


# Incidence, risk factors and outcomes of early post-operative stroke in a university-based, tertiary care hospital

## A 7-year retrospective case-control study

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### Abstract

Most post-operative stroke cases occur within 24 hours. This retrospective case-control study aimed to investigate the incidence, risk factors, and outcomes of early post-operative stroke that occurred within 24 hours after surgery in a university-based tertiary care hospital. Medical records were collected and reviewed between 2015 and 2021. Early post-operative stroke cases were compared with age-matched controls in a 1:3 ratio, and data regarding patient characteristics, intra-operative events, and post-operative outcomes were analyzed. Multiple logistic regression was performed to identify the risk factors for post-operative stroke. The incidence of early ( $\leq 24$  hours) post-operative stroke was 0.015% (43 out of 284,105 cases). The multivariable analysis revealed that American Society of Anesthesiologists (ASA) physical status  $\geq 3$  (adjusted odds ratio [OR]: 3.12; 95% confidence interval [CI]: 1.22–7.99,  $P = .017$ ), operation time  $> 120$  minutes (adjusted OR: 10.69; 95% CI: 3.95–28.94,  $P < .001$ ), and intra-operative hypotension and inotrope/vasopressor use (adjusted OR: 2.80; 95% CI: 1.08–7.24,  $P = .034$ ) were risk factors for early post-operative stroke. Compared to the controls, stroke patients had higher rates of planned and unplanned intensive care unit (ICU) admission, length of stay, ventilator use, and death. Despite its low incidence (0.015%), stroke is associated with poor clinical outcomes and increased mortality. Stratification of potential risks and establishment of risk optimization may help reduce stroke incidence.

**Abbreviations:** ASA = American Society of Anesthesiologists, BP = blood pressure, CI = confidence interval, ICU = intensive care unit, OR = odds ratio, TIA = transient ischemic attack.

**Keywords:** cerebrovascular disease, complications, post-operative, risk factors, stroke

### 1. Introduction

Post-operative adverse events involving major organ dysfunction or even death occasionally occur. Stroke is a complication that results in high morbidity and mortality. The incidence of peri-operative stroke observed until 30 days after surgery in patients undergoing non-cardiac and non-neurological surgery ranges from 0.1% to 1.0% worldwide.<sup>[1]</sup> However, in Thailand, research regarding stroke remains limited. The incidence of stroke for all types of surgery within 24 to 72 hours post-operation in Thailand was 0.036% to 0.067%<sup>[2,3]</sup> and 0.075% for non-cardiac surgery within 30 days post-operation.<sup>[4]</sup> Age, sex, renal disease, prior transient ischemic attack (TIA) or stroke, myocardial infarction within 6 months, atrial fibrillation, hypertension, chronic obstructive pulmonary disease, current smoking, and migraine history

have been reported as risk factors.<sup>[1,5]</sup> The incidence of stroke varies among different types of surgery and is considerably higher in cardiac, neurological, vascular, and emergency surgeries.<sup>[1,3–8]</sup> Other intra-operative risk factors include intra-operative hypotension in patients with large vessel stenosis<sup>[9]</sup> and hypoxemia.<sup>[10]</sup>

The majority of post-operative strokes were reported within 24 hours post-operation and are thus regarded as early post-operative strokes<sup>[11,12]</sup> with increased post-operative death.<sup>[13]</sup> As a result, it may be worthwhile to investigate early post-operative stroke events and their relationship to potential causal factors, including surgery and anesthesia. In our institutional practice, post-anesthesia care service members visit patients the day after the operation and report and record anesthesia-related complications. Anesthetic agents can remain in the body for up to 24

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hours after administration.<sup>[14–16]</sup> However, difficulty in awakening or fully recovering from anesthesia may be the first indication of post-operative stroke.<sup>[5]</sup>

The present study objectives were to explore the incidence and risk factors of early (24 hours) post-operative stroke and to determine the patients' outcomes. Considering that anesthetic agents persist in the body for <24 hours, it could be compelling to investigate relevant stroke risk factors, which might include anesthesia. With the information obtained from this study, the quality of patient preparation and optimization can be improved to achieve better clinical outcomes after surgery.

## 2. Methods

### 2.1. Study design

This retrospective case-control study was initiated in a university-based tertiary care hospital after approval by the Siriraj Institutional Review Board (SI 214/2565). This study was registered in the Thai Clinical Trials Registry (<https://www.thaiclinicaltrials.org/show/TCTR20220317006>).

### 2.2. Participants

Patients with complete medical records who were 18 years or older and scheduled for surgery at a university-based tertiary care hospital between January 2015 and December 2021 were recruited for the study. Patients who did not undergo surgery for any reason (e.g., a change in the treatment plan, cancellation of surgery, or incomplete medical records) were excluded. Cases with evidence of in-hospital post-operative stroke within 24 hours after anesthesia were included for further analysis. All records of in-hospital post-operative stroke cases at any time point in the hospital database also conformed to the guidelines outline by the International Classification of Diseases, Tenth Revision.

Stroke was defined as the sudden onset of a neurological deficit in the cerebral hemispheres, brainstem, or cerebellum, which is related to the vascular territory. Stroke can be further classified as hemorrhagic stroke, ischemic stroke, and TIA.<sup>[17,18]</sup> Patients having stroke onset within 24 hours after operation and then lasting >24 hours without spontaneous recovery were selected for further study; hence, TIA was not included. Strokes with causes other than vascular origin were also not considered. Stroke diagnosis must be confirmed by neuroimaging studies and a certified neurologist. Patients who underwent surgery and did not develop post-operative stroke within 24 hours were matched for exact age ( $\pm 1$ –2 years) and surgery day. Non-stroke controls were matched to stroke cases at a 3:1 ratio.

### 2.3. Data collection

Patients' pre-operative demographic characteristics, including age, sex, body weight, height, comorbidities, American Society of Anesthesiologists (ASA) classification of physical status, abnormal pre-operative testing, surgery type, and surgery timing, were collected. A history of cerebrovascular disease included stroke and TIA. Hypertension (any patient with blood pressure [BP]  $\geq 140/90$  mm Hg), well-controlled hypertension (treated hypertensive patients with BP < 140/90 mm Hg), and uncontrolled hypertension (treated patients with BP  $\geq 140/90$  mm Hg) were described according to the American College of Cardiology/American Heart Association (ACC/AHA) and the International Society of Hypertension (ISH) clinical practice guidelines.<sup>[19,20]</sup> To define chronic kidney disease stages and estimated glomerular filtration rate, the Kidney Disease Improving Global Outcomes practice guidelines<sup>[21]</sup> were used. Metabolic acidosis was defined as a decrease in serum bicarbonate below 22 mmol/L.<sup>[22]</sup>

The following intra-operative data were collected: anesthesia type, operation duration, blood component transfusion, intra-operative hypotension and inotrope/vasopressor use, and intra-operative hypoxemia. Intra-operative hypotension was defined as an absolute mean arterial pressure <65 mm Hg or a relative, a reduction of mean arterial pressure or systolic blood pressure of  $\geq 20\%$  from baseline.<sup>[23,24]</sup> Intra-operative desaturation was defined as an oxygen saturation of <90%, as reported previously.<sup>[1,25]</sup>

Post-operative data relating to the incidence of planned and unplanned intensive care unit (ICU) admissions, length of ICU stay, total hospital stay, ventilator use, duration of ventilator use, and discharge status were collected.

### 2.4. Sample size calculation

Similar to previous literature,<sup>[26]</sup> our work reported the actual number of stroke cases observed between January 2015 and December 2021. We did not perform a priori sample size calculation because this was an observational study. Cases were matched with controls at a ratio of 1:3, which was proven to be sufficient for analysis.<sup>[27]</sup>

### 2.5. Statistical analysis

According to the normality of the distribution, continuous data were reported as mean, standard deviation, or median and interquartile range and analyzed using an independent Student *t* test or Mann–Whitney *U* test. Categorical variables were reported as frequency and percentage and compared using the Chi-square test or Fisher exact test. Variables with a *P* value < .10 from the univariate analysis were included for multivariable logistic regression using the forward-stepwise analysis. The associated factors were presented as crude odds ratio (OR), adjusted OR, and 95% confidence intervals (CI). As reported previously, most medical studies frequently adopt small sample sizes for regression analyses, which might cause a problem in result reproducibility. We circumvented this issue by selecting the variables of interest with the optimal number of events required for multivariable regression analysis ( $n \geq 25$ ).<sup>[28]</sup> The cutoff value for the operation time was calculated from the area under the receiver operator characteristic curve. Statistical analysis was performed using SPSS version 28.0 (IBM Corp, Armonk, NY). Statistical significance was determined by a *P* < .05.

## 3. Results

During the period 2015 to 2021, a total of 284,105 patients aged  $\geq 18$  years were scheduled for surgery. Of this population, 43 post-operative stroke cases were reported, resulting in an incidence of 0.015% or 1.5/10,000. Figure 1 displays the annual distribution of incidences. A total of 129 age- and day-matched non-stroke controls were also recruited for the study. The majority of stroke cases (88.4%) were ischemic, and the middle cerebral arteries were the most affected area (32.6%) (Supplementary Table 1, <http://links.lww.com/MD/J299>).

Patients' pre-operative demographics were comparable between the non-stroke and stroke groups. Univariate analysis revealed significant variables (*P* < .10) that were associated with early post-operative stroke ( $\leq 24$  hours after surgery), including cerebrovascular diseases with neurological deficit, chronic kidney disease  $\geq$  Stage 4, ASA physical status  $\geq 3$ , pre-operative metabolic acidosis, abnormal chest radiography, cardiothoracic and intra-cranial surgery, emergency surgery, administration of isoflurane and midazolam, operation time >120 minutes, and intra-operative events such as blood component transfusion, intra-operative hypotension and inotrope/vasopressor use, and intra-operative desaturation. The median operation time in the non-stroke group

was significantly lower than that in the stroke group (98 vs 280 minutes,  $P < .001$ ). The operation cutoff time of 120 minutes was considered the best sensitivity/specificity ratio determined by area under a receiver operator characteristic curve (0.756). The proportion of patients whose operation

time exceeded 120 minutes was significantly higher in the stroke group (86%) than in the non-stroke group (34.9%) (Tables 1 and 2).

The 4 variables with  $P$  values  $< .10$  and sample sizes ( $n$ )  $\geq 25$ , such as  $ASA \geq 3$ , abnormal pre-operative chest

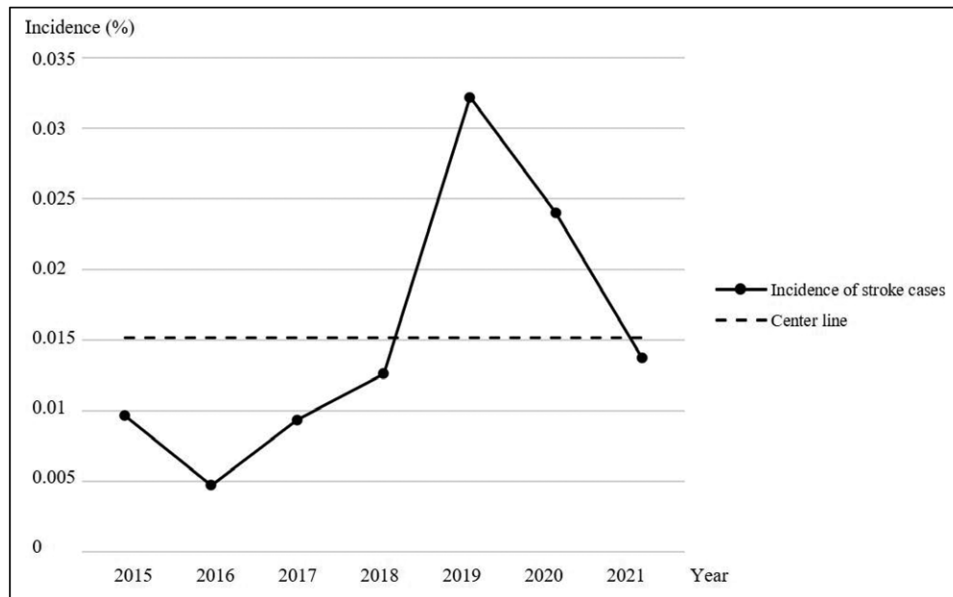


Figure 1. Early postoperative stroke incidence from 2015 to 2021.

Table 1

Preoperative characteristics of the non-stroke and stroke groups.

Variables	Non-stroke (n = 129)	Stroke (n = 43)	P value
Age (yr)	65.2 ± 13.9	66.0 ± 14.5	.764
Sex			
Male (%)	45 (34.9%)	21 (48.8%)	
Female (%)	84 (65.1%)	22 (51.2%)	.105
Body mass index (kg/m <sup>2</sup> )	24.1 ± 5.2	23.6 ± 4.4	.587
Comorbidities (%)			
History of cerebrovascular disease (CVD)			
CVD without neurological deficit	9 (7.0%)	4 (9.3%)	.739
CVD with neurological deficit	2 (1.6%)	4 (9.3%)	.035*
Type 2 diabetes mellitus	32 (24.8%)	11 (25.6%)	.919
Hypertension			
Well controlled hypertension	30 (23.3%)	12 (27.9%)	.544
Uncontrolled hypertension	53 (41.1%)	23 (53.5%)	.162
Dyslipidemia	71 (55.0%)	25 (58.1%)	.723
Chronic kidney disease			
Stage 2–3 (eGFR 30–89.9 mL/min/1.73 m <sup>2</sup> )	81 (62.8%)	27 (62.8%)	1.000
Stage ≥ 4 (eGFR ≤ 29.9 mL/min/1.73 m <sup>2</sup> )	8 (6.2%)	8 (18.6%)	.028*
Liver cirrhosis	3 (2.3%)	1 (2.3%)	1.000
Atrial fibrillation	8 (6.2%)	6 (14.0%)	.117
Coronary artery disease	19 (14.7%)	9 (20.9%)	.342
Structural heart disease	7 (5.4%)	4 (9.3%)	.374
Respiratory disease	9 (7.0%)	2 (4.7%)	.592
ASA physical status classification (%)			
1–2	75 (58.1%)	11 (25.6%)	
≥3	54 (41.9%)	32 (74.4%)	<.001*
Preoperative testing abnormalities (%)			
Metabolic acidosis	5 (3.9%)	17 (39.5%)	<.001*
Abnormal electrocardiogram	43 (33.3%)	20 (46.5%)	.122
Abnormal chest radiography	44 (34.1%)	25 (58.1%)	.006*

Data presented as mean ± standard deviation (SD) or number (%).

ASA = American Society of Anesthesiologists, CVD = Cerebrovascular disease, eGFR = estimated glomerular filtration rate.

\* $P$  value  $< .05$  considered statistically significant.

**Table 2**  
**Intraoperative characteristics of the non-stroke and stroke groups.**

Variables	Non-stroke (n = 129)	Stroke (n = 43)	P value
Type of surgery (%)			
Non-cardiothoracic, non-intracranial	115 (89.1%)	20 (46.5%)	
Cardiothoracic and Intracranial	14 (10.9%)	23 (53.5%)	<.001*
Timing of surgery (%)			
Elective	114 (88.4%)	29 (67.4%)	
Emergency	15 (11.6%)	14 (32.6%)	<.001*
Type of anesthesia (%)			
General	89 (69.0%)	33 (76.7%)	.438
Regional	19 (14.7%)	2 (4.7%)	.102
Combined general + regional	9 (7.0%)	7 (16.3%)	.173
Others†	12 (9.3%)	1 (2.3%)	.159
Anesthetic agents			
Nitrous oxide	12 (9.3%)	2 (4.7%)	.344
Desflurane	48 (37.2%)	11 (25.6%)	.167
Sevoflurane	39 (30.2%)	15 (34.9%)	.570
Isoflurane	8 (6.2%)	11 (25.6%)	.001*
Midazolam	27 (20.9%)	18 (41.9%)	.008*
Operation time (%)			
≤120 minutes	84 (65.1%)	6 (14.0%)	
>120 minutes	45 (34.9%)	37 (86.0%)	<.001*
Blood component transfusion (%)	15 (11.6%)	25 (58.1%)	<.001*
Intraoperative hypotension and inotrope/vasopressor use (%)	59 (45.7%)	35 (81.4%)	<.001*
Intraoperative desaturation (%)	1 (0.8%)	6 (14.0%)	.006*

Data presented as number (%) or median (Interquartile range, IQR).

\*P value < .05 considered statistically significant.

†Intravenous sedation or monitored anesthesia care.

radiography, operation time >120 minutes, and intra-operative hypotension and inotrope/vasopressor use, were included in the multivariable logistic regression. Only 3 variables were independent risk factors for early post-operative stroke: ASA  $\geq 3$  (adjusted OR: 3.12; 95% CI: 1.22–7.99,  $P = .017$ ), operation time > 120 minutes (adjusted OR: 10.69; 95% CI: 3.95–28.94,  $P < .001$ ), and intra-operative hypotension and inotrope/vasopressor use (adjusted OR: 2.80; 95% CI: 1.08–7.24,  $P = .034$ ) (Table 3).

The post-operative outcomes of the stroke group differed significantly from those of the non-stroke group. Post-operative stroke patients had a higher rate of planned and unplanned ICU admission following surgery, longer length of ICU stay, greater need for mechanical ventilation, longer duration of ventilator use, longer hospital stay, and a higher death rate (Table 4). The causes of death in the non-stroke group were respiratory complications and underlying medical conditions, whereas all deaths in the stroke group were complications from ischemic stroke.

#### 4. Discussion

The incidence of post-operative stroke within 24 hours post-surgery in this study was 2.4 times lower than what was reported previously in a study of 24-hours post-operative stroke conducted among the major hospitals across Thailand (0.015% vs 0.036%).<sup>[2]</sup> We hypothesized that this might be due to medical advancements over the years, higher medical personnel experience, and better knowledge and enhanced vigilance in preventing post-operative complications. In addition, other international studies considered post-operative stroke as an event occurring from the immediate post-operative period until 30 days after the operation. Therefore, the overall incidence could be higher: 0.52% to 1.1% in non-cardiac and non-neurological surgery or up to 10% in cardiac and neurological surgery.<sup>[1,29]</sup>

The mean age of the patients predisposed to post-operative stroke was  $66.0 \pm 14.5$  years, which is similar to previous reports.<sup>[3,30]</sup> In contrast to previous reviews,<sup>[1,3–5]</sup> we did not find a significant association between stroke and sex, or comorbidities such as diabetes mellitus, valvular heart disease, and atrial fibrillation. This could be due to the limited sample size of this study.

Our study proposed that the risk factors for stroke that occurred within 24 hours after surgery based on multivariable logistic regression were ASA physical status  $\geq 3$ , operation time > 120 minutes, and intra-operative hypotension and inotrope/vasopressor use. Considering that higher ASA contributed to post-operative mortality and complications,<sup>[31,32]</sup> we speculated that patients with high ASA might have a high tendency for adverse events, including stroke. However, we presumed that a longer operation time might increase the chance of exposure to hemodynamic derangement during the operation. We reported that intra-operative hypotension and administration of inotrope/vasopressor could pose a risk for stroke. This could be because inotrope/vasopressor administration reflected severe hypotensive events that required medical treatment.

The rates of post-operative ICU admission, ventilator need, and days of hospital care were clearly higher in stroke cases than in the non-stroke controls. From our findings, most post-operative strokes were ischemic, with unfavorable outcomes. Previous studies have confirmed a higher mortality rate of ischemic stroke than of its hemorrhagic counterpart.<sup>[33,34]</sup>

This study has several limitations. First, our work was performed in a single center; thus, there could be a lower incidence of post-operative stroke or under-reported cases that presented with TIA, which was not within the scope of our study, or minor stroke with rapid self-recovery. Second, we collected only in-hospital stroke cases. Therefore, any stroke events outside the hospital that occurred within 24 hours post-operatively could have been overlooked.

**Table 3**  
**Risk factors associated with early postoperative stroke.**

Variables	Crude OR (95% CI)	Adjusted OR (95% CI)	P value
ASA physical status classification $\geq 3$	4.04 (1.87–8.72)	3.12 (1.22–7.99)	.017*
Abnormal preoperative chest radiography	2.68 (1.32–5.44)	1.72 (0.70–4.24)	.238
Operation time	1	1	<.001*
$\leq 120$ minutes	11.51 (4.52–29.34)	10.69 (3.95–28.94)	
>120 minutes			
Intraoperative hypotension and inotrope/vasopressor use	5.19 (2.24–12.05)	2.80 (1.08–7.24)	.034*

Data presented as crude and adjusted odds ratio (OR) (95% confidence interval [CI]).

ASA = American Society of Anesthesiologists.

\*P value < .05 considered statistical significant.

**Table 4**  
**Postoperative outcomes of the non-stroke and stroke groups.**

Variables	Non-stroke (n = 129)	Stroke (n = 43)	P value
ICU admission (%)	16 (12.4%)	35 (81.4%)	<.001*
Planned ICU admission	15 (11.6%)	27 (62.8%)	<.001*
Unplanned ICU admission	1 (0.8%)	8 (18.6%)	<.001*
Length of ICU stay (d, IQR)†	1 [1–4]	10 [5–19]	<.001*
Ventilator use (%)	13 (10.1%)	27 (62.8%)	<.001*
Duration of ventilator (d, IQR)#	1 [1–2]	14 [4–20]	<.001*
Length of hospital stay (d, IQR)	5 [3–8]	19 [11–39]	<.001†
Discharge status (%)			<.001*
Improved	126 (97.7%)	34 (79.1%)	
Death	3 (2.3%)	9 (20.9%)	

Data presented as number (%) or median (Interquartile range, IQR).

ICU = intensive care unit.

\*P value < .05 considered statistical significant.

†Analyzed from patients who were admitted in the ICU (Total n = 51, non-stroke = 16, stroke = 35).

#Analyzed from patients who were on postoperative ventilators (Total n = 40, non-stroke = 13, stroke = 27).

Despite these limitations, our study has some strengths. This study is the first to determine intra-operative risk factors for surgery and anesthesia for early post-operative stroke, as well as post-operative outcomes. Despite the small sample size, which might result in a wide CI in the multivariable regression, our study performed a methodical analysis and displayed comparable statistical parameters to previous publications.<sup>13,41</sup> We overcame the small sample size issue by adopting the previously proposed solution to the minimal sample size for regression analysis.<sup>128</sup> As recommended, we selected only the variables with  $n \geq 25$  for multivariable analysis to avoid false negative and false positive results. Importantly, too small a sample size could cause a wide 95% CI. Our strategy of variable selection for multivariable analysis could narrow the variables' CIs, thus resulting in a better representation of the population mean.

The study results could be implemented into a guide for peri-operative patient preparation and optimization, as well as prerequisite monitoring in cases with risks for post-operative stroke. Future studies should explore other variables potentially related to post-operative stroke by recruiting a larger study population or performing a multi-institutional study.

## 5. Conclusion

Our study explored pre- and intra-operative factors contributing to post-operative stroke and demonstrated post-operative outcomes. Pre-operative ASA physical status  $\geq 3$ , operation time > 120 minutes, and intra-operative hypotension and inotrope/vasopressor use were potential risk factors among patients scheduled for surgery. Patients at risk can be prepared and closely monitored to mitigate stroke risk. Despite the low

incidence, stroke patients experienced a higher rate of ICU admission, ventilator use, length of stay, and mortality than non-stroke patients.

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