

# Epidemiology of stroke after cardiac surgery in the current era

Ani C. Anyanwu, MD, FRCS,<sup>a</sup> Farzan Filsoofi, MD,<sup>a</sup> Sacha P. Salzberg, MD,<sup>a</sup> David J. Bronster, MD,<sup>b</sup> and David H. Adams, MD<sup>a</sup>



Earn CME credits at <http://cme.ctsnetjournals.org>



Supplemental material is available online.

**Objective:** Previous studies of the epidemiology of stroke in patients undergoing cardiac surgery have been based primarily on patients having coronary bypass surgery and therefore have limited applicability to the more heterogeneous populations seen in the current era. We examine the epidemiology of stroke after cardiac surgery in a contemporary surgical population.

**Methods:** Retrospective analysis was conducted of a prospective database of 5085 adults (coronary bypass 2401, isolated valve 1003, valve/coronary bypass 546, thoracic aorta 517, transplant/assist device 179, adult congenital 124, other 315) who had cardiac surgery at a single institution over a 6-year period (1998–2004).

**Results:** Stroke occurred in 134 (2.6%) patients. Incidence varied according to procedure (coronary bypass 1.7%, isolated valve 1.8%, valve/coronary bypass 4.4%, and ascending aorta 4.6%). Patients who had a stroke had a higher perioperative mortality rate than that of patients who did not (32.8% vs 4.9%;  $P < .0001$ ) and a longer period of hospitalization (median 30 days vs 7 days;  $P < .0001$ ). Multivariate logistic analysis identified 10 preoperative predictors of stroke: gender, age, aortic surgery, previous stroke, critical preoperative state, poor ventricular function, diabetes, peripheral vascular disease, unstable angina, and pulmonary hypertension. A logistic model was developed on the basis of these risk factors to predict the likelihood of stroke.

**Conclusions:** We have demonstrated a relatively low incidence of stroke in a diverse contemporary cardiac surgical cohort. By enabling preoperative identification of patients at risk, our logistic model has the potential to improve preoperative patient counseling and selection and could help to define high-risk cohorts for research into stroke prevention.

From the Departments of Cardiothoracic Surgery<sup>a</sup> and Neurology,<sup>b</sup> Mount Sinai Medical Center, New York, NY.

Received for publication March 5, 2007; revisions received June 5, 2007; accepted for publication June 15, 2007.

Address for reprints: David H. Adams, MD, Professor and Chairman, Cardiothoracic Surgery, Mount Sinai Hospital, 1190 Fifth Ave, New York, NY 10029 (E-mail: david.adams@mounsinai.org).

J Thorac Cardiovasc Surg 2007;134:1121-7  
0022-5223/\$32.00

Copyright © 2007 by The American Association for Thoracic Surgery

doi:10.1016/j.jtcvs.2007.06.031

Stroke remains one of the most devastating complications of cardiac surgery. Early studies conducted primarily on patients undergoing coronary artery bypass grafting (CABG) provided great insight into the mechanisms and risk factors associated with perioperative stroke. These studies documented a high morbidity and mortality rate associated with stroke.<sup>1</sup> Present surgical cohorts, however, are more heterogeneous than are historical series, with a lesser proportion of patients undergoing CABG and increasingly older patients with more comorbidities. Management strategies have also changed in recent years. Additionally, although several studies have examined predictors of stroke, most include intraoperative and postoperative variables, thus preventing use for *preoperative* risk stratification. There is, therefore, a need for re-description of the epidemiology of stroke. The objective of this study was to examine the epidemiology of stroke in the current era and to develop a predictive model that is applicable to contemporary patient cohorts.

**Abbreviations and Acronyms**

CABG	= coronary artery bypass graft
CPB	= cardiopulmonary bypass
IQR	= interquartile range

**Materials and Methods****Patient Population and Data**

Institutional review board approval with a waiver of individual consent was obtained for this study. All patients in our center had data entered prospectively into a New York State mandated cardiac surgical database at the time of surgery. At time of hospital discharge, complications occurring during the hospitalization (including stroke) are entered into the database. Retrospective analysis of this prospective database forms the basis for this study. This study was conducted on 5085 consecutive adult patients undergoing cardiac procedures at our institution between 1999 and 2004. Patient characteristics and procedures performed are shown in Table 1. Summary of data collection routines and data definitions are available from the New York State Department of Health.<sup>2</sup> Stroke was defined as a permanent new neurologic deficit occurring either intraoperatively or postoperatively during the hospitalization. Transient neurologic deficits with complete resolution at the time of discharge or exacerbation of a previous cerebral vascular accident with no new neurologic deficit were not recorded. There was no systematic evaluation of patients for postoperative stroke; recording of stroke was based on clinical diagnosis in the course of standard patient management. In-hospital mortality was defined as death within the same admission, regardless of cause. Subsequent deaths were tracked from the Social Security Death Index.

**Surgical Techniques**

The anesthesia, cardiopulmonary bypass (CPB), and surgical techniques were varied according to physician preference. Some broad patterns of practice were observed, however. Preoperatively, we did not systematically screen for carotid or aortic disease. All patients had intraoperative transesophageal echocardiographic assessment of the thoracic aorta for atheroma. More recently, we have routinely applied epiaortic ultrasound to identify optimal sites for cannulation and clamping. For CPB, the ascending aorta was the preferred site for arterial cannulation. For aortic procedures, in patients with aortic atheroma, and in selected reoperative procedures, the axillary artery was the preferred site for arterial inflow. CPB was maintained with nonpulsatile blood flow between 2.0 and 2.5 L · min<sup>-1</sup> · m<sup>-2</sup> body surface area with a target perfusion pressure between 60 and 80 mm Hg. Degree of systemic cooling varied between 25°C and 34°C according to surgeon preference, except for procedures requiring circulatory arrest, in which profound hypothermia (16°C–20°C) was uniformly used. Cold blood cardioplegic solution given intermittently via the antegrade and/or retrograde route, with or without topical cooling, was the preferred method of myocardial protection. A single clamp technique was generally used for on-pump CABG. For off-pump CABG, proximal aortic anastomoses were performed with side-biting clamps or with an anastomotic device. Carbon dioxide insufflation into the

**TABLE 1. Patient characteristics**

Variable	n	%
Age in years, median (IQR)	65 (54–74)	
Gender: female	1856	36.5
Extracardiac vascular disease	551	10.8
Surgery on thoracic aorta	680	13.4
Surgery on aortic arch	163	3.2
Previous stroke	382	7.5
Severe aortic calcification	297	5.8
Critical preoperative state	269	5.3
Left ventricular function		
Poor	758	14.9
Moderate	2538	49.9
Chronic obstructive pulmonary disease	349	6.7
Coronary graft performed	2947	57.6
Reoperation	691	13.6
Unstable angina	469	9.2
Renal failure	266	5.2
Pulmonary hypertension > 60 mm Hg	132	2.6
Diabetes	1319	25.9
Emergency operation	292	5.7
Recent myocardial infarction	607	11.9
Valve surgery performed	1549	30.5
Endocarditis	120	2.4
Operation type		
Congenital	124	2.4
Isolated valve	1003	19.7
CABG	2401	47.2
Valve with CABG	546	10.7
Ascending aorta	517	10.2
Transplant or ventricular assist device	179	3.5
Other	315	6.2

IQR, Interquartile range; CABG, coronary artery bypass graft.

operative field has been used liberally in recent years. Deairing and venting procedures varied among surgeons. Transesophageal echocardiography was routinely used to facilitate deairing.

**Database Validation**

Our prospective database is kept in accordance with the requirements of the New York State Department of Health for the purpose of auditing of cardiac surgical results in New York State. As part of this audit process, all hospitals in the state provide information to the Department of Health on every patient undergoing cardiac surgery. Approximately 45 risk factor variables and 8 outcome variables, including perioperative stroke, are collected on each patient. Our database is validated periodically by the New York State Department of Health. Validation consists of review of unusual reporting frequencies, cross-referencing of our database with other data sources, and periodic site visits to review the medical records on a selected sample of cases.<sup>2</sup>

**Statistical Analysis**

Categorical variables are shown as a percentage and comparisons were made with  $\chi^2$  tests as appropriate. Continuous data are shown as medians with interquartile range (IQR), with comparisons made

**TABLE 2. Risk of stroke according to risk of death**

Predicted operative mortality risk by EuroSCORE	n	Incidence of stroke (%)
Low (<3%)	1505	19 (1.3%)
Moderate (3%–9%)	2050	31 (1.5%)
High (10%–24%)	1014	46 (4.5%)
Very high (≥25%)	519	38 (7.3%)

There is a higher risk of stroke in patients at higher risk of death ( $P < .0001$ ).

by the Wilcoxon test. We used the Kaplan–Meier method for survival analysis and the log–rank test to compare survival strata. EuroSCORE was calculated by the logistic method.<sup>3</sup> Univariate logistic regression was used to define relationships between categorical or continuous variables and the occurrence of stroke. Variables with a  $P$  value of .20 or less were entered into a multivariate logistic regression analysis. We used multivariate logistic regression with stepwise selection to determine independent predictors of stroke, retaining variables with a  $P$  value below .10 in a final model. Confidence intervals were calculated as appropriate. The area under the receiver operating characteristic curve was used to assess the performance of the model. All statistical analysis was performed with SAS for Windows version 9.1 (SAS Institute, Cary, NC).

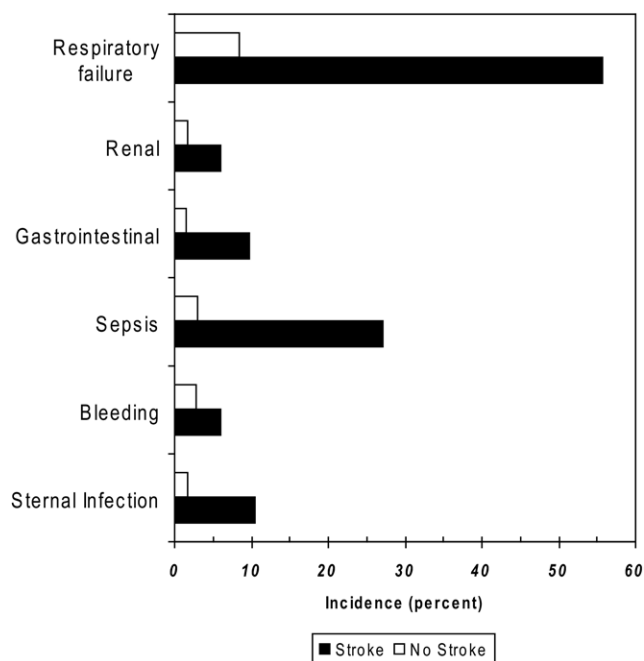
## Results

### Incidence of Stroke

During the study period, postoperative stroke was observed in 134 patients (incidence 2.6%). Of these, 80 (60%) were observed in the immediate postoperative period after reversal of anesthesia. The remaining 54 strokes were first observed after the first postoperative day. The incidence of stroke varied significantly by procedure: CABG 1.7% (40/2401), isolated valve 1.8% (18/1003), valve with CABG 4.4% (24/546), ascending aortic graft 4.6% (24/517), congenital 1.0% (1/124), ventricular assist device or transplant 6.2% (11/179), and other (including aortic arch) 5.4% (16/315). When patients were stratified according to EuroSCORE predicted risk of operative mortality, we observed an increasing risk of stroke, with increased predicted mortality (Table 2).

### Burden of Stroke

The hospital mortality for patients who had a stroke was substantially higher than that for patients who did not have a stroke (44/134 [32.8%] vs 242/4951 [4.9%]; odds ratio 9 [95% CI 6.1–13.2]). Strokes were also associated with substantially longer periods of hospitalization (median 30 days, IQR 13–62) than seen in patients who did not have a stroke (median 7 days, IQR 5–12;  $P < .0001$ ). We observed a higher incidence of all major complications in patients who had a stroke (Figure 1). The burden of stroke continued beyond the initial hospitalization, with a higher rate of death over the first postoperative year. By the end of the first year



**Figure 1. Association between stroke and perioperative morbidity.**

there was a 35% absolute survival difference between patients who did not have a stroke and those who had a stroke (Figure 2). The increased morbidity and mortality associated with stroke were seen across all EuroSCORE risk categories. Although there were more stroke deaths in high-risk patients, the *relative* risk of dying after a stroke was highest in low-risk patients (Table 3).

### Predictors of Stroke

Sixteen of the 22 factors examined on univariate analysis met criteria for inclusion into multivariate analysis (Table E1). On multivariate analysis, 10 preoperative factors were found to be independently predictive of stroke (Table 4). These 10 factors can be broadly categorized into 3 groups:

- Markers of general patient risk—gender, age, and diabetes
- Markers of vascular risk—previous stroke, peripheral vascular disease, and aortic surgery
- Markers of severity of cardiac disease—poor left ventricular function, pulmonary hypertension, critical preoperative state (inotropic, mechanical, or ventilatory support), and acute coronary syndromes

By means of the logistic equation, the risk of stroke in a given patient or patient group can be easily determined with a calculator or spreadsheet (Table E2). For example, a 76-year-old diabetic man with peripheral vascular disease and a prior

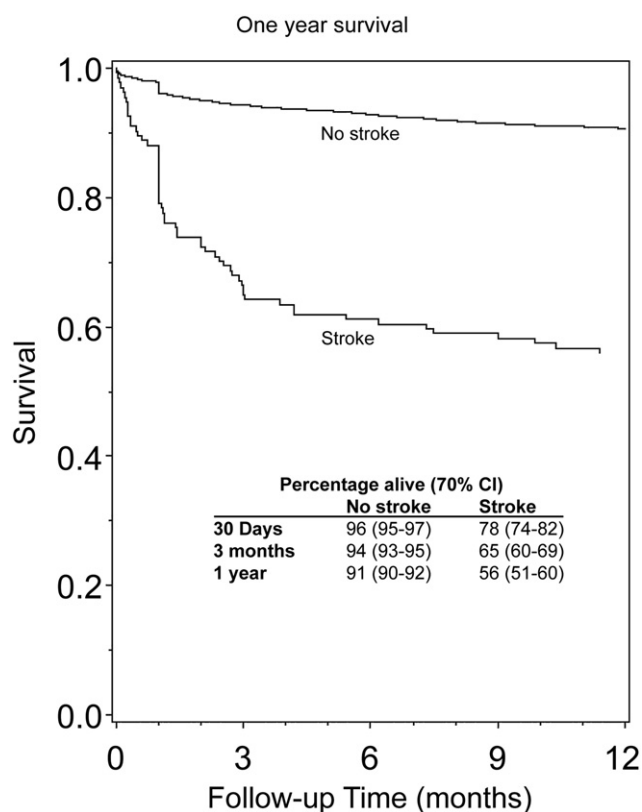


Figure 2. One-year survival after heart surgery stratified by occurrence of stroke. *CI*, Confidence interval.

stroke having an operation for aortic aneurysm has a 22% risk of stroke. The area under the receiver operating characteristic curve for the predictive model was 0.73.

## Discussion

### Incidence

In a heterogeneous and contemporary population of patients undergoing cardiac surgery, we found a 2.6% incidence of stroke. Prior series defining the epidemiology of stroke after cardiac surgery variously define the incidence of perioperative stroke after cardiac surgery between 0.8% and 5.2%.<sup>4,5</sup> Most of these studies are based on patients operated on in the 1980s or early 1990s; thus they do not reflect increasing comorbidity of current cohorts or recent advances in intraoperative management,<sup>1,6,7</sup> or they have consisted predominantly of patients undergoing CABG.<sup>8-10</sup> McKhann,<sup>5</sup> Bucerius,<sup>11</sup> and their colleagues have recently published data on more contemporary and heterogeneous groups undergoing cardiac surgery. McKhann and colleagues<sup>5</sup> keep a prospective stroke database at Johns Hopkins University and recorded a stroke incidence of 4.1% for CABG, 3.1% for valve, 7.9% for valve with CABG, and 8.7% for aortic surgery for the years 2001 to 2004; these figures compare

TABLE 3. One-year mortality after stroke according to risk category

Risk group	Mortality rate		Odds ratio (95% CI)
	Patients with stroke	Patients without stroke	
Low	15.0%	1.3%	14 (3.9–55.6)
Moderate	26.7%	2.8%	12 (5.3–29.3)
High	32.6%	7.4%	6 (3.1–11.8)
Very high	44.7%	21.1%	3 (1.5–5.9)

Occurrence of stroke in the low risk patient increases the probability of death several-fold.

with 1.8%, 2.0%, 4.6%, and 5%, respectively, in our series. Bucerius and coworkers<sup>11</sup> studied a heterogeneous population of 16,184 patients who were operated on between 1996 and 2001. They reported an incidence of stroke of 4.6% overall, with an 8.8% incidence after mitral valve surgery, 4.5% for aortic valve surgery, and 3.8% for on-pump CABG. Although our study methodology does not provide us with means of determining the reasons that our incidence of stroke is lower than that in these two contemporary series, we believe the key to a low stroke rate lies in systematic application of adjunctive stroke prevention measures. For example, epiaortic ultrasound, which we now routinely apply, identifies significant atheromatous lesions that are not evident on digital palpation<sup>12,13</sup> and may reduce the risk of perioperative stroke.<sup>14</sup> Similarly, our low threshold for use of axillary artery cannulation may be protective, inasmuch as less cerebral microemboli occur with this technique than with aortic cannulation.<sup>15</sup> Single clamp techniques,<sup>16</sup> carbon dioxide flooding,<sup>17</sup> maintenance of high perfusion pressures,<sup>18</sup> adequate hematocrit on bypass,<sup>19</sup> and hypothermia may also have contributed to our low incidence of stroke.

### Causation Versus Association

The continued hazard associated with perioperative stroke months to years after the stroke occurs raises the possibility that stroke may be a marker of predisposition to death rather than a direct cause of death. Table 2 provides some argument against causation, because there is direct correlation between risk of death (predicted by EuroSCORE) and incidence of stroke. This implies that at least some patients who die after a stroke were independently predisposed to perioperative death regardless of occurrence of the stroke. In such patients, stroke often coexists with other major complications such as bleeding, low cardiac output, and sepsis (Figure 1) such that stroke may have been a surrogate for a complicated postoperative course or a mechanism of death in a critically ill patient, rather than the direct cause of death. Such high-risk patients who do survive a stroke will, by virtue of their pre-existing comorbidity, still be more

**TABLE 4. Multivariate predictors of postoperative stroke**

Factor	Coefficient	Odds ratio	95% CI	P value
Aortic surgery	1.36	3.9	2.5–5.9	<.0001
Previous stroke	0.74	2.1	1.4–3.7	.0007
Critical preop state	0.90	2.5	1.4–4.5	.0008
Age > 60 y (per 5-y intervals)	0.14	1.2	1.0–1.3	.003
Left ventricle function, poor	0.69	2.0	1.3–3.2	.003
Gender, female	0.50	1.7	1.1–2.4	.006
Diabetes	0.50	1.7	1.2–2.6	.007
Peripheral vascular disease	0.58	1.8	1.1–2.9	.01
Unstable angina	0.51	1.7	0.9–2.8	.05
Pulmonary hypertension	0.79	2.2	0.9–4.5	.08

likely to die months or even years after surgery, partly explaining the persistence of an increased death rate for several years in patients who survive perioperative stroke.

In some patients, however, there is a definite causative influence of stroke on mortality. This is well demonstrated by our observation that low-risk patients, who should otherwise survive without major complications, had a mortality rate of 15% if they had a postoperative stroke (Table 3), an excess mortality that cannot otherwise be explained by preoperative risk factors. In the very high-risk patient, however, many strokes may be surrogates rather than the cause of adverse outcomes, because the relative impact of a stroke was less in the higher risk groups (Table 3).

#### Preoperative Risk Factors for Perioperative Stroke

Several studies have reported predictive factors for perioperative stroke.<sup>7,10,11,20-27</sup> Most of these have based their risk models on cohorts of patients undergoing CABG. In the current era, the frequency of CABG surgery is decreasing rapidly, such that existing models are not applicable to a substantial proportion of patients undergoing cardiac surgery. Our study is unique in the stroke literature inasmuch as only half of our patients had isolated CABG; this provides sufficient heterogeneity to allow determination of risk factors applicable to the entire spectrum of adult cardiac surgery. Predictive variables in prior models have generally been limited to markers of vascular disease and age; because they have limited risk factors, they invariably lack sufficient discriminatory ability. For example, in the risk model of McKhann and coworkers,<sup>21</sup> a 65-year-old diabetic and hypertensive man with no history of stroke has an estimated 9% risk of stroke, a risk we would consider excessive (on the basis of our model such a patient has a stroke risk of 1.5%). By contrast, a 75-year-old diabetic woman with peripheral vascular disease and a history of previous stroke, who required an intra-aortic balloon for hemodynamic support after an acute coronary syndrome, would have a stroke risk of 12%, a risk we would consider too low (in our model such a risk would be 33%). Such

inability to differentiate patients, whose risks of developing an event are clearly not similar (referred to as a lack of model discrimination), is a problem with most predictive models for perioperative stroke. Lack of discrimination arises largely because of the homogeneity of the populations from which the models were defined (most were defined based on low-risk CABG populations and therefore, by definition, are not calibrated to predict outcomes in higher risk patients). Bucarius and colleagues<sup>11</sup> did study a more heterogeneous population, but applicability of their risk model is limited because they included operative variables such as duration of CPB, hemofiltration, and transfusion requirement, thus preventing application in preoperative risk stratification.

In our study, the risk factors are broad and include not just markers of vascular disease (which predominate most risk models) but also markers of general patient risk and surgical complexity. The latter two are important because markers of vascular disease alone will not capture increased stroke risk in patients who are independently predisposed to embolism or hypoperfusion (such as a patient having emergency CABG after complications of angioplasty), both of which are important etiologic mechanisms of stroke after cardiac surgery. By capturing a diversity of patient morbidity, our 10-factor model has improved discriminatory ability compared with existing models. Because we have limited our analysis to preoperative risk factors, risk stratification can be applied preoperatively. This may prove particularly useful to the cardiologist and cardiac surgeon when counseling a patient with comorbidities about the risks of a particular cardiac surgical intervention. Because of a lack of data, often the focus is on mortality risk, but ideally the stroke risk would also be available for consideration when balancing the risks and benefits of a potential operation. A relatively high probability of stroke in the setting of a low or moderate operative mortality risk and minimal cardiac symptomatology would be particularly relevant in the decision-making process. Another potential application of our

model is to define high-risk cohorts for research into mechanisms and prevention of stroke, such as for testing of novel neuroprotective drugs, devices, and techniques. Use of low-risk cohorts for studies of stroke prevention are challenged because several thousands of patients are required to demonstrate a difference. For example, although Banbury and colleagues<sup>28</sup> randomized 1289 patients to receive an intra-aortic filter that captures particulate emboli which could potentially cause stroke, they did not find any clinical difference between the intervention and control arm. The incidence of stroke in the control arm (2.2%) was, however, so low that up to 30,000 patients would have been required to demonstrate the differences they sought. With a preoperative stroke risk model such as ours, a high-risk population can be defined that requires realistic and smaller numbers to show relevant clinical differences.

### Burden of Stroke

Perioperative stroke has a high clinical and economic burden. We found patients who had a stroke 6 times more likely to die during hospital admission than were those who did not. Bucerius and colleagues<sup>11</sup> also found a 6-fold increase in mortality. The mortality associated with perioperative stroke has remained constant over the past 3 decades (mortality 32% in our series compared with 29% in the 1970s<sup>1</sup>). This suggests that in some patients stroke, once it occurs, is a lethal condition that is minimally influenced by subsequent medical management. This highlights the importance of stroke prevention as the primary approach to lessen the burden of stroke. We observed increased morbidity and length of stay in patients with stroke—these patients often require intense medical therapy and therefore use a large amount of resources. Patients with perioperative stroke also require longer periods of intensive care (55% required prolonged ventilatory support in our series). Our observation of a continued hazard of death, even after successful hospital discharge, is supported by data from Dacey and coinvestigators<sup>8</sup> from the Northern New England Cardiovascular Disease Study Group, who found a reduced survival at 10 years in patients who had perioperative stroke compared with those who did not (27% vs 62%).

The epidemiologic and economic burden of stroke after cardiac surgery is huge. Some studies have suggested that as many as 35,000 new strokes per year occur as a result of cardiac surgery.<sup>29</sup> On the basis of our findings of an incremental length of stay of 30 days in stroke patients, at a conservative cost of \$1000 per day, the health care costs of stroke after cardiac surgery in the United States may approach \$1 billion annually.

### Limitations

Although our database is prospective, all databases have a potential for underreporting or misreporting of events and

risk factors. We, however, believe this underreporting to be minimal as our data are based on a government-mandated quality assurance database. The New York State Department of Health periodically undertakes validation visits to each center, and there has not been any question of the quality of our data or underreporting of adverse events in our center. Although we recorded data on complications at time of discharge, rather than when the stroke occurred, it is unlikely that this delayed recording would have resulted in underreporting, because stroke was defined as permanent deficits, which would still have been present at the time data were entered. Because our definition of stroke was very restrictive (permanent deficits only), our study did not pick up subtle strokes. However, by recording only permanent strokes, our study has the advantage of focusing on those strokes that are most important to the patients and clinicians. Another problem all databases face is incomplete data. Statistical tests did not, however, find any missing data to be systematically informative, such that it is unlikely that incomplete data biased our results. Some risk factors are unknown and other factors of interest may not have been systematically collected (such as preoperative identification of aortic calcification and preoperative atrial fibrillation), preventing their inclusion in the model. We believe, however, that there is sufficient colinearity such that the effects of any potentially useful variable that was not considered in our study will be captured by variables included in our model. For example, although atrial fibrillation has been associated with a higher perioperative stroke rate on univariate analysis, it is likely that this a confounding effect from associated poor cardiac function and advanced valve disease, because the association is lost on multivariate analysis.<sup>10,11</sup>

### Conclusions

In a diverse population of patients undergoing cardiac surgery, we have shown a low incidence of stroke in a contemporary surgical cohort. Although our incidence of stroke is lower than that seen in historical cohorts, the impact of stroke remains substantial in terms of mortality, morbidity, and duration of hospitalization. Improved ability to predict those patients who are at increased risk of stroke may allow more targeted research and better informed consent. Cardiologists, surgeons, and patients may benefit from such information when making decisions regarding referral, timing, and acceptance for surgery. External validation of our model in other settings is required.

### References

1. Coffey CE, Massey EW, Roberts KB, Curtis S, Jones RH, Pryor DB. Natural history of cerebral complications of coronary artery bypass graft surgery. *Neurology*. 1983;33:1416-21.

2. Adult cardiac surgery in New York State 2001–2003. Available at: [http://www.nyhealth.gov/nysdoh/heart/pdf/2001-2003\\_cabg.pdf](http://www.nyhealth.gov/nysdoh/heart/pdf/2001-2003_cabg.pdf). Accessed August 3, 2006.
3. Roques F, Michel P, Goldstone AR, Nashef SA. The logistic EuroSCORE. *Eur Heart J*. 2003;24:881-2.
4. Bronster DJ. Neurologic complications of cardiac surgery: current concepts and recent advances. *Curr Cardiol Rep*. 2006;8:9-16.
5. McKhann GM, Grega MA, Borowicz LM Jr, Baumgartner WA, Selnes OA. Stroke and encephalopathy after cardiac surgery: an update. *Stroke* 2006;37:562-71.
6. Breuer AC, Furlan AJ, Hanson MR, Lederman RJ, Loop FD, Cosgrove DM, et al. Central nervous system complications of coronary artery bypass graft surgery: prospective analysis of 421 patients. *Stroke* 1983;14:682-7.
7. McKhann GM, Goldsborough MA, Borowicz LM Jr, Mellits ED, Brookmeyer R, Quaskey SA, et al. Predictors of stroke risk in coronary artery bypass patients. *Ann Thorac Surg*. 1997;63:516-21.
8. Dacey LJ, Likosky DS, Leavitt BJ, Lahey SJ, Quinn RD, Hernandez F Jr, et al. Perioperative stroke and long-term survival after coronary bypass graft surgery. *Ann Thorac Surg*. 2005;79:532-6.
9. Likosky DS, Marrin CA, Caplan LR, Baribeau YR, Morton JR, Weintraub RM, et al. Determination of etiologic mechanisms of strokes secondary to coronary artery bypass graft surgery. *Stroke* 2003;34:2830-4.
10. D'Ancona G, Saez de Ibarra JL, Baillet R, Mathieu P, Doyle D, Metras J, et al. Determinants of stroke after coronary artery bypass grafting. *Eur J Cardiothorac Surg*. 2003;24:552-6.
11. Bucerius J, Gummert JF, Borger MA, Walther T, Doll N, Onnasch JF, et al. Stroke after cardiac surgery: a risk factor analysis of 16,184 consecutive adult patients. *Ann Thorac Surg*. 2003;75:472-8.
12. Bolotin G, Domany Y, de Perini L, Frolkis I, Lev-Ran O, Neshet N, et al. Use of intraoperative epiaortic ultrasonography to delineate aortic atheroma. *Chest*. 2005;127:60-5.
13. Royse C, Royse A, Blake D, Grigg L. Screening the thoracic aorta for atheroma: a comparison of manual palpation, transesophageal and epiaortic ultrasonography. *Ann Thorac Cardiovasc Surg*. 1998;4:347-50.
14. Zingone B, Rauber E, Gatti G, Pappalardo A, Benussi B, Dreas L, et al. The impact of epiaortic ultrasonographic scanning on the risk of perioperative stroke. *Eur J Cardiothorac Surg*. 2006;29:720-8.
15. Hedayati N, Sherwood JT, Schomisch SJ, Carino JL, Markowitz AH. Axillary artery cannulation for cardiopulmonary bypass reduces cerebral microemboli. *J Thorac Cardiovasc Surg*. 2004;128:386-90.
16. Aranki SF, Sullivan TE, Cohn LH. The effect of the single aortic cross-clamp technique on cardiac and cerebral complications during coronary bypass surgery. *J Card Surg*. 1995;10:498-502.
17. Svenarud P, Persson M, van der Linden J. Effect of CO2 insufflation on the number and behavior of air microemboli in open-heart surgery: a randomized clinical trial. *Circulation*. 2004;109:1127-32.
18. Gold JP, Charlson ME, Williams-Russo P, Szatrowski TP, Peterson JC, Pirraglia PA, et al. Improvement of outcomes after coronary artery bypass: a randomized trial comparing intraoperative high versus low mean arterial pressure. *J Thorac Cardiovasc Surg*. 1995;110:1302-11.
19. DeFoe GR, Ross CS, Olmstead EM, Surgenor SD, Fillinger MP, Groom RC, et al. Lowest hematocrit on bypass and adverse outcomes associated with coronary artery bypass grafting. Northern New England Cardiovascular Disease Study Group. *Ann Thorac Surg*. 2001;71:769-76.
20. Newman MF, Wolman R, Kanchuger M, Marschall K, Mora-Mangano C, Roach G, et al. Multicenter preoperative stroke risk index for patients undergoing coronary artery bypass graft surgery. Multicenter Study of Perioperative Ischemia (McSPI) Research Group. *Circulation*. 1996;94(9 Suppl):II74-80.
21. McKhann GM, Grega MA, Borowicz LM Jr, Bechamps M, Selnes OA, Baumgartner WA, et al. Encephalopathy and stroke after coronary artery bypass grafting: incidence, consequences, and prediction. *Arch Neurol*. 2002;59:1422-8.
22. Engelman DT, Cohn LH, Rizzo RJ. Incidence and predictors of TIAs and strokes following coronary artery bypass grafting: report and collective review. *Heart Surg Forum*. 1999;2:242-5.
23. Ascione R, Reeves BC, Chamberlain MH, Ghosh AK, Lim KH, Angelini GD. Predictors of stroke in the modern era of coronary artery bypass grafting: a case control study. *Ann Thorac Surg*. 2002;74:474-80.
24. Charlesworth DC, Likosky DS, Marrin CA, Maloney CT, Quinton HB, Morton JR, et al. Development and validation of a prediction model for strokes after coronary artery bypass grafting. *Ann Thorac Surg*. 2003;76:436-43.
25. Stamou SC, Hill PC, Dangas G, Pfister AJ, Boyce SW, Dullum MK, et al. Stroke after coronary artery bypass: incidence, predictors, and clinical outcome. *Stroke*. 2001;32:1508-13.
26. Libman RB, Wirkowski E, Neystat M, Barr W, Gelb S, Graver M. Stroke associated with cardiac surgery. Determinants, timing, and stroke subtypes. *Arch Neurol*. 1997;54:83-7.
27. Rao V, Christakis GT, Weisel RD, Ivanov J, Peniston CM, Ikonomidis JS, et al. Risk factors for stroke following coronary bypass surgery. *J Card Surg*. 1995;10:468-74.
28. Banbury MK, Kouchoukos NT, Allen KB, Slaughter MS, Weissman NJ, Berry GJ, et al. Emboli capture using the Embol-X intraaortic filter in cardiac surgery: a multicentered randomized trial of 1,289 patients. *Ann Thorac Surg*. 2003;76:508-15.
29. Stamou SC. Stroke and encephalopathy after cardiac surgery: the search for the Holy Grail. *Stroke*. 2006;37:284-5.

TABLE E1. Univariate analysis of predictors of stroke

Factor	Stroke rate (%)		Odds ratio	95% CI	P value
	Patients with risk factor	Patients without risk factor			
Age > 60 y (per 5-y intervals)			1.1	1.1–1.3	<.0001
Extracardiac vascular disease	5.4	2.3	2.4	1.6–3.7	<.0001
Surgery on thoracic aorta	5.6	2.2	2.6	1.8–3.9	<.0001
Surgery on aortic arch	8.6	2.4	3.7	2.1–6.6	<.0001
Previous stroke	5.8	2.4	2.7	1.7–4.3	<.0001
Aortic calcification*	9.8	2.2	5.0	3.2–7.8	<.0001
Critical preoperative state	6.7	2.4	2.8	1.7–4.8	<.001
Left ventricular function, poor	4.4	2.3	1.9	1.2–2.9	.001
Gender, female	3.5	2.1	1.6	1.2–2.3	.004
Obstructive airways disease	4.9	2.5	2.0	1.2–3.5	.005
Coronary graft performed	2.2	3.3	0.63	0.4–0.9	.008
Reoperation	4.1	2.4	1.7	1.1–2.7	.009
Unstable angina	4.3	2.5	1.6	1.0–2.6	.04
Renal failure	4.5	2.5	1.8	1.0–3.3	.05
Pulmonary hypertension	5.3	2.6	1.9	0.9–4.3	.08
Diabetes	3.2	2.4	1.34	0.92–1.9	.11
Emergency operation	3.8	2.6	1.5	0.7–2.8	.2
Carotid disease†	3.9	2.6	1.4	0.7–2.9	.35
Recent myocardial infarction	3.1	2.6	1.2	0.7–2.0	.43
Valve surgery performed	2.7	2.6	1.1	0.7–1.5	.75
Left ventricular function, moderate	2.6	2.6	1.0	0.7–1.4	.88
Endocarditis	2.5	2.6	1.0	0.3–3.1	.97

\*Because aortic calcification was often determined intraoperatively, this variable was not included in the multivariate analysis. †Because we did not routinely screen for carotid disease, these data were incomplete in a substantial proportion of patients.

TABLE E2. Logistic model for estimating the risk of stroke

Factor	$x$ (yes = 1; no = 0)	$b$	$xb$
Aortic surgery		1.36	
Previous stroke		0.74	
Critical preoperative state		0.9	
Age > 60 y (per 5-y intervals)		0.14	
Left ventricular function, poor		0.69	
Gender, female		0.5	
Diabetes		0.5	
Peripheral vascular disease		0.58	
Unstable angina		0.51	
Pulmonary hypertension		0.79	
Intercept (a)		−4.99	−4.99
Total		$\sum xb + a =$	
$\text{Odds (stroke)} = \exp \sum xb + a$ $P (\text{stroke}) = \text{odds}/(1 + \text{odds})$			

Logistic model for estimating the risk of stroke. Numeric values ( $x$ ) are assigned to each factor.  $xb$  refers to the product of  $x$  and the coefficient  $b$ . The odds are then calculated as the exponent of the sum of all product coefficients  $xb$  and the intercept ( $a$ ). The probability of a stroke is odds/(1 + odds). The model can easily be applied using a spreadsheet.