Incidence and Risk Factors of Perioperative Stroke in Siriraj Hospital

Pachara Leemingsawat MD*,
Suneerat Kongsayreepong MD**, Chulaluk Komoltri DrPH (Biostatistics)***,
Naraporn Prayoonwiwat MD*, Yongchai Nilanont MD*

** Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
*** Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
**** Division of Clinical Epidemiology, Department of Research Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *Data concerning perioperative stroke incidence and risk factors are lacking in Thailand.*
Objective: *To study incidence and risk factors of perioperative stroke in Siriraj Hospital, Bangkok, Thailand.*
Material and Method: *The authors conducted a nested case-control study between July 2007 and June 2010. Consecutive perioperative stroke cases were compared with age-matched controls that had undergone surgery without having a stroke at a 1:4 ratio. Patients' characteristics, co-morbidities, clinical manifestation, stroke subtypes, duration, and types of surgery were collected. Multiple logistic regression analysis was performed to identify factors associated with a stroke during perioperative period.*
Results: *Sixty-six patients with perioperative stroke from 99,283 that underwent surgery were included. This resulted in an incidence of 66.5/100,000. Men comprised 65.2%. Mean age of stroke patients was 66.6-years-old. Age-match controls included 264 consecutive patients who underwent surgery without having a stroke. A multivariate analysis showed that male sex (adjusted OR 3.1, $p = 0.003$), surgical types: open heart surgery (adjusted OR 54.3, $p < 0.0001$), vascular surgery (adjusted OR 20.6, $p < 0.0001$) and endovascular procedure (adjusted OR 15.4, $p < 0.0001$), emergency surgery (adjusted OR 8.3, $p < 0.0001$), the presence of diabetes mellitus (adjusted OR 2.6, $p = 0.018$), chronic kidney disease (adjusted OR 2.6, $p = 0.027$), and coronary artery disease (adjusted OR 0.4, $p = 0.039$) were associated with perioperative stroke.*
Conclusion: *Incidence of perioperative stroke was higher than a previous report. Male, type of surgery, emergency operation, diabetes mellitus, and chronic kidney disease were risk factors of perioperative stroke.*

Keywords: *Perioperative stroke, Incidence, Risk factors*

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Stroke is one of the most common causes of death and disability worldwide. It is also one of the most feared complications of surgery that can increase mortality and morbidity. Although the incidence and risk factors of perioperative stroke are well documented in developed countries, there is still a lack of recognition and data in the developing world. The incidence of perioperative stroke in Western countries was 0.08-0.7% in general surgery, 1.4-3.8% in coronary artery bypass graft (CABG), 7.4% in combined CABG and valve surgery and 8.7% in aortic repair[1]. The Thai Anesthesia Incidence Study showed an incidence of 28 stroke cases among 172,592 anesthetics (16.2/100,000)[2]. Studies concerning factors associated with perioperative stroke, stroke subtypes as well as incidence and prognosis in Thailand are still lacking. The authors performed a prospective nested case-control single center study assessing the perioperative stroke incidence and risk factors.

Correspondence to:
Nilanont Y, Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Prannok Road, Bangkoknoi, Bangkok 10700, Thailand.
Phone: 0-2419-7101, Fax: 0-2412-3009, 0-2411-1103
E-mail: siysl@mahidol.ac.th

Material and Method

This was a nested case-control single center study conducted at Siriraj Hospital, a tertiary care hospital in Bangkok Thailand between July 2007 and June 2010. Study participants included consecutive perioperative stroke patients over 18 years of age. Age-matched controls were enrolled from consecutive patients who underwent surgical or catheter related

procedures without having stroke or transient neurological deficit. Controls were matched to cases at a 4 to 1 ratio. Patients who underwent brain surgery, minor surgery, and dental procedures were excluded from the present study. The diagnosis of stroke must be confirmed by neuroimaging studies and a certified neurologist. Stroke was defined according to the World Health Organization as the rapidly developing signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin[2-4]. Perioperative stroke was defined as any stroke that occurred within 72 hours postoperatively.

Data including age, sex, underlying diseases, medications used, discontinuation of antiplatelet and/or anticoagulant medication(s), types of surgery, timing (elective versus emergency surgery) and duration of surgery, types of anesthesia, stroke symptoms and signs, time interval between the operation and stroke onset as well as stroke subtypes were collected.

Type of surgery was divided into six categories: general/non-cardiac surgery, open-heart surgery, orthopedic surgery, obstetric-gynecologic surgery vascular surgery, and endovascular surgery. Endovascular surgery included those who underwent any of the following procedures, coronary angiography, percutaneous coronary intervention, carotid stent placement, and peripheral artery angioplasty.

Concerning timing of surgery, emergency surgery was defined by The American Society of Anesthesiologist (ASA) physical status classification as any procedure that could not be delayed, when delay in treatment would significantly increase the threat to the patient's life or body part.

The present study was approved by the Research Ethics Committee of Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Statistical analysis

Baseline characteristics were analyzed using mean ± SD and median for continuous variables according to their distributions. Categorical variables were analyzed in terms of their relative frequencies. Chi-square and Mann-Whitney U tests were applied to compare categorical and continuous variables respectively. Statistical analysis was performed using commercially available SPSS software (version 15.0). All tests were 2-tailed and multivariable analysis was performed by logistic regression analysis, and a probability value of less than 0.05 was considered statistically significant[5,6].

Results

There were 99,283 consecutive patients who underwent surgery or catheter related procedures between July 2007 and June 2010. Of these, 66 patients experienced perioperative stroke resulting in an incidence of 66.5/100,000.

Ischemic stroke comprised of 89.4% with a mean age of 66.6 years and 65.2% were male. Diabetes mellitus, hypertension, dyslipidemia, chronic kidney disease, atrial fibrillation, coronary artery disease (CAD) and previous stroke were documented in 39.4, 71.2, 42.4, 30.3, 13.6, 50 and 9.1% respectively in patients experiencing perioperative stroke, whereas these risk factors were found in 25.8, 62.9, 40.9, 7.2, 5.7, 30.7 and 2.3% respectively in the control group. Data regarding patients' characteristics of both cases and controls are demonstrated in Table 1.

Concerning surgical types, open heart, vascular and catheter-related procedures accounted for 39.4, 16.7, and 28.8% respectively among stroke cases. In age-matched controls, there were 7.2, 5.3, 21.2% of patients who underwent open heart, vascular and catheter-related procedures respectively as are shown in Table 1. Regarding timing of surgery, emergency surgery was performed in 19.7% in perioperative stroke whereas in 6.8% of the control group.

General, regional, and local anesthesia was applied in 69.7, 4.5, and 25.8% among stroke cases, respectively whereas they were used in 55.3, 20.8, and 23.9% respectively in the control group. Duration of surgery was significantly longer in stroke cases when compared with controls (180 versus 110 minutes, $p = 0.018$) (Table 1).

Patients experienced unilateral motor deficit in 63.6%, impaired level of consciousness in 21.2%, seizure in 6.1%, aphasia in 3%, dysarthria in 3%, and vertigo in 3%. More than one-third of stroke (37.9%) occurred intra-operatively or immediately after the operation. At discharge, 19.7% of stroke cases died whereas no death was found in the control group ($p < 0.0001$).

The use of antiplatelets was more prevalent in stroke cases (59.1% vs. 35.2%, $p < 0.0001$). However, the authors did not find any difference concerning the use of other medications such as, anticoagulation, antihypertensive, and statins. Discontinuation of antithrombotic medications was not found to be significantly different between the two groups.

In a logistic regression model, risk factors of perioperative stroke included 1) male sex (adjusted OR 3.1, $p = 0.003$), 2) type of surgery; open heart

Table 1. Characteristics and risk factors in the stroke group and controlled group

	Stroke		p-value	Crude OR (95% CI)
	No (n = 264)	Yes (n = 66)		
Sex: male (%)	109/264 (41.3)	43/66 (65.2)	0.001	2.7 (1.5, 4.7)
Mean age (years)	65.75	66.56		
Type of surgery				
General/non-cardiac (%)	115/264 (43.6)	7/66 (10.6)		1
Open heart (%)	19/264 (7.2)	26/66 (39.4)		22.5 (8.6, 59.1)
Orthopedic (%)	41/264 (15.5)	2/66 (3)		0.8 (0.2, 4.0)
OB-GYN (%)	19/264 (7.2)	1/66 (1.5)		0.9 (0.1, 7.4)
Vascular (%)	14/264 (5.3)	11/66 (16.7)		12.9 (4.3, 38.7)
Endovascular (%)	56/264 (21.2)	19/66 (28.8)		5.6 (2.2, 14.0)
Timing of surgery				
Emergency (%)	18/264 (6.8)	13/66 (19.7)	0.001	3.4 (1.6, 7.3)
Type of anesthesia				
Regional (%)	55/264 (20.8)	3/66 (4.5)		1
General (%)	146/264 (55.3)	46/66 (69.7)		5.8 (1.7, 19.2)
Local (%)	63/264 (23.9)	17/66 (25.8)		5.0 (1.4, 17.8)
Duration (minutes)[#]	110 (13, 640)	180 (13, 720)	0.018	(-86.6, -26.5)
Co-morbid diagnosis				
Diabetes mellitus (%)	68/264 (25.8)	26/66 (39.4)	0.028	1.9 (1.1, 3.3)
Hypertension (%)	166/264 (62.9)	47/66 (71.2)	0.206	1.5 (0.8, 2.6)
Dyslipidemia (%)	108/264 (40.9)	28/66 (42.4)	0.823	1.1 (0.6, 0.8)
Chronic kidney disease (%)	19/264 (7.2)	20/66 (30.3)	<0.0001	5.6 (2.8, 11.3)
Cerebrovascular disease (%)	6/264 (2.3)	6/66 (9.1)	0.008	4.3 (1.3, 13.8)
Atrial fibrillation (%)	15/264 (5.7)	9/66 (13.6)	0.026	2.6 (1.1, 6.3)
Coronary artery disease (%)	81/264 (30.7)	33/66 (50.0)	0.003	2.3 (1.3, 3.2)
Prior medication				
Antiplatelet (s) (%)	93/264 (35.2)	39/66 (59.1)	<0.0001	2.7 (1.5, 4.6)
Discontinuation of antiplatelet (s) (%)	34/93 (36.6)	17/39 (46)	0.449	1.3 (0.6, 2.9)
Anticoagulant (s) (%)	16/264 (6.1)	7/66 (10.6)	0.195	1.8 (0.7, 4.7)
Discontinuation of anticoagulant (s) (%)	11/16 (68.8)	6/7 (85.7)	0.394	2.7 (0.3, 29.1)
Bridging of anticoagulant (%)	4/16 (25)	2/7 (28.6)	0.858	1.2 (0.2, 8.8)
Statin (s) (%)	119/264 (45.1)	32/66 (48.5)	0.619	1.2 (0.7, 1.9)
Antihypertensive (s) (%)	163/264 (62.7)	48/66 (72.7)	0.096	1.7 (0.9, 2.9)

[#] Median (min, max)

(adjusted OR 54.3, $p < 0.0001$), vascular (adjusted OR 20.6, $p < 0.0001$) and endovascular procedure 15.4, $p < 0.0001$), 3) emergency surgery (adjusted OR 8.3, $p < 0.0001$), 4) the presence of diabetes mellitus (adjusted OR 2.6, $p = 0.018$) and 5) chronic kidney disease (adjusted OR 2.6, $p = 0.027$) as is shown in Table 2. However, the presence of coronary artery disease was significantly associated with lower perioperative stroke risk (adjusted OR 0.4, $p = 0.039$).

Discussion

Our study has provided an incidence and risk factors of perioperative stroke in a tertiary care hospital in Thailand. The following factors including male sex, open-heart surgery, vascular and endovascular procedures, emergency surgery, the presence of diabetes, and chronic kidney disease were found to be associated with perioperative stroke.

An incidence rate in the present study was approximately four times higher when compared to a previous multicenter report from Thailand (66.5/100,000 vs. 16.2/100,000)[17]. Possible explanations for the observed difference include a single center study taking place in a tertiary care hospital, a greater stroke awareness of medical personnel, a difference in type of surgery, a thorough neurological examination by a

Table 2. Result of multiple logistic regression analysis

	p-value	Adjusted OR (95% CI)
Sex: male	0.003	3.1 (1.5, 6.4)
Type of surgery		
General	-	1
Open heart	<0.0001	54.3 (15.5, 190.1)
Orthopedic	0.434	2.0 (0.4, 11.7)
OB-GYN	0.358	3.0 (0.3, 31.0)
Vascular	<0.0001	20.6 (5.6, 17.1)
Endovascular procedures	<0.0001	15.4 (4.5, 52.7)
Emergency surgery	<0.0001	8.3 (2.6, 24.1)
Co-morbid diagnosis		
Diabetes mellitus	0.018	2.6 (1.2, 5.8)
Chronic kidney disease	0.027	2.6 (1.1, 6.2)
Atrial fibrillation	0.052	3.1 (0.9, 9.5)
Coronary artery disease	0.039	0.4 (0.2, 0.9)

certified neurologist and a complete neuroimaging study.

In agreement with other studies, similar perioperative stroke risk factors were confirmed in the authors' findings including male sex, type and timing of surgery, diabetes mellitus, and chronic kidney disease[7-11]. However, the authors found that the presence of coronary artery disease was associated with lower perioperative stroke risk, which was different from previous reports[7,12]. Despite an unclear explanation, secondary prevention strategies for atherosclerotic diseases in patients with coronary artery disease including the use of statins, antihypertensive agent(s), antithrombotic medication(s) and vascular risk factors modification might partly explain this finding. In addition, the authors found a significant difference in duration of operation between those who experienced perioperative stroke and the controls. This finding may indicate an association between more complex surgical procedure and the risk of perioperative stroke.

In agreement with other studies, patients with stroke had a significantly higher mortality rate (19.7% vs. 0% at discharge). The mortality rate was also similar when compared with previous reports (15 to 46%)[2,7,13-15]. Discontinuation of antithrombotic medications was not significantly associated with perioperative stroke in our study. A small number of patients who discontinued the medication(s), and a low stroke incidence, may explain this finding[7-9].

There were several limitations in the present study required acknowledgement. Firstly, the study was conducted in a single tertiary care center, which may have led to a selection bias of study participants. More complicated surgical procedures as well as more emergency surgeries were performed. Patients were more likely to have several co-morbidities. These factors may result in a higher perioperative stroke incidence. Secondly, stroke cases with unusual presentations, for example, those who presented with post-operative cognitive dysfunction, abnormal movement, or very mild and transient symptoms might be missed. Finally, data concerning previously described risk factors such as the presence of congestive heart failure, prior cardiac surgery, valvular heart disease, cardiac bypass time, and estimated blood loss were not available in the authors' cohort[7,16,17].

In spite of its limitations, this was the first prospective nested case-control study assessing the incidence and perioperative stroke risk factors in Thailand. The present findings indicate a need for establishing preoperative prophylaxis as well as perioperative stroke detection and management strategies among patients who undergo surgical procedures.

Conclusion

Perioperative stroke incidence rate was higher than previous reports. Male, type of surgery, emergency surgery, diabetes mellitus, and chronic kidney disease were stroke risk factors among patients who underwent surgery.

Potential conflicts of interest

None.

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อุบัติการณ์และปัจจัยเสี่ยงของโรคหลอดเลือดสมองระหว่างการผ่าตัดในโรงพยาบาลศิริราช

พชร ลี้มิ่งสวัสดิ์, สุณีรัตน์ คงเสรีพงศ์, จุฬาลักษณ์ โกมลตรี, นาราพร ประยูรวิวัฒน์, ยงชัย นิละนนท์

ภูมิหลัง: *ปัจจุบันข้อมูลเกี่ยวกับอุบัติการณ์และปัจจัยเสี่ยงของโรคหลอดเลือดสมองระหว่างการผ่าตัดในประเทศไทยยังมีจำกัด*
วัตถุประสงค์: *เพื่อศึกษาอุบัติการณ์และปัจจัยเสี่ยงของโรคหลอดเลือดสมองระหว่างการผ่าตัดในโรงพยาบาลศิริราช ประเทศไทย*
วัสดุและวิธีการ: *เก็บข้อมูลผู้ที่เข้ารับการผ่าตัดที่โรงพยาบาลศิริราชแบบไปข้างหน้าระหว่างเดือนกรกฎาคม พ.ศ. 2550 ถึงเดือนมิถุนายน พ.ศ. 2553 โดยรวบรวมผู้ป่วยที่เกิดโรคหลอดเลือดสมองระหว่างการผ่าตัดหรือภายใน 72 ชั่วโมงหลังการผ่าตัด เพื่อหาอุบัติการณ์ และเก็บข้อมูลพื้นฐานของผู้ป่วยรวมทั้งรายละเอียดการผ่าตัด ทำการเปรียบเทียบข้อมูลผู้ป่วยที่เข้ารับการผ่าตัดแล้วเกิดโรคหลอดเลือดสมองกับผู้ป่วยที่เข้ารับการผ่าตัดแล้วไม่เกิดโรคหลอดเลือดสมอง แบบ nested case-control study ในอัตราส่วน 1:4 เพื่อศึกษาปัจจัยเสี่ยง*
ผลการศึกษา: *ผู้ป่วยเกิดโรคหลอดเลือดสมองระหว่างหรือหลังการผ่าตัดรวมทั้งสิ้น 66 ราย จากการผ่าตัดทั้งหมด 99,283 ครั้ง คิดเป็นอุบัติการณ์เท่ากับ 66.5/100,000 เป็นเพศชายร้อยละ 66.5 อายุเฉลี่ย 66.6 ปี ผลการวิเคราะห์แบบพหุตัวแปรพบปัจจัยที่สัมพันธ์กับการเกิดโรคหลอดเลือดสมองระหว่างการผ่าตัดดังนี้ เพศชาย มีค่า odds ratio 3.1 ที่ความเชื่อมั่นร้อยละ 95 เท่ากับ 0.003 ประเภทของการผ่าตัด ได้แก่ การผ่าตัดหัวใจแบบเปิดช่องอก การผ่าตัดหลอดเลือด และการทำหัตถการที่เกี่ยวข้องกับการใส่สายสวนหลอดเลือดโดยมีค่า odds ratio เท่ากับ 54.3, 20.6 และ 15.4 ตามลำดับ ค่าความเชื่อมั่นร้อยละ 95 น้อยกว่า 0.05 การผ่าตัดฉุกเฉินมีค่า odds ratio เท่ากับ 54.3 โดยมีค่าความเชื่อมั่นร้อยละ 95 น้อยกว่า 0.001 การพบมีโรคเบาหวาน โรคไตวายเรื้อรัง และโรคหลอดเลือดหัวใจ โดยมีค่า odds ratio เท่ากับ 2.6, 2.6 และ 0.4 ตามลำดับ ที่ค่าความเชื่อมั่นร้อยละ 95 น้อยกว่า 0.05*
สรุป: *พบอุบัติการณ์การเกิดโรคหลอดเลือดสมองระหว่างหรือหลังการผ่าตัดสูงกว่าการศึกษาในอดีต โดยพบว่า เพศชาย ชนิดของการผ่าตัด การผ่าตัดฉุกเฉิน โรคเบาหวาน โรคไตวายเรื้อรัง เป็นความเสี่ยงต่อการเกิดโรคหลอดเลือดสมองระหว่างการผ่าตัด*