Outcomes of patients with untreated severe aortic stenosis in real-world practice

Suresh Perera, Namal Wijesinghe, Elene Ly, Gerard Devlin, Sanjeevan Pasupati

Abstract

Background Surgical aortic valve replacement remains the gold standard of the treatment of severe symptomatic aortic stenosis but is often not considered due to excessive risk factors and comorbidities especially in elderly patients. We describe the burden of untreated severe aortic stenosis at a tertiary care hospital in New Zealand.

Method Consecutive patients with severe aortic stenosis presented between January-December, 2005 were studied retrospectively. Outcome assessment included mortality, hospital stay and on going symptoms (angina >CCS class II, dyspnoea >NYHA class II and syncope).

Results A total of 105 patients with severe aortic stenosis were identified (mean age 76±13 years, 51% men). Patients were divided into 3 groups according to the management strategy. (Group 1: Not referred for surgery as asymptomatic (n=25), Group 2: Declined for surgery (n=41), Group 3: Accepted for surgery (n=39)). Median follow-up was 34 months (interquartile range: 16–36 months). All-cause mortality in Group 1, Group 2 and Group 3 were 36%, 73% and 18% respectively while hospital days per 100 patient-years were 3.5, 10.1 and 6.4 and symptoms on last follow-up were 0%, 64% and 0% respectively. Almost half of symptomatic patients (Group 2 versus 3) were denied valve surgery due to comorbidities. Symptomatic patients had a significant mortality (p<0.0001) benefit with less hospitalisations (p<0.0001) post surgery.

Conclusions Untreated symptomatic severe aortic stenosis is associated with a poor prognosis and significant morbidity. For symptomatic patients with severe aortic stenosis who are denied surgery, alternative therapies such as transcatheter aortic valve implantation could be a viable option.

Aortic stenosis accounts for the vast majority of aortic valve disease, with a prevalence of approximately 1–2% among people over 65 years and 4% among people over 85 years.1 The aetiology is mainly calcific stenosis due to senile degenerative valve disease. Management of aortic stenosis has been tailored based on the severity of the condition, presence of comorbidities, age of the patient and their operative risk. Usually, treatment is only needed when aortic stenosis is severe and patients are symptomatic.

Aortic stenosis is the commonest acquired valvular lesion with a prevalence of 1–2% in the over 65s.1 Calcific aortic stenosis, the commonest cause of aortic stenosis, shares the predisposing factors of coronary artery disease: age, male sex and hypercholesterolaemia.
The onset of symptoms in patients with aortic stenosis is a poor prognostic indicator without valve replacement. More than half the patient will die within the next 12–18 months of symptom onset, unless the aortic valve is replaced relieving the afterload on the ventricle. In addition, quality of life is adversely affected with frequent hospital admissions during the remaining years of lives.

The management of the asymptomatic patient with severe aortic stenosis is less straightforward. Asymptomatic patients have an almost normal life expectancy without valve replacement with <1% incidence of sudden cardiac death precluding the need for aortic valve surgery. In patients in whom surgery is considered necessary, prompt aortic valve replacement (AVR) can return age-corrected prognosis to that of a normal population.

Procedural mortality for isolated aortic valve replacement in the surgically accepted group is low (<4%) and long-term results are excellent. Worldwide, however, over 30% of patients with severe symptomatic AS are not accepted for surgery due to comorbidities or are not indeed referred for surgery.

The emergence of transcatheter valve implantation techniques offers opportunities to expand treatment options to these patients. It is essential, therefore, in the assessment of this new technology, to understand the burden of untreated disease, not only for clinicians but also for the health administrators.

We describe our attempts to define the burden of aortic stenosis in a large tertiary care centre in New Zealand with the intent to improve the care of patients with aortic stenosis in our region with a better understanding of patient demographics and impact of the disease on not only mortality but also morbidity and cost to the health care system.

This study evaluates the burden of untreated severe aortic stenosis at Waikato Hospital.

The study aims to:

- Assess the outcome of patients with severe aortic stenosis who are managed with the surgical and medical option.
- Improve the management of severe aortic stenosis by understanding the patients’ demographics.
- Assess the impact on the patients’ quality of life.
- Assess the impact to the health care system.
- Assess the impact on the survival of the patient.

**Methods**

All consecutive patients, with severe aortic stenosis who presented to the Echocardiography Laboratory at Waikato Hospital, New Zealand between 1 January 2005 and 31 December 2009, were identified retrospectively.
**Definition of severe aortic stenosis**—Echocardiography criteria for diagnosing severe aortic stenosis applied according to ACC/AHA guidelines\(^3\).

We used at least one of the following parameters:
- Aortic valve area <1 cm\(^2\).
- Maximum velocity across aortic valve >4 m/s.
- Mean pressure gradient across aortic valve >40 mmHg.

If there was any discrepancies with these parameters, the Dimensionless Index was used to confirm severe aortic stenosis.

Long-term outcome data was obtained by review of medical records and telephone contact with patients and their primary care physicians. All of the patients identified with severe aortic stenosis (106 patients) were divided into 3 groups according to the management strategy:
- Group 1: Asymptomatic aortic stenosis.
- Group 2: Symptomatic aortic stenosis not treated surgically.
- Group 3: Symptomatic aortic stenosis treated surgically.

The history of symptomology was assessed by the cardiologist and asymptomatic patients were followed 6–12 monthly if felt they were operable in the future. All symptomatic patients were discussed at the combined meeting with cardiac surgeons and cardiologist for eligibility for surgery. The mortality, number of days spent in hospital per year and symptomatic status (angina >CCS class II, dyspnoea >NYHA class II, syncope) during follow-up were compared between these three groups.

**Statistical analysis**—Continuous variables were presented as the mean value±SD. These variables were compared, in between the groups, by using Student t-test. Discrete variables including the outcome measures of severe aortic stenosis were compared using Chi-squared test (double classification) with Yates correction. Event-free survival was plotted using Kaplan-Meir curves (censored data).

**Results**

A total of 105 patients with severe aortic stenosis were identified (mean age 76±13 years, 51% men) over the 12-month study period. The majority (76% (80/105)) were symptomatic with aortic stenosis. The median follow-ups in Group 1, Group 2 and Group 3 were 35 months (interquartile range: 27–37 months), 24 months (interquartile range: 11–36 months) and 36 months (interquartile range: 32-37 months) respectively. The baseline demographics of these groups are shown in Table 1. Clinical endpoints are shown in Table 2. At 36-month follow-up patients with symptomatic severe aortic stenosis treated surgically with aortic valve replacement had an excellent survival outcome compared to symptomatic patients who were declined for surgery (82% versus 27%, p<0.0001) (Figure 1). Of interest, mortality was also increased in patients with asymptomatic aortic stenosis compared to mortality of patients with symptomatic aortic stenosis treated surgically with aortic valve replacement (36% versus 18%, p<0.001). Unfortunately, the precise cause of death in-group 1 is unknown as the majority (8 out of 9 patients) died in the community.
### Table 1. Baseline demographic data

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Group 1 (n=25)</th>
<th>Group 2 (n=41)</th>
<th>Group 3 (n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (± SD)</td>
<td>81.7±14.4</td>
<td>83.4±7.6</td>
<td>66.1±12.2</td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>44%</td>
<td>56%</td>
<td>44%</td>
</tr>
<tr>
<td>Male</td>
<td>56%</td>
<td>44%</td>
<td>57%</td>
</tr>
<tr>
<td>Prior MI</td>
<td>22%</td>
<td>41%</td>
<td>17%</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>34%</td>
<td>59%</td>
<td>50%</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>4%</td>
<td>10%</td>
<td>17%</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>0%</td>
<td>13%</td>
<td>26%</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>20%</td>
<td>15%</td>
<td>2%</td>
</tr>
<tr>
<td>Prior TIA</td>
<td>16%</td>
<td>15%</td>
<td>7%</td>
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<tr>
<td>Peripheral vascular disease</td>
<td>16%</td>
<td>18%</td>
<td>12%</td>
</tr>
<tr>
<td>COPD</td>
<td>24%</td>
<td>31%</td>
<td>7%</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>40%</td>
<td>49%</td>
<td>43%</td>
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<td>Diabetes Mellitus</td>
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<td>21%</td>
<td>24%</td>
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<tr>
<td>Hypertension</td>
<td>64%</td>
<td>69%</td>
<td>60%</td>
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<tr>
<td>Smoking:</td>
<td></td>
<td></td>
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<tr>
<td>Current smoker</td>
<td>12%</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Ex smoker</td>
<td>28%</td>
<td>44%</td>
<td>36%</td>
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<tr>
<td>Logistic Euro Score</td>
<td>16%</td>
<td>26%</td>
<td>10%</td>
</tr>
<tr>
<td>-&gt;&lt;10%</td>
<td>32%</td>
<td>19%</td>
<td>68%</td>
</tr>
<tr>
<td>-10%~20%</td>
<td>36%</td>
<td>19%</td>
<td>17%</td>
</tr>
<tr>
<td>-&gt;&gt;20%</td>
<td>32%</td>
<td>62%</td>
<td>15%</td>
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<tr>
<td>NYHA class I-II</td>
<td>100%</td>
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<td>NYHA class III-IV</td>
<td>0%</td>
<td>36%</td>
<td>40%</td>
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<tr>
<td>CCS class I-II</td>
<td>100%</td>
<td>90%</td>
<td>83%</td>
</tr>
<tr>
<td>CCS class III-IV</td>
<td>0%</td>
<td>10%</td>
<td>17%</td>
</tr>
<tr>
<td>Syncope</td>
<td>8%</td>
<td>15%</td>
<td>10%</td>
</tr>
</tbody>
</table>

PCI=Percutaneous coronary intervention, CABG=Coronary artery bypass surgery, TIA=Transient ischemic accident, COPD=Chronic obstructive pulmonary disease, NYHA=New York Heart Association, CCS=Canadian Cardiovascular Society.

### Table 2. Outcomes of patient groups during follow-up

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of patients</th>
<th>All-cause mortality</th>
<th>Hospital days per 100 pt-years</th>
<th>Symptoms at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>25 (24%)</td>
<td>9 (36%)</td>
<td>3.5</td>
<td>0%</td>
</tr>
<tr>
<td>Group 2</td>
<td>41 (39%)</td>
<td>30 (73%)</td>
<td>10.1</td>
<td>64%</td>
</tr>
<tr>
<td>Group 3</td>
<td>39 (37%)</td>
<td>7 (18%)</td>
<td>6.4</td>
<td>0%</td>
</tr>
</tbody>
</table>

Patients with symptomatic severe aortic stenosis managed conservatively (Group 2) had significantly more recurrent hospitalisation and time in hospital related to cardiovascular causes compared to patients who underwent surgical valve replacement (10.1 versus 6.4 days/100 patient-years, p<0.0001).

Similarly, 2 of 3 symptomatic patients who were managed conservatively (Group 2) had on going symptoms, (greater than CCS class II angina or NYHA class II...
dyspnoea or syncope). Asymptomatic patients and patients with aortic valve replacement had remained free from significant valve related symptoms during follow-up.

**Figure 1. Kaplan-Meier survival of the 3 patient groups**

![Kaplan-Meier survival graph]

**Limitations**—As our study was a retrospective analysis and most death in our cohorts occurred in the community there were major limitations in finding the actual cause of death. This limits our ability to define the actual valve related mortality.

**Discussion**

Aortic stenosis is a common valvular heart disease in the western world. It is a disease that is increasing in prevalence as the population ages. The onset of symptoms in the patient with severe aortic stenosis is a poor prognostic sign. These patients should be closely monitored and should be treated with aortic valve replacement if appropriate.

While surgical aortic valve replacement offers excellent result for patients with symptomatic severe aortic stenosis, those who are not considered as suitable surgical candidates have poor survival.2,12–14

Almost half of the symptomatic patients in our study were declined for aortic valve replacement surgery. This was mainly due to presumed high-risk involved with open-heart surgery because of their multiple comorbidities and age. The mean logistic EuroScore in this group was significantly high compared to a mean logistic EuroScore of the symptomatic patients treated surgically (26.1±16.0 versus 10.4±12.3,
p < 0.0001). This implies that non-surgical patients had more co-morbidity and were of higher risk compared to the surgical patients. In addition, they were much older compared to the surgical group (mean age: 83.4±7.6 versus 66.1±12.2, p < 0.0001). Hence in our study as patients who were declined for surgery could have been done so appropriately due to multiple comorbidities which could have lead to an early mortality, we cannot assess the actual valve related mortality due to this decision. Usually, symptomatic aortic stenosis patients, who are declined for aortic valve replacement surgery due to excessive risk, have a poor survival. In our study, their survival was as low as 27% at 36 months, which is consistent with the published literature. In a retrospective study of 144 symptomatic patients, survival at 3 years was 87% in 125 patients who underwent valve replacement compared to 21% in 19 patients who were managed conservatively. In our study, symptomatic patients treated surgically had not only a significant reduction in mortality (18% versus 73%, p value < 0.001) but also in days spent in hospital for cardiac causes (6.4 versus 10.1 days/100 patient-years, p < 0.0001) compared to those were declined for surgery. Although randomised trials comparing surgery to continued conservative therapy for severe symptomatic aortic stenosis have not been performed, observational studies have found that aortic valve replacement surgery in this setting is almost always followed by symptomatic improvement and a substantial increase in survival.

In our study, symptomatic patients treated surgically had not only a significant reduction in mortality (18% versus 73%, p value < 0.001) but also in days spent in hospital for cardiac causes (6.4 versus 10.1 days/100 patient-years, p < 0.0001) compared to those were declined for surgery. Although randomised trials comparing surgery to continued conservative therapy for severe symptomatic aortic stenosis have not been performed, observational studies have found that aortic valve replacement surgery in this setting is almost always followed by symptomatic improvement and a substantial increase in survival. There have been major advances in cardiac surgery, which affect the consideration of surgical treatment in elderly patients who in the past may not have been surgical candidates. Among patients who survive the surgery and perioperative period, the level of function, quality of life and survival are the same as in a general population of age-matched subjects. As a result, the classic view that surgery should be considered only for elderly patients in excellent general condition is being challenged as higher success rates for isolated aortic valve replacement is obtained in patients with comorbidities with pre-existing good functional level.

An unexpected finding of our study was that 1 in 3 of asymptomatic patients dying during the follow-up. Our study is also limited by being unable to define the exact cause of death in this group especially where the majority were elderly. Objective defining of the symptom status with a treadmill may have better categorise this group. Although exercise testing is contraindicated in patients with symptomatic aortic stenosis, it has been shown to be safe in asymptomatic patients and can identify the presence of exercise-induced haemodynamic compromise, which is a relative indication for elective surgery.

High-risk echocardiographic features (presence of moderate to severe valvular calcification, a rapid progression in the aortic jet velocity (0.3 m/sec within one year) and a high aortic jet velocity > 4.5 m/sec), advance age (> 50 years) and raised plasma B-type natriuretic peptide concentration may help to identify the patients who are likely to rapidly progress to symptomatic state needing aortic valve surgery or dying from a cardiac cause. For symptomatic patients who are declined surgery, alternative therapies such as transcatheter aortic valve implantation may be an option. This is a promising approach that is now being used at many highly...
specialised centres around the world for specific patients (elderly, surgically declined symptomatic aortic stenosis population).

Randomised study data using the Edwards SAPIEN™ valve (PARTNER NCT00530894) will be available in 2010 that looks at outcomes against surgery in the high-risk population and also in patients declined from surgery. Data on cost effectiveness and long-term durability of this valve will allow wider application of this program.

**Conclusion**

Untreated symptomatic severe aortic stenosis is associated with a poor prognosis and significant morbidity while aortic valve replacement surgery results in improved survival and quality of life. A significant number of patients with symptomatic aortic stenosis are declined surgical aortic valve replacement due to comorbidities and new therapies such as transcatheter aortic valve implantation may be of value as alternative treatment options to manage these patients. Asymptomatic patients with severe aortic stenosis should be carefully monitored objectively for development of symptoms and early referral for surgery should be recommended.

**Competing interests:** None.

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**References:**


