The impact of age and severity of comorbid illness on outcomes after isolated aortic valve replacement for aortic stenosis

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Objectives: This study examines outcomes in a national sample of patients undergoing isolated aortic valve replacement (AVR) for aortic stenosis, with particular focus on advanced-age patients and those with extreme severity of comorbid illness (SOI).

Methods: Data were obtained from the Nationwide Inpatient Sample and included all patients undergoing AVRs performed from January 1, 2006 to December 31, 2008. Patients with major concomitant cardiac procedures, as well as those aged <20 years, and those with infective endocarditis or aortic insufficiency without aortic stenosis, were excluded from analysis. The analysis included 13,497 patients. Patients were stratified by age and further stratified by All Patient Refined Diagnosis Related Group SOI into mild/moderate, major, and extreme subgroups.

Results: Overall in-hospital mortality was 2.96% (n=399); in-hospital mortality for the ≥80-year-old group (n=139, 4.78%) was significantly higher than the 20- to 49-year-old (n=9, 0.84%, P<0.001) or 50- to 79-year-old (n=251, 2.64%, P<0.001) groups. In-hospital mortality was significantly higher in the extreme SOI group (n=296, 15.33%) than in the minor/moderate (n=22, 0.35%, P<0.001) and major SOI groups (n=81, 1.51%, P<0.001). Median in-hospital costs in the mild/moderate, major, and extreme SOI strata were $29,202.08, $36,035.13, and $57,572.92, respectively.

Conclusion: In the minor, moderate, and major SOI groups, in-hospital mortality and costs are low regardless of age; these groups represent >85% of patients undergoing isolated AVR for aortic stenosis. Conversely, in patients classified as having extreme SOI, surgical therapy is associated with exceedingly high inpatient mortality, low home discharge rates, and high resource utilization, particularly in the advanced age group.

Keywords: cardiac surgery, outcomes, risk stratification

Introduction

Aortic stenosis (AS) is the most common valvular disorder in the US.1 Aortic valve replacement (AVR) remains the gold standard for treatment of extreme symptomatic AS.1 However, with broader indications for transcatheter AVR (TAVR), understanding outcomes across a broad population of patients is increasingly important.2

The purpose of this study was to characterize outcomes, including mortality, discharge disposition, length of stay, and cost, in a national cohort of patients undergoing isolated AVR for AS. Secondary analysis stratified patients by age and severity of comorbid illness (SOI). This study is important because it provides current clinical and economic benchmarks for surgical AVR in a national sample of patients.
Methods
Data source
Use of data in this analysis is consistent with the regulations of our institutions’ Internal Review Boards. The Nationwide Inpatient Sample (NIS), which is sponsored by the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project, is a 20% sampling of abstracted discharge data from a national survey of all nonfederal acute care hospitals in the US. The dataset contains discharge records from over 1,000 hospitals in up to 44 states, depending on the year of the study. The NIS contains up to 15 procedure codes per patient using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure code index. During the years of study (2006–2008), 24,276,621 hospital discharges were captured in the NIS.

Study population
The NIS was used to identify all patients aged ≥20 years with discharges related to AVR that occurred between January 1, 2006 and December 31, 2008 (n=39,729). The analysis included patients undergoing AVRs (ICD-9-CM: 35.21, 35.22) performed on patients with AS (ICD-9-CM: 39.5, 39.6, 42.41, 74.63). Patients were excluded if they had a diagnosis of aortic insufficiency (ICD-9-CM: 39.51, 74.64) without a diagnosis of AS (n=2,653). In order to avoid the potential confounding effect of multiple procedures, patients undergoing other major concomitant cardiac procedures (n=23,579) – including coronary artery bypass grafting, aortic surgery, mitral valve surgery, tricuspid valve surgery, atrial septal defect (ASD) or ventricular septal defect (VSD) closure, and arrhythmia surgery – were excluded.

Patients were divided into three age groups: 20–49 years, 50–79 years, and ≥80 years. Patients were further stratified by the All Patient Refined Diagnosis Related Group (APR-DRG) SOI scale developed by 3M. APR-DRGs allow analysis of outcomes across large cohorts for a given diagnostic group. SOI is defined as the extent of organ system derangement or physiologic decompensation for a patient. The APR-DRG subclasses are determined by using discharge billing codes and are based on primary and secondary discharge diagnosis, age, and pre-existing medical conditions; the sub classes do not include codes reflecting in-hospital complications. The APR-DRG SOI system stratifies patients into four SOI subclasses – mild, moderate, major, and extreme – for each base APR-DRG, of which there are more than 300. To simplify the presentation of data in our analysis, minor and moderate were collapsed into a single group.

Clinical outcomes
The primary outcome of interest was in-hospital mortality and in-hospital cost. Secondary measures include discharge disposition (ie, home, rehabilitation or skilled nursing facility, and dead) and length of stay (LOS).

Cost outcomes
Total billed charges for each hospitalization are present in the NIS dataset. These data reflect the amount hospitals billed for services rendered rather than the costs for the specific hospitalization or the amount hospitals received in payments. Estimated institutional cost data were obtained by multiplying Healthcare Cost and Utilization Project-supplied cost-to-charge ratios by total charges. Grouped average cost-to-charge ratios are a weighted average for the hospitals in the group (defined by state, urban/rural, investor owned/other, and number of beds) and use the proportion of group beds as the weight for each hospital.

Analysis
For clinical data, continuous variables were reported as mean ± standard error and were compared using the Student’s t-test or Wilcoxon rank sum test when noted. Categorical variables were reported as percentages and compared using the chi-squared or Fisher’s exact test when appropriate. Since measures of resource utilization (eg, medical costs and LOS) are typically right skewed, as they cannot be negative, we report median cost and LOS in the analysis, unless otherwise specified. For all analyses, the conventional P-value of 0.05 or less was used to determine the level of statistical significance. All reported P-values are two-sided. NIS–provided discharged-based weights were used when noted in order to estimate frequency relative to the national experience. All statistical analyses were performed using Stata 11.2 (Stata Corp, College Station, TX, USA). The authors had direct access to data and take responsibility for the analysis.

Results
Study population
There were a total of 13,496 patients who underwent isolated AVR for AS between 2006 and 2008. Patient characteristics, including prevalence of comorbidities based on ICD-9-CM codes, are summarized in Table 1. A total of 61.6% (n=8,312) of cases received a tissue valve, while 38.4% (n=5,185) received a mechanical valve. The study population was stratified into three age groups: 20–49 years (n=1,075; 7.97%), 50–79 years (n=9,510; 70.46%), and ≥80 years (n=2,911, 21.57%). In addition, the study population was also stratified
by SOI: minor/moderate (n=6,199, 45.90%), major (n=5,366, 39.80%), and extreme (n=1,931, 14.30%).

### In-hospital mortality

Overall in-hospital mortality was 2.96% (n=399); in-hospital mortality for the ≥80-year-old (4.78%, n=139) group was significantly higher than for the 20- to 49-year-old (0.84%, n=9, \( P < 0.001 \)) or 50- to 79-year-old (2.64%, n=251, \( P < 0.001 \)) groups (outcomes summarized in Table 2). Regardless of age, in-hospital mortality was significantly higher in the extreme SOI group (n=296, 15.33%) than in the minor/moderate (n=22, 0.35%, \( P < 0.001 \)) and major SOI groups (n=81, 1.51%, \( P < 0.001 \)). Figure 1 demonstrates that within each SOI stratum, inpatient mortality increases significantly (\( P < 0.001 \)) with age strata.

### Table 2 Outcomes of patients undergoing aortic valve replacement

<table>
<thead>
<tr>
<th>N</th>
<th>In-hospital mortality (%)</th>
<th>Discharge home (%)</th>
<th>Median cost ($)</th>
<th>25% cost ($)</th>
<th>75% cost ($)</th>
<th>Median length of stay (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>13,496</td>
<td>2.96</td>
<td>74.2</td>
<td>33,953</td>
<td>26,456</td>
<td>45,821</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–49 years</td>
<td>1,075</td>
<td>0.84</td>
<td>94.6</td>
<td>30,870</td>
<td>24,932</td>
<td>40,568</td>
</tr>
<tr>
<td>50–79 years</td>
<td>9,510</td>
<td>2.64</td>
<td>79.9</td>
<td>33,554</td>
<td>26,066</td>
<td>45,216</td>
</tr>
<tr>
<td>≥80 years</td>
<td>2,911</td>
<td>4.78</td>
<td>47.7</td>
<td>37,593</td>
<td>29,249</td>
<td>51,125</td>
</tr>
<tr>
<td>Severity of comorbid illness subgroup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild/moderate</td>
<td>6,199</td>
<td>0.35</td>
<td>88.1</td>
<td>29,202</td>
<td>22,668</td>
<td>39,223</td>
</tr>
<tr>
<td>Major</td>
<td>5,366</td>
<td>1.51</td>
<td>72.6</td>
<td>36,035</td>
<td>28,023</td>
<td>48,156</td>
</tr>
<tr>
<td>Extreme</td>
<td>1,931</td>
<td>15.3</td>
<td>42.9</td>
<td>57,573</td>
<td>48,870</td>
<td>71,505</td>
</tr>
</tbody>
</table>

### Location of discharge

Figure 2 demonstrates that discharge to home was correlated with age and SOI, respectively. In the mild/moderate SOI group, the vast majority (>60%) of patients were discharged, even in the ≥80-year-old group home. Conversely, in the extreme SOI group, a minority of patients in the ≥80-year-old group (<25%) were discharged home.

### Resource utilization

Median in-hospital costs in the mild/moderate, major, and extreme SOI strata were $29,202.08, $36,035.13, and $57,572.92, respectively. Figures 3 and 4 illustrate that within the mild/moderate and major SOI strata, LOS and cost increase significantly (\( P < 0.001 \)) with age strata; however, in the extreme stratum, there are no differences in LOS and cost by age.

### Discussion

Findings here are consistent with previous analyses examining outcomes after isolated AVR for AS. Overall in-hospital mortality was less than 3% for the entire study population, and less than 5% in patients aged ≥80 years. This observed in-hospital mortality is similar to other recently published series, including a recent study from the Society of Thoracic Surgeons (STS) database reporting an inpatient mortality of 2.6% for AVR in 2006. In a similar analysis of the NIS, Astor et al7 reported a 4.5% mortality for patients undergoing AVR in 1994, thus providing additional data to suggest that outcomes in patients undergoing surgical AVR are improving measurably over time.

### Mild, moderate, and major severity of comorbid illness

This analysis provides further evidence that isolated surgical AVR provides excellent outcomes in well-selected patients regardless of age. Among patients in the mild/moderate and major SOI strata (which includes 85% of the total study population), in-hospital mortality for the entire study population...
was 0.35% and 1.51%, respectively. Though in-hospital mortality was threefold to fourfold higher in the ≥80-year-old group compared with those aged <50 years, among mild/moderate SOI, inpatient mortality was significantly less than 1% for all age strata, and less than 2% among mild/moderate/major SOI across all age strata. Furthermore, more than 50% of ≥80-year-old patients were discharged home (Figure 2). Finally, though total inpatient costs increased significantly with increasing age, the absolute differences were relatively small (Figure 4). Notably, median total in-hospital costs in the mild/moderate stratum are less than the cost of a transcatheter aortic valve device alone. These findings suggest that surgical AVR should remain the gold standard for treatment across a large proportion of patients with isolated AS.

Extreme severity of comorbid illness

Not surprisingly, in patients with multiple comorbidities, thus classified as extreme SOI, in-hospital mortality was significantly higher, and the discharge to home rate was lower across all age strata. In the extreme stratum, which comprised approximately 15% of patients— or approximately 3,800 patients annually based on NIS weight discharge estimates—surgical AVR was associated with exceedingly high morbidity, mortality, and resource utilization. These findings support the expanded role of other nonsurgical therapies, including transcatheter valve implantation, balloon aortic valvuloplasty, or apical–aortic conduits, in managing these complex patients.

Thus, the need for better risk stratification, particularly in high-risk AS patients, is clear. Conventional scores such
as STS and euroSCORE perform poorly when applied to extreme populations. Furthermore, these scores are often inappropriately applied to assess patient risk for nonsurgical therapies such as TAVR. Therefore, given the increased rate of intervention in high-risk and advanced-age patients, broader application of nonsurgical therapies in these populations, and repeat findings of excess mortality in these populations, appropriately developed tools are needed to understand the competing risks of the various treatment approaches, particularly in high-risk patients. With growing TAVR and balloon aortic valvuloplasty experiences, this should be possible in the near future.

APR-DRG, SOI, and risk stratification

In this analysis, APR-DRG was used to stratify patients by SOI. However, APR-DRG is not comparable with clinical risk stratification scores such as the STS score or euroSCORE. APR-DRG is calculated based on ICD-9-CM billing codes and thus calculated after hospital discharge, not preoperatively. Furthermore, APR-DRG does not incorporate specific clinical data such as ejection fraction or pulmonary function tests. Therefore, it has no role in clinical decision making. Nevertheless, APR-DRG has become a preferred method for assessing SOI and risk of death in the analysis and understanding of administrative data. It is used by thousands

Figure 3 Median length of stay by Severity of comorbid illness (SOI) by age.

Figure 4 Median cost by Severity of comorbid illness (SOI) by age.
of health care organizations worldwide to standardize disparate patient populations.

In the context of this analysis, APR-DRG SOI was a proxy for patient risk. As previously stated, this analysis suggests that lower-risk patients, who represent nearly 85% of the cohort, achieve excellent outcomes with surgical AVR. However, a minority of patients with higher SOI, unsurprisingly, experience more adverse events and higher resource utilization. Though no direct comparisons can be made, it is interesting to note that the TAVR arm of the Placement of Aortic Transcatheter Valves (PARTNER) A cohort suffered a 30-day mortality in excess of 3.4% and inpatient costs of approximately $73,000 for the transfemoral cohort and $90,000 for the transcathodal cohort, similar to the extreme SOI subgroup in the analysis. Further, the AVR arm of the PARTNER A cohort had a 6.5% 30-day mortality, with inpatient costs totaling around $74,000 in the transfemoral cohort and $79,000 in the transcathodal cohort.11,12 This suggests that the PARTNER B cohort is comparable in risk with the extreme SOI group, and that the PARTNER A cohort has less morbidity than the extreme SOI group, but increased morbidity when compared to the major SOI group.

**Limitations**

There are numerous limitations to this study. First, use of administrative data for the purposes of clinical outcomes research has disadvantages. These include variability in data as a result of differences in coding procedures across institutions, difficulty distinguishing pre-existing comorbidities from postoperative complications such as stroke, and lack of detailed clinical information such as ejection fraction and creatinine clearance. In addition, only 20% of nationwide institutions are sampled within the NIS; thus, there exists the potential for limitations in the number of hospitals surveyed that perform comprehensive cardiac surgery. Nevertheless, use of the NIS presents several advantages, including providing experience from over 500 hospitals. Because of large sample size, trends in disease and disease management are more likely to be generalizable to the larger population.

A second limitation of our study is that follow-up did not extend beyond the index hospitalization; consequently, important events, complications, or costs that may have occurred after discharge were not captured.

Third, the use of ICD-9-CM codes to identify clinical events is imperfect. Nonetheless, regardless of the disadvantages, ICD-9-CM coding of complications remains a well-established technique.13 In a series of recent reports by the Complications Screening Project, the ICD-9-CM coding of several surgical complications was found to be clinically valid. The study reports that when comparing ICD-9-CM coding and the clinical record, the positive predictive value for complications varied from 84.2% to 96.8%, with kappa scores of 0.69–0.88.14,15

Finally, the cost-to-charge ratios used in the analysis, and thus the reported costs, may be subject to bias. This is because variability exists in state reporting of cost-to-charge ratios (eg, variability in individual participating institutional ratios versus aggregate state ratios). However, many of the limitations in this analysis must be understood in the context of the strengths of the NIS, which include its large size, representative quality, standardized methodology of survey, and availability of economic end points.

**Conclusion**

In the minor, moderate, and major SOI groups, in-hospital mortality and costs are low, regardless of age; these groups represents >85% of patients undergoing isolated AVR for AS. These findings provide further evidence that surgical AVR provides excellent outcomes for a significant population of patients with AS, and advanced age alone should not preclude patients from undergoing surgical therapy. Conversely, in patients classified as having extreme SOI, surgical therapy was associated with exceedingly high inpatient mortality, low discharge to home rates, and high resource utilization, particularly in the advanced age group; the more widespread application of alternative procedures such as transcatheter valve therapies may offer the greatest potential benefit in this subgroup.

**Disclosure**

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