Age-related Morphological Changes in Cardiac Valves

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Valvular heart disease is a common cardiac problem. There are many age-associated changes that can occur in otherwise healthy heart valves. These commonly develop in the aortic valve and, to a lesser extent, in the mitral valve. In both cases there is fibrosis and thickening of the tissues with the deposition of calcium salts in the aortic valve cusps and in the annulus of the mitral valve. These changes can contribute to progressive secondary changes in the heart (left ventricle and left atrium), which can be associated with significant morbidity related to complications of valvular disease, such as congestive heart failure, infective endocarditis and sudden death.

Key words: heart valves, age-related changes, calcified aortic valve, mitral annular calcification.

Introduction

The mandate of quality health care includes improved neonatal survival, better maternal and neonatal health and an improved life expectancy, resulting in an increasingly older population with the largest growth in the 65+ age group. Therefore, there is a growing need for an improved awareness of age-related changes in the body in general and in the heart in particular. In addition to risk factors such as diabetes mellitus, abnormal lipid levels and hypertension, increasing age is a major independent risk factor for cardiovascular disease. In a previous issue of Geriatrics & Aging, the age-related changes in the myocardium were highlighted. In this paper we review age-related cardiac valvular changes and briefly discuss their sequelae and treatment.

Heart Valves: Structure and Function

Heart valves serve the important function of preventing backflow, or regurgitation, in the healthy heart. It is well known that cardiac valves can and do suffer congenital and acquired disease (Table 1) and that neoplasms are exquisitely rare. Congenital valvular disease manifesting in childhood is usually seen in right-sided valves, while acquired disease is more common in left-sided valves (higher pressure). All four valves have a similar basic structure and are divided morphologically into atrioventricular valves (mitral [MV] and tricuspid [TV]) and the semilunar valves (aortic [AV] and pulmonary [PV]). The valves on the left side (MV, AV) are exposed to higher closing pressures than those on the right side (TV, PV), and they consequently show structural differences such as a thicker zona fibrosa, a thicker spongiosa and a more prominent nodulus Arantius.

The valve function of maintaining unidirectional blood flow requires the integrated movement of all anatomic components of the valve, collectively referred to as the valve apparatus. The atrioventricular valve apparatus is comprised of the annulus, leaflets, chordae tendineae, papillary muscles and the myocardium of the chamber on either side. The semilunar valve apparatus is comprised of the annulus (aortic valve only), cusps, commissures, vessels and the ventricular myocardium. Endothelial cells cover the valve surfaces. While appearing structurally similar throughout the cardiovascular system, endothelial cells likely have different functional effects at different sites, including the heart valves.

Histologically, all valves have four basic layers: the soft compressible spongiosa; the firm collagen-rich fibrosa; the ventricularis (continuation of the ventricular endocardium) and; the atrialis (continuation of the left and right atrial endocardium, the aorta or the pulmonary arterial intima). The tip of the AV is composed only of fibrosa and spongiosa. The fibrosa, the central layer of the valve composed of collagen and elastic fibres, provides strength and structural support to the valve. The zona spongiosa provides flexibility and allows the valve to “fold and unfold” as it opens and closes. Chordae tendineae are thin, cord-like (or tendon-like) structures composed of endothelium-covered collagen and elastic tissue extending from the valve leaflet to the endocardial surface of papillary muscles. They are the “tensor” apparatus that allows the MV to stay closed against the left ventricular closing or ejection pressures.

The predominant glycosaminoglycans (GAGs) in heart valves are hyaluronic acid, chondroitin sulphate and heparan sulphate. With advancing age, there is a striking increase in elastin and GAGs with a concomitant decrease in collagen in the MV. Increased thickness of valves is noticed with aging in both males and females. This thickening is more prominent in left-sided valves (MV, AV) that are subject to higher pressures compared to right-sided valves (PV, PV).

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TV), as well as in the basal or annular third compared to the rest of the valve (greater stress localization). The PV shows the least noticeable change with aging (Table 1). The PV differs from the other three valves in that its cusps arise from the right ventricular outflow tract endomycocardium and not from the PV “annulus”. This is relevant to the way the tissues are removed for the Ross or “valve switch” procedure for treating aortic valve disease.

**Aortic Valve: Age-related Changes**

The aortic valve shows the most significant age-related changes, often requiring valve replacement with prostheses (Figure 1). The AV cusps thicken with age, with fibrosis most marked in the posterior or non-coronary aortic cusp (Figure 2).6 Histologically, the thickening is seen primarily in the fibrosa and in the ventricularis (Figure 3).6 Thickening also is seen as plaque-like lesions on the cusps, especially at their bases. These plaques show a striking increase in elastin with a modest decrease in collagen, but no change in GAGs.5

The late morphologic hallmark is a heaped-up or nodular calcific mass(es) along the aortic or non-flow surface of the cusps that gradually becomes anchored to the annulus and prevents the smooth opening of cusps. Calcific deposits are often seen at the base and body of the cusps, especially along the “line of closure or rough zone” and rarely at the free edges (Figure 2). In addition, there is an increase in the number of adipocytes in the leaflet and increased prominence of the nodulus Arantius. This thickening and calcification of the AV is referred to as aortic sclerosis, which increases with age and is associated with mineral deposits (calcium apatite salts) in the zona fibrosa.

Aortic sclerosis is seen in over 20% of people older than 65 years and in 35% of people older than 75 years.7 In the Helsinki Aging study, some degree of calcification was seen in 53% of people older than 75 years, and age was found to be a significant independent predictor of aortic valve calcification7—findings that were confirmed by the Cardiovascular Health Study.8 This calcification is believed to be a degenerative change and can lead to significant aortic valve stenosis. Aortic valve sclerosis and stenosis are considered to be stages in calcific valve disease and occur in valves that were apparently previously normal and had three well-functioning cusps.8 Hemodynamically significant aortic stenosis is seen in 2–3% of the population older than 65 years.8 Calcific AV disease is the most common valvular lesion among older people, accounting for over half the number of cases needing prosthetic replacement of aortic valves.9 Most of these patients present in the seventh decade with symptoms of exercise intolerance (most common), angina syncope and orthopnea.

Calcific AV disease needs to be differentiated from aortic stenosis secondary to calcification of the congenitally abnormal AV. The bicuspid (congenitally abnormal) aortic valve (BAV) is seen in 2–3% of the population and undergoes relatively accelerated calcification compared to a three-cuspid AV. Why some BAVs progress more rapidly to the symptomatic stage remains to be clarified. However, only a small percentage of this group will need AV replacement. Patients with a calcific BAV present in their 50s and 60s. Commonly appears before the seventh decade with symptoms of exercise intolerance.

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In a study by Christie, et al., maximum radial elastic extensibility (also referred to as stretch) of human aortic valves decreased with age.13 Stretch loss in the leaflets can be a contributing factor to the development of aortic incompetence.13 Fenestrations are variably sized defects in the lunules of valve cusps ranging in size from pinpoint to over 1.0cm in diameter, and are increasingly apparent with advancing age. They may be congenital defects that gradually increase in size or may form due to wear and tear. Fenestrations are usually seen near commissures, in the lunule above the line of closure. If they extend beyond the line of closure they

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**Table 1**

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Aortic</th>
<th>Mitral</th>
<th>Tricuspid</th>
<th>Pulmonary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital</td>
<td>yes</td>
<td>very rare</td>
<td>yes*</td>
<td>yes**</td>
</tr>
<tr>
<td>Acquired</td>
<td>yes</td>
<td>yes</td>
<td>rare</td>
<td>rare</td>
</tr>
<tr>
<td>Chronic inflammation†</td>
<td>yes</td>
<td>yes</td>
<td>rare</td>
<td>very rare</td>
</tr>
<tr>
<td>Acute inflammation‡</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes**</td>
</tr>
<tr>
<td>Age-related††</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>

* In association with other changes; isolated valvular abnormality is rare.
** In pulmonary valve, congenital changes and infective endocarditis are common.
† Rheumatic process.
‡ Infective endocarditis.
Aging Cardiac Valves

Figure 1.
Age-related Morphological Changes in the Aortic Valve

Aortic valve changes and sequelae with aging:

- cusp sclerosis and thickening
- stiffening of cusps/ decreased mobility
- stenosis of orifice
- progressive left ventricular hypertrophy
- left ventricular decompensation
- left ventricular dilatation
- mitral valve incompetence
Aging Cardiac Valves

may cause valve incompetence or regurgitation. The size of the aortic valve ring or annulus increases with advancing age. Although rare, the aortic valve ring has been reported to be as large as the mitral valve in patients older than 90 years.

Mitral Valve: Age-related Changes

In the MV, the closing edge (rough zone) of each leaflet is thicker than the rest of the valve and this is more pronounced in the anterior leaflet than in the posterior. MV leaflets become less translucent with age and adipocytes and lipid deposits accumulate within the leaflet tissue, especially on the ventricular surface and in the zona spongiosa. Nodular thickening often can be seen along the lines of closure on both leaflets, likely due to repeated trauma caused by valve closure. With increasing age, collagen deposition, degeneration, lipid accumulation and dystrophic calcification of the annulus is seen. Lamb’s excrescences are increasingly found with advancing age and were reported in almost all subjects over 60 years of age. They are found on the atrial surface of the leaflets, usually along the line of closure.

Mitral annular calcification (MAC) is considered a degenerative disease similar to aortic sclerosis or stenosis. The prevalence of MAC increases with aging. Crescent-shaped calcific deposits of varying severity and significance can be seen at the basal end and in the annulus of the MV leaflets in about half of the older population, on echocardiography. Any condition that increases the stress on the MV (e.g., hypertension, mitral valve prolapse) enhances this degenerative process. Increasingly, the basal part of the posterior mitral leaflet (PML) adheres to this annular calcific mass that bulges into the left ventricular cavity, immediately behind the PML.

Complications of MAC include calcific erosion of the PML, perforations of the PML, infective endocarditis and "liquefaction" necrosis of this calcific mass. MAC can result in mitral regurgitation and/or mitral stenosis, left atrial enlargement, atrial fibrillation and an increased incidence of thromboembolic phenomena. In the prospective Framingham Heart Study, MAC was found to be associated with stroke; this association was found to be independent of atrial fibrillation, congestive heart failure (CHF) and coronary heart disease. The risk of stroke, embolic in two-thirds of cases, was found to double in the presence of MAC. Other complications of MAC include complete heart block or other conduction defects because of extension of calcification from the mitral ring into the conduction system. Other changes in the mitral annulus include annular dilatation (often seen in CHF and dilated cardiomyopathy).

Redundancy of the leaflet tissue, with increasing hooding of the MV leaflets (occurring due to increased closing pressures over the years) and MV incompetence, is seen in older patients. This is due partly to shortening of the overall base to apex length of the left ventricle, causing the mitral valve chordae to become “redundant” and to appear longer, leading to mild mitral leaflet tissue prolapse.

Development of “atheroma” on the MV anterior leaflet is increasingly noticed with aging. Lipid deposits can occur in both leaflets, and are found on the ventricular surface and sometimes can involve the chordae tendineae.

Surgical Management of Damaged Heart Valves

Cardiac surgery may be required to replace aging or damaged heart
Aging Cardiac Valves

Valves. Although cardiac surgeons are very familiar with the location and distribution of calcium deposits in heart valves, removing these poses a number of problems. Multiple fragments of calcium may result during debridement of a calcified valve annulus. Great care must be taken to avoid embolization of these calcium fragments, which could otherwise cause a stroke. Calcium that extends deep into the annulus and surrounding tissues is particularly dangerous. If the calcium is not carefully removed, a new valve prosthesis may not seat well. On the other hand, radical debridement of the annulus can lead to aortoventricular or atrial ventricular separation which, if unrecognized, is usually fatal. Finally, older patients who require aortocoronary bypass surgery frequently have associated valvular sclerosis. Even though the main indication for surgery is the presence of coronary heart disease, there is often controversy about the best management of mildly sclerotic valves that are identified at the time of coronary bypass surgery. The surgeon must make a judgment about adding an unplanned valve replacement procedure to a planned aortocoronary bypass surgery. This has to be balanced against the likelihood that at some time in the future sclerotic valves eventually cause hemodynamically significant problems. This, in turn, may expose the patient to the risk of a re-operation, often in the face of functioning bypass grafts.

Conclusion

In this review, age-associated changes in cardiac valves have been summarized. Some of these, such as lipid insulation, may remain trivial morphological curiosities, while others, such as aortic valve calcification and mitral annular calcification, can lead to significant clinical consequences and often to heart valve replacement with one of the many excellent prosthetic heart valves available today.28,29 Many other complications, such as thromboemboli and infective endocarditis, can occur on these diseased valves (Table 2). It is therefore essential to be aware of these changes, to order the appropriate investigations and to seek appropriate surgical intervention when required.

No competing financial interests declared.

References


