MVA ≥4.0 cm ²	MVA <4.0 cm ²
Grasping Zone Length	>10 mm	<7 mm
Primary MR	Flail width <15 mm; flail gap <10 mm; single segment pathology Normal leaflet thickness	<ul style="list-style-type: none"> ■ Flail width >15 mm and flail gap >10 mm ■ Multisegment pathology; highly mobile flail leaflet with multiple ruptured chords ■ Severely and diffusely thickened (5 mm in diastole) and redundant leaflets (Barlow's type valve); LVESD >55 mm
Secondary MR	Coaptation depth <11 mm; coaptation length (overlap length) ≥2 mm	LVESD >70 mm

*Knowledge continues to evolve regarding case selection; highly experienced operators at comprehensive valve centers may achieve good procedural results in selected cases with unfavorable anatomic features.

LVESD = left ventricular end-diastolic dimension; MR = mitral regurgitation; MV = mitral valve; MVA = mitral valve area.

in 2013 was based on the results of the EVEREST (Endovascular Valve Edge-to-Edge REpair Study) Trials and outcomes reported in the REALISM (Real World Expanded Multicenter Study of the MitraClip System) Registry (105,106). Appropriate selection of patients with severe primary MR for TMVr is critically dependent on rigorous echocardiographic assessment and MDT consensus. **Table 7** includes key echocardiographic parameters used to assess suitability for TMVr using a clip device for primary MR. Cardiac CT is required for assessment of investigational TMVR systems. Procedural and outcome data for 2952 patients (median age 82 years, STS PROM 6.1%, 86% with pure primary MR) treated at 145 centers in 2013 to 2015 were reported from the STS/ACC TVT Registry in 2017. Acute procedural success was reported in 92% of patients, with device embolization in 0.1% and stroke in 0.4%. Among the 1,867 patients with CMS linkage data, 30-day and 1-year mortality rates were 5.2% and 25.8%, respectively—likely a reflection of the high-risk patient cohort. By 1 year, stroke occurred in 2.7% of patients and rehospitalization for HF in 20.2%, while 2.1% of patients underwent open surgery and 6.2% had a second clip procedure. In a subsequent learning curve analysis, visual inflection points for procedural time, procedural success, and procedural complications were evident after ~50 institutional cases, with continued improvements observed up to 200 cases (107).

TMVr using the clip device is usually performed by a single operator (interventional cardiologist or cardiac surgeon) in a cardiac catheterization laboratory under TEE guidance in collaboration with an expert interventional echocardiographer. A second operator may be needed or

preferred on an individual basis and according to institutional protocols. Recommended performance standards are provided in the 2019 AATS/ACC/SCAI/STS Expert Consensus Systems of Care Document: Operator and Institutional Recommendations and Requirements for Transcatheter Mitral Valve Intervention (8). Other TMVr systems that may become available for clinical use to treat primary MR in future years will dictate the need to establish new criteria for patient selection, as well as operator and institutional requirements. Joint participation by an interventionalist and surgeon is anticipated for novel TMVR systems that gain future approval for clinical use.

6.3.2. Secondary MR

Transcatheter intervention for moderate to severe or severe secondary MR should not be undertaken until appropriate guideline-recommended management for HF has been fully optimized as assessed by the MDT with guidance from HF and electrophysiology experts as needed.

Previous registry reports suggested that edge-to-edge TMVr was associated with improved symptoms, functional capacity, and quality of life in selected patients with severe secondary MR (108). Approximately 9% of patients in the 2017 STS/ACC TVT registry report treated with TMVr had secondary MR, and an additional 9% had mixed MR. The efficacy and safety of edge-to-edge TMVr for moderately severe or severe MR using a clip device were evaluated in 2 large RCTs reported in 2018: MITRA-FR (Percutaneous Repair with the MitraClip Device for Severe Functional/Secondary Mitral Regurgitation) (NCT01920698) (4) and COAPT (Cardiovascular Outcomes

Assessment of the MitraClip Percutaneous Therapy) (NCT01626079) (5). In each trial, patients with at least moderately severe secondary MR were randomized to either transcatheter therapy using an edge-to-edge clip device plus GDMT (including CRT when indicated) or to GDMT alone. Whereas the MITRA-FR trial showed no between-group difference in a 1-year primary composite endpoint of all-cause death and unplanned HF hospitalization, the COAPT trial demonstrated significant reductions in the 2-year rates of HF hospitalization (primary endpoint) and all-cause mortality (secondary endpoint) with device therapy. The MITRA-FR investigators also reported no significant between-group difference in their composite endpoint at 2 years (109).

There were important differences between these 2 studies with respect to trial design, sample size, patient entry criteria, the manner in which medical therapy for HF was intensified, MR severity, LV volumes, procedural success rates, duration of follow-up, and durability of MR reduction. Patients enrolled in the COAPT trial appear to have had a greater burden of HF refractory to rigorous medical therapy supervised by an HF expert prior to randomization, as well as more severe MR (higher mean EROAs), smaller ventricles (lower mean LV end-diastolic volumes), and more complete and durable MR reduction following device therapy. A third trial, RESHAPE-HF (A Randomized Study of the MitraClip Device in Heart Failure Patients with Clinically Significant Functional Mitral Regurgitation) (NCT01772108), comparing the clip device plus GDMT versus GDMT alone for severe secondary MR, is ongoing. On the basis of the results of the COAPT trial, in March 2019, the FDA approved the use of the clip device for the treatment of patients with moderately severe or severe secondary MR, LVEF 20% to 50%, LV end-systolic diameter <7.0 cm, and persistent symptoms despite maximally tolerated GDMT as assessed by an MDT experienced in the evaluation and treatment of HF and MV disease (5). The fundamental importance of echocardiographic, HF, and interventional expertise, as well as the contributions from other members of the MDT in decision making, cannot be overstated. Whether the results of the COAPT trial can be duplicated in practice across a wider spectrum of clinical sites remains to be seen. Approximately one-third to one-half of patients randomized to device therapy in the MITRA-FR and COAPT trials either died or were hospitalized for HF at 1 year. These outcomes are a testimony to the severity of LV dysfunction and advanced symptoms observed in these patient cohorts and speak to the need for additional research into risk stratification.

Several TMVr systems focusing on leaflet modification (such as leaflet ablation and space occupation between leaflets) or annular reduction, as well as TMVR platforms, are in various stages of development and not available outside of clinical trials. This space is evolving very rapidly, and it is anticipated that future iterations of this ECDP will address novel systems as they are introduced into clinical practice. The foundational elements embodied by the MDT are likely to remain the same as these procedures will require similar preprocedural clinical and multimodality imaging assessment, intraprocedural personnel and equipment, operator experience and skill, and postprocedural care.

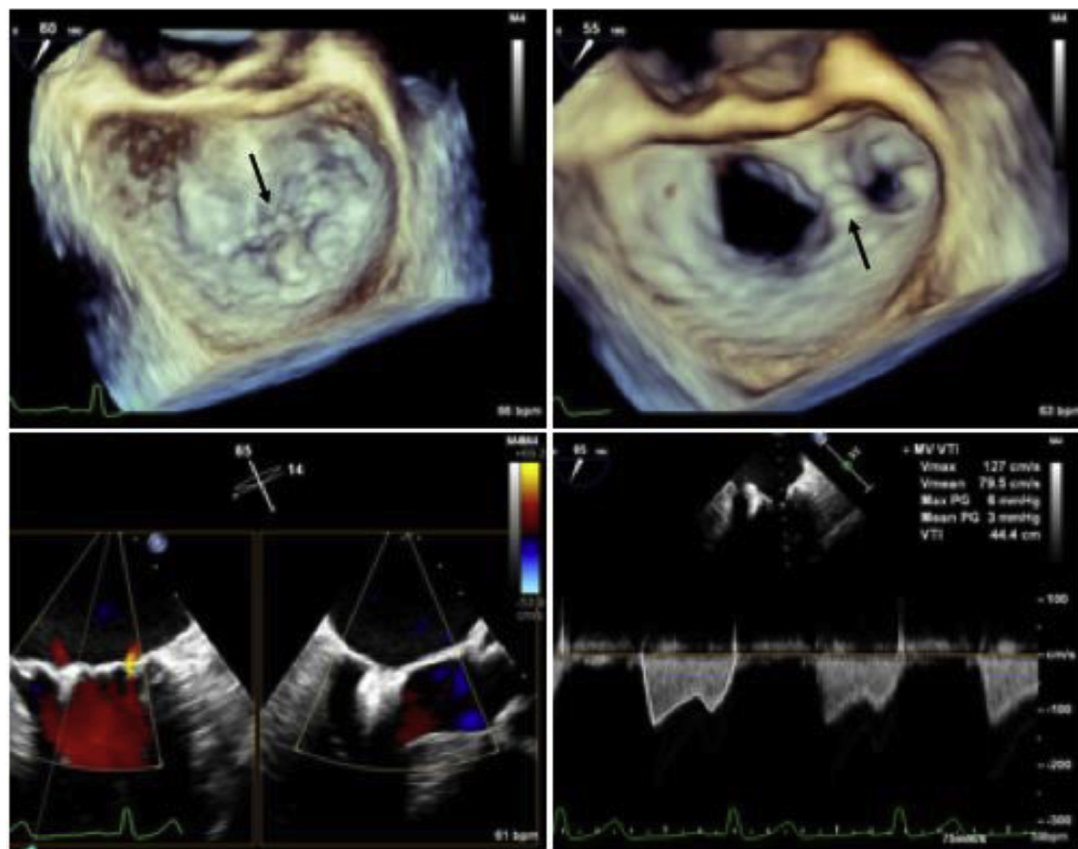
6.3.3. Edge-to-Edge Leaflet Coaptation

Transcatheter edge-to-edge leaflet coaptation using a clip is based on the surgical technique described by Alfieri *et al.* (110) and results in the creation of a double-orifice MV and reduction in the severity of MR (Figure 11). Successful deployment can result in improved hemodynamics and patient outcomes (111–114). Appropriate patient selection is critically dependent on rigorous clinical and echocardiographic assessment (115) (Figure 12, Table 7). Intraprocedural and postprocedural management algorithms facilitate best practices. Operator and institutional criteria for the performance of transcatheter MV interventions are available in a joint, multisocietal expert consensus document (8). A search in the STS/ACC TVT Registry in January 2020 showed that TMVr using a clip device is currently offered at more than 420 sites within the United States.

6.3.3.1. Feasibility of Edge-to-Edge Leaflet Coaptation

Table 7 and Figure 13 include the key echocardiographic parameters used to assess suitability for TMVr using a clip device (115). The procedure is usually performed by a single operator in a cardiac catheterization laboratory under TEE guidance provided by an expert interventional echocardiographer. Procedural personnel (interventionalist plus surgeon) and venue (hybrid suite, operating room) may differ among institutions. The MDT, which includes at a minimum a clinical heart valve specialist, cardiologist with experience managing HF and MR, multimodality cardiac imaging expert, interventional cardiologist, and cardiac surgeon, is required for patient evaluation, selection, and periprocedural management. The participation of each MDT member may vary as a function of MR etiology (primary vs. secondary) or whether input is needed regarding the adequacy and rigor of HF management. Other TMVr systems introduced into

FIGURE 11 Transcatheter Edge-to-Edge MV Clip Device



Transcatheter edge-to-edge MV clip. Top left: 3D en face view showing flail posterior leaflet middle scallop (P2) with torn chords (arrow). Top right: Transcatheter edge-to-edge clip creates tissue bridge between anterior and posterior leaflets (arrow). Bottom left: Color flow image showing trace MR after edge-to-edge MV clip. Bottom right: Continuous wave Doppler showing mean gradient 3 mm Hg after transcatheter edge-to-edge clip placement. 3D = 3-dimensional; MR = mitral regurgitation; MV = mitral valve.

clinical use in future years may dictate the need for new criteria for patient selection and MDT member participation.

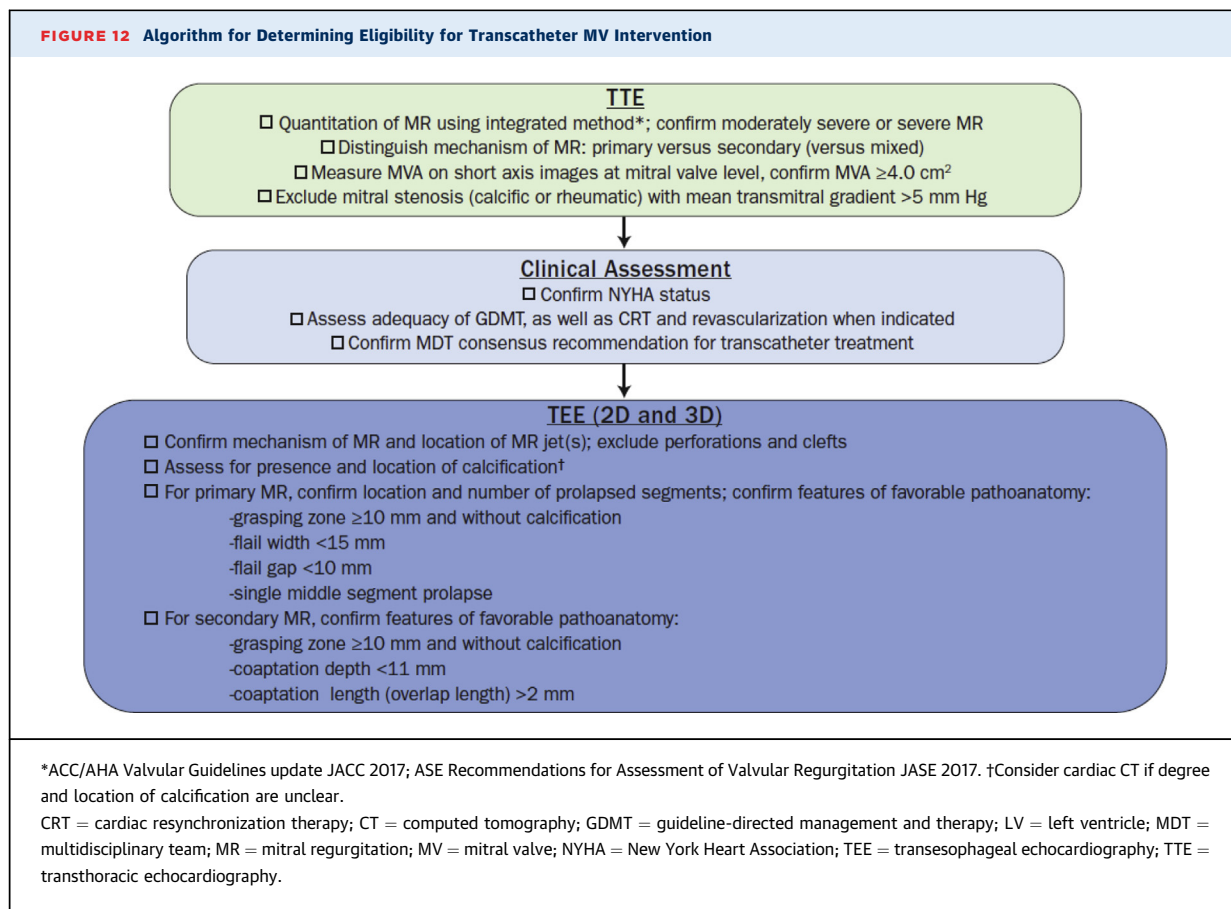
7. DISCUSSION AND INTENDED USE OF PATHWAY

The last several years have witnessed important advances in the evaluation and management of patients with chronic MR. Building upon the [2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease](#) (2), its [2017 focused update](#) (3), and the results of RCTs reported in 2018, this ECDP provides the clinician with additional tools to improve the care of MR patients. It can serve as a guide to patient assessment and individualized decision making. MDTs composed of

experienced valve experts, HF specialists, multimodality imaging experts, interventionalists, surgeons, anesthesiologists, nurse practitioners, physician assistants, certified nurse specialists, and others are vital to the provision of advanced care to challenging patients at heart valve centers. Closing the existing knowledge and treatment gaps in the management of these patients requires ongoing collaboration across primary care, cardiology, and cardiac surgical specialties, as emerging technologies for the treatment of MR are evaluated with a dedicated focus on high-quality outcomes.

7.1. Key Points

- Once MR is recognized, its etiology, mechanism, and severity should be defined using semiquantitative and

FIGURE 12 Algorithm for Determining Eligibility for Transcatheter MV Intervention

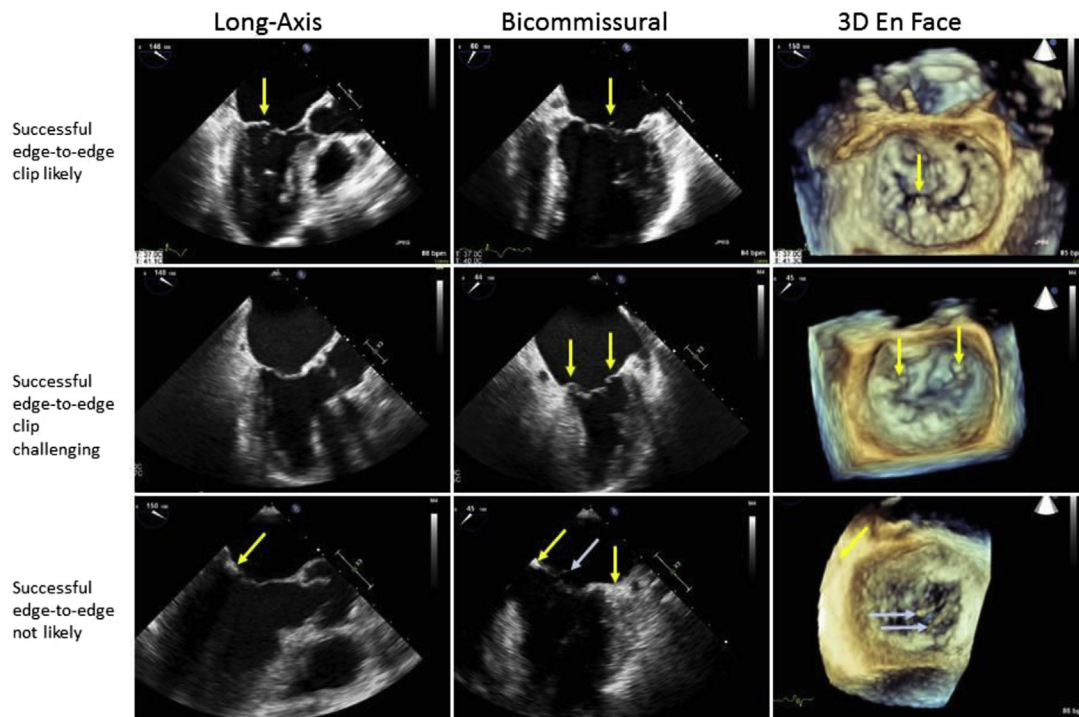
quantitative echocardiography and other imaging and physiological testing as indicated.

- Standardized echocardiographic reporting and timely access to accurate information are critical for effective patient management.
- The prognostic, evaluative, and management differences between primary and secondary MR should be recognized.
- An MDT consensus treatment recommendation should be discussed with the patient and family to enable shared decision making.
- Ongoing communication between members of the MDT and the referring clinician is strongly endorsed, especially at critical junctures in the course of treatment and at times of transition of care.
- The indications for and techniques utilized in surgical treatment of primary and secondary MR differ. Referral for repair to an experienced MV surgeon at a heart valve center should be considered for patients with severe MR in whom other cardiac diseases require concomitant operative management (e.g., coronary artery

disease), for those in whom complex repair of primary MR is contemplated, or for those with primary MR who wish to pursue a minimally invasive or robotic approach.

- Use of TMVr with an edge-to-edge clip device in the United States has expanded from the treatment of severely symptomatic patients with primary, severe MR who are poor operative candidates to carefully selected secondary MR patients with persistent HF symptoms despite rigorous GDMT (and CRT when indicated). The roles of the MDT and its individual members are critical to decision making and consensus treatment recommendations. Other TMVr and TMVR systems are under active investigation and are anticipated to become clinically available in the near to intermediate term. Introduction of these systems into clinical practice will require iterative updates to this ECDP.
- Long-term follow-up of patients after surgical or transcatheter MV intervention is essential for assessment of durability of MR reduction, functional outcome, quality of life, and survival.

FIGURE 13 Mitral Anatomy in Transcatheter Edge-to-Edge MV Clip



TEE images showing examples of mitral anatomy with varying degrees of difficulty for transcatheter edge-to-edge clip therapy. The top row of panels shows flail posterior middle scallop (arrows) in long-axis, bicommisural, and 3D en face views. This anatomy favors successful reduction with transcatheter edge-to-edge repair. The center row of panels shows a challenging case with no significant pathology of the middle segments (long-axis) but flail P1 and P3 segments (yellow arrows; bicommisural and 3D en face). The diastolic mitral area was 4.8 cm^2 , allowing room for clips in both commissures. The bottom row of panels shows a patient with severe mitral annular calcification (yellow arrows) and a flail P3 segment (blue arrows). The MV area was 2.8 cm^2 , which is below the threshold value (4.0 cm^2) and would likely result in mitral stenosis.

3D = 3-dimensional; MR = mitral regurgitation; TEE = transesophageal echocardiography.

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KEY WORDS ACC Expert Consensus Decision Pathway, heart failure, mitral regurgitation, mitral valve, registry, transcatheter mitral valve repair, transcatheter mitral valve replacement

APPENDIX 1. AUTHOR RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES (RELEVANT)—2020 FOCUSED UPDATE OF THE 2017 ACC EXPERT CONSENSUS DECISION PATHWAY ON THE MANAGEMENT OF MITRAL REGURGITATION

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Patrick T. O'Gara (Vice-Chair)	Harvard Medical School—Professor of Medicine; Brigham and Women's Hospital Cardiovascular Division—Director, Clinical Cardiology	None	None	None	None	■ Edwards Lifesciences* ■ Medtronic	None
David H. Adams	Mount Sinai Health System—Cardiac Surgeon-in-Chief; Icahn School of Medicine at Mount Sinai and The Mount Sinai Hospital—Marie-Josee and Henry R. Kravis Professor and Chairman, Department of Cardiovascular Surgery	None	None	None	■ Medtronic ■ NeoChord	■ Edwards Lifesciences† ■ Medtronic†	None
Vinay Badhwar	West Virginia University—Gordon F. Murray Professor; Chair, Department of Cardiovascular and Thoracic Surgery; Executive Chair, WVU Heart & Vascular Institute	None	None	None	None	■ Abbott Laboratories‡	None
Joseph E. Bavaria	Hospital of the University of Pennsylvania—Director, Thoracic Aortic Surgery Program	■ St. Jude Medical/Abbott	None	None	■ Edwards Lifesciences* ■ Medtronic Cardiovascular* ■ St. Jude Medical/Abbott*	■ Medtronic*‡ ■ Edwards Lifesciences*‡	None
Sammy Elmariah	Massachusetts General Hospital—Director, Interventional Cardiology Research, Division of Cardiology	■ AstraZeneca ■ Medtronic	None	None	■ Edwards Lifesciences*	■ Abbott‡ ■ Medtronic‡ ■ St. Jude‡	None
Judy W. Hung	Massachusetts General Hospital—Associate Director, Echocardiography, Division of Cardiology	None	None	None	None	■ Edwards Lifesciences§	None
JoAnn Lindenfeld	Vanderbilt University Medical Center—Director, Advanced Heart Failure; Professor of Medicine	■ Abbott Laboratories ■ Boston Scientific ■ Edwards Lifesciences ■ ResMed† ■ V-WAVE†	None	None	■ AstraZeneca* ■ Novartis†	■ AstraZeneca‡	None
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APPENDIX 1. CONTINUED

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Ruby Satpathy	Baptist Medical Center—Medical Director, Structural Heart Program; Associate Director, Cardiac Catheterization Laboratory	None	None	None	None	None	None
Brian Whisenant	Intermountain Heart Institute Cardiology—Medical Director, Heart Valve and Structural Heart Disease	<ul style="list-style-type: none"> ■ Boston Scientific† ■ Edwards Lifesciences† ■ Johnson & Johnson† 	None	None	<ul style="list-style-type: none"> ■ Edwards Lifesciences* 	<ul style="list-style-type: none"> ■ Abbott Laboratories‡ ■ Edwards Lifesciences‡ ■ Medtronic‡ 	None
Y. Joseph Woo	Stanford University School of Medicine—Norman E. Shumway Professor; Chair, Department of Cardiothoracic Surgery	None	None	None	None	None	None

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\$Dr. Hung is Director of the Massachusetts General Hospital Echo Core Laboratory, which is funded by Edwards Lifesciences through Edwards' acquisition of Harpoon Medical. Dr. Hung's relationship with Edwards/Harpoon was disclosed after the initial publication of this document.

AATS = American Association for Thoracic Surgery; ACC = American College of Cardiology; AHA = American Heart Association; SCAI = Society for Cardiovascular Angiography and Interventions; STS = The Society of Thoracic Surgeons.

APPENDIX 2. PEER REVIEWER INFORMATION—2020 FOCUSED UPDATE OF THE 2017 ACC EXPERT CONSENSUS DECISION PATHWAY ON THE MANAGEMENT OF MITRAL REGURGITATION

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ACC = American College of Cardiology; SSOC = Solution Set Oversight Committee.

APPENDIX 3. ABBREVIATIONS

ACC = American College of Cardiology

AF = atrial fibrillation

AHA = American Heart Association

CFD = color flow Doppler

CMR = cardiac magnetic resonance

COAPT = Cardiovascular Outcomes Assessment of the
MitraClip Percutaneous Therapy

CRT = cardiac resynchronization therapy

ECDP = Expert Consensus Decision Pathways

EROA = effective regurgitant orifice area

GDMT = guideline-directed management and therapy

HF = heart failure

LA = left atrial

LV = left ventricle

LVEF = left ventricular ejection fraction

MDT = multidisciplinary team

MR = mitral regurgitation

MV = mitral valve

PISA = proximal isovelocity surface area

PROM = predicted risk of mortality

RCT = randomized controlled trial

RF = regurgitant fraction

RVol = regurgitant volume

STS = Society of Thoracic Surgeons

TEE = transesophageal echocardiography

TMVR = transcatheter mitral valve replacement

TMVr = transcatheter mitral valve repair

TTE = transthoracic echocardiography