Aortic stenosis: even mild disease is significant

Catherine M. Otto*

Division of Cardiology, University of Washington, Seattle, USA

Received 2 December 2003; accepted 4 December 2003

The spectrum of calcific aortic valve disease ranges from aortic sclerosis, without obstruction to ventricular outflow, to severe aortic stenosis. The natural history of symptomatic and asymptomatic severe aortic valve stenosis has been evaluated by Doppler echocardiography in several retrospective and prospective studies. In addition, there is substantial data on the rate of haemodynamic progression of aortic stenosis of all degrees of severity. However, there is much less data on clinical outcomes in adults with asymptomatic mild-moderate stenosis.1–3 Knowledge of the expected outcomes with mild aortic valve disease is especially important given that aortic sclerosis is present in about 25% of adults over age 65 years and progression to aortic stenosis occurs within 7 years in 16% of patients with aortic sclerosis.4

In this issue of the European Heart Journal, Rosenhek and colleagues5 provide an important contribution to our understanding of the natural history of mild to moderate aortic stenosis. This consecutive cohort of 176 initially asymptomatic adults was identified over a 1-year period, with detailed clinical outcomes ascertained over an average of 4 years. Although earlier studies based on patient groups identified at catheterization suggested a relatively benign prognosis, the findings in the current study extend the observations from the Seattle aortic stenosis study that both adverse clinical outcomes and progression to severe aortic stenosis occur at a very high rate in adults with mild-moderate aortic stenosis (Table 1).

Progression of aortic stenosis

About 50% of these patients with mild to moderate stenosis at baseline had progressive valve calcification leading to haemodynamically severe aortic stenosis (defined as an aortic jet velocity >4.0 m/s) and 18% required valve replacement for onset of aortic stenosis symptoms. The average rate of increase in aortic jet velocity of 0.24±0.30 m/s/year is similar to previous studies.3 The observation that there is a wide standard deviation in haemodynamic progression again emphasizes the individual variability in this disease process. In fact, the wide range of progression rates is one of the features of this disease that suggests there may be interventions to slow or prevent leaflet calcification. After all, if we understood why some patients have rapid disease progression and others do not, we potentially could provide treatments or lifestyle changes to convert the rapid progressors into slow progressors.

In this study, a faster rate of haemodynamic progression was associated with age over 50 years, coexisting coronary artery disease and moderate to severe valve calcification. While these factors are difficult to modify, they should be taken into consideration, in addition to aortic stenosis severity, in clinical decision making. For example, when deciding whether aortic valve replacement should be performed for moderate aortic stenosis at the time of coronary bypass grafting or other cardiac surgery, the presence of severe valve calcification might weight the balance towards aortic valve replacement. Although, no significant association with haemodynamic progression was found for more modifiable clinical factors, this apparent lack of association may simply be due to a small sample size. The magnitude of the association between calcific aortic valve disease and clinical factors demonstrated in large population based studies is unlikely to be demonstrated in a study this size. Thus, we should not discount the possibility that interventions to modify these clinical factors, such as hypertension, hypercholesterolaemia, smoking and diabetes, might slow progression of aortic valve disease.

Sudden death and left ventricular dysfunction

In addition to the rate of haemodynamic progression, this study addresses two other areas of clinical concern in adults with aortic stenosis: the risk of sudden death and
the likelihood that left ventricular systolic dysfunction will precede symptoms. Of the 15 cardiac deaths, only one occurred in a patient without symptoms, supporting the concept that sudden death is rare in adults with asymptomatic aortic stenosis. In studies where patients have been followed prospectively, there have been no sudden deaths, possibly because these patients were educated about the expected symptoms and were followed closely. Left ventricular systolic dysfunction also was uncommon and was observed only in a few patients, all of whom had progressed to severe aortic stenosis.

Clinical outcome

The overall mortality rate observed by Rosenhek and colleagues was 1.8 times higher than expected for an age and gender matched population. Although this high mortality rate is only partly explained by progression to severe outflow obstruction, it is not surprising in the context of the 50% increased risk of cardiovascular mortality associated with aortic sclerosis, in which there is no obstruction to ventricular outflow.

The strongest predictors of clinical outcome were aortic valve calcification, aortic jet velocity and coronary artery disease, but over 50% of the deaths were non-cardiac, similar to the Seattle study, with death due to a wide range of causes. One wonders if some of these deaths might be related to having moderate aortic stenosis at the time of a substantial haemodynamic stress, particularly if aortic stenosis was not recognized by the physicians caring for the patient at that time. In adults with severe aortic stenosis, we are all aware of the importance of careful haemodynamic monitoring and optimization of loading conditions during times of haemodynamic stress, such as non-cardiac surgery. Perhaps the same considerations apply to moderate aortic stenosis.

Another concern is the association between aortic stenosis and coronary artery disease. In the Cardiovascular Health Study, the presence of aortic sclerosis was associated with an approximately 50% increase in the risk of myocardial infarction. In the Seattle Aortic Stenosis Study, atherosclerotic events were frequent with coronary revascularization in 4%, myocardial infarction in 3%, and a cerebrovascular event in 6% of subjects. In the study by Rosenhek and colleagues, coronary artery disease was present in 52% of those with the endpoint of death or valve replacement but in only 23% those without an adverse outcome. Event free survival at 3 years was only 63±7% in those with coronary disease compared to 86±3% in those with no coronary disease.

Table 1

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection criteria</th>
<th>n</th>
<th>Mean age</th>
<th>Subgroups</th>
<th>Follow-up (years)</th>
<th>Event-free survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horstkotte 1988</td>
<td>Cath for other reasons</td>
<td>142</td>
<td>58±19</td>
<td>Mild AS (AVA &gt;1.5 cm²)</td>
<td></td>
<td>92% at 10 years</td>
</tr>
<tr>
<td></td>
<td>Cath for other reasons</td>
<td>236</td>
<td></td>
<td>Mod AS (AVA 0.8–1.5 cm²)</td>
<td></td>
<td>80% at 10 years</td>
</tr>
<tr>
<td>Kennedy 1991</td>
<td>Cath AYA 0.7–1.2 cm²</td>
<td>28</td>
<td>67±10</td>
<td>AVA 0.92±0.13 (0.7&lt;1.2)</td>
<td>2.9</td>
<td>72% at 4 years</td>
</tr>
<tr>
<td>Seattle AS Study</td>
<td>Abnormal valve with Vmax ≥2.6 m/s</td>
<td>97</td>
<td>63±16</td>
<td>Vmax &lt;3 m/s (n=29)</td>
<td>2.5±1.4</td>
<td>84±16% at 2 years</td>
</tr>
<tr>
<td>Rosenhek 2004</td>
<td>Aortic stenosis with Vmax 2.5–3.9 m/s</td>
<td>176</td>
<td>58±19</td>
<td>Vmax 3–4 m/s (n=68)</td>
<td>4±1.6</td>
<td>66±13% at 2 years</td>
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<td></td>
<td></td>
<td></td>
<td>66±13% at 2 years</td>
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</tbody>
</table>

Clinical outcomes in adults with asymptomatic mild to moderate aortic stenosis

- AS=aortic stenosis; AVA=aortic valve area; Cath=cardiac catheterization; Mod=moderate; Ca++=calcification; Vmax=maximum aortic stenosis jet velocity.
- Only the asymptomatic patients are shown.
- Only the subgroups with mild-moderate aortic stenosis (defined as an aortic jet velocity <4.0 m/s are shown).

Practical applications

In clinical decision making in adults with asymptomatic aortic stenosis, the primary factors predicting clinical outcome are aortic jet velocity, the severity of valve calcification and the presence of coronary artery disease. Thus, echocardiography reports should include a description of the severity of valve calcification, in addition to measures of stenosis severity, such as jet velocity, mean gradient, valve area and the outflow tract to aortic jet velocity ratio. A detailed clinical history to elicit symptoms and determine functional status also is a key factor in decision making.

Despite the low prevalence of sudden death and asymptomatic left ventricular dysfunction, the fact that they do occasionally occur highlights the importance of patient education and periodic echocardiography. Patients who understand the expected disease course, prognosis and typical symptoms are likely to report promptly at the onset of even mild symptoms, hopefully minimizing the risk of sudden cardiac death. My practice is to perform echocardiography annually in patients with an aortic jet velocity >3.5 m/s. Based on the expected rate of disease progression, this ensures detection of a change in haemodynamic severity or left ventricular function and provides repeated opportunities for patient education and periodic echocardiography.
education. In patients with a jet velocity of 2.5 to 3.5 m/s, echocardiography every 2–3 years is reasonable in most cases, although more frequent studies are appropriate if the valve is severely calcified, coronary artery disease is present, or there is a rapid rate of progression on serial studies.

Even though definitive data showing an association between clinical risk factors for atherosclerosis and progression of aortic stenosis is lacking, clearly we should assess and treat coronary risk factors in all our patients, especially those with aortic valve disease. If nothing else, preventing coronary disease in our aortic stenosis patients will improve clinical outcome. At best, we may be slowing disease progression in the valve leaflets with conventional approaches to atherosclerosis risk factor modification. More aggressive approaches to preventing disease progression in adults with calcific aortic stenosis await the result of prospective randomized intervention trials.

References