Perioperative Acute Ischemic Stroke in Noncardiac and Nonvascular Surgery

Incidence, Risk Factors, and Outcomes

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Background: Perioperative acute ischemic stroke (AIS) is a recognized complication of noncardiac, nonvascular surgery, but few data are available regarding incidence and effect on outcome. This study examines the epidemiology of perioperative AIS in three common surgeries: hemicolectomy, total hip replacement, and lobectomy/segmental lung resection.

Methods: Discharges for patients aged 18 yr or older who underwent any of the surgical procedures listed above were extracted from the Nationwide Inpatient Sample, an administrative database that contains 20% of all discharges from non-Federal hospitals each year, for years 2000 to 2004. Using appropriate International Classification of Diseases, 9th revision, Clinical Modification codes, patients with perioperative AIS were identified, as were comorbid conditions that may be risk factors for perioperative AIS. Multivariate logistic regression was performed to identify independent predictors of perioperative AIS and to ascertain the effect of AIS on outcome.

Results: A total of 0.7% of 131,067 hemicolectomy patients, 0.2% of 201,235 total hip replacement patients, and 0.6% of 39,339 lobectomy/segmental lung resection patients developed perioperative AIS. For patients older than 65 yr, AIS rose to 1.0% for hemicolectomy, 0.3% for hip replacement, and 0.8% for pulmonary resection. Multivariate logistic regression analysis revealed renal disease (odds ratio, 3.0), atrial fibrillation (odds ratio, 2.0), history of stroke (odds ratio, 1.6), and cardiac valvular disease (odds ratio, 1.5) to be the most significant risk factors for perioperative AIS.

Conclusions: Perioperative AIS is an important source of morbidity and mortality associated with noncardiac, nonvascular surgery, particularly in elderly patients and patients with atrial fibrillation, valvular disease, renal disease, or previous stroke.

◇ This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 9A.

◆ This article is accompanied by an Editorial View. Please see: Auroy Y, Benhamou D, Amalberti R. Time to widen our horizons in perioperative medicine: A plea in favor of using patient-centered outcomes. ANESTHESIOLOGY 2008; 109:209–11.

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PERIOPERATIVE acute ischemic stroke (AIS) is a well recognized complication of cardiac and certain vascular surgeries, and it has been extensively studied in these settings.[1] Other types of surgery, although lacking the stroke risks associated with use of a cardiopulmonary bypass pump and direct manipulation of the heart and/or major vessels, are subject to other risk factors for perioperative AIS that have been recognized in cardiovascular surgery, including postoperative atrial fibrillation, perioperative myocardial infarction, hypotension, and surgery-induced hypercoagulability.[1] Although it has been shown that there is a stroke risk associated with noncardiac and nonvascular surgeries,[2] relatively few data are available regarding the incidence, risk factors, and effect on outcome of perioperative AIS for these surgeries. We therefore undertook an analysis of perioperative AIS using a large, nationwide administrative dataset looking at three common, noncardiac surgeries: hemicolectomy, total hip replacement, and segmental/lobar lung resection. These operations were used to represent major intraabdominal, orthopedic, and noncardiac thoracic surgical procedures, respectively.

Materials and Methods

Study data were derived from the Nationwide Inpatient Sample (NIS) for the years 2000 through 2004. The NIS is the largest public use database of hospital discharges available in the United States. The database encodes data from approximately 20% of all discharges from non-Federal, acute care hospitals in the United States. The sampling strategy used to create the NIS uses five hospital characteristics to generate a sample that is maximally representative of all hospitalizations in the United States: geographic region, ownership, location (urban or rural), teaching status, and bed size. During the years considered in this study, between 986 and 1004 hospitals from 28 to 37 states reported discharges to the database. The annual number of total discharges contained in the database ranged from 7,450,992 to 8,004,571 for the years considered. The data-
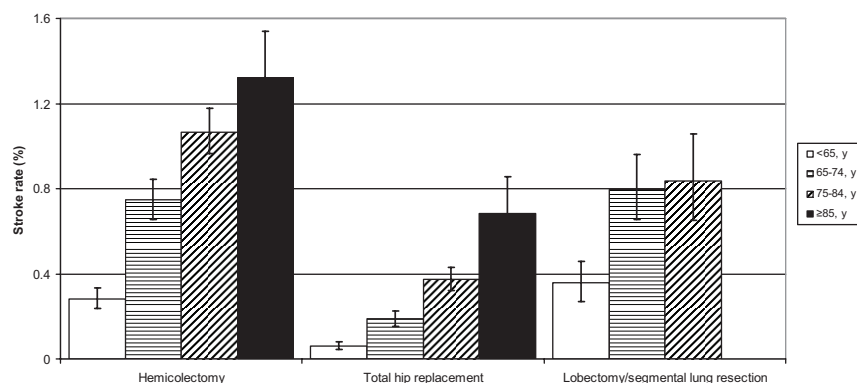
Fig. 1. The rate of perioperative acute ischemic stroke by surgery and patient age group. The rate of perioperative acute ischemic stroke is shown with 95% confidence intervals for each patient group. Figures for the 85 yr-old and older age group cannot be shown for the lobectomy/segmental resection group as it contains less than 10 patients, in accordance with the rules governing the use of the Nationwide Inpatient Sample dataset.

base includes patient information coded at the time of discharge, including age, up to 15 diagnoses and 15 procedures, discharge destination, hospital charges, and length of stay. The diagnoses codes include both acute and chronic conditions. The database is maintained by the Healthcare Utilization Project of the Agency for Healthcare Research and Quality.‖

Patients aged 18 yr or older whose list of discharge procedures included a procedure code from the International Classification of Disease-Clinical Modification, 9th revision indicating right or left hemicolectomy (ICD-9 CM 45.73, 45.75), total hip replacement (ICD-9 CM 81.51), or segmental resection or lobectomy of lung (ICD-9 CM 32.3, 32.4) were selected for analysis. We selected these ICD-9 procedure codes because they very specifically identify these common and representative surgeries. There are, in some instances, other procedure codes that overlap and include procedures that are the same or similar to the procedures we selected to study, but we chose to sacrifice an element of inclusiveness in our procedure selections for specificity. Demographic characteristics of the surgical population, including age, gender, and race, were recorded directly from the dataset. Categorization of race was simplified to white and nonwhite. Race was not coded for 27.5% of the cohort studied and was imputed as white, which is the majority race group in our cohort, to avoid unnecessarily excluding a large component of our cohort in regression analyses. Gender was missing for 0.1% of the cohort. These cases were excluded from all regression analyses.

Patients who had perioperative ischemic strokes while in-hospital were identified using ICD-9 CM diagnostic codes consistent with AIS, including 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, and 436.[3–5] Patients coded as having an iatrogenic stroke (ICD-9 CM 997.02) who did not have diagnostic codes indicating hemorrhage (ICD-9 CM 430-432) were also considered to have had a perioperative ischemic stroke; the vast majority of perioperative strokes are ischemic and not hemorrhagic.[1] Codes for an acute stroke are distinct from codes relating to strokes that occur before the incident admission. Patients were classified as having suffered a stroke if the appropriate code appeared anywhere in their list of discharge diagnoses.

The rate of perioperative AIS has been extensively studied in coronary artery bypass grafting. Therefore, to validate our method for detecting perioperative AIS, we identified all admissions in the NIS from 2000 to 2004 for coronary artery bypass grafting (CABG) without concurrent valve replacement surgery, and we identified perioperative AIS events using the ICD-9 coding schema described above. The rate of perioperative AIS was then determined and compared with the rates of stroke in CABG without valve replacement previously reported in the literature.

We identified risk factors for perioperative AIS from published review articles, case series, and by clinical plausibility, and we identified the presence or absence of these comorbid conditions for each patient within the surgical cohort by querying the database using the appropriate ICD-9 codes. The comorbidities considered included diabetes mellitus, atrial fibrillation, congestive heart failure, chronic obstructive pulmonary disease and associated conditions including chronic bronchitis and asthma, history of stroke, renal disease, cardiac valvular disease, ischemic heart disease, and peripheral vascular disease. For some of the conditions analyzed, including atrial fibrillation, the ICD-9 coding schema does not differentiate between conditions that existed before the admission for surgery and those that first occurred during the admission.

The NIS dataset reports up to 15 diagnoses and procedures per patient admission; some states have a higher maximum number of reported diagnoses and procedures. In the rare instances where more than 15 diagnoses or procedures are reported, the NIS truncates the list of discharges and procedures. In our dataset, only 0.8% of the discharges had a truncated diagnosis list, and 0.1% had a truncated procedure list.

For each discharge in the cohort, we recorded the identifier for the hospital at which the patient underwent surgery. Hospital-based variables such as hospital teaching status and size (discharges per year) were also recorded. Teaching status was missing for 0.03% of the cohort, and these cases were excluded from the primary regression analysis.

‖ Information about the database is available at http://www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed July 29, 2008.

Table 1. Patient and Hospital Characteristics and Their Initial Bivariate Analyses Relating to Acute Perioperative Stroke

	Entire Cohort, n (%)	Patients without Stroke, n (%)	Patients with Stroke, n (%)	OR (95% CI)	P
Totals	371,641	370,040	1601		
Surgery type					
Total hip replacement	201,235 (54.1)	200,815 (54.3)	420 (26.2)	Ref	
Hemicolectomy	131,067 (35.3)	130,128 (35.2)	939 (58.7)	3.45 (3.07–3.87)	< 0.001
Lobectomy, segmental resection	39,339 (10.6)	39,097 (10.6)	242 (15.1)	2.96 (2.53–3.47)	< 0.001
Age, yr (continuous)	66 ± 14	66 ± 14	74 ± 11		< 0.001
Age (categorical)					
< 65 yr	146,855 (39.5)	146,609 (39.6)	246 (15.4)	Ref	
65–74 yr	106,052 (28.5)	105,581 (28.5)	471 (29.4)	2.66 (2.28–3.10)	< 0.001
75–84 yr	95,051 (25.6)	94,407 (25.5)	644 (40.2)	4.07 (3.51–4.71)	< 0.001
> 85 yr	23,683 (6.4)	23,443 (6.3)	240 (15.0)	6.10 (5.10–7.29)	< 0.001
Gender, female (*vs.* male)	207,229 (55.8)	206,288 (55.7)	941 (58.8)	1.13 (1.02–1.25)	0.017
Race, nonwhite (*vs.* white)	41,202 (11.1)	41,002 (11.1)	200 (12.5)	1.15 (1.00–1.33)	0.073
Comorbid diagnoses					
Diabetes mellitus	45,346 (12.2)	45,082 (12.2)	264 (16.5)	1.42 (1.25–1.62)	< 0.001
Atrial fibrillation	32,687 (8.8)	32,246 (8.7)	441 (27.5)	3.98 (3.57–4.45)	< 0.001
Congestive heart failure	20,874 (5.6)	20,587 (5.6)	287 (17.9)	3.71 (3.26–4.22)	< 0.001
COPD and associated conditions	63,576 (17.1)	63,177 (17.1)	399 (24.9)	1.61 (1.44–1.81)	< 0.001
History of stroke	9131 (2.5)	9048 (2.4)	83 (5.2)	2.18 (1.75–2.72)	< 0.001
Renal disease	12,954 (3.5)	12,698 (3.4)	256 (16.0)	5.36 (4.68–6.13)	< 0.001
Valvular disease	13,659 (3.7)	13,520 (3.7)	139 (8.7)	2.51 (2.10–2.99)	< 0.001
Ischemic heart disease	51,985 (14.0)	51,631 (14.0)	354 (22.1)	1.75 (1.56–1.97)	< 0.001
Peripheral vascular disease	9492 (2.6)	9405 (2.5)	87 (5.4)	2.20 (1.77–2.74)	< 0.001
Hospital teaching status, teaching hospital (*vs.* nonteaching hospital)	171,891 (46.3)	171,260 (46.3)	631 (39.4)	0.75 (0.68–0.83)	< 0.001
Annual number of discharges (number of hospitals in group)					
< 3000 (803)	16,741 (4.5)	16,671 (4.5)	70 (4.4)	Ref	
3000–9999 (899)	89,102 (24.0)	88,710 (24.0)	392 (24.5)	1.05 (0.82–1.36)	0.69
>10,000 (841)	265,798 (71.5)	264,659 (71.5)	1,139 (71.1)	1.02 (0.80–1.31)	0.84

Where reference category is not marked, categorical comparisons are for the occurrence of stroke in patients with or without the demographic characteristic or medical diagnosis. Overall chi-square was $P < 0.001$ for perioperative stroke versus categorical age groups and $P = 0.87$ for stroke versus categories of annual number of hospital discharges. Data are expressed as mean ± SD or n (%).

CI = confidence interval; COPD = chronic obstructive pulmonary disease; OR = odds ratio.

Statistical Analyses

The primary outcome for the main analysis was AIS occurring during an admission with one of the three surgical procedures: lung resection, hemicolectomy, or total hip replacement. The admissions were all included in one dataset, with the type of surgery identified as a categorical variable.

The data were then split into an estimation dataset (70%) and a validation dataset (30%). An initial bivariate analysis was used to detect association between patient or hospital-related variables and AIS. Unpaired *t* test and chi-square test were used as indicated in table 1. These variables were then tested for colinearity. Excluding age, which is expected to correlate with comorbid disease states, variance inflation factor scores ranged from 1.01 to 1.32, averaging 1.09, with a condition index of 6.4. Even with age included in the colinearity testing, the mean variance inflation factor was 1.10, with a condition index of 17.6. With variance inflation factor scores far below 10, and condition index below 30, colinearity was judged to not be a problem for the current analysis.[6]

Multivariate analysis was performed on the estimation data set using generalized estimating equations (GEE) for logistic regression with an exchangeable working correlation matrix (compound symmetry). The hospital identifier was used as the grouping variable. Unlike standard logistic regression, GEE logistic regression allows for dependence within clusters, presumably clustering by hospital in this case.[7] All of the patient and hospital-related variables in table 1 were included in the multivariate GEE logistic model for model selection: age, gender, and race were forced in all models. After the first step of model selection, variables with limited clinical significance (odds ratios, > 0.9 or < 1.1) or with $P > 0.1$ were removed, and the model was refit. In the second step of model selection, $P < 0.05$ was applied as the criterion to include variables in the model. No interaction terms were included in the model.

Two continuous variables, patient age and total hospital discharges per year, were examined in the multivariate model and were tested for continuity and linearity.[8] The coefficients were visually linear in a graphical analysis, although total hospital discharges was eventually dropped from the model for lack of statistical significance.

The final model was tested for discrimination and calibration on both the estimation dataset and the validation

dataset, using three methods. To test discrimination, we used the area under the receiver operating curve.[8] A chi-square goodness-of-fit test was performed on the validation dataset by comparing predicted to observed proportion of stroke for the entire validation set. Lastly, to test calibration (the degree of correspondence with outcome over the range of risk), we examined the goodness of fit for 10 patient groups of equal size and increasing risk using the Hosmer-Lemeshow test.[8] The sensitivity of the Hosmer-Lemeshow test, however, is related to sample size, and the test may not be useful as an absolute criterion in studies involving large amounts of data. Simulation with large datasets (greater than 5000 data points) has shown that the Hosmer-Lemeshow test detects small deviations from model predictions when the true lack of fit is very small and that a model will be judged a good fit on a small simulated dataset but a poor fit on an identically simulated large dataset.[9] See Supplemental Digital Content 1, which shows the receiver operating curves for the generalized estimating equation logistic model in the estimation and validation samples, http://links.lww.com/A669, and Supplemental Digital Content 2, which shows the predicted *versus* the observed stroke rate for the estimation and validation samples, http://links.lww.com/A670.

We ascertained the effect of perioperative stroke on various outcomes after surgery, including in-hospital mortality, death or discharge to a facility other than home, and hospital-free days in a 30-day period. Hospital-free days were calculated by subtracting the reported length of stay from 30 for all patients surviving to hospital discharge. Patients who died in-hospital were considered to have 0 hospital-free days. The NIS does not allow tracking of patients across hospital admission; therefore, it is impossible to include readmission in the calculation of outcome measures. The effect of stroke on in-hospital mortality and death or discharge to a facility other than home was estimated using a GEE logistic model and on hospital-free days using a GEE linear model; both used the entire cohort of 371,641 discharges. As before, the hospital delivering care was used as the clustering variable. In both cases, the regression was adjusted for age, race, sex, and Charlson index of comorbidity as modified by Goldstein *et al.*[3] The Charlson Index of comorbidity is a standard method in which comorbid medical conditions (*e.g.*, diabetes, cardiac or pulmonary disease, and other conditions) are identified using the ICD-9 codes of a patient's hospitalization. Comorbid conditions are assigned weights between 1 and 6 and summed to create a Charlson index score for each patient.[3]

Statistical procedures were performed using SAS version 9.1.3 for the GEE models (SAS Institute, Inc., Cary, NC) and Stata version 10 for all other analyses (StataCorp LP, College Station, TX). Data are expressed as means ± SD or percentages and their corresponding 95% confidence interval. *t* Tests were two-tailed, and $P < 0.05$ was considered significant for all final analyses. It should be noted that NIS

provides weighting parameters for use with their data for predictions of disease burden made for the entire United States population. However, use of weighting is not indicated for the analyses in our study, and would inappropriately power the logistic regressions.

Results

Among patients having reached an age of 18 yr, we identified 131,067 admissions with patients undergoing right or left hemicolectomy, 201,235 admissions with total hip replacement, and 39,339 admissions with pulmonary lobectomy/segment resection recorded in the NIS database for the years 2000 to 2004.

We identified 939 cases of perioperative AIS in the hemicolectomy cohort for a rate of 0.7% (95% CI, 0.7–0.8%), 420 cases of perioperative AIS in the total hip replacement cohort for a rate of 0.2% (95% CI, 0.2–0.2%), and 242 cases of perioperative AIS in the lobectomy/segmental lung resection cohort for a rate of 0.6% (95% CI, 0.6–0.7%). When only patients aged 65 yr or older were considered, the rate of AIS rose to 1.0% (95% CI, 0.9–1.0) for hemicolectomy, 0.3% (95% CI, 0.3–0.3%) for total hip replacement, and 0.8% (95% CI, 0.7–0.9%) for lobectomy/segmental resection. As shown in figure 1, the rate of perioperative AIS increased with age for each type of surgery examined.

Table 1 shows the characteristics of the entire surgical cohort and examines the bivariate association of perioperative AIS with these patient and hospital variables. Table 2 shows the results of our GEE logistic regression model. As described in the Materials and Methods, the model was based on a randomly selected 70% sample of the entire cohort. The model had good discrimination in the estimation sample (area under the receiver operating curve 0.77). The Hosmer-Lemeshow statistic, a measure of calibration over a range of probabilities of perioperative stroke in the estimation sample was $P = 0.03$. This indicates a statistically significant difference between predicted and observed in the estimation sample, but it may reflect the limited utility of the Hosmer-Lemeshow statistic in very large datasets, as discussed in Statistical Analyses.[9]

The model was validated on the 30% sample of the cohort that was excluded from the estimation data. The overall chi-square goodness-of-fit test comparing the predicted percentage of strokes over all risk ranges to the observed number of strokes showed no significant difference between predicted and observed ($P = 0.50$). The model also showed good discrimination in the validation set (area under the receiver operating curve, 0.78). The Hosmer-Lemeshow statistic evaluating the calibration of the regression on the validation dataset produced $P = 0.17$, confirming that predicted outcomes over the range of stroke risk were not statistically different from observed. Figures comparing predicted to ob-

Table 2. Final Predictors of Postoperative Stroke Using Generalized Estimating Equation Logistic Model in the Estimation Sample

	ß Coefficient (95% CI)	Odds Ratio (95% CI)	P
Surgery type			
Total hip replacement	Ref	Ref	
Hemicolectomy	0.886 (0.744–1.029)	2.43 (2.10–2.80)	< 0.001
Lobectomy, segmental resection	0.965 (0.769–1.162)	2.63 (2.16–3.20)	< 0.001
Age (per 10 years)*	0.359 (0.303–0.415)	1.43 (1.35–1.51)	< 0.001
Gender, female (vs. male)*	0.188 (0.065–0.311)	1.21 (1.07–1.36)	0.003
Race, nonwhite (vs. white)*	0.097 (−0.091–0.285)	1.10 (0.913–1.33)	0.313
Comorbid diagnoses			
Diabetes mellitus	0.168 (0.009–0.327)	1.18 (1.01–1.39)	0.038
Atrial fibrillation	0.669 (0.523–0.814)	1.95 (1.69–2.26)	< 0.001
Congestive heart failure	0.361 (0.193–0.529)	1.44 (1.21–1.70)	< 0.001
History of stroke	0.492 (0.222–0.762)	1.64 (1.25–2.14)	< 0.001
Renal disease	1.09 (0.922–1.265)	2.98 (2.52–3.54)	< 0.001
Valvular disease	0.433 (0.223–0.643)	1.54 (1.25–1.90)	< 0.001
Hospital teaching status, teaching hospital (vs. nonteaching)	−0.212 (−0.339 to −0.085)	0.809 (0.713 – 0.918)	0.001

* Age, gender and race were forced throughout model selection.

served stroke rates over the range of risk (from which the HL statistics were generated) are available online for both the estimation and validation data sets.

Independent risk factors in the final GEE logistic regression model included hemicolectomy or lung resection (compared with total hip replacement), advancing age, female gender, diabetes mellitus, atrial fibrillation, congestive heart failure, history of prior stroke, renal disease, and cardiac valvular disease. Teaching hospital status was associated with lower odds of stroke.

Table 3 shows an analysis of the effect of perioperative AIS on various measures of outcome, adjusting for age, race (white vs. nonwhite), sex, and modified Charlson comorbidity index. Perioperative AIS was consistently associated with worse outcomes. Most notably, the adjusted odds of in-hospital mortality associated with perioperative AIS was 6.0 (95% CI, 5.1–7.0) for hemicolectomy, 21.4 (95% CI, 14.3–32.1) for total hip replacement, and 13.3 (95% CI, 10.0–17.5) for lobectomy/segmental resection.

To validate our method of estimating perioperative stroke rates using the ICD-9 coding structure of the National Inpatient Sample, we performed a simple analysis of stroke after cardiac surgery using the same dataset. We identified 327,628 patients admitted for CABG without concurrent valve replacement in the NIS during years 2000 to 2004. In this cohort, there were 6,316 cases of perioperative AIS, for a rate of 1.9%. Of those with perioperative AIS, 1018 (16.1%) died prior to hospital discharge. As addressed in the discussion, these results for stroke following cardiac surgery were compared to existing studies that used other methods for estimating perioperative stroke rates.

Discussion

This study, which uses the largest publicly available discharge dataset in the United States, establishes a rate

Table 3. Influence of Perioperative Stroke on Outcome

	Patients without Stroke, n (%)	Patients with Stroke, n (%)	OR (95% CI) or ß Coefficient (95% CI)	P
Hemicolectomy				
Died	7000 (5.4)	291 (31.1)	6.0 (5.1–7.0)	< 0.001
Died or discharged to location other than home	27,917 (21.5)	743 (79.3)	11.4 (9.5–13.7)	< 0.001
Hospital-free days	19 ± 8	8 ± 8	−9.9 (−9.3 to −10.4)	< 0.001
Total hip replacement				
Died	603 (0.3)	50 (12.0)	21.4 (14.3–32.1)	< 0.001
Died or discharged to location other than home	101,634 (51.0)	363 (87.1)	3.4 (2.6–4.5)	< 0.001
Hospital-free days	26 ± 3	18 ± 9	−6.8 (−5.9 to −7.6)	< 0.001
Lobectomy, segmental resection				
Died	1231 (3.2)	79 (32.6)	13.3 (10.0–17.5)	< 0.001
Died or discharged to location other than home	4942 (12.7)	174 (71.9)	16.7 (12.2–23.0)	< 0.001
Hospital free days	21 ± 7	9 ± 9	−10.7 (−9.5 to −11.9)	< 0.001

Comparisons of outcome performed using generalized estimating equation logistic model (death or discharge to other than home) and generalized estimating equation linear model (hospital-free days). All regressions adjusted for age, race, sex, and Charlson comorbidity index. Hospital-free days demonstrate negative β coefficients, indicating fewer hospital-free days in the stroke group. Outcome data were missing for 1,675 (0.45%) of the cohort and were excluded from this analysis. Data are expressed as mean ± SD or n (%).

CI = confidence interval, OR = odds ratio.

for perioperative AIS of 0.7% for hemicolectomy, 0.2% for total hip replacement surgery, and 0.6% for lobectomy/segmental lung resection. Further, when only patients aged 65 yr or older are considered, the rate of AIS rises to 1.0% for hemicolectomy, 0.3% for total hip replacement, and 0.8% for lobectomy/segmental resection. Our study confirmed that perioperative AIS has a profoundly deleterious effect on outcome after surgery, greatly increasing the odds of in-hospital mortality or discharge to a medical or chronic care facility (as opposed to discharge to home), as well as decreasing the number of hospital free days. This study, therefore, establishes perioperative ischemic stroke as an important source of morbidity and mortality in noncardiac, nonvascular surgery, particularly for elderly patients.

Rates for perioperative stroke that have been previously reported for general surgery have varied widely, ranging from 0.08–0.7% depending on the methods and populations studied,[1,10,11] and most of these incidence data derive from studies that are now quite dated. Our study provides a contemporary assessment of the burden of perioperative stroke in a well-defined and representative surgical population.

The strength of using a national dataset such as the NIS resides in the large number of cases that we were able to analyze in developing our estimates of the incidence and risk factors for perioperative AIS. The greatest limitation is the dependence on ICD-9 coding of AIS in discharge abstracts to identify cases, raising the possibility of underascertainment or misclassification of perioperative strokes. ICD-9 coding has been used to identify acute stroke in discharge databases for a variety of purposes in the neurology literature, and the accuracy has been studied in detail. Transient ischemic attacks and other conditions that do not represent acute stroke are sometimes included in the acute stroke coding,[4,5] and some inaccuracy in coding is a limitation of this, and indeed all, studies using administrative datasets.

Some authors have limited their datasets to patients with stroke coded as the primary discharge diagnosis, to maximize specificity and positive predictive value.[5] However, Tirschwell and Longstreth used all listed diagnoses (nine were available in their dataset) to show that limiting stroke to the primary diagnosis underestimates the number of AIS and that outcome is significantly worse for patients in whom stroke is not coded in the primary position.[4] We chose to use all 15 discharge diagnoses available in our dataset; in our study, the first few diagnoses are generally related to the primary surgical diagnosis. Although imperfect, the sensitivity and specificity of ICD-9 coding for AIS was found to be 86% and 95%, respectively, when appropriate modifier codes are employed and all diagnosis fields are queried.[4]

As an additional verification of the validity of our method for identifying perioperative AIS in the NIS dataset, we analyzed discharges in the NIS of patients admit-

ted for CABG without valve replacement, a population in which perioperative AIS has been well studied. Using the same ICD-9 coding schema that we employed in identifying perioperative AIS in the noncardiac, nonvascular procedures, we found a stroke rate of 1.9% for CABG patients. Further, we calculated the in-hospital mortality rate of CABG patients with AIS to be 16.1%. The incidence of stroke in CABG that has been reported previously is 1.2–2.3%, and the rate of early mortality among patients with stroke has been reported as 18–26%.[12-16] Thus, the rates for stroke and stroke-related early mortality that we find are concordant with those reported in the literature, suggesting that our method for identifying perioperative AIS is reliable.

In the process of generating our model, age, sex, and gender were kept in the regression for standard demographic adjustment, but other variables were excluded if their effect size resulted in an odds ratio less than 1.1 or greater than 0.9. In the final model, four of six medical conditions associated with perioperative stroke had odds ratios greater than 1.5. These included atrial fibrillation, history of stroke, cardiac valvular disease, and renal disease.

A particularly important and potentially modifiable risk factor for AIS in our cohort was atrial fibrillation. Although the NIS dataset does not include information concerning the timing of onset for atrial fibrillation (as such, it represents a composite of preexisting and new-onset atrial fibrillation), it was a comorbid diagnosis in 27.6% of the cases of postoperative strokes, making it the most common risk factor in the stroke patients. Atrial fibrillation can cause ischemic stroke either through cardioembolism or through cerebral hypoperfusion in patients who develop rapid ventricular response and hypotension. Perioperative electrolyte abnormalities, hyperadrenergic states, and pulmonary complications may predispose patients to new-onset atrial fibrillation after surgery. For cardiac surgery, several meta-analyses have found that the occurrence of postoperative atrial fibrillation can be reduced by the prophylactic use of β-blockers, antiarrhythmics such as amiodarone, or mixed agents like sotalol.[17] Patients treated in this manner demonstrated a trend towards decreased cerebrovascular events. However, in the recent POISE trial,[18] which examined patients undergoing noncardiac surgery, the use of β-blockers was associated with a lower risk of atrial fibrillation but a higher risk of perioperative stroke (due largely to an increase in hypotension) and of overall mortality. The dose of metoprolol administered in this study was high, and it was started immediately before surgery. More studies are needed to better define the role of pharmacologic prophylaxis of atrial fibrillation in noncardiac surgery patients, particularly among patients who carry a strong risk of developing postoperative atrial fibrillation.

Also, potentially important in modulating the risk of perioperative atrial fibrillation–related stroke is appropriate anticoagulation. The decision to anticoagulate must

balance the risks of bleeding in the surgical site and the generally self-limited history of postoperative atrial fibrillation against the potential benefits of cardioembolism prevention. Expert opinion recommends consideration of anticoagulation with warfarin in cardiac surgery patients with new onset of atrial fibrillation in the perioperative period if it lasts more than 48 h if bleeding risks are acceptable.[19] This recommendation may be applicable to patients who develop postoperative atrial fibrillation after noncardiac surgery, but more data are needed to clarify the risks and potential benefits in this population. Similarly, for patients with preexisting atrial fibrillation, the risk of thromboembolism must be balanced against the bleeding risk in deciding whether and when to anticoagulate the patient in the perioperative period; this decision is particularly challenging in patients at highest risk for thromboembolism, including those with previous thromboembolism, valvular heart disease, or left ventricular dysfunction. It is interesting in this context to note that patients undergoing total hip replacement carried the lowest risk of perioperative stroke of the surgeries we studied; the aggressive fashion in which these patients are anticoagulated to prevent venous thrombosis and embolism may contribute to their lower rate of stroke. However, the majority of patients who undergo colectomy and lung resection have an underlying malignancy; this factor may increase the stroke rate in these groups.[20]

Renal disease, previous stroke, and valvular disease were the other medical conditions representing the largest risk factors for perioperative AIS. Renal disease is a well-documented risk factor for perioperative stroke in cardiac surgery.[14,15,21] The association of renal disease and perioperative stroke may be accounted for by the accelerated atherosclerosis associated with renal disease[22]; also contributory may be the hypotension and susceptibility to fluid shifts seen in patients who are dependent on dialysis. As is well known, history of stroke is a strong risk factor for future stroke in general, [23] and our study suggests that the perioperative period may be especially dangerous for patients with history of stroke. Likewise, valvular heart disease is a known risk factor for stroke in the general population[24]; diseased valves can act as a nidus for embolus formation and, in certain situations, may compromise perfusion by decreasing cardiac output. Surgery induced hypercoagulability, cessation of anticoagulation, and the hemodynamic changes associated with surgery may make the perioperative period a time of elevated risk in patients with valvular disease.

There are a number of limitations associated with this study, in addition to those discussed earlier related to ICD-9 coding. We are limited in the range of variables that we can explore as risk factors for perioperative AIS by what is included in the dataset; a variety of potential risk factors of special interest to anesthesiologists, including intraoperative hypotension, type of anesthetic, and/or management of anticoagulation are not recorded. Our analysis of outcome after perioperative stroke is hindered by the lack of follow-up. We cannot detect if a patient dies after discharge or is discharged and subsequently readmitted, and our results likely underestimate the morbidity and mortality associated with perioperative AIS. Further, we lack the clinical and temporal detail necessary to define what specific components of the perioperative period place the patients at risk for stroke, because the dataset does not record whether a stroke occurred intraoperatively or during the milieu of physiologic changes that occur postoperatively.

Despite these limitations, our study establishes perioperative ischemic stroke as an important source of morbidity and mortality in the perioperative period of noncardiac, nonvascular surgery, particularly for elderly patients. As the population ages and the number of elderly and advanced elderly undergoing surgery and anesthesia expands,[25,26] the incidence of perioperative stroke will likely increase. While the issue of perioperative stroke in cardiac surgery has received considerable attention in the literature, there is a relative dearth of studies examining the issue in noncardiac surgery. We hope that our study will draw attention to this issue, and promote further investigation of this topic. New prospective studies that include more detailed patient characteristics and intraoperative variables are now indicated to better clarify the basis of this devastating complication.

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