CHAPTER 2
Mitral regurgitation

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Introduction

Mitral regurgitation (MR) is the most frequent adult valvular lesion and the second most frequent reason for valvular surgery (after aortic stenosis). This chapter illustrates the evaluation of the patient with an asymptomatic pansystolic murmur. However, other typical clinical scenarios in which evaluation of MR is critical are the following:

1 The patient presenting with chronic dyspnea and a murmur suggesting MR.
2 The patient with severe dyspnea of abrupt new onset and a new murmur suggesting MR, with or without fever and signs of infection.
3 The patient with acute or chronic dyspnea, chronic coronary artery disease, an impaired left ventricle, and clinical or invasive evidence of MR.
4 The patient with acute severe dyspnea in the context of an acute coronary syndrome.

As in all forms of valvular regurgitation, assessment of severity is difficult, and no single parameter exists that is both easy to obtain and reliable for grading MR. Clinical assessment of MR therefore relies on gathering information on several characteristics and parameters, including mechanism, severity, duration, impact on the left ventricle, cardiac rhythm, amenability to repair, and other clinical data. These issues can almost always be resolved by careful clinical evaluation and application of modern imaging techniques (Table 2.1). Additionally, clinical and echocardiographic signs of the underlying etiology of MR should be sought systematically (Table 2.2).

Case Presentation

A 55-year-old man presents to his family physician for a routine check-up examination. He is physically active, completely asymptomatic, and in regular heart rhythm. A pansystolic murmur is heard over the apex, radiating to the axillary region. MR is suspected on clinical grounds and he is referred to a cardiologist for further evaluation.

Table 2.1 Imaging goals in mitral regurgitation.

Assessment of severity: mild, moderate, severe, and intermediary degrees, based on qualitative (color jet configuration, Doppler saturation, pulmonary venous flow) or quantitative (effective regurgitant orifice, regurgitant fraction, regurgitant volume) evaluation
Assessment of mechanism: normal/excessive/restricted mobility, degenerative changes (thickening, calcification, shortening), dilated annulus, structural damage, hypertrophic obstructive cardiomyopathy with systolic anterior motion, congenital anomaly
Assessment of location of regurgitant lesion (Fig. 2.4): anterior/posterior leaflet, anterolateral, central, posteromedial scallops (Carpentier nomenclature: P1–3, A1–3)
Assessment of left ventricular function: ejection fraction, left ventricular end-diastolic and end-systolic diameter (or volume), contractile reserve during stress
Other echocardiographic signs of underlying etiology: wall motion abnormalities for ischemic MR, leaflet thickening for mitral valve prolapse, doming and thickening for rheumatic valvular disease

Table 2.2 Etiology of mitral regurgitation.

Degenerative chordal rupture with consecutive flail leaflet , typically in mitral valve prolapse
Degenerative fixation of a leaflet (in particular the posterior leaflet)
Ischemic:
• Impaired left ventricular function with dilatation causing eccentric pull of papillary muscles, restricted leaflet motion, and incomplete closure, together with mitral annular dilatation
• Papillary muscle rupture following myocardial infarction
Dilated cardiomyopathy (similar mechanism as in ischemic impaired left ventricular function)
Infective endocarditis with valvular destruction
Rheumatic valve disease
Hypertrophic obstructive cardiomyopathy
Congenital disease, e.g. mitral valve cleft
Mitral prosthetic dysfunction:
• Postoperative suture dehiscence
• Bioprosthetic degeneration
• Bioprosthetic endocarditis with leaflet destruction
• Ring abscess with large paraprosthetic leak or prosthetic dehiscence
• Prosthetic thrombosis with fixed position of occluder
• Fracture of mechanical prosthetic valve with occluder embolization
Rare causes: trauma, postvalvotomy regurgitation, Libman–Sacks endocarditis (systemic lupus erythematosus)

Chest X-ray

In a patient with dyspnea, a chest X-ray usually is performed as part of the basic work-up. Although heart and heart chamber enlargement resulting from MR

(e.g. left ventricular and left atrial enlargement) can be diagnosed on chest X-ray, echocardiography is much more specific and accurate for these findings. Thus, nowadays the main information from a chest X-ray in MR is assessment of pulmonary congestion, ranging from mild pulmonary hypervolemia to frank pulmonary edema and pleural effusion. The absence of at least some degree of pulmonary congestion makes severe MR an unlikely cause for symptoms.

Case Presentation (Continued)

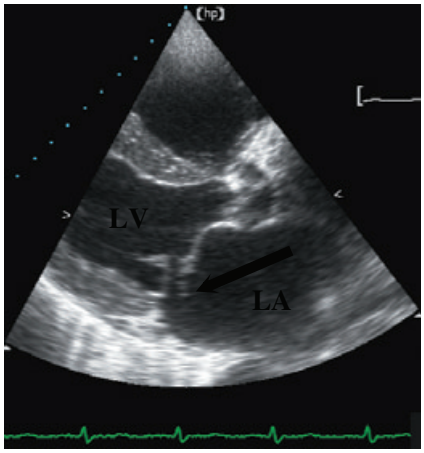
A chest X-ray demonstrates cardiac enlargement and mild pulmonary congestion. Kerley lines and pleural effusions are absent.

Which imaging modality for definite diagnosis?

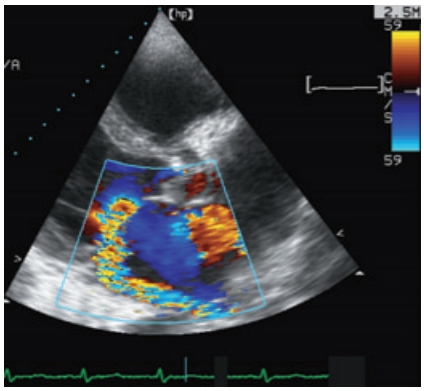
In clinical practice, two imaging modalities are used to evaluate MR: echocardiography and contrast ventriculography by cardiac catheterization. Contrast ventriculography is invasive, costly, carries a small risk, is operator-dependent, and subject to large interobserver variabilities in interpretation.[1] Nevertheless, a well-performed ventriculogram showing no or minimal MR excludes substantial regurgitation. With higher degrees of regurgitation, the influence of injection technique, amount of contrast, catheter position, left ventricular function, and premature ventricular beats become more pronounced. It is particularly difficult to separate moderate from moderate-to-severe or severe degrees of regurgitation. Ventriculography should not be considered a "gold standard," and evaluation of MR per se is only very rarely the indication for cardiac catheterization. None the less, a left ventriculogram is usually part of coronary angiography.

Echocardiography, while operator-dependent and having substantial interobserver variability, is now the dominant imaging technique to evaluate severity of MR, identify its mechanism, and devise therapy. Every patient with substantial MR should have an echocardiogram, and the decision to send a patient to surgery (especially if mitral repair is considered) mandates a thorough echocardiographic work-up, often with transesophageal echocardiography (Figs 2.1 & 2.2). Transesophageal echocardiography also is essential intraoperatively during repair surgery to assess results before the chest is closed.[2]

The use of three-dimensional (3D) echocardiography can improve the anatomic visualization of the different mitral valve scallops. For example, the location of prolapsing or flail leaflet segments is often immediately recognizable on 3D echocardiography, but requires expertise to pinpoint by conventional 2D echocardiography (Fig. 2.3). Communication with the surgeon may be aided by displaying "surgeon's views" from 3D data sets. Other benefits that may prove extremely useful, not only for diagnostic purposes, but also to help the surgeon in defining the feasibility and type of valve repair include a better appreciation



(a)



(b)

Figure 2.1 **(a)** Severe mitral regurgitation caused by a flail anterior mitral leaflet. Echocardiographic parasternal long axis view. The arrow points at the systolic position of the tip of the anterior mitral leaflet within the left atrium, thus creating a large regurgitant opening between anterior and posterior leaflet. **(b)** Color Doppler echocardiography, same patient and view as in (a). A large eccentric, posteriorly directed (away from the flail leaflet) turbulent, high-velocity jet is visible in the left atrium. LA, left atrium; LV, left ventricle.

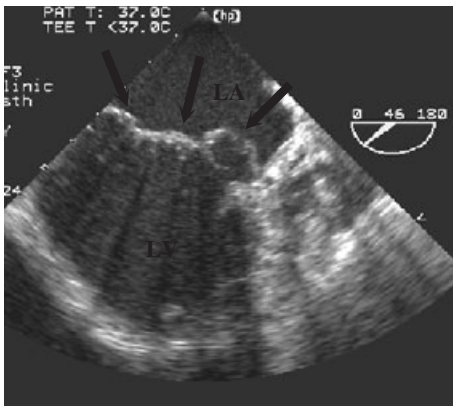


Figure 2.2 Mitral valve prolapse of both leaflets (arrows). Transesophageal view.

of the extension of the prolapse above the mitral annulus plane, the precise location of the diseased portion of the leaflets, its relation to important anatomic landmarks such as the valve commissures, and even the quantification of the volume of prolapsing tissue.[3] Furthermore, 3D echo is superior to 2D echo in calculating left ventricular volumes and ejection fraction.[4]

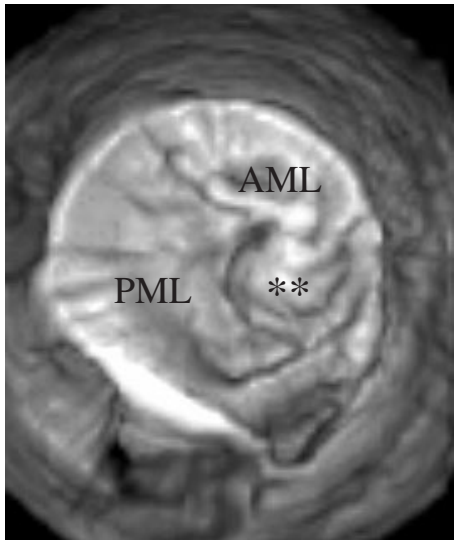


Figure 2.3 Three-dimensional echocardiography of a patient with prolapse (**) of the anterior leaflet of the mitral valve. AML, anterior mitral leaflet; PML, posterior mitral leaflet.

Magnetic resonance imaging (MRI) is the most recent imaging technique in the field. The morphologic and functional information MRI can provide is very similar to echocardiography, with somewhat lesser time and space resolution than transesophageal echocardiography. Atrial fibrillation substantially degrades image quality. Morphologic abnormalities of the leaflets can be detected, as well as high-velocity regurgitant jets. Regurgitant fraction can be calculated as the difference between left ventricular inflow and outflow, or between the difference of end-diastolic and end-systolic left ventricular volume on the one hand and aortic stroke volume on the other hand.[5] Left ventricular volumes and ejection fraction are assessed very accurately by MRI. Moreover, MRI can potentially provide much supplemental information in one examination, such as data on the presence and extent of myocardial scar, regional perfusion, and non-invasive coronary angiography (which, although currently rudimentary, is steadily improving). While these advantages, often summarized in the concept of "one-stop shopping" are impressive, practical reasons, apart from cost, nowadays and most likely in the future too will prevent MRI from superseding echocardiography, which will remain the first, and most often also the only, imaging technique needed. MRI at this time may be seen as an alternative technique if echocardiography cannot provide the necessary data. MRI can be safely performed in the presence of prosthetic valves, but is hazardous in the presence of a pacemaker.

Echocardiography in mitral regurgitation

Mitral valve morphology

Severe MR is always accompanied by morphologic abnormalities of the mitral

valve structure or configuration. Specific morphologic assessment of the mitral valve apparatus includes the following:

- *Leaflet morphology:* leaflets are thickened in myxomatous (classic) mitral valve prolapse, degenerative disease, and rheumatic disease. Endocarditic lesions may manifest as vegetations, pseudoaneurysms (a form of abscess), defects, and rupture of subvalvular structures as chordae. Calcification, especially of the posterior annulus and leaflet, occurs in advanced age, hypertension, renal insufficiency, and rheumatic valve disease.
- *Leaflet mobility:* mobility can be conceptually divided into normal, excessive, and restricted.[6,7] Excessive mobility is present in prolapse and flail (Fig. 2.3), while restricted mobility is caused by calcification or rheumatic disease. The most important cause of restricted mobility is eccentric pull (tethering) via the papillary muscles in a dilated ventricle resulting from coronary heart disease with ventricular remodeling (ischemic cardiomyopathy) or dilated cardiomyopathy, leading to incomplete closure of the mitral leaflets. In these circumstances, the mitral annulus is usually also dilated to some degree. Importantly, ischemic MR may be dynamic (i.e. may dramatically increase from minor to severe during acute ischemia).[8,9] This mechanism can be unmasked by exercise stress.
- *Damage to the subvalvular apparatus:* typical examples are (degenerative or endocarditic) chordal or (ischemic) papillary muscle rupture, leading to a flail leaflet or scallop with severe regurgitation. In rheumatic heart disease, the subvalvular apparatus, in particular the chordae, are thickened, calcified, and shortened.

Morphologic assessment should include not only the type of damage, but also the location of the lesion (Fig. 2.4). The posterior leaflet can be subdivided into three scallops, and the anterior leaflet can also be divided in three corresponding segments, although these are anatomically less well-defined than the posterior leaflet scallops. The nomenclature is either anatomic or follows the Carpentier classification (P1–3 and A1–3). The scallops of the posterior leaflet are usually designated anterolateral (P1, adjacent to the A1 region of the anterior leaflet), central (P2, adjacent to A2), and posteromedial (P3, adjacent to A3). The location of mitral valve pathology (e.g. a prolapse) has important implications for repairability.[2] It is also important to correlate morphologic findings with Doppler findings. Restricted leaflet motion leads to regurgitant jets directed towards the side of the affected leaflet, while excessive leaflet motion leads to regurgitant jets directed away from the affected leaflet.

Doppler assessment of hemodynamics

MR should be evaluated by color Doppler using all available windows, especially the apical views. Mitral regurgitant jets are often eccentric (Fig. 2.1b). Visual estimation of the maximal color Doppler jet and relating it to left atrial area yields a rough estimate of severity, but moderate and severe degrees cannot be reliably separated in this way, and eccentric, wall-hugging jets are severely underestimated by the jet area method. While very small and very large jets are

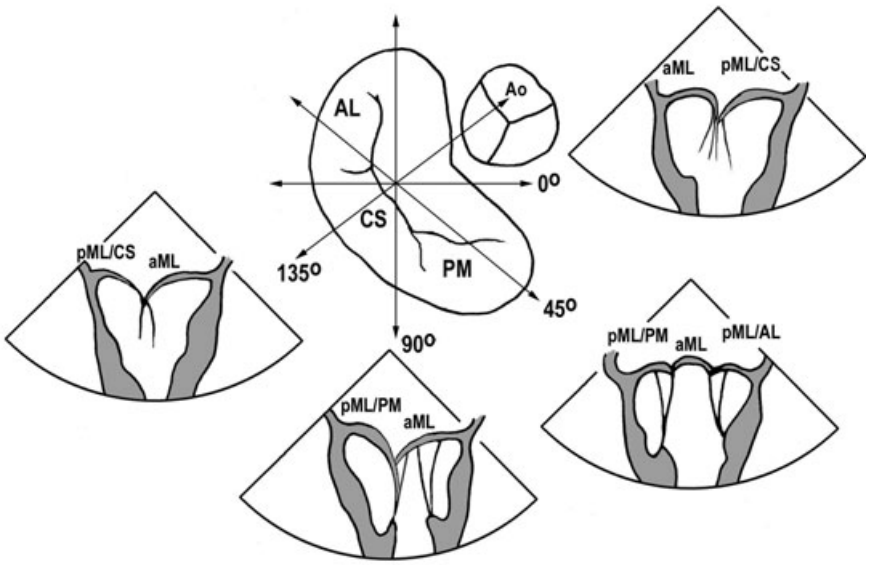


Figure 2.4 Mapping of the mitral valve by multiplane transesophageal echocardiography (schematic drawing). Four cross-sections from a transesophageal transducer position centered on the mitral valve are shown in a "surgeon's view" of the mitral valve, together with the relationship of the mitral leaflets as they are seen in these cross-sections: at 0°, corresponding to a four-chamber view; at 45°, representing an intermediate view; at 90°, corresponding to a two-chamber view; and at 135°, corresponding to a long axis view of the left ventricle. Different scallops of the posterior leaflet (pML) are visualized in the different views: the central scallop (pML/CS, corresponding to P2 in the Carpentier nomenclature) is seen in the four-chamber and the long axis view; the anterolateral scallop (pML/AL, corresponding to P1) in the 45° intermediate view; and the posteromedial (pML/PM, corresponding to P3) in the two-chamber and in the intermediate view. AML, anterior mitral leaflet; AO, aortic valve. (Reproduced with permission from Flachskampf FA, Decoodt P, Fraser AG, Daniel WG, Roelandt JRTC. Recommendations for performing transesophageal echocardiography. *Eur J Echocardiogr* 2001;**2**:8–21.)

usually well identified, the intermediate severities are impossible to grade reliably by color jet area. An important sign of severe MR that should always be evaluated is reduced or reversed systolic pulmonary venous flow (Fig. 2.5). In eccentric jets, it may be useful to sample both upper pulmonary veins to detect flow reversal.

Several quantitative approaches to evaluating MR severity have been validated and are clinically feasible, if image quality is good.[10]

1 Measurement of the proximal jet diameter, which evaluates the regurgitant orifice by measuring the smallest diameter of the regurgitant jet immediately downstream from its passage through the leaflet.

2 The proximal convergence zone method (PISA method). This technique an-

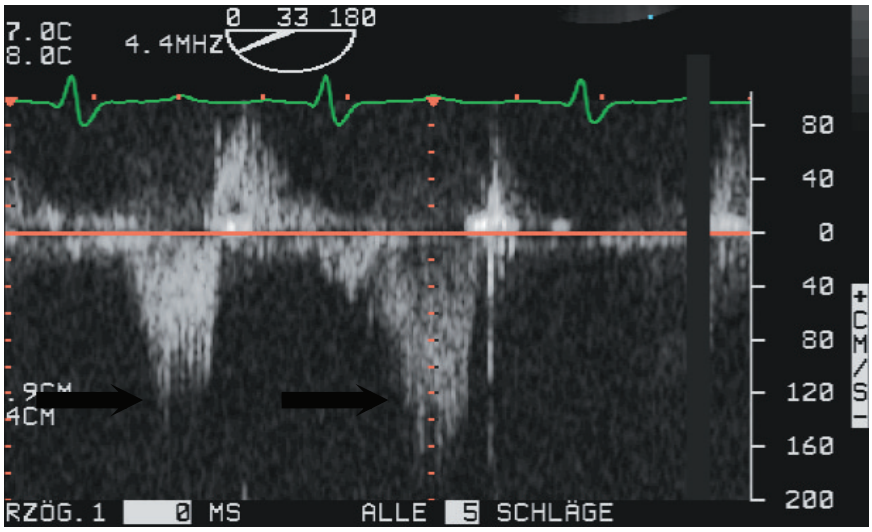


Figure 2.5 Pulsed wave Doppler recording from the left upper pulmonary vein in severe mitral regurgitation (MR) (same patient as Fig. 2.1). Systolic backward flow is present (arrows), indicating severity of regurgitation.

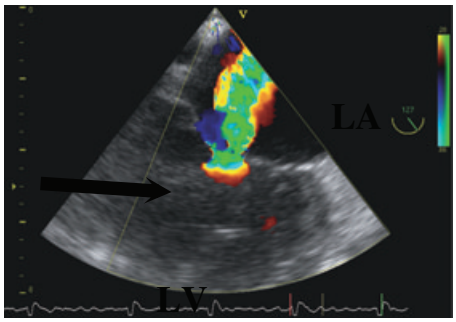


Figure 2.6 Transesophageal view of mitral regurgitation with large central jet and prominent proximal convergence zone (arrow).

alyzes the flow field upstream from the regurgitant orifice (i.e. on the ventricular side of the mitral valve; Fig. 2.6).

3 Calculation of regurgitant fraction based on the difference between transmitral stroke volume, calculated from pulsed-wave Doppler and mitral annular diameter, and transaortic stroke volume or the difference between end-diastolic and end-systolic left ventricular volume.

Right ventricular systolic pressure as assessed by measuring tricuspid regurgitation velocities is elevated in substantial MR, sometimes to severe pulmonary hypertension levels.

Evaluation of left heart morphology and left ventricular function

Quantitative morphologic parameters of the left ventricle important for the management of severe MR are as follow:

1 *End-systolic and end-diastolic left ventricular diameters (or volumes):* chronic (but not acute!) MR of more than mild severity leads to end-diastolic enlargement (dilatation) of the left ventricle as a consequence of volume overload. Initially, end-systolic diameter remains unaffected, thus leading to an increased shortening fraction, reflecting a hyperkinetic, volume-loaded ventricle. Increase in the end-systolic left ventricular dimension signals contractile impairment. A cut-off of 45 mm has been shown to predict persistent impaired left ventricular function after surgical correction of MR.[11]

2 *Left atrial enlargement:* more than mild chronic regurgitation leads to left atrial enlargement. In chronic severe MR, atrial fibrillation inevitably ensues, further promoting left atrial dilatation. The anteroposterior systolic diameter classically measured by M-mode is a relatively insensitive measure of left atrial enlargement. Left atrial enlargement is best assessed by planimetry of the left atrium in the four-chamber view.

3 *Left ventricular ejection fraction*, similar to fractional shortening, is of paramount importance in assessing MR and identifying candidates for surgical correction, especially in asymptomatic patients. Because MR initially leads to a hyperkinetic ventricle by increasing preload and decreasing afterload, even a low-normal ejection fraction (less than 60%) should be taken as a sign of beginning contractile dysfunction. Exercise ejection fraction may be used to unmask latent contractile dysfunction. Patients with severe MR who are unable to raise their ejection fraction in response to physical exercise (i.e. lacking contractile reserve) are candidates for surgical repair even in the presence of a normal ejection fraction.[12]

With state-of-the-art echocardiographic equipment most if not all these data can be acquired from the transthoracic echo. In patients difficult to image or with questionable results, transesophageal echocardiography is the next diagnostic step. Confirmation of the underlying mitral pathology and its location by transesophageal echocardiography, especially if the patient is a surgical candidate, will usually be sought to give the surgeon as much preoperative information as possible.

Ejection fraction calculation by echocardiography has considerable interobserver, intraobserver, methodologic (e.g. monoplane or biplane disk summation method), and day-to-day variability, the latter mostly resulting from changes in loading conditions such as arterial blood pressure. This variability needs to be kept in mind. Substantially more accurate and reproducible measurements of left ventricular volumes and ejection fraction are possible with 3D echoechocardiography or MRI, although this does not address the problem of load dependency of ejection fraction. Thus, in a few selected patients difficult to image or with inconclusive echocardiographic findings, an MRI may be clinically helpful.

Case Presentation (Continued)

Transthoracic echocardiography reveals a dilated left ventricle (end-diastolic diameter 59 mm; end-systolic diameter 41 mm). The ejection fraction is calculated to be 54%. The mitral valve is mildly and diffusely thickened, with a flail portion of the posterior leaflet well visible in the apical four-chamber view, indicating flail of P2 (central scallop of the posterior leaflet). There is an anteriorly directed, eccentric jet of MR with a proximal diameter of 8 mm, a reproducible proximal convergence zone on the left ventricular side of the mitral valve, and clearly reduced systolic forward pulmonary venous flow in the right upper pulmonary vein. The left atrium is mildly enlarged. There is moderate tricuspid regurgitation, with right ventricular systolic pressure calculated from the peak tricuspid regurgitant velocity to be 38 mmHg plus right atrial pressure.

In summary, this patient has asymptomatic, severe MR with low normal left ventricular function, sinus rhythm, and a presumably repairable lesion. Following the guidelines,[13,14] this constitutes a recommendation[14] or "IIa recommendation" ("weight of evidence/opinion is in favor of usefulness/efficacy"[13]) for mitral valve repair.

If ejection fraction was clearly in the upper normal range (more than 60%), stress echocardiography might be useful to determine whether ejection fraction increases during exercise. Failure to increase ejection fraction would indicate incipient impairment in myocardial contractility in spite of normal resting function.[12] A transesophageal echocardiogram would be additionally useful to confirm location and repairability of the regurgitant lesion.

Other important clinical situations

Acute severe mitral regurgitation

Acute MR is usually ischemic (e.g. papillary muscle rupture) or endocarditic in origin. Some typical features of severe chronic MR are missing in severe acute regurgitation:

1 Regardless of the severity of regurgitation, neither the left atrium nor the left ventricle are necessarily enlarged. At least initially, sinus rhythm is often preserved. However, the presence of enlargement does not exclude acute regurgitation, because concomitant or previous disease may have led to previous chamber enlargement.

2 Global left ventricular dysfunction is not a typical feature of acute MR, and typically there is left ventricular hyperkinesis as a response to the volume loading of acute regurgitation. However, left ventricular dysfunction does not exclude this condition, because there may be concomitant myocardial disease.

Mitral prosthetic regurgitation

With ever-increasing numbers of patients with mitral valve replacement, this scenario is becoming increasingly important. Importantly, the size of the left atrium and ventricle, as well as the level of pulmonary hypertension are influenced by pre-existing disease and therefore have to be interpreted with caution with respect to the severity of MR. Because of the difficulties inherent in imaging valve prostheses, transesophageal echocardiography is usually necessary for evaluation. Mitral prosthetic regurgitation can have several etiologies:

1 *Bioprosthetic degeneration:* the wear-and-tear lesions of bioprostheses may remain entirely clinically silent before a large tear suddenly manifests as torrential regurgitation.

2 *Infective endocarditis:* endocarditis often leads to ring abscesses which destroy the anchoring of the prosthesis in its bed. Regurgitation may range from paravalvular leakage to dehiscence, defined as abnormal mobility ("rocking") of the whole prosthesis, to embolism of the entire prosthesis. Furthermore, endocarditis can affect bioprosthetic leaflets in a similar manner as native valve leaflets.

3 *Paravalvular leakage or dehiscence* (Fig. 2.7): may occur as the result of suture insufficiency.

4 *Mechanical (and rarely, biological) prosthetic thrombosis or pannus interference:* may fix the occluder or leaflets in a half-open, half-shut position, leading to both severe stenosis and regurgitation.

5 *Prosthetic strut fracture:* this is a very rare cause of acute massive prosthetic regurgitation, leading to embolization of the occluder.

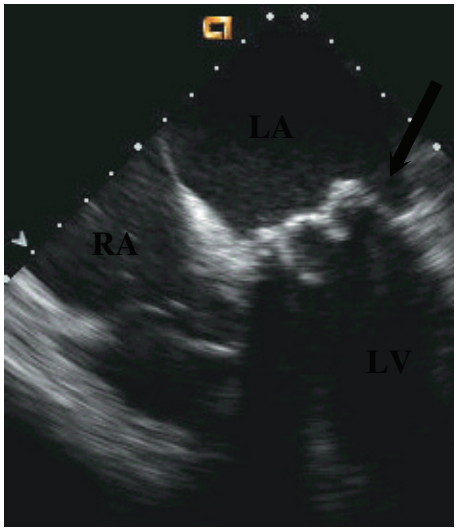


Figure 2.7 Lateral dehiscence (arrow) of a mitral bioprosthesis. Transesophageal four-chamber view in systole, showing displacement and tilting of the prosthesis towards the left atrium. RA, right atrium. (Reproduced with permission from Lambertz H, Lethen H. *Atlas der Transösophagealen Echokardiographie*. Stuttgart: Thieme, 2000.)

Role of imaging in management decisions in mitral regurgitation

The decision to treat MR surgically depends on careful appreciation of the following issues:[13,14]

- Presence of severe MR, at least if MR is the principal reason for surgery.
- Symptom status (dyspnea).
- Left ventricular function. Even mildly impaired or borderline left ventricular function constitutes an indication for valve surgery, even in the absence of symptoms. On the other hand, severely impaired left ventricular function (ejection fraction less than 30%) may render valve replacement a high surgical risk.
- Amenability of mitral pathology to repair surgery, especially if sinus rhythm can likely be preserved.

These issues can almost always be resolved by careful clinical and echocardiographic evaluation of the patient. In a few cases, contrast ventriculography, together with right heart catheterization, or MRI may be helpful.

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