Mitral Valve Insufficiency

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Mitral valve insufficiency is characterized by the presence of systolic reflow from the left ventricle to the atrium.

2.1 Classification and Etiology

The causes of mitral valve insufficiency may largely be divided into two categories: organic or primary and functional or secondary.

In the first case, the cause of insufficiency is due to a morphological change of the valve. Numerous diseases may damage the valve. Of the degenerative disease we may list myxomatous degeneration, fibroelastic deficiency or annular calcifications. Of the phlogistic diseases we may note rheumatic or bacterial endocarditis. Congenital defects include the isolated cleft of the anterior leaflet of the mitral valve (not to be confused with the cleft of the atrioventricular septal defect, which is a congenital malformation affecting the entire mitral valve apparatus), double orifice, parachute mitral valve etc. Ischemic diseases include fibrosis or rupture of the papillary muscles after acute myocardial infarction.

In the so-called “functional” form, the valve is described as morphologically normal (below we shall see that in reality this is not so) but insufficient due to a modification in the geometry of the left ventricle with which it is intimately connected. The changes to the left ventricle that cause insufficiency may be classified as localized (the most conventional case is inferoposterior infarction with “asymmetrical” transmission on the medial portions of the two leaflets) or diffuse (dilated cardiomyopathy with “symmetrical” traction on the entire valve closure). In this chapter we shall describe organic or primary, mitral insufficiency. In the next chapter we shall discuss functional, or secondary, mitral valve insufficiency.

One classification that has been particularly successful is the one of Carpentier [1], which differentiates insufficiency into three categories: mitral valve insufficiency with “normal” leaflet movement (type I), due to perforation or erosion of the leaflet(s) (generally in endocarditis) or dilatation of the annulus (e.g. in atrial fibrillation); mitral valve insufficiency with “excessive” leaflet movement (type II), such as prolapse or rupture of the chordae tendineae; and finally mitral valve insufficiency with reduced leaflet movement (type III), which can further be subdivided into type IIIa, where reduced movement is diastolic (mitral valve stenosis) and type IIIb, where the reduced movement occurs in systole due to leaflet traction or dilatation/deformation of the left ventricle.

In Western countries the most common cause of mitral valve insufficiency is due to degenerative changes, occurring in 60 % of cases, followed by “functional” changes (approximately 20–30 %), endocarditis (5–10 %), rheumatic (2–5 %) and a group of miscellaneous causes such as inflammation, trauma and congenital conditions (2 %) [2].
2.2 Degenerative Mitral Valve Insufficiency

Three types of degenerative mitral valve disease that are able to cause valve regurgitation can be distinguished: calcification of the mitral annulus, myxomatous degeneration and fibroelastic deficiency.

2.2.1 Calcification of the Mitral Annulus

Calcification of the mitral annulus is a degenerative process generally found in elderly people and particularly in women. The etiology is unknown but the fact that it occurs primarily in older age may imply a phenomenon related to hydraulic stress on the valve. Pathological conditions such as advanced-phase myxomatous valves, hypertension, chronic renal insufficiency and diabetes mellitus may accelerate calcification of the annulus. In such cases large calcificous formations can sometimes be observed. In approximately half of the cases of mitral annular calcification, the aortic cusp is also found to have calcifications. Initially calcification of the mitral annulus involves a nodular calcium deposit, generally located in the central part of the posterior annulus, then as degradation gradually progresses, a rigid, curved band of calcifications deposit or calcifications is formed that follows the outline of the annulus. In this state the calcification of the annulus may be considered a relatively common and benign condition in elderly patients. In fact, it causes mild valve insufficiency due possibly to the lack of the sphincter-like action of the annulus or to deformation and traction of the leaflets. When the entire annulus is involved, insufficiency may be associated with an atrioventricular gradient. Even in these cases the gradient is generally moderate. However, if calcification is considerably diffuse along the circumference of the annulus, extending to the body of the valve leaflets, the atrioventricular gradient may be large. These are examples of degenerative mitral stenosis (this stenosis being different from rheumatic stenosis, where calcifications first affect the commissures and leaflets). When widespread calcifications are present, it is possible that calcium deposit claws infiltrate the ventricular myocardium. If isolated, calcification can in rare cases lead to insufficiency requiring surgical correction; in this case the finding is uncommon. When calcification is associated with severe mitral valve insufficiency of a different etiology (e.g. myxomatous degeneration of the valve) or when it causes severe mitral stenosis, valve replacement may be necessary. The suture of the prosthesis on a calciferous annulus is a complicated surgical procedure: if the suture line is moved higher on the atrial wall, parts of the left atrium will be exposed to ventricular pressure in future. Suturing through a calcification mass means using smaller prostheses and anchoring the prosthesis on brittle tissue. Suturing the prosthesis around the calcification (including in the suture points) risks damaging the circumflex artery. Decalcifying the annulus before suture is possible but not always easy (especially if the calcification has infiltrated the ventricular myocardium) [3]. A little-used technique, but one that causes little trauma and yields convincing results, is decalcification with ultrasound.

Finally, it is possible that in large calciferous masses of the posterior annulus there is central “liquefaction”. This rare variant of annular calcification (0.6 % of annular calcifications) is known as caseous calcification of the annulus, or calciferous aseptic abscess of the annulus, and is generally an uncommon echocardiographic finding that does not appear to be correlated to any specific symptom; the internal part of the calcification is made up of a mix of calcium, fatty acids and cholesterol, with a “toothpaste” consistency [4].

2.2.1.1 Transthoracic and Transesophageal Two-Dimensional Echocardiography

The finding is often uncommon in the context of examinations performed for other reasons. A hyperechogenic formation infiltrating the
annulus and casting a cone-shaped shadow is sufficient for diagnosis.

Hyperechogenicity that characterizes the calciferous structures is not pathognomonic for calcium. It is worth remembering how a normal pericardium often shows equivalent hyperechogenicity but is not, in normal subjects, calciferous. Therefore, the key of interpretation cannot be based only on hyperechogenicity, but other information, such as the position and overall movement of the calciferous structure, must also be taken in consideration.

The extension of calcification can vary: nodular or affecting the whole posterior annulus with a semi-circumference (Fig. 2.1) or, finally, involving both the posterior and anterior annulus.

Regurgitation, in general, is mild if there are no associated valve diseases. In extensive forms, even the base of the leaflets is involved, reducing excursion and sometimes creating an atrioventricular gradient (which, in most cases, is moderate).

Widespread calcification of the mitral-aortic junction with involvement of the anterior leaflet becomes the determining factor for the development of an atrioventricular gradient. In fact, in such cases, it is the reduced excursion of the anterior leaflet that causes the decrease in the valve area. It is interesting to note that echocardiography shows how the excursion of the anterior leaflet is limited to only the distal portion of the leaflet, with the hinge point moved toward its free margin (Fig. 2.2).

Caseous degeneration has a particular and characteristic echocardiographic presentation enabling quick diagnosis: the presence of a large hyperechogenic case with an irregularly echolucent internal area (Fig. 2.3).

2.2.1.2 Transthoracic and Transesophageal Three-Dimensional Echocardiography

The possibility of distinguishing between annular calcifications using variations in the grayscale (or color), as in two-dimensional echocardiography, becomes more difficult using three-dimensional echocardiography. The grayscale variations are, in fact, used by the system to provide meaning to the depth: light gray (or beige in a blue/bronze color map) shows a structure closer to the observer, while increasingly darker tones of gray (or darker blue to black in the blue/bronze color map) are used for structures further away. However, calcifications that are at the same depth as other

![Fig. 2.1 a Transthoracic parasternal short-axis slice showing widespread calcification extending to the entire posterior annulus; b transesophageal two-chamber slice of the same patient. LA left atrium, LV left ventricle, RV right ventricle, LAA left atrial appendage](image)
non-calciferous structures maintain a substantially similar grayscale or color tone (Fig. 2.4).

It is, however, possible to distinguish between the presence of calcified and non-calcified areas. Seen from above, calcifications are generally depicted as an irregular protuberance from the annulus, of varying extent, above the surrounding structures (Figs. 2.5a, b). A second characteristic is their “rigidity” during the cardiac cycle: they move as a single unit, giving the careful observer the correct interpretation.

Even in case of caseous calcifications it is difficult to make a correct diagnosis with three-dimensional echocardiography when observing it from the left atrium. From this perspective they appear simply as a swelling of the atrial wall, which reduce the area of the valve annulus; only by obtaining a slice of the swelling, we realize that it is a caseous form, since the interior has characteristics that are different from the calciferous case (Fig. 2.6).

### 2.2.2 Myxomatous Degeneration

The macroscopic picture of the severe form is that of a large, thickened valve, often with a gelatinous consistency, with excess tissue (especially for the posterior leaflet, which can reach the same length as the anterior leaflet), clear annular dilatation, and thickening and lengthening of the chordae tendineae. Myxomatous degeneration of the valve has been defined using various names. In this text we shall refer to the disease using the name Barlow’s disease, which defines all the possible variants (rupture or otherwise of the chordae tendineae, diffuse or localized myxomatous degeneration, etc.). The exuberance of the leaflets and the lengthening of the chordae tendineae almost invariably lead to the protrusion of one or both leaflets (or part of them) over the plane of the mitral annulus (prolapse) in the left atrium. The prolapse is the “dysfunction” caused by this excess tissue and may also occur for other reasons (such as fibrosis and lengthening of the papillary muscles, as described below). Barlow provided the greatest contribution to the definition of the disease by showing that meso-systolic click syndrome and telesystolic regurgitation were a clinical entity apart [5]. Before then this auscultation finding was considered to be an “innocent” event caused, according to many authors, by...
pleuropericardial or extra-cardial adhesion. Barlow et al., in a study published in the American Heart Journal in 1966, succeeded in showing, with the help of cineventriculography, that the meso-telesystolic click was of mitral origin. He called this abnormality an “aneurysmal protrusion” of the posterior leaflet. The name “mitral valve prolapse” was coined by Criley in

Fig. 2.4 a Parasternal short-axis two-dimensional images showing extensive and irregular calcification involving the entire posterior annulus; b three-dimensional image of the same patient obtained with the apical approach, rotated and sliced in order to visualize the mitral valve from above. It is noted how the calcifications appear as an irregular mass, which nevertheless maintains color tones that are not dissimilar from neighboring structures.

Fig. 2.5 a Three-dimensional echocardiographic images of the mitral valve seen from the atrium in a patient with extensive calcification of the posterior portion of the annulus. It is noted how the calcification, being at the same depth as the leaflets, has the same beige tone. However, it can be distinguished due to its irregular shape (arrows) and the fact that it is slightly higher than the posterior leaflet; b nodular calcification inserted in the center of the posterior portion of the annulus. Once again, it is not the color tone (similar blue to the surrounding structures) but rather the fact that it is slightly higher that enables diagnosis (arrows).
the same year in a study published in the British Heart Journal [6].

Myxomatous degeneration leads to degradation of the extracellular matrix: the spongiosa layer of the valve is filled with mucopolysaccharide material and thickens. The mucopolysaccharide substance overflows onto other layers, altering the organization and architecture of the collagenous fibers of the fibrosa and the elastic fibers present in the atrialis and ventricularis. Increasingly thicker mucoid tissue areas are present between the collagenous fibers, separating them. The collagenous fibers are reduced, taking on a spiral form. Even the structural characteristics of the fibers are changed, with a reduction in type I collagen and an increase in type III, which is less resistant to traction. The elastic fibers of the atrialis and ventricularis have a similar fate, being fragmented [7]. Finally, even the chordae tendineae experience mucoid infiltration, which fragments the fibrous core. Depending on the accumulation of mucous substances and the fragmentation of collagen, the chordae may appear either flexible or swollen, but functionally weaker. The main cause of this structural “chaos” seems to be
excessive proteolytic activity (affecting collagen and elastic fibers too) by the cell population that is present in the spongiosa with degradation of collagen and elastin and accumulation of proteoglycans [8]. The changes described above, whether affecting the connective fibers or the elastic fibers, weaken the leaflets and chordae tendineae, representing the histopathological substrate of the structural weakness of the valve. It is likely that myxomatous degeneration of the mitral valve is the joint outcome of a mix of genetic changes that weaken the connective tissue of the valve, leading to the macroscopic and microscopic picture described above [9].

The diagnosis of mitral valve prolapse is made, other than by clinical assessment, obviously (and especially) with echocardiographic examination. There are at least three reasons why echocardiography is the technique of choice in studying this disease:

1. it is the most widespread technique in cardiology. Even a small cardiology unit has echocardiographic equipment and a cardiologist able to interpret the images: echocardiography is part of a cardiologist’s training in all specialist medical schools;
2. it often provides all the information required for correct management: from the morphology of the valve to the regurgitation entity, from the overall and regional left ventricular function to the involvement of other valves; it has, moreover, a primary role in intraoperative and postoperative assessment;
3. the introduction of three-dimensional echocardiography (transthoracic and transesophageal) has made it possible to visualize the mitral valve from perspectives that were previously impossible with traditional echocardiography (the most common being the so-called “surgical view” of the valve, seen from the left atrium, the same point of observation as in surgery).

The first diagnosis of mitral valve prolapse was made using the M-mode technique: the image of a posterior movement od more than 2 mm of the valve leaflets during systole or in meso-telesystole. The study was published by the Feigenbaum group in Circulation in 1971. The diagnostic image for mitral valve prolapse in the M-mode was similar to a holo-telesystolic “hammock” [10]. With the arrival of two-dimensional echocardiography, it was realized that the diagnostic accuracy of M-mode echocardiography was moderate. In fact, a small variation in the angle of a single ultrasound beam compared to the mitral valve was sufficient to make the “hammock” image appear and disappear as required. With the advent of two-dimensional echocardiography, M-mode echocardiography was no longer used.

Two-dimensional echocardiography started to be used in the 1970s and, unlike M-mode echocardiography, had the essential prerequisites to become the reference method for the diagnosis of mitral valve prolapse: it was a technique that provided images of the valve in “real time”, depicting the annulus or valve leaflets, i.e. the two structures used for diagnosis and, above all, defined the spatial relationship between these even in a single plane. However, with this method mitral valve prolapse was diagnosed with unexpected frequency: 13% of the general population and an additional 34% of young women with aspecific symptoms [11]. A real and genuine epidemic! It also achieved the unexpected, since the “echocardiographic” diagnosis of mitral valve prolapse in otherwise normal individuals with absolutely normal leaflet morphology (except for small prolapses) was associated with a worrying prognosis, with a considerable risk of endocarditis, stroke or unexpected death.

Today we know that this diagnosis was due to the erroneous notion that the mitral annulus was located on one plane: all the longitudinal echocardiographic slices, however, remained suitable, including the two points of the annulus, so that by joining them with a line, the hypothetic annular plane (which in normal subjects could not be exceeded by the leaflets) could be established.

It was Robert Levine who sorted things out [12]. In a work that brought him international renown, he showed that the mitral annulus was not located on one plane but had a three-dimensional “saddle-like” shape. For this reason
the diagnosis of prolapse may only be made with echocardiographic slices that visualize the more cranial portions of the annulus (anterior and posterior), i.e. in parasternal or apical long-axis slices. With this premise, the diagnosis of mitral valve prolapse became much less diffuse and in most cases (i.e. those with normal valve morphology) it was considered to be a benign syndrome. The Italian co-author of this work was Marco Triulzi, who at that time was an intern in Boston in the laboratory of Arthur Weyman and Bob Levine. Marco died a few years later from leukemia, but today Bob and colleagues at Massachusetts General Hospital in Boston still remember his contribution with affection.

2.2.2.1 Transthoracic and Transesophageal Echocardiography

Prolapse of the mitral valve occurs when one or more valve leaflets exceed the parasternal or apical long-axis annular plane in systole at least 2 mm. With these precise “coordinates”, mitral valve prolapse occurs in approximately 2–3% of the population and is equally distributed between men and women.

Using this cut-off point, even small prolapses with normal leaflets are included, and minimal telesystolic regurgitation is often observed in hyperkinetic patients with abnormal ribcages and fluid depletion, etc. Certainly, these patients cannot be considered at high risk for endocarditis, stroke, malignant arrhythmia or progression of regurgitation. In reality, one of the characteristics mitral valve prolapse due to myxomatous degeneration is tissue exuberance and irregular leaflet thickness (generally more acute in the pars rugosa). The coaptation area of the leaflets itself is higher, often at the height of the mitral orifice. If both characteristics are present, the leaflets exceed the mitral annulus more than 2 mm. Now, however, they are considered patients at risk as they are carriers of “classic” prolapse, with the characteristics of exuberance and thickening of the leaflets associated with protrusion of one or more leaflets by >5 mm [13]. In other cases we refer to small benign abnormalities, if not variations from the norm.

A transthoracic two-dimensional study is able not only to establish a diagnosis of prolapse but also to accurately define the location of the prevalent lesion. We have seen in Chap. 1 how the various regions of the leaflets can be identified with two-dimensional echocardiography. The same concept is applied when we shall identify the part of the leaflet(s) that prolapses: a transthoracic parasternal (or apical) long-axis view that shows the prolapse (or flail, with rupture of the chorda(e) tendinea(e)) of the posterior leaflet shows that the prolapse involves the central portion of the leaflet (or P2) (Fig. 2.7a). On the other hand, if the protrusion occurs with the anterior leaflet, this is an A2 prolapse. An apical “two-chamber” approach in which the prolapsed part of the leaflet is seen inserted on the lateral annulus (next to the left atrial appendage) (recognizable because the ventricular wall in continuity with the annulus is the anterior wall) suggests involvement of the lateral portion of the posterior leaflet (or P1) (Fig. 2.7b); when, however, the prolapse is found on the opposite portion, this means involvement of the medial part of the posterior leaflet, or P3.

The direction of the regurgitation flow is helpful as well. In fact, due to the obstacle caused by the prolapsed tissue, regurgitation flow is generally in the opposite direction from the prolapse. In prolapse of the posterior leaflet, reflow is toward the posterior part of the aorta, and for prolapse of the anterior leaflet toward the posterior wall of the atrium.

Regarding the transthoracic study, the transesophageal approach has the advantage of a better acoustic window (from the esophagus neither the ribcage nor the lungs are located between the transducer and the heart); furthermore, the proximity of the transducer to the posterior structures of the heart (including the mitral valve) enables the use of high-frequency beams with greater resolution. In expert hands, using a systematic approach (including the long-axis, two-chamber, four-chamber, transgastric short-axis, and off-axis slices) enables a
generally accurate diagnosis of mitral valve prolapse, defining sufficiently accurately which portion of the valve is prolapsed (Fig. 2.8).

Even in this case the direction of regurgitation flow helps us to better define the anatomy of prolapse (Fig. 2.9).

However, the diagnosis of prolapse with transthoracic and transesophageal two-dimensional echocardiography is not always precise due to individual anatomical variability. For example, a very wide prolapsed P3 scallop may be detected in a long-axis slice and therefore erroneously classified as P2. Moreover, only part of a scallop may be prolapsed (for example, the lateral segment of P2) or parts of various scallops (the lateral half of P2 and the medial part of P3), in these cases careful transesophageal assessment can be imprecise. Finally, in complex

Fig. 2.7  a Parasternal long-axis view showing evident prolapse of the central part (P2) of the posterior leaflet (arrows); b apical two-chamber view showing a small prolapse of the lateral part (P1) of the posterior leaflet (arrow). LV left ventricle, LA left atrium, Ao aorta, LAA left atrial appendage

Fig. 2.8  a Transesophageal long-axis slice showing prolapse of the central part (P2) of the posterior leaflet (arrows); b transesophageal two-chamber slice showing a small prolapse of the lateral part (P1) of the posterior leaflet (arrow). LV left ventricle, LA left atrium, Ao aorta, LAA left atrial appendage
lesions involving more scallops, it is objectively difficult to establish whether in a given slice the prolapse belongs to P2 or P3 and so forth. The new mesh catheter (which enables the acquisition of three-dimensional images) also has the capacity to simultaneously obtain two two-dimensional images with perpendicular slices (e.g., long-axis and two-chamber). The possibility of simultaneously visualizing two-dimensional images helps in the definition of valve morphology (Fig. 2.10).

**Fig. 2.9** a, b Same patient as in Fig. 2.5. It can be seen how the regurgitation flow is directed toward the posterior wall of the aorta; c, d wide flail of the anterior leaflet. In this case regurgitation flow is directed toward the opposite part. **LV** left ventricle, **LA** left atrium, **Ao** aorta

### 2.2.2 Transthoracic and Transesophageal Three-Dimensional Echocardiography

A peculiarity of three-dimensional echocardiography (transthoracic and transesophageal) makes it possible to visualize the whole valve in a single image. A second advantage is that, once volumetric data are acquired, we have the possibility of observing the valve from a virtually infinite number of perspectives. Even some which are not possible to see with two-dimensional
echocardiography. We shall see how, in general, three-dimensional echocardiography makes it possible to observe the surface face on. The mitral valve, when closed, is a surface that can be visualized either from the atrium (i.e. by observing it from the atrium in the so-called surgical vision) or from below (i.e. observing from the left ventricle).

It is necessary to state that transthoracic three-dimensional echocardiography has a frame rate resolution that is inferior to two-dimensional echocardiography (even if the latest generation of “mesh” transducers enables the acquisition of two-dimensional images derived from three-dimensional volumetric data, with better quality than two-dimensional images). However, this retains, that all the peculiarities above and therefore in face-on images can provide additional information compared to two-dimensional studies, especially in mitral valve prolapse. The valve may be observed face on either from the ventricular perspective or the atrial perspective. Unfortunately, both perspectives have limitations, which we shall discuss below.

With the parasternal approach, the ultrasound beam finds the tangential valve: this penalizes the quality of the image since it is mainly acquired with scattered echoes rather than specular echoes. If two-dimensional echocardiographic images are of good quality, the overall vision of the valve makes it possible to establish, with some certainty, the anatomical characteristics of prolapse by confirming and enriching the two-dimensional diagnosis. Sometimes, by rotating the image slightly, the software adds new tones that facilitate depth perception by helping the operator to better define the structural characteristics of the valve. Figure 2.11 shows an example of myxomatous valve prolapse seen from the atrium in diastole (Fig. 2.11a) and in systole (Fig. 2.11b). The image face-on does not precisely explain the prolapsed areas; however, by slightly rotating the image in direction of the arrow, the variation in color tones with the appearance of new “shadow areas” provides a more precise characterization of the anatomical structure of the valve (Fig. 2.8c), which presents prolapse of P3 and A2 (asterisks).

The apical approach is theoretically ideal, since the pyramid of ultrasound beams is perpendicular to the mitral valve and, in constructing the image, the system most often uses specular echoes, with a net improvement in resolution. However, we must bear in mind that as the beam gets further from the transducer, it diverges, with a net deterioration in lateral resolution. For this reason, with the apical transthoracic approach, the best images of the mitral valve are obtained by visualizing the valve from the left ventricle since the ultrasound beams do not diverge to

![Fig. 2.10 Wide flail of the anterior mitral leaflet (a) in a long-axis view and, simultaneously, (b) in a two-chamber view. LV left ventricle, LA left atrium, Ao aorta, LAA left atrial appendage](image)
a considerable degree. While this point of observation is ideal for mitral stenosis since the minimal valve area is at the apex of the bottleneck inside the left ventricle (see chapter on mitral valve stenosis), it is less so for prolapse. The surgical vision, if possible, does not always appear able to provide optimal images, since the others are much more distant, the ultrasound beams diverge, and the resolution of the three-dimensional image is penalized; in cases with an optimal acoustic window it is possible to distinguish the scallops and assess the extent of prolapse. Figure 2.12 shows a myxomatous valve with images obtained from the apical approach in diastole (Fig. 2.12a) and systole (Fig. 2.12b). Once again, a slight rotation of the image enables a better definition (Fig. 2.12c).

Three-dimensional images using slices that correspond to two-dimensional images generally do not add any data compared to simple two-dimensional echocardiography, and thus the quality of the image is inferior. Figure 2.13 shows an apical four-chamber view of the prolapsed posterior leaflet obtained with two-dimensional imaging and three-dimensional imaging. As can easily be ascertained, the three-dimensional image, if we exclude the possibility of seeing the trabeculae of the left ventricular wall on a deeper plane (irrelevant information for the diagnosis of prolapse), does not provide any additional data compared to two-dimensional imaging.

However, if we use the same volumetric data, but orient the image in order to have the mitral valve opposite the left atrium and rotate it in order to visualize the mitral valve as seen in surgery (Fig. 2.14b), we realize how the prolapse is restricted to the central zone of the posterior leaflet. Until the quality of the three-dimensional image is inferior to the two-dimensional image, the added value of this technique compared to two-dimensional imaging (and this is the reason that it is worth using it) lies simply in its ability to see structures face on.

The so-called “vision from the atrium or surgical vision” obtained with three-dimensional transesophageal echocardiography is optimal for various reasons: (a) a perpendicular incidence angle between the pyramidal ultrasound beam and the valve; (b) the proximity of the transducer (in the esophagus) enables the use of high frequencies (7 MHz), the maximum possible resolution; (c) the absence of interference due to structures with high acoustic
impedance such as ribs and lungs. Figure 2.15 shows the same patient as in Fig. 2.14, who was studied with transthoracic (Fig. 2.15a) and transesophageal (Fig. 2.15b) three-dimensional echocardiography. The difference in image quality between the two techniques is obvious. As with transthoracic three-dimensional echocardiography, transesophageal three-dimensional echocardiography provides a dynamic vision of the whole mitral valve in a single image. The prolapse of one or more parts of the valve may be seen in movement and the extension of the prolapsed part can be visualized in vivo, represented as a protuberance in the left atrial cavity (Fig. 2.16a), while, when observing the prolapse from the left ventricle, this appears as a depression (Fig. 2.16b).

In the case of chordal rupture, with an overall view, it is easier to establish the position and number of ruptured chordae, even if, it must be
admitted, due to poor lateral resolution the ruptured chordae appear thicker than they really are (Fig. 2.17).

Once the “volumetric data” are acquired, they can be “modeled” electronically (with slices in different perpendicular planes or with a free plane that enables slices on any plane) in order to obtain an image of the mitral valve without the surrounding tissue that conceals it. Images obtained by this means may therefore be rotated and angled in an infinite number of positions that make it possible to explain any information regarding, for example, prolapses close to commissures. Finally, “tangential” observation points on the prolapsed leaflet make it possible to visualize the regurgitation orifice which when “seen from above” generally covers the leaflet itself (Fig. 2.18).

In many cases, the lesions on the mitral valve are complex, involving several scallops. In these cases transesophageal three-dimensional echocardiography provides a greater contribution.

Fig. 2.14  a Same image as in the preceding Fig. 2.10, and b after having excluded the atrial wall and rotated the image in order to see the mitral valve from the left atrium. From this perspective it can be seen how the prolapse is restricted to the central part of the posterior leaflet (P2). LA left atrium, RV right ventricle, RA right atrium, AML anterior mitral leaflet, PML posterior mitral leaflet, TV Tricuspid valve.

Fig. 2.15 (a) Transthoracic and (b) transesophageal three-dimensional echocardiography. The difference in resolution between the two approaches is evident. Red circle ruptured chordae.
Figure 2.19 shows mitral valve insufficiency with a complex morphology. Two-dimensional echocardiography clearly shows a flail at P2. However, even P3 appears prolapsed and there is a calcification concealing P1 (arrow). Three-dimensional echocardiography confirms and clarifies the complex morphology of this valve: the flail is limited to P2 with the rupture of two small chordae. P3 is prolapsed while P1 is basically normal. The calcification is limited to the anterolateral portion of the annulus (near the fibrous trigone).

An accurate analysis of the three-dimensional image often makes it possible to verify that the lesion is much more complex than expected in the two-dimensional examination (Fig. 2.20).

It is not exaggerating to say that this technique has become a true gold standard in the evaluation of mitral valve disease. A comparison study recently conducted at the Mayo Clinic...
Fig. 2.18 a–d Multiple ruptured chordae tendineae of the anterior leaflet. Gradual rotation of the image in direction of the arrows, shows the regurgitation orifice (little white arrow)

Fig. 2.19 a Two-dimensional image of a complex valve lesion; b corresponding three-dimensional image (see text). LA left atrium, LV left ventricle, Ao aorta
yielded sensitivity and specificity rates of almost 100 % compared to surgical findings (considered the gold standard). The hypothesis that the residual differences between transesophageal three-dimensional echocardiography and surgery are due to inaccuracy in surgical assessment, can be surmised. It is doubtful that surgery may detect a small lateral or medial focal prolapse in a stable and weak heart that accompanies a large prolapse. This work was bravely exhibited by Dr. Giovanni La Canna in his recent study. In this excellent study, transesophageal three-dimensional echocardiography was performed in 222 patients with mitral valve prolapse or flail undergoing reparative surgery [11]. La Canna classified echocardiographic lesions as dominant when prolapse was \( \geq 5 \) mm and secondary, or mild, when prolapse was \( \geq 2 \) mm but \( < 5 \) mm. The latter are not easy to recognize with surgery. The clinical impact that uncorrected small prolapses may have in the patient’s later course is not clear. La Canna formulates the hypothesis that in time these prolapses may deteriorate and may be the cause of a certain number of repeat surgical interventions.

Figure 2.21 illustrates three examples of our cases with the corresponding surgical images, showing how three-dimensional echocardiography speaks the same language as heart surgery. Off-line evaluation with dedicated programs makes it possible to obtain from three-dimensional images a series of parameters such as the surface area of the prolapsed valve, the height of prolapse and the dimensions of the annulus (diameters, circumference and area) (Fig. 2.22). This information can be very useful for surgery (showing the amount of valve tissue to be removed); moreover, it makes it possible to distinguish prolapse due to fibroelastic deficiency from prolapse due to myxomatous degeneration (see below), and to assess the feasibility of transcutaneous repair using a mitral clip.

### 2.2 Degenerative Mitral Valve Insufficiency

#### 2.2.3 Fibroelastic Deficiency

Fibroelastic deficiency is a degenerative process affecting the mitral valve that develops in advanced age and presents a completely different histopathological picture from myxomatous degeneration [15]. In this degenerative form there is a net loss of collagenous tissue and, in particular, elastic tissue, which leads to a marked reduction of thickness of the leaflets and chordae tendineae but with a preserved layer architecture (pellucid being the term coined by Carpentier to describe the macroscopic appearance).
The valve becomes generally weaker and the rupture of one or more flexible chordae is the mechanism leading to insufficiency. The causes are unknown but seem to have a certain correlation with the patient’s age, with greater incidence after the 7th decade of life. The macroscopic picture is the one of a flexible, translucid valve with normal dimensions. It is interesting to compare the two pictures of degenerative change of the mitral valve: myxomatous degeneration and fibroelastic deficiency. Myxomatous degeneration appears earlier in the course of life compared to fibroelastic deficiency and therefore the clinical history of insufficiency is known for several years; patients with myxomatous degeneration arrive at need for surgery at a younger age (mean age approximately 50 years); fibroelastic degeneration is more common in elderly patients and has a relatively short clinical history of insufficiency that requires surgery much later on (mean age 70 years). In the first case there is an accumulation of mucopolysaccharide substances that alter the layered architecture of the leaflets, and in the second case the layered structure is preserved and connective and elastic tissue is reduced. Macroscopically, in myxomatous degeneration you can observe swollen, opaque leaflets with a clear excess of tissue, a dilated annulus and thickened chordae tendineae;
fibroelastic deficiency is characterized by translucent, flexible leaflets, with no excess tissue, with an annulus of normal dimensions and flexible chordae tendineae. The appearance of regurgitation in such cases is invariably due to ruptured chordae tendineae with the involvement of a single scallop, while in the case of myxomatous degeneration regurgitation is present even in absence of chordal rupture.

2.2.3.1 Transthoracic and Transesophageal Two-Dimensional and Three-Dimensional Echocardiography

The possibility of using echocardiography to distinguish between the two classical degenerative forms, fibroelastic deficiency and myxomatous valve, is principally based on the observation that in the former only one scallop is usually involved and the remaining parts of the valve do not have a myxomatous appearance (Fig. 2.23).

Using dedicated software, a recent study with transesophageal three-dimensional echocardiography indicated the quantitative cut-off point that made it possible to distinguish more objectively between these two entities. Taking the heart surgeon’s judgment during tactile examination of the valve as gold standard, the height of the prolapsed valve of more than 1 mm separated the valves with degenerative disease from a control group with no mitral valve disease, while an underlying volume of prolapsed tissue equal to or greater than 1.15 ml separated the myxomatous valves from those affected by fibroelastic degeneration [15].

Figure 2.24 shows a second case of fibroelastic deficiency in our case history. The flail of the medial part of the anterior leaflet (A3) with a
Fig. 2.23  a Transesophageal long-axis two-dimensional image of an 84-year-old patient with prolapse and rupture of a chorda tendinea of the posterior leaflet. The arrow indicates rupture of a small chorda tendinea of the central segment of the posterior leaflet. It is shown how the anterior leaflet does not have the characteristics of a myxomatous leaflet, but appears substantially normal;  
b transesophageal three-dimensional echocardiography of the same patient. The image is rotated in order that the observer is to the right of the valve. The orifice of the left atrial appendage (LAA) is seen face on. This perspective confirms that the only part of the mitral valve that is prolapsed is the central part of the posterior leaflet (PML). The anterior leaflet (AML) is not prolapsed and does not appear myxomatous. With these characteristics fibroelastic deficiency was diagnosed.

Fig. 2.24  Three-dimensional image of the mitral valve seen from the left atrium in an 86-year-old patient with severe mitral valve insufficiency (a) in diastole and (b) in systole. Prolapse with rupture of a chorda tendinea (arrow) of the medial portion of the anterior leaflet (A3). The rest of the valve appears normal.
ruptured chorda tendinea (arrow) can be observed. Once again it can be seen how all the rest of the valve is substantially normal with no prolapsed or redundant tissue.

### 2.3 Inflammatory Disease: Bacterial Endocarditis

Despite progress in antibiotic therapy, with new and potent drugs, bacterial endocarditis remains a “malign disease” as defined by Sir William Osler in the pre-antibiotic era. The term endocarditis seems to limit inflammation only to endocarditis; even if this may be true in the early stages of infection, since the endocardium is the port of entry for microorganisms to take root, when infection is severe the lesions extend through the whole valve tissue. Bacterial endocarditis may affect all four heart valves and even valve prostheses, catheters or any other intracardiac device [16]. Here we shall discuss endocarditis of the mitral valve.

The mitral valve may be affected by infection in various ways, of which many lead to valve insufficiency. The classic anatomical and pathological picture is characterized by the presence of so-called endocardial “vegetation”: a mass of variable dimensions formed of fibrin, platelets, inflammatory cells, red blood cells, bacteria and a variable quantity of necrotic tissue. These vegetations are generally attached to the atrial surface of the valve, often, but not always, in areas that are already morphologically changed due to previous lesions (rheumatic or congenital). However, even though this is less common, the vegetation may also form in normal valve structures. The action of some virulent microorganisms may be so severe as to lead to destruction of healthy valve tissue and/or the progression of infective process inside the myocardial tissue with the formation of abscess cavities after a few hours or days. The first stage in the formation of endocardial vegetation is the adhesion of platelets and fibrin together with coagulation factors in endocardial microlesions. In normal conditions, these lesions are relatively common and their reappearance is a completely normal process. It is probable that these microlesions heal spontaneously with no sequelae, unless they are infected due to bacteremia (even transitory), with the entry of bacteria that initiates the formation of vegetation.

It is not a case of the microlesions on the mitral valve (and therefore the possible entry of bacteria) being almost exclusively located on the atrial surface of the coaptation area. In this area, in fact, there are two mechanisms that can cause microlesions: tangential stress (shear stress) of trans-valvular flow that may cause minor exfoliation of the endothelium on surfaces that are not perfectly smooth; and erosion that occurs along the coaptation line of the leaflets that enter into contact with each other with considerable acceleration due to intraventricular pressure. These microlesions happen more easily when the valve is altered: the turbulent flow caused by the regurgitation flow (whether diastolic as in mitral valve stenosis, or systolic as, for example, in mitral valve prolapse) promotes microlesions and therefore the entry of bacteria.

The ensuing valve insufficiency may be caused by rupture of the chordae tendinea, leaflet perforation, or erosion of the free margins. Even if the valve tissue is not damaged, the presence of vegetation itself may disturb normal leaflet coaptation and lead to valve regurgitation. It is interesting to note how it is possible that the mitral valve can be infected even on the left ventricular surface. In this case, valve infection is caused by endocarditis on the aortic cusps (secondary involvement). This may occur through contact; the phenomenon has been called mitral kissing vegetation [17]. A large amount of aortic vegetation that prolapses in the outflow tract of the left ventricle has contact with the ventricular surface of the anterior mitral leaflet during diastole, causing secondary infection. The infection may take root, which promotes further microlesions produced by the insufficient aortic flow hitting the ventricular surface of the mitral valve. The echocardiographer has to conduct a series of careful assessments of the mitral valve when large-scale
aortic endocarditis is observed, in order to avoid damage caused by the “kiss of death”. Another path for involvement of the mitral valve caused by aortic infection is by contiguity through the mitral-aortic junction. In general, the first structure to be affected is the anterior portion of the mitral valve annulus, with formation of an abscess in this area. Rheumatic endocarditis will be discussed in the chapter on mitral valve stenosis since its activity generally causes fusion of the commissures and reduction of the valve area.

2.3.1 Transthoracic and Transesophageal Two-Dimensional Echocardiography

Echocardiography is the main technique for studying endocarditis of the mitral valve. The echocardiographic diagnosis of this disease is based on morphological criteria and anatomical outcomes of the infectious process (annular abscesses, ruptured chordae tendineae). When echocardiographic images are clear, the diagnosis is relatively simple. The presence of an irregular mass on the atrial surface of one of the leaflets, oscillating with a motion independent of the leaflets, with a texture similar to the myocardium, makes the diagnosis of endocarditis fairly easily, especially when inflammatory indices are high and blood cultures are positive (Fig. 2.25).

Even if the most common location for the implantation of vegetation is the atrial surface, in the coaptation area microorganisms, especially if they are particularly aggressive, may be implanted in any part of the valve, including the chordae tendineae and papillary muscles. The anatomical sequelae of endocarditis of the mitral valve are chordal rupture, perforation of the leaflet, and formation of a peri-annular abscess (which is often complicated by fistulization in another chamber). Transesophageal echocardiography has considerably improved the diagnostic accuracy. While in ideal conditions transthoracic echocardiography can identify masses up to 3 mm, transesophageal echocardiography, thanks to its superior resolution, can identify masses up to 1 mm. Following the recommendations of the European Association of Echocardiography, transthoracic and transesophageal echocardiography must always be performed in patients with suspected endocarditis. The only clinical situation where a

Fig. 2.25 Large-scale endocarditic vegetation (arrows). Image obtained (a) with a transesophageal and a (b) transgastric approach. LA left atrium, LV left ventricle
The transesophageal study can be avoided in patients in whom the pre-test probability of endocarditis is low and the transthoracic study is negative and of high-quality [18].

The dimensions of the vegetations are considered to be a risk factor for systemic embolism. Sanfilippo et al. [19] observed that, starting from 6 mm, the risk of embolism grows linearly with the increase in the dimensions of vegetations. In general, the risk of embolism is three times higher in patients with an endocardial mass >10 mm compared to those with vegetations of minor dimensions. Even the mobility of vegetations plays a role: the more mobile the mass, the greater the risk of embolism.

In an early phase of infection, echocardiography, even the transesophageal approach, may be negative, despite the strong clinical suspicion. The negativity of echocardiographic findings must not lead to the ruling out of infection (it is worth remembering that echocardiography is not 100% sensitive) [20]. In such cases, it is possible that the dimension of the vegetation is still under the resolution power of echocardiography. Therefore it is worth conducting a second examination after 2–3 days. In other clinical situations, echocardiography may be negative despite the strong clinical suspicion due, for example, to massive calcifications (in such cases small endocarditic masses with a characteristic texture may be completely hidden by the calciferous mass or the cone-shaped shadow it casts); even small abscesses on the posterior leaflet may be missed when the leaflet is calcified. On the other hand, echocardiography is not

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**Fig. 2.26** Large-scale endocarditic vegetation (*arrows*). Image obtained with a transesophageal three-dimensional approach. Ao aorta, LV left ventricle

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**Fig. 2.27** Endocarditic vegetation on the anterior leaflet (*arrow*). (a) Two-dimensional and (b) three-dimensional image. Definition of the vegetation is better in the three-dimensional image. LA left atrium, LV left ventricle, Ao aorta
specific to 100%: it may also be difficult to identify vegetations when we are faced with a ruptured chorda tendinea in a myxomatous valve where the prolapsed leaflet may assume a very similar appearance to a vegetation. Three-dimensional echocardiography (especially transesophageal) may be useful to better define the position of the vegetation, even if in our experience it does not provide essential data to confirm or rule out the diagnosis of endocarditis (Figs. 2.26, 2.27, 2.28).

References

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