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Clinical commentary

Carotid artery disease and perioperative stroke risk after surgical aortic valve replacement: A nationwide inpatient sample analysis

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ABSTRACT

To study the role of carotid stenosis (CS) and cerebrovascular disease as independent risk factors for perioperative stroke following surgical aortic valve replacement (SAVR). The National Inpatient Sample (NIS) database was used for our study. All patients who underwent SAVR from 1999 to 2011 were identified using ICD-9 codes. Univariate and multivariate analysis of baseline characteristics, Elixhauser comorbidities and other covariates were examined to identify independent predictors of perioperative strokes following SAVR. Data on 50,979 patients who underwent SAVR from 1999 to 2011 was obtained. The mean age of the study cohort was 60.5. The study patients were predominantly Caucasian (79.3%) and males (60.01%). The incidence of perioperative stroke was 2.48%. CS (OR 1.8, 95%CI 1.1–2.8, $p = 0.009$) and cerebral arterial occlusion (OR 3.4, 95% CI 1.3–8.9) significantly increased perioperative stroke risk following SAVR. Infective endocarditis (OR 4.6, 95%CI 3.8–5.6, $p = 0.00$) and neurological disorders (OR 4.8, 95% CI 4–5.8, $p = 0.00$) appeared to be the strongest risk factors for strokes. Other risk factors found to be significant predictors of perioperative strokes ($p < 0.05$) were – age, higher VWR scores, CS, cerebral arterial occlusion, infective endocarditis, DM, HTN, renal failure, neurological disorders, coagulopathy and hypothyroidsm. In conclusion, perioperative stroke risk has remained more or less constant despite advancements in surgical techniques with risk having gone up in patients <65 years of age. CS and cerebral arterial occlusion significantly increase stroke risk following SAVR. Improved patient selection with pre-operative risk stratification and institution of preventive strategies are necessary to improve operative outcomes following SAVR.

1. Introduction

Perioperative strokes, defined as neurological deficits which develop within 30 days of the procedure are common complications with an incidence of 2% following surgical aortic valve replacement (SAVR) [1,2]. Their implications on post-operative mortality rates and quality of life are devastating with serious economic ramifications due to longer stays in hospitals and chronic care facilities [3,4]. AVR is the most common cardiac valve surgery performed in the US with 22,000 procedures done annually [5] and reported operative mortality of 2.5–3% [1,2,5]. Previous studies on timing of the strokes show that 55–72% of perioperative strokes occur in the first 24 h and the PARTNER trial reported 51% of post-operative strokes in the first 10 days following AVR making it important for us to study the periprocedural causes of neurological events in the hospital [6–8]. Beyond the first post-operative week the surgery or its associated risks were no longer implicated to contribute to strokes [6].

Previous studies have shown history of cerebrovascular disease or carotid stenosis (CS) with prior stroke to be the strongest independent risk factor of perioperative stroke following cardiac surgery [9,10]. The common risk factors contributing to perioperative strokes following SAVR include: pre-operatively – age >65 years, female sex, history of cerebrovascular disease (stroke/transient ischemic attacks), cardiac failure, atrial fibrillation, diabetes, hypertension, prior cardiac surgery and endocarditis, etc. [3,9,10]. Intra-operatively, cerebral hypoperfusion or embolic phenomena [4] and post-operatively, new onset atrial fibrillation and low cardiac output syndrome were found culpable [10]. Although several studies have examined the relationship of carotid stenosis with stroke risk following coronary artery bypass

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surgery and cardiac surgeryin general [9,10], a large scale risk analysis of perioperative stroke following aortic valve intervention has not been done before. Some studies also implicate intracranial artery stenosis and vertebral artery stenosis in the etiology of perioperative strokes [11,12].

The primary aim of our study is to identify whether carotid artery disease is an independent risk factor for perioperative stroke following SAVR. We will also evaluate vertebral, basilar and intracranial stenosis and occlusion as a risk factor for perioperative stroke following SAVR. Finally we will evaluate the trends in perioperative stroke and its relationship with carotid disease over a ten year period. Identifying the significance of carotid artery disease in the incidence of perioperative stroke will help us formulate preoperative screening and risk-stratification of patients on the need for carotid revascularization before or after SAVR. Further the need for intra-operative neurophysiological monitoring to cerebral hypoperfusion [13–15] or intense medical management for intracranial stenosis can be evaluated [16].

2. Methods

The National Inpatient Sample (NIS) database was used to select the study population over a period of 11 years from 1999 to 2011 for SAVR. International Classification of Diseases, Ninth Revision-Clinical Modification (ICD-9-CM) codes were used to identify diagnoses and risk factors in the NIS database. Patients were identified using ICD-9 codes 35.21 and 35.22 for SAVR and extracted for our analysis. Patients below the age of 18 years were excluded from our study. Baseline characteristics such as age, gender, race, admission status and comorbid conditions commonly observed in the patient demographic undergoing SAVR were studied for our analysis. The NIS database provides 29 Elixhauser comorbidities based on standard ICD-9 codes [17]. Other additional risk factors studied were carotid stenosis, cerebral arterial occlusion, vertebral and basilar artery stenosis, atrial fibrillation, infective endocarditis, left ventricular dysfunction (LVD), previous history of stroke or transient ischemic attack (TIA), previous history of any cardiac surgery and use of cardioplumonary bypass. The ICD-9 codes used to identify the covariates and outcomes are listed in supplement Table 1.

The primary outcome studied was perioperative stroke following SAVR. Carotid stenosis was used as the independent variable. Risk stratification was done using Van Walraven (VWR) score. It is a summary score developed for Elixhauser Comorbidities by modeling in-hospital mortality with inpatient admission data [18]. The summary score is a weighted combination of the 29 Elixhauser comorbidities, where a larger comorbidity weight indicates a stronger association between comorbidity and in-hospital mortality.

3. Statistical analysis

All data are presented as mean ± SD or percentages. Univariate comparisons between groups were done using unpaired t-tests for continuous variables and a survey-adjusted Wald test for variables that were categorical in nature. In our multivariable analysis, we included variables that were statistically significant in the univariate analysis, that had alarge enough group population, that lacked missing data, and were established as risk factors in previous studies. We elected to exclude each individual Elixhauser Comorbidity and use the van Walraven score as a surrogate, as we did not want to risk overloading our model with variables that may have been either statistically insignificant or not relevant to our outcome of interest. Data extraction was performed using SAS 9.3 (SAS Institute, Inc., Cary, NC), as was the creation of the Elixhauser comorbidity index and the generation of the van Walraven score [19]. All subsequent statistical analyses were performed using Stata version.14 (StataCorp, College Station, TX).

4. Results

4.1. Baseline characteristics

The study population comprised of 50,979 patients who underwent surgical aortic valve replacement from 1999 to 2011. The baseline data of the study cohort and univariate analysis of risk factors is provided in Table 1. The mean age of the study cohort was 60.58, with majority of the population (58.13%) under the age of 65. The study patients were predominantly Caucasian (79.3%) and males (60.01%). The perioperative stroke incidence was found to be the same irrespective of gender. The procedure was done electively in 68.47% of the cases. The incidence of perioperative stroke was 2.48% in our study. The patients were stratified based on their Van Walraven (VWR) scores into low/intermediate and high risk groups. The average VWR score was found to be 2.15 with 75.2% of the study patients categorized as low risk.

4.2. Univariate analysis of pre-operative predictors for perioperative strokes

Univariate analysis of risk factors (see Tables 1 and 2) suggests the following significant predictors of perioperative stroke ($p < 0.05$)-advancing age, higher VWR scores, males, African American race, elective procedures, CS, cerebral arterial occlusion, infective endocarditis, CHF, valve disease, cardiopulmonary bypass use, CLD, paralysis and other neurological disorders, complicated DM, RF, coagulopathy, weight loss, fluid and electrolyte abnormalities, hypertension and drug abuse. Carotid stenosis and other precerebral artery stenosis was seen in 1.2% and 0.43% of our study patients and were both significant predictors of strokes (OR 2.01, 95%CI 1.3–3.0, $p = 0.001$ and OR 2.1, 95%CI 1.1–4.1, $p = 0.016$ respectively). No patients coded for vertebral or basilar artery stenosis and were not included on our analysis. Infective endocarditis, seen in 4.8% of study patients was another significant predictor (OR 4.8, 95%CI 4.1–5.7, $p = 0.00$). CBP was used in 88.9% of patients and showed a significantly decreased perioperative stroke risk (OR 0.7, 95%CI 0.6–0.9, $p = 0.006$). A statistically significant stroke risk was seen in patients with higher VWR scores ($p < 0.05$).

4.3. Independent predictors of perioperative strokes by multivariate analysis

The following risk factors were found to be significant predictors of perioperative strokes ($p < 0.05$) – age, higher VWR scores, CS, cerebral arterial occlusion, infective endocarditis, DM, HTN, renal failure, neurological disorders, coagulopathy and hypothyroidsm (Table 3). Carotid stenosis (OR 1.8, 95%CI 1.1–2.8, $p = 0.009$) and cerebral arterial occlusion (OR 3.4, 95% CI 1.3–8.9) were significantly associated with an increased perioperative stroke risk following SAVR. Infective endocarditis (OR 4.6, 95%CI 3.8–5.6, $p = 0.00$) and neurological disorders (OR 4.8, 95% CI 4–5.8, $p = 0.00$) appeared to be the strongest risk factors for strokes.

4.4. Trend analysis

An analysis of the trends in perioperative stroke incidence and the average age and VWR scores of patients who underwent SAVR from 1999 to 2011 is depicted in Table 4. The average age of patients undergoing the procedure has remained the same over the years (61.4 years). The VWR score shows an increasing trend over the years from an average score of 1.4 in 1999 to 2.5 in