Trends, Predictors, and Outcomes of Stroke After Surgical Aortic Valve Replacement in the United States

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Background. **Postoperative stroke is a devastating complication after aortic valve replacement (AVR). Our objective was to use a large national database to identify the incidence of and risk factors for stroke after AVR, as well as to determine incremental mortality, resource use, and cost of stroke.**

Methods. **We identified 360,437 patients who underwent isolated surgical AVR between 1998 and 2011 from the National Inpatient Sample (NIH) database. Mean age was 66 ± 32 years. Multivariable regression and propensity matching were used to identify risk factors and the effect of stroke on outcomes. Patients were stratified according to the Elixhauser comorbidity score (ECS) into low- (0–5), medium- (6–15), and high-risk (16+) categories.**

Results. **Stroke after AVR occurred in 5,092 (1.45%) patients. The incidence of stroke declined from 1.69% in 1999 to 0.94% in 2011 ($p < 0.001$). Increasing age and higher comorbidities were the main predictors of stroke (each $p < 0.001$). The highest-volume centers (>200 AVRs/y) had the lowest rate of stroke (1.2%). After multivariable adjustment, high-volume centers had lower odds of stroke in medium-risk (odds ratio [OR], 0.59; 95% confidence interval [CI], 0.37–0.94) and high-risk patients (OR, 0.39; 95% CI, 0.22–0.68) compared with the lowest-volume centers. For low-risk patients, volume was not associated with stroke. Patients who experienced stroke were hospitalized for 4 days longer, had an average of $10,496 higher costs, and had 2.74 (95% CI, 1.97–3.80) times higher odds of in-hospital mortality compared with those who did not experience stroke (all $p < 0.001$).**

Conclusions. **The incidence of stroke after AVR has decreased but remains a significant cause of morbidity in medium- and high-risk patients. Superior outcomes can be achieved in medium- to high-risk patients at high-volume centers.**

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Surgical aortic valve replacement (AVR) is 1 of the most commonly performed cardiac procedures in the United States and is the treatment of choice for symptomatic patients with aortic valve disease [1–4]. Over the past few decades, development of new techniques and advancements in health care have substantially improved outcomes. According to a recent analysis of The Society of Thoracic Surgeons (STS) database from 2002 to 2010, mortality after isolated surgical AVR was 3% [2]. At high-volume centers, mortality from surgical AVR is even lower: between 2011 and 2013 at the Cleveland Clinic, mortality for all surgical AVR was 0.6%, 0.4%, and 0.7%, respectively [5]. Despite these improvements, postoperative stroke remains a major cause of morbidity after AVR, especially in high-risk and elderly patients, and the true incidence of this complication from a population-based perspective remains unclear [2–10].

The reported risk of stroke after AVR varies widely. A recent analysis of the STS database showed that the rate of stroke after isolated AVR in the United States was 1.5% [3] and has been declining since 1997 [6]. Among high-risk patients, there is considerable variability in stroke rates. Thourani and colleagues [2] reported that high-risk patients undergoing surgical AVR with STS preoperative risk of mortality greater than 10% had a risk of stroke as high as 4.4%. Among high-risk patients enrolled in the pivotal Placement of Aortic Transcatheter Valve

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(PARTNER) trial, the risk of stroke after surgical AVR was 2.1% [7], whereas the incidence of stroke in the surgical arm of the US CoreValve trial was noted to be as high as 6.2% [9]. Clearly, a contemporary real-world appraisal of postoperative stroke risk after surgical AVR is lacking and necessary in order to set a benchmark for comparison to transcatheter aortic valve replacement (TAVR) [7, 11–14].

Our objective was to use a large national database to identify the incidence of and risk factors for stroke after AVR, as well as to determine incremental mortality, resource use, and cost of stroke.

Patients and Methods

Data

The National Inpatient Sample (NIS) Healthcare Cost Utilization Project (HCUP) database was queried from 1998 to 2011 for patients undergoing isolated surgical AVR in the United States. Patients were identified using the 2003 International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes. The NIS is the largest all-payer inpatient discharge database and represents a 20% stratified sample of all discharges occurring in a given year. It includes information on demographics, comorbidities, cost, hospital length of stay, procedures, outcomes, and discharge. Discharge weights allow extraction of national-level estimates from the unweighted database information. Weighted estimates are reported throughout. Patients who underwent AVR were identified using the ICD-9-CM procedure codes 35.21 and 35.22 (replacement of aortic valve with a tissue prosthesis; replacement of the aortic valve with other). Patients undergoing additional cardiovascular procedures during the same hospital admission as well as those younger than 18 years and older than 100 years were excluded. The Institutional Review Board at Cleveland Clinic confirmed that the use of NIS publically available data does not contain any identifiable information and is not considered "human subject research." Institutional review board approval therefore is not required.

Population

From 1998 to 2011, 883,430 patients underwent AVR with or without concomitant cardiac operations. This resulted in 360,437 isolated AVR procedures for analysis.

Statistical Analysis

The mean, median, and standard deviation were calculated for all continuous outcomes, and the categorical outcomes are presented as frequency counts and percentages. Appropriate statistical tests were used for categorical (χ^2 test) and continuous (Student's *t* test) outcomes to compare unadjusted differences between the stroke after AVR and no stroke after AVR groups.

Covariables

Patient-level variables included age, sex, race, insurance status, admission status, admission location, and comorbidities. Race/ethnicity was categorized as white, black, Hispanic, and other/missing. Insurance status was categorized as Medicare, Medicaid, private insurance, uninsured, and other based on the primary payer listed on the discharge record. Comorbidities for risk adjustment were derived from secondary ICD-9-CM diagnosis codes using a modification of the approach developed by Elixhauser and colleagues [15]. The Elixhauser comorbidity scores (ECSs) are most commonly used for analyzing administrative data. The score allocation is based on the number of comorbidities per patient, comprising 30 comorbidities in total (Supplemental Tables 1–3). Previous studies have shown that the comorbidities identified by the Elixhauser comorbidity measure are significantly associated with in-hospital mortality, including acute as well as chronic conditions. It is a reliable predictor model for postoperative outcomes. Alternatively, The Society of Thoracic Surgeons (STS) risk score (http://riskcalc.sts.org/stswebriskcalc/#/calculate) has also been used for risk stratification in some studies. For the current analysis, it was not the ideal choice because the NIS database is based on ICD-9 diagnosis codes, and a significant proportion of variables included in the STS risk score model are very specific—not all of which are reliably available in the NIS database. Therefore, we used the ECS for risk stratification because it is more commonly used for analyzing large administrative data sets. For this study, patients were stratified using the ECS into low- (0–5), medium- (6–15), and high-risk (16+) categories. Results of patient-level stratification based on the ECS are shown in Supplemental Table 1.

Hospital-level characteristics included hospital location, bed size, teaching status, and annual hospital AVR volume. A hospital was considered to be a teaching hospital if it had an American Medical Association–approved residency program, was a member of the Council of Teaching Hospitals, or had a ratio of full-time equivalent interns and residents to beds of 0.25 or higher. Hospital region was classified by the US Census Bureau as Northeast, Midwest, South, or West. Hospital bed size was classified as small, medium, or large based on an algorithm developed by HCUP. Additionally, categories of hospital surgical AVR volume were determined based on the number of annual surgical AVRs performed during the study period: 1 to 49, 50 to 99, 100 to 199, and 200+ AVRs/y. The distribution of AVR procedures according to hospital volume and risk is shown in Supplemental Fig 1. Individual surgeon volume was not available for all hospitals or was inconsistently coded across all states, or both, and therefore was not included.

Matching

Propensity scores, or the conditional probability of having the complication of postoperative stroke after isolated AVR, were estimated for each participant using a multivariable logistic regression model in which the occurrence of postoperative stroke was the dependent variable, whereas patient demographics, payer status, comorbidities, and hospital characteristics, including hospital AVR volume, were the independent variables. The purpose of