H CONT. dilatation (end-systolic diameter >50 mm or indexed end-systolic dimension >25 mm/m^2). Aortic valve repair without valve replacement may be performed in centers of expertise. Follow-up of asymptomatic patients is based on severity of regurgitation and other factors (see Table 23). H

Medical therapy, preferably with dihydropyridine calcium channel blockers (nifedipine, isradipine, felodipine, nicardipine, nisoldipine, lacidipine, and amlodipine), ACE inhibitors, or angiotensin receptor blockers, is recommended in patients with chronic aortic regurgitation in the setting of hypertension. In the absence of hypertension, medical therapy is appropriate for symptomatic patients who are not surgical candidates.

KEY POINTS

- Characteristic physical findings of chronic aortic regurgitation include bounding peripheral pulses, displacement of the left ventricular apex, and a diastolic decrescendo murmur heard along the right sternal border or left sternal border.
- Emergent surgery is indicated for patients with acute aortic regurgitation due to aortic dissection.
- In cases of chronic aortic regurgitation, surgery with traditional open aortic valve replacement is advised for patients with symptoms, those with left ventricular dysfunction, or patients undergoing other cardiac surgery.
- Medical therapy with dihydropyridine calcium channel blockers, ACE inhibitors, or angiotensin receptor blockers is recommended for patients with aortic regurgitation and hypertension; in the absence of hypertension, medical therapy is appropriate in symptomatic patients who are not surgical candidates.

Bicuspid Aortic Valve Disease

Bicuspid aortic valve disease affects approximately 1% to 2% of the general population. Bicuspid morphology leads to abnormal shear forces and predisposes to early degeneration of the valve, resulting in stenosis in most patients (up to 75%) (see Figure 20) and pure regurgitation in a small minority of patients (2%-10%). Patients with a bicuspid aortic valve typically present with an incidental systolic ejection murmur in adolescence or young adulthood and gradually progress to severe disease in the fifth or sixth decade of life. More than one third of those older than 70 years with severe aortic stenosis have an underlying bicuspid valve.

A bicuspid aortic valve is often accompanied by abnormalities in the aortic arch, independent of the severity of aortic stenosis or regurgitation, and may be associated with aneurysms, dissection, or coarctation. Therefore, in patients with a bicuspid aortic valve, the aortic arch should be examined for aortopathy with CMR imaging, echocardiography, or cardiac CT; serial imaging is indicated if abnormalities are detected. The imaging modality and frequency depend on several factors, including the location and severity of the abnormalities, age of the patient, family history, and candidacy for surgery (see Diseases of the Aorta). Importantly, bicuspid aortic valve disease is heritable, and first-degree relatives should be screened for its presence with echocardiography.

Management of bicuspid aortic valve disease depends on the predominant lesion type (aortic stenosis or regurgitation) and its severity. In patients with a bicuspid valve who are undergoing surgery for severe aortic stenosis or regurgitation, surgical repair of the ascending aorta is advised when the aortic diameter is greater than 4.5 cm. In the absence of surgical indications for a stenotic or regurgitant aortic valve, surgical repair of the ascending aorta or aortic sinuses is advised when the aortic diameter is greater than 5.5 cm or when the diameter is greater than 5.0 cm with additional risk factors for dissection (family history, rate of progression ≥0.5 cm/year).

No medical therapies slow aortic dilatation in patients with aortopathy and a bicuspid aortic valve. Blood pressure should be controlled in patients with concomitant hypertension.

KEY POINTS

- Bicuspid morphology predisposes to early degeneration of the aortic valve, resulting in stenosis in most patients and pure regurgitation in few patients.
- Patients with a bicuspid aortic valve typically present with an incidental systolic ejection murmur in adolescence or young adulthood and gradually progress to severe disease in the fifth or sixth decade of life.
- Management of bicuspid aortic valve disease follows the recommendations for the predominant valve lesion type (aortic stenosis or regurgitation) and severity of the valvular disease.

Mitral Stenosis

Clinical Presentation and Evaluation

The leading cause of mitral stenosis is rheumatic heart disease, which has a higher predilection for women than men (female-to-male ratio of 4:1). Although relatively uncommon in the United States, rheumatic heart disease is frequent in populations with limited access to treatment for streptococcal pharyngitis. Rheumatic heart disease results in fusion of the mitral commissures and, in more advanced forms, calcification of the valve and abnormalities in the subvalvular apparatus (**Figure 23**). Other causes of mitral stenosis are parachute mitral valve, chest radiation, and severe mitral annular calcification. Mitral annular calcification is more common in the elderly and is associated with inflammatory disorders, peripheral artery disease, and chronic kidney disease.

The natural history of mitral stenosis is characterized by a slow progression over decades, with gradual enlargement of the left atrium (LA) and preservation of LV function. Symptoms

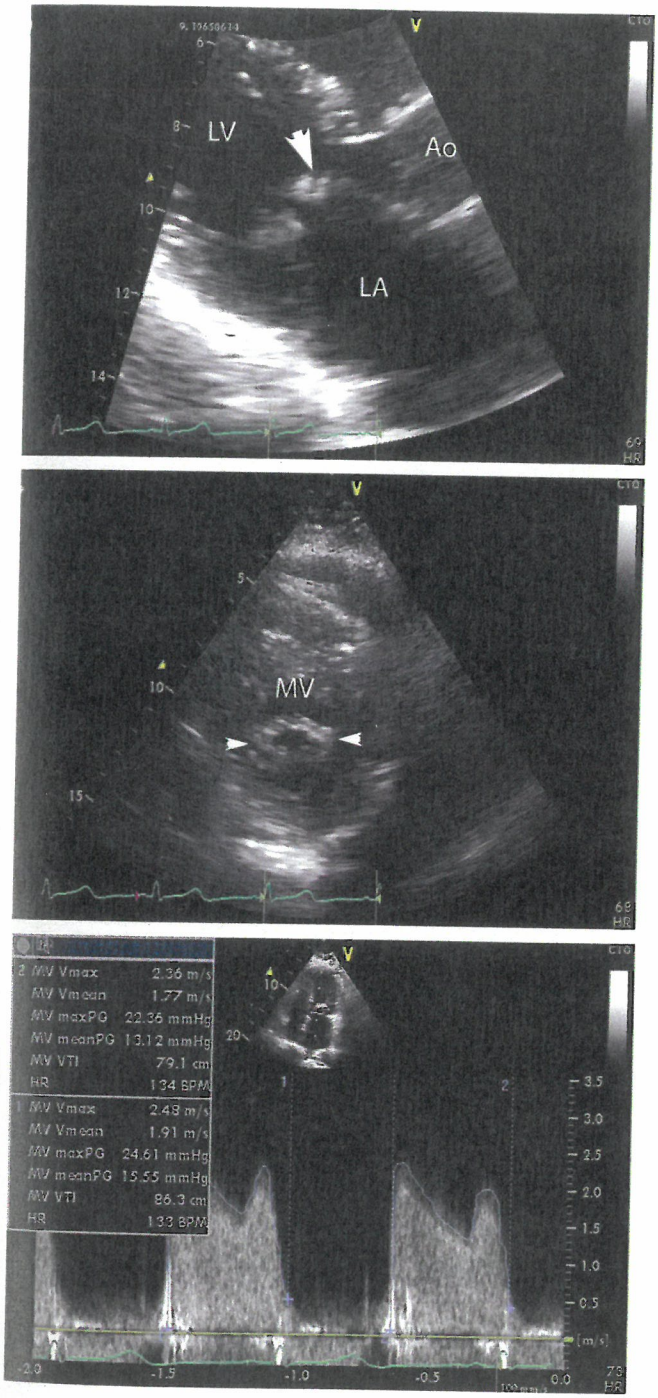

FIGURE 23. Rheumatic mitral stenosis. *Top panel:* Diastolic doming (*arrowhead*) is present with a "hockey stick" deformity from mitral stenosis. *Middle panel:* Commissural fusion (*arrowheads*) of the mitral valve (MV) is present. *Bottom panel:* Doppler echocardiogram showing a mitral gradient of 13 mm Hg, consistent with severe stenosis. Ao = ascending aorta; LA = left atrium; LV = left ventricle.

of mitral stenosis may arise from low cardiac output (fatigue), pulmonary congestion (dyspnea), and pulmonary hypertension with right-sided heart failure (lower extremity edema). Symptoms typically occur with exertion because exercise shortens diastolic filling time and increases the transvalvular flow and diastolic mitral gradient, leading to worsening of LA hypertension. Symptoms may first occur during pregnancy owing to increased blood volume and cardiac output. Patients can also present with systemic embolization, atrial fibrillation, or, in severe cases, hemoptysis. Heart failure is the cause of death in approximately 60% of patients with mitral stenosis, and thromboembolism is the cause in most others.

On physical examination, the findings of mitral stenosis when the valve is pliable include a tapping LV impulse in the precordium, a loud S_1, an increased pulmonic component of S_2, a diastolic opening snap, and a diastolic rumble or low-pitched murmur at the apex (see Table 21). Signs of pulmonary or systemic congestion may be present depending on the severity of the lesion and the patient's volume status.

TTE is highly accurate for assessing mitral stenosis severity, pulmonary pressures, and right ventricular function (see Table 23). Additional imaging or cardiac catheterization is rarely required. Severe mitral stenosis is defined by a mitral valve area of 1.5 cm^2 or less, which usually corresponds to a mean mitral gradient of more than 5 to 10 mm Hg at a normal heart rate. In patients with a discrepancy between the clinical findings and the echocardiographic findings, stress echocardiography with pharmacologic or physical stressors should be pursued to assess the response of the mitral gradient and pulmonary pressures.

Management

The procedure of choice for patients with significant rheumatic mitral stenosis and a pliable mitral valve is percutaneous balloon mitral commissurotomy (PBMC). PBMC is indicated for symptomatic patients with severe mitral stenosis and favorable valve morphology. PBMC may be considered in asymptomatic patients with critical mitral stenosis when the valve area is less than 1.0 cm^2. In patients with LA thrombus, moderate mitral regurgitation, or a severely calcified valve, PBMC should not be performed. In appropriately selected patients, success rates with PBMC are 95%, and complications occur in less than 5% of patients. Surgery for mitral stenosis should be performed in patients with severe symptoms (New York Heart Association functional class III or IV) and a nonpliable valve or concomitantly in patients undergoing other cardiac surgical procedures.

Nearly 50% of patients with mitral stenosis have atrial fibrillation, and without anticoagulation therapy, these patients have a risk for thromboembolism of 20% to 25%. Patients with mitral stenosis and atrial fibrillation should receive warfarin, with a goal INR of 2.0 to 3.0. Other indications for anticoagulation are a history of LA thrombus or systemic embolization. Notably, clinical trials of non–vitamin K antagonist oral anticoagulants in atrial fibrillation excluded patients with mitral stenosis; therefore, the efficacy and safety of these agents in this population have not been demonstrated.

Because the mitral gradient is heavily dependent on transvalvular flow, medical therapy with negative chronotropic agents, diuretics, and long-acting nitrates can be effective for

symptom palliation in patients who are not candidates for interventional or surgical therapy.

KEY POINTS

- Transthoracic echocardiography is highly accurate for assessing the severity of mitral stenosis, pulmonary hypertension, and right ventricular function.
- Percutaneous balloon mitral commissurotomy is indicated for symptomatic patients with severe mitral stenosis and favorable valve morphology.
- Warfarin therapy is recommended for patients with mitral stenosis and a history of atrial fibrillation, left atrial thrombus, or systemic embolization.

Mitral Regurgitation

Clinical Presentation and Evaluation

Mitral regurgitation may arise from any portion of the complex valve apparatus (such as the leaflets, annulus, chordae, papillary muscles, or LV free walls) and may present acutely or chronically. Causes of acute mitral regurgitation are infective endocarditis, papillary muscle ischemia or rupture, trauma (for example, injury from PBMC), or degenerative disease with chordal rupture and flail leaflet. Chronic mitral regurgitation is classified as primary or secondary. Chronic primary mitral regurgitation relates to processes involving any portion of the mitral annulus. Common causes of primary mitral regurgitation are mitral valve prolapse (also known as myxomatous or degenerative mitral valve disease), radiation therapy, rheumatic disease, and cleft mitral valve. Chronic secondary mitral regurgitation involves causes other than the annulus, such as ventricular dysfunction.

Mitral regurgitation results in volume overload with LV dilatation and LA hypertension, which may progress and cause pulmonary hypertension and right ventricular failure. In acute mitral regurgitation, heart failure symptoms often occur abruptly because there has not been time for adaptive chamber dilatation, and patients may present with cardiogenic shock. The systolic murmur in acute mitral regurgitation may be brief because of the rapid equalization of LA and LV pressures. Echocardiography with color flow imaging can underestimate the severity of the regurgitation. Thus, when acute mitral regurgitation is suspected, comprehensive assessment to identify the potential causes should be pursued, and additional imaging with TEE should be considered. Aggressive evaluation and accurate diagnosis are crucial for patients with acute mitral regurgitation.

Chronic primary mitral regurgitation is predominantly caused by mitral valve prolapse, which affects approximately 2% of the general population or roughly 500,000 persons in the United States. Echocardiography in patients with chronic primary mitral regurgitation may show a range of abnormalities, including prolapse, gross degeneration of one or both leaflets (Barlow syndrome), or chordal rupture with flail leaflet (**Figure 24**). Barlow syndrome is more common in young adult patients. In patients who are relatively older, fibroelastic deficiency predominates and frequently results in chordal rupture. The mitral valve apparatus is normal in patients with chronic secondary mitral regurgitation (**Figure 25**). In these patients, ventricular dysfunction causes mitral regurgitation through papillary muscle displacement and tethering of the mitral leaflets, which impairs coaptation.

The physical examination in patients with chronic mitral regurgitation is notable for a blowing holosystolic murmur at the apex. In patients with mitral valve prolapse, one or more systolic clicks may precede the murmur, and variation in severity, preload, and afterload can lead to differences in murmur onset (holosystolic, midsystolic, or late systolic). In patients with LV dilatation, the apical impulse may be displaced laterally, and an S_3 may be audible, especially in patients with secondary mitral regurgitation due to LV dysfunction.

TTE readily assesses the severity of primary mitral regurgitation, with a high degree of accuracy and precision. Severe primary mitral regurgitation is defined by using several parameters; the most common is an effective regurgitant orifice area of 0.4 cm^2 or larger, regurgitant volume of 60 mL or more, or vena contracta of 0.7 cm or larger. In some instances, TEE may be required to further elucidate the mechanism of the mitral regurgitation, particularly when surgical or interventional therapy is planned. TEE may be especially useful in evaluating for acute mitral regurgitation, in which rapid systolic equalization of LV and LA pressures can pose challenges for both the bedside examination and TTE imaging.

Appropriate follow-up of asymptomatic patients with mitral regurgitation is outlined in Table 23.

Management

Medical therapy and surgical intervention can be life-saving in patients with acute severe mitral regurgitation. Vasodilator therapy with a titratable drug, such as nitroprusside, decreases aortic impedance and mitral regurgitation, thereby improving forward cardiac output. An intra-aortic balloon pump can be used to decrease afterload and augment systemic and coronary perfusion pressures. Prompt surgical correction should be considered for all patients with acute severe mitral regurgitation.

Patients with chronic severe primary mitral regurgitation generally do poorly without surgery, particularly when there are significant symptoms, flail leaflet, or LV dilatation. In one study of 458 patients with asymptomatic severe primary mitral regurgitation, the 5-year survival rate was only 58%. Surgical treatment with repair of the mitral valve is indicated for chronic severe primary mitral regurgitation in (1) symptomatic patients with left ventricular ejection fraction (LVEF) greater than 30%, (2) asymptomatic patients with LV dysfunction (LVEF of 30%-60% and/or LV end-systolic diameter ≥40 mm), or (3) patients undergoing another cardiac surgical procedure. Surgical repair is reasonable in asymptomatic patients with preserved LV function when the expected repair success rate is

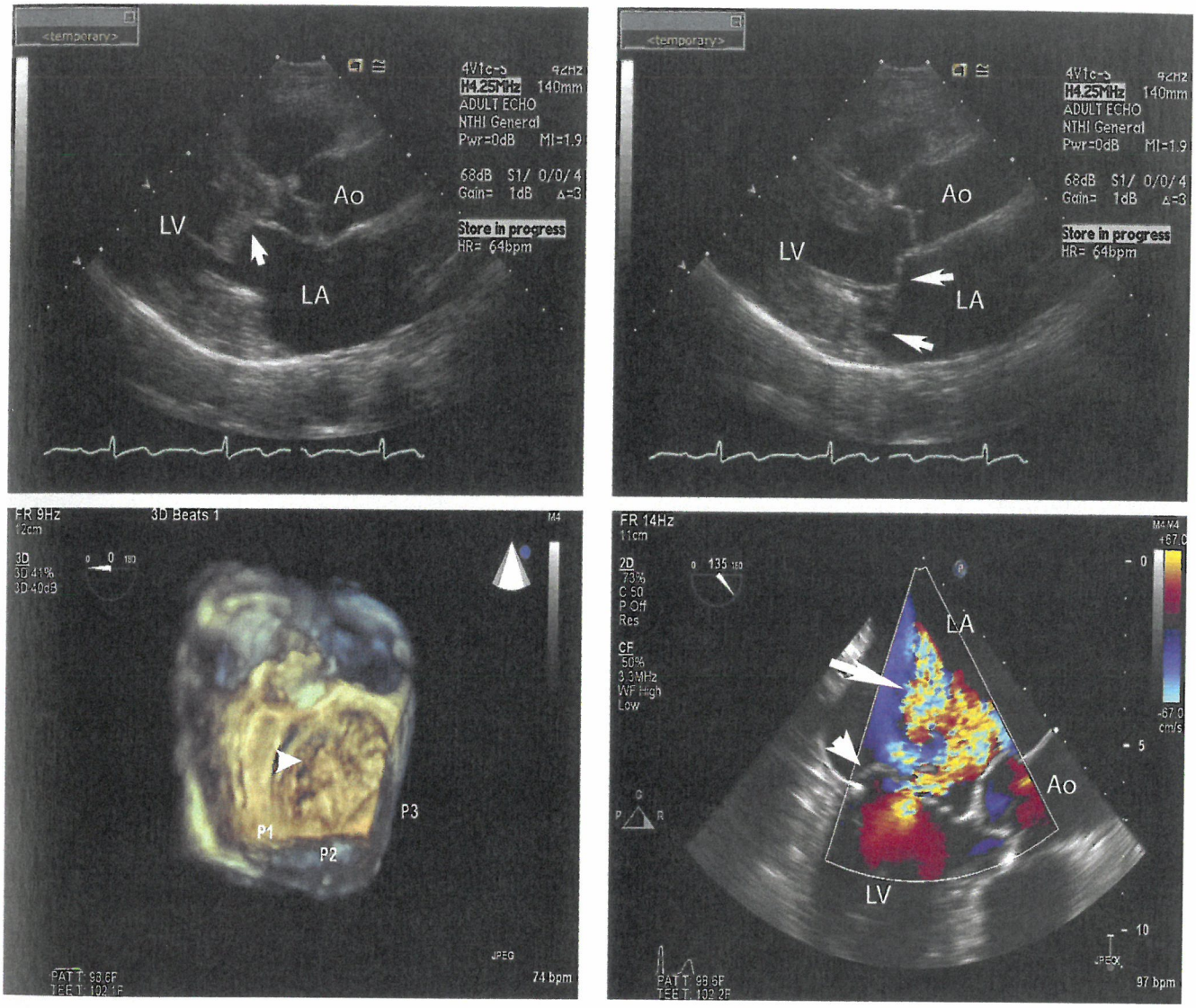

FIGURE 24. Mitral valve prolapse. Echocardiogram showing normal opening of the mitral valve (*arrow, top left panel*), which then prolapses into the left atrium during systole (*arrows, top right panel*). In a different patient with myxomatous degeneration, a flail portion of the posterior mitral valve is present (*bottom panels*); torn chordae are seen (*arrowheads*), leading to severe regurgitation seen on color flow imaging (*arrow, bottom right panel*). Ao = ascending aorta; LA = left atrium; LV = left ventricle.

greater than 95% and the operative risk is less than 1% or when serial imaging studies have demonstrated a progressive increase in LV size or decrease in LVEF. Mitral valve repair should also be considered in asymptomatic patients with chronic severe primary mitral regurgitation who have new-onset atrial fibrillation or pulmonary hypertension (pulmonary artery systolic pressure >50 mm Hg). Surgical repair is preferred over replacement in all patients, and patients should be referred to a surgical center with expertise in valve repair. Medical therapy with vasodilators in patients with primary mitral regurgitation is not beneficial in the absence of symptoms or LV dysfunction.

For patients who are not surgical candidates, mitral valve repair with a catheter-based clip device was approved by the FDA in 2013. The percutaneously delivered clip improves coaptation of the mitral valve leaflets, leading to increased valve closure and a reduction in regurgitation. In selected patients with primary mitral regurgitation, success rates with implantation of the device are approximately 90%, with a procedural mortality of approximately 2%.

In patients with chronic secondary mitral regurgitation, the primary goal of therapy is to address the underlying ventricular dysfunction with guideline-directed medical therapy and, if indicated, cardiac resynchronization therapy (see Heart Failure). Guideline-directed medical therapy for ventricular dysfunction includes ACE inhibitors, angiotensin receptor blockers, an angiotensin receptor–neprilysin inhibitor, β-blockers, diuretics, and/or aldosterone antagonists. Benefits of valve repair or replacement in patients with secondary mitral regurgitation are less certain, although studies have

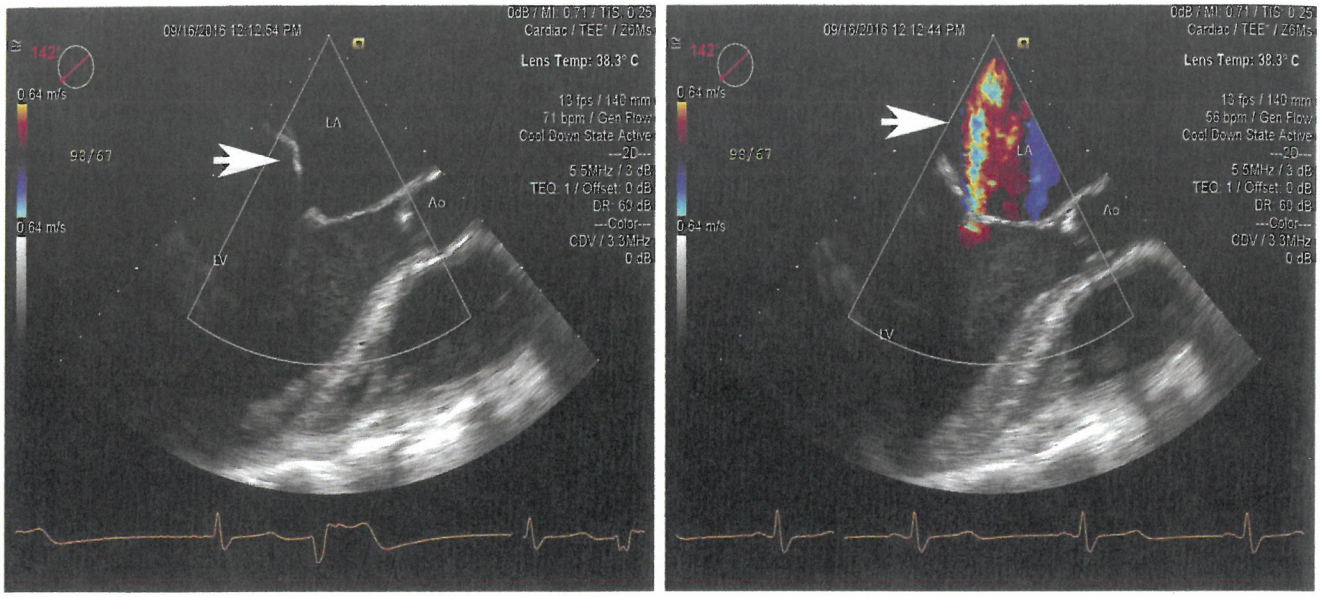

FIGURE 25. Secondary mitral regurgitation in a patient with prior inferior myocardial infarction. Tethering of the posterior leaflet (*arrow*) is present due to the prior infarction and left ventricular remodeling (*left panel*). Mitral regurgitation (*arrow*) is evident on color flow imaging (*right panel*). Ao = ascending aorta; LA = left atrium; LV = left ventricle.

demonstrated favorable LV remodeling after surgery. Surgery for secondary mitral regurgitation is generally advised for those undergoing concomitant cardiac surgical procedures (for example, coronary artery bypass grafting), but mitral regurgitation may recur after repair because of primary LV dysfunction. Trials of transcatheter mitral valve replacement for patients with secondary mitral regurgitation and high surgical risk are ongoing.

KEY POINTS

- Patients with acute mitral regurgitation may present with acute heart failure; these patients may be difficult to diagnose clinically or with echocardiography.
- The most common cause of chronic primary mitral regurgitation is mitral valve prolapse.
- Surgery for chronic severe primary mitral regurgitation is indicated in the presence of symptoms, left ventricular dilatation, or need for concomitant cardiac surgery.
- Surgical repair is preferred over replacement in patients with chronic primary mitral regurgitation, and patients should be referred to a surgical center with expertise to improve the chances of repair.
- Transcatheter mitral valve repair with implantation of a clip device is indicated for patients with chronic primary mitral regurgitation who are at high surgical risk.
- Patients with chronic secondary mitral regurgitation should be treated with guideline-directed medical therapy for ventricular dysfunction, although surgical intervention may be considered for those undergoing concomitant cardiac surgery.

Tricuspid Valve Disease

Tricuspid regurgitation, the most common form of tricuspid valve disease, is frequently functional and clinically asymptomatic. Causes of tricuspid regurgitation include cor pulmonale (or pulmonary hypertension) with right ventricular failure, pacemaker or defibrillator lead placement, trauma, congenital abnormalities, and infective endocarditis. When symptomatic, patients can present with fatigue from low cardiac output and symptoms and signs of right-sided failure, such as elevated jugular venous pulse (a large *c-v* wave), a palpable right ventricular lift, hepatic congestion with pulsatile liver, and peripheral edema. The murmur of tricuspid regurgitation is typically a holosystolic murmur heard along the left sternal border that increases during inspiration due to increased venous return.

Tricuspid regurgitation should be evaluated by TTE, which also allows assessment of right ventricular function and estimation of pulmonary pressures. In patients with tricuspid regurgitation due to pacemaker or defibrillator lead placement, TEE may be required to more clearly evaluate the regurgitant murmur.

Medical therapy with loop diuretics and aldosterone antagonists is effective in improving symptoms of right-sided congestion; however, caution should be exercised to minimize the potential for creating a low-flow state with impaired cardiac output. Surgery is recommended for patients with severe tricuspid regurgitation who are undergoing left-sided valve surgery. Additionally, surgery may be considered in patients with symptomatic tricuspid regurgitation who are unresponsive to medical therapy or have right-sided heart failure.

Tricuspid stenosis is nearly always caused by rheumatic disease. Other causes include radiation therapy, carcinoid