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Risk of Surgery and Anesthesia for Ischemic Stroke

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Background: **The goal of this study was to determine if the combination of surgery and anesthesia is an independent risk factor for the development of incident (first-time) ischemic stroke.**

Methods: **All residents of Rochester, MN, with incident ischemic stroke from 1960 through 1984 (1,455 cases and 1,455 age- and gender-matched controls) were used to identify risk factors associated with ischemic stroke. Cases and controls undergoing surgery involving general anesthesia or central neuroaxis blockade before their stroke/index date of diagnosis were identified. A conditional logistic regression model was used to estimate the odds ratio of surgery and anesthesia for ischemic stroke while adjusting for other known risk factors.**

Results: **There were 59 cases and 17 controls having surgery within 30 days before their stroke/index date. After adjusting for previously identified risk factors, surgery within 30 days before the stroke/index date (perioperative period) was found to be an independent risk factor for stroke ($P < 0.001$; odds ratio, 3.9; 95% confidence interval, 2.1–7.4). In an analysis that excluded matched pairs where the case and/or control underwent surgery considered "high risk" for stroke (cardiac, neurologic, or vascular procedures), "non–high-risk surgery" was also found to be an independent risk factor for perioperative stroke ($P = 0.002$; odds ratio, 2.9; 95% confidence interval, 1.5–5.7).**

Conclusion: **Our results suggest that there is an increased risk of ischemic stroke in the 30 days after surgery and anesthesia. This risk remains elevated even after excluding surgeries (cardiac, neurologic, and vascular surgeries) considered to be high risk for ischemic stroke. (Key words: Cerebrovascular accident; case-control study; morbidity.)**

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STROKES during the perioperative period are uncommon events. Rates of stroke after general surgery and anesthesia have ranged from approximately 0.08 to 0.4%.[1-3] It has also been established that certain surgeries, such as cardiac, neurologic, and vascular procedures, have higher rates of associated stroke ranging from 2.2 to 5.2%.[4-9] Although these events are uncommon, perioperative stroke can be associated with a mortality rate of up to 26%.[3]

Although not completely uniform among all studies, certain risk factors have been identified to be independently associated with the development of stroke. These factors include older age, male gender, history of transient ischemic attacks (TIA), hypertension, cigarette smoking (current or former), diabetes mellitus, ischemic heart disease, atrial fibrillation, and mitral valve disease.[10-14] However, the risk of the combination of surgery and anesthesia as a predictor for stroke has not been adequately evaluated. Existing studies have focused primarily on the determination of rates of perioperative stroke.[1-3,5,6] These studies are often limited by small numbers of cases, and the specific types of stroke are often not described. Any evaluation of risk has been directed toward identification of comorbid conditions associated with perioperative stroke. However, the risk of the event of surgery and anesthesia itself, independent of other known risk factors for the development of stroke, has not been determined.

Previous work identified all residents of Rochester, MN, who were newly diagnosed with ischemic stroke (incident cases) during a 25-yr period between 1960 and

1984.[10] This database has allowed the study and identification of certain risk factors associated with ischemic stroke.[10] The purpose of this study was to determine, by reviewing existing medical records, if the combination of surgery and anesthesia is an independent risk factor for the development of incident ischemic stroke.

Methods

This investigation was approved by the Mayo Institutional Review Board. The population of Rochester, MN, is suitable for epidemiologic studies because medical care is provided primarily by the Mayo Clinic (and its two large affiliated hospitals: Rochester Methodist and Saint Mary's) and one smaller group practice, the Olmsted Medical Group (and its affiliated hospital: Olmsted Community). All diagnoses at any of these facilities that are made for residents of Rochester are entered into a central index. The computerized file makes it possible to identify Rochester residents with a variety of different types of stroke. In addition, the original medical records for these patients are readily available for review. The medical records include the details of medical care provided by physicians of the community, in the office, during hospitalizations, at emergency department visits, and during home or nursing home visits as well as information recorded at autopsy, on death certificates, and on correspondence with patients or family members. The result is a comprehensive file of the records of the health care received by the population of Rochester.

The medical record linkage system for the Rochester Epidemiology Project has been previously used to retrieve the records of 1,444 residents of Rochester who were diagnosed as having an incident ischemic stroke from 1960 through 1984.[10,15] The previously described work, identifying 1,444 incident ischemic stroke cases,[10] has subsequently been further clarified, identifying a new total of 1,455 cases, which was used for our investigation. An ischemic stroke, which is a cerebral infarct, has been defined in previous work as a focal neurologic deficit of acute onset, persisting for > 24 h, that could not be attributed to another disease process.[15] Patients who, ≥ 24 h after the onset of stroke, had only persistent sensory symptoms with minimal sensory signs or mild impairment of dexterity with normal muscle strength were included. Patients who, after 24 h, had only deep tendon reflex changes or Babinski's signs were excluded. Computed tomography of the head or autopsy, when performed, did not show evidence of an intracerebral hematoma. Potential cases of stroke were excluded if (1) the patient had no clinical history of stroke, and the only evidence of stroke was either a diagnosis on the death certificate, an area of low density on a computed tomography head scan, or an old lesion in the brain at autopsy; (2) the patient had a clinical diagnosis of stroke and died within 24 h of the onset of symptoms and had no focal neurologic deficit, no autopsy, and no computed tomography head scan; or (3) the patient had lived in Rochester for < 1 yr before their first stroke occurred.

The controls were selected from an enumeration of the population through the medical records of the Rochester Epidemiology Project.[16] For each case, a pool of all same-sex Rochester residents who had a medical visit within $\pm$ 1 yr of the year of the diagnosis of the case and were born within $\pm$ 2 yr of the year of birth of the case was created. For example, if a 71-yr-old man had a stroke in 1971, the pool of potential controls would include all male residents in Rochester in 1971 who had a medical visit in 1970, 1971, or 1972 and were born in 1898, 1899, 1900, 1901, or 1902. Beginning with the earliest stroke case within the 1960-1984 time interval, controls were selected from these pools by first selecting the individual who had a registration number that was the nearest to that of the case. Registration numbers are sequentially assigned, and matching on them assures comparable length of the calendar time for a case-control pair of individual medical records. It was then validated that: (1) the selected individual had a recorded blood pressure determination within $\pm$ 1 yr of the case stroke, and the date of that blood pressure became the control's index date; (2) the individual had been a resident of Rochester for at least 1 yr before the index date; (3) the individual had not had a cerebral infarct before the reference date; and (4) the individual had not been selected as a control for an earlier stroke case. If the selected individual failed any of these matching conditions, then he/she was ineligible to serve as a control for this case, and another individual was selected from the pool. The one who qualified and had the next nearest registration number was always selected as the control for that case. Thus, for all 1,455 cases of stroke, there were age- and gender-matched controls with similar index dates. Because this process covered a 25-yr span of time, an individual selected initially as a control could potentially become a case subsequently. Thinking of the population of Rochester for the period of 1960-1984 as the cohort, this study design essentially describes a case-control study nested within the cohort.

Using the Mayo Surgical Information Retrieval System and the Rochester Epidemiology Project data, which contains information regarding every anesthesiologist-attended surgical procedure performed in Rochester, MN, over the period of interest, we identified all stroke cases who had a surgical procedure at Mayo Rochester (in one of two hospitals) or Olmsted Community Hospital within 1 yr before their stroke date. The medical records of these stroke cases who received a general anesthetic or central neuroaxis local anesthetic block (spinal or epidural local anesthetic block) during this period were reviewed. Surgical procedures involving monitored anesthesia care or peripheral nerve block were not included. This methodology was then repeated for the age- and gender-matched control group. Information for the cases and controls were abstracted from the medical record by a single nurse abstractor.

Statistical Analysis

Statistical analysis for this case-control study compared indexed cases and controls in a matched-pair design to determine if the combination of surgery and anesthesia was associated with ischemic stroke using a conditional logistic regression model.[17] For each patient, a continuous variable was calculated as the length of time between the stroke/index date and the most recent surgery before this date. This variable was assigned a value of 366 days for all subjects who had no prior surgeries or who did not have surgery in the 1 yr before the stroke date or index date. Time since most recent surgery was assessed as both a continuous variable and categorically with three categories: 0-30 days (perioperative period—a frequently used time period to evaluate short-term, postsurgical outcomes), 31-365 days, and 366+ days. Using this grouping, subjects with no prior surgeries were classified as 366+ days. With time since most recent surgery treated as a continuous variable, we assessed both linear and nonlinear associations between time and the risk for ischemic stroke. Because there was not an exact matching of age and stroke/index date, adjusting variables for these were incorporated into the model. Time from most recent surgery was included in a multivariate model along with the variables from the "final" model identified by Whisnant *et al*, which included seven risk factors that are well defined in their report.[10] These factors included TIA, hypertension, current smoking, diabetes mellitus, ischemic heart disease, atrial fibrillation, and mitral valve disease (other than prolapse). The following interactions were also included in the final model of Whisnant *et al.*: TIA by gender and age, hypertension by age, current smoking by age, and type of atrial fibrillation by hypertension. Using multiple conditional logistic regression, we examined the main effect of time since most recent surgery and the interaction of time since most recent surgery with each of the other variables included in the final model. In addition, to assess whether the risk of surgery for the development of ischemic stroke changed over calendar time, we evaluated the two-way interaction between length of time since most recent surgery and calendar time. Patients undergoing cardiac, neurologic, or vascular surgeries are known to be at increased risk for perioperative stroke (stroke within 30 days after surgery).[4-9] Therefore, an additional analysis was performed to evaluate the effect of "non-high-risk" surgery on the development of stroke by removing the matched pairs of cases and/or controls who underwent cardiac, neurologic, or vascular surgeries in the previous 30 days.

Data regarding cigarette smoking were available only for the last 15 yr of the study (1970-1984). For this reason, an analysis that did not adjust for current smoking was performed using the data from the entire time period. In addition, an analysis that adjusted for current smoking was performed using only the data from the last 15 yr of the study. In all cases, tests were two-sided with P values ≤ 0.05 considered as evidence of findings not attributable to chance.

Results

This report includes 1,455 incident cases of ischemic stroke in the Rochester, MN, population in the 25 yr of this study from 1960 through 1984, matched 1:1 with controls from the population as described by Whisnant *et al.*[10] For the 15-yr period from 1970-1984, there were 942 cases. A complete description of the demographics and risk factors for the cases and controls is presented in the original work.[10]

We found 9.1% (132 of 1,455) cases and 5.8% (85 of 1,455) controls who underwent one or more surgical procedures requiring a general anesthetic or central neuroaxis local anesthetic block in the 1-yr period before their stroke/index date, respectively. Using only the previous surgery closest to their stroke/index date, figure 1 displays the frequency of surgery for cases and controls weekly for the 1-yr period before their stroke/index date. Surgery occurred within 30 days before the stroke/index date in 4.1% (59 of 1,455) cases and 1.2% (17 of 1,455) controls (tables 1 and 2), and 31-365 days before the stroke/index date in 5.0% (73 of 1,455) cases and 4.7% (68 of 1,455) controls. There was a nonlinear asso-

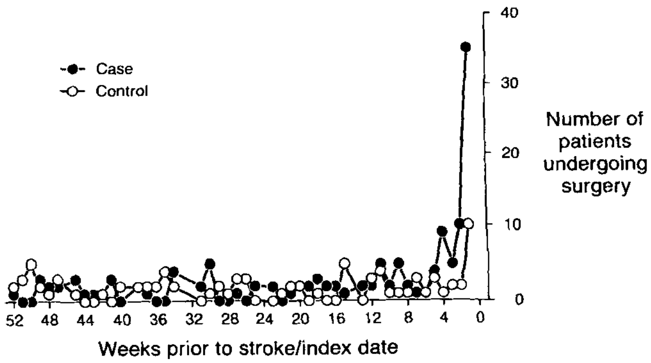

Fig. 1. Weekly frequency of surgery for 52 weeks (1 yr) before the stroke/index date for cases (n = 132) and controls (n = 85). Only the surgery closest to the stroke/index date was considered in individuals with multiple surgeries.

ciation between time since most recent surgery (treated as a continuous variable) and risk for ischemic stroke ($P = 0.019$).

Using data from the entire period, surgery within 30 days before the stroke/index date was found to be a univariate risk factor for ischemic stroke ($P < 0.001$; odds ratio, 4.2; 95% confidence interval, 2.3–7.6). After adjusting for all variables in the final model of Whisnant *et al.*, with the exception of smoking status, surgery within 30 days before the stroke date was also found to be an independent risk factor for ischemic stroke ($P < 0.001$; odds ratio, 3.9, 95% confidence interval, 2.1–7.4; table 3). There was no significant evidence to suggest that the risk of surgery for the development of ischemic stroke changed over the calendar period studied ($P = 0.113$ for the test of the two-way interaction of calendar time and surgery within 30 days). When the analysis was repeated using data from the 1970–1984 period and adjusting for all variables in the final model of Whisnant *et al.* (including current smoking), surgery within 30 days was again found to be an independent risk factor ($P < 0.001$; odds ratio, 6.0; 95% confidence interval, 2.5–14.2).

There were no significant interactions between time since most recent surgery and each of the other variables in the final model of Whisnant *et al.* The inclusion of surgery within 30 days had very little impact on the estimated odds ratios associated with the other risk factors. In all cases, the odds ratios obtained after adjusting for surgery within 30 days were within ± 10% of those

Table 1. Percent of Cases or Controls Undergoing Surgery Within 30 Days Before the Stroke/Index Date*

	Controls (N = 1455)		Cases (N = 1455)	
Type of surgery	*n*	%	*n*	%
General	13	0.9	28†	1.9
Orthopedic	4	0.3	13	0.9
Cardiac	0	0.0	11	0.8
Vascular	0	0.0	5‡	0.3
Neurologic	0	0.0	2	0.1

* There were 17 (1.2%) controls and 59 (4.1%) cases that underwent one or more surgical procedures in the 30-day period before the index date.

† Five cases included in the general surgery group underwent multiple general surgeries in the 30 days prior to their stroke date (three patients underwent two general surgeries and two patients underwent three general surgeries).

‡ One case included in the vascular surgery group underwent both a vascular surgery and an orthopedic surgery in the 30 days before their stroke date.

Table 2. Surgeries Performed within 30 Days Before Stroke/Index Date*

Type of surgery	Controls (n)	Cases (n)
General†		
Bowel procedure	5	7
Transurethral resection of prostate	5	4
Bladder procedure	0	5
Cholecystectomy	1	4
Hernia repair	0	3
Penile procedure	0	2
Dilatation and curretage	0	2
Perianal procedure	0	2
Abdominal exploration	0	2
Esophogus procedure	1	1
Lung procedure	0	1
Mediastinoscopy	0	1
Lumbar sympathectomy	0	1
Orchiectomy	1	0
Orthopedic‡		
Open reduction/internal fixation of hip or ankle	4	13
Lower extremity amputation	0	1
Cardiac		
Heart valve procedure	0	5
Coronary artery bypass graft	0	3
Pacemaker implant	0	1
Atrial septal defect repair	0	1
Extracorporeal circulation repair	0	1
Vascular‡		
Thoracic or abdominal aortic aneurysm repair	0	3
Femoral embolectomy	0	1
Translumbar arteriogram	0	1
Neurologic		
Carotid endarterectomy	0	2

* There were 17 (1.2%) controls that underwent a total of 17 surgical procedures in the 30-day period before the index date and 59 (4.1%) cases who underwent a total of 67 surgical procedures in the 30-day period before the stroke date.

† Five cases underwent multiple general surgeries in the 30 days before their stroke date (three patients underwent two general surgeries and two patients underwent three general surgeries).

‡ One case underwent both a vascular surgery and an orthopedic surgery in the 30 days before the stroke date.

Table 3. Relative Risk for Ischemic Stroke After Surgery (within 30 days)

		Controls		Cases		Conditional Logistic Regression Results*		
Risk Factor	N	n	%	n	%	O.R.	95% C.I.	p-value
Any surgery within 30 days before index date	1455	17	(1.2)	59	(4.1)	3.9	2.1 to 7.4	<0.001
Any non-high-risk surgery within 30 days before index date†	1437	17	(1.2)	41	(2.9)	2.9	1.5 to 5.7	0.002
Non-high-risk surgery (by type) within 30 days before index date†	1437							
General surgery		13	(0.9)	28	(1.9)	2.5	1.1 to 5.6	0.021
Orthopedic surgery		4	(0.3)	13	(0.9)	4.0	1.1 to 15.2	0.041

* Data were analyzed using conditional logistic regression making use of the 1:1 matched pair design (Breslow and Day, 1980).[17] An indicator variable for surgery within 30 days before the index date was included in a multivariate model along with all variables from the "final" model identified by Whisnant (Neurology, 1996)[10] with the exception of smoking status. The odds ratio (OR) and corresponding P value cannot be computed directly from the information provided.

† There were 18 cases and 0 controls that underwent one or more high-risk (cardiac, neurologic, or vascular) surgeries in the 30 day period before the index date. To determine whether non-high-risk surgery was associated with ischemic stroke, an analysis was performed that excluded these 18 cases and their matched controls.

obtained from the unadjusted model. In addition, with the exception of those associated with TIA, no adjusted odds ratio changed by more than ± 0.1 units of that obtained from the unadjusted model.

A summary of the types of most recent surgeries performed in the 30-day period before the stroke/index date for cases and controls is given in tables 1 and 2. There were 18 of 1,455 cases and 0 of 1,455 controls who underwent one or more surgeries that are high risk for stroke (cardiac, neurologic, or vascular procedures) in the 30 days before their stroke/index date. To determine whether non-high-risk surgery was associated with ischemic stroke, the analysis was repeated after removing the 18 cases (with their matched controls) who underwent a cardiac, neurologic, or vascular procedure in the 30 days before the stroke date (fig. 2). From this univariate analysis, non-high-risk surgery within 30 days before the stroke/index date was found to be a predictor of ischemic stroke ($P < 0.001$; odds ratio, 3.0; 95% confidence interval, 1.6-5.5). After adjusting for all variables in the final model of Whisnant *et al.* except smoking status, non-high-risk surgery within 30 days was still found to be a significant risk factor for ischemic stroke ($P = 0.002$; odds ratio, 2.9; 95% confidence interval, 1.5-5.7; table 3). There was no significant evidence to suggest that the role of non-high-risk surgery for the development of ischemic stroke changed over the calendar period studied ($P = 0.212$ for the test of the two-way interaction of calendar time and non-high-risk surgery within 30 days). When this analysis was repeated using only data for the time period from 1970 to 1984, and adjusting for all variables in the final model of Whisnant *et al.*, including smoking status, non-high-risk surgery within 30 days was again found to be a significant risk factor ($P = 0.003$; odds ratio, 4.1; 95% confidence interval, 1.6-10.4).

The majority of surgeries occurring within 30 days before the stroke/index date were performed with general anesthesia. General anesthesia was used in 93% (62 of 67) of surgeries in the cases and in 65% (11 of 17) of surgeries in the controls.

Discussion

The major finding of this study is that the combination of surgery and anesthesia is an independent risk factor for development of ischemic stroke during the perioperative period (within 30 days after the surgery date). In addition, the combination of surgery and anesthesia re-

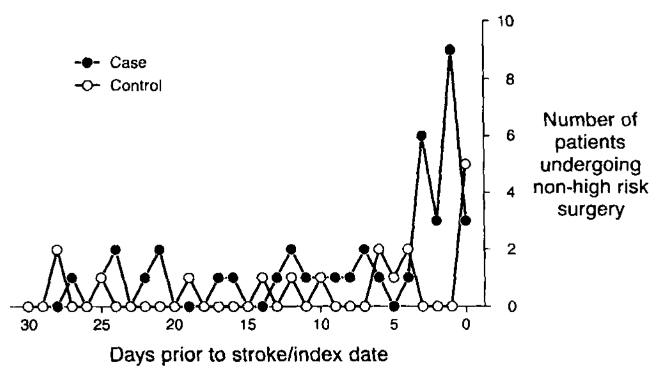

Fig. 2. Daily frequency of non-high-risk surgery before the stroke/index date for cases (n = 41) and controls (n = 17) during the perioperative period. Only the surgery closest to the stroke/index date was considered in those individuals with multiple surgeries.

mained an independent risk factor for ischemic stroke during the perioperative period after excluding matched pairs where cases and/or controls had surgical procedures (cardiac, neurologic, and vascular surgeries) at high risk for ischemic stroke.

Previous retrospective studies of stroke after surgery and anesthesia have primarily focused on determining rates of stroke, often without describing the specific subtypes of stroke.[1-3,5,6] In addition, these studies have not evaluated the event of surgery and anesthesia itself as an independent risk factor for the development of stroke. The risk of stroke after surgery is likely to be highest during the perioperative period, which is typically defined as the period from the time of hospitalization for surgery until the time of discharge (up to 30 days after surgery).[2,3,5,9,18,19] There may be other factors associated with surgery such as bed rest, medications, and diagnostic tests that may contribute to ischemic stroke risk during the perioperative period. However, retrospective review of existing medical records does not allow us to evaluate all these possible associations.

Our population-based, case-control design to evaluate the risk of surgery for ischemic stroke used a unique and powerful set of data because it included previously identified risk factors from a large number of incident ischemic stroke cases and matched controls.[10] In contrast to other investigations, the purpose of our study was to evaluate the effect of the event of surgery and anesthesia itself as an independent risk factor for ischemic stroke, while accounting for other known risk factors including age, gender, TIA, hypertension, smoking, diabetes mellitus, ischemic heart disease, atrial fibrillation, and mitral valve disease. However, the determination of the absolute risk of stroke (stroke rate) for all patients undergoing surgery and anesthesia was not the goal of our investigation. Our population database does not allow us to determine the exact number of all patients (residents of Rochester, MN) undergoing surgery and anesthesia during this time period, which would be necessary to calculate the stroke rate after surgery and anesthesia. In addition, the data used for our study is restricted to incident stroke events.

The findings from our study show that the risk for ischemic stroke is increased during the first 30 days after surgery, a frequently used time period to evaluate short-term, postoperative outcomes. Our approach to this analysis was to use the case-control methodology and look backward in time to identify patients who underwent surgery and anesthesia before their stroke/index date. As displayed in figures 1 and 2, considering each individual's most recent surgery before their stroke/index date, the stroke group seems to have a significant time-related trend with respect to the frequency of surgery preceding ischemic stroke, with most surgeries occurring in the week immediately preceding the stroke. Using a matched pair, conditional logistic regression analysis, we did not detect a significant trend within the 30 days before the stroke/index date with respect to the odds ratio of stroke and time since most recent surgery. However, this analysis is highly influenced by five control patients whose index date corresponded to the date of a surgical procedure. Although five patients represent a very small percentage of the overall control group, they represent the largest number of surgeries performed on any given day for this group. There is a limitation of the control selection methodology in that control patients were required to have had a medical visit with a blood pressure determination. The date of this blood pressure measurement was then used as the index date for controls. This medical visit may have corresponded to a surgical procedure or a follow-up visit related to a surgical procedure. Because only individuals with at least one health care encounter were eligible as potential controls, these patients were perhaps more likely than the general population to have undergone a surgical procedure. If the frequency of recent surgery is overly represented in the control group, the relative risk of ischemic stroke associated with recent surgery would be underestimated using the case-control design. For these reasons, our findings may actually be underestimating the odds ratio of surgery for the development of incident ischemic stroke, especially during the early perioperative period.

As with all retrospective studies, the results of this investigation must be carefully interpreted. We found surgery/anesthesia to be an independent risk factor for ischemic stroke using an analysis that adjusted for other known risk factors. Nonetheless, we cannot definitively determine whether surgery is itself causative or whether it simply represents a marker for a high-risk group that was not accounted for by the other risk factors included in the model. We found no significant evidence to suggest that the risk of surgery for the development of ischemic stroke changed over the study period from 1960 through 1984. We believe that changes in surgical technique, anesthesia technique, and postoperative care, which occurred during the time period of this study, are more dramatic than changes that have occurred subsequent to this time period. However, we cannot assess the effects of changes in surgical practice since 1984 on the findings of our study.

There is a higher rate of perioperative stroke associated with cardiac, neurologic, and vascular procedures.[4-7,9] For these high-risk surgeries, the mechanism of perioperative stroke likely involves thromboembolic events. The risk of thromboembolic events may be greater in these patients because of the pathophysiology of their disease requiring surgery, the type of surgical technique used to treat their disease process, or a combination of both.[8,19]

Previous studies have found perioperative stroke rates or neurologic events (neurologic deficits, stupor, or coma) ranging from 2.8 to 5.2% of patients undergoing coronary artery surgery.[4,5,9] The cause of these neurologic events after cardiopulmonary bypass may be related to mechanical, temperature, hemodynamic, metabolic, infectious, or pharmacologic causes.[8] For neurologic surgeries, previous studies have found perioperative stroke rates ranging from 2.2 to 2.4% of patients undergoing carotid endarterectomy surgery.[6,7] Carotid endarterectomies are performed in patients who are prone to neurologic events caused by ischemic episodes from decreased cerebral perfusion and embolic events from manipulation of carotid artery plaques. Our data also suggest that these procedures are associated with a higher risk of stroke, as 18 of 1,455 cases but no controls underwent high-risk surgery (cardiac, neurologic, or vascular surgery) in the 30 days before their stroke/index date. Our finding is consistent with previous studies suggesting a high degree of association between high-risk surgery and perioperative stroke.

However, we were surprised to find that even after excluding matched pairs, where cases and/or controls had cardiac, neurologic, or vascular procedures, surgery remained a significant risk factor for perioperative stroke. This finding is interesting because the mechanism of association between non-high-risk surgery and ischemic stroke is not as obvious as the association between high-risk surgery and ischemic stroke. Previous studies have suggested that alterations in the coagulation system resulting from stress responses related to surgery might be an explanation.[19-23] Perioperative changes in hemostasis have been theorized to contribute to the development of thromboembolic phenomena after surgery.[20] Increased plasma concentrations of coagulation factors,[21] decreased concentrations of coagulation inhibitors,[22] and alterations in fibrinolysis[23] have been reported postoperatively, suggesting a "hypercoagulable state." Under certain conditions, an increased tendency for blood to coagulate may be considered advantageous. However, in patients with cerebrovascular or other vascular lesions, these hemostatic changes may increase the potential for thromboembolic complications such as stroke.

Previous studies have attempted to identify other comorbid conditions or risk factors that may be associated with perioperative stroke.[2,6,18] Most of these studies were able to identify only a limited number of stroke cases, and risk factor determination has been limited by a lack of statistical power. A previous neurologic event, such as stroke and TIA, has been found to be a risk factor for perioperative stroke after both general surgery[2] and carotid endarterectomy surgery.[6] However, in our study, we were not able to evaluate the history of stroke as a risk factor because all of the stroke cases were first-time events (incident cases). In addition, we found no significant interactions between our finding of recent surgery as a risk factor and the other known risk factors for stroke in the model of Whisnant *et al.*[10] However, we cannot rule out the possibility of lack of statistical power to detect such interactions.

Cardiogenic embolism from cardiac arrhythmia has been suggested to be a mechanism in the development of perioperative stroke.[3,19] In addition, cardiac arrhythmias may cause a reduction in cerebral blood flow associated with increases in arterial resistance.[24] Hart and Hindman reviewed the records of 12 surgical patients who developed postoperative cerebral infarctions and found atrial fibrillation present in four patients (33%).[19] Atrial fibrillation has also been previously identified to be an independent risk factor for ischemic stroke in the model of Whisnant *et al.*[10] However, in our study, we did not detect any significant interactions between time since most recent surgery and each of the other variables in the final model of Whisnant *et al.*, including the presence or absence of atrial fibrillation.

The majority of surgeries occurring within 30 days before the stroke/index date were performed with general anesthesia as opposed to central neuroaxis blockade. There was a higher percentage of surgery in the cases (93%) receiving general anesthesia compared with the controls (65%), which might suggest that anesthetic type influences the risk of perioperative ischemic stroke. However, the relatively small number of patients receiving central neuroaxis block and the potential biases involved in the selection of anesthetic type make these findings difficult to fully interpret.

The results of our study suggest that there is an increased risk of ischemic stroke after surgery and anesthesia during the perioperative period. In addition, the risk of perioperative ischemic stroke remains increased even after general, non-high-risk surgeries. Understanding the mechanism of stroke after surgery and anesthesia will require further investigation.

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