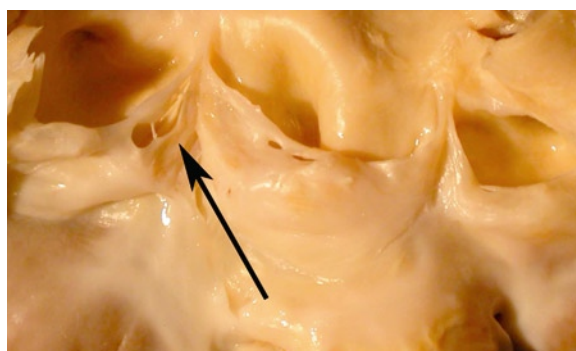


Like all visceral organs, the heart ages. The fibrous skeleton of the heart becomes sclerotic and calcifies, the valve closing margins thicken, the aorta dilates and tilts rightward on the interventricular septum making the latter seem prominent, the ventricles decrease in size, the left atrium enlarges, valves calcify and/or become myxomatous and amyloid may deposit in the heart.

## Fenestrations

Fenestrations of semilunar valve cusps are very commonly noted at pathology examination and at surgery and may be detected by imaging studies. Fenestrations are an acquired degenerative change whose frequency increases with age. Fenestrations are typically found in the region of the lunula, which is the portion of the valve cusp between the line of closure and the free edge of the cusp (Figs. 2.1, 2.2). They may extend from the region of the commissures all the way to the nodule of Arantius in the middle of the cusp. Fenestrations are not usually associated with aortic regurgitation as they are located distal to the line of closure. Acute aortic insufficiency due to rupture of fenestrated aortic valve cusp has been reported [1]. This occurs when the fenestration is large and extends beyond the line of closure into the body of the cusp, or the fenestration is located at the commissure and its rupture leads to cusp prolapse. If dilation of the aortic root moves the line of valve closure towards the cusp free edge, the fenestration may be incorporated into the functional portion of the valve, and regurgitation through the fenestration may develop [2].

Un-ruptured aortic fenestrations are not detectable echocardiographically, because they are located in the lunula region beyond the line of closure. Ruptured

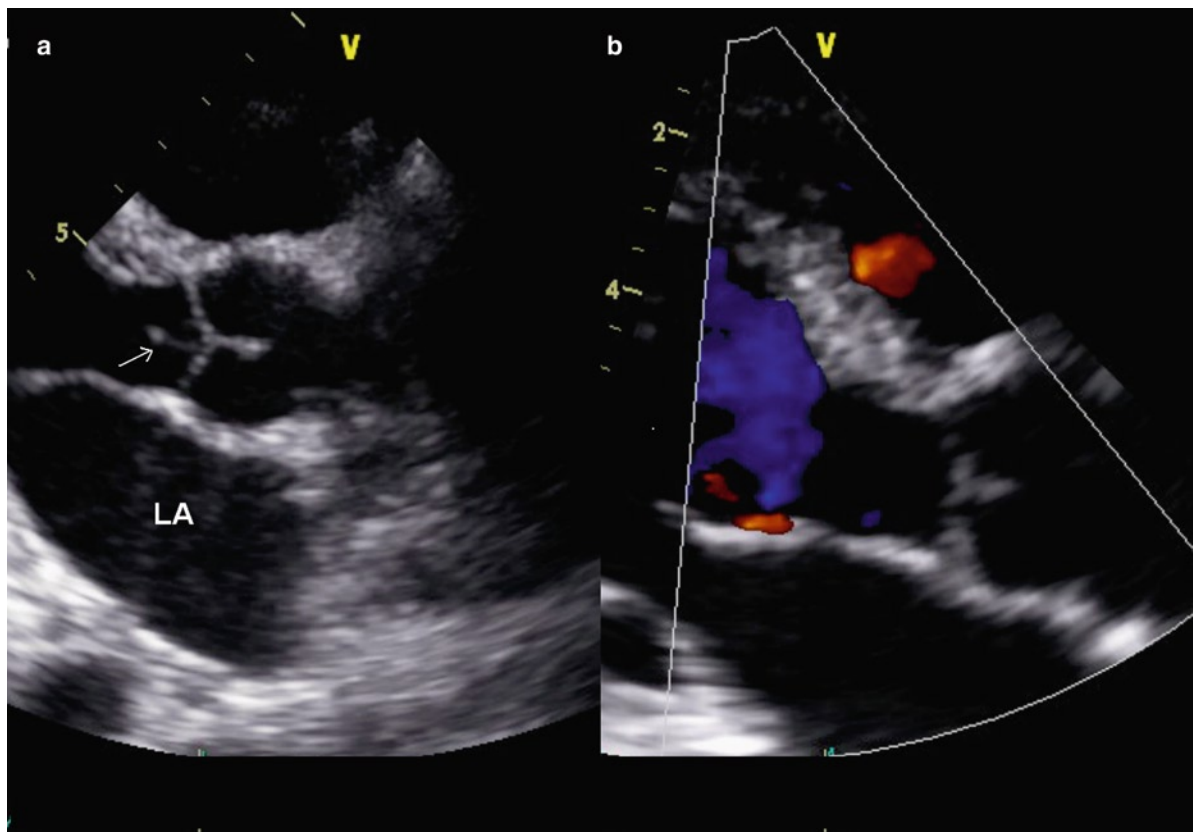


**Fig. 2.1** Opened aortic valve with fenestrations (*arrow*) visible. Note they are above the line of valve closure near the commissures laterally

fenestrations can be identified as long linear strands arising from the aortic cusps. They are best seen in the left ventricular outflow tract during aortic valve closure (Fig. 2.2). They are differentiated from vegetations by their long linear appearance and the absence of aortic regurgitation as previously discussed.

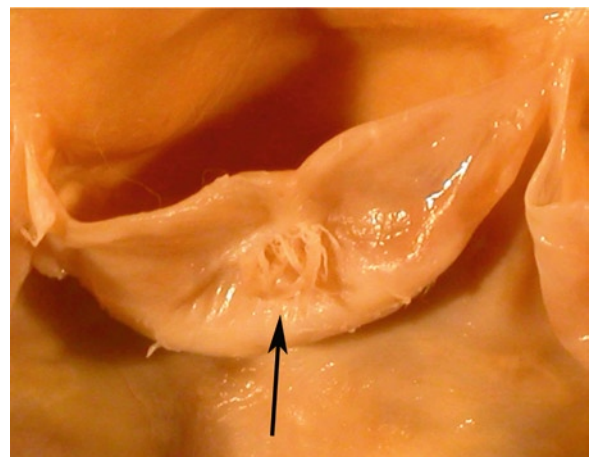
## Lambl's Excrescences

Lambl's excrescences and fibrous tags are thought to represent a common valvular degenerative or age-related lesion, often thought to reflect wear and tear. Some consider these to represent repetitive trauma-related endothelial proliferations or organized thrombi. They may occasionally be found in much younger patients, including children. Thrombi have a tendency to form on these areas of endocardial roughening (non-bacterial thrombotic endocarditis). On gross examination Lambl's excrescences commonly occur at lines of valve closure and are most common on the left sided

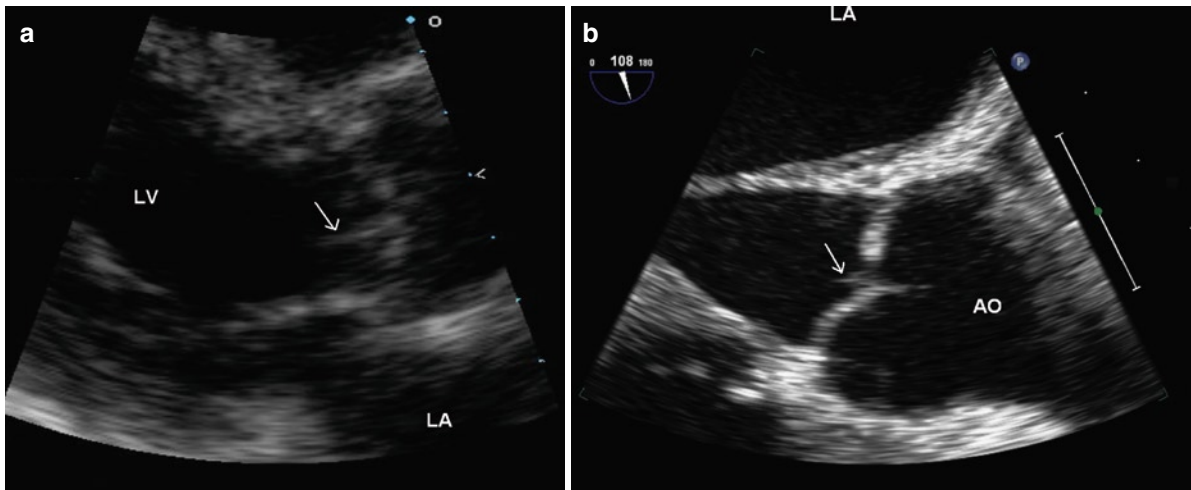


**Fig. 2.2** The parasternal long-axis view (a) of a 43-year-old woman shows that there is long linear density (arrows) attaching to the tip of the aortic valve and prolapsing into the left ventricular outflow tract in diastole. Color flow imaging shows no aortic regurgitation (b). This linear mobile density likely represents a ruptured aortic fenestration. *LA* left atrium

valves, including the aortic valve near the nodulus of Arantius. The excrescences appear as tiny tags of fibrous material and are best visualized immersed under water (Fig. 2.3). These morphologic features have been observed on echocardiography (Fig. 2.4). These excrescences are grossly similar to papillary fibroelastoma neoplasms, but differ in size and location. On microscopic examination they are similar to papillary fibroelastomas with endothelial covered fibroelastic cores, sometimes associated with adherent thrombi. They can cause turbulence, and are a site of relative stasis where thrombosis may occur and thus may provide a site for the development of infective endocarditis. Coronary ostial obstruction and embolization of fragments or excrescences have been reported. It is probable that the emboli originate from thrombus on the Lambl's, rather than the fibroelastic material itself.



**Fig. 2.3** Close up view of an aortic valve cusp. In the center of the cusp, midline, along the line of closure, there are multiple small whisker like Lambl's excrescences (arrow)



**Fig. 2.4** (a) Small whisker-like mobile densities (*arrow*) consistent with Lambl's excrescences are seen on the aortic valve in this 87-year-old woman. (b) These are more clearly demonstrated (*arrow*) by transesophageal echocardiography. Ao aorta, LA left atrium, LV left ventricle

## Mitral Annular Calcification

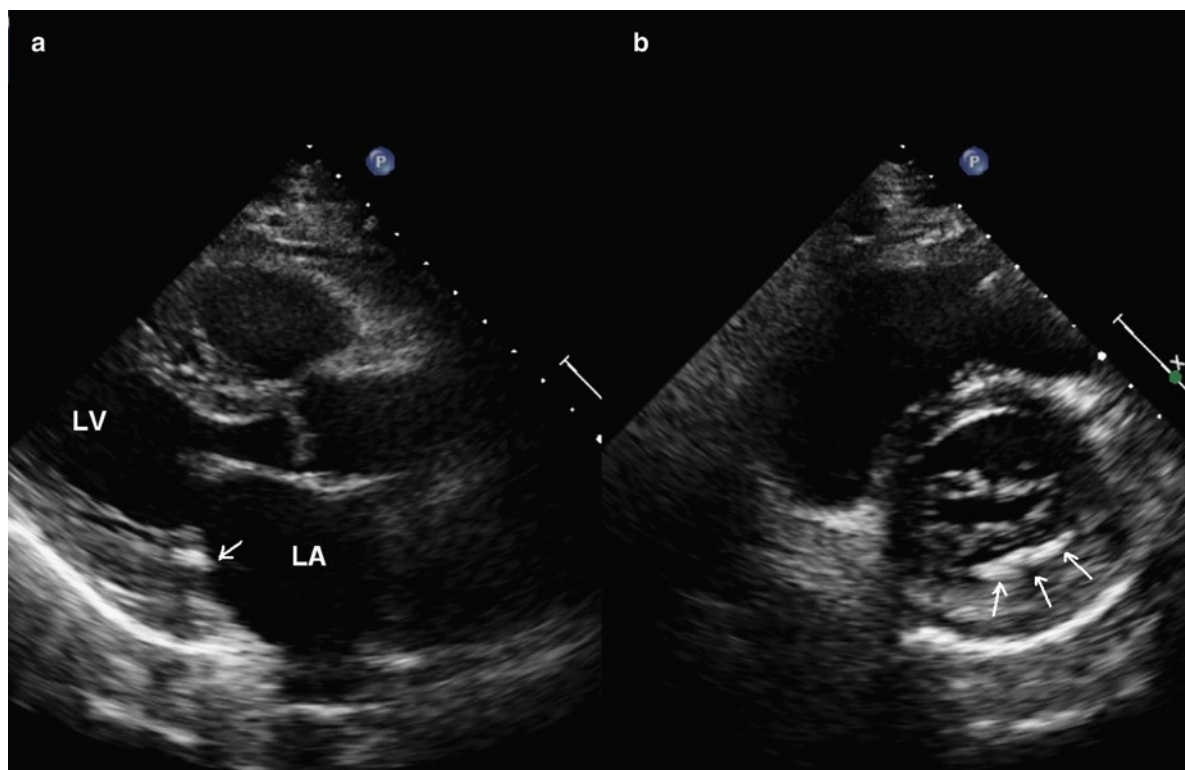
Mitral annular calcification (MAC) is a common finding in the hearts of elderly patients, especially females. Although MAC has been considered to be an age-related finding, it probably is a pathological process due to degenerative changes in the mitral annulus. Its incidence is low in those under the age of 50 years; however, the incidence of MAC increases to become common in the elderly. It is a progressive process, albeit at a slow pace in most patients. In association with mitral valve disease, especially mitral valve prolapse (myxomatous/floppy mitral valve), the condition may occur in younger patients. MAC occurs at an earlier age, is more exaggerated and has a more rapid progression in those with calcium metabolic abnormalities such as hyperparathyroidism and chronic renal failure, especially in those who are dialysis dependent.

Mitral annular calcification is usually localized to the mitral ring, invariably the most common site being the base of the posterior mitral leaflet (Fig. 2.5). Rarely the calcium extends onto the mitral leaflet (Fig. 2.6). This process generally starts at the base of the leaflets and the tips of leaflets remain mobile (Fig. 2.7). MAC may be distinguished from post-rheumatic changes by the lack of leaflet commissural fusion and the fact that the leaflet is not diffusely diseased. MAC may also fix or tether the posterior leaflet

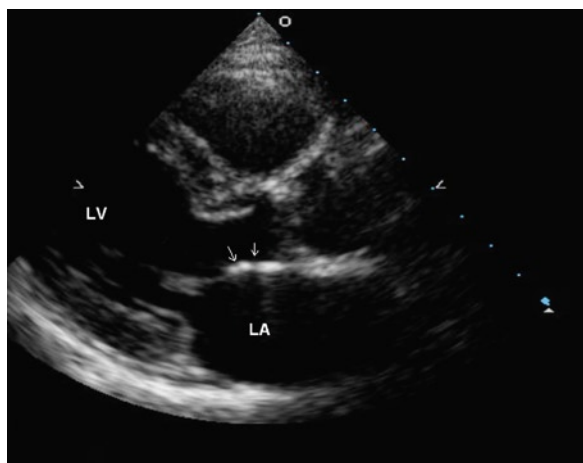


**Fig. 2.5** The mitral valve has been opened laterally demonstrating severe calcification of the posterior annulus between the left atrium and the left ventricle

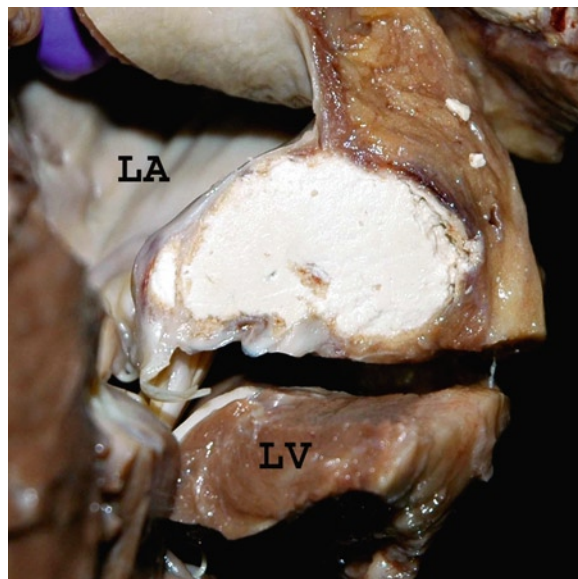
to the underlying calcified mass, restricting the leaflet motion and contributing to valve insufficiency. Loss of the normal left ventricle squeezing motion during systole due to rigidity, also contributes to mitral insufficiency. When liquefactive degeneration of the calcific mass occurs, extension to the posterior left atrial wall has been described (Figs. 2.8, 2.9). In these cases, the mass may mimic a valvular mass (Fig. 2.10). MAC with liquefaction necrosis may grossly mimic a gumma, an abscess or more commonly a necrotizing granuloma (Fig. 2.9). MAC may also ulcerate with thrombus deposition with the potential for embolization (Fig. 2.11). MAC was associated with a doubled risk of stroke, independent of traditional risk factors for stroke, in longitudinally followed population-based cohort (Framingham Heart Study). MAC may



**Fig. 2.6** Mitral annular calcification is demonstrated in the parasternal long- (a) and short-axis (b) views as localized, bright density at the base of the posterior mitral leaflet (arrow). The circumferential extent is clearly shown on the short-axis view (arrows). LA left atrium, LV left ventricle

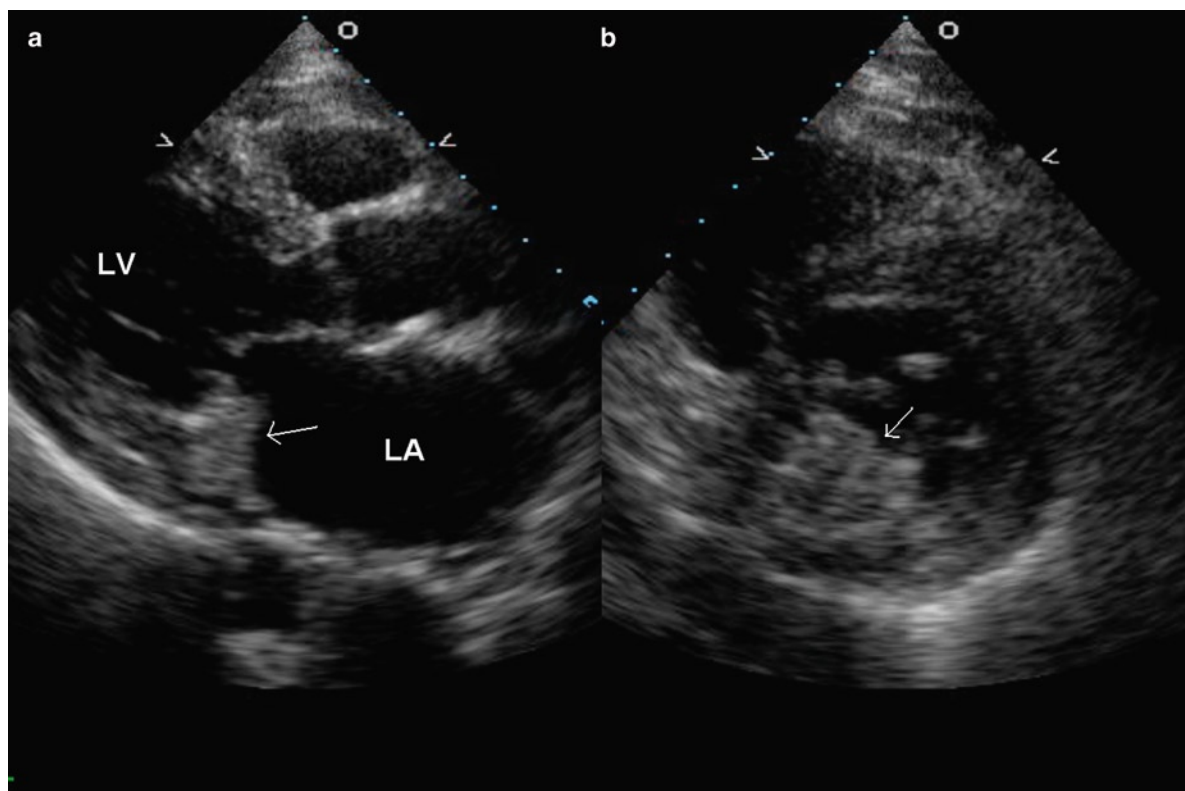


**Fig. 2.7** In this 86-year-old woman, the sclerotic changes involve the aortic root and extend to involve the basal two thirds of the anterior mitral leaflet. Mitral stenosis should be suspected when both mitral annular calcification and sclerotic involvement of the mitral leaflets are present. LA left atrium, LV left ventricle



**Fig. 2.8** Liquefaction of a large mitral annular calcific deposit. It extends under the left atrium (LA) wall and fixes the posterior mitral leaflet to it. LV left ventricle





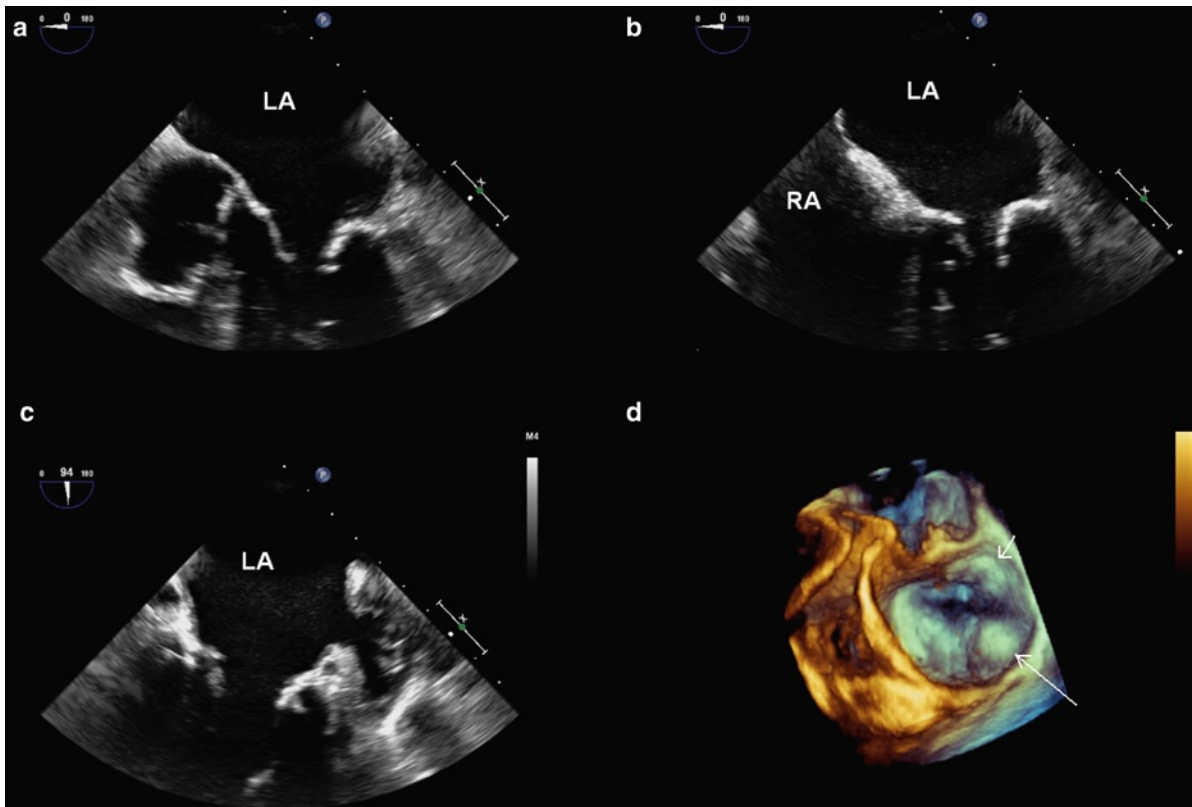
**Fig. 2.9** This 88-year-old woman has a large calcific mass at the posterior mitral annulus which may be confused with an abscess or necrotizing granuloma. The mitral annular calcification is less echo dense in keeping with liquefaction, and is shown (arrows) in the parasternal long-axis (a) and short-axis (b) views. LA left atrium, LV left ventricle

also become ulcerated and infected, giving rise to emboli. If infected, there is usually leaflet perforation and myocardial abscess formation. Thus when MAC is noted in an echocardiographic examination to assess for a source of emboli, it should be remembered that MAC is not only a risk factor for thromboembolism but may have a direct causative role.

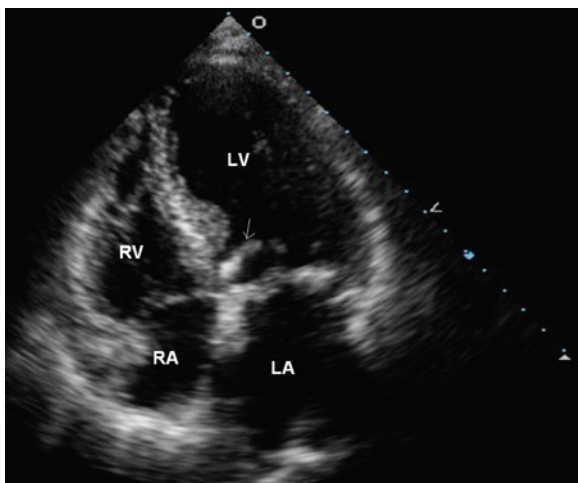
## Calcific Aortic Valve Changes

Age-related “degenerative change” of aortic valves is the most common cause of adult aortic valve stenosis encountered in North America. Traditionally valve “degenerative” calcification was thought to be passive in nature representing dystrophic calcification of degenerated material from wear and tear of the valve tissue. Increasingly, this theory has been shown to be

incomplete. Early there is endothelial dysfunction from wear and tear, and hemodynamic shear stresses, followed by lipid accumulation, inflammation, alteration of cytokines, growth factors and valve matrix metalloproteinases [3]. The process of valve calcification has much in common with atherosclerosis and bone formation [4–6]. Progression of aortic valvular disease in patients from the general population has been associated with many of the traditional risk factors for atherosclerotic disease including systemic arterial hypertension, hyperlipidemia, and diabetes mellitus [7–10]. Stenotic aortic valves have a larger amount of lipid compared to non-stenotic valves [11]. The lipid may oxidize and attract inflammatory cells. Early cusp yellow discoloration and fibrosis eventually evolves into an arch of calcium extending from the base of each cusp like an inverted “u” (Fig. 2.12). With repetitive valve deformation, endothelial damage, inflammation and lipid oxidation, nodules of calcium form and the cusp becomes sclerotic.



**Fig. 2.10** The extent of mitral annular calcification and involvement of the mitral leaflet are shown in these transesophageal echo views (a–c). The calcification extends and limits the excursion of both leaflets. The 3D view of the mitral orifice from the left atrial perspective (d) shows that the calcification involves the basal half of the entire anterior mitral leaflet (*short arrow*), and a large calcific mass in the medial aspect of the annulus (*long arrow*). LA left atrium, RA right atrium

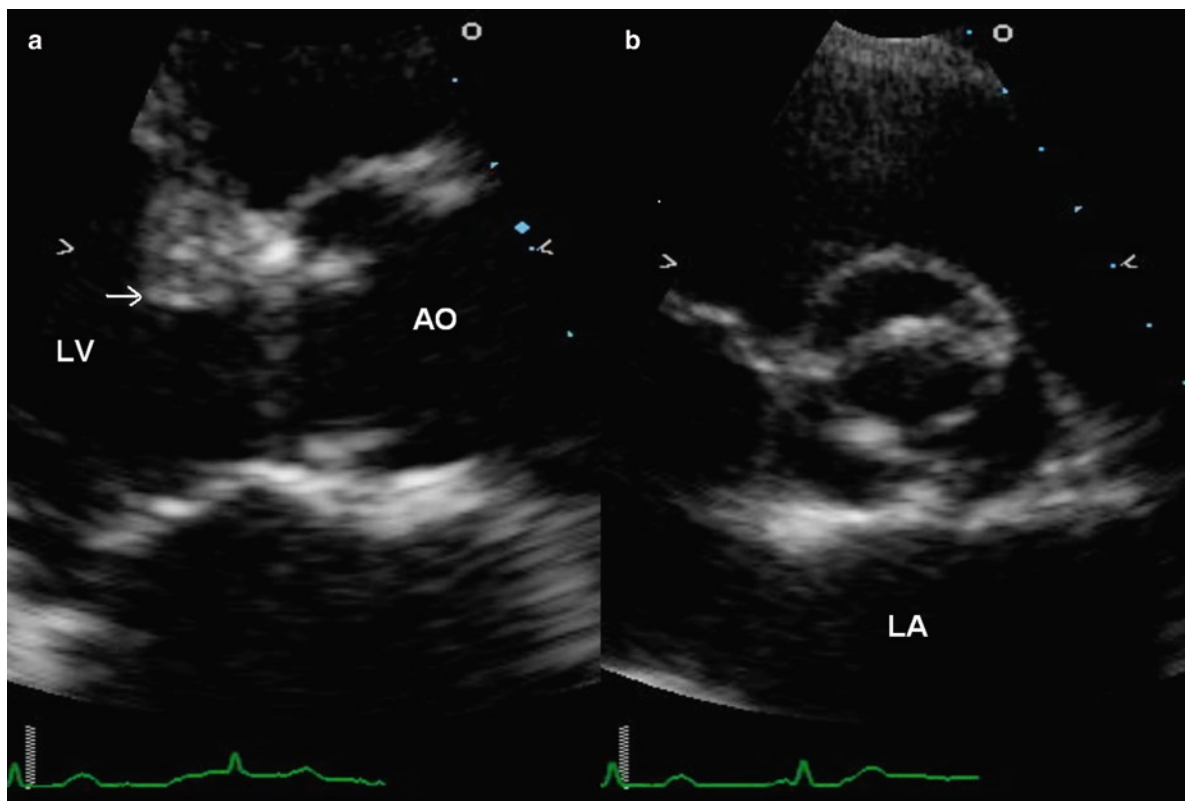


**Fig. 2.11** There is a mobile mass (*arrow*) attaching to the ventricular surface of the mitral annulus calcification in this 73-year-old man with coronary artery disease. The mass is likely a thrombus because it resolves following anticoagulation treatment. LA left atrium, LV left ventricle, RA right atrium, RV right ventricle

Nodular thickening of one or more of the aortic cusps is an early sign of age-related degeneration [12]. The thickening is usually located at the nodule of Arantius or the base of the commissures (Fig. 2.13). In a follow-up of 3–5 years, about 10% of individuals with aortic sclerosis will progress to develop aortic stenosis. Aortic stenosis is also a progressive process, and individuals with more extensive valvular calcification have a more rapid rate of progression. Recent trials have showed that cholesterol lowering with statin does not have an effect on the progression of aortic stenosis.

When aortic valve cusp calcification is present, it is not unusual to note calcification of the sinotubular junction above the aortic valve (Figs. 2.14, 2.15). Pathologically, the sinotubular calcium deposits are similar to those observed in MAC. This calcification is usually benign and clinically silent. However, if the deposit becomes large it may extend to and obstruct the coronary arterial ostia.

**Fig. 2.12** Excised aortic valve with degenerative calcification. The calcium is localized and the free edge of the cusp is relatively spared. Small fenestrations at the lateral area of each cusp are also evident

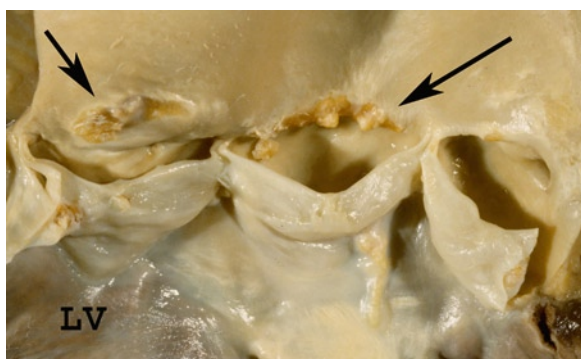


**Fig. 2.13** The age-related sclerotic changes are shown in the parasternal long-axis (a) and short-axis (b) views. The aortic valve is tricuspid with diffuse thickening of the right cusp and thickening of the nodule of Arantius of the non-coronary cusp. The left cusp is relatively unaffected. There is mild restriction in excursion of the aortic cusps. The aortic root is also involved, as it has increased thickness. *Ao* aorta, *LA* left atrium, *LV* left ventricle

## Age-Related Amyloidosis

Amyloid deposition is common in the elderly heart. Amyloidosis is a disease process, with a common staining characteristic – eosinophilic amorphous on routine stains, and birefringence with polarized light

using a Congo red stain. The heart may be involved by primary amyloid, secondary amyloid, and senile or age-related systemic and familial transthyretin types. The prevalence of cardiac involvement and the resultant clinical consequences vary considerably between the groups. Amyloid may be clinically silent, or may



**Fig. 2.14** Calcification of the sinotubular junction (*arrows*) above the aortic valve and the aortic sinuses. *LV* left ventricle

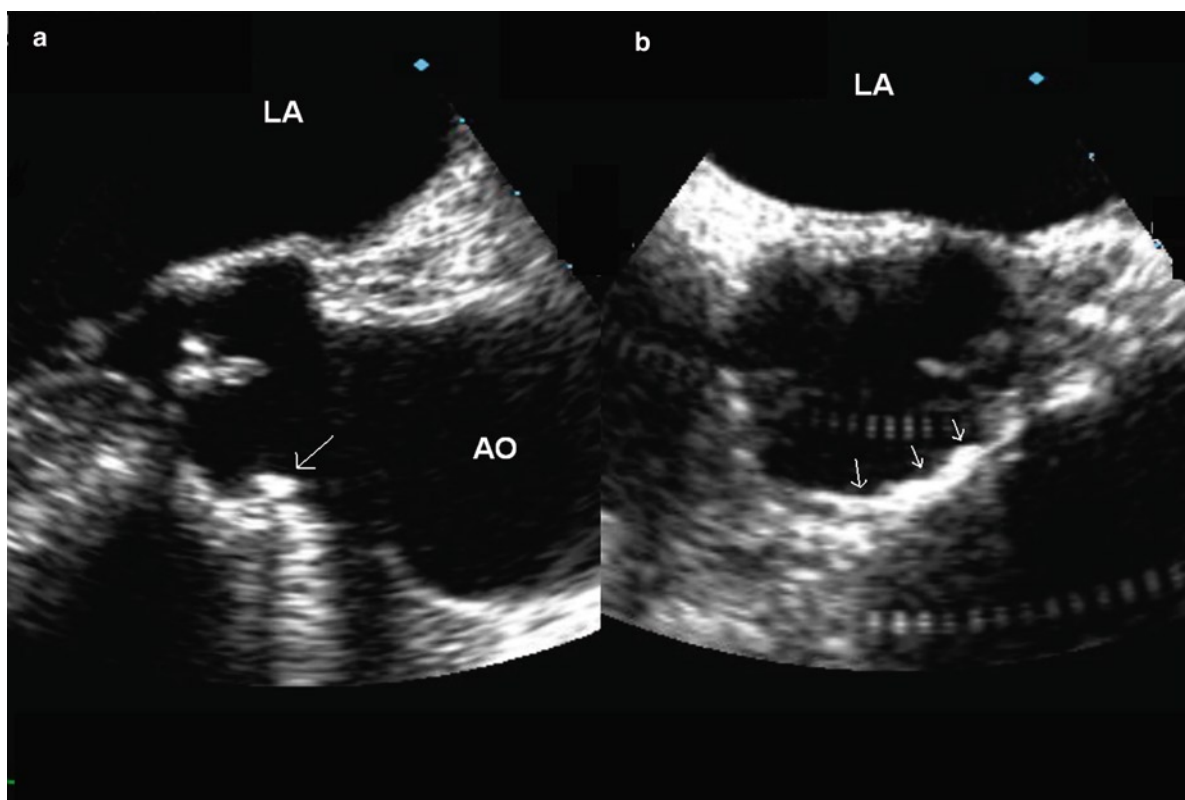
be associated with arrhythmias, diastolic dysfunction and restrictive myocardial findings, asymmetrical septal hypertrophy, systolic dysfunction, conduction disturbances, and coronary insufficiency [13].

Senile or age-related transthyretin amyloid is often without clinical complication. Histologically it cannot be distinguished on routine stains from the other

amyloid types, so immunostaining is informative. Age-related amyloid may be found in any chamber, the coronary arteries, the valves and the pericardium. Commonly it deposits in a pericellular location around the myocytes, and if significant, it may contribute to diastolic dysfunction. Endocardial and valve amyloid deposits may cause stiffening. Epicardial vascular amyloid is often silent, but the small vessel disease may cause microinfarcts. The fibrosis associated with these infarcts aggravates the diastolic dysfunction.

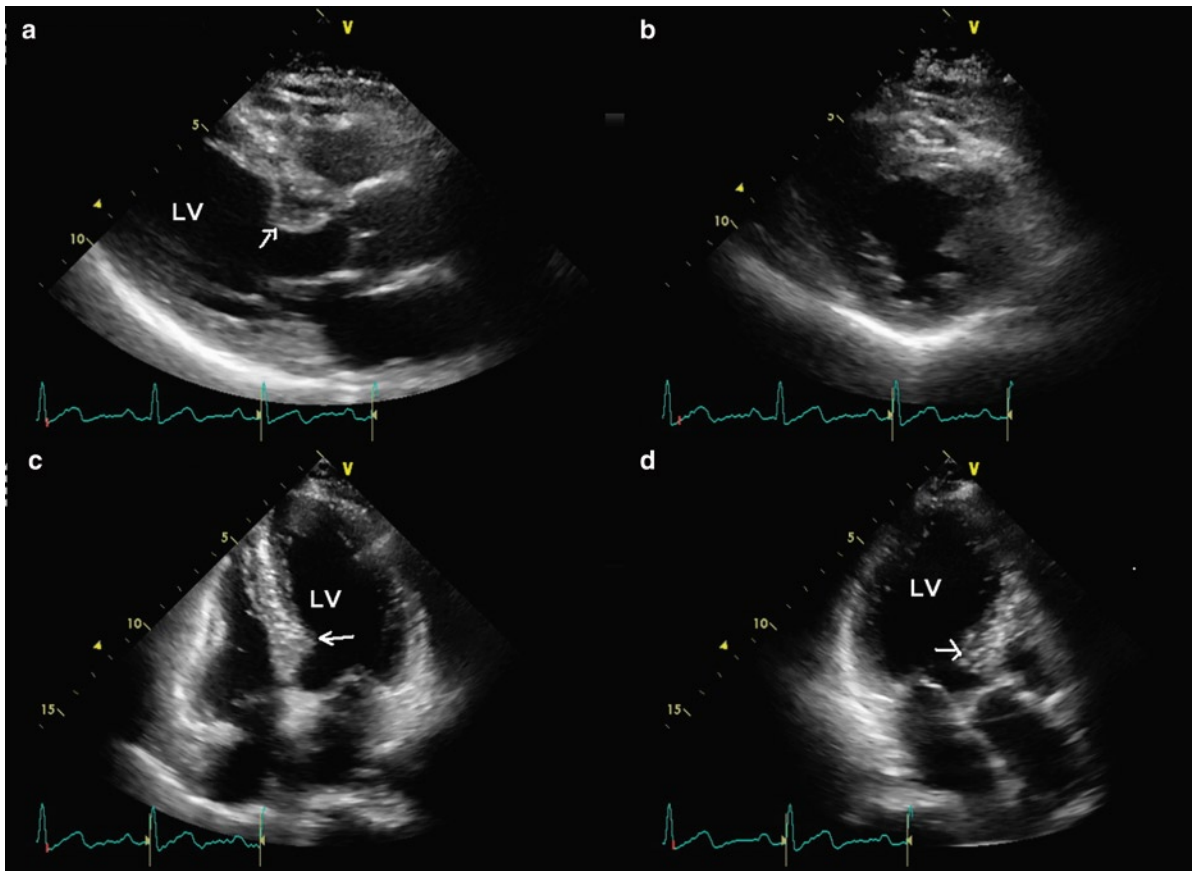
## Age-Related Cardiac Chamber Changes

With age, studies have found that the heart weight remains relatively constant in men but the heart weight increases in women, up to about the tenth decade and then the heart weight decreases in both men and women [14]. The heart stiffens and the volume of the left ventricle decreases with a decrease in base to apex dimension [15–20]. The interventricular septum may slightly



**Fig. 2.15** This 84-year-old woman with aortic stenosis has calcification at the sinotubular junction (*arrows*) shown in the transesophageal aortic long-axis (a) and short-axis (b) views. *Ao* aorta, *LA* left atrium

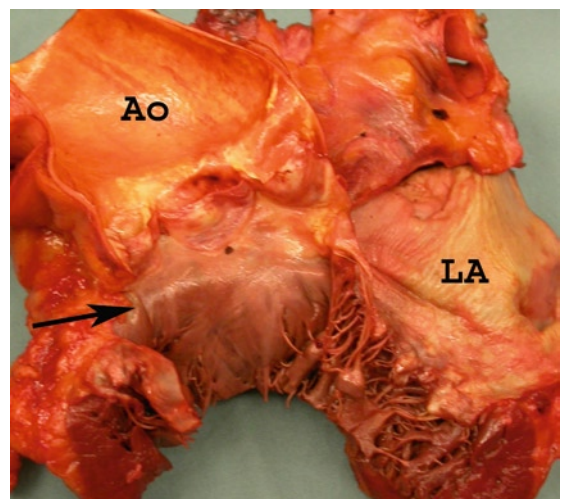




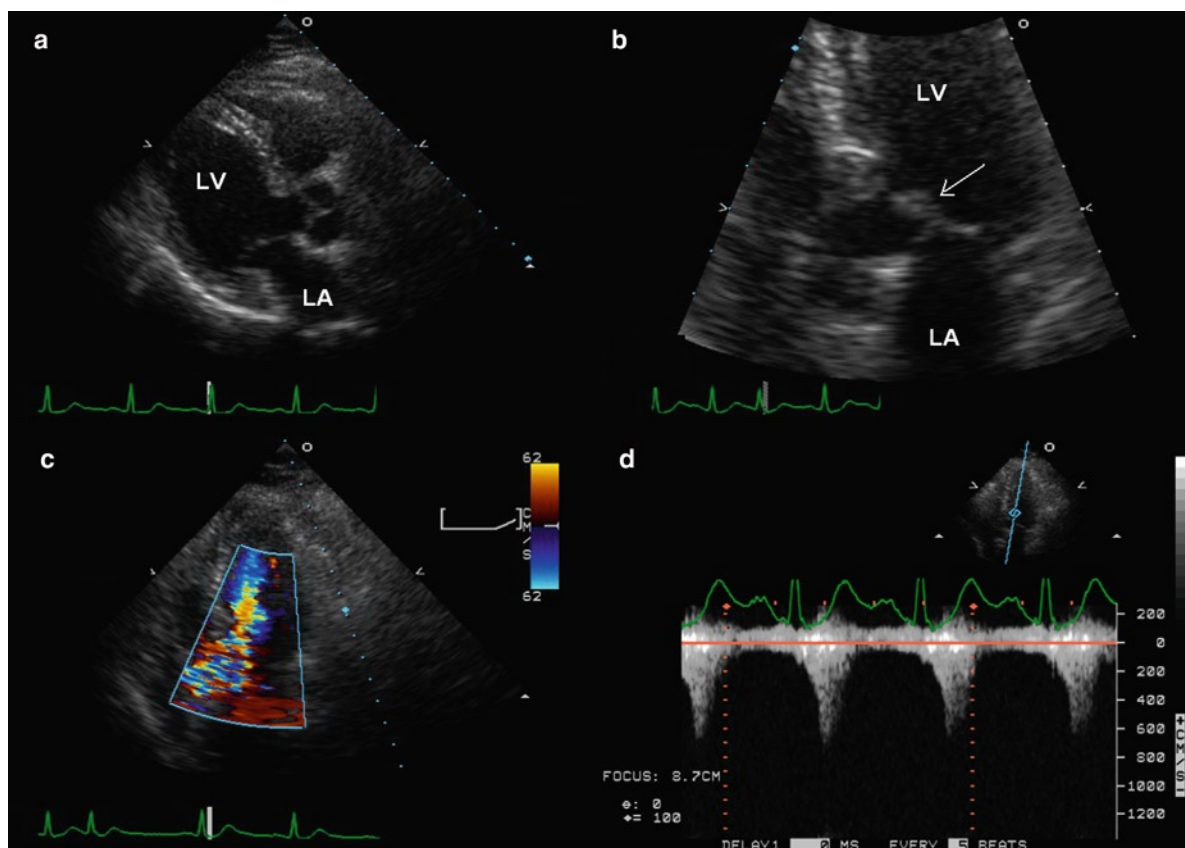
**Fig. 2.16** These are the parasternal long-axis (a), short-axis (b), apical four chamber (c) and apical long-axis (d) views of a 71-year-old woman. The ventricular septum is angulated with a sigmoid shape (arrow) and the left ventricular wall thickness is mildly increased. LV left ventricle

increase in thickness (Fig. 2.16). This needs to be considered in the assessment of patients suspected to have hypertrophic cardiomyopathy [14, 21]. The left atrium increases in volume and dilates with age [21, 22].

With age, the aorta dilates and tilts to the right on the interventricular septum, thus the ventricular septum under the aortic valve becomes protuberant or prominent in the left ventricle outflow tract (Figs. 2.16, 2.17). This has been termed the “sigmoid” septum due to the shape of the left ventricle outflow tract. It is generally not clinically significant but it can contribute to systolic anterior motion of the mitral valve leaflet and may contribute to left ventricle outflow obstruction in hearts with significant left ventricular hypertrophy (Fig. 2.18). It is sometimes removed as a surgical myomectomy specimen during aortic valve replacement (as the individuals have aortic stenosis related left ventricular hypertrophy exacerbating the prominence of the septum).



**Fig. 2.17** The heart has been opened to show the left ventricle outflow tract. The upper part of the ventricle septum is prominent (arrow), as the aorta (Ao) has shifted slightly rightward with age. LA left atrium



**Fig. 2.18** This 69-year-old woman undergoes dobutamine stress echocardiography because of exertional dyspnea and tiredness. The parasternal long-axis view is shown in (a), apical long-axis view in (b), color flow imaging of the apical long-axis view in (c) and continuous wave Doppler assessment of the left ventricular outflow tract in (d). During dobutamine infusion, systolic anterior motion of the mitral valve (arrow) develops associated with a high subaortic gradient. LA left atrium, LV left ventricle

## Summary

An understanding of the age-related changes is crucial to the interpretation of echocardiographic findings. The presence of a sigmoid septum is likely normal in an elderly individual but should raise the possibility of hypertrophic cardiomyopathy in a young person. Sclerotic changes and calcification of cardiac structures are common in the elderly, and should not be confused with abnormalities such as tumors.

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