Guideline for the Management of Patients With Valvular Heart Disease

Mitral Regurgitation

Derived From:

Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, O'Gara PT, Rigolin VH, Sundt TM, Thompson A, Toly C. 2020 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;143:e1-e156. doi: 10.1161/CIR.0000000000000923.

Copublished in *Journal of the American College of Cardiology* 2021:e1-e173
doi: 10.1016/j.jacc.2020.11.018

American College of Cardiology
www.acc.org

The American Heart Association
professional.heart.org

Full-text guidelines available in both *Circulation and JACC.*

Key Points

- **Disease stages in patients with valvular heart disease should be classified (Stages A, B, C, and D) on the basis of symptoms, valve anatomy, the severity of valve dysfunction, and the response of the ventricle and pulmonary circulation.**
- **In the evaluation of a patient with valvular heart disease, history and physical examination findings should be correlated with the results of noninvasive testing (i.e., ECG, chest x-ray, transthoracic echocardiogram). If there is discordance between the physical examination and initial noninvasive testing, consider further noninvasive (computed tomography, cardiac magnetic resonance imaging, stress testing) or invasive (transesophageal echocardiography, cardiac catheterization) testing to determine optimal treatment strategy.**
- **All patients with severe valvular heart disease being considered for valve intervention should be evaluated by a multidisciplinary team, with either referral to or consultation with a Primary or Comprehensive Valve Center.**
- **A mitral transcatheter edge-to-edge repair is of benefit to patients with severely symptomatic primary mitral regurgitation who are at high or prohibitive risk for surgery, as well as to a select subset of patients with secondary mitral regurgitation who remain severely symptomatic despite guideline-directed management and therapy for heart failure.**

Treatment

Note: the numbering of tables and figures in this pocket guide differs from that of the Clinical Practice Guideline.

Table 1. Evaluation of Patients With Known or Suspected VHD

Reason	Test	Indication
Initial evaluation: All patients with known or suspected valve disease	TTE*	Establishes chamber size and function, valve morphology and severity, and effect on pulmonary and systemic circulation
	History and physical	Establishes symptom severity, comorbidities, valve disease presence and severity, and presence of HF
	ECG	Establishes rhythm, LV function, and presence or absence of hypertrophy
Further diagnostic testing: Information required for equivocal symptom status, discrepancy between examination and echocardiogram, further definition of valve disease, or assessing response of the ventricles and pulmonary circulation to load and to exercise	Chest x-ray	Important for the symptomatic patient; establishes heart size and presence or absence of pulmonary vascular congestion, intrinsic lung disease, and calcification of aorta and pericardium
	TEE	Provides high-quality assessment of mitral and prosthetic valve, including definition of intracardiac masses and possible associated abnormalities (e.g., intracardiac abscess, LA thrombus)
	CMR	Provides assessment of LV volumes and function, valve severity, and aortic disease
	PET CT	Aids in determination of active infection or inflammation
	Stress testing	Gives an objective measure of exercise capacity
	Catheterization	Provides measurement of intracardiac and pulmonary pressures, valve severity, and hemodynamic response to exercise and drugs

Table 1. Evaluation of Patients With Known or Suspected VHD *(cont'd)*

Reason	Test	Indication
Further risk stratification: Information on future risk of the valve disease, which is important for determination of timing of intervention	Biomarkers	Provide indirect assessment of filling pressures and myocardial damage
	TTE strain	Helps assess intrinsic myocardial performance
	CMR	Assesses fibrosis by gadolinium enhancement
	Stress testing	Provides prognostic markers
	Procedural risk	Quantified by STS (Predicted Risk of Mortality) and TAVI scores
	Frailty score	Provides assessment of risk of procedure and chance of recovery of quality of life
Preprocedural testing: Testing required before valve intervention	Dental examination	Rules out potential infection sources
	CT coronary angiogram or invasive coronary angiogram	Gives an assessment of coronary anatomy
	CT: peripheral	Assesses femoral access for TAVI and other transcatheter procedures
	CT: cardiac	Assesses suitability for TAVI and other transcatheter procedures

* TTE is the standard initial diagnostic test in the initial evaluation of patients with known or suspected VHD.

Table 2. Stages of Progression of VHD

Stage	Definition	Description
A	At risk	Patients with risk factors for development of VHD
B	Progressive	Patients with progressive VHD (mild-to-moderate severity and asymptomatic)
C	Asymptomatic severe	Asymptomatic patients who meet the criteria for severe VHD: C1: Asymptomatic patients with severe VHD in whom the left or right ventricle remains compensated C2: Asymptomatic patients with severe VHD, with decompensation of the left or right ventricle
D	Symptomatic severe	Patients who have developed symptoms as a result of VHD

Table 3. Frequency of Echocardiograms in Asymptomatic Patients With VHD and Normal Left Ventricular (LV) Function

	Valve Lesion			
Stage	**AS***	**AR**	**MS**	**MR**
Progressive (stage B)	Every 3–5 y (mild severity; V_{max} 2.0–2.9 m/s)	Every 3–5 y (mild severity)	Every 3–5 y (mitral valve area [MVA] >1.5 cm^2)	Every 3–5 y (mild severity)
	Every 1–2 y (moderate severity; V_{max} 3.0–3.9 m/s)	Every 1–2 y (moderate severity)		Every 1–2 y (moderate severity)
Severe asymptomatic (stage C1)	Every 6–12 mo (V_{max} ≥4 m/s)	Every 6–12 mo	Every 1–2 y (MVA 1.0–1.5 cm^2)	Every 6–12 mo
		Dilating LV: more frequently	Every year (MVA <1.0 cm^2)	Dilating LV: more frequently

Patients with mixed valve disease may require serial evaluations at intervals earlier than recommended for single-valve lesions. These intervals apply to most patients with each valve lesion and do not take into consideration the etiology of the valve disease.

* With normal stroke volume.

Table 4. Risk Assessment for Surgical Valve Procedures

Criteria	Low-Risk SAVR (Must Meet ALL Criteria in This Column)	Low-Risk Surgical Mitral Valve Repair for Primary MR (Must Meet ALL Criteria in This Column)	High Surgical Risk (Any 1 Criterion in This Column)	Prohibitive Surgical Risk (Any 1 Criterion in This Column)
STS-predicted risk of death*	<3% AND	<1% AND	>8% OR	Predicted risk of death or major morbidity (all-cause) >50% at 1 y OR
Frailty†	None AND	None AND	≥2 Indices (moderate to severe) OR	≥2 Indices (moderate to severe) OR
Cardiac or other major organ system compromise not to be improved postoperatively‡	None AND	None AND	1 to 2 Organ systems OR	≥3 Organ systems OR
Procedure-specific impediment§	None	None	Possible procedure-specific impediment	Severe procedure-specific impediment

* Use of the STS Predicted Risk of Mortality (http://riskcalc.sts.org/stswebriskcalc/#/) to predict risk in a given institution with reasonable reliability is appropriate only if institutional outcomes are within 1 standard deviation of the STS average observed/expected mortality ratio for the procedure in question. The EUROSCORE II risk calculator may also be considered for use and is available at http://www.euroscore.org/calc.html.

† Seven frailty indices: Katz Activities of Daily Living (independence in feeding, bathing, dressing, transferring, toileting, and urinary continence) plus independence in ambulation (no walking aid or assistance required, or completion of a 5-m walk in <6 s). Other scoring systems can be applied to calculate no, mild, or moderate to severe frailty.

‡ Examples of major organ system compromise include cardiac dysfunction (severe LV systolic or diastolic dysfunction or RV dysfunction, fixed pulmonary hypertension); kidney dysfunction (chronic kidney disease, stage 3 or worse); pulmonary dysfunction (FEV1 <50% or D_{LCO_2} <50% of predicted); central nervous system dysfunction (dementia, Alzheimer's disease, Parkinson's disease, cerebrovascular accident with persistent physical limitation); gastrointestinal dysfunction (Crohn's disease, ulcerative colitis, nutritional impairment, or serum albumin <3.0); cancer (active malignancy); and liver dysfunction (any history of cirrhosis, variceal bleeding, or elevated INR in the absence of VKA therapy).

§ Examples of procedure-specific impediments include presence of tracheostomy, heavily calcified (porcelain) ascending aorta, chest malformation, arterial coronary graft adherent to posterior chest wall, and radiation damage.

Table 5. Median Operative Mortality Rates for Specific Surgical Procedures (STS Adult Cardiac Surgery Database, 2019)

Procedure	Mortality Rate (%)
AVR	2.2
AVR and CABG	4
AVR and Mitral Valve replacement	9
Mitral Valve replacement	5
Mitral Valve replacement and CABG	9
Mitral Valve repair	1
Mitral Valve repair and CABG	5

2.6. The Multidisciplinary Heart Valve Team and Heart Valve Centers

COR	LOE	Recommendations
1	C-EO	Patients with severe VHD should be evaluated by a Multidisciplinary Heart Valve Team (MDT) when intervention is considered.
2a	C-LD	Consultation with or referral to a Primary or Comprehensive Heart Valve Center is reasonable when treatment options are being discussed for 1) asymptomatic patients with severe VHD, 2) patients who may benefit from valve repair versus valve replacement, or 3) patients with multiple comorbidities for whom valve intervention is considered.

Table 6. Stages of Chronic *Primary* MR

Stage	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
A	At risk of MR	• Mild MV prolapse with normal coaptation • Mild valve thickening and leaflet restriction	• No MR jet or small central jet area <20% LA on Doppler • Small vena contracta <0.3 cm	None	None
B	Progressive MR	• Severe MV prolapse with normal coaptation • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE	• Central jet MR 20%–40% LA or late systolic eccentric jet MR • Vena contracta <0.7 cm • RVol <60 mL • RF <50% • ERO <0.40 cm^2 • Angiographic grade 1+ to 2+	• Mild LA enlargement • No LV enlargement • Normal pulmonary pressure	None
C	Asymptomatic severe MR	• Severe MV prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • RVol ≥60 mL • RF ≥50% • ERO ≥0.40 cm^2 • Angiographic grade 3+ to 4+	• Moderate or severe LA enlargement • LV enlargement • PHTN may be present at rest or with exercise • **C1:** LVEF >60% and LVESD <40 mm • **C2:** LVEF ≤60% and LVESD ≥40 mm	None
D	Symptomatic severe MR	• Severe MV prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • RVol ≥60 mL • RF ≥50% • ERO ≥0.40 cm^2 • Angiographic grade 3+ to 4+	• Moderate or severe LA enlargement • LV enlargement • PHTN present	• Decreased exercise tolerance • Exertional dyspnea

* Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence.

7.2.2.1. Diagnostic Testing: Initial Diagnosis

COR	LOE	Recommendations
1	B-NR	In patients with known or suspected primary MR, TTE is indicated for baseline evaluation of LV size and function, RV function, LA size, pulmonary artery pressure, and the mechanism and severity of primary MR (Stages A to D).
1	C-EO	In patients with primary MR, when TTE provides insufficient or discordant information, TEE is indicated for evaluation of the severity of MR, mechanism of MR, and status of LV function (Stages B to D).
1	B-NR	In patients with primary MR, CMR is indicated to assess LV and RV volumes and function and may help with assessing MR severity when there is a discrepancy between the findings on clinical assessment and echocardiography.
1	B-NR	In patients with severe primary MR undergoing mitral intervention, intraoperative TEE is indicated to establish the anatomic basis for primary MR (Stages C and D) and to guide repair.

7.2.2.2. Diagnostic Testing: Changing Signs or Symptoms

COR	LOE	Recommendation
1	B-NR	In patients with primary MR (Stages B to D) and new-onset or changing symptoms, TTE is indicated to evaluate the mitral valve apparatus and LV function.

7.2.2.3. Diagnostic Testing: Routine Follow-Up

COR	LOE	Recommendations
1	B-NR	For asymptomatic patients with severe primary MR (Stages B and C1), TTE is indicated every 6 to 12 months for surveillance of LV function (estimated by LVEF, LVEDD, and LVESD) and assessment of pulmonary artery pressure.
2b	B-NR	In asymptomatic patients with severe primary MR (Stages B and C1), use of serum biomarkers and novel measurements of LV function, such as global longitudinal strain, may be considered as an adjunct to guide timing of intervention.

7.2.2.5. Diagnostic Testing: Exercise Testing

COR	LOE	Recommendation
2a	B-NR	In patients with primary MR (Stages B and C) and symptoms that might be attributable to MR, hemodynamic exercise testing using Doppler echocardiography or cardiac catheterization or cardiopulmonary exercise testing is reasonable.

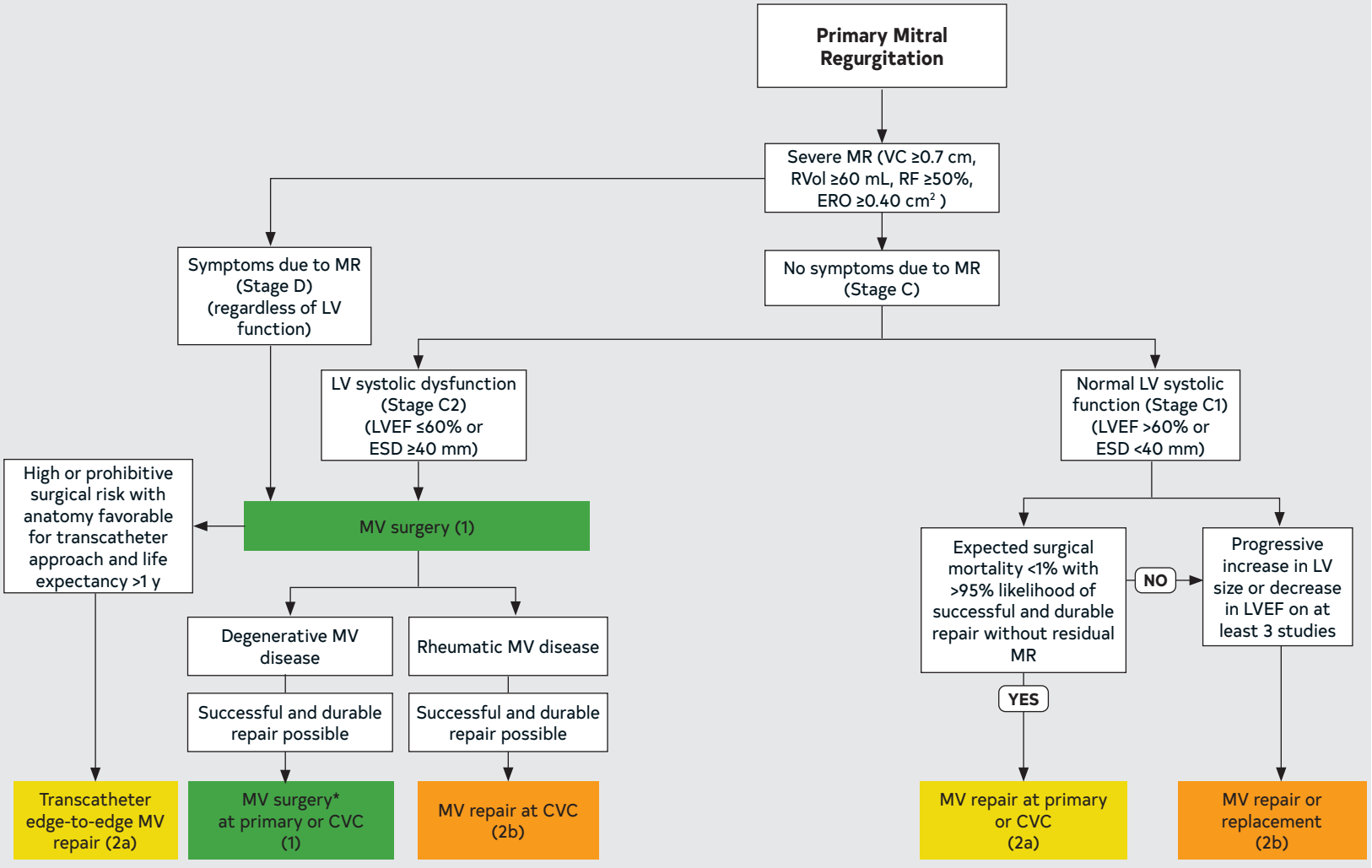
7.2.3. Medical Therapy

COR	LOE	Recommendations
2a	B-NR	In symptomatic or asymptomatic patients with severe primary MR and LV systolic dysfunction (Stages C2 and D) in whom surgery is not possible or must be delayed, GDMT for systolic dysfunction is reasonable.
3: No Benefit	B-NR	In asymptomatic patients with primary MR and normal LV systolic function (Stages B and C1), vasodilator therapy is not indicated if the patient is normotensive.

7.2.4. Intervention

COR	LOE	Recommendations
1	B-NR	In symptomatic patients with severe primary MR (Stage D), mitral valve intervention is recommended irrespective of LV systolic function.
1	B-NR	In asymptomatic patients with severe primary MR and LV systolic dysfunction (LVEF ≤60%, LVESD ≥40 mm) (Stage C2), mitral valve surgery is recommended.
1	B-NR	In patients with severe primary MR for whom surgery is indicated, mitral valve repair is recommended in preference to mitral valve replacement when the anatomic cause of MR is degenerative disease, if a successful and durable repair is possible.
2a	B-NR	In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF ≥60% and LVESD ≤40 mm) (Stage C1), mitral valve repair is reasonable when the likelihood of a successful and durable repair without residual MR is >95% with an expected mortality rate of <1%, when it can be performed at a Primary or Comprehensive Valve Center.
2b	C-LD	In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF >60% and LVESD <40 mm) (Stage C1) but with a progressive increase in LV size or decrease in EF on ≥3 serial imaging studies, mitral valve surgery may be considered irrespective of the probability of a successful and durable repair.
2a	B-NR	In severely symptomatic patients (NYHA class III or IV) with primary severe MR and high or prohibitive surgical risk, transcatheter edge-to-edge repair (TEER) is reasonable if mitral valve anatomy is favorable for the repair procedure and patient life expectancy is at least 1 year.
2b	B-NR	In symptomatic patients with severe primary MR attributable to rheumatic valve disease, mitral valve repair may be considered at a Comprehensive Valve Center by an experienced team when surgical treatment is indicated, if a durable and successful repair is likely.
3: Harm	B-NR	In patients with severe primary MR where leaflet pathology is limited to less than one half the posterior leaflet, mitral valve replacement should not be performed unless mitral valve repair has been attempted at a Primary or Comprehensive Valve Center and was unsuccessful.

Figure 1. Primary MR



* See Prosthetic Valve section (11.1.2) for choice of mitral valve replacement if mitral valve repair is not possible.

Colors correspond to the Class of Recommendation on page 20-21.

Table 7. Stages of *Secondary* MR

Stage	Definition	Valve Anatomy	Valve Hemodynamics*	Associated Cardiac Findings	Symptoms
A	At risk of MR	• Normal valve leaflets, chords, and annulus in a patient with coronary disease or cardiomyopathy	• No MR jet or small central jet area <20% LA on Doppler • Small vena contracta <0.30 cm	• Normal or mildly dilated LV size with fixed (infarction) or inducible (ischemia) regional wall motion abnormalities • Primary myocardial disease with LV dilation and systolic dysfunction	• Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
B	Progressive MR	• Regional wall motion abnormalities with mild tethering of mitral leaflet • Annular dilation with mild loss of central coaptation of the mitral leaflets	• ERO <0.40 cm^2 † • Regurgitant volume <60 mL • Regurgitant fraction <50%	• Regional wall motion abnormalities with reduced LV systolic function • LV dilation and systolic dysfunction due to primary myocardial disease	• Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
C	Asymptomatic severe MR	• Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet • Annular dilation with severe loss of central coaptation of the mitral leaflets	• ERO ≥0.40 cm^2 † • Regurgitant volume ≥60 mL‡ • Regurgitant fraction ≥50%	• Regional wall motion abnormalities with reduced LV systolic function • LV dilation and systolic dysfunction due to primary myocardial disease	• Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
D	Symptomatic severe MR	• Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet • Annular dilation with severe loss of central coaptation of the mitral leaflets	• ERO ≥0.40 cm^2 † • Regurgitant volume ≥60 mL‡ • Regurgitant fraction ≥50%	• Regional wall motion abnormalities with reduced LV systolic function • LV dilation and systolic dysfunction due to primary myocardial disease	• HF symptoms due to MR persist even after revascularization and optimization of medical therapy • Decreased exercise tolerance • Exertional dyspnea

* Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence.

† The measurement of the proximal isovelocity surface area by 2D TTE in patients with secondary MR underestimates the true ERO because of the crescentic shape of the proximal convergence.

‡ May be lower in low-flow states.

7.3.2. Diagnosis of Chronic Secondary MR

COR	LOE	Recommendations
1	B-NR	In patients with chronic secondary MR (Stages B to D), TTE is useful to establish the etiology and to assess the extent of regional and global LV remodeling and systolic dysfunction, severity of MR, and magnitude of pulmonary hypertension.
1	C-EO	In patients with chronic secondary MR (Stages B to D), noninvasive imaging (stress nuclear/PET, CMR, or stress echocardiography), coronary CT angiography, or coronary arteriography is useful to establish etiology of MR and to assess myocardial viability.
1	B-NR	In patients with chronic secondary MR with severe symptoms (Stage D) that are unresponsive to GDMT who are being considered for transcatheter mitral valve interventions, TEE is indicated to determine suitability for the procedure.
1	C-EO	In patients with chronic secondary MR undergoing transcatheter mitral valve intervention, intraprocedural guidance with TEE is recommended.

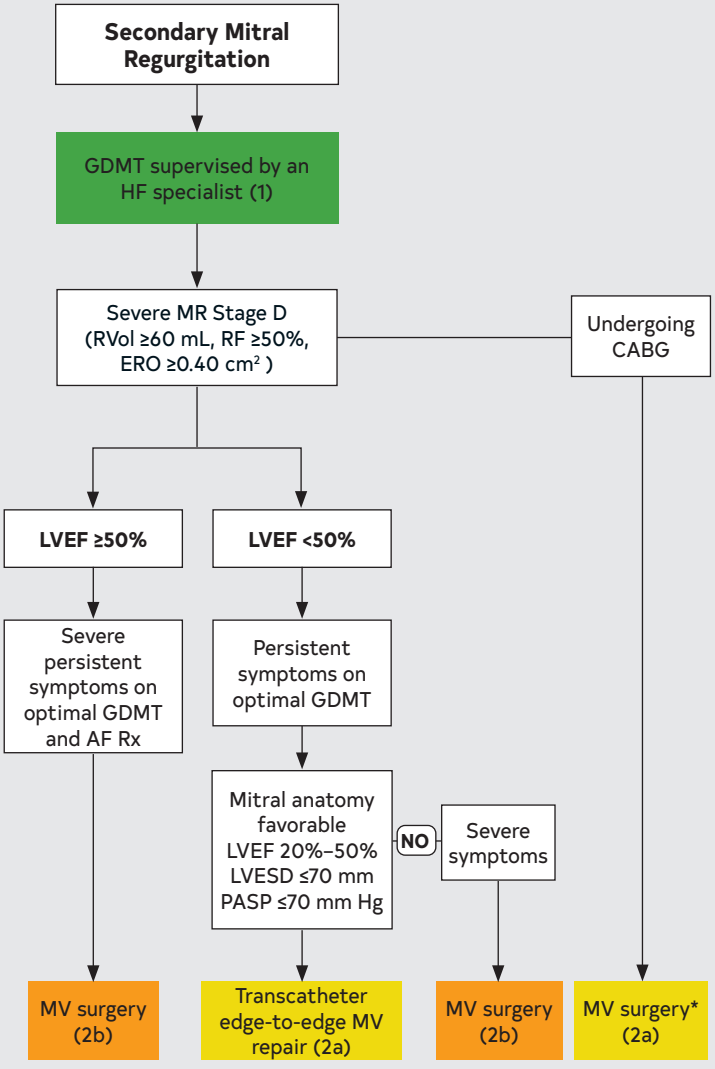
7.3.3. Medical Therapy for Secondary MR

COR	LOE	Recommendations
1	A	Patients with chronic severe secondary MR (Stages C and D) and HF with reduced LVEF should receive standard GDMT for HF, including ACE inhibitors, ARBs, beta blockers, aldosterone antagonists, and/or sacubitril/valsartan, and biventricular pacing as indicated.
1	C-EO	In patients with chronic severe secondary MR and HF with reduced LVEF, a cardiologist expert in the management of patients with HF and LV systolic dysfunction should be the primary MDT member responsible for implementing and monitoring optimal GDMT.

7.3.4. Intervention for Secondary MR

COR	LOE	Recommendations
2a	B-R	In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) who have persistent symptoms (NYHA class II, III, or IV) while on optimal GDMT for HF (Stage D), transcatheter edge-to-edge mitral valve (TEER) repair is reasonable in patients with appropriate anatomy as defined on TEE and with LVEF between 20% and 50%, LVESD ≤70 mm, and pulmonary artery systolic pressure ≤70 mm Hg.
2a	B-NR	In patients with severe secondary MR (Stages C and D), mitral valve surgery is reasonable when CABG is undertaken for the treatment of myocardial ischemia.
2b	B-NR	In patients with chronic severe secondary MR from atrial annular dilation with preserved LV systolic function (LVEF ≥50%) who have severe persistent symptoms (NYHA class III or IV) despite therapy for HF and therapy for associated AF or other comorbidities (Stage D), mitral valve surgery may be considered.
2b	B-NR	In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) who have persistent severe symptoms (NYHA class III or IV) while on optimal GDMT for HF (Stage D), mitral valve surgery may be considered.
2b	B-R	In patients with CAD and chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) (Stage D) who are undergoing mitral valve surgery because of severe symptoms (NYHA class III or IV) that persist despite GDMT for HF, chordal-sparing mitral valve replacement may be reasonable to choose over downsized annuloplasty repair.

Figure 2. Secondary MR



* Chordal sparing mitral valve replacement may be reasonable to choose over downsided annuloplasty repair.

Colors correspond to the Class of Recommendation on page 20-21.

Table 8. AS/MR Mixed Valve Disease

Severe AS	Severe MR	Surgical Risk	Procedure
SAVR candidate	• Primary MR • Repairable valve	Low intermediate	• SAVR • Surgical MV repair
SAVR candidate	• Primary MR • Valve not repairable	Low intermediate	• SAVR • Surgical mitral valve replacement
TAVI candidate	• Primary • Repairable valve	High prohibitive	• TAVI • Mitral TEER*
SAVR candidate TAVI candidate	Secondary MR	Low intermediate	• SAVR • Surgical mitral valve repair/mitral valve replacement ***or*** • TAVI • Mitral TEER*
TAVI candidate	Secondary MR	High prohibitive	• TAVI • Mitral TEER*

* Consider TEER as a later staged procedure if symptoms and severe MR persist after treatment of the AS.

AMERICAN COLLEGE of CARDIOLOGY

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:

- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS 2a (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:

- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS 2b (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:

- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well-established

CLASS 3: No Benefit (MODERATE) — **Benefit = Risk**

(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:

- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS 3: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:

- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A

- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R — **(Randomized)**

- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR — **(Nonrandomized)**

- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD — **(Limited Data)**

- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO — **(Expert Opinion)**

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; RCT, randomized controlled trial.

Abbreviations

2D, 2-dimensional; **ACE**, angiotensin-converting enzyme; **AF**, atrial fibrillation; **AR**, aortic regurgitation; **AS**, aortic stenosis; **AVR**, aortic valve replacement; **BAV**, bicuspid aortic valve; **CABG**, coronary artery bypass graft surgery; **CAD**, coronary artery disease; **CMR**, cardiac magnetic resonance; **COR**, Class of Recommendation; **CT**, computed tomography; **ECG**, electrocardiogram; **GDMT**, guideline-directed management and therapy; **HF**, heart failure; **IE**, infective endocarditis; **INR**, international normalized ratio; **LA**, left atrium (left atrial); **LOE**, Level of Evidence; **LV**, left ventricle (left ventricular); **LVEDD**, left ventricular end-diastolic dimension; **LVEF**, left ventricular ejection fraction; **LVESD**, left ventricular end-systolic dimension; **MDT**, multidisciplinary team; **MR**, mitral regurgitation; **MS**, mitral stenosis; **NYHA**, New York Heart Association; **RCT**, randomized controlled trial; **RV**, right ventricle (right ventricular); **SAVR**, surgical aortic valve replacement; **TAVI**, transcatheter aortic valve implantation; **TEE**, transesophageal echocardiography (echocardiogram); **TEER**, transcatheter edge to edge repair; **TTE**, transthoracic echocardiography (echocardiogram); **VHD**, valvular heart disease; **VKA**, vitamin K antagonist

Source

Otto CM et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;143:e1-e156. doi: 10.1161/CIR.0000000000000923

Copublished in *Journal of the American College of Cardiology* 2021:e1-e173
doi: 10.1016/j.jacc.2020.11.018

Disclaimer

This pocket guide attempts to define principles of practice that should produce high-quality patient care. It is applicable to specialists, primary care, and providers at all levels. This pocket guide should not be considered exclusive of other methods of care reasonably directed at obtaining the same results. The ultimate judgment concerning the propriety of any course of conduct must be made by the clinician after consideration of each individual patient situation. Neither IGC, the medical associations, nor the authors endorse any product or service associated with the distributor of this clinical reference tool.

GuidelineCentral.com®
TEL: 407.878.7606 • FAX: 407.878.7611
Order additional copies at GuidelineCentral.com

AHAVHD12203a_MR

MitraClip™

Transcatheter Mitral Valve Repair

IMPORTANT SAFETY INFORMATION

MITRACLIP CLIP DELIVERY SYSTEMS

℞ ONLY

INDICATION FOR USE

- The MitraClip™ G4 System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus [degenerative MR] in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.
- The MitraClip™ G4 System, when used with maximally tolerated guideline-directed medical therapy (GDMT), is indicated for the treatment of symptomatic, moderate-to-severe or severe secondary (or functional) mitral regurgitation (MR; MR ≥ Grade III per American Society of Echocardiography criteria) in patients with a left ventricular ejection fraction (LVEF) ≥ 20% and ≤ 50%, and a left ventricular end systolic dimension (LVESD) ≤ 70 mm whose symptoms and MR severity persist despite maximally tolerated GDMT as determined by a multidisciplinary heart team experienced in the evaluation and treatment of heart failure and mitral valve disease.

CONTRAINDICATIONS

The MitraClip™ G4 System is contraindicated in patients with the following conditions:

- Patients who cannot tolerate, including allergy or hypersensitivity to, procedural anticoagulation or post procedural anti-platelet regimen
- Patients with known hypersensitivity to clip components (nickel / titanium, cobalt, chromium, polyester), or with contrast sensitivity
- Active endocarditis of the mitral valve
- Rheumatic mitral valve disease
- Evidence of intracardiac, inferior vena cava (IVC) or femoral venous thrombus

WARNINGS

- **DO NOT use MitraClip™ outside of the labeled indication.**
- The MitraClip™ G4 Implant should be implanted with sterile techniques using fluoroscopy and echocardiography (e.g. transesophageal [TEE] and transthoracic [TTE]) in a facility with on-site cardiac surgery and immediate access to a cardiac operating room.
- Read all instructions carefully. Use universal precautions for biohazards and sharps while handling the MitraClip™ G4 System to avoid user injury. Failure to follow these instructions, warnings and precautions may lead to device damage, user injury or patient injury including:
  - MitraClip™ G4 Implant erosion, migration or malposition
  - Failure to deliver MitraClip™ G4 Implant to the intended site
  - Difficulty or failure to retrieve MitraClip™ G4 system components
- Use caution when treating patients with hemodynamic instability requiring inotropic support or mechanical heart assistance due to the increased risk of mortality in this patient population. The safety and effectiveness of MitraClip™ in these patients has not been evaluated.
- Patients with a rotated heart due to prior cardiac surgery in whom the System is used may have a potential risk of experiencing adverse events such as atrial perforation, cardiac tamponade, tissue damage, and embolism which may be avoided with preoperative evaluation and proper device usage.
- For the Steerable Guide Catheter and Delivery Catheter only:
  - The Guide Catheter: the distal 65 cm of the Steerable Guide Catheter with the exception of the distal soft tip, is coated with a hydrophilic coating.
  - The Delivery Catheter: coated with a hydrophilic coating for a length of approximately 131 cm.
  - Failure to prepare the device as stated in these instructions and failure to handle the device with care could lead to additional intervention or serious adverse event.
- The Clip Delivery System is provided sterile and designed for single use only. Cleaning, re-sterilization and / or re-use may result in infections, malfunction of the device and other serious injury or death.
- Note the product "Use by" date specified on the package.
- Inspect all product prior to use. Do not use if the package is open or damaged, or if product is damaged.

PRECAUTIONS

- Prohibitive Risk Primary (or degenerative) Mitral Regurgitation
  - Prohibitive risk is determined by the clinical judgment of a heart team, including a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, due to the presence of one or more of the following documented surgical risk factors:
    - 30-day STS predicted operative mortality risk score of
      - ≥8% for patients deemed likely to undergo mitral valve replacement or
      - ≥6% for patients deemed likely to undergo mitral valve repair
  - Porcelain aorta or extensively calcified ascending aorta.
  - Frailty (assessed by in-person cardiac surgeon consultation)
  - Hostile chest
  - Severe liver disease / cirrhosis (MELD Score > 12)
  - Severe pulmonary hypertension (systolic pulmonary artery pressure > 2/3 systemic pressure)
  - Unusual extenuating circumstance, such as right ventricular dysfunction with severe tricuspid regurgitation, chemotherapy for malignancy, major bleeding diathesis, immobility, AIDS, severe dementia, high risk of aspiration, internal mammary artery (IMA) at high risk of injury, etc.
  - Evaluable data regarding safety or effectiveness is not available for prohibitive risk Primary patients with an LVEF < 20% or an LVESD > 60 mm. MitraClip™ should be used only when criteria for clip suitability for Primary have been met.
  - The heart team should include a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease and may also include appropriate physicians to assess the adequacy of heart failure treatment and valvular anatomy.
- Secondary Mitral Regurgitation
  - Evaluable data regarding safety or effectiveness is not available for secondary MR patients with an LVEF < 20% or an LVESD > 70 mm.
  - The multidisciplinary heart team should be experienced in the evaluation and treatment of heart failure and mitral valve disease and determine that symptoms and MR severity persist despite maximally tolerated GDMT.

POTENTIAL COMPLICATIONS AND ADVERSE EVENTS

The following ANTICIPATED EVENTS have been identified as possible complications of the MitraClip™ G4 procedure.

- Allergic reactions or hypersensitivity to latex, contrast agent, anaesthesia, device materials (nickel / titanium, cobalt, chromium, polyester), and drug reactions to anticoagulation, or antiplatelet drugs
- Vascular access complications which may require transfusion or vessel repair including:
  - wound dehiscence
  - catheter site reactions
  - Bleeding (including ecchymosis, oozing, hematoma, hemorrhage, retroperitoneal hemorrhage)
  - Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture, vascular occlusion
  - Emboli (air thrombotic material, implant, device component)
  - Peripheral Nerve Injury
- Lymphatic complications
- Pericardial complications which may require additional intervention, including:
  - Pericardial effusion
  - Cardiac tamponade
  - Pericarditis
- Cardiac complications which may require additional interventions or emergency cardiac surgery, including:
  - Cardiac perforation
  - Atrial septal defect
- Mitral valve complications, which may complicate or prevent later surgical repair, including:
  - Chordal entanglement / rupture
  - Single Leaflet Device Attachment (SLDA)
  - Thrombosis
  - Dislodgement of previously implanted devices
  - Tissue damage
  - Mitral valve stenosis
  - Persistent or residual mitral regurgitation
  - Endocarditis
- Cardiac arrhythmias (including conduction disorders, atrial arrhythmias, ventricular arrhythmias)
- Cardiac ischemic conditions (including myocardial infarction, myocardial ischemia, and unstable / stable angina)
- Venous thromboembolism (including deep vein thrombosis, pulmonary embolism, post procedure pulmonary embolism)
- Stroke / Cerebrovascular accident (CVA) and Transient Ischemic Attack (TIA)
- System organ failure:
  - Cardio-respiratory arrest
  - Worsening heart failure
  - Pulmonary congestion
  - Respiratory dysfunction / failure / atelectasis
  - Renal insufficiency or failure
  - Shock (including cardiogenic and anaphylactic)
- Blood cell disorders (including coagulopathy, hemolysis, and Heparin Induced Thrombocytopenia (HIT))
- Hypotension / hypertension
- Infection including:
  - Urinary Tract Infection (UTI)
  - Pneumonia
  - Septicemia
- Nausea / vomiting
- Chest pain
- Dyspnea
- Edema
- Fever or hyperthermia
- Pain
- Death
- Fluoroscopy, Transesophageal echocardiogram (TEE) and Transthoracic echocardiogram (TTE) -related complications:
  - Skin injury or tissue changes due to exposure to ionizing radiation
  - Esophageal irritation
  - Esophageal perforation
  - Gastrointestinal bleeding

Abbott 3200 Lakeside Dr., Santa Clara, CA. 95054 USA, Tel: 1.800.227.9902

Caution: This product is intended for use by or under the direction of a physician. Prior to use, reference the Instructions for Use provided inside the product carton (when available) or at eifu.abbottvascular.com or at medical.abbott/manuals for more detailed information on Indications, Contraindications, Warnings, Precautions and Adverse Events.

Abbott