



The Mitral Valve

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In 1972, David E. Perloff, a cardiologist, and William Roberts, an anatomist, wrote the most educational paper on the mitral valve. These authors clarified that the mitral valve is not merely a couple of connective tissue flaps closing and opening secondary to the pressure gradient; it is a much more complex apparatus formed by several components working together in synchrony. Indeed, a perfect systolic competence of the valve and an unrestricted inflow requires precise spatial and temporal coordination. Only a reciprocal interaction between all the components will enable the normal function of the valve as a whole. Any anatomic change or disruption of one or more components inevitably causes mitral regurgitation. Anatomically, the valve consists of the mitral annulus, anterior and posterior leaflets, and the subvalvular apparatus of the chordae tendineae and papillary muscles. Because each of these components has a specific function, we will discuss them individually.

Mitral Annulus

In the cardiology community, the *mitral annulus* is commonly perceived as a circular ring of dense connective tissue from which the leaflets are suspended. The real architec-

ture of the mitral annulus is different from this “traditional” description, and in many aspects the mitral annulus is just a *concept* rather than a well-defined anatomic entity. Moreover, anatomists, surgeons, imagers, and others have used terms such as *atrio-ventricular orifice*, *atrio-ventricular plane*, *valve hinge*, and *mitral hinge line* to describe the same structure, causing confusion. The aim of this chapter therefore is to provide a clear description of this essential component of the mitral valve complex. For simplicity, we will continue to name this part of the valve the *annulus*. The posterior and anterior segments of the mitral annulus differ in structure and function, so they are described separately.

The Posterior Annulus

The posterior annulus, longer than its anterior partner, suspends the posterior leaflet and can be portrayed roughly as a letter “C” extending posteriorly from the left to the right trigones.

From an anatomical point of view, it can be described as the convergence of three structures: the atrial wall, the leaflet hinge, and the marginal free wall of the left ventricle. These structures are thought to be connected by a discrete band of fibrous tissue, giving the impression of a solid annulus (Fig. 1.1a). In reality, however, the fibrous band often is discontinuous, and when present, may have different consistency and robustness. There are differences in thickness and density not only among different individuals but also along different segments of the same annulus. In those parts in which the fibrous band is absent, the posterior leaflet is inserted directly on the ventricular myocardium. Because of this anatomical arrangement, the posterior annulus follows the myocardial contraction and relaxation, playing a fundamental role in the sphincter action (Fig. 1.1b).

From a surgeon’s viewpoint (that is, viewing from the left atrial side), this fibrous band is not visible. When present, it is located 2–3 mm external to the hinge line of the leaflet. What

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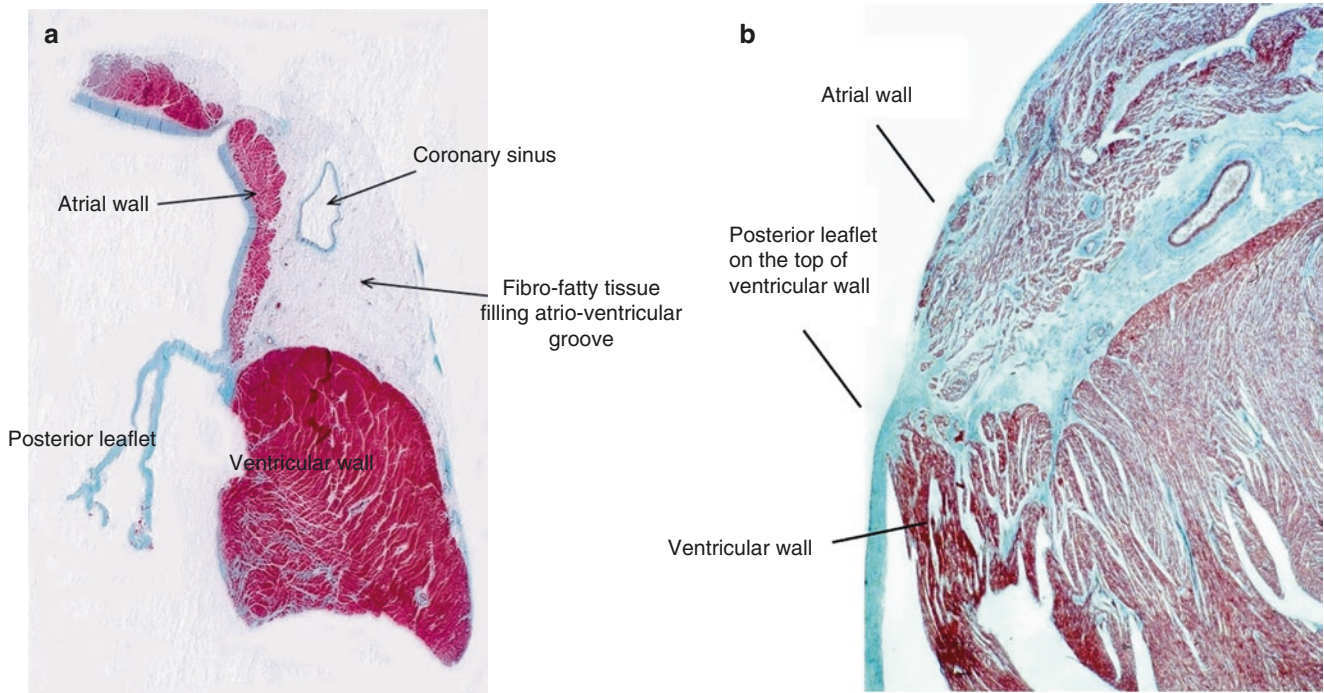


Fig. 1.1 (a) Histologic section of normal mitral valve stained in Masson's trichrome stain showing fibrous tissue in green and myocardium in red. Note the fibrofatty tissue plane separating atrial from ventricular myocardium. (b) Histologic section of another normal mitral

valve shows a less well-formed 'annulus'. Trichrome stain colors fibrous tissue green and myocardium in red. The posterior leaflet is inserted directly on the top of ventricular wall and has fibrous extensions into the atrial wall and atrioventricular groove

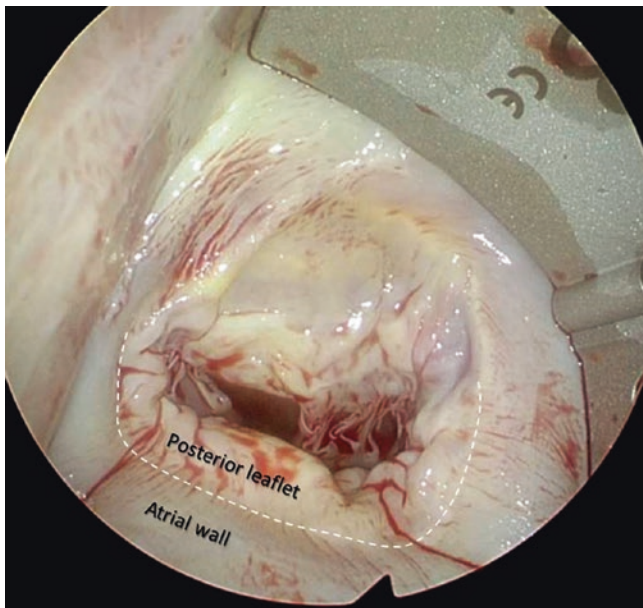


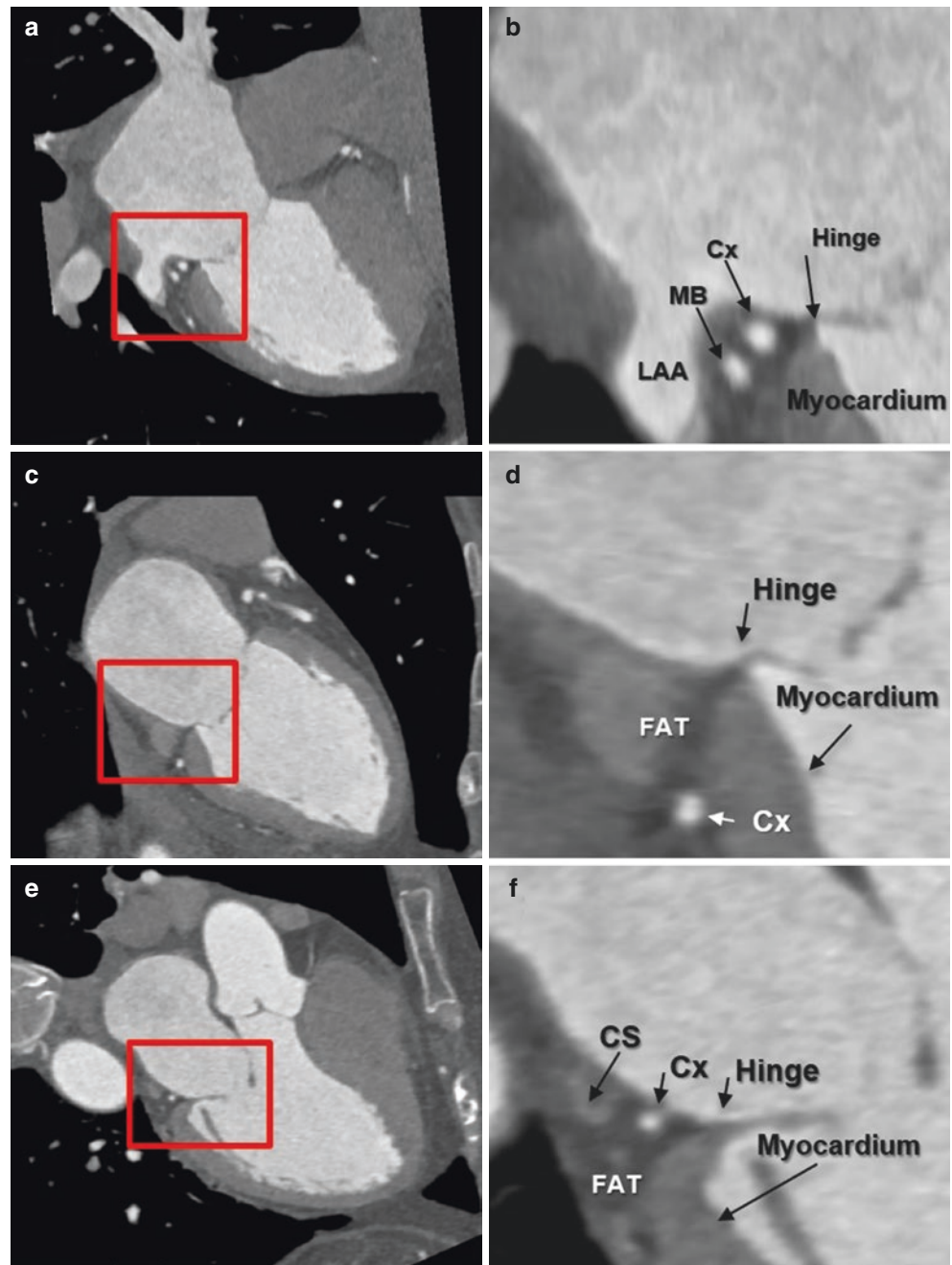
Fig. 1.2 Surgical view of the mitral valve. The dotted line marks the transition zone between the atrial wall and the posterior leaflet

the surgeons are clearly able to see is the "transition zone" between the atrial wall and the leaflet—the so-called *atrio-ventricular junction* (Fig. 1.2).

Finally, *from an imager's point of view*, the cross sections obtained by computed tomography (CT), cardiac magnetic resonance (CMR), transthoracic echocardiography (TTE), and transesophageal echocardiography (TEE) show the line of insertion of the posterior leaflet (hinge line). This line is the fulcrum upon which the leaflet opens and closes during the cardiac cycle. The CT scan is the best imaging modality to clarify the anatomy of this region. The spatial resolution of this technique, with the voxel as small as 0.6 mm, allows precise definition of the anatomy of the region. Different slices show the extreme variability of the anatomical relationship between the hinge line of the posterior leaflet and the vessels lying in the atrioventricular groove, reflecting the changeable relationships of the vessels as they course through the fat-filled groove (Fig. 1.3).

On the other hand, the unique ability of cine sequences of CMR to obtain strong signals from both blood and fat, coupling with weak signal from myocardium, provides images

Fig. 1.3 CT images showing cross sections of the posterior annulus in the four-chamber view (a), two-chamber view (c), and long-axis view (e). Magnified images of the areas in the red squares are shown in panels (b), (d), and (f), respectively. The variable spatial relationship between fat, leaflet hinge, myocardium, and vessels is evident. *Cx* circumflex artery, *CS* coronary sinus, *LAA* left atrial appendage, *MB* marginal branch



that reveal the adipose tissue that envelops the coronary arteries in the atrioventricular groove. This tissue contributes to the electrical insulation between left atrium and ventricle. Moreover, its presence is supposed to provide mechanical protection of the coronary arteries, buffering them against the torsion induced by the arterial pulse wave and cardiac contraction (Fig. 1.4).

TTE and TEE cross sections parallel images of CT and CMR, but the spatial resolution of the 2D TTE and TEE images is inferior to CT, and the tissue differentiation (differentiating fat from muscle) is less than with CMR because of the minimal differences in acoustic impedance between these two tissues. On the other hand, 3D TEE from an overhead perspective (surgical view) shows unique images of the

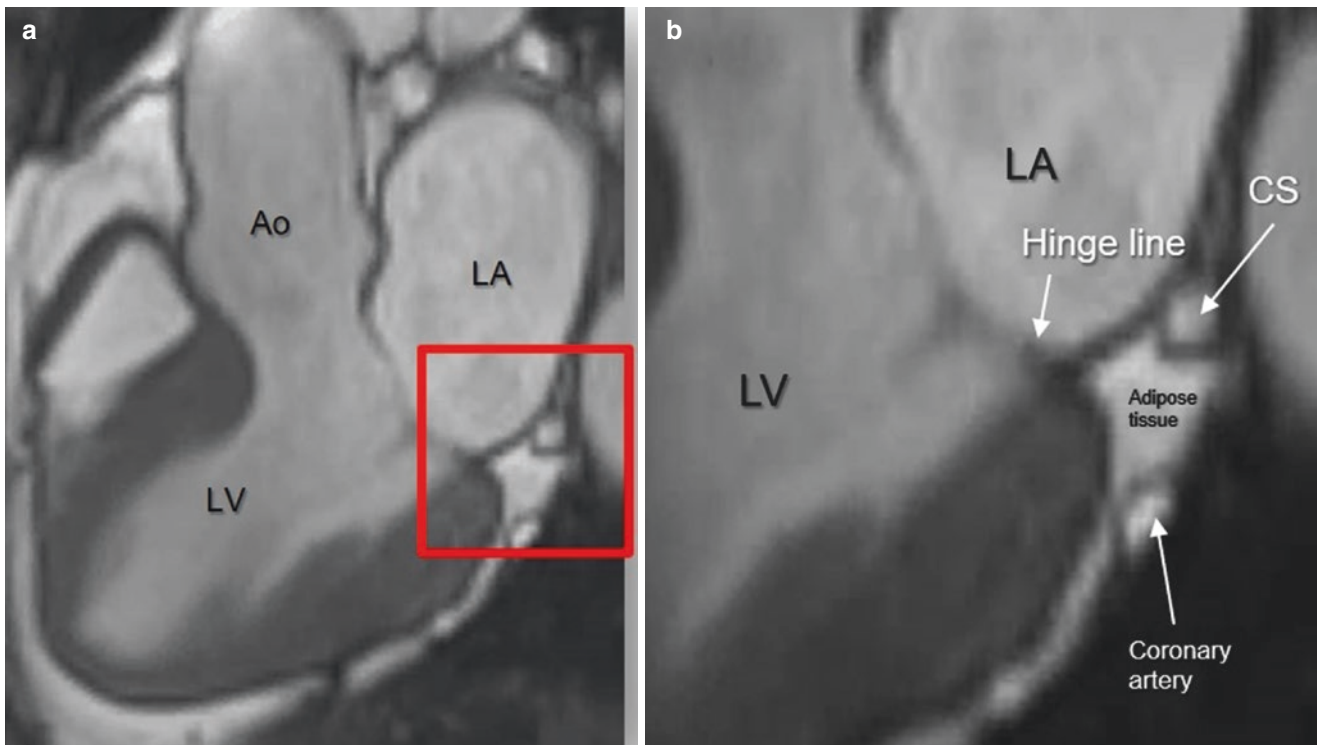


Fig. 1.4 (a) Cardiac magnetic resonance (CMR) cine images in long-axis view, obtained with steady-state free precession (SSFP). (b) The magnified image (*red square*) shows the atrioventricular groove with high-signal fat accumulation and vessels. The muscular

tissue has a low signal and is easily distinguishable from blood and fat. The coronary sinus (CS) is often located in a more atrial position with respect to the atrioventricular groove. *Ao* aorta, *LA* left atrium, *LV* left ventricle

“sphincteric” action of the annulus (Fig. 1.5). Still, neither CT, CMR, or TTE and TEE are capable of detecting the fibrous band as a distinct structure.

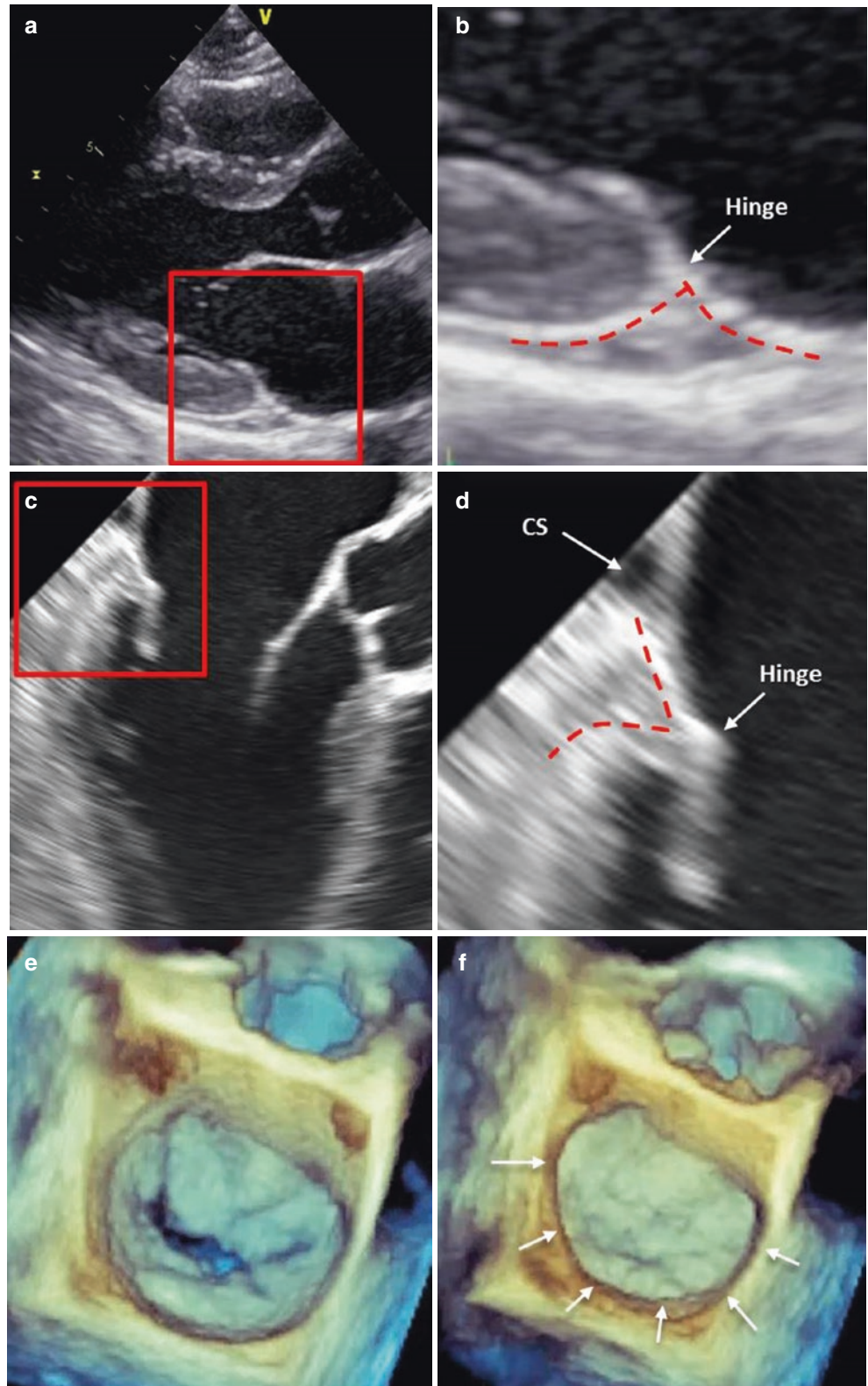
Two vessels are usually close to the posterior mitral annulus: the circumflex artery and the great cardiac vein continuing into the coronary sinus. The circumflex artery runs between the base of the left atrial appendage and the anterior-lateral commissure, initially a few millimeters from the hinge of the posterior leaflet; it then moves away from the posterior annulus. The great cardiac vein continuing into the coronary sinus borders the attachment of the posterior leaflet laterally, posteriorly, and then medially, opening in the right atrium just close to the medial commissure. The relationship between the hinge line of the posterior mitral leaflet and the coronary sinus is of particular relevance because of the potential percutaneous treatment of functional mitral regurgitation through a device placed inside the coronary sinus. In a significant number of individuals, in fact, the coronary sinus lies superior to the plane of the atrioventricular junction and the leaflet hinge line. In these cases, mitral annulus reduction through this percutaneous intervention may

result in traction applied on the left atrial wall rather than on the hinge line of the posterior mitral leaflet, with relatively minor impact on annular area reduction and mitral regurgitation (Fig. 1.6).

The spatial arrangement between the hinge line, muscular crest of the left ventricle, coronary arteries, and coronary sinus is also important in surgical valve reconstruction, as the stitches used to sew the prosthetic ring must be placed on the atrial wall about 2 mm above the hinge line, in order to be attached to a more resilient tissue, securing the ring and simultaneously preserving the motion of the leaflet. In the new percutaneous direct annuloplasty strategies using a flexible ring (such as Cardioband [Valtech Cardio Ltd. for Edwards Lifesciences, Nyon, Switzerland]), the anchors must be placed into the muscular/fibrous tissue around the posterior annulus, 2–3 mm externally from the hinge line of the leaflet.

The absence of a continuous dense band of connective tissue makes the posterior annulus prone to dilatation. Moreover, it is also a frequent target of extensive calcifications, the so-called mitral annular calcification (MAC).

Fig. 1.5 (a, b) Two-dimensional (2D) transthoracic echocardiography (TTE) long-axis view showing the posterior leaflet insertion. In the magnified image of the structures inside the *red square* (b), the hinge line of the posterior leaflet is clearly seen. The *dotted red line* marks the atrioventricular groove, but the vessel running in the groove cannot be visualized because of insufficient spatial resolution. (c, d) 2D transesophageal echocardiography (TEE) images of the posterior leaflet insertion. Although TEE has better spatial resolution than TTE, vessels in the atrioventricular groove also cannot be distinguished. (e, f) 3D TEE of the mitral valve from an overhead perspective in early diastole (e) and end systole (f), showing how the posterior annulus (*arrows*) contributes to the reduction of annular area (sphincteric action) following the left ventricular contraction. CS coronary sinus



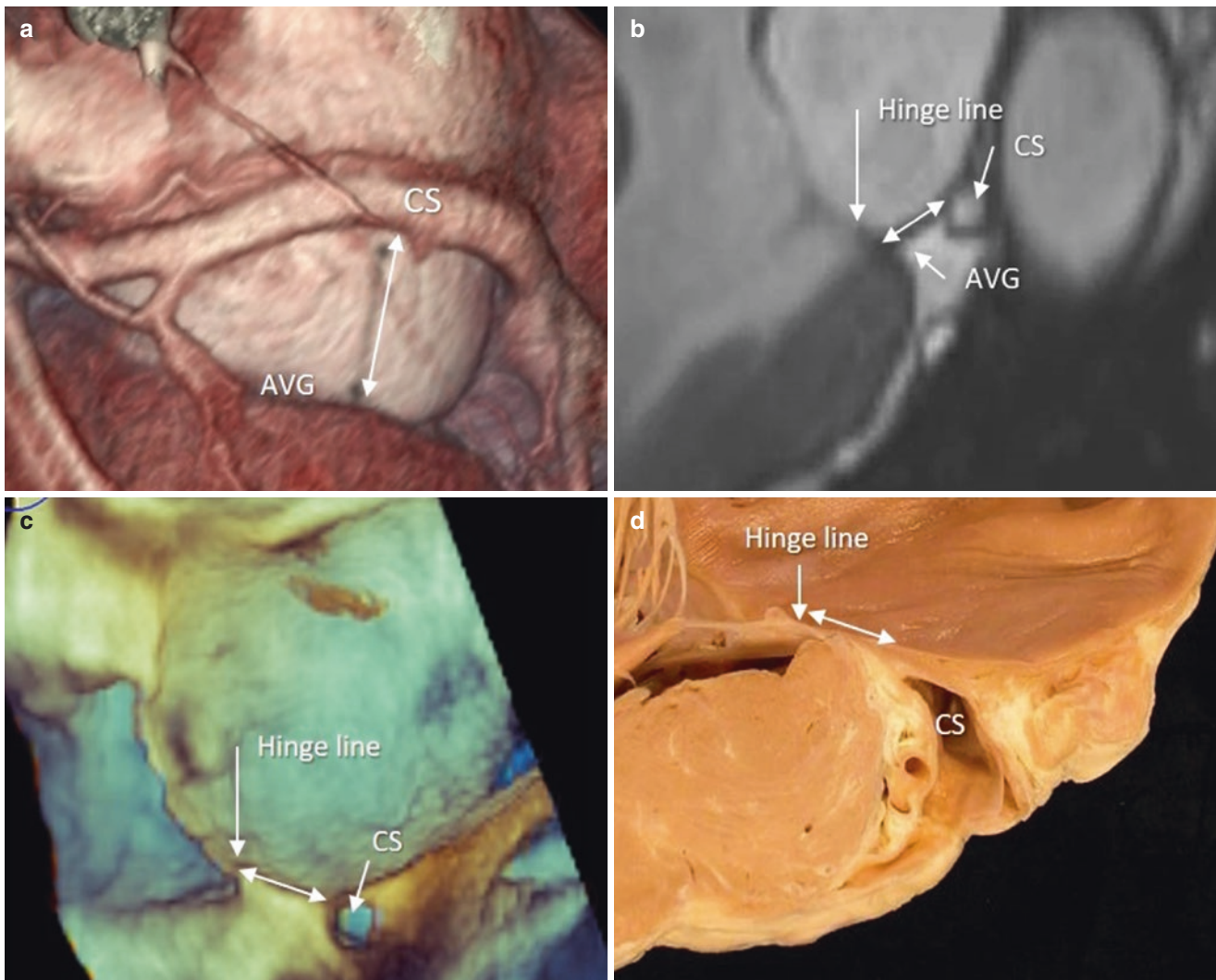


Fig. 1.6 The coronary sinus (CS) lies superior to the atrioventricular groove (AVG) and leaflet hinge line (*double-headed arrow*), as seen on CT volume-rendered acquisition (a), CMR SSFP sequence (b), 3D TEE (c), and an anatomic specimen (d)

Although often described as a passive, degenerative age-related process, accumulating evidence suggests that MAC is closely associated with vascular atherosclerosis and cardiovascular risk factors. MAC is also frequently observed in patients with renal failure, owing to abnormal calcium-phosphorus metabolism.

The Anterior Annulus

The anterior mitral annulus, considered as a band of connective tissue that anchors the anterior leaflet, simply *does not exist*. From a ventricular perspective, the anterior leaflet is, in fact, in continuity with a sheet of fibrous tissue (called the *mitral-aortic curtain*, *mitral aortic continuity*, or *mitral aortic intervalvular fibrosa*), which continues imperceptibly

into the left inter leaflet triangle. We will hereinafter refer to this area as the *mitral-aortic curtain*.

The mitral-aortic curtain is more or less rectangular and is delimited medially and laterally by two fibrous nodules, the right and left fibrous trigones. Compared with the body of the anterior mitral leaflet, this region presents a slight increase in thickness.

Seen from the atrial perspective, the mitral-aortic curtain comprises the atrial wall that extends up to the hinge line of the anterior mitral leaflet, which lies lower than the hinge line of the aortic leaflet. Thus, the space between the two hinge lines is occupied on the ventricular side by the mitral-aortic curtain (Fig. 1.7).

This region is well known to surgeons and imagers because in patients with aortic endocarditis or an aortic prosthesis, this area is predisposed to the development of abscess,

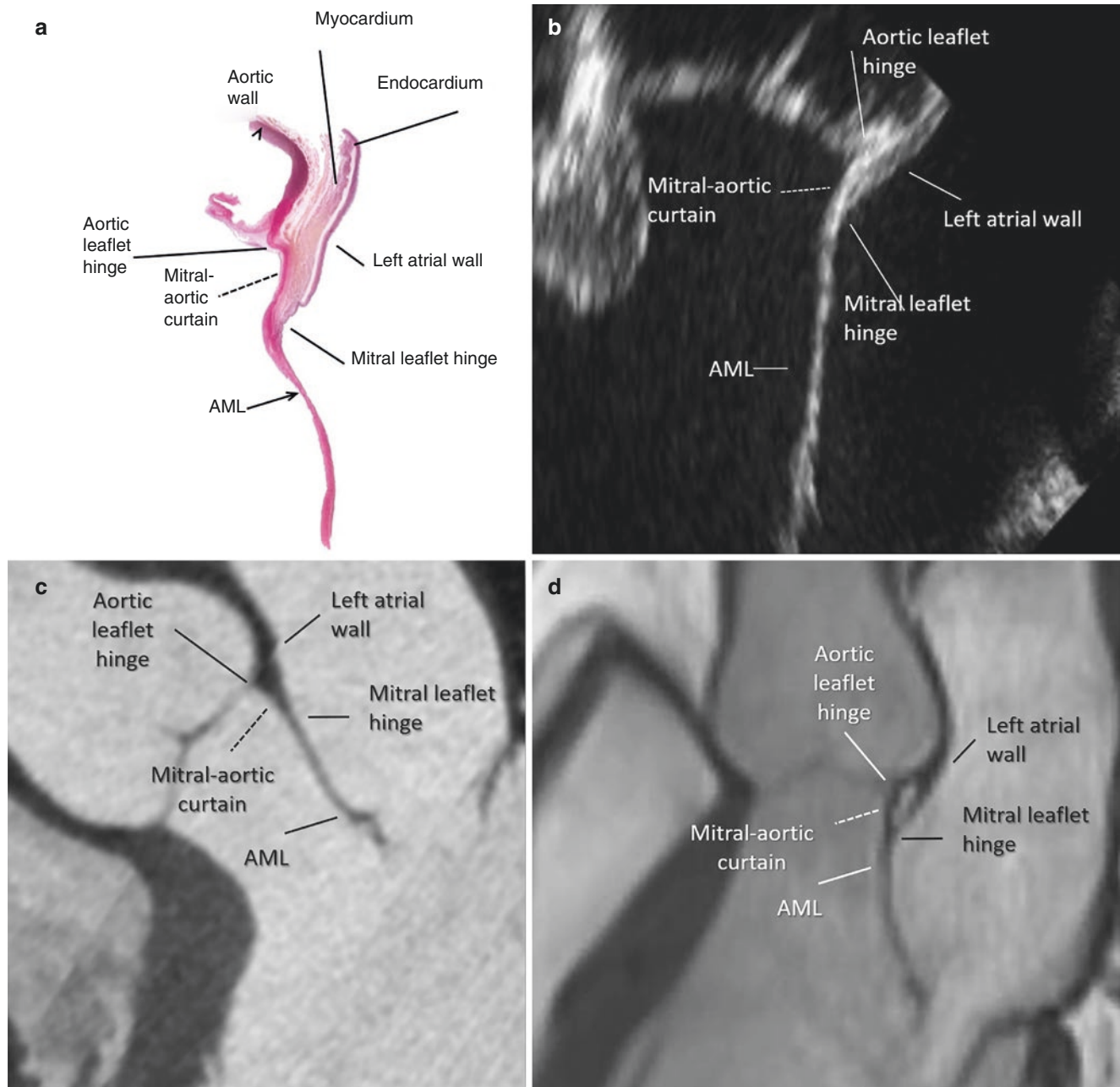


Fig. 1.7 (a) Histologic section of mitral-aortic curtain stained with elastic van Gieson stain showing fibrous tissue in red, myocardium in yellow, and elastic tissue in dark purple. (b) The corresponding echocardiographic image. The mitral aortic curtain is present only on the ventricular side of the anterior leaflet. On the atrial side, this space is

occupied by atrial wall. (c) CT multiplanar images. Despite the high resolution power CT does not allow a clear distinction between aortic and atrial wall. (d) Unlike CT, CMR is capable of visualizing even a thin leaf of epicardial adipose tissue in between the two walls. AML anterior mitral leaflet

aneurysm, and perforation into the left atrium or the base of the anterior leaflet. The reason why the mitral-aortic curtain is a frequent target of aortic endocarditis is its continuity with the aortic leaflets. The infection may, in fact, propagate either by direct extension of the infected tissue inferiorly or

as the result of infected regurgitant jet striking this region. Moreover, the mitral-aortic curtain is avascular, so it offers little resistance to infections. Exquisite images of this area can be obtained using 3D TEE from a ventricular perspective (Figs. 1.8 and 1.9).

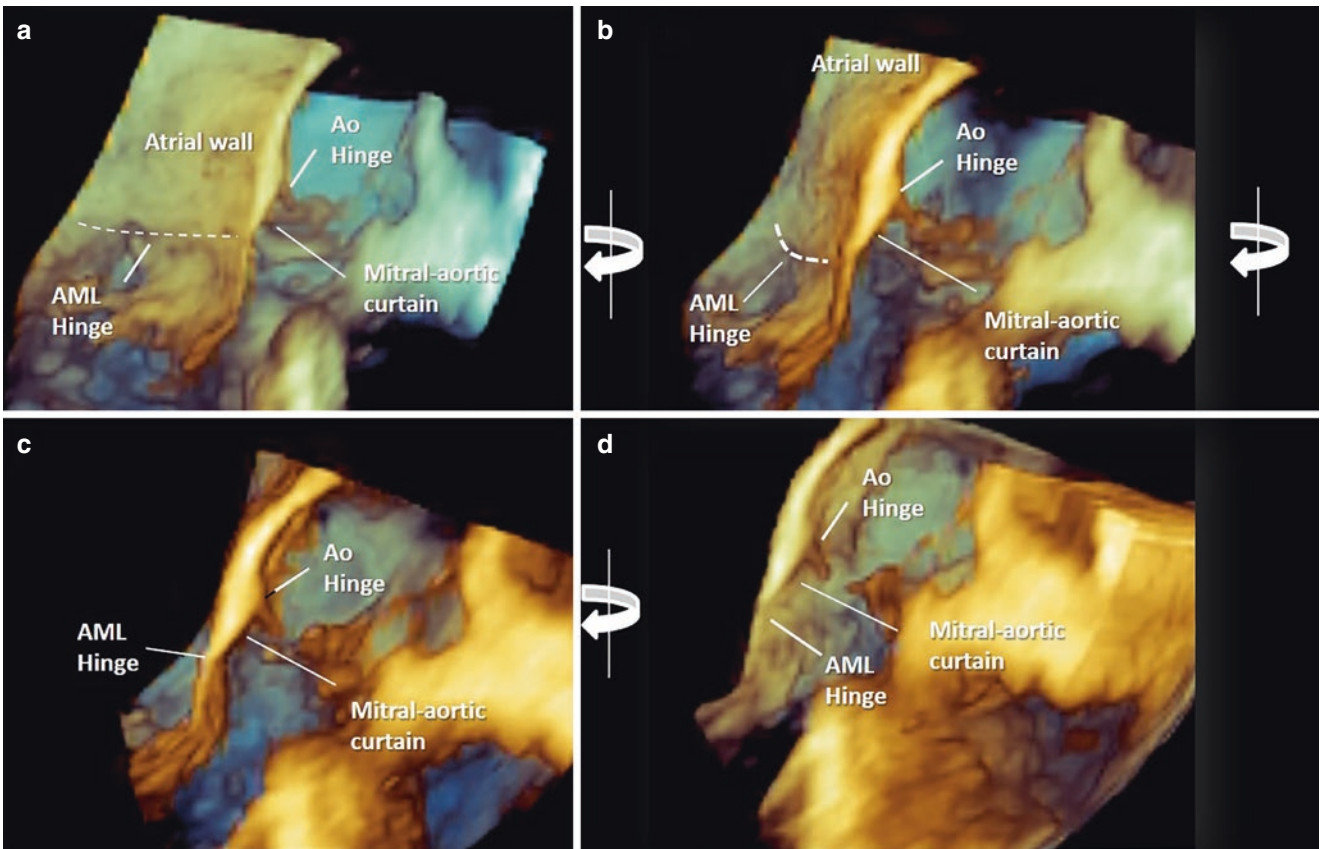


Fig. 1.8 The mitral-aortic curtain and its anatomical relationship with the anterior mitral leaflet (AML) hinge, the aortic (Ao) hinge, and the atrial wall, as illustrated by 3D TEE. (a) 3D zoom modality image show-

ing the atrial aspect of mitral-aortic curtain from an oblique perspective. (b–d) Rotation right to left around Y-axis (*curve arrows*) progressively displays the mitral-aortic curtain from ventricular perspective

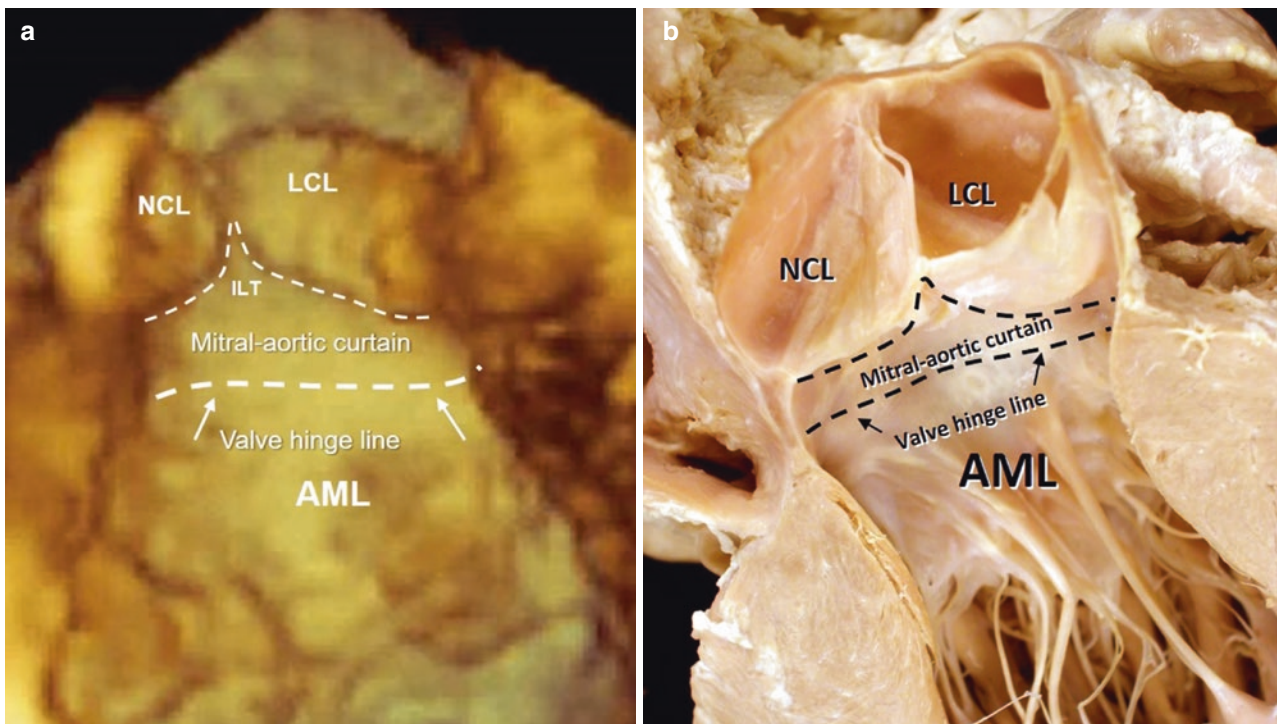


Fig. 1.9 (a) 3D TEE image from the ventricular perspective showing the anterior mitral leaflet (AML) in systole. The hinge line (*i.e.*, the fulcrum around which the leaflets move) is marked by the thicker dotted line, and the insertion of the aortic leaflets is marked by the thinner dot-

ted line. The interleaflet triangle (ILT) is well recognizable between the aortic leaflets. (b) Anatomic specimen in similar display. *LCL* left coronary leaflet, *NCL* noncoronary leaflet

The Shape of the Annulus

In systole, the hinge of the mitral leaflets along the atrio-ventricular junction takes the form of a “D” (Fig. 1.10). The anteroposterior (or septal-lateral) diameter of the orifice is significantly shorter than the commissural diameter. In diastole, the annulus becomes more circular and the two diameters are almost equivalent. 3D TEE, being able to visu-

alize the mitral complex from an overhead perspective, is certainly the best imaging technique to illustrate the shape of the annulus. What 3D TEE shows from this perspective is the hinge line of leaflets. This perspective is the same as the exposed view seen during cardiac surgery, so it takes the name of *surgical view*.

The three-dimensional saddle-shaped configuration of the annulus was described by Robert Levine and colleagues in

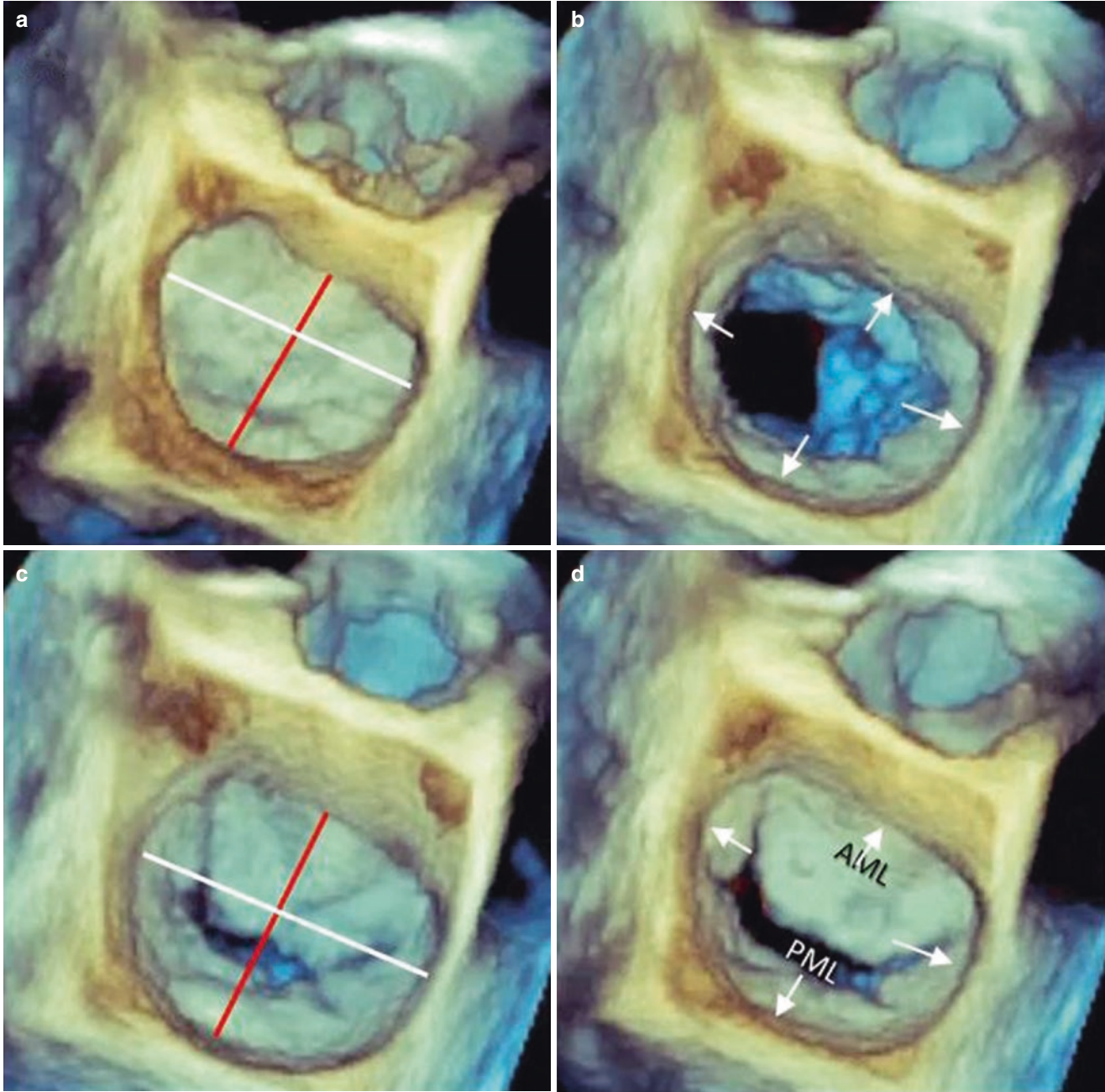


Fig. 1.10 The shape of the annulus as seen with 3D TEE at different time points of the cardiac cycle. (a) In mid-systole, the shape assumes an elliptical configuration (like a letter “D” lying down). The anteroposterior diameter (*red line*) is shorter than the commissural diameter

(*white line*). (c) In late diastole, the annulus is almost circular. Thus, the anterior-posterior and the commissural diameters are equivalent. (b) and (d) are intermediate phases. *AML* anterior mitral leaflet, *PML* posterior mitral leaflet

the 1980s. Instead of a planar configuration, they reported variable heights of the hinge of the leaflets in relation to the apex, with the highest edge being located at the level of the midpoints of the anterior and posterior leaflets and the lowest edge at the commissural level. This description generated a profound conceptual reconsideration of the echocardiographic diagnosis of mitral valve prolapse. This configuration explains the reduced stress on the leaflets, and most of the rings currently used by surgeons are designed to respect this three-dimensional geometry. The best way to visualize the saddle-shaped aspect of the annulus is by using 2D slices obtained from the 3D data set. The hinge line is manually traced in several adjacent long-axis planes, and the reconstructed annulus is then displayed as a color-coded 3D-rendered surface (Fig. 1.11). It must be emphasized that both in the original paper and in current 3D TEE color-coded rendered surface reconstruction, the contour traced to reconstruct the saddle-shaped configuration is the hinge line of leaflets, rather than the annulus. Thus, the correct definition should refer to the *saddle-shaped configuration of the mitral hinge line*.

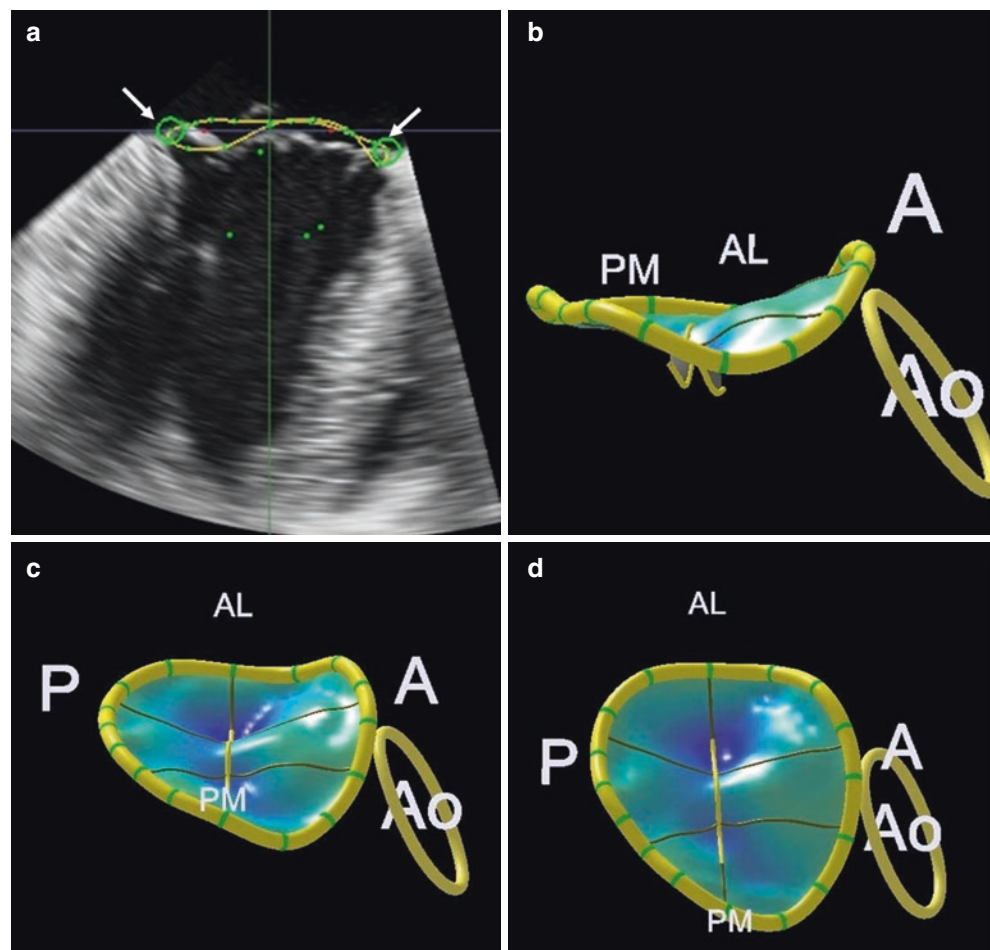
Annulus Motion

During the cardiac cycle, the mitral annulus (or more precisely, the leaflet hinge line) undergoes three types of motions: a sphincteric-like contraction, a translation motion, and an annular folding.

A *sphincteric-like contraction* occurs specifically at the level of the posterior annulus as a consequence of the contraction of basal helical fibers. The “sphincter” mechanism reduces the orifice area by 20–30%, thereby increasing the coaptation surface of the leaflets and ensuring perfect valve competence. The orifice area is minimum in mid to end systole (see Fig. 1.10a) and maximum in isovolumetric relaxation to early diastole (see Fig. 1.10c).

The *translation motion* is a consequence of the long-axis reduction of the left ventricle (LV); it is functionally linked to atrial and ventricular filling and emptying. In diastole, the annulus is pulled away from the LV apex, promoting LV filling by displacing a column of blood initially present in the left atrium beneath mitral leaflets. In systole, because the LV apex is fixed to the diaphragm by the pericardial sac,

Fig. 1.11 3D TEE color-coded rendered surface reconstruction of the saddle-shaped configuration of the annulus. (a) The operator follows the hinge line (arrows). The fulcrum (around which the leaflets open and close) is clearly visible (arrows). (b–d) Color-coded 3D rendered surface shows the saddle-shaped configuration from three different perspectives. Because the contour traced to reconstruct the saddle-shaped configuration is the hinge line of the leaflets, a better description should be the *saddle-shaped configuration of the mitral hinge line*. A anterior, AL anterior-lateral, Ao aorta, P posterior, PM posterior-medial



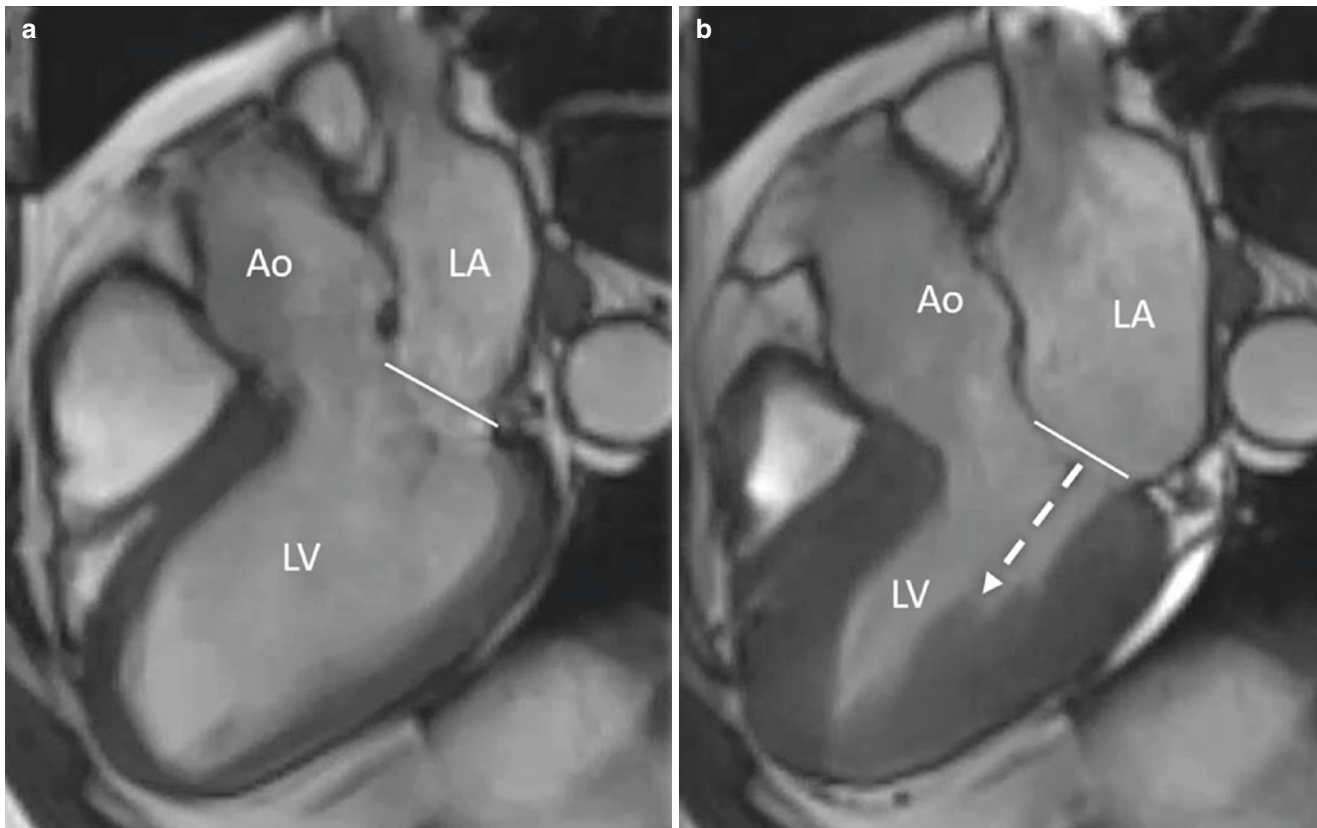


Fig. 1.12 (a, b) Frames captured from cine sequences of CMR, showing the movement of the mitral annulus towards the apex

the longitudinal LV shortening causes the base of the heart (and consequently of the annulus) to move towards the apex. This longitudinal shortening of the left ventricle reflects the contribution of the contraction of endocardial and epicardial muscular fibers, which have a prevalent longitudinal/oblique orientation. This motion displaces a column of blood, which is ejected into the aorta and simultaneously enlarges the left atrium, causing a drop in atrial pressure that facilitates the pulmonary venous return. This apical excursion of 5–10 mm has been shown to generate at least one fourth of the LV stroke volume. The excursion of the annulus can be best appreciated (and measured) in cine CMR sequences using a long-axis view plane (Fig. 1.12). It must be said that the degree of displacement of the anterior and posterior portions of the leaflet hinge line is not equal; the anterior annulus is tethered by the aortic root and translates less than the posterior annulus.

The *annular folding*, an accentuation of the saddle-shaped configuration, occurs during the systole. This conformational change avoids leaflet distortion along the hinge line, a potential consequence of annular contraction. As mentioned above, an accentuated saddle-shaped configura-

tion blunts the stress on leaflets that occurs as LV pressure rises. Another mechanism that favors the annular folding is the expansion of the aortic root, which displaces the mitral-aortic curtain posteriorly.

Mitral Leaflets

The most remarkable components of the mitral valve are undoubtedly the leaflets. The well-known description of the mitral valve with two leaflets is actually imprecise from a strict anatomical point of view. The two incisures, called *commissures* (a name that literally refers to the junction line between two adjacent structures), which divide the valve tissue into two halves, *do not* reach the hinge line. Thus, the presence of valve tissue along the entire circumference of the hinge creates an anatomical continuity between the two leaflets, thus making the mitral valve a continuous, uninterrupted veil. Because these incisures are consistently present in any normal mitral valve, however, the term *bicuspid valve* is justified. Therefore, we continue to describe the mitral valve as having two leaflets and two commissures.

The Commissures

The commissures are the deepest incisures of the valve leaflets. Because of the oblique orientation of the longitudinal axis of the left ventricle inside the thorax (from right to left, from top to bottom, and from posterior to anterior), the anterior-lateral commissure is higher than the posterior-medial commissure. The position of the commissures can be easily appreciated by using a new technology based on the “fusion” of fluoroscopy and 3D TEE (Fig. 1.13).

The unique chordal arrangement arising from the tip of the papillary muscles as a single stem, branching radially

and embracing the commissures, is used by anatomists to define the limits of the commissural area. Frequently, the commissural tissue takes the shape of a small Y-shaped segment called a *commissural scallop*. In the same mitral valve, one commissure may have a small commissural scallop while the other is represented by a simple strip of valve tissue. Whatever the configuration, this additional tissue is critical for obtaining a sufficient area of coaptation in this region. The best way to visualize the commissures remains 3D TEE, in which both commissures are clearly depicted from an overhead perspective (Fig. 1.14).

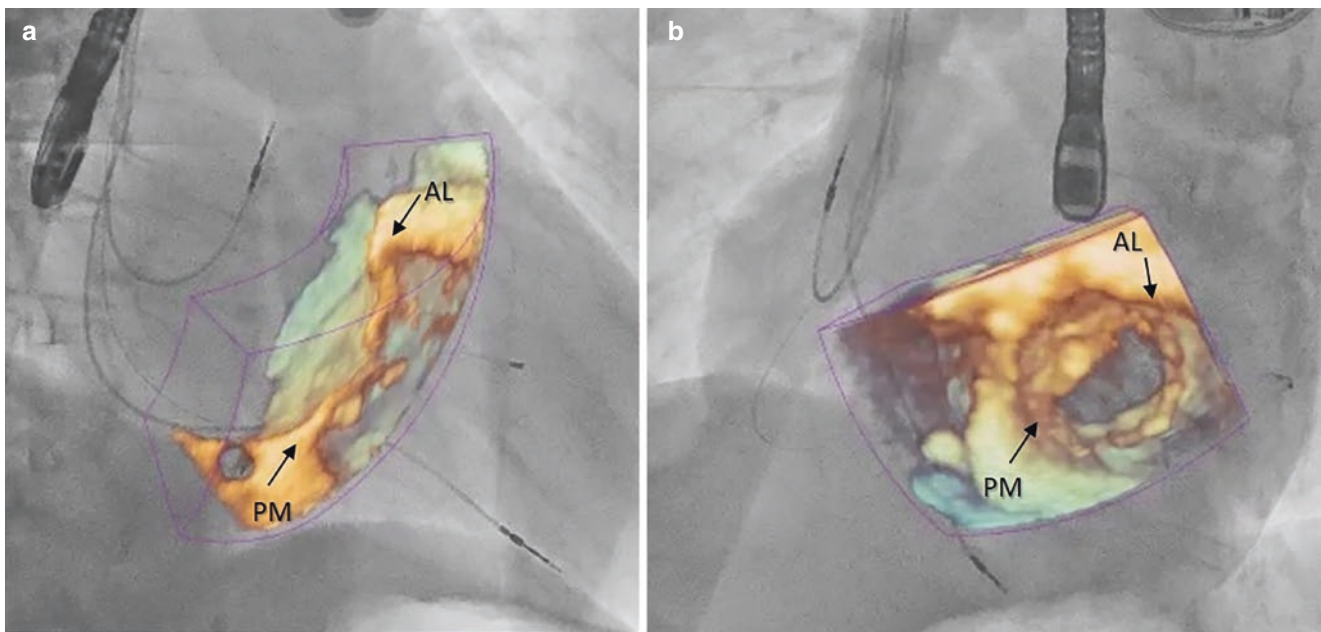


Fig. 1.13 Fusion images of fluoroscopy and 3D TEE showing the positions of the anterior-lateral commissure (AL) and posterior-medial commissure (PM) of the mitral valve, in a right anterior oblique projection (a) and in a left anterior oblique projection (b)

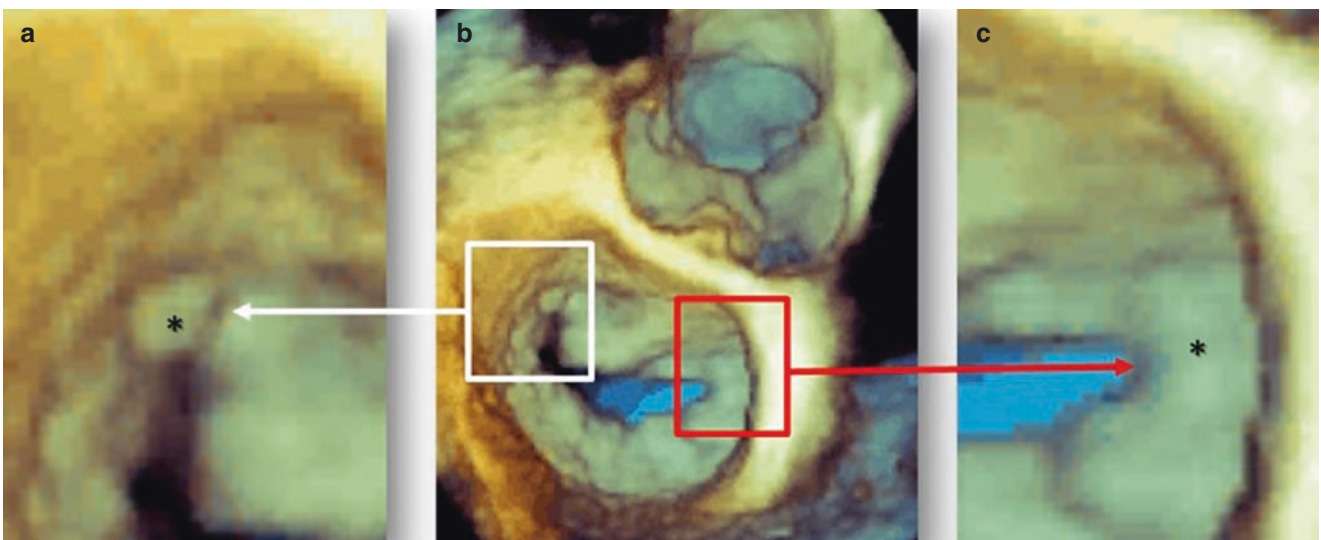


Fig. 1.14 (a) Magnified 3D TEE image (white square from panel b) showing the Y-shaped anterior-lateral commissure (*asterisk*). (c) Magnified image (red square from panel b) showing the posterior-medial commissure without any well-defined commissural scallop (*asterisk*)

The Leaflets

The commissures divide the mitral valve into two leaflets: *the anterior leaflet* (or, given its strict continuity with the aortic valve, the *aortic leaflet*) and the *posterior leaflet* (or, given its strict continuity with the margin of the left ventricle, the *mural leaflet*). The anterior leaflet has almost a triangular shape, and its hinge line occupies approximately one third of the annulus. The length from the hinge point to the free margin varies from 1.5 to 2.5 cm. The free margin is usually devoid of incisures (Fig. 1.15a). The posterior leaflet reveals a relatively quadrangular shape, and its

hinge line occupies the remaining two thirds of the mitral annulus (Fig. 1.15b). The distance between the insertion and the free margin is shorter than for the anterior leaflet, measuring less than 1 cm, but given its longer hinge line, the areas of the two leaflets are almost equal. In contrast to the anterior leaflet, the posterior leaflet usually has two indentations, which divide the leaflet into three parts called *scallops*. According to Carpentier's classification, these scallops, from lateral to medial, are named P1, P2, and P3. These indentations usually extend as deep as half of the distance between the free margin and the hinge line of the posterior leaflet and are supported by numerous chordae. The scallops have a

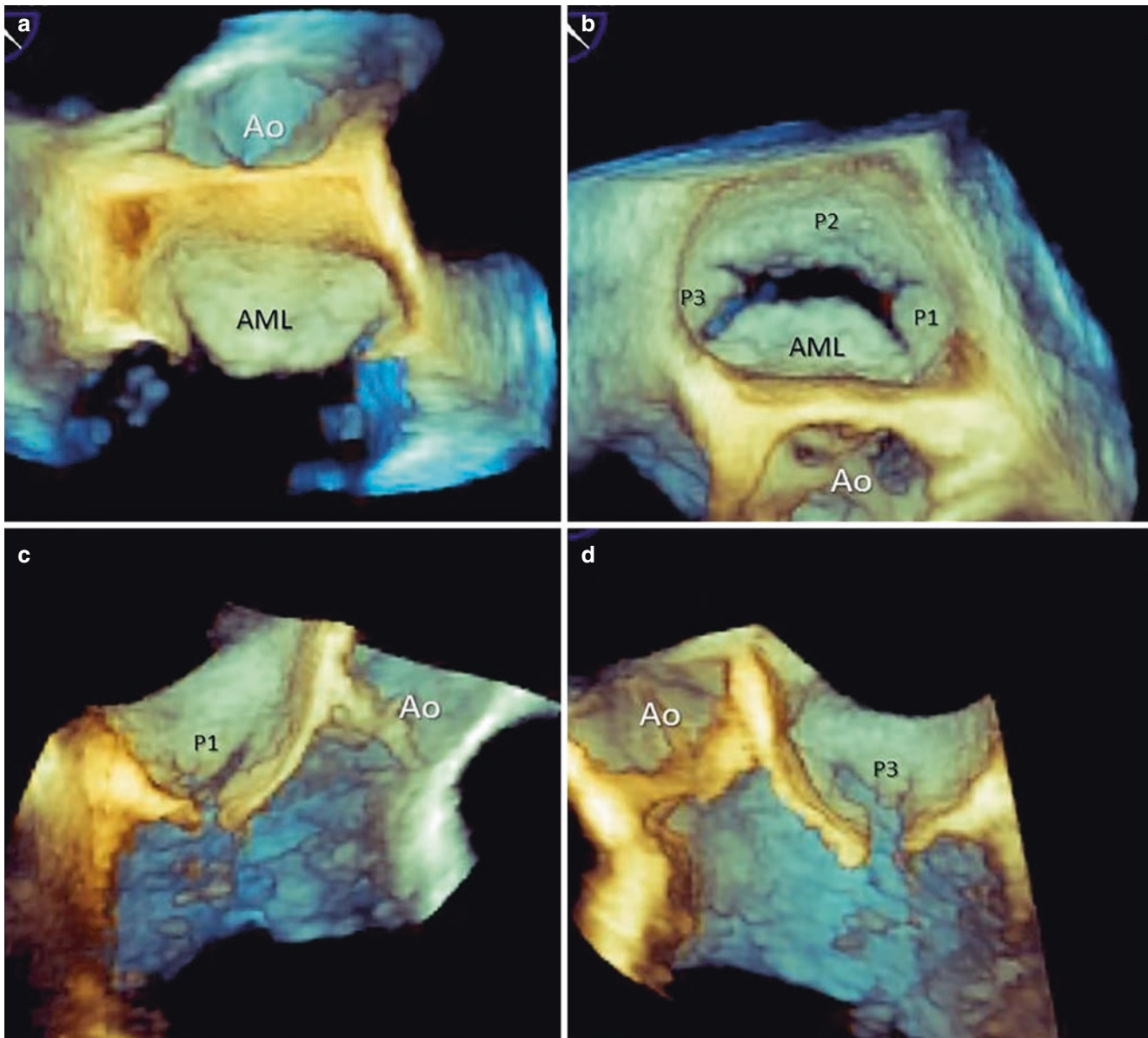


Fig. 1.15 (a–d) 3D TEE images of mitral leaflets as visualized from different perspectives (a, cropped image of surgical perspective; b, anterior perspective from overhead; c and d, cropped image of long-

axis perspective showing P1 and P3 scallop). P1, P2, and P3 denote the three scallops of the posterior mitral leaflet. *AML* anterior mitral leaflet, *Ao* aorta

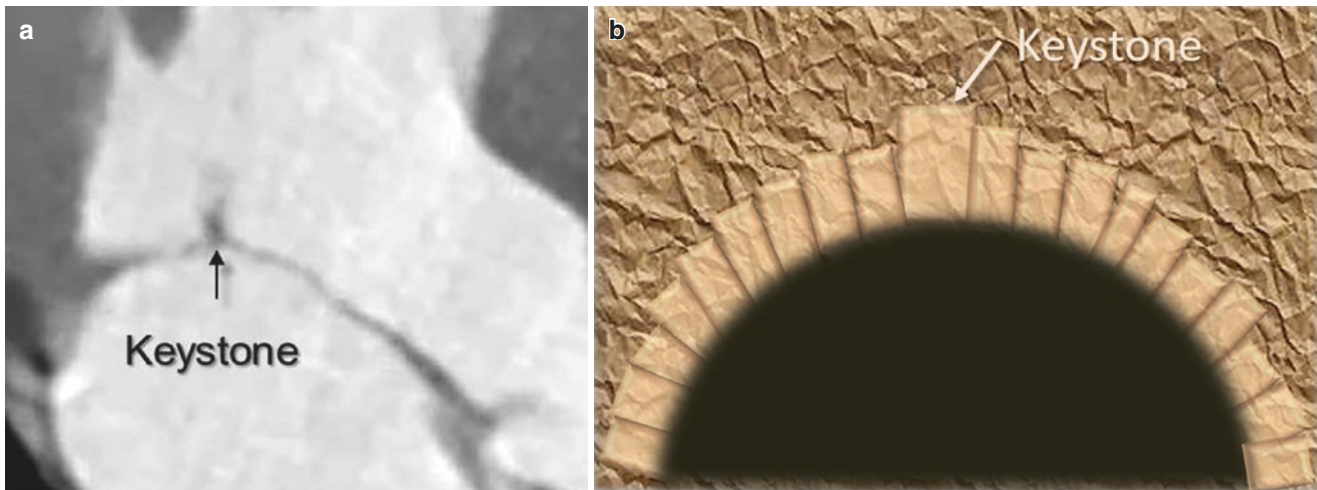


Fig. 1.16 (a, b) The keystone mechanism of leaflet coaptation attenuates the stress on the leaflets and chordal apparatus

semi-elliptical shape, and frequently, the central one is the largest. They act exactly as the commissures, facilitating a larger opening in diastole and favoring an effective closure in systole. Other smaller incisures may subdivide a single scallop into subunits. The term *cleft* should be used to indicate a deeper indentation that extends from the free edge to the hinge line and, when present, results in regurgitation. Clefts are usually present in degenerative valve disease (large prolapse or Barlow disease). The best imaging technique to explore the leaflets is the 3D TEE, in which the valve can be visualized in its entirety.

The ventricular surface of the two leaflets can be divided into two portions: the rough zone (*pars rugosa*) and the clear, translucent zone (*pars liscia*). The rough zone is thicker and has an irregular surface owing to the insertion of chordae tendineae onto the underside of the leaflets. This area is wider in the central zone of both leaflets and gradually fades as it approaches the commissures. In the anterior leaflet, the clear zone is rather thin, translucent, relatively wide, and elastic. In systole, it may therefore acquire a convex shape towards the atrial cavity. This systolic shape, though frequently misdiagnosed as a prolapse, is far from being pathological. Instead, it is rather beneficial, because the convexity reduces the mechanical stress by distributing the systolic pressure more evenly. In the posterior leaflet, the clear zone is a narrow, flexible band. Characteristically, the rough zone corresponds, on its atrial surface, to the coaptation surface of the valve leaflets. The coaptation surface is critical for a perfect valve competence. The leaflets “coapt” over a height of 6–8 mm, thus endowing the valve with a kind of “valvular reserve” that preserves valve function even in the event of “moderate” annular dilatation. The coaptation forms an arc-shaped closure line, which is obliquely situated relative to the orthogonal plane of the body. The posterior leaflet provides an anchor against which the anterior leaflet abuts

to maintain valve competence. This “keystone” mechanism (as for an ancient arch made of stones) considerably reduces the tension and the pressure on the leaflets and the chordal apparatus, as the LV pressure is exerted simultaneously on the two opposite sides of the leaflets (Fig. 1.16). Because of the different lengths of the anterior and posterior leaflets, in normal individuals, this area is asymmetrical, with an anterior leaflet dominance. Echocardiography, CMR, and CT scans may offer excellent images of the coaptation surface (Fig. 1.17).

Microstructure of the Leaflets

The leaflets are tacitly perceived as two flaps of inert tissue, but this belief is far from accurate. The mitral valve leaflets in an adult must open and close over 100,000 times a day (more than three trillion times in a lifetime) in order to maintain unidirectional blood flow. This goal could not be achieved with inert tissue. Mitral leaflets are made of living tissue with a highly organized connective tissue system that provides unique mechanical properties. Indeed, cross sections reveal three well-defined layers: the atrialis is on the flow side of the leaflet, the spongiosa in the middle, and the fibrosa or ventricularis on the ventricular side. This three-layered structure is covered on both the ventricular and the atrial surfaces with a single layer of endothelial cells. Each layer has different molecular characteristics, which impart unique mechanical properties to the leaflets. The *atrialis*, for example, contains lamellar collagen and elastin sheets, thus forming a robust yet elastic network that counteracts the systolic deformation in systole and enables elastic recoil in diastole. The *spongiosa* contains loose connective fibers and glycosaminoglycans, which counteract the compressive forces generated by coaptation by absorbing tension and

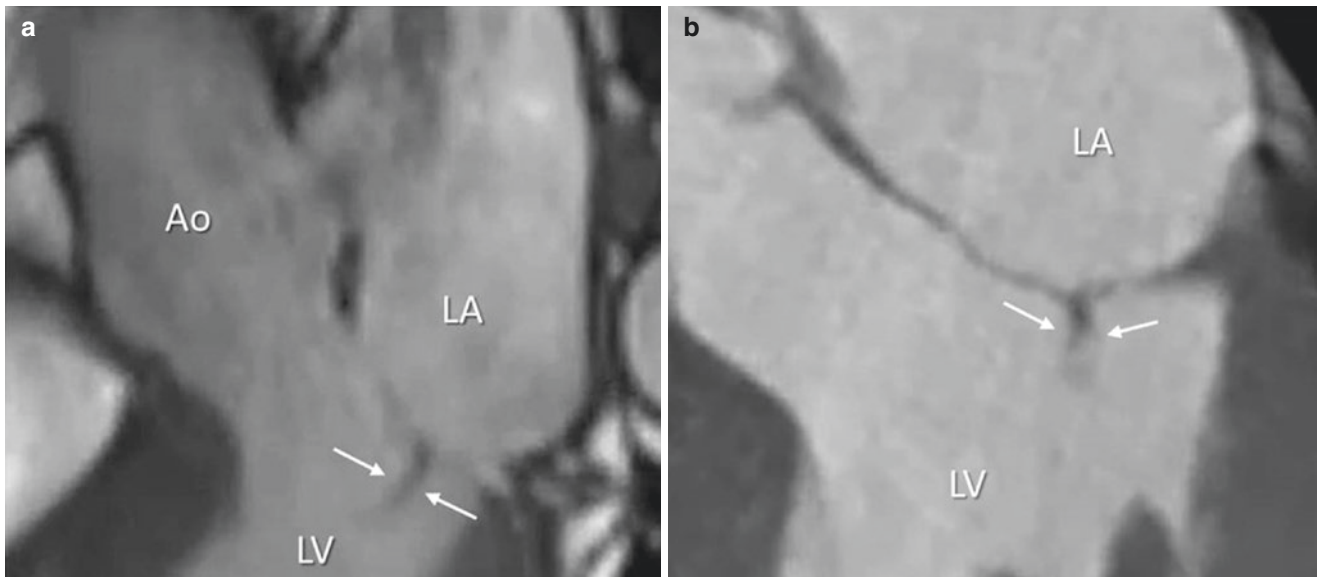


Fig. 1.17 CMR image (a) and CT scan (b) showing the coaptation surface (*arrows*) in systole. *Ao* aorta, *LA* left atrium, *LV* left ventricle

friction between the layers, like a lubricant cushion. Finally, the *fibrosa*, made of collagen densely packed in robust fibers and arranged parallel to the free margin of the leaflet, confers strength and stiffness. At sites of chordal insertion, the fibrosa is in continuity with a robust cylindrical strand of collagen fibers that form the “core” of the chordae tendineae. This architecture faces the high LV pressure with a gradual transition of forces between leaflets and chordae (Fig. 1.18).

The most striking feature of the microstructure of the mitral leaflets is the cellular population. Mitral leaflets contain mainly two types of cells: valvular endothelial cells, covering the leaflet surface, and the interstitial cells, with at least five different types distributed throughout the leaflets. Both cellular components are essential to maintain the matrix network that forms the mechanical scaffold to sustain the dynamic activity of the leaflets and to confer robustness and durability.

Notably, in medical textbooks and guidelines, functional mitral regurgitation (both ischemic and non-ischemic) is described as a “secondary” regurgitation. This term emphasizes the fact that mitral regurgitation is a result of geometric distortion of the papillary muscles due to the enlargement of the left ventricle, while the valve leaflets and chordal apparatus are structurally normal. Consequently, therapies have focused on reducing annular and ventricular remodeling. But this paradigm is not completely true. Indeed, preclinical and clinical studies have shown leaflets that are larger and thicker than normal in patients with longstanding functional mitral regurgitation. In other words, the leaflets are not innocent bystanders in functional mitral regurgitation. Mechanical stretching of the leaflets may activate fibroblast-like cell populations, which increase collagen production and render the

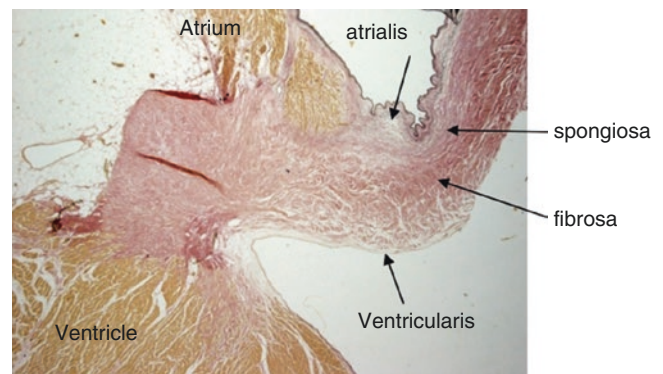


Fig. 1.18 Histologic section through mitral leaflet (elastic van Gieson stain)

leaflets larger and thicker in order to compensate for annular dilation and/or geometric remodeling of the left ventricle. The knowledge of this “adaptive” mechanism (though still at an early stage) shifts away from the well-accepted model in which the leaflets are structurally normal and the insufficiency is a matter of unbalanced closing against tethering forces due to abnormal LV geometry. The new paradigm focuses on leaflet remodeling. The histological remodeling of leaflets leading to active valve enlargement can be seen as an adaptive mechanism to restore effective coaptation, but it is not illogical to consider the possibility that excessive remodeling may result in a stiffer leaflet with decreased mobility, which in turn may interfere with effective closure and exacerbate mitral regurgitation. Thus the mechanisms of functional mitral regurgitation are likely to be more complex than previously thought. Indeed, it seems to be not simply a balance between closing versus tethering forces but also an

adaptive versus a maladaptive fibrosis. As effective closure requires thin, flexible, and elastic leaflets that expand nearly 15% in systole to form a coaptational seal, stiffer leaflets may increase mitral regurgitation, rather than reducing it.

Chordae Tendineae

The simplest and most effective classification divides the chordae into three categories: the first-order or *marginal* chordae, the second-order *strut* or *stay* chordae, and the third-order *basal* chordae (Fig. 1.19). Despite marked variability in number and distribution among individuals, the general design of the chordal apparatus is rather constant. The chordae originate from the tip or heads of the papillary muscles, as single stems that split radially into several branches. Only the basal chordae may originate directly from the left ventricular wall. Before inserting into the leaflets, the chordal branches form numerous interconnections, thus ensuring a balanced distribution of forces and robust structural stability.

These three types of chordae exert different functions. The *marginal chordae* insert on the free margin of the leaflets, and the rupture of a main marginal chorda is responsible for flail and severe mitral regurgitation. Commissural chordae are considered to be part of marginal chordae. The *strut* or *stay chordae* are attached close to the boundary between the rough and the clear zone on both leaflets. Of particular interest are two strut chordae that are inserted on the anterior leaflet at an angle of 45°. They are located at a distance approximately one third of the way from the free edge and two thirds from the annulus; sometimes they divide

before their insertion into two or three branches. These chordae are particularly thick and robust. Indeed, in the animal model, the tension exerted during systole on these chordae is three times higher than the force exerted on the marginal chordae, and these chordae remain tense during the entire cardiac cycle. The function of these chordae is still not completely understood. Their main function does not seem to be the prevention of mitral regurgitation. In the animal model, transection of these chordae does not result in either mitral regurgitation or changes in leaflet coaptation; it results in global LV systolic dysfunction. In fact, these chordae maintain a fibrous connection between the mitral valve and the papillary muscles and may contribute to the preservation of LV geometry by favoring long-axis LV shortening. They also reduce the motion of the peripheral part of the anterior mitral leaflet, thus leaving the central part more mobile. In systole, therefore, the leaflet takes a concave shape on the side of the LV outflow tract, which facilitates the blood flow transit towards the aorta. In diastole, the concavity faces the inflow tract and facilitates the inflow of the blood into the left ventricle.

It is interesting to note that in the setting of secondary mitral regurgitation of ischemic or idiopathic origin, strut chordae are believed to exacerbate leaflet tethering. Therefore, some authors have suggested the transection of strut chordae as an adjunct technique to valve annuloplasty to improve leaflet coaptation. This mechanism has decreased mitral regurgitation in the experimental setting, but surgeons remain skeptical about implementing the procedure in standard mitral surgery because of their awareness that the cutting of the anterior strut chordae may have detrimental effects on LV function.

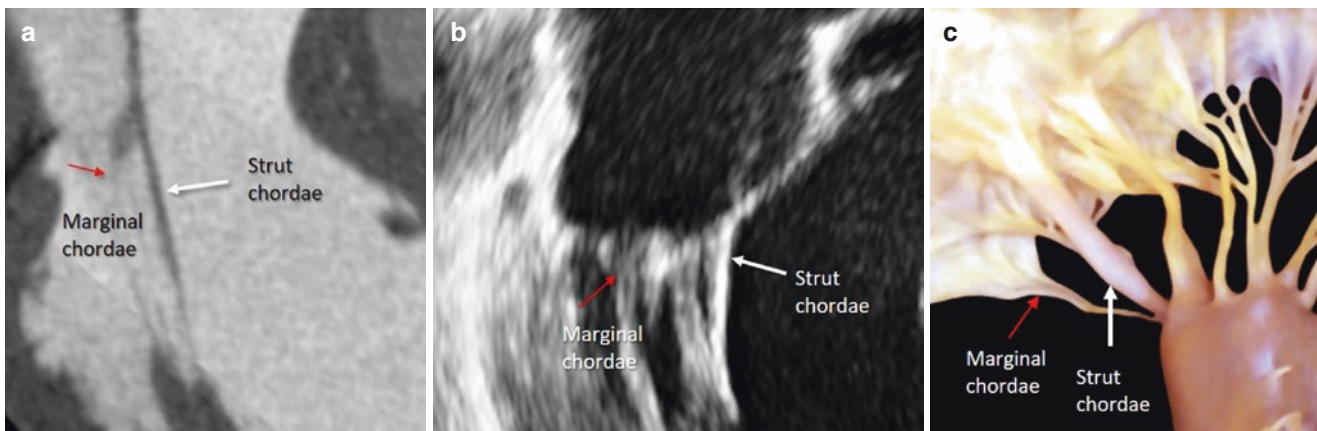


Fig. 1.19 CT scan (a), echocardiogram (b), and anatomic specimen (c) showing the strut chordae (white arrow) and the marginal chordae (red arrow)

The *basal chordae* originate directly from the ventricular wall and insert only on the posterior leaflet. Theoretically, the function of the basal chordae is to reduce the mobility of the leaflet by anchoring the valve to the ventricular wall. The absence of similar chordae on the anterior leaflet is due to the fact that the basal portion of the anterior leaflet continues with the mitral aortic curtain and has no anatomical connection with the ventricular wall.

Microstructure of Chordae Tendineae

The chordae tendineae consist of a core of densely packed collagen fibers in continuity with the fibrosa of the leaflets, surrounded by a layer of loose connective tissue of elastic fibers interspersed with collagen fibrils, and an outer layer of endothelial cells. This histological composition allows sustaining of the cyclic stress to which the chordae are continuously subjected. Moreover, the presence of vessels in the middle layer of the thicker chordae, running longitudinally from the papillary muscles to the mitral leaflets, strongly indicate that chordae tendineae are not simply passive collagenous structures, but represent live tissue with its own metabolism and an additional important role in leaflet nutrition. Moreover, in functional mitral regurgitation, chordal elongation may occur as part of the adaptive process to preserve leaflet coaptation.

Papillary Muscles

The papillary muscles (PM) originate from the apical third of the left ventricle and are usually organized into the anterior-lateral and the posterior-medial groups, which are positioned just below the corresponding commissures. Each of the two groups of PMs gives rise to a dozen or so main chordae tendineae, which insert into the medial and lateral halves of the anterior and posterior leaflets respectively. Considerable differences in shape and size have been described among individuals. Papillary muscles have been described as arising from the inner part of the left ventricle wall as a single body or as two or three bodies. The axis of these bodies is usually parallel to the long axis of the left ventricular cavity. Generally, the thickness of the PM matches with the thickness of the LV free wall, with a slight difference between the two PM (the anterior-lateral PM being larger than the posterior-medial PM), but considerable variation in size,

length, and configuration (single PM with or without multiple heads or multiple PMs) may occur.

In the 1960s, PM came to be appreciated as an essential component of the mitral valve apparatus, with a role in the closure process of the mitral leaflets. When the LV contracts and shortens, the PM contract and shorten as well, keeping the distance between the tips of the PM and the leaflets constant. The contraction of the PM prevents eversion of the leaflets during systole. The best imaging modalities to appreciate PM shortening are undoubtedly CMR and echocardiography.

Transient isolated PM ischemia or necrosis and fibrosis may result in leaflet prolapse with mitral regurgitation. In such a case, the regurgitation (and murmur) starts after the isometric contraction, when the ventricle begins to shorten. Involvement of both the PM and surrounding LV wall in the ischemic process causes asymmetric tethering of the leaflet. In these cases, the consequent mitral regurgitation (and murmur) starts at the beginning of the isometric contraction.

It is important to discuss PM vascularization, which may be responsible for different clinical presentations. Indeed, myocardial infarction involving the posterior myocardial wall usually results in necrosis of the posterior-medial PM, while anterior myocardial infarction may spare the anterior-lateral PM. In fact, the anterior-lateral PM has a dual blood supply from both the anterior descending and the circumflex coronary arteries, whereas the posterior-medial PM is dependent only on the coronary artery that gives origin to the posterior descending coronary artery. Because of this “asymmetric” blood supply, the posteromedial PM is considered to be more vulnerable to an ischemic insult.

Several articles and textbooks have described PM as arising directly from the compact myocardium, but this belief was recently challenged by CT scans and 2D echocardiography revealing that PM arise from a network of trabeculations rather than from a single pillar originating from the compact myocardium layer (Fig. 1.20). Such an arrangement of the PM suggests that by distributing the systolic pressure more uniformly on a larger base, a broad, mesh-like architecture with multiple points of attachment could protect PM from ventricular pressure more effectively than a pillar-like attachment. Furthermore, multiple trabecular origins allow PM to draw blood supply from numerous pathways, thus ensuring diffuse collateral perfusion protecting against ischemic insults.

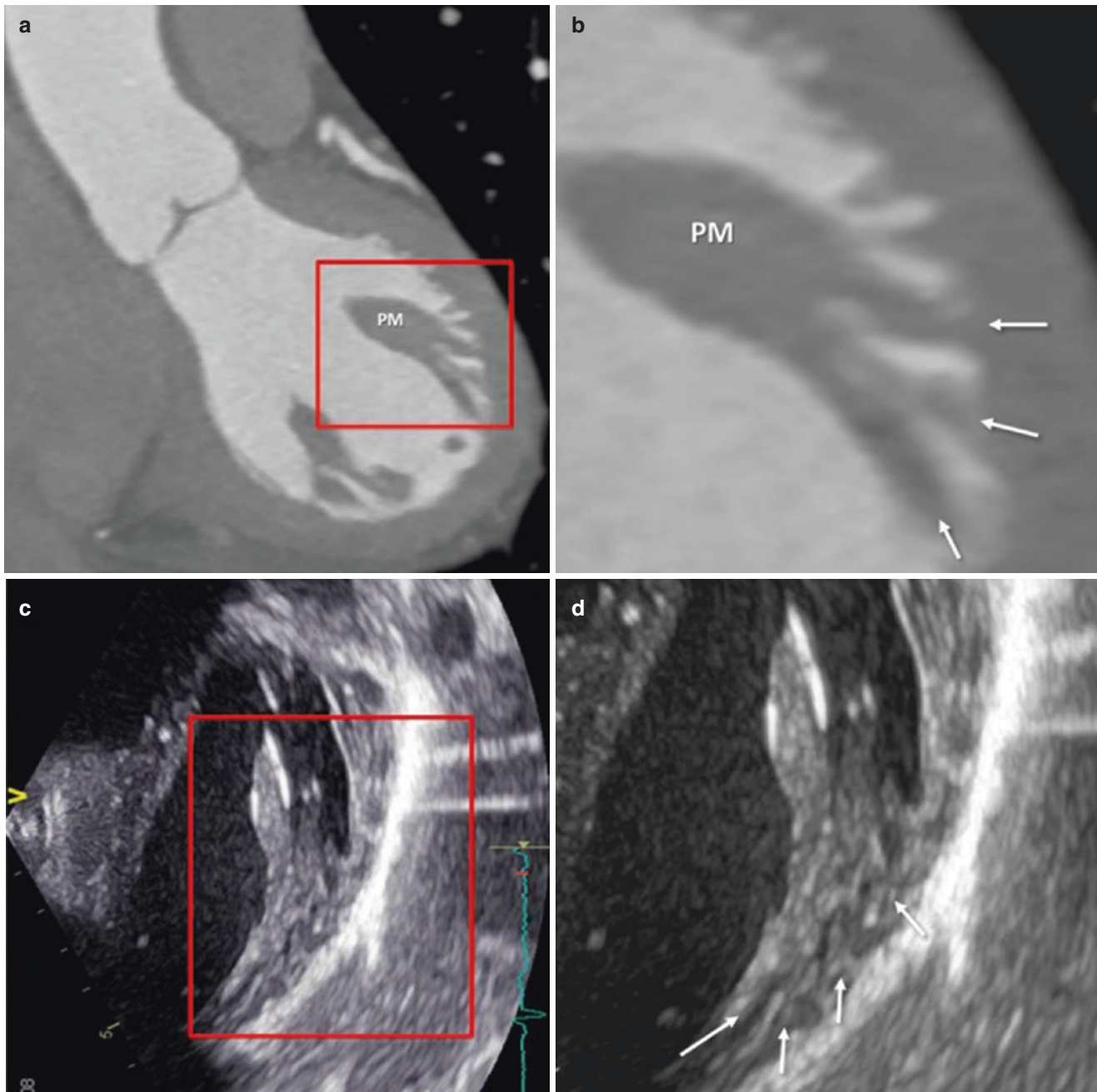


Fig. 1.20 The base of a papillary muscle (PM), seen on a CT scan (a) and 2D TTE (c). In the magnified images (b and d), it can be seen that the PM arises from a network of trabeculations (*arrows*), not as a single pillar from the compact myocardium

Suggested Reading

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