Outcomes of elderly patients aged 80 and over with symptomatic, severe aortic stenosis: impact of patient’s choice of refusing aortic valve replacement on survival

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Summary

Background: Aortic valve replacement (AVR) can be performed safely in selected elderly patients with aortic stenosis (AS). However, the survival benefits of AVR over conservative treatment have not been convincingly demonstrated in AS patients aged above 80.

Aim: To investigate the outcomes of patients aged 80 and over with symptomatic, severe AS and by analyzing the effects of patient’s choice in either agreeing or refusing to undergo AVR, determine the survival benefits afforded by AVR.

Design: Cohort study.

Methods: Subjects aged 80 and over with severe symptomatic AS, diagnosed between 2001 and 2006 were segregated into three groups: subjects who underwent AVR (Group A); patients who were fit for AVR but declined surgery due to personal choice (Group B) and those who were not fit for surgery and were managed conservatively (Group C). Follow-up was conducted by out-patient attendances, review of medical records and telephone interviews. The primary endpoint was all-cause mortality.

Results: A total of 103 patients (86.0 ± 4.2 years, 41% male) were identified and no patient was lost during follow-up. In Group A (n = 17), all 15 patients who underwent AVR were alive after 3.6 ± 1.4 years follow-up and 2 died whilst awaiting AVR. Seventy-four percent of Group B (n = 24) and 76% of Group C (n = 62) died during follow-up. Group A had significantly better survival than B and C. (P < 0.01) Amongst patients fit for AVR with similar operative risks (Groups A and B), refusal to undergo surgery (hazard ratio 12.61, P = 0.001) was the only predictor of mortality in a multivariate model.

Conclusions: For elderly AS patients fit for surgery, the patient’s decision to refuse AVR is associated with a >12-fold increase in mortality risk. These findings have significant implications for informed decision-making when managing the fit, elderly patient with AS.

Introduction

Aortic stenosis (AS) is predominantly a disease of the elderly, with significant mortality and morbidity. The only definitive therapy is aortic valve replacement (AVR) and surgical units operating on large numbers of elderly patients have reported reasonable operative mortality rates of <10%.1–9 Some of these studies have concluded that patients who undergo AVR have better outcomes compared to those who are treated conservatively. However, the conservatively managed ‘control’ group tended to be older, more frail and had a higher incidence of co-morbidities. Community-based studies have
shown that only a minority of elderly patients with operable AS were referred to tertiary centers for surgery, subjecting case series from high-volume tertiary centers to potential referral bias.10–12 The aims of this study are 2-fold: first, to provide community-based data about the outcomes of elderly patients with AS; and secondly to quantify the survival benefits of AVR by comparing the survival of elderly subjects post-AVR with the survival of patients with similar pre-operative risks but had declined surgery due to personal choice.

**Methods**

**Patient selection**

Hemel Hempstead General Hospital is a district general hospital based in Hertfordshire, United Kingdom. It is the sole provider of echocardiographic services to a population of ~266,000 people. Patients aged 80 and over, diagnosed with symptomatic, severe AS in a 5-year-period from September 2001 to 2006 were identified by analysis of our comprehensive clinical database. This study was performed with institutional ethics approval.

AS was graded as severe if peak systolic velocity measured by Doppler echocardiography was >4 m/s or valve area measured by the continuity equation was ≤1 cm².13 Based on a holistic clinical assessment incorporating patient’s health, presence of co-morbidities and operative risks (measured by EuroSCORE), attending clinicians decided whether patients would be suitable surgical candidates for referral to the local tertiary centers, St Mary’s Hospital or Harefield Hospital in London for AVR.

Patients were divided into three groups:

Group A—patients who were considered suitable candidates for surgery and underwent AVR with or without concomitant coronary artery bypass grafting (CABG)

Group B—patients with severe AS who were considered suitable candidates for surgery with equivalent operative risks as Group A but declined surgery due to personal choice

Group C—patients who were considered to be inappropriate candidates for surgery due to frailty, high operative risks or significant co-morbidities

**Clinical data**

Operative risks were assessed by the use of the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), a validated scoring system based on the knowledge of 12 clinical variables.14–16 Clinical factors recorded included the presence of cardiovascular co-morbidities such as hypertension, history of strokes, extracardiac arteriopathy, atrial fibrillation; other significant co-morbidities such as chronic pulmonary disease and renal failure (defined as a serum creatinine >200 µmol/l) and use of aspirin, β-adrenergic blocker therapy, ACE-inhibitors and statins. Subjects were considered to have lost the ability to self-care if they resided in a place where assisted care was available such as a residential or nursing home.

**Echocardiographic and Doppler measurements**

All patients underwent a comprehensive 2-dimensional and Doppler echocardiographic evaluation. Left ventricular ejection fraction was assessed from M-mode measurements of changes in left ventricular cavity and wall dimensions in the parasternal long-axis view. Continuous-wave Doppler was used at multiple windows to obtain the maximal jet velocity. The maximal instantaneous pressure gradient across the aortic valve was calculated by a modified Bernoulli equation. In patients with atrial fibrillation, velocities from several acquisitions were averaged. The aortic valve area was derived from the continuity equation.

**Primary end-point and follow-up**

The primary endpoint was all-cause mortality. Clinical information was obtained by out-patient attendances, review of medical records and telephone interviews with patients or their general practitioners. Information about place and date of mortality was recorded. Furthermore, at the end of the study (July 2007), the status of all patients known to be alive was confirmed by telephone interviews with their general practitioners.

**Statistical analysis**

Survival of the three groups was analyzed by the Kaplan–Meier method. The effects of the clinical, electrocardiographic and echocardiographic variables as well as the decision to undergo AVR on mortality were studied with Cox proportional-hazards regression analysis. Comparison between groups was analyzed with one-way analysis of variance (ANOVA) with Bonferrri’s post-tests. Statistical significance was established at $P<0.05$.

**Results**

**Baseline characteristics**

One hundred and three patients with severe, symptomatic AS aged 80 and over were identified from
out our clinical database (mean age of 86.0 ± 4.2 years, 41% male). Complete follow-up, available for all 103 patients averaged 1.6 ± 1.4 years (maximum of 5.9 years).

Groups A and B were similar in terms of age, operative mortality risks as assessed by the EuroSCORE, pattern of clinical presentation, incidence of hypertension, vascular disease, diabetes, atrial fibrillation and ability to self-care. However Group A had a higher proportion of male patients, history of coronary artery disease and renal failure (defined as a creatinine of > 200 µmol/l). Group B had a higher incidence of chronic obstructive pulmonary disease and were more likely to be female and be inpatients compared to Group A. In comparison to Groups A and B, Group C was older, had a higher incidence of syncope, more likely to be inpatients and had higher loss of ability to self-care. Consequently, the EuroSCORE for Group C was significantly higher than Groups A and B. Clinical characteristics are listed in Table 1.

Mean aortic peak velocity for all patients was 4.0 ± 0.7 m/s and aortic valve area averaged 0.65 ± 0.20 cm². Echocardiographic parameters were similar between all three groups and are listed in Table 2.

**Survival analysis**

The primary endpoint of all-cause mortality was reached in 64 (62%) patients. All 15 Group-A patients who underwent AVR were still alive in July 2007 (mean follow-up of 3.6 ± 1.4 years). Two subjects in Group A died whilst awaiting cardiac surgery.

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**Table 1** Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 17)</th>
<th>Group B (n = 24)</th>
<th>Group C (n = 62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>82.1 ± 2.3</td>
<td>83.6 ± 3.6</td>
<td>87.2 ± 4.2*</td>
</tr>
<tr>
<td>male (%)</td>
<td>59</td>
<td>29</td>
<td>40</td>
</tr>
<tr>
<td>Presenting complaint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina (%)</td>
<td>18</td>
<td>21</td>
<td>6</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>71</td>
<td>67</td>
<td>71</td>
</tr>
<tr>
<td>Syncope/pre-syncope</td>
<td>12</td>
<td>13</td>
<td>29</td>
</tr>
<tr>
<td>Inpatients (%)</td>
<td>12</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Coronary artery disease (%)</td>
<td>41</td>
<td>13</td>
<td>31</td>
</tr>
<tr>
<td>Previous cardiac surgery (%)</td>
<td>0</td>
<td>0</td>
<td>6 (all CABG)</td>
</tr>
<tr>
<td>Atrial fibrillation (%)</td>
<td>24</td>
<td>25</td>
<td>32</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>65</td>
<td>50</td>
<td>32</td>
</tr>
<tr>
<td>CVA/PVD (%)</td>
<td>12</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>6</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Renal failure (%)</td>
<td>12</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (%)</td>
<td>6</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>Logistic EuroSCORE (%)</td>
<td>10.3 ± 5.9</td>
<td>12.0 ± 7.8</td>
<td>20.2 ± 13.4*</td>
</tr>
<tr>
<td>Loss of ability to self-care (%)</td>
<td>0</td>
<td>4</td>
<td>31</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin (%)</td>
<td>88</td>
<td>50</td>
<td>35</td>
</tr>
<tr>
<td>β-blockers (%)</td>
<td>59</td>
<td>13</td>
<td>31</td>
</tr>
<tr>
<td>ACE-inhibitors (%)</td>
<td>35</td>
<td>29</td>
<td>16</td>
</tr>
<tr>
<td>Statin (%)</td>
<td>65</td>
<td>29</td>
<td>26</td>
</tr>
</tbody>
</table>

*P < 0.05 for Group C compared to A and B.

**Table 2** Echocardiographic parameters

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve peak velocity (m/s)</td>
<td>4.4 ± 0.6</td>
<td>3.9 ± 0.6</td>
<td>3.9 ± 0.7</td>
</tr>
<tr>
<td>Aortic valve area (cm²)</td>
<td>0.66 ± 0.29</td>
<td>0.63 ± 0.18</td>
<td>0.65 ± 0.19</td>
</tr>
<tr>
<td>Contractile function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>60.1 ± 16.5</td>
<td>67.3 ± 12.3</td>
<td>58.1 ± 13.7</td>
</tr>
<tr>
<td>Percentage of patients with ejection fraction &lt;50%</td>
<td>24</td>
<td>29</td>
<td>34</td>
</tr>
<tr>
<td>Pulmonary artery pressure (mmHg above right atrial pressure)</td>
<td>30.5 ± 18.0</td>
<td>43.7 ± 22.0</td>
<td>43.2 ± 13.5</td>
</tr>
</tbody>
</table>
surgery and were analyzed on an intention-to-treat basis. Seventy-four percent (18) of Group B subjects and 75% (46) of Group C subjects died during follow-up. The Kaplan–Meier probabilities of survival at 1 year was 94, 66 and 51% for Groups A, B and C, respectively (Figure 1). The likelihood of survival in Group A was statistically greater than for Group B and C (\( P < 0.01 \)). Group B had a better chance of survival compared to Group C with the median survival times of 20.6 and 12.2 months, respectively (\( P = 0.04 \)).

Univariate and multivariate analysis

Regression models were used to adjust for the effect of any potential confounding variables on mortality. The analysis was performed for all 103 patients in our cohort and repeated for the 41 patients in Groups A and B, which were of particular interest in this study. Univariate and multivariate models for all cause mortality are shown in Table 3.

In the univariate analysis of all 103 patients, increased age, raised pulmonary artery pressures, higher EuroSCORE, in-patient status and loss of ability to self-care were associated with increased mortality. AVR and the use of ACE-inhibitors were associated with decreased mortality. In the multivariate model, in-patient status and loss of ability to self-care were significant predictors of mortality, whilst only AVR significantly predicted improved survival.

The analysis was repeated with subjects from Groups A and B only. Univariate analysis showed that increased age and refusal to undergo AVR predicted increased mortality whilst use of ACE-inhibitors and statins were associated with reduced mortality. Refusal to undergo AVR was the only independent predictor of mortality in multivariate analysis.

Operative details

All 15 Group-A patients underwent AVR at either St Mary’s Hospital, London or Harefield Hospital, Middlesex, performed by five different cardiothoracic surgeons. Nine patients (60%) had concomitant CABG (2.3 ± 1.0 grafts per subject). All patients received porcine aortic valve replacements with a median size of 22 mm. One patient developed a post-operative stroke, with near-complete recovery when assessed during follow-up. Average length of stay was 20.6 ± 13.1 days.

Discussion

In this present study, we have demonstrated, for the first time, the impact of elderly, fit AS patients refusing AVR is >12-fold increase in mortality. Therefore, AVR confers significant survival benefits to elderly patients with severe, symptomatic AS. In our cohort, AVR is associated with low operative risks but the majority of elderly patients aged 80 and over with severe symptomatic AS was not appropriate AVR candidates.
Aortic stenosis in the elderly

AS is a disease of the elderly and its impact is becoming more significant in the ageing world population. According to the 2001 United Kingdom census, there were 9790 people aged 80 and above in our local catchment area, which approximates to a local prevalence of 1.1% for severe symptomatic AS in this age group.17

It is well recognized that the prognosis of untreated AS is poor.18 As there is no effective medical therapy and percutaneous valvotomy or replacement are currently not acceptable alternatives to surgery, current guidelines recommend that all elderly patients with severe symptomatic AS should be considered for AVR, regardless of age.19 These recommendations are based on the following observations: first, the operative risk of AVR in octogenarians and even nonagenarians are reasonable, ranging from 5.2% to 9.6% for isolated AVR. Secondly, surgical patients achieve improved post-operative quality of life scores, comparable to the general population.1,5,7,8,20–28 Furthermore, econometric analysis has also shown that AVR is cost-effective for patients up to the age of 90.29 In keeping with previous studies, only 40% of our cohort was considered to be eligible for AVR. Therefore, the excellent operative results reported by large-volume tertiary centers in elderly patients undergoing AVR for severe AS could be in part due to referral bias.8,30

Survival benefits conferred by AVR

The impact of AVR on improving survival has not been convincingly demonstrated in the literature. In one study, survival in more than 2000 post-AVR patients in Sweden were compared with the expected survival of their general population.31 The investigators found excellent relative survival rates with 83% of AVR patients alive at 5 years. However, there was an excess of mortality in the AVR group throughout the entire 12 years of follow-up.

To our knowledge, only two retrospective cohort studies have attempted to determine the survival benefits of undergoing AVR. In 1982, Schwarz et al.32 retrospectively studied 144 patients with isolated AS whom were all offered surgery. A 3-year survival rate in 125 operated patients was 87% in contrast to 21% in 19 unoperated patients, who refused due to personal choice. However, in this report, the mean age of AVR subjects was only 49 years and therefore such data may not be applicable to older patients. In a later Dutch prospective registry of 280 patients aged 70 and over with severe AS, overall survival in the surgical group was significantly higher than the ‘medically’ treated group.8 When subjects were stratified according to their individual baseline risk (judged according to left ventricular function, presence of mitral regurgitation, NYHA status, age and sex), the survival benefit of AVR was only seen in subjects with high baseline risk. In the groups with low or intermediate baseline risk, there was no significant difference between surgical and medical treatment. In a later report by the same authors, they also concluded that patients above the age of 80 without other cardiac co-morbidity gained little survival benefit from AVR.33 In the aforementioned registry, patients above the age of 80 (16% of the surgical group) were also less likely to be offered surgery and subjects who refused AVR due to personal choice were excluded from analysis. The inclusion of more elderly and frail subjects with a higher prevalence of co-morbidities resulted in a higher-risk medical cohort, which rendered the control group a poor comparator to assess the benefits of AVR.

Whilst a randomized controlled trial of AVR is clearly ethically unfeasible, a reliable estimate of the survival benefits of AVR in the elderly can be made by the use of a control group which consisted of patients suitable for AVR with equivalent baseline operative risk to the surgical group but had chosen not to undergo AVR due to personal choice. In keeping with a larger Dutch registry, a higher percentage of female patients (71%) in our study considered fit for surgery declined AVR compared to 44% of men. The reason for this difference is unclear.

Based on the current findings, clinicians must be cognisant of the low operative risks of AVR as seen in our cohort and larger surgical series, the significant survival benefits conferred by AVR in patients above the age of 80 and clearly communicate the poor prognosis associated with refusal to undergo surgery during the decision-making process.

Limitations

The possibility that angiographically significant coronary artery disease could be a confounding factor could not be excluded as only patients who agreed to undergo AVR had coronary angiography. However, only 60% of our AVR cohort had significant coronary artery disease that required CABG, suggesting that the survival benefits seen in Group A is unlikely to be solely due to revascularization. The zero peri-operative and follow-up mortality during follow-up of AVR patients was unexpectedly low and much lower than the predicted EuroSCORE of 10.3%. This is in part due to the small size of our surgical cohort. For the same reason, it is possible
that the mortality in Group B was higher than expected. Nevertheless, the benefit of surgery is clear. The low operative mortality could also be due to physicians’ selection criteria by which <40% of elderly patients with severe symptomatic AS in the community are considered for surgery with an even smaller proportion being referred to regional cardiothoracic units.

**Conclusions**

Amongst patients aged 80 and over with severe symptomatic AS and fit for AVR, the mortality risk is 12 times greater for those who refused surgery compared to subjects undergoing AVR. These findings have significant implications for informed decision-making when managing the fit, elderly patient with AS. However, most elderly patients with severe symptomatic AS are not suitable candidates for AVR and have a poor prognosis.

**Conflict of interest:** None declared.

**References**


