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Aortic stenosis: current treatment options for a common condition in old age

D Tiwari[1], J Radvan[1] and SC Allen[2]
[1]The Royal Bournemouth Hospital and [2]Centre for Postgraduate Medical Research and Education, Bournemouth University, Poole, UK

Summary

Degenerative-calcific aortic stenosis is mainly a disease of old age. Patients with mild to moderate stenosis without symptoms and those with aortic valve sclerosis do not require mechanical intervention. There is no firm evidence that the rate of progression can be modified by medical therapies, though statins might have some effect. Patients who develop severe stenosis with symptoms have a very poor prognosis if managed medically. Surgical aortic valve replacement greatly improves symptoms and mortality rates and remains the treatment of choice for those fit for major surgery, even above the age of 80 years. For those not suitable for surgery, or who are unwilling to have an operation, outcomes can be significantly improved by trans-catheter aortic valve replacement, which has become an important option for frail elderly patients. Balloon aortic valvuloplasty improves symptoms and short-term survival, but has a less clear impact on mortality beyond 1 year. It is useful as a palliative treatment and as a bridging procedure for patients who are not ready for valve replacement. There is less agreement on the best approach to patients with asymptomatic severe aortic stenosis. Trials indicate that early valve replacement results in outcomes that are comparable to those seen in symptomatic patients, though guidelines advocate delaying surgery until symptoms occur or left ventricular function begins to decline rapidly. All elderly patients with severe aortic stenosis should be considered for a mechanical intervention unless there is a properly considered reason for not doing so, or they are not willing to receive such treatment.

Key words: aortic stenosis, aortic valve replacement, elderly, old age.

Introduction

Aortic valve disease is commonly encountered in the clinical assessment of elderly patients. Until the middle of the 20th century many cases were due to inflammatory, mostly post-rheumatic, valve damage and the burden of disease fell on the young and middle-aged. However, despite the decline of rheumatic fever in most parts of the world, the prevalence of aortic valve disease is rising. This is due to the increase in mean life expectancy to unprecedented levels in many countries, which has enabled a large number of people to live long enough to develop degenerative-calcific aortic valve damage in late life. Patients with bicuspid aortic valves also tend to progress to significant aortic stenosis. Consequently, aortic stenosis (AS) is now mainly a disease of old age.[1–4]

Until recently, the range of treatment options for moderate to severe AS was limited in old age, particularly for the very old and those with significant co-morbidities that rendered them unfit for the rigours of major cardiac surgery. Further, the evidence for benefit from aortic valve replacement (AVR) in very elderly patients had not, until recently, been confidently established. This generated a very conservative approach to the management of symptomatic AS among general practitioners, geriatricians and cardiologists, particularly for patients above the age of 80 years, and a rate of referral for AVR that was probably too low. However, over the last 15 years there has been a great improvement in the quality of evidence for benefit from several interventions for AS, and the arrival of new technologies has widened the range of options for treatment in old age. This review sets out to examine that evidence, with particular reference to outcomes in older patients, and to frame the subject in the context of new insights into the epidemiology and pathology of aortic valve disease.

Search methods

We used the terms 'aortic stenosis', 'aortic valve disease', 'elderly', 'older adults', 'old age' and

Address for correspondence: Professor S.C. Allen, Postpoint A10, The Royal Bournemouth Hospital, Castle Lane East, Bournemouth BH7 7DW, UK. Email: Stephen.allen@rbch.nhs.uk

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'aortic valve replacement' to search PubMed, Medline, Exerpta Medica and Ovid from 1990 to 2010. Ninety-four articles were identified for initial screening. Further selection was made according to the quality of the research, including methodology and sampling for trials, and large size for series and case ascertainment studies. Forty-nine were selected for reading in depth. We also searched relevant national guidelines. Some older review articles and several textbooks were also consulted to provide background information and a historical perspective.

Definitions

There are no universally agreed definitions for AS or aortic valve sclerosis (AVS). It is usual in clinical practice, and research, to measure the degree of stenosis in terms of the actual valve cross-sectional area. Nevertheless, the size of the patient needs to be taken into account during clinical evaluation; a small elderly person can remain asymptomatic with a degree of stenosis that would cause critical haemodynamic embarrassment in a larger or younger individual. One of the factors complicating the interpretation and comparison of published studies is the lack of standardization in the definitions of severity of AS. A further degree of variation results from the relatively operator-dependent nature of pressure and flow measurements derived from echocardiographic imaging.

Typical definitions,[5] which will be used in this review, are as follows:

AVS is defined as focal or diffuse thickening of the aortic valve cusps while the valve cross-sectional area is in or only slightly below the normal adult range (>1.8 cm^2) and the trans-valvular pressure gradient and maximum flow velocity (V_{max}) at rest remain in the normal range (<12 mmHg and <2 m s^{-1}, respectively). AVS is now often regarded as very mild AS, rather than a separate clinical entity.

AS is defined as focal or diffuse thickening of the aortic valve cusps with an abnormally low valve cross-sectional area, taking into account the size of the patient, and a raised transvalvular pressure gradient and V_{max} (though the last two factors can be normal or low if left ventricular contractility is severely reduced).

The prefix 'calcific' is used when there is calcification present, usually near the base of the valve leaflets. This is found in almost all elderly patients with aortic valve disease.

AS is usually referred to as mild when it is causing no symptoms and the valve cross-sectional area is >1.5 cm^2, moderate when 1.0–1.5 cm^2 and severe when <1.0 cm^2. Patients with severe AS and normal, or near-normal, left ventricular systolic function usually have a trans-valvular pressure gradient >40 mmHg.

These indices are usually measured by trans-thoracic echocardiography and there is a broad relationship between the severity of the valve narrowing and symptoms. Other factors contribute, particularly coronary artery disease, the degree of left ventricular hypertrophy, the presence of other valve lesions and the individual's level of physical activity and metabolic rate. There is considerable individual variation in the clinical presentation. Therefore in elderly patients it is usual to include the presence of symptoms, and their intensity, in the overall assessment of severity of AS. Symptoms play a crucial part in deciding the thresholds for intervention in older people. Typically, patients with significant AS complain of chest pain, breathlessness, faintness and sometimes blackouts on exertion. Mechanical limitation of the cardiac output, excessive left ventricular systolic pressure and impeded coronary perfusion are the main denominators. Those with very severe AS have symptoms at rest.[5] In such cases the valve cross-sectional area is usually <0.8 cm^2.

For the purposes of this review we have not included congenital aortic valve stenosis, or sub-valvular stenotic pathologies.

Prevalence

Large scale echocardiographic studies have shown a prevalence of 40–54% for AVS in asymptomatic community-dwelling people over the age of 75 years, most of whom did not have an aortic systolic murmur on auscultation. The majority had some degree of valve calcification. AS of at least moderate degree was found in 1.6–2.5% of those in the 75–84 year age band and 6–8.5% of those aged 85 years or more. Most of those subjects had no symptoms.[1,4,5] Those with more pronounced AS tended to have more extensive valve calcification. Symptomatic AS has been found to have a prevalence of around 1.5–2.5% in people over the age of 75 years.[4,5] The limited

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life expectancy of that group if untreated, and the increasing use of effective interventions, is probably the main explanation for the apparently low residual prevalence.

Pathogenesis and natural history

Aortic valve sclerosis, and stenosis, is usually caused by the same pathological process that leads to arteriosclerosis. The general risk factors are therefore: age, male sex (though female sex is associated with a higher risk of severe symptomatic AS), smoking, hypertension, diabetes mellitus, high plasma low-density lipoprotein and low plasma high-density lipoprotein concentrations, and short stature. The molecular mechanisms underlying these changes are not fully delineated, though it is becoming apparent that low amplitude systemic, and localized endothelial, inflammatory processes are involved, mediated by macrophage adhesion and migration, leading to pathological expression of genes coding for fibrosis and calcium deposition.[6–12] Patients with AVS have a higher risk of other vascular morbidities, such as stroke, coronary artery disease and peripheral vascular disease.[6] There is some evidence to show that the rate of progression of AVS and AS might be slowed by treatment with statins to correct disordered lipids,[13] though that has not been established with confidence. Also, it has not been shown that treating hypertension slows the rate of progression.[14] There are no credible data on the effects of smoking cessation or improved diabetic control on the echocardiographic time course of AS. On the other hand, patients with chronic renal failure on long-term haemodialysis appear to have accelerated deterioration of their aortic valve disease.[15]

There is no doubt that the natural history of AS is progressive in almost all subjects.[4,16,17] However, there are wide between-subject variations in the rate of progression. AVS is also a progressive disease, and a rising proportion over time will come to meet the criteria for AS. In one 5-year follow-up study of patients with AVS, 32% developed some degree of AS. Most were mild, though 14% were moderate and 8% severe.[17] Some patients with established AS appear to progress very rapidly.[18] Other than haemodialysis, there are no reliable factors that can be used to predict rapid progression.[15]

Post-inflammatory aortic valve disease, for example due to rheumatic fever or vasculitis, now accounts for <20% of all aortic valve replacements (AVR) and <5% of AVRs for AS in people above the age of 75 years.[19]

Management

A full review of the cardiological work up of patients with suspected or established AS is outside the purpose and scope of this review. There are a number of clear guidelines that can be consulted if required.[5,19] When an older person is found to have an aortic ejection systolic murmur, with or without symptoms or other physical signs of AS, the initial investigations should include an ECG, chest radiograph and trans-thoracic echocardiogram. As well as being a screen for important co-morbidities, this minimum set will provide preliminary information on the condition of the valve, left ventricular performance and hypertrophy. Further management will depend on the findings of these first-line investigations and the individual patient's symptoms, physiological condition, functional status and wishes. In this paper we intend to give an overview of the options for intervention in AS in old age and to discuss the potential benefits and risks.

AVS and mild AS

Elderly people with AVS or mild AS without symptoms do not require any form of mechanical intervention.[5,19] There is unanimity about this in the cardiac literature, in agreed guidelines and in practice. Control of cardiovascular risk factors is prudent despite the paucity of evidence for benefit in slowing the progression to significant AS, because there is clear evidence of benefit in other vascular domains in early old age and some evidence for the very old.[19] There are no agreed recommendations for surveillance but it is usual practice to monitor asymptomatic patients with mild aortic valve disease in the primary care setting with a view to further echocardiography if symptoms occur or physical signs change. However, there is some evidence that progression is faster in those above the age of 80 years[20] so a case can be made for regular, perhaps 2-yearly, echocardiographic surveillance in elderly people with mild AS. Antibiotic prophylaxis for dental

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procedures is no longer routinely recommended.[21] Prophylactic AVR for mild–moderate AS at the time of coronary artery bypass grafting (CABG) may not improve survival.[22]

Moderate AS

Most elderly people with moderate AS do not have symptoms caused by the valve lesion. The diagnosis has usually come to light when an aortic ejection murmur has been found during routine physical examination, or when echocardiography or cardiac catheterization has been performed for another reason. Elderly people with moderate asymptomatic AS do not require a mechanical intervention.[5,19] As with AVS and mild AS there are good reasons to control vascular risk factors, though there is no firm evidence that such measures will alter the rate of progression of moderate AS. In the published literature it is apparent that much of the data regarding the progression of AS is based on echocardiographic follow-up of people with moderate AS, most of whom are aged 65 years or more. In that group the rate of progression varies from zero to more than 0.3 cm^2 per year, with an average of 0.12 cm^2 per year, and an average rise of 8 mmHg per year in the trans-valvular pressure gradient.[19] About half of those followed up show very slow progression over 3–9 years.[3] There is some evidence that older subjects, particularly those above the age of 80 years, with heavily calcific disease have faster progression.[20,23] The rate of rise of the systolic trans-valvular pressure gradient can also be used to gauge progression though it will obviously be faster in those who already have a relatively low valve cross-sectional area, as the relationship between area, pressure and flow is not linear. Monitoring echocardiography is therefore usually performed more frequently as the valve becomes more stenotic.

There is no consensus on the frequency of surveillance in asymptomatic moderate AS. The first review is usually at 1 year after which the frequency can be reduced, or suspended, if there is little or no change.

Severe AS

Although degenerative-calcific AS has a long latent period in most cases, once the echocardiographic definition for severe AS is reached and/or symptoms occur, the prognosis worsens steeply.[24,25] There is plentiful evidence of improvements in symptoms, function and survival in elderly people who undergo an aortic valve intervention.[26–28] The management of the condition in an elderly individual will clearly be predicated on whether the patient is likely to benefit from an intervention, is willing to undergo such treatment and has the capacity to consent to any proposed procedures. In most cases the diagnosis will have been established initially by echocardiography. When there is a poor concordance between symptoms and the degree of stenosis in an individual there is a need to proceed to cardiac catheterization to confirm the pathology and to assess the state of the coronary circulation and other valves, and catheter studies are virtually always performed prior to AVR. The range of interventions available at this stage includes medical therapy, balloon aortic valvuloplasty (BAV), transcatheter aortic valve intervention (TAVI), and open AVR with or without CABG. We will now examine the evidence that can help clinicians decide which approach to recommend for their elderly, and frail elderly, patients with AS.

Severe AS with symptoms

The natural prognosis for severe AS in old age is poor.[24,25,28,29] There is around 75% mortality within 5 years when symptomatic patients are treated with medical therapies alone.[29] This was found to apply equally to patients who were fit for AVR but declined, and those not fit for AVR.[30] In a large American study of octogenarians with AS, the 1-, 2- and 5-year survival rates for patients managed medically were 52, 40 and 22%, respectively, and 87, 78 and 68% for those who received AVR.[28] These studies concord with the prevailing narratives among geriatricians and cardiologists that advocate AVR as the intervention of choice for older people with symptomatic AS who are fit enough to have the operation.

AVR – the best option for elderly patients in good physiological condition

Medical therapies do not improve the long-term prognosis, but are clearly useful as short-term treatments for episodes of ischaemic cardiac pain

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and/or left ventricular failure.[5,19] However, there is a substantial body of evidence that AVR gives the best medium- and long-term outcomes in terms of symptom control and survival.[5,19,26–28,30] In recent years improvements in valve design, operation techniques and cardiac anaesthesia have greatly improved the safety and utility of AVR in old age. In one study, the 5-year mortality risk for those declining AVR was increased 12-fold.[30]

There are no internationally agreed exclusion criteria for offering an elderly patient AVR though there is broad agreement that the outcomes, both post-operative and long term, are much poorer in patients with significant uncorrectable left ventricular dysfunction, moderate or severe dementia, renal failure with a glomerular filtration rate (GFR) below 30 ml min^{-1}, significantly reduced pulmonary reserve, advanced malignancy, uncontrolled sepsis or any other contra-indication to major surgery and prolonged general anaesthesia.[5,19,26] Although those with heart failure have less good outcomes than those without, there are survival benefits, compared with medical therapies, of performing AVR in elderly people with New York Heart Association (NYHA) class 1–4 heart failure.[19] There are sometimes technical constraints, particularly in small elderly women with very narrow aortic roots. A need for CABG at the time of AVR does not carry a significant additional risk of prosthetic valve failure, but does predict a higher rate of other adverse vascular outcomes.[27]

Selection should be the result of team discussion between the cardiologists, surgeons and anaesthetists; this approach enables the patient to be offered the best information regarding risks and benefits prior to giving consent to proceed. Formal risk scoring systems, such as the Society of Thoracic Surgeons Predicted Risk of Mortality Score[31] and the EuroSCORE,[32] are often used to stratify patients for overall risk, though they have not been validated for use in elderly patients, or specifically for AS. Such scores, and other frailty indices, can be used as one of the factors to determine the suitability for AVR and for less invasive treatments, though the final decision is one of clinician judgement and should not rely solely on any scoring system.[5,19,33] The decision as to whether to use a mechanical or tissue AVR is a matter of technical suitability and operator preference. There is evidence that outcomes in old age are similar for both types, including long-term survival.[34]

When AVR is planned for frail people there is narrative evidence that outcomes are improved by deploying the holistic approach to care encapsulated in comprehensive geriatric assessment, and by the inclusion of geriatricians in the pre- and post-operative management.[35]

Options for patients unable or unwilling to receive AVR

For very frail individuals, usually those with advanced pathologies and short life expectancy, and people with contra-indications to any form of invasive cardiac intervention, a palliative approach is appropriate. This also applies to those unwilling to undergo any treatment other than drug therapy. Under these circumstances episodes of left ventricular failure, angina and arrhythmias should be treated with drugs in the conventional way and need not be rehearsed in this review. Opioids are often needed to control distressing end-stage breathlessness and/or chest pain.

TAVI

This relatively new approach to the treatment of severe AS has been shown to be very effective, but does not displace AVR as the best option for elderly patients fit enough for open surgery.[5,19,36] It has been shown in several studies that TAVI gives substantially better outcomes, for symptoms and survival, than medical therapy and/or BAV for patients considered at too high a risk for AVR.[37–42] The technology is evolving, so it is possible that TAVI could rival AVR as an option for fit elderly patients in future, though there is no trial evidence to that effect at present.

There are no universally agreed selection criteria for TAVI, though guidance has been published by the National Institute for Clinical Excellence for the UK.[36] However, it appears that the technology in its current state positions TAVI ideally for patients with symptomatic AS who have a life expectancy of a few years, well-preserved cognitive function, a GFR above 30 ml min^{-1}, and who either do not wish to have AVR or are considered to be at high risk for open surgery.

Some patients require concomitant coronary artery interventions (PCI), such as angioplasty or stent insertion, with no apparent adverse influence on outcomes.[42]

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TAVI can be performed under general anaesthesia or sedation with local anaesthesia. A trans-luminal approach via the femoral artery is usually employed, though the alternatives are to approach via the femoral vein, which requires puncture of the interatrial septum, or by apical puncture of the left ventricle, which requires a small thoracotomy. The procedure was completed in 75–88% of attempted cases in three UK series, with various technical reasons for abandonment or failure.[36]

There is usually an immediate resolution of the symptoms of AS. There are immediate haemodynamic improvements, including a lower trans-valvular pressure gradient and lower systolic peak jet velocity. Longer-term improvements in left ventricular function occur as hypertrophy recedes and myocardial contractility and diastolic relaxation become less disordered. In various follow-up series the 1-year survival rate has been 75% or better. As TAVI is usually used for frailer patients the causes of late mortality are usually due to co-morbidities and not related to the valve replacement.[39] Mechanical failure of the TAVI prosthesis has been very rarely reported. Para-valvular aortic regurgitation is relatively common. Five-year survival data are scanty but appear to be considerably better than medical treatment.[36,39]

The role of BAV

BAV gained ground in the 1980s as an alternative means of improving the flow characteristics of the valve, acutely or electively, in symptomatic patients with severe AS who were considered to be unfit for AVR. The approach is trans-luminal, usually from the femoral artery. A balloon is positioned in the valve and inflated to separate the valve leaflets and thereby increase the cross-sectional area. Early series were disappointing, with frequent operative complications, high re-stenosis rates and little impact on survival.[43] It came to be seen as a palliative procedure. However, recent improvements in catheter and balloon technology have given BAV a new lease of life. There is again growing interest in BAV and the technique is finding a new position in the range of options for severe AS.

There is broad agreement that BAV is not an acceptable alternative to AVR for older patients fit for open surgery.[5,19] However, BAV series conducted in the last 5 years have shown improved survival rates, compared with medical treatment, and when BAV is used as a holding procedure for patients expected to have AVR but who are not yet ready.[46] Further, in a recent series of the use of BAV as an alternative for patients unable or unwilling to have AVR, the outcomes have been considerably better than those observed in the early years of BAV, and much better than the outcomes for medical therapy at 1 year.[5,19,44–46] Combining BAV and PCI in selected cases does not worsen the outcomes for the valve.[46] BAV can be repeated with further extension of survival and control of symptoms.[47] Longer-term survival data are awaited.

Despite the improved early mortality rates, morbidity remains high in the immediate follow-up after BAV, particularly when it has been used in an emergency setting.[43] Some of this is a consequence of operative complications, but a substantial proportion appears to be more related to the clinical condition of patients receiving BAV in the context of old age and frailty, particularly those with cardiogenic shock and multi-organ failure caused by their severely compromised cardiac output.

Therefore, BAV certainly has a place, in selected patients, as a palliative procedure, a bridging treatment prior to AVR or TAVI and possibly, for some, as a definitive treatment for severe AS. It appears to be unlikely that it will displace TAVI as the preferred option for those unable to have AVR, though there are no head-to-head randomized trials that have compared TAVI and BAV to date.

Aortic valve preservation surgery (AVPS)

AVPS has been advocated as an alternative to AVR for elderly people with severe AS who have an aortic annulus that is too small for AVR (and possibly for TAVI), or have a contra-indication to long-term anticoagulation for a mechanical valve prosthesis, but are fit enough for open cardiac surgery.[48–50] The technique consists of manual repair of the aortic valve by commissurotomy, re-shaping and ultrasonic decalcification. There is little in the published literature that has properly evaluated this treatment, and no randomized trials. One follow-up series showed short- and long-term mortality rates that were much less favourable than usual AVR outcomes.[49] Another showed rates

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that were comparable with AVR for 1- and 5-year survival.[50] Few cardiac surgical units employ AVPS, and it seems likely that it will be superseded as AVR, TAVI and BAV technologies evolve.

Severe AS without symptoms

A substantial proportion of elderly patients with echocardiographic evidence of severe AS have none of the classical symptoms. Deciding how best to manage and advise this group, in the light of the prevailing evidence and technology, has now become a frequently encountered issue for clinicians. This is a controversial area, and there is a range of opinion that extends from watchful waiting to early elective AVR. At present, national guidelines do not recommend AVR for asymptomatic elderly patients with AS unless symptoms occur on exercise testing or there is clear evidence of worsening left ventricular dysfunction. Exercise testing for such patients is itself a topic of debate and many clinicians avoid it because of the risk of acute haemodynamic decompensation, syncope and sudden death. However, there is evidence that the mortality rate in asymptomatic AS is higher than was once believed,[24,25] with most of the cardiac deaths being due to acute left ventricular failure or arrhythmias. There is also evidence that AVR significantly improves the survival in that group.[51] There certainly appear to be no credible clinical reasons to avoid AVR in asymptomatic severe AS. Indeed, after AVR the survival rates are similar in patients with pre-operative symptoms of AS and those without.[52] Further, in one large series the strongest predictor of mortality in asymptomatic AS patients who declined AVR compared with those who received it was the omission of surgery.[52] Other studies have shown that delaying surgery until symptoms arise does not lead to excess mortality in patients with slowly progressive disease.[51]

It has been suggested, based on a comparative series, that asymptomatic patients with rapidly progressive (jet velocity increase of 0.3 m s^{-1} or more in 1 year) severe calcific AS have a high rate of progression to urgent surgery and a high 1-year mortality, so should be considered for early elective AVR.[51]

Conflict of interest

The authors have no conflicts of interest.

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