

CLINICAL PRACTICE

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Secondary Mitral Regurgitation

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This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors’ clinical recommendations.

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A 75-year-old man presents with dyspnea and fatigue that occur with less than moderate physical activity. He had an ST-segment elevation myocardial infarction involving the inferior and posterior segments of the left ventricle 10 years ago, and since then the left ventricular ejection fraction (LVEF) has decreased from 40% to 25%, accompanied by increasing mitral regurgitation. An implantable cardioverter–defibrillator (ICD) was placed for primary prevention 6 months ago. His medications include metoprolol succinate, spironolactone, and torsemide. How would you further evaluate and treat this patient?

THE CLINICAL PROBLEM

MITRAL REGURGITATION DERIVES FROM ANATOMICAL OR FUNCTIONAL impairment of one or more components of the mitral apparatus that are necessary for normal valve function, including the left ventricle, papillary muscles, chordae tendineae, leaflets, and annulus.¹ The two broad categories of mitral regurgitation are primary (or degenerative) mitral regurgitation, which is most commonly caused by leaflet prolapse or flail, and secondary (or functional) mitral regurgitation. Primary mitral regurgitation is a disease of the valve (or chordae), and secondary mitral regurgitation is a disease of the left ventricle or left atrium.



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In the United States, mitral regurgitation is the most common cause of moderate-to-severe valvular heart disease among adults older than 55 years of age.² In a cross-sectional cohort study involving persons older than 65 years of age, the prevalence of moderate-to-severe mitral regurgitation detected on transthoracic echocardiography was 2.3%.³ In another study,⁴ moderate-to-severe mitral regurgitation was identified in 0.59% of 29,390 adults residing in Olmsted County, Minnesota. The mitral regurgitation was classified as secondary in 65% of the cases, of which 60% were attributed to left ventricular remodeling or dysfunction and the remainder were attributed to atrial fibrillation or flutter or to idiopathic annular dilation.⁵

The severity of secondary mitral regurgitation may vary dynamically as a function of left ventricular loading conditions, heart rhythm, conduction system disease, and myocardial ischemia. Ischemic mitral regurgitation is a type of secondary mitral regurgitation that occurs after myocardial infarction. Several studies have shown high risks of illness and death from cardiovascular disease among patients with symptomatic heart failure, reduced left ventricular systolic function,

KEY CLINICAL POINTS

SECONDARY MITRAL REGURGITATION

- Mitral regurgitation can be broadly classified into two different categories — primary and secondary mitral regurgitation. The evaluation, treatment, and prognosis in patients with these conditions differ. Primary mitral regurgitation is usually caused by leaflet abnormalities (prolapse), whereas secondary mitral regurgitation results from abnormal left ventricular size, shape, or function.
- Transthoracic echocardiography is the most frequently used test to determine the cause, mechanism, and severity of mitral regurgitation.
- Guideline-directed medical therapy is the first-line approach in the treatment of patients who have heart failure with secondary mitral regurgitation and a reduced left ventricular ejection fraction (LVEF). Surgical or transcatheter intervention should be undertaken only after the patient has received the maximal dose of medical therapy without adverse effects.
- Surgical treatment of secondary mitral regurgitation consists of downsized annuloplasty repair or replacement. Surgery has not been shown to improve long-term survival among these patients.
- In one of two randomized trials of transcatheter edge-to-edge repair (TEER) involving patients with secondary mitral regurgitation and a reduced LVEF, guideline-directed medical therapy plus TEER significantly decreased the incidence of hospitalization for heart failure or death from any cause at 2 years.
- The concept of differentiating mitral regurgitation as proportionate or disproportionate has been proposed to explain the benefit of TEER for secondary mitral regurgitation. Prospective validation of this concept is needed.

and moderate or greater degrees of ischemic mitral regurgitation.⁶⁻⁸ Secondary mitral regurgitation is associated with lower event-free survival than primary mitral regurgitation of similar magnitude. Adverse outcomes with secondary mitral regurgitation can occur in association with smaller regurgitant volumes than are observed in patients with remodeled primary mitral regurgitation. Whether secondary mitral regurgitation is simply a marker of poor outcomes due to left ventricular dysfunction or whether it contributes independently to the long-term prognosis in these patients is uncertain.

STRATEGIES AND EVIDENCE

DIAGNOSIS AND EVALUATION

The clinical recognition of secondary mitral regurgitation begins with detection and characterization of a systolic heart murmur that is considered within the context of the patient's history, symptoms at presentation, and other evidence of an underlying cardiac condition (e.g., abnormalities on electrocardiography or chest radiography). Although the murmur can be difficult to detect, bedside maneuvers to increase left ventricular afterload may increase its intensity.

The identification of the cause, mechanism, severity, and consequences of mitral regurgitation relies primarily on performance of trans-

thoracic echocardiography with assessment of the morphologic characteristics and motion of the mitral-valve leaflets, size and calcification of the annulus, left ventricular and left atrial volumes, global and regional left ventricular systolic function, pulmonary-vein flow, pulmonary-artery pressures, right ventricular function, and the presence of tricuspid regurgitation (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org; and Fig. 1).⁹ The nature of secondary mitral regurgitation is dynamic, so the patient's blood pressure and heart rate and rhythm should be recorded. Transthoracic echocardiography often reveals more mitral regurgitation than can be detected on physical examination.

CLASSIFICATION AND ASSESSMENT

The Carpentier classification,¹⁰ which categorizes mitral regurgitation on the basis of normal, excessive, or restrictive leaflet mobility, can be useful for clinical categorization and surgical planning (Fig. S1). In Carpentier type IIIB disease, which is the main focus of this article, mitral regurgitation is attributable to restricted mitral-valve leaflet motion during systole in patients with an ischemic or nonischemic (dilated) cardiomyopathy. In patients with ischemic mitral regurgitation, the mitral-valve leaflets are also thickened and fibrotic, with reduced lengthening.¹¹ Mitral

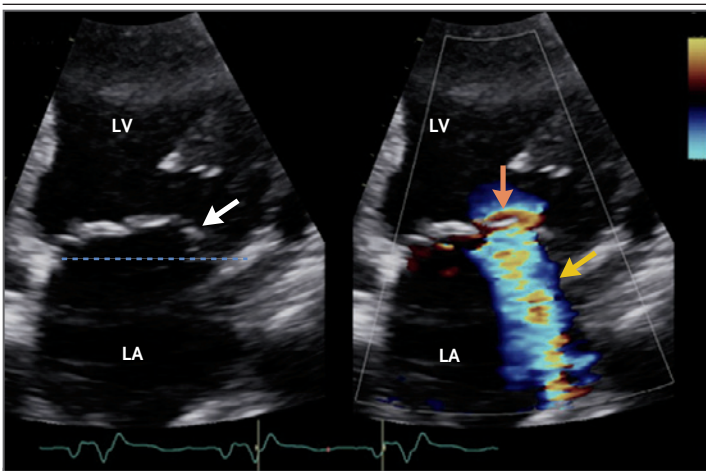


Figure 1. Secondary Mitral Regurgitation on Transthoracic Echocardiography.

An enlarged apical four-chamber view without color Doppler (left side) and with color Doppler (right side) is shown. On the left side, the posterior mitral-valve leaflet (white arrow) is tethered, and there is tenting of both leaflets above the valve plane (dashed blue line) during systole. The left ventricle (LV) and left atrium (LA) are enlarged. On the right side, there is an eccentric jet of mitral regurgitation (yellow arrow) directed posteriorly and laterally into an enlarged LA with an area of accelerated flow convergence at its cap (orange arrow). The mitral regurgitation was severe according to multiple criteria.

regurgitation occurs most often as a consequence of adverse left ventricular remodeling with papillary muscle displacement, leaflet tethering, reduced mitral-valve closing forces, annular dilation, and failure of leaflet coaptation. In some patients with ischemic mitral regurgitation, however, the left ventricle is not substantially remodeled. With atrial functional mitral regurgitation (Carpentier type I), mitral-valve leaflet motion is normal and the mitral regurgitation is due to left atrium and annular enlargement with insufficient leaflet lengthening, as occurs in some patients with chronic persistent atrial fibrillation.¹²

The severity of mitral regurgitation should be measured objectively. However, quantitative assessment of secondary mitral regurgitation is difficult because of geometric assumptions and technical challenges.¹³ In patients with ischemic mitral regurgitation, measurement may be inaccurate because of the eccentric nature of the jet and the crescentic shape of the regurgitant orifice.^{13,14} Professional societies have published various thresholds for the classification of severe mitral regurgitation. The American College of Cardiology–American Heart Association (ACC–

AHA) guidelines define severe secondary mitral regurgitation on the basis of an effective regurgitant orifice area of at least 0.4 cm² and a regurgitant volume of 60 ml or more (the same thresholds as those applied to primary mitral regurgitation).^{15,16} In contrast, the guidelines of the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery use lower cutoff points (effective regurgitant orifice area ≥ 0.2 cm² and regurgitant volume ≥ 30 ml)¹⁷; these cutoff points are based on data on the natural history of this condition that link these lower values with poor outcomes. The American Society of Echocardiography guidelines¹⁴ caution that secondary mitral regurgitation may be severe even with an effective regurgitant orifice area of 0.3 cm² or more because of limitations in the technique used to measure it. One echocardiographic finding in isolation cannot define the severity of mitral regurgitation, and thus an integrative approach is needed.

ADDITIONAL TESTING

When assessment of the anatomy and function of the mitral valve by means of transthoracic echocardiography is not adequate, transesophageal echocardiography and cardiac magnetic resonance imaging (MRI) can provide more specific anatomical and hemodynamic detail.¹⁴ Because the patient has to be sedated during transesophageal echocardiography, the performance of this test can result in favorably altered left ventricular loading conditions and reduced severity of secondary mitral regurgitation. Thus, observations made on transthoracic echocardiography while the patient is awake should be used in clinical decision making. Cardiac MRI can provide accurate measurement of left ventricular volumes, detect areas of myocardial scarring, and assess for regional ischemia. Exercise transthoracic echocardiography may be useful when there are discrepancies between the clinical findings and data from other noninvasive testing. Cardiac catheterization with hemodynamic assessment, coronary angiography, and left ventriculography has a role in selected patients, particularly those with known or suspected coronary artery disease.⁹

MEDICAL THERAPY OR DEVICES

Recommendations regarding the treatment of secondary mitral regurgitation are based on multi-

ple variables, including the type (ventricular or atrial), severity, and hemodynamic consequences of secondary mitral regurgitation; coexisting conditions; and the experience and expertise of the multidisciplinary team providing care. Guideline-directed medical therapy (Table S2) is the first-line approach in patients who have heart failure with a reduced LVEF and secondary mitral regurgitation, and it is provided preferably with the supervision of a heart failure specialist. Randomized trials involving patients who have heart failure with a reduced ejection fraction (some of whom had secondary mitral regurgitation) have shown functional and survival benefits of beta-blockers, inhibitors of the renin-angiotensin-aldosterone system, angiotensin receptor-neprilysin inhibitors, and sodium-glucose cotransporter 2 inhibitors.¹⁸⁻²¹ Stepped therapy with these agents and others is implemented over a period of weeks to months. Both carvedilol²² and sacubitril-valsartan²³ have been shown to reduce the degree of secondary mitral regurgitation.

Cardiac resynchronization therapy can improve left ventricular function, decrease left ventricle size, and reduce the magnitude of mitral regurgitation in selected patients who have heart failure with a reduced ejection fraction and left bundle-branch block, particularly when the QRS duration exceeds 150 msec.^{24,25} In patients with atrial functional mitral regurgitation due to atrial fibrillation, restoration and maintenance of sinus rhythm can reduce the left atrium size, the mitral annular dimensions, and the degree of mitral regurgitation.²⁶ Attention to the principles of secondary prevention of coronary artery disease events (including lipid management) and reduction in the risk of sudden death (with an ICD) and stroke (with anticoagulation for atrial fibrillation) is important.

SURGERY

In contrast to primary mitral regurgitation, for which valve repair is indicated when symptoms develop or when certain thresholds for left ventricle size, function, or both are met,¹⁴⁻¹⁶ surgical or transcatheter intervention for secondary mitral regurgitation should be pursued only in patients with persistent symptoms and residual moderately severe or severe mitral regurgitation despite an adequate 3-month trial of guideline-directed medical therapy.⁹ Surgery for secondary mitral

regurgitation consists chiefly of either repair with a downsized annuloplasty ring or valve replacement with chordal sparing. In patients with ischemic mitral regurgitation, coronary-artery bypass grafting (CABG) is performed when appropriate. Surgical ablation for atrial fibrillation, amputation of the left atrial appendage, and other valve surgery is undertaken when indicated.

Although a case series showed improvement in left ventricular function and shape in patients with dilated cardiomyopathy and secondary mitral regurgitation with insertion of a downsized annuloplasty ring,²⁷ a subsequent propensity-matched cohort study from the same institution showed that survival was not longer among patients who underwent repair than among those who received medical therapy.²⁸ Data from randomized trials comparing mitral-valve surgery with medical therapy or transcatheter therapy in patients with ischemic mitral regurgitation are lacking. In a randomized trial comparing mitral-valve repair with chordal-sparing mitral-valve replacement in 251 patients with severe ischemic mitral regurgitation (mean effective regurgitant orifice area, 0.4 cm²), those assigned to mitral-valve replacement had a lower incidence of moderate-to-severe mitral regurgitation after surgery, fewer serious adverse events related to heart failure, and fewer readmissions for cardiovascular causes at 2 years, although there was no significant difference in survival at 2 years.²⁹ Thus, in contrast to severe primary mitral regurgitation (for which valve repair is preferred over replacement), valve replacement may be preferred for treatment of severe ischemic mitral regurgitation. In another randomized trial involving patients with moderate ischemic mitral regurgitation (mean effective regurgitant orifice area, 0.2 cm²), there was no difference between mitral-valve repair plus CABG and CABG alone with respect to the magnitude of left ventricular reverse remodeling, and survival was not longer with mitral-valve repair plus CABG than with CABG alone.³⁰

TRANSCATHETER REPAIR OR REPLACEMENT

In transcatheter intervention for mitral regurgitation, the use of a clip (MitraClip, Abbot Vascular) to create an edge-to-edge approximation of the midportion of the mitral-valve leaflets results in a double-orifice mitral valve (Fig. 2,

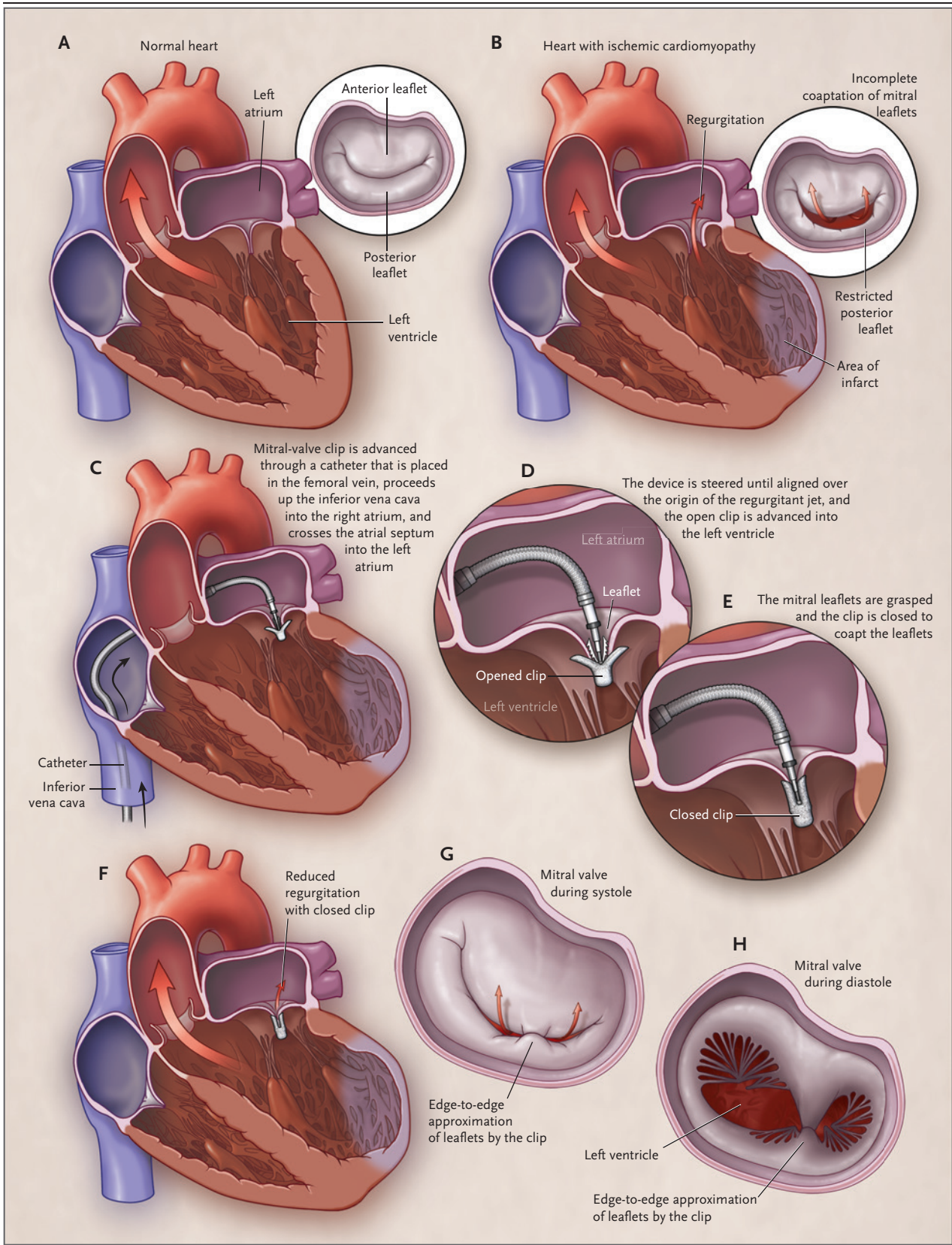


Figure 2 (facing page). Transcatheter Intervention for Mitral Regurgitation.

As shown in A (upper left), in the normal heart, the mitral valve is competent and systolic flow is directed out of the aorta. As shown in B, the left ventricle remodels after myocardial infarction with displacement of the papillary muscles and restricted movement of the posterior mitral-valve leaflet, resulting in mitral regurgitation. As shown in C, a catheter containing the mitral-valve clip device is threaded up the inferior vena cava into the right atrium, across the interatrial septum, into the left atrium, and across the mitral-valve leaflets. This procedure is performed with transesophageal and fluoroscopic guidance. As shown in D and E, the device is positioned to grasp the mitral-valve leaflets and clip them together in the region of the jet of mitral regurgitation. As shown in F and G, edge-to-edge clipping results in a decrease in the magnitude of mitral regurgitation. Placement of the clip results in the creation of a double-orifice mitral valve. The view in H is from the left atrial side of the valve, looking down into the left ventricle. In this example, the clip has been placed across the middle scallops of the anterior and posterior leaflets, creating a ridge of tissue that separates the two orifices.

Video 1, and Video 2). The favorable outcomes in both randomized and observational studies resulted in the 2013 Food and Drug Administration (FDA) approval of the clip for the treatment of patients with primary mitral regurgitation who are at high risk for surgery-related complications or death.³¹

Subsequently, the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT) trial randomly assigned 614 patients with secondary mitral regurgitation (approximately 60% of whom had ischemic cardiomyopathy) and symptomatic heart failure with a reduced LVEF to either transcatheter edge-to-edge repair (TEER) plus guideline-directed medical therapy or guideline-directed medical therapy alone.³² The addition of TEER to medical therapy resulted in significantly fewer hospitalizations for heart failure and improved survival at 2 years, with a low incidence of device-related complications.

A second randomized trial that used the same device, the Percutaneous Repair with the MitraClip Device for Severe Functional/Secondary Mitral Regurgitation (MITRA-FR) trial, involved 304 patients. The 1-year³³ and 2-year³⁴ follow-up results of that trial showed no significant differences between patients who received guideline-directed

medical therapy plus TEER and those who received guideline-directed medical therapy alone with respect to a composite outcome of death from any cause or unplanned hospitalization for heart failure. Possible reasons proposed for these discordant results include differences between the trial sample sizes and in end points, as well as differences in the severity of baseline mitral regurgitation, baseline left ventricle size, rigor of medical therapy, degree and durability of the reduction in mitral regurgitation, and operator experience.³⁵ Another proposed explanation is that the benefits of TEER in patients with secondary mitral regurgitation may depend on the relationship between the left ventricle size and the severity of mitral regurgitation.³⁶ These benefits are greater when the degree of mitral regurgitation exceeds — or is disproportionate to — that which would be expected for the size of the ventricle alone. Such disproportionate mitral regurgitation was more common in patients in the COAPT trial, who had more mitral regurgitation and smaller ventricles than patients in the MITRA-FR trial. Although a COAPT substudy of echocardiographic findings showed consistent benefits of TEER across numerous baseline echocardiographic measures,³⁷ a post hoc analysis involving a small subgroup of patients in the COAPT trial who more closely resembled patients in the MITRA-FR trial and who had mitral regurgitation that was considered to be proportionate to the degree of left ventricular dilatation did not show a benefit with TEER.³⁸

Patient selection for TEER is a nuanced process and must involve consideration of numerous clinical, imaging, and hemodynamic variables.^{39,40} In patients with secondary mitral regurgitation, important transesophageal echocardiographic findings to predict the feasibility of TEER include leaflet coaptation depth, coaptation length, grasping zone distance between leaflets, and the presence, extent, and distribution of calcification.⁹ The FDA approved the MitraClip device in March 2019 for use in patients with secondary mitral regurgitation who meet the inclusion criteria of the COAPT trial. These criteria are symptomatic heart failure with an ejection fraction of 20 to 50% and moderate-to-severe or severe mitral regurgitation despite guideline-directed medical therapy (plus cardiac resynchronization therapy, if indicated), a left



Videos showing transcatheter repair are available at [NEJM.org](https://www.nejm.org)

Table 1. 2017 Guidelines for Intervention in Patients with Chronic Severe Secondary Mitral Regurgitation.***American College of Cardiology–American Heart Association**

Class IIa recommendation

Mitral-valve surgery is reasonable for patients with chronic severe secondary mitral regurgitation who are undergoing CABG or aortic-valve replacement. (Level of evidence: C)

It is reasonable to choose chordal-sparing mitral-valve replacement over repair with a downsized annuloplasty ring if the operation is considered for severely symptomatic patients with chronic severe ischemic mitral regurgitation and persistent symptoms despite the use of maximal doses of guideline-directed medical therapy without adverse effects. (Level of evidence: B)

Class IIb recommendation

Mitral-valve repair or replacement may be considered for severely symptomatic patients with chronic severe secondary mitral regurgitation who have persistent symptoms despite the use of maximal doses of guideline-directed medical therapy without adverse effects. (Level of evidence: B)

European Society of Cardiology and the European Association for Cardio-Thoracic Surgery

Class I recommendation

Surgery is indicated in patients with severe secondary mitral regurgitation who are undergoing CABG and who have an LVEF >30%. (Level of evidence: C)

Class IIa recommendation

Surgery should be considered in symptomatic patients with severe secondary mitral regurgitation and an LVEF <30% who have an indication for revascularization and evidence of myocardial viability. (Level of evidence: C)

Class IIb recommendation

When revascularization is not indicated, surgery may be considered in patients with severe secondary mitral regurgitation and an LVEF >30% who remain symptomatic despite the use of maximal doses of medical therapy without adverse effects (and cardiac resynchronization therapy if indicated) and have a low risk of surgery-related complications or death. (Level of evidence: C)

When revascularization is not indicated and the risk of surgery-related complications or death is not low, a percutaneous edge-to-edge procedure may be considered in patients with severe secondary mitral regurgitation and an LVEF >30% who remain symptomatic despite the use of maximal doses of medical therapy without adverse effects (and cardiac resynchronization therapy, if indicated) and who are found to have suitable valve morphologic characteristics on echocardiography, if the heart team thinks there is a reasonable chance for clinical improvement. (Level of evidence: C)

In patients with severe secondary mitral regurgitation and an LVEF <30% who remain symptomatic despite the use of maximal doses of medical therapy without adverse effects (and cardiac resynchronization therapy if indicated) and who have no option for revascularization, the heart team may consider a percutaneous edge-to-edge procedure or valve surgery after careful evaluation for a left ventricular assist device or heart transplantation according to individual patient characteristics. (Level of evidence: C)

* The class of recommendation indicates the strength of the recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk. In general, a class I recommendation indicates that the intervention is indicated or useful and should be performed. A class IIa recommendation implies that the intervention is reasonable and can be effective, whereas a class IIb recommendation implies that the usefulness or effectiveness of the intervention is less certain. The guidelines differ with respect to methods and language, although the recommendations are directionally concordant. The level of evidence rates the quality of scientific evidence that supports the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources. Level B evidence may derive from randomized trials, observational studies, and registries, and it is considered to be of moderate quality. Level C evidence relies on limited data, expert opinion, or both. These guideline recommendations reflect the strength of the evidence base in existence in 2017. CABG denotes coronary-artery bypass grafting, and LVEF left ventricular ejection fraction.

ventricular end-systolic dimension of less than 7.0 cm, and a pulmonary-artery systolic pressure of less than 70 mm Hg.

Other transcatheter approaches to repair secondary mitral regurgitation include devices that target the mitral-valve leaflets or reduce the size

of the dilated annulus. Devices for mitral-valve replacement are also under investigation.⁴¹ Early studies have focused on feasibility, device performance, safety, and short-term efficacy in patients with a high or prohibitive risk of surgery-related complications or death.

 GUIDELINES

International practice guidelines for the care of patients with valvular heart disease were most recently updated in 2017, before the publication of the results of the COAPT and MITRA-FR trials in 2018, and these guidelines were conservative in their recommendations regarding surgery for secondary mitral regurgitation (Table 1).^{16,17} Mitral-valve surgery was recommended¹⁶ or considered to be reasonable¹⁷ for patients with severe secondary mitral regurgitation who are undergoing CABG. The guidelines noted that isolated mitral-valve surgery could be considered for severe secondary mitral regurgitation in selected patients with severe symptoms despite the use of maximal doses of guideline-directed medical therapy without adverse effects. The surgical approach was not rigorously specified, although the ACC–AHA guidelines stated that it is reasonable to choose replacement in preference to repair with a downsized annuloplasty ring for patients with severe ischemic mitral regurgitation.¹⁶

The 2017 guidelines of the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery also suggested a possible role for TEER in the treatment of severe secondary mitral regurgitation in patients who have heart failure with a reduced ejection fraction and persistent symptoms despite the use of maximal doses of guideline-directed medical therapy without adverse effects. Both guidelines are currently undergoing revision. The present article differs from the current guidelines¹⁵⁻¹⁷ by taking into account the results of the COAPT and MITRA-FR trials.

 AREAS OF UNCERTAINTY

The disparate results of the COAPT and MITRA-FR trials have confused the clinical community. A third trial (A Clinical Evaluation of the Safety and Effectiveness of the MitraClip System in the Treatment of Clinically Significant Functional Mitral Regurgitation [RESHAPE-HF2]) (ClinicalTrials.gov number, NCT02444338) of the same device in similar patients is currently recruiting patients and is designed to provide additional data to guide the appropriate use of TEER in patients with secondary mitral regurgitation.

Currently, more than 380 U.S. centers offer TEER for mitral regurgitation (www.sts.org/registries-research-center/stsacc-tvt-registry). Whether they can reproduce the rigor applied in the COAPT trial to achieve similar results in a real-world setting is uncertain. Regulatory criteria for approval of new transcatheter repair and replacement devices need to be developed. Prospective validation of the concept of differentiating secondary mitral regurgitation as proportionate or disproportionate to guide patient selection for mitral-valve intervention is needed.^{35,38-40,42}

Despite clear recommendations for guideline-directed medical therapy, treatment is often not sufficient, and mortality among patients who have heart failure with a reduced ejection fraction and secondary mitral regurgitation remains high (e.g., 29% at 2 years in the device group of the COAPT trial); effective strategies are needed to improve guideline adherence.^{43,44} Given the results of the COAPT trial, the role of surgery in the management of secondary mitral regurgitation has become less clear for patients in whom there is no other primary indication for operation, such as severe coronary artery disease, for which CABG would be preferred over percutaneous coronary intervention.

 CONCLUSIONS AND
 RECOMMENDATIONS

In the patient described in the vignette, the cause, mechanism, and severity of mitral regurgitation should be evaluated by means of transthoracic echocardiography, and an assessment of myocardial ischemia and viability should be performed. The first-line approach should be to initiate a regimen for heart failure that includes a low dose of an angiotensin-converting-enzyme inhibitor (or an angiotensin-receptor blocker), adjusted with attention to the patient's blood pressure, renal function, and potassium level, followed by an attempt to switch to an angiotensin receptor–neprilysin inhibitor. Efforts should be made to administer the doses of medications that have been shown to be useful in randomized heart failure trials. Cardiac resynchronization therapy should be considered if indicated.⁴⁵

If severe heart failure symptoms persist after the use of maximal doses of guideline-directed medical therapy without adverse effects for

3 months, TEER can be considered if the patient meets the inclusion criteria of the COAPT trial noted above and transesophageal echocardiographic assessment of the leaflet structure and motion indicates that this is feasible. We would consult with a multidisciplinary team that includes a heart failure specialist, an echocardiog-

rapher, an interventionalist, and a surgeon to seek a consensus recommendation regarding the best treatment strategy, and we would pursue a shared decision-making process with the patient and his family.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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