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Perioperative strokes after coronary artery bypass grafting with staged carotid endarterectomy: A nationwide perspective

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ABSTRACT

Study Objective: To examine the risk of perioperative stroke on in-hospital morbidity and mortality in staged coronary artery bypass grafting (CABG) and carotid endarterectomy (CEA) procedures.
Design: The National Inpatient Sample (NIS) database was used to extract data on all patients who underwent staged CABG CEA procedures. They were identified using the ICD-9 (International Classification of Diseases, Ninth Revision-Clinical Modification) diagnosis and procedure codes.
Setting: Multi-institutional.
Patients: Patients who underwent staged CABG and CEA from 1999 to 2011.
Interventions: Staged CABG and CEA procedures.
Measurements: Various pre-operative, and perioperative risk factors and their association with in-hospital mortality and morbidity were studied.
Main Results: The study cohort was grouped into 2761 patients who underwent staged CEA and CABG. The average age of the patient population was 69 years. An in-hospital mortality of 4.96% (137) was observed. Staged procedures showed a morbidity rate of 69.21%. Patients with perioperative strokes had a mortality rate of 16.73% following staged procedures. Other notable risk factors for mortality and morbidity were post-operative myocardial infarction (MI) and congestive heart failure (CHF).
Conclusion: Analysis of 2761 patients over a period of 12 years (1999–2011) indicate perioperative stroke to be a strong post-operative predicator of in-hospital mortality and morbidity for staged procedures. Other significant factors such as advancing age, female gender and comorbidities like CHF, left ventricular dysfunction (LVD) and post-operative MI should also be considered when determining patient risk. Further investigative studies on staged CABG and CEA procedures are needed for better patient selection and for implementing preventative strategies such as neuroprotective medication and neuromonitoring to minimize the risk of ischemic strokes.

1. Introduction

Carotid endarterectomy (CEA) staged with coronary artery bypass grafting (CABG) has been increasingly done for secondary prevention of stroke [1]. However, a six-folds increase (6.1% to 0.9%) in in-hospital mortality has been associated with secondary CEA procedures [2]. Current literature does suggest that staged CABG + CEA procedures have significantly lowered the risk of long term mortality and morbidity compared to combined procedures with similar short term results [3–5]. However, some studies show that performing CEA prior to CABG increases the risk for myocardial infarction (MI) [6]and performing CEA after CABG increases the risk of perioperative strokes. Carotid artery stenting (CAS) with CABG has been suggested as a safer alternative to staged CABG + CEA procedures and a few randomized studies have compared the two [5,7]. More research into the mechanism behind the difference in mortality and morbidity of CABG + CEA procedures is needed. It is suggested that the high rates of perioperative strokes associated with staged CABG + CEA procedures account for the relatively higher mortality rates [5].

CABG procedures have a perioperative strokes rate of 3–5% [8–10]. Neurological deficits after CABG are the leading cause for post-operative morbidity and has also been shown to increase short and long-term mortality [11,12]. With advances in technology and in-hospital care overall complications for CABG have decreased, but the perioperative stroke rate has remained relatively the same [13]. Carotid stenosis potentiated by intra-operative cerebral hypoperfusion, impaired autoregulation and embolization have been attributed to the etiology of

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perioperative cerebral ischemia following CABG [10,14–16]. In order to implement therapeutic and preventive strategies like intensive medical management and intra-operative neurophysiological monitoring it would be necessary to examine the relationship between perioperative strokes and early post-operative outcomes following staged CABG + CEA [17,18].

The primary aim of this study is to use the National Inpatient Sample (NIS) database to investigate the role of perioperative stroke on in-hospital mortality and mortality following staged CABG + CEA. We will also evaluate the trends in perioperative stroke, morbidity and mortality following CEA and CABG between 1999 and 2011, a 12 year period.

2. Methods

2.1. Study population

Data from the Nationwide Inpatient Sample (NIS) was used for this study. The NIS is an administrative discharge level database with diagnoses and procedures coded in primarily for billing purposes. Patients who underwent staged CABG and CEA procedures were included in our study and were identified using the ICD-9 (International Classification of Diseases, Ninth Revision-Clinical Modification) diagnosis and procedure codes. Staged procedures were those with the same admission date for CEA and CABG but with differing dates of surgery. Patients under the age of 18 and over the age of 100 were excluded from the study. The following baseline characteristics of patients were available for analysis: age (categorized as <65, 65–74, 75–84, 85+), gender, race/ethnicity, admission status, transfer status, Elixhauser comorbidities and other additional covariates including aortic atherosclerosis, left ventricular dysfunction and cardiac failure, prior cardiac surgery, previous MI, history of thromboembolic events, previous history of cerebrovascular disease (stroke/TIA), perioperative stroke, and cardiac arrest. A list of 29 Elixhauser comorbidities with their respective ICD-9 codes provided in the NIS database was used for the analysis [19]. A complete list of covariates and their ICD-9 codes can be found in Supplemental Table 1. Institutional review board approval was not obtained for this study as the NIS database is available at most institutions for review purposes. The STROBE guidelines were followed for this retrospective study and a checklist has been provided in the supplement.

2.2. Outcome

The primary outcome studied was in-hospital mortality and the secondary outcome examined was post-operative morbidity, characterized by a long length of hospital stay (i.e. >14 days) [20] or discharge to a place other than home. The independent variable analyzed was perioperative stroke.

3. Statistical analysis

The initial data extraction was done using SAS version 9.3 (SAS Institute, Inc., Cary, NC). The Hospital Weight Files provided by the NIS was merged into each individual year's dataset to ensure each hospital was accounted for at least once. We then combined each individual year into an aggregated database. The Elixhauser comorbidity index was created using the "Comorbidity Software" available at the HCUP website [19,21]. The van Walraven score was created using the van Walraven macro created by the Cleveland Clinic [22]. Risk stratification was done using van Walraven (VWR) score, which is a summary score for the Elixhauser Comorbidities developed by modeling in-hospital mortality with inpatient admission data. 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 [22]. All subsequent analyses were performed using Stata version 14 (StataCorp, College Station, TX). Univariate analysis was done using the unpaired *t*-test for continuous variables and a survey-adjusted Wald test for all variables that were categorical in nature. Variables with p value < 0.05 were considered significant. We ran several multivariate regression models for the outcomes of mortality and morbidity and have reported one model in Table 5. We elected not to include individual covariates with very few members in the group. An analysis of trends in average age of the patient cohort, perioperative stroke rates, morbidity and mortality rates over the 12 year period was also performed.

4. Results

4.1. Baseline characteristics

Demographic data was obtained from a total population of 2761 patients who underwent staged CABG from1999 to 2011 (Table 1). The average age of the patient population was 69 ± 12 years. Majority of the study patients were male (66.76%) and between the ages 65–74 years. An in-hospital mortality of 4.96% (n = 137) was observed. Staged procedures showed a morbidity rate of 69.21%. Risk stratification was done using van Walraven (VWR) score. The average VWR score observed for the patient cohort was 3.31 ± 5.99. The majority (46.97%)of patients were categorized as high risk (VWR > 14) in staged procedures. Significant increases in adverse outcomes were observed in patients with higher scores.

4.2. Staged CABG + CEA: in-hospital mortality and morbidity

Following staged CABG and CEA, 6.21% (n = 171) of the cohort developed perioperative strokes and 32.85% of the patients (n = 906) developed post-operative MI. Patients who developed perioperative strokes had a mortality rate of 16.73% and a morbidity rate of 91.97%. Patients with post-operative MI had an in-hospital mortality rate of 7.87% and a morbidity of 77.11% (Table 2).

4.3. Univariate predictors of in-hospital mortality and morbidity

Significant univariate predictors of in-hospital mortality and morbidity were—congestive cardiac failure, multivalvular heart disease, pulmonary circulation disorders, peripheral vascular disease, lymphoma, metastatic cancer, collagen vascular disorders, coagulopathy, weight loss, fluid and electrolyte disorders, hypertension, drug abuse, nutritional anemia, perioperative strokes and post-operative cardiac arrest/myocardial infarction (Tables 3 & 4).

4.4. Independent predictors of in-hospital mortality and morbidity by multivariate analysis

Perioperative stroke was found to be the strongest independent predictor with for post-operative mortality (OR 7.13, 95%CI 2.4–7.1, $p < 0.001$) and morbidity (OR 5.16, 95%CI 2.7–9.7, $p < 0.001$) respectively. Age and female gender were found to be significant independent predictors of in-hospital mortality and morbidity as well. Other variables that were found to be independent predictors of in-hospital morbidity are: increasing van Walraven scores, congestive cardiac failure, coronary artery disease/angina and post-operative cardiac arrest/myocardial infarction (Table 5).

4.5. Trend analysis (1999–2011)

A trend analysis for the period 1999 to 2011 was done to study average age of patients who underwent staged CABG and CEA, the average VWR score, the incidence of perioperative strokes, in-hospital mortality and morbidity rates (Table 6). The average age of the patient cohort has gradually decreased from 70.5 in 1999 to 68.4 in 2011 while the average VWR score has increased from 2.5 to 5over