

EXPERT CONSENSUS DECISION PATHWAY

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

A Report of the American College of Cardiology Task Force on
 Expert Consensus Decision Pathways

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ABSTRACT

Mitral regurgitation (MR) is a complex valve lesion that can pose significant management challenges for the cardiovascular clinician. This Expert Consensus Document emphasizes that recognition of MR should prompt an assessment of its etiology, mechanism, and severity, as well as indications for treatment. A structured approach to evaluation based on clinical findings, precise echocardiographic imaging, and when necessary, adjunctive testing, can help clarify decision making. Treatment goals include timely intervention by an experienced heart team to prevent left ventricular dysfunction, heart failure, reduced quality of life, and premature death.

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PREFACE

The American College of Cardiology (ACC) develops a number of policy documents to provide members with guidance on clinical topics. Although clinical practice guidelines remain the primary mechanism for offering evidence-based recommendations, such guidelines may contain gaps in how to make clinical decisions, particularly when equipoise is present in a topic. Expert Consensus Documents are intended to provide guidance for clinicians in areas where evidence may be limited or new and evolving, or where data are insufficient to fully inform clinical decision making.

In an effort to increase the impact of ACC policy on patient care, an ACC Presidential Task Force was formed in 2014 to examine the ACC's clinical documents. The main recommendation of the Task Force was a new focus on concise decision pathways and/or key points of care, instead of the traditional longer documents. The Task Force also established criteria for identifying high-value clinical topics to be addressed, as well as an innovative approach to collecting stakeholder input through a roundtable or think tank meeting. To complement the new focus on brief decision pathways and key points, Expert Consensus Documents were rebranded "Expert Consensus Decision Pathways" (ECDPs).

Although ECDPs have a new format, they maintain the same goal of Expert Consensus Documents to develop policy based on expert opinion in areas for which important clinical decisions are not adequately addressed by available data. ECDPs are designed to complement the guidelines and bridge the gaps in clinical guidance that remain. In some cases, topics covered by ECDPs will be addressed subsequently by ACC/American Heart Association (AHA) guidelines as the evidence base evolves. The writing groups are charged with developing algorithms that are more actionable and can be implemented into tools or apps to accelerate the use of these documents at point of care. Decision Pathways are not intended to provide a single correct answer, but to encourage clinicians to ask certain questions and consider important factors as they come to their own decision on a treatment plan to be recommended and discussed with their patients. There may be multiple pathways that can be taken for treatment decisions, and the goal is to help clinicians make a more informed decision.

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1. INTRODUCTION

Improvements in multimodality imaging, surgical techniques, and outcomes, as well as the introduction of transcatheter replacement and repair, have transformed the approach to patients with valvular heart disease. Long-term natural history studies have informed clinical decision making regarding the appropriate timing for valve intervention. 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 the heart valve team approach to patients with calcific aortic stenosis, in large measure due to improvements in transcatheter and surgical therapies. The evaluation and management of patients with mitral regurgitation (MR), a highly prevalent valve lesion among aging U.S. adults, are more complex, in part related to 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 the valve's normal function, including the left ventricle, papillary muscles, chordae tendineae, leaflets and annulus.

This document contains clinical expert consensus recommendations to guide the approach to patients identified with MR. The document emphasizes clinical and echocardiographic assessment, establishment of etiology and mechanism, consideration of associated hemodynamic consequences, recognition of the triggers for surgical referral, appreciation of the graded complexity of mitral valve repair as a function of pathoanatomy, and understanding the currently limited role for transcatheter mitral valve edge-to-edge repair in the United States. Recommendations are based on the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (1) and its 2017 focused update (2), and augmented with additional clinical context and practical advice for medical and surgical decision making in complex patient scenarios.

2. METHODS

The writing committee was assembled in September 2015. In addition to the master document, figures, and tables contained herein, the writing committee developed a template for structured echocardiographic reporting of MR etiology, mechanism, Carpentier (functional) classification, severity, and associated findings, as well as a checklist for use when contemplating referring

patients for advanced imaging or surgical/interventional therapy. The 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 (1), its 2017 focused update (2), additional literature review through March 2017, and, when evidence was lacking or limited, expert consensus. The writing committee (see Appendix 1) included representatives from the following areas and career stages: general cardiology, heart valve disease, heart failure, imaging, interventional/structural heart disease, valve surgery, fellows-in-training, and early career professionals.

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

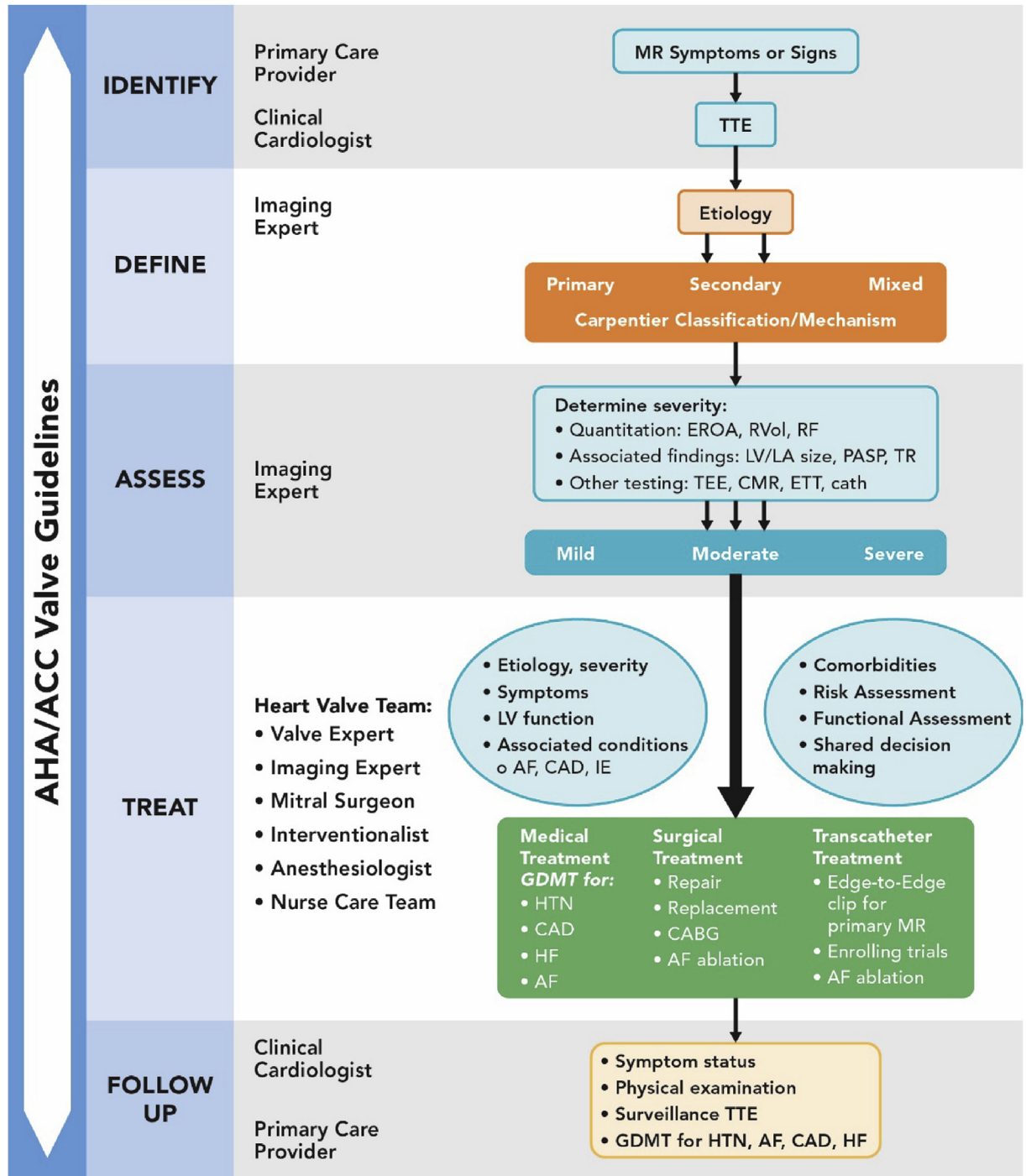
This effort was neither conceived nor designed to rewrite or reinterpret the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (1) or its 2017 focused update (2). The writing committee did not stipulate the means by which MR may first be appreciated and did not focus on 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 (functional) MR is characterized by incompetence due to adverse changes in left ventricular 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., mitral valve 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 (3). Previous publications regarding institutional and operator requirements for transcatheter heart valve intervention programs were acknowledged (4). The writing committee did not define a comprehensive valve center or stipulate the criteria by which a mitral valve surgeon or interventionalist is considered experienced or highly experienced. The latter 2 issues are of intense interest to the community and are the focus of collaborative, multisocietal deliberations. The members of the heart valve team and their roles have been reviewed in previous guideline and multisocietal publications (1,4).

4. CENTRAL ILLUSTRATION

Figure 1 provides an overview of what is covered in the decision pathway. See each section for more detailed considerations and guidance.

FIGURE 1 Pathway for Management of MR



Abbreviations:

AF = atrial fibrillation; 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 medical therapy; HF = heart failure; HTN = hypertension; IE = infective endocarditis; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; PASP = pulmonary artery systolic pressure; RF = regurgitant fraction; RVol = regurgitant volume; TEE = transesophageal echocardiogram; TR = tricuspid regurgitation; TTE = transthoracic echocardiogram

5. DESCRIPTION AND RATIONALE

Mitral regurgitation is the most common type of moderate or severe heart valve disease among U.S. adults older than 55 years of age. Its prevalence increases further as a function of age (5). The 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (1) 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) left ventricular (LV) function, or having symptomatic severe MR (Stage D). Indications for treatment depend on disease stage, characterization of which relies on an accurate assessment of MR severity, coupled with an appreciation for symptom status and the limits of intervention. A recent 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 volume and quality of surgical repair at their institution (6).

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

6. EVALUATION OF THE PATIENT

6.1. 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) (7). 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

patient what is the most vigorous activity he/she currently undertakes and compare that with what he/she 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 he/she 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 (8). In addition to exertional dyspnea, common symptoms include fatigue and palpitations. Incorporation of a patient questionnaire on health status into the medical record is encouraged. The Society of Thoracic Surgeons/ACC Transcatheter Valve Therapy (TVT) Registry (NCT01737528) includes an entry for the Kansas City Cardiomyopathy Questionnaire (9,10). The Patient Reported Outcomes Measurement Information System is an alternative assessment tool (11).

If the patient is asymptomatic, exercise testing may be performed safely and may elicit symptoms or demonstrate reduced exercise capacity. 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 (12-15). 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 (16).

In patients with primary MR, the presence of a diastolic filling complex (S3 plus short diastolic murmur) suggests a significant RVol and severe MR (17). In secondary MR, an S3 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 is limited in timing to late systole only, it is likely that the regurgitation is not severe. One or more nonejection clicks may be audible. 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 with posterior leaflet flail radiate anteriorly and can be confused with systolic ejection murmurs. With functional 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 make the examination more challenging, particularly when the heart rate is rapid (17).

6.2. Hemodynamic Effects of MR

The hemodynamic effects of chronic, severe primary MR are well-known. Chronic 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 left ventricular ejection fraction (LVEF), which is typically supranormal. As the LV dilates, LV wall stress increases. Incipient and irreversible myocardial dysfunction may occur due to the long-standing LV volume overload. Because ejection fraction is a load-dependent measure of LV function, it can be preserved even as myocardial contractile function becomes abnormal. Current clinical practice guidelines recommend surgical intervention in asymptomatic patients with primary MR and LVEF <60% or LV end-systolic dimension >40 mm (1). These thresholds, however, may already indicate LV dysfunction, and mitral valve surgery is also now considered 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%) (2). In secondary MR, the relationship between LVEF and the associated volume overload is confounded by the fact that LV dilation and decreased function are the cause rather than the consequence of MR; however, the presence of any degree of secondary MR is associated with worsened prognosis in patients with ischemic or nonischemic cardiomyopathy (9,18-24). To date, neither valve repair nor replacement has been shown to improve survival in patients with severe, functional MR.

In addition to its effects on LV size, chronic severe MR results in LA dilation, increased LA pressure, and pulmonary venous hypertension. Accordingly, AF is common in chronic severe MR. Persistent or long-standing persistent AF may also cause or worsen MR due to the associated dilation of the LA and mitral annulus. Therefore, the assessment of MR severity must take into account the pathoanatomy of the mitral apparatus, LV size and function, LA size/volume, pulmonary artery pressure, and the presence of AF.

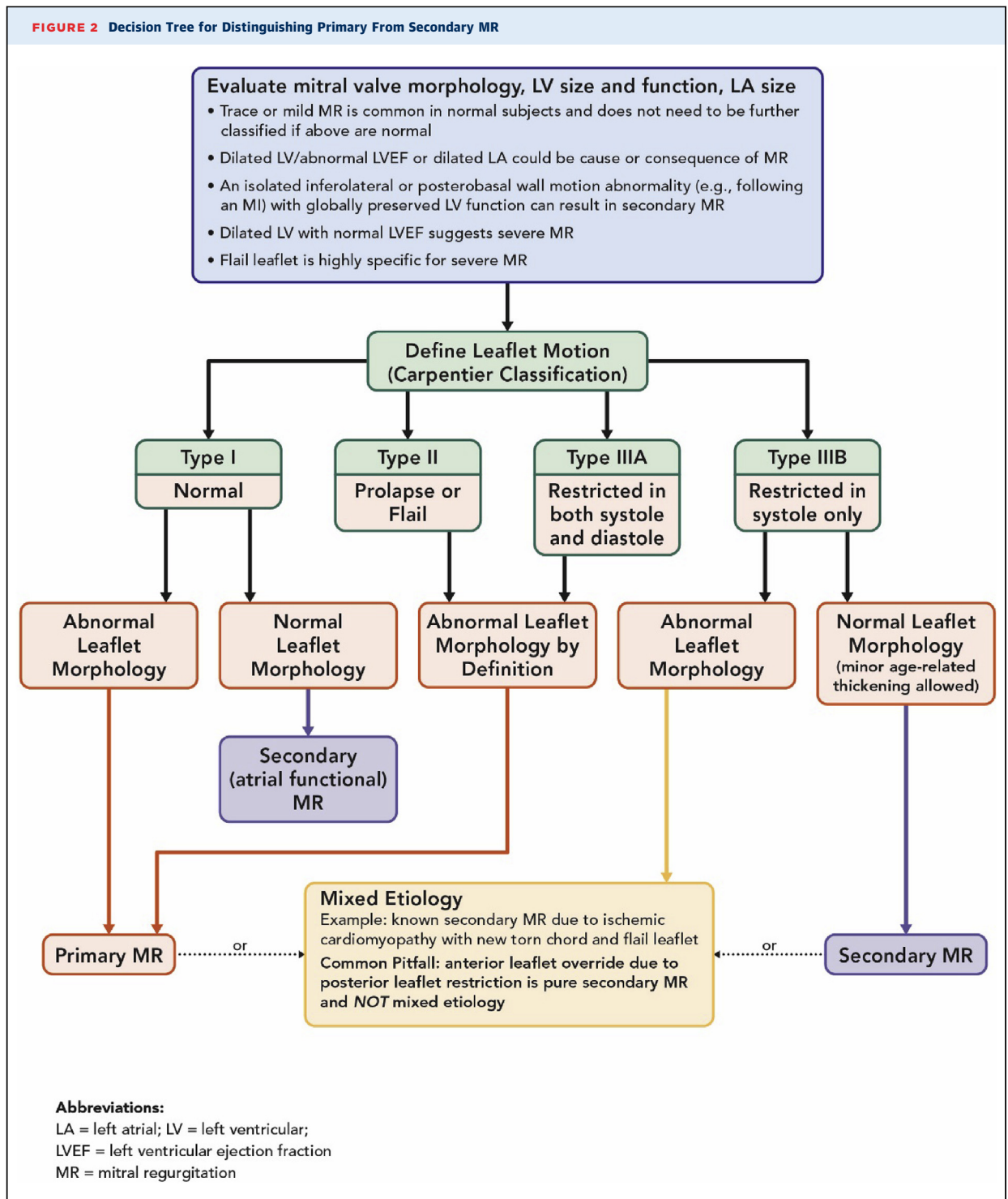
6.3. Determining the Mechanism and Etiology of MR

The identification of MR mechanism and etiology is most commonly achieved by transthoracic echocardiography (TTE) (Figure 2). Mitral valve morphology should be carefully assessed in multiple views using B-mode imaging to evaluate structure and motion and color flow Doppler (CFD) to localize the origin of MR jet(s). If image quality is poor with TTE, transesophageal echocardiography (TEE) may often be needed to define anatomy and function more precisely. TEE may identify lesions such as vegetations or flail segments not detected by TTE (6,25-28). Careful measurement of LV and LA volumes and of LV dimensions should be performed according to American Society for Echocardiography guidelines for chamber quantification (29). Mitral valve morphology, LV and LA volumes, and LV size and systolic function are

used together to classify the mechanism and etiology 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 may involve chordal rupture, thickening, fusion, vegetations, and masses, which should similarly be described in detail by size and location. Abnormal annular morphology comprises dilation and/or calcification. Mitral annular calcification can be localized posteriorly or extend into the LV outflow tract or LV myocardium. When MR is due to primary mitral valve pathology, left-sided chamber dilation should be considered a clue that the MR is both chronic and severe. Chronic primary MR with normal LV and LA size, function, and volume is unlikely to be severe (2). 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 (30-35); however, isolated regional wall motion abnormalities, particularly in the inferobasal or posterobasal segments, may cause severe secondary MR despite preserved LV function and dimensions. It is also possible to have MR secondary to pure annular dilation in patients with severe LA dilation (36). This has been termed "atrial functional MR" and it is most commonly seen in persistent or long-standing persistent AF or in restrictive cardiomyopathies, such as that due to amyloid.

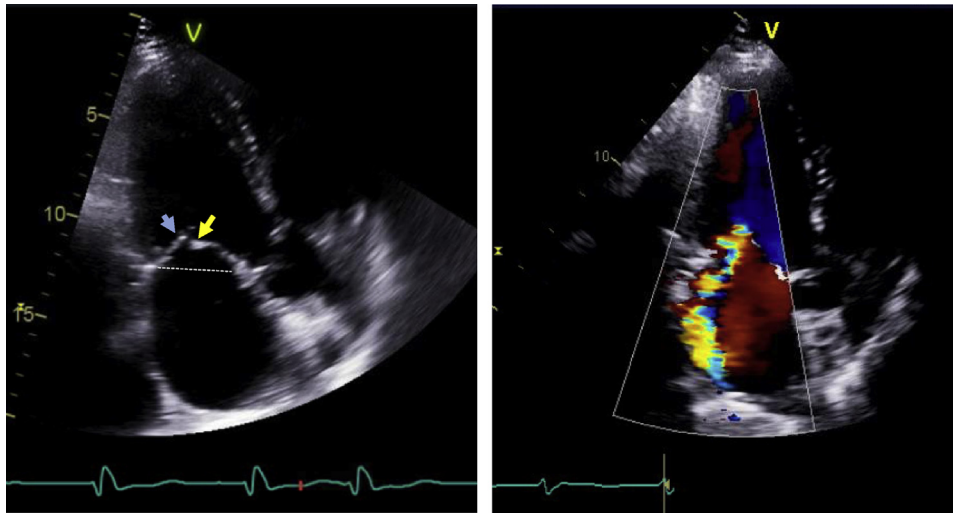
Once the leaflet morphology is characterized, leaflet motion should be described using Carpentier's classification system (37) (Figure 2). Normal leaflet motion (Type I) may be seen in primary MR due to endocarditis, perforation, or clefts and in primary or secondary MR due to isolated annular dilation. Excessive leaflet motion (Type II) is most commonly seen with mitral valve 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 (38). 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 mitral valve disease, radiation- or drug-induced injury, or other inflammatory conditions. The latter is typical of MR secondary to ischemic or nonischemic cardiomyopathy.

It is also important to note that mixed pathology can and does occur. Untreated primary MR eventually results in irreversible LV dilation/dysfunction in which both leaflet prolapse and tethering may coexist. Other

FIGURE 2 Decision Tree for Distinguishing Primary From Secondary MR

examples include patients with long-standing secondary MR due to ischemic heart disease or AF who subsequently rupture a chord, or patients with mitral valve prolapse who have a myocardial infarction or develop a cardiomyopathy. 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

FIGURE 3 Anterior Leaflet Override in Functional MR

Anterior leaflet override in secondary MR due to ischemic cardiomyopathy. Apical long-axis views 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 mitral valve prolapse, but cannot be such because the AML never moves superiorly to the mitral annulus (**dotted line**). AML = anterior mitral leaflet; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; PML = posterior mitral leaflet.

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 1](#) lists the descriptors of MR mechanism and severity that should be included in standardized echocardiographic reports.

6.3.1. Spectrum of Functional MR

Functional MR occurs across a spectrum of severity of LV dysfunction. At one end of the spectrum is a severely dilated, spherical LV with markedly depressed LV systolic function and functional MR. Treatment of MR may not improve symptoms or quality of life or result in reverse LV remodeling because the primary problem is severe LV dysfunction. Heart transplantation or destination LV assist device therapy may be a more effective treatment strategy than mitral valve surgery in this context. At the other end of the spectrum, a patient with an isolated inferobasal myocardial infarction may develop severe functional MR due to posterior leaflet tethering, despite normal LV size and global ejection fraction. In such patients, the severe MR is the cause of heart failure, and surgery may be indicated for symptom relief. In the middle of the spectrum, it can be very hard to determine whether MR, LV dysfunction, or both are contributing to heart failure symptoms.

6.4. Assessment of MR Severity

6.4.1. CFD Jet Size

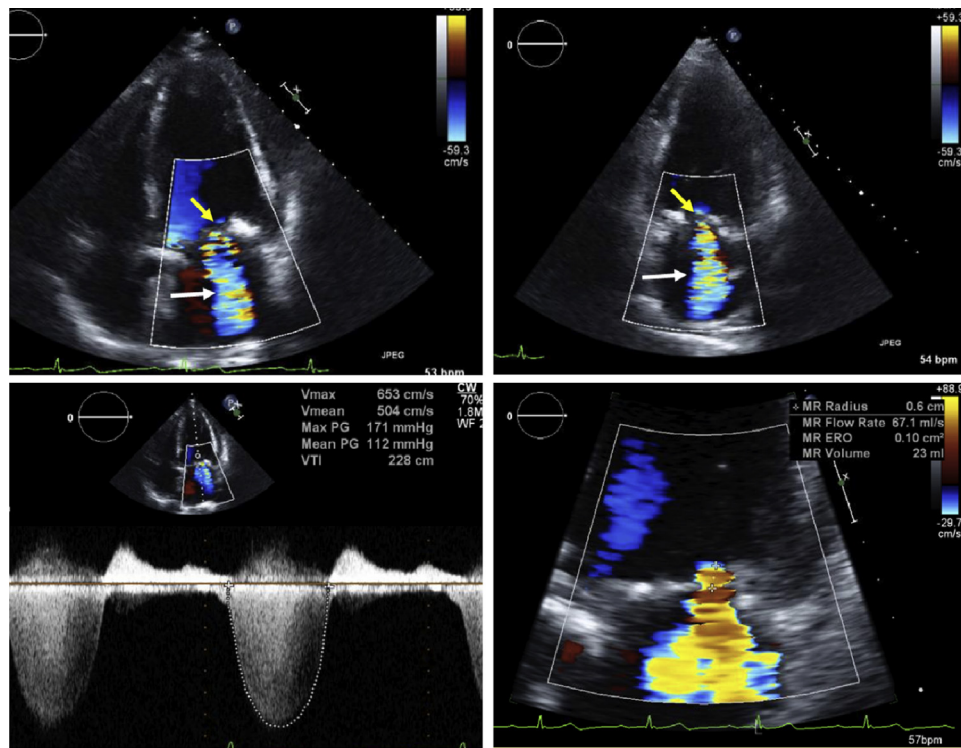
Severity of MR is most commonly assessed using CFD during TTE or TEE. CFD is a misnomer because it is not actually a flow image—it is an image of the spatial distribution of velocities within the image plane and is profoundly affected by instrument settings and hemodynamic factors (3). If these are held constant, the size of a jet through a given effective regurgitant orifice area (EROA) is determined by its momentum flux, ρAv^2 , where ρ is blood density, A is orifice area, and v^2 is velocity squared (39). 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 (3). The tendency for CFD to overestimate MR severity has recently been shown in a study comparing TTE with cardiac magnetic resonance (CMR) imaging for quantitation (40). This also explains why healthy individuals with no heart murmur often have mild MR on CFD (41). MR can be significantly underestimated when jets have a low driving velocity or are markedly eccentric as momentum is

TABLE 1 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 	<p>Mitral stenosis</p> <ul style="list-style-type: none"> Rheumatic Degenerative Other <p>Carpentier Classification</p> <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) <p>Submitral morphology:</p> <ul style="list-style-type: none"> Thickening Calcification Retraction Tumor Vegetation <p>MR Mechanism:</p> <ul style="list-style-type: none"> Primary Secondary <ul style="list-style-type: none"> Dilated Cardiomyopathy Ischemic Cardiomyopathy Other Mixed <p>MR Jet Duration (CW Doppler and frame-by-frame analysis of color flow Doppler):</p> <ul style="list-style-type: none"> Holosystolic Early systolic Midsystolic Late systolic Bimodal CW Doppler density <p>MR Jets:</p> <ul style="list-style-type: none"> Single Multiple <p>MR Jet Direction:</p> <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 <p>Pulmonary Vein Flow Profile:</p> <ul style="list-style-type: none"> Normal Systolic flow blunting Systolic flow reversal Number of veins exhibiting systolic reversal 	<p>Mitral Inflow Profile:</p> <ul style="list-style-type: none"> E dominant pattern A dominant pattern (incompatible with severe MR)
QUALITATIVE PARAMETERS		QUANTITATIVE PARAMETERS
<p>Leaflet Morphology:</p> <ul style="list-style-type: none"> Structurally normal Nonspecific thickening Focal calcific or nodular thickening Diffusely calcified Myxomatous Vegetations Tumor Clefts Perforation <p>Chordal Morphology:</p> <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 <p>Annulus Size and Morphology (commisure-commisure and anterior-posterior measurements)</p> <ul style="list-style-type: none"> Normal Dilated Calcified (location and extent) <p>Leaflet Mobility:</p> <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 <p>Restricted or Tethered Leaflets</p> <ul style="list-style-type: none"> AML PML Both 		<p>Vena Contracta:</p> <ul style="list-style-type: none"> Vena contracta width: mm Vena contracta area (cm²) <p>Threshold values specific for severe MR</p> <ul style="list-style-type: none"> EROA >0.4cm² Regurgitant volume >60 mL/beat Regurgitant fraction >50% <p>Left Atrial Size:</p> <ul style="list-style-type: none"> Left atrial dilation Left atrial volume index: mL/m² <p>Mitral Valve Area: cm² (for patients with coexisting rheumatic or degenerative mitral stenosis or for planning edge-to-edge clip)</p> <ul style="list-style-type: none"> 2D planimetry (biplane) 3D planimetry (multiplanar Reconstruction) Pressure half-time Continuity equation PISA <p>Mean transmitral Doppler gradient:</p> <ul style="list-style-type: none"> mm Hg @ heart rate (input HR concurrently recorded during CW Doppler acquisition) <p>Left Ventricular Function:</p> <ul style="list-style-type: none"> Ejection fraction (normal > 60%) Global LV dysfunction Regional LV dysfunction (detail wall motion) <p>Left Ventricular Size:</p> <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 <p>Right Ventricular Size (tricuspid annular and midventricular measurements)</p> <ul style="list-style-type: none"> Normal Dilated <p>Right Ventricular Systolic Function:</p> <ul style="list-style-type: none"> Normal Impaired <p>Tricuspid Annulus:</p> <ul style="list-style-type: none"> Normal Dilated <p>Tricuspid Valve Regurgitation:</p> <ul style="list-style-type: none"> Mild Moderate Severe <p>PA Systolic Pressure: mm Hg</p> <p>Estimated RA pressure: mm Hg</p>
	<p>*Above criteria applicable for native mitral valve disease only and not for assessing MR post mitral valve repair (surgical or transcatheter).</p>	<p>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</p>

transferred to the LA wall (42). 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 (43). Thus, both U.S. and European guidelines recommend that MR jet size assessed by CFD not be used alone to assess MR severity (3,44).

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**) Large MR jet (**white arrows**) penetrating deep into LA in apical 4-chamber (**left**) and 2-chamber (**right**) 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 of 6.5 m/s, corresponding to an LV-LA pressure gradient of 170 mm Hg. 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.

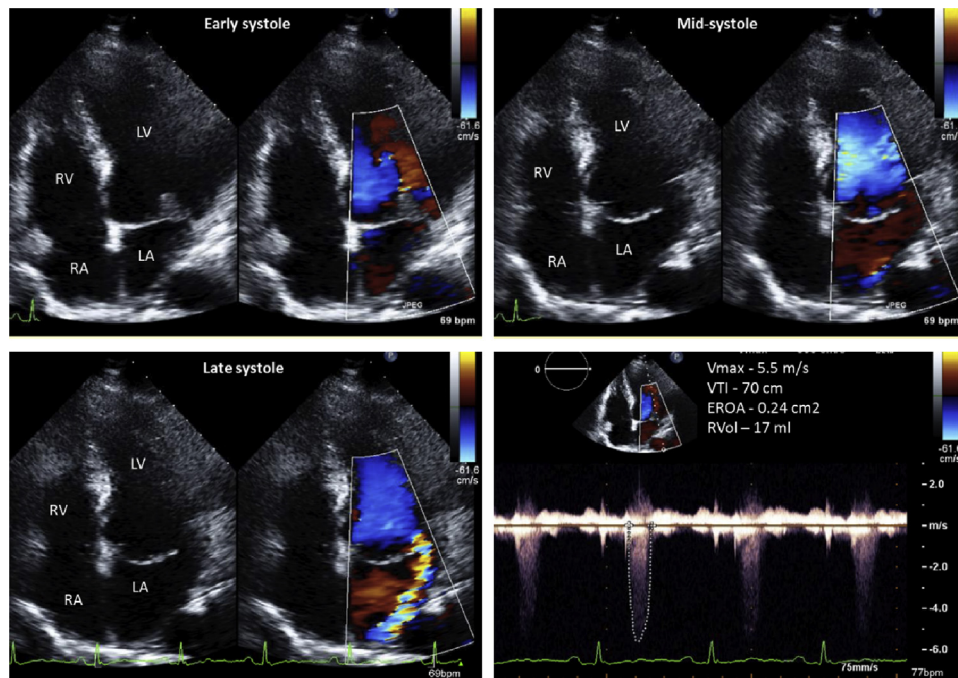
6.4.2. Quantitative Parameters

Calculation of EROA, a marker of lesion severity, as well as RVol and regurgitant fraction (RF), is strongly recommended for assessing MR severity (3). They 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 area, can markedly overestimate MR severity when the jet is limited to early or late systole (Figure 5) (45). 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) (46-55). 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. The addition of multiple EROA 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.

6.4.3. Integration of Multiple Parameters

A comprehensive approach is recommended whereby multiple parameters are evaluated and integrated to form

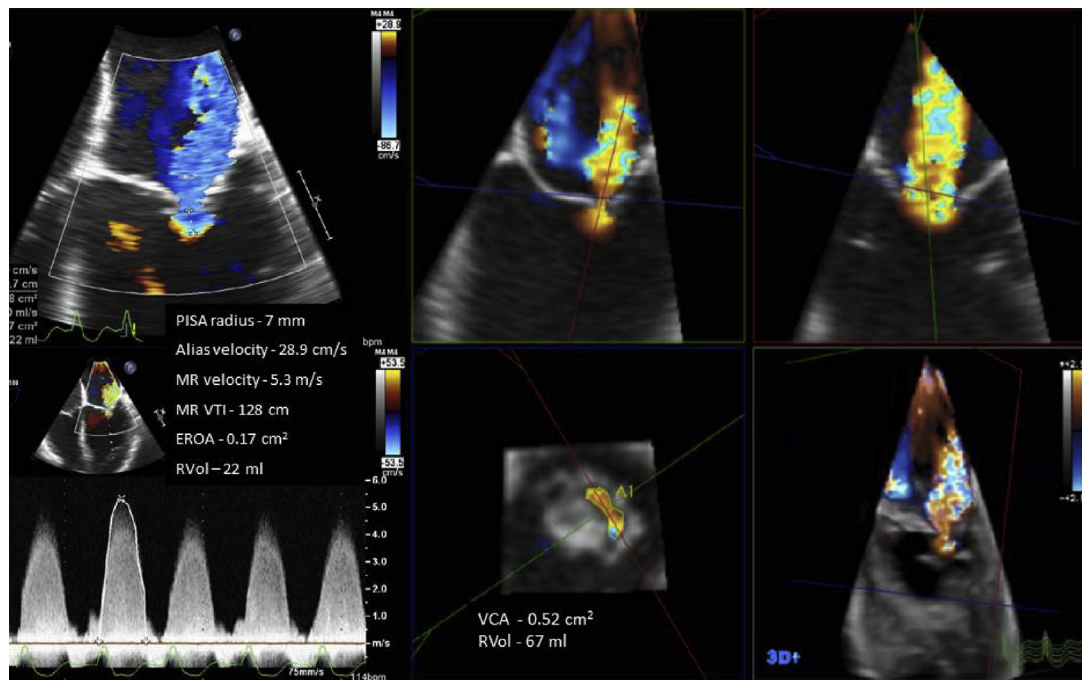
FIGURE 5 MR Limited to Late Systole in Mitral Valve Prolapse

Example of nonholosystolic MR in mitral valve prolapse. (Top) No MR by color Doppler in early systole (left) and midsystole (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 was 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.

a final determination of MR severity (3,44) (Figure 7). The strengths and limitations of these parameters are listed in Table 2 and described in detail in the 2017 American Society for Echocardiography Guidelines for Assessment of Native Valve Regurgitation (3). 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 (56-58). 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 be considered only 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 mitral valve; however, when different parameters are discordant among themselves or with 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 general 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 (3,59-63).

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 cm^2 and RVol of 22 mL. (**Middle and right**) 3-dimensional reconstruction of the vena contracta in the same patient showing vena contracta-derived area of 0.52 cm^2 (**middle, lower panel**), yielding an RVol of 64 mL ($0.5 \text{ cm}^2 \times 128 \text{ cm}$). The EROA is underestimated by 2-dimensional PISA, which assumes circular orifice geometry, because of the crescent-shaped MR jet. CW = continuous wave; EROA = effective regurgitant orifice area; MR = mitral regurgitation; PISA = proximal isovelocity surface area; RVol = regurgitant volume.

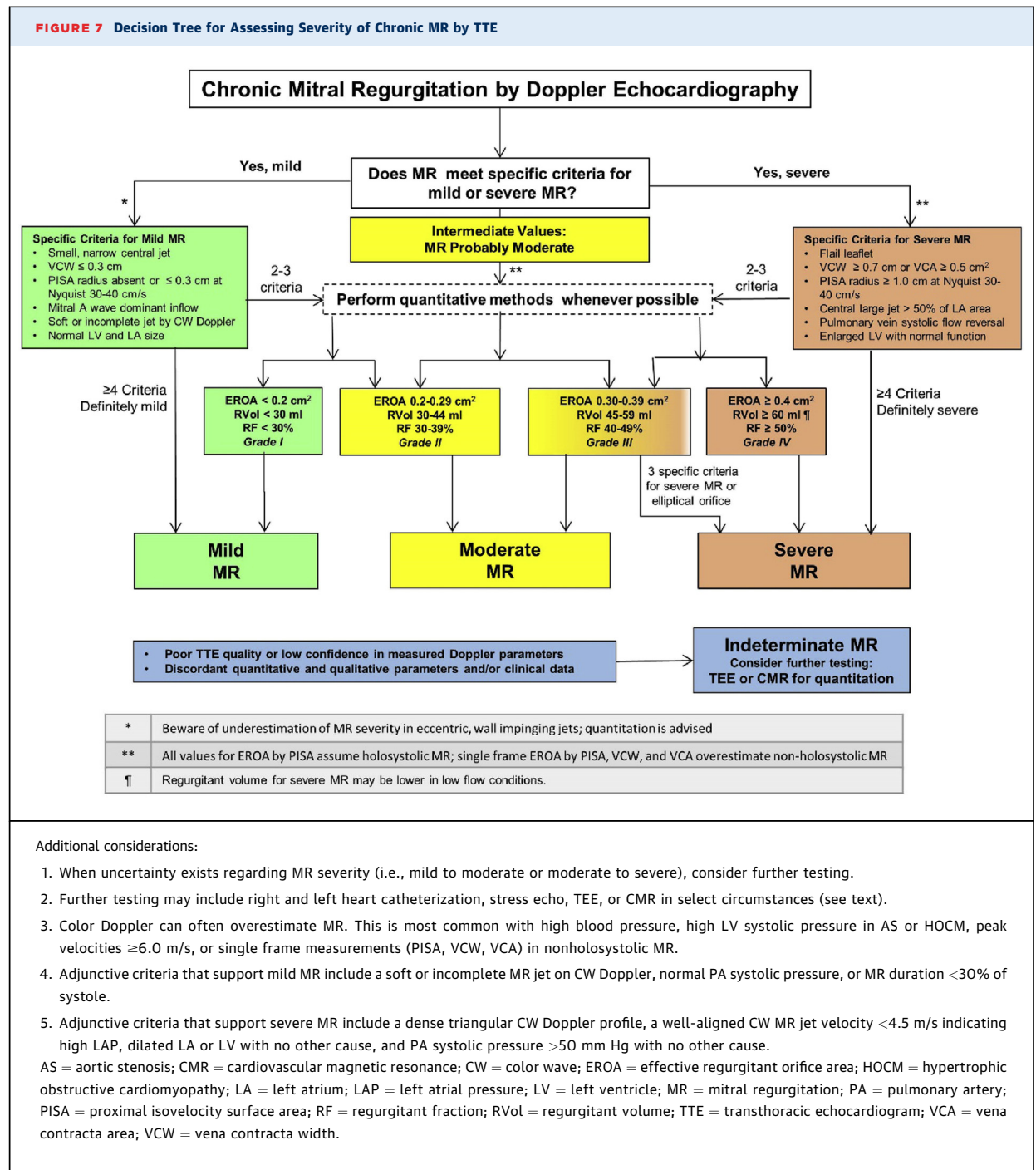
Right and left heart catheterization may be indicated to assess hemodynamics. Despite its known limitations, a high-quality biplane LV angiogram can also be helpful in resolving uncertainty. Invasive measurement of pressures, cardiac output, and pulmonary vascular resistance allows a comprehensive assessment, 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 left/right ventricular 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 can be given to referring such patients to a comprehensive valve center for multidisciplinary evaluation and treatment.

An evidence-based algorithm for the evaluation and management 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 (1) and its 2017 focused update (2), this algorithm attempts to mitigate any potential gaps in the clinical approach to MR (6).

Decisions regarding when to follow and when to refer patients with MR for further assessment or valve intervention can be challenging. Once the diagnosis of MR is established 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, which is discussed further in the following text.

6.4.4. Dynamic Nature of MR

MR is a dynamic condition, and its severity can change with LV loading parameters (56). 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 mitral valve prolapse (64) as well as in patients with

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

hypertrophic obstructive cardiomyopathy. Afterload reduction would also be expected to increase MR severity in hypertrophic obstructive cardiomyopathy. Guideline-directed medical therapy, revascularization, and cardiac resynchronization (when indicated) may improve MR severity in functional 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 (57,58). The classic example is late systolic MR due to 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 (45). It is possible to correct EROA for duration of systole, but this method has not been

TABLE 2 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
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); flow convergence at Nyquist limit of 50–60 cm/s alerts reader to significant MR	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; PISA = proximal isovelocity surface area; PW = pulsed wave; RF = regurgitant fraction; RVol = regurgitant volume.

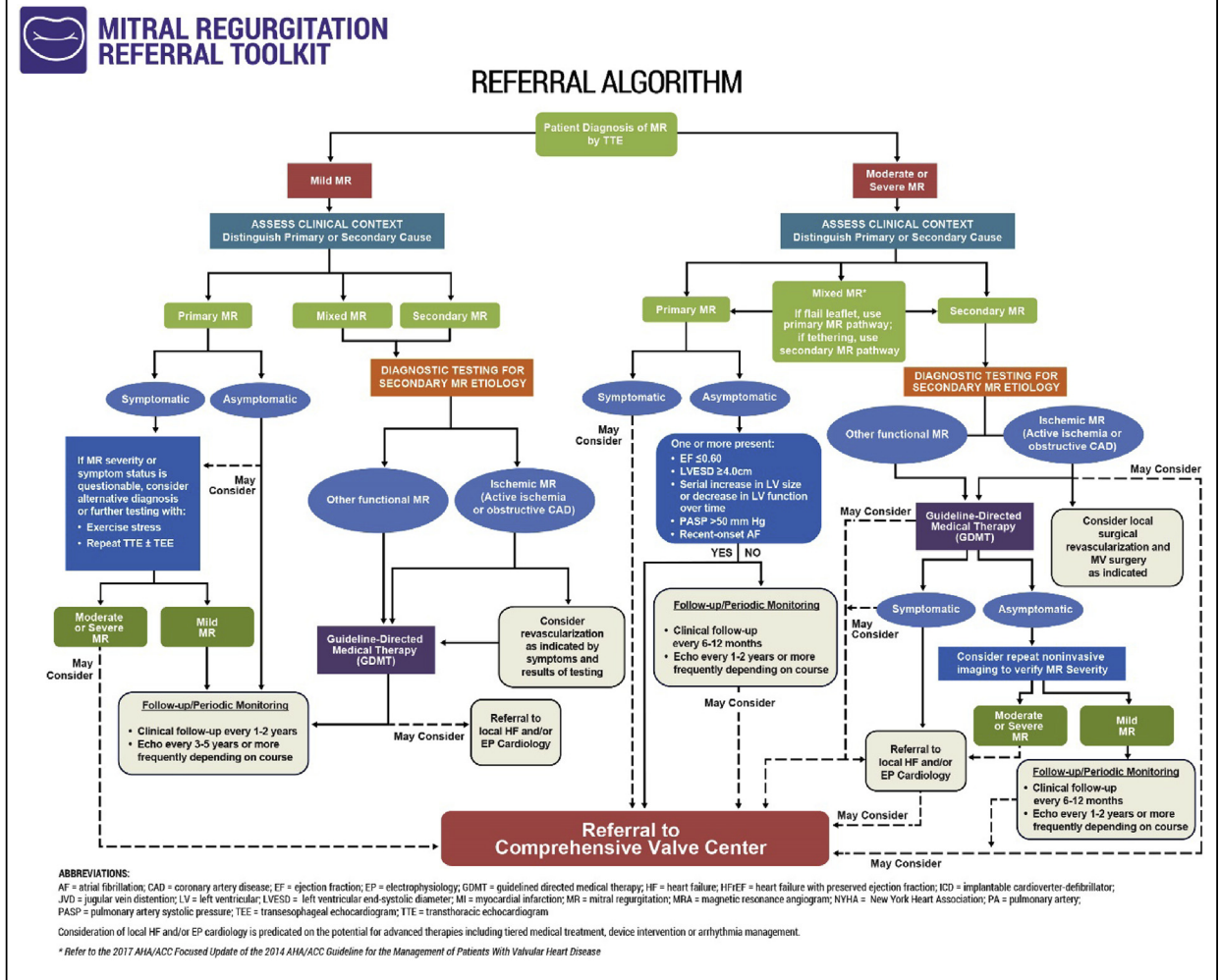
validated. In secondary MR, a biphasic pattern can be seen in which MR improves during midsystole when LV pressure (i.e., closing force) is at its maximum (57). It is important for the sonographer not to “overgain” the machine to make this phenomenon disappear. It is also important to measure PISA radius and MR peak velocity at the same point in the cardiac cycle (3). 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 the single-frame technique (65).

6.4.5. 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, severe leaflet retraction without visible coaptation, or leaflet destruction and perforation due to endocarditis, are specific markers of severe MR. LV or LA dilation in chronic primary MR is most often a consequence of the MR and is a strong clue that the MR is severe. Exceptions could occur if a patient with long-standing mitral valve 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 brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide; 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 are therefore 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 because the latter assumes a circular orifice (46–55). This inaccuracy can be ameliorated by 3-dimensional PISA measurements or direct 3-dimensional measurement of EROA by TTE or TEE (Figure 6). Such measurements have been validated against CMR (52,54). Importantly, EROA and RVol thresholds that define severe MR are related to LV volumes (66). As an example, consider 2 patients with LVEF 30% but LV end-diastolic volumes of 200 and 400 mL, respectively. The former has a total stroke volume of 60 mL; the latter, 120 mL. In the former patient, an EROA 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 an RF of 75% (45/60 mL),

FIGURE 8 Clinical Algorithm for the Management of Chronic MR Based on TTE



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 ejection fraction. It is recognized that the accepted EROA threshold for severe MR (≥ 0.40 cm²) can be lower in patients with secondary MR and elliptical orifices, emphasizing the need for an integrative assessment of severity (3).

6.4.6. Prognosis in MR

Table 3 lists prognostic variables important in the assessment of primary MR. Some of these are clinical (age, heart failure, coronary artery disease, and functional class); others relate to MR itself or the effects of MR on the LV or LA. LVEF <60%, LV end-systolic diameter >40 mm, and LA systolic volume index >60 mL/m² have all been associated with worse prognosis (67-70). Flail leaflet is

associated with an adverse prognosis and is usually a specific sign for severe MR (7,67,68), although occasionally patients with flail leaflets only have moderate MR by integrative assessment. Rare patients with flail leaflet may experience sudden cardiac death (71). Early referral of the patient with flail leaflet might be considered. Secondary MR has been associated with an adverse prognosis in multiple studies (9,18-24). 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 ≥ 0.2 cm² has been shown to be a predictor of adverse outcomes in some studies of patients with functional MR (19,21,23). 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 (9,22). Surgical correction of secondary MR may improve symptoms and quality of life but has not been shown to improve survival (72).

TABLE 3 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 >4 cm) ■ 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 ■ 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

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; MV = mitral valve.

7. TREATMENT OF CHRONIC MR

7.1. General Considerations

Decisions regarding the optimal treatment of chronic MR are based on multiple variables, including MR type and severity, hemodynamic consequences, disease stage, patient comorbidities, and the experience of the heart valve team and its members (73). Evidence-based management may be aided by use of the algorithm in Figure 8. The use of standardized nomenclature when reporting echocardiographic findings helps to guide surgical/interventional decision making (37) (Table 1). The anterior and posterior leaflets are divided into 3 anatomic sections from lateral to medial (A1, A2, and A3, and P1, P2, and P3, respectively). The 2 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 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 (midesophageal 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 60 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 mitral valve operation is beyond the scope of this document.

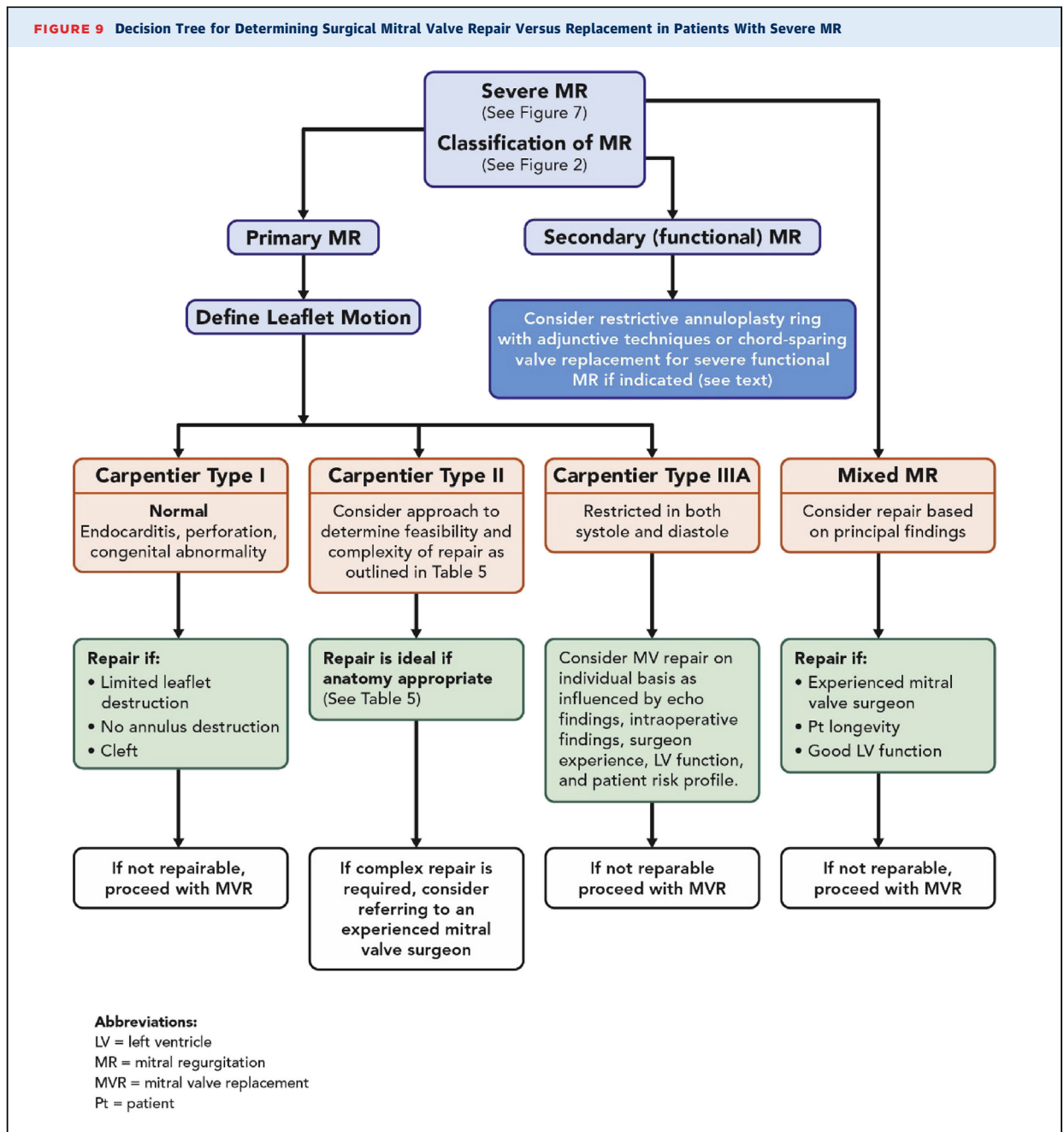
The principal treatment modality for primary MR is surgery. At present, transcatheter mitral repair using an edge-to-edge clip has a very limited role for the treatment of patients with primary MR and severe symptoms who are

felt to be poor surgical candidates. Surgical treatment for secondary MR is undertaken only after appropriate medical and device therapies have been instituted. Transcatheter repair systems other than the edge-to-edge clip, as well as transcatheter mitral valve replacement devices, are currently not approved for clinical use in the United States but remain the subject of clinical trial investigation.

7.2. Surgical Treatment of MR

Mitral valve 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) (1). Mitral valve repair is strongly preferred over replacement for primary MR whenever anatomically feasible and as dictated by the experience and skill of the operating surgeon. Mitral valve repair is reasonable for patients with primary MR and preserved LV size and systolic function (LV end-systolic dimension <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 if resting pulmonary artery pressures are elevated (>50 mm Hg at rest) (2). Mitral valve 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 comprehensive heart valve center by a reference surgeon (2). 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 (74,75). Timely surgical referral for primary MR must take into account the feasibility of repair as well as surgeon and institutional outcomes. The latter is particularly relevant when considering referral of an asymptomatic patient.

Indications for mitral valve surgery for moderate or severe secondary MR are more limited, in part due to the recognition that although valve intervention in this patient group may improve symptoms and quality of life, it has not been shown to improve survival (1). Mitral valve repair (usually with an undersized annuloplasty ring) may be considered at the time of other cardiac surgery (e.g., CABG) for patients with moderate functional MR, although its benefit is uncertain (76-78). In patients with severe functional MR, mitral valve surgery (either replacement or repair) is reasonable at the time of other cardiac surgery (e.g., CABG) and can be considered as an isolated procedure for patients with advanced New York Heart Association functional class despite guideline-directed medical therapy and cardiac resynchronization when indicated (2). The decision to replace or repair the valve can be challenging (72) and is deferred to an

FIGURE 9 Decision Tree for Determining Surgical Mitral Valve Repair Versus Replacement in Patients With Severe MR

experienced surgeon in consultation with the heart valve team; however, for severely symptomatic patients with severe ischemic MR, it is reasonable to choose chordal-sparing mitral valve replacement over downsized annuloplasty repair (2). This recommendation reflects the results of a randomized controlled trial 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 heart failure events and cardiovascular readmissions in follow-up (71). Whether

more advanced repair techniques or better patient selection might improve upon these results remains to be determined in prospective trials.

7.2.1. Feasibility of Surgical Repair

Mitral valve repair is a complex operation comprising a wide spectrum of available techniques to achieve durable success (79). The principal goals of mitral valve 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

TABLE 4 Pathoanatomically Directed Contemporary Surgical Techniques for MR**Primary Mitral Regurgitation****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 mitral valve leaflet

Secondary Mitral Regurgitation**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 mitral valve 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

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

MR = mitral regurgitation; PTFE = polytetrafluoroethylene.

feasibility are pathoanatomy and surgeon experience (Figure 9).

The surgical spectrum of primary MR with Carpentier type II motion ranges from focal prolapse in the setting of an otherwise anatomically normal mitral valve, known as fibroelastic deficiency, to a more diffuse process with excess, redundant, billowing tissue as noted in Barlow's syndrome (80). Alternatively, primary MR with

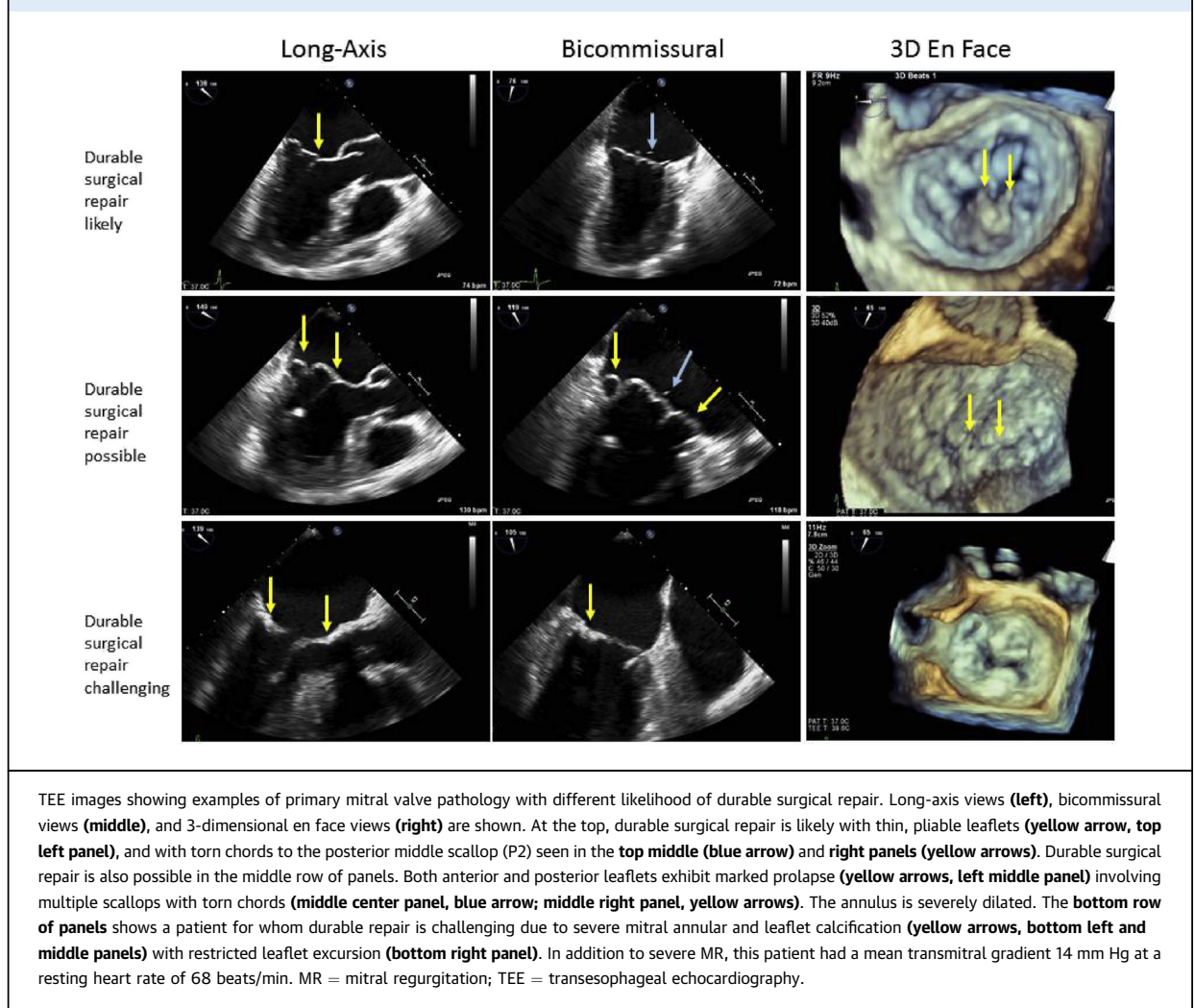
Carpentier type II motion may take an intermediate form between these 2 extremes referred to as a *forme fruste*. In primary MR with Carpentier type IIIA motion, the surgical spectrum includes focal or diffuse leaflet and subvalvular thickening and commissural fusion due to rheumatic heart disease, prior 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.

Common techniques of mitral valve repair are listed in Table 4 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 mitral valve leaflet. A suggested approach to determine the feasibility and complexity of repair is described in Table 5. The majority of experienced valve surgeons can perform successful and durable repairs for patients with echocardiographic findings of focal posterior prolapse or flail without annular or leaflet calcium. However, when additional annular, commissural, or bileaflet pathoanatomic complexities arise, in isolation or combination, more specific experience with mitral valve repair is often required. Other confounding factors impacting reparability that may necessitate advanced mitral surgical evaluation include mitral reoperations, prior mitral endocarditis, basal septal hypertrophy with echocardiographic predictors of postoperative systolic anterior motion of the anterior mitral leaflet, and congenital anomalies (27,79,80). 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 (1). Alternatively, patients

TABLE 5 Feasibility of Surgical Mitral Valve Repair

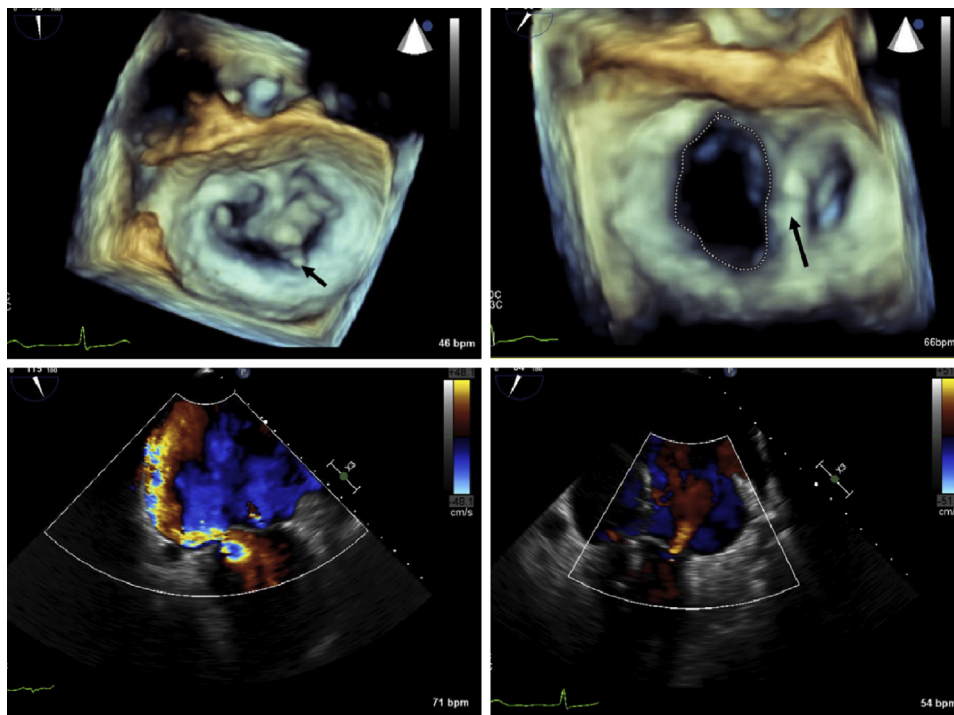
	Ideal Pathoanatomy	Challenging Pathoanatomy	Relative Pathoanatomic Contraindications
Primary lesion location	Posterior leaflet only	Anterior leaflet or bileaflet	None
Leaflet calcification	None	Mild	Moderate to severe
Annular calcification	None	Mild to moderate with minimal leaflet encroachment	Severe 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 forme fruste 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	Mitral valve reoperation with paucity of leaflet tissue; diffuse radiation valvulopathy; papillary muscle rupture with shock

MR = mitral regurgitation.

FIGURE 10 Examples of Valve Morphology That is Amenable to Surgical Repair in Patients With Primary MR

with severe anterior, bileaflet, Barlow's, or mixed disease that may require extensive and complex reparative techniques should be preferentially referred to an experienced mitral valve surgeon at a high-volume institution. The most important predictor of long-term failure is the presence of moderate or greater residual MR at the time of the index operation (81-83). 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 9 provides a more detailed guide to decision making for mitral repair or replacement based on Carpentier's classification (37). Figure 10 shows echocardiographic examples of mitral valve morphologies that are likely, possible, or challenging for successful mitral valve repair (see also Table 5).

Surgeon experience has been recognized as a primary determinant of successful repair. Registry data from 2005 to 2007 estimated a nearly 3-fold greater likelihood of successful repair when surgeon experience was over 100 cases/year compared with 5 to 10 cases/year, with a threshold for frequency of successful repair being >50 mitral surgical cases/year (repair or replacement) (84); however, data from the last 5 years have shown a doubling of the frequency of mitral valve repair over replacement, and the initial success rate for isolated mitral valve repair for primary MR is now >75% across the United States, with >10% being performed using non-sternotomy minimally invasive or robotic approaches (85). For asymptomatic Stage C1 patients, those with complex mitral pathoanatomy (1), and those who desire a minimally invasive or robotic approach, consideration should be given to referral to an experienced mitral surgeon at a comprehensive valve center.

FIGURE 11 Transcatheter Edge-to-Edge Mitral Valve Clip

(Top left) 3-dimensional en face view showing flail anterior leaflet with torn chord (**arrow**). **(Top right)** Transcatheter edge-to-edge clip creates tissue bridge between anterior and posterior leaflets (**arrow**). **(Bottom left)** Color flow image showing severe mitral regurgitation at beginning of case. **(Bottom right)** Reduction of mitral regurgitation from severe to trace after transcatheter edge-to-edge clip placement.

TTE is recommended either prior to discharge or within 3 months after mitral repair. Longitudinal TTE studies thereafter are dictated by clinical findings.

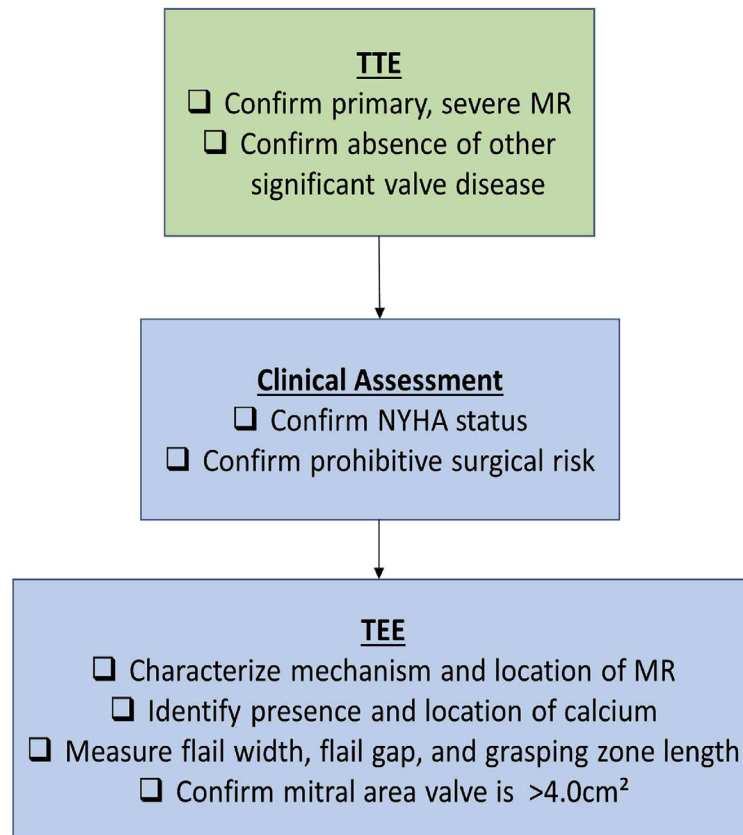
7.2.2. Determination of Risk for Surgery

Assessment of peri-operative risk includes the use of a standardized Predicted Risk of Mortality developed by the Society of Thoracic Surgeons, which is based on the outcomes of large numbers of patients who have undergone surgery (86,87). Additional factors not included in this risk score also contribute to procedural and post-procedural risk, including liver disease, pulmonary hypertension, porcelain aorta, and post-radiation scarring, as well as reduced patient ability to recover from the trauma of surgery due to frailty. Measures of frailty such as the 5-meter or 6-minute walk test and hand grip strength have become part of the heart team evaluation of elderly patients for surgical or transcatheter therapy. The 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (1) includes a risk assessment tool that incorporates these considerations.

7.3. Transcatheter Treatment of MR

The desirability of transcatheter options for the treatment of MR is driven by the increasing prevalence of this valve lesion among an aging population with significant comorbidities that render many patients poor candidates for surgical intervention. Developing lower-risk procedures that effectively reduce the severity of MR and improve clinical outcomes is the goal of transcatheter interventions.

The complex, functional anatomy of the mitral apparatus has challenged the development of effective transcatheter strategies for the management of MR. Patients vary widely in the individual contributions of each component (leaflets, annulus, chordae, papillary muscles, and subjacent myocardium) to the emergence and progression of MR. Transcatheter repair techniques can be targeted to the leaflets, annulus, or chordae, either solely or in combination. At present, edge-to-edge mitral leaflet coaptation using a clip to approximate opposing segments of the anterior and posterior leaflets is the only system approved by the Food and Drug Administration for

FIGURE 12 Algorithm for Determining Eligibility for Transcatheter Edge-to-Edge Mitral Valve Clip

Note: Transcatheter edge-to-edge clip repair not approved in US for patients with functional MR

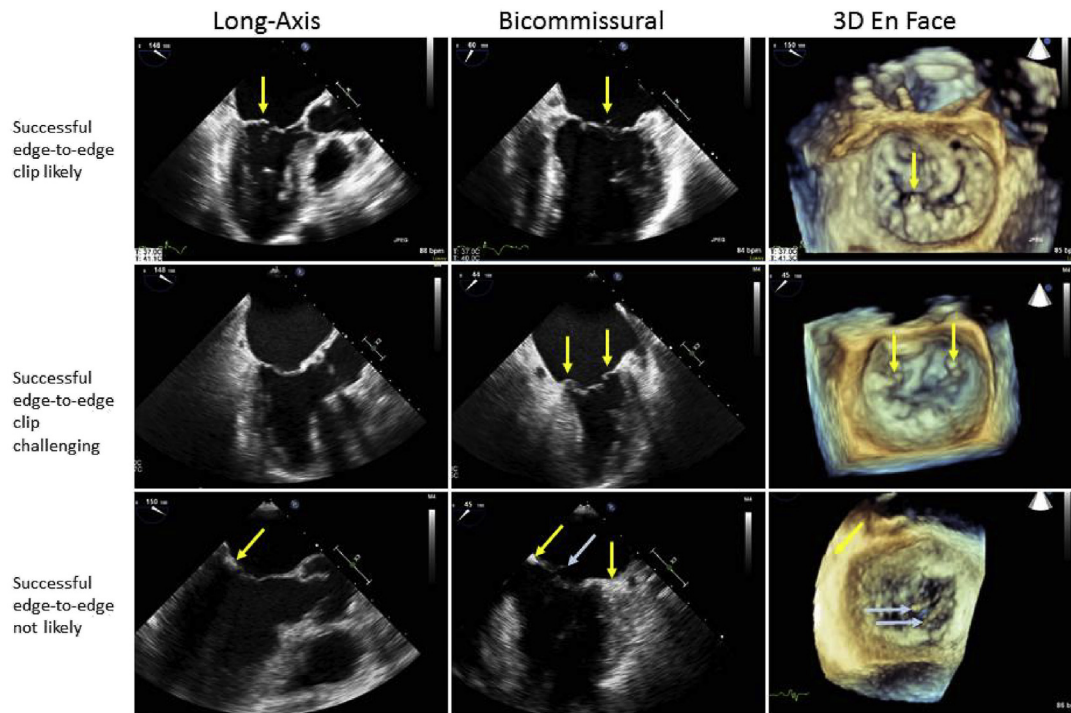
Abbreviations: MR = mitral regurgitation; NYHA = New York Heart Association; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography

TABLE 6 Feasibility of Transcatheter Edge-to-Edge Clip Repair

	Ideal Echo Features	Challenging Echo Features	Relative Echo Contraindications
Location of pathology	■ Segment 2	■ Segments 1 or 3	■ Body of leaflet (i.e., perforation or cleft/deep fold)
Calcification	■ None	■ Mild, outside grasping zone ■ Extensive annular calcification	■ Severe calcification at site of grasping zone
Mitral valve area/gradient	■ >4 cm ² ■ ≤4 mm Hg	■ >3.5 and <4 cm ² with small BSA or very mobile leaflets ■ ≥4 mm Hg	■ <4.0 cm ² ■ >5 mm Hg Especially if severe MAC
Grasping zone Length	■ >10 mm	■ 7-10 mm	■ <7 mm
Functional MR	■ Normal thickness and mobility ■ Coaptation depth <11 mm	■ Carpentier IIIB (restricted) ■ Coaptation depth >11 mm	■ Carpentier IIIA (rheumatic thickening and restriction)
Degenerative MR	■ Flail width <15 mm ■ Flail gap <10 mm ■ Leaflet separation <2 mm	■ Flail width <15 mm with large valve area and option for >1 MitraClip ■ Flail gap >10 mm with possibility of adjunctive measures	■ Barlow's disease with significant regurgitation in segments 1-3
Other pathology		■ Annuloplasty ring with adequate mitral valve area and leaflet length ■ HOCM with systolic anterior motion ■ Extreme disease (markedly dilated annulus or EROA ≥70.8 mm ²)	

Note: Transcatheter edge-to-edge clip repair is approved for use in the United States only for patients with primary MR, severe symptoms, and high or prohibitive operative risk. Adapted from Hahn (96).

BSA = body surface area; EROA = effective regurgitant orifice area; HOCM = hypertrophic obstructive cardiomyopathy; MAC = mitral annular calcification.

FIGURE 13 Transcatheter Edge-to-Edge Mitral Valve 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 cm², 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 mitral valve area was 2.8 cm², which is below the threshold value (4.0 cm²) and would likely result in mitral stenosis. TEE = transesophageal echocardiography.

transcatheter repair in the United States (88,89). Furthermore, its use is restricted to the management of symptomatic (New York Heart Association functional class III or IV) patients with severe primary MR, reasonable life expectancy, and prohibitive surgical risk due to comorbidities (1,89). The safety and efficacy of this technology for the treatment of patients with symptomatic, severe functional MR are being studied in a randomized controlled trial (COAPT [Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy] trial [NCT01626079]). Edge-to-edge leaflet repair for patients with functional MR is used more frequently in centers outside of the United States (90). Several other transcatheter repair systems are in development (e.g., annular devices) but are not currently available for clinical use (91). Transcatheter repair and replacement devices/techniques are undergoing rapid change and intense investigation (86,91,92).

7.3.1. 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.

(93) and results in the creation of a double orifice mitral valve and reduction in the severity of MR (Figure 11). Successful deployment can result in improved hemodynamics and patient outcomes (89,90,94,95). Appropriate patient selection is critically dependent on rigorous clinical and echocardiographic assessment (96) (Figure 12). Intraoperative and postoperative management algorithms facilitate best practices. Operator and institutional criteria for the performance of transcatheter mitral valve repair have been published in a joint, multisocietal expert consensus document (4). This procedure is offered at more than 200 sites within the United States (97).

7.3.1.1. Feasibility of Edge-to-Edge Leaflet Coaptation

Table 6 and Figure 13 include the key echocardiographic parameters used to assess suitability for transcatheter edge-to-edge repair (96). The procedure is usually performed by 1 or 2 operators in a cardiac catheterization laboratory or hybrid suite. A multidisciplinary team, which includes at a minimum a clinical heart valve specialist, multimodality cardiac imaging expert,

interventional cardiologist, and cardiac surgeon, is required for patient evaluation, selection, and periprocedural management. Other transcatheter mitral valve repair systems for primary MR may become available for clinical use in future years and will dictate new requirements for patient assessment and selection.

8. 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 (1) and its 2017 focused update (2), this expert consensus decision pathway 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. Multidisciplinary heart teams composed of experienced surgeons, interventionalists, expert imagers, and others are vital to the provision of advanced care to challenging patients at comprehensive 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.

8.1. Key Points

- Once MR is recognized, its etiology, mechanism, and severity should be defined using quantitative echocardiography and other 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.

- A heart valve team consensus treatment recommendation should be discussed with the patient and family to enable shared decision making.
- Ongoing communication between members of the heart team at the valve treatment center and the referring provider is strongly endorsed, especially at critical junctures in the course of the patient's 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 mitral valve surgeon at a comprehensive valve center should be considered for asymptomatic stage C1 patients, patients in whom complex repair is required, and patients who wish to pursue a minimally invasive or robotic approach.
- Current use of transcatheter edge-to-edge repair in the United States is limited to symptomatic patients with primary, severe MR who are poor operative candidates. Other transcatheter mitral valve repair and replacement systems are under active investigation.
- Evidence-based medical and device therapy should be optimized in patients with secondary MR before decision making for surgical intervention.
- Long-term follow-up of patients after surgical or transcatheter intervention is essential for assessment of durability, functional outcomes, and survival.

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KEY WORDS Expert Consensus Decision Pathway, echocardiography, mitral regurgitation, mitral valve, transcatheter, valve repair, valve surgery

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

To avoid actual, potential, or perceived conflicts of interest that may arise as a result of industry relationships or personal interests among the writing committee, all members of the writing committee, as well as peer reviewers of the document, are asked to disclose all current healthcare-related relationships, including those existing 12 months before initiation of the writing effort. The ACC Task Force on Expert Consensus Decision Pathways reviews these disclosures to determine what companies make products (on market or in development) that pertain to the document under development. Based on this information, a writing committee is formed to include a majority of

members with no *relevant* relationships with industry (RWI), led by a chair with no *relevant* RWI. RWI is reviewed on all conference calls and updated as changes occur. Author RWI pertinent to this document is disclosed in the table below and peer reviewer RWI is disclosed in [Appendix 2](#). Additionally, to ensure complete transparency, authors' *comprehensive disclosure information*—including RWI not pertinent to this document—is available online (see [Online Appendix 1](#)). Disclosure information for the ACC Task Force on Expert Consensus Decision Pathways is also available [online](#), as well as the [ACC disclosure policy for document development](#).

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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Continued on the next page

APPENDIX 1. CONTINUED

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This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of $\geq 5\%$ of the voting stock or share of the business entity, or ownership of $\geq \$5,000$ of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Please refer to <http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy> for definitions of disclosure categories or additional information about the ACC Disclosure Policy for Writing Committees.

*Significant relationship.

†No financial benefit.

ACC = American College of Cardiology; DSMB = data safety monitoring board.

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

This table represents the individuals, organizations, and groups that peer reviewed this document. A list of corresponding comprehensive healthcare-related disclosures for each reviewer is available as [Online Appendix 2](#).

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AATS = American Association for Thoracic Surgery; ACC = American College of Cardiology; AHA = American Heart Association; ASE = American Society of Echocardiography; DSMB = data safety monitoring board; NHLBI = National Heart, Lung, and Blood Institute; NIH = National Institutes of Health; SCMR = Society for Cardiovascular Magnetic Resonance; STS = Society of Thoracic Surgeons; UCLA = University of California = Los Angeles.

APPENDIX 3. ABBREVIATIONS

ACC = American College of Cardiology

AF = atrial fibrillation

AHA = American Heart Association

CFD = color flow doppler

CMR = cardiac magnetic resonance

ECDP = Expert Consensus Decision Pathways

EROA = effective regurgitant orifice area

LA = left atrial

LV = left ventricular

LVEF = left ventricular ejection fraction

MR = mitral regurgitation

PISA = proximal isovelocity surface area

RF = regurgitant fraction

RVol = regurgitant volume

TEE = transesophageal echocardiography

TTE = transthoracic echocardiography
