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A Comparison of Perioperative Complications and Outcomes in Patients Undergoing Cerebral Aneurysm Clipping Performed Ultra-Early ($\leq$ 24 hours) versus Late ($>$ 24 hours): A 7-Year Retrospective Study of 302 Patients

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Abstract

Objectives The intracerebral aneurysm with subarachnoid hemorrhage (SAH) has a high morbidity and mortality rate. This study aimed to compare the incidences of perioperative complications in ultra-early surgery (within 24 hours) with those in late surgery ($>$ 24 hours).

Methods Retrospective data were reviewed for 302 patients who underwent craniotomies with aneurysm clipping between January 2014 and December 2020. Perioperative data were obtained from the medical records and reviewed by the investigators. The complications were compared between ultra-early and late operations. We were interested in major complications such as delayed ischemic neurologic deficit (DIND), intraoperative aneurysm rupture (IAR), and anesthesia-related complications. The short-term (in hospital) and long-term (1 year) outcomes in patients with or without DIND and IAR were compared. The collected data was statistically analyzed.

Results Three hundred and two patients were analyzed, and 264 patients had completed follow-up. The ultra-early cases (150 patients) had a higher American Society of Anesthesiologists physical status, a lower Glasgow Coma Scale, and higher Hunt and Hess scales. The surgeons operated on more cases of the anterior cerebral artery as ultra-early operations. The incidence rates of DIND, IAR, severe hemodynamic instability, and cardiac arrest were 5.6, 8.3, 6.3, and 0.3%, respectively, which were not different between groups. However, the reintubation rate was higher in the ultra-early surgery cases (0 vs. 3.3%, $p = 0.023$). The DIND and IAR patients had poorer short-term (in hospital) outcomes.

Conclusions There were no differences in major complications between ultra-early and late craniotomy with aneurysm clipping. However, the reintubation rate was strikingly higher in the ultra-early group. Patients with major complications had early, unfavorable outcomes.

Keywords
- aneurysm rupture
- cerebral aneurysm
- complications
- delayed ischemic neurologic deficit
- outcome
- reintubation
- ultra-early surgery

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Introduction

Intracerebral aneurysms are dilations of intracranial arteries that cause subarachnoid hemorrhage (SAH), a serious condition with high mortality and disability rates. Despite advancements in treatments, up to 31% of patients still have poor outcomes.[1–5] Surgical clipping has been the gold standard for treating early ruptured aneurysms,[6,7] particularly in developing countries, due to its low cost and feasibility. Early treatment is advised to prevent rebleeding and vasospasm.[8]

Recently, the timing of microsurgical clipping has remained controversial,[7] but recent studies[6,7,9] suggested that ultra-early clipping within 24 hours may result in fewer complications and better outcomes. Unfortunately, the traditional concerns of ultra-early treatment were revealed, including suboptimal operating conditions in emergency surgery, brain swelling from cerebral edema, difficulty in dissection, a higher risk of intraoperative rebleeding leading to devastating outcomes. Nevertheless, none of these studies has addressed the potential anesthesia-related complications that may arise from the suboptimal conditions of these emergent patients.

Our hospital provides 24-hour anesthetic care for these patients, based on the neurosurgeon's consideration and decision. Many operations take place outside of regular office hours, when anesthetic providers may have less experiences. However, there had been reports of factors impacting anesthesia-related complications during nighttime work.[10] The aim of this study is to compare the incidence of major procedure-related or anesthesia-related complications following aneurysm clipping between ultra-early ($\leq$ 24 hours) and late ($>$ 24 hours) surgical groups.

Materials and Methods

Following approval from the Institutional Ethics Committee (SI 520/2020), data were collected from all patients aged more than 18 years who underwent aneurysm clipping for a SAH in a tertiary teaching hospital over a 7-year period (2014–2020). Patients were excluded if their medical data were incompletely recorded and there was insufficient information about the outcomes of interest.

Patients' demographics, clinical and aneurysmal characteristics, and perioperative details were noted. The patients were then divided into two groups based on the timing of surgery which was mainly considered and decided by the surgical team. Ultra-early surgery was defined as emergency surgery performed within 24 hours after diagnosis and most of the time these procedures were taken care of by younger anesthesiologists at out of office hours, while late surgery was defined as surgery performed after 24 hours of admission that is called elective and urgent conditions. The elective or urgent operations mostly were performed within 48 to 72 hours. The perioperative complications were compared between the two groups. The perioperative complications were distinguished between major complications and anesthesia-related complications. Major complications included delayed ischemic neurologic deficit (DIND), intraoperative aneurysm rupture (IAR), hemodynamic instability, and cardiac arrest. The anesthesia-related complications were reintubation, difficult intubation, and pulmonary aspiration.

DIND was defined as a new neurological deficit or worsening of a previous one when the Glasgow Coma Scale (GCS) decreased by two points for 1 hour. Any decrease in the level of consciousness must be distinguished from an acute ischemic event and other causes of neurological deterioration.[11,12]

IAR is a SAH due to the rupture of a cerebral aneurysm, either by itself or by an iatrogenic method. Rupture generally occurs at the following three stages during surgery: predissection, dissection, and during clipping.[13]

Hemodynamic instability is defined as a systolic blood pressure of 90 mm Hg that necessitated the use of vasopressors, bleeding with a blood loss of 500 mL, transfusion, or gaseous embolism.[14–16] A cardiac arrest is defined as an event requiring cardiopulmonary resuscitation. The judgment of cardiac arrest is based on whether the electrocardiogram showed ventricular fibrillation, the disappearance of direct arterial blood pressure, and the reduction in mean arterial pressure to less than 20 mm Hg.[17]

Reintubation was defined as reintubation within 24 hours after extubation; difficult intubation was defined as intubation three times or more by an experienced anesthesiologist or more than 10 minutes; and pulmonary aspiration was defined as the entry of liquid or solid material into the trachea and lungs.[18]

All the patients were followed up for short-term and long-term outcomes and were compared between patients with and without major complications. The ventilator days, intensive care unit (ICU) stay, length of hospital stay, and the Glasgow Outcome Scale at 3, 6, and 12 months were also recorded and compared in patients with and without major procedure-related perioperative complications. Good long-term outcomes are defined as a Glasgow Outcome Scale of 4 and 5.[19]

Statistical Analysis

The sample size for rare events was calculated based on the incidence of major perioperative complications from the previous studies of 0.66 to 5.5%.[11–13,20,21] We estimated the complication rate at 1% with a 95% confidence interval, which requires a sample size of 300 subjects. In terms of lost data awareness, we increased the number of subjects by another 10%. Therefore, the final required number of patients was 330.

The statistical analysis was conducted by using SPSS software version 18.0 (IBM coporation, Chicago, IL, United states). The categorical data were compared with the Pearson chi-square test or Fisher's exact test, the continuous variables with normal distribution were compared with the Student's *t*-test, while nonparametric variables were compared with the Mann–Whitney *U* test. The *p*-value of less than 0.05 is considered statistically significant.

Results

During the study period, we identified 330 patients with a mean age of 56 years who underwent clipping aneurysm surgery. Of the 330 patients who met our study criteria,

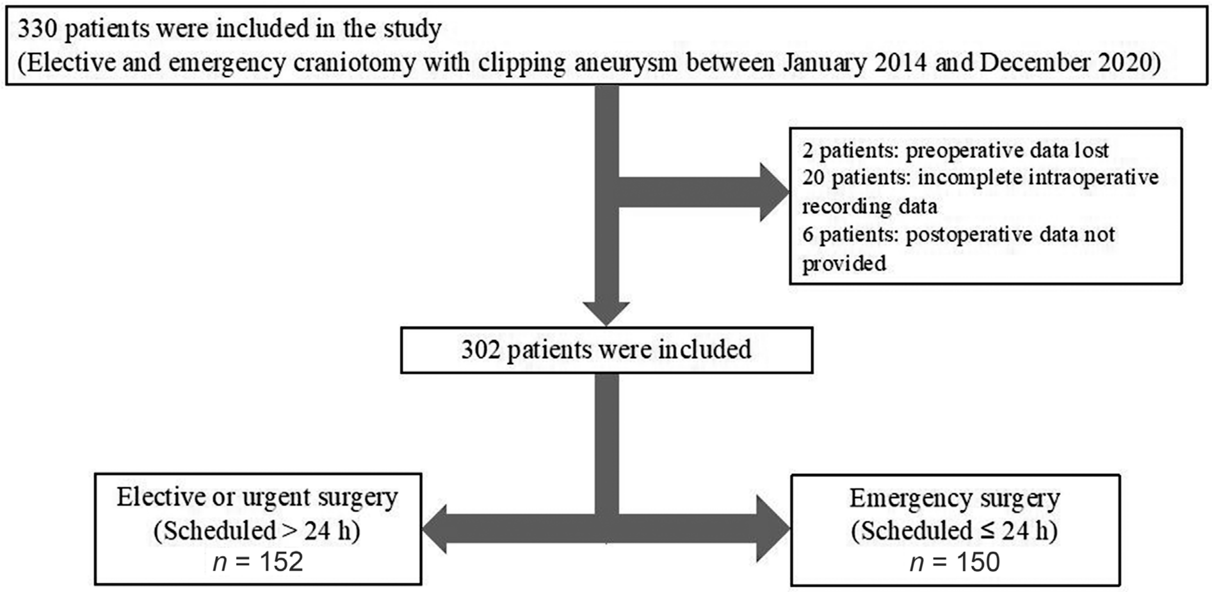

Fig. 1 Flowchart documenting inclusion criteria, exclusion criteria, and the number of individuals included in the study population.

preoperative data was not provided for 2 patients, incomplete intraoperative data were recorded for 20 patients, and postoperative data were missed for 6 patients. Finally, 302 patients were included in the analysis (►**Fig. 1**). Only 264 patients had completed 1 year of follow-up.

The population was predominantly female (66.6%). The ultra-early-surgery cases (150 patients) had higher American Society of Anesthesiologists (ASA) physical status (p-value < 0.001), lower GCS (p-value < 0.001), higher Hunt and Hess scales (p-value < 0.001), and more cases of the anterior cerebral artery and its communicating artery (p-value < 0.001; ►**Table 1**). The incidence rates of major complications such as DIND, IAR, severe hemodynamic instability, and cardiac arrest were 5.6, 8.3, 6.3, and 0.3%, respectively (►**Table 2**). No rebleeding before surgery occurred in either group. However, there were two cases admitted to medical wards due to medical problems, and then rebleeding occurred and SAH was the final diagnosis. The anesthesia-related complications, such as reintubation, difficult intubation, and pulmonary aspiration, were presented at 1.7, 0.3, and 1%, respectively. There are no statistically significant differences in the incidence rates of major complications between ultra-early and late surgery cases except the incidence rate of reintubation that was significantly higher in the ultra-early surgery group (0 vs. 3.3%, p-value $= 0.023$; ►**Table 2**).

Forty patients in the major complication group stemmed from those who were affected by DIND, IAR, or both (two patients had two complications) and had worse short-term outcomes, including prolonged ventilator use, a longer ICU and hospital stay, as well as worse general outcomes at hospital discharge. Nevertheless, improved outcomes at discharge were found in 80 and 90.5% of patients with and without major complications. The patients with or without major complications who survived at hospital discharge had good long-term outcomes at 3 months, 6 months, and 1 year following the surgery (►**Table 3**).

Discussion

This study demonstrated postoperative adverse events following surgical aneurysmal clipping in a detailed comparison between ultra-early (emergency) and late surgery. As per our expectation, the population of the ultra-early surgery group had significantly higher ASA physical status, lower GCS, and greater Hunt and Hess scales, compared with the other group. The anterior circulation aneurysm was more commonly operated on compared with the posterior circulation as an emergency procedure. Even though we could not find a significant difference in the incidences of major complications between these two conditions, except for reintubation, which happened only in emergency situations.

A previous peer-reviewed study[7] reported that the ultra-early treatment of cerebral aneurysms within 24 hours of rupture was associated with younger age and poorer SAH grades as determined by the World Federation of Neurological Surgeons (WFNS) grading scale. A good grade was defined as WFNS 1 to 3, while a poor grade was defined as WFNS 4 to 5. Our study confirmed that patients in the ultra-early treatment group had a more severe grade of disease at admission, which was reflected in lower GCS scores and higher Hunt and Hess scores. However, our study did not find a significant difference in age between the two groups, which was consistent with another recent retrospective study.[9]

Furthermore, our study identified a significant association between ultra-early treatment and aneurysms located in the anterior cerebral artery and its communicating artery. This may be explained by the fact that anterior communicating artery aneurysms (ACoAAs) are the most frequently occurring intracranial aneurysms, approximately 30%[22,23] of all intracranial aneurysms. From surgical point of view, the ACoAAs is easier clipped and need less equipment than other locations.

Table 1 Demographic data

Characteristics	Total ($n = 302$)	Surgery > 24 hours ($n = 152$)	Surgery ≤ 24 hours ($n = 150$)	*p*-Value
Gender: female	201 (66.6)	104 (68.4)	97 (64.7)	0.542
Age (years)	56.5 ± 14.9	56.3 ± 15.3	56.8 ± 14.6	0.791
Body mass index (kg/m^2)	23.5 ± 3.9	22.9 ± 3.9	24.2 ± 3.9	0.004[a]
ASA physical status				
I–II	79 (26.1)	54 (35.5)	25 (16.6)	< 0.001[a]
III	167 (55.3)	91 (59.9)	76 (50.7)	
IV	56 (18.5)	7 (4.6)	49 (32.7)	
Glasgow Coma Scale				
13–15	209 (69.2)	131 (86.2)	78 (52.0)	< 0.001[a]
9–12	52 (17.2)	15 (9.9)	37 (24.7)	
3–8	41 (13.6)	6 (3.9)	35 (23.3)	
Hunt and Hess scale				
1	54 (17.9)	50 (32.9)	4 (2.7)	< 0.001[a]
2	132 (43.7)	71 (46.7)	61 (40.7)	
3	68 (22.5)	21 (13.8)	47 (31.3)	
4	26 (8.6)	7 (4.6)	19 (12.7)	
5	22 (7.3)	3 (2.0)	19 (12.7)	
Site of aneurysm				
Anterior cerebral artery and its communicating artery	99 (32.8)	35 (23)	64 (42.7)	< 0.001[a]
Middle cerebral artery	50 (16.6)	19 (12.5)	31 (20.7)	
Internal carotid artery	37 (12.3)	29 (19.1)	8 (5.3)	
Posterior cerebral artery and its communicating artery	82 (27.2)	45 (29.6)	37 (24.7)	
Basilar artery	26 (8.6)	17 (11.2)	9 (6.0)	
Size of aneurysm (cm)	0.4 (0.11, 1.6)	0.36 (0.18, 1.30)	0.4 (0.11, 1.6)	0.778
Blood loss (mL)	350 (10, 5,300)	350 (30, 5,300)	350 (10, 2,300)	0.954
Operative time (minutes)	237.5 (45, 610)	247.5 (60, 610)	227.5 (45, 490)	0.017[a]
Anesthesia: TIVA	91 (30.1)	40 (26.3)	51 (34)	0.146

Abbreviations: ASA, American Society of Anesthesiologists; TIVA, total intravenous anesthesia.
Data presented as mean ± standard deviation (SD), median (min, max), or number (%) as appropriate.
[a]*p*-Value < 0.05 considered statistically significant.

Several prior publications have indicated that human or situational factors such as decreased alertness, teamwork, performance, and quality of care may contribute to the higher incidence of intraoperative adverse events during nighttime hours.[24–27] One study[25] evaluated 13 pairs of day-night matched anesthesia cases performed by anesthesia residents and found that mood and task performance were worse at night, leading the investigators to speculate that fatigue may have played a role. Another study[28] involving 21 anesthesiologists found that reaction times were worse with sleep deprivation.

From this study, reintubation was significantly more likely to occur in the ultra-early group. This finding aligns with the results of a large cohort study, which showed that nighttime surgeries had a higher incidence of postoperative pulmonary complications (PPCs).[10] Our study highlights the importance of considering the balance between the risks and benefits of extubation during out-of-office hours.[29,30] If there are any questionable conditions, extubation should be postponed. To help determine this balance, utilizing risk scores for PPCs may be useful in predicting which patients run the highest risk of developing PPCs during nighttime.[31]

When compared with a noncomplication group, patients with major adverse complications in terms of DIND and IAR required significantly longer ICU stays, ventilator support, and total length of hospital stays and had unfavorable postoperative outcomes (no improvement, disability, and death). All these complications could lead to a detrimental quality of life and a long-term, deleterious national problem. These findings were undoubtedly similar to those of the previous study.[32]

Table 2 Perioperative procedure-related and anesthesia-related adverse events

Major complications	Total ($n = 302$)	Surgery > 24 hour ($n = 152$)	Surgery ≤ 24 hour ($n = 150$)	*p*-Value
Procedure-related adverse events				
Rebleeding before surgery	0	0	0	1.000
Delayed ischemic neurologic deficits	17 (5.6)	10 (6.6)	7 (4.7)	0.471
Intraoperative aneurysm rupture	25 (8.3)	11 (7.2)	14 (9.3)	0.509
Hemodynamic instability	19 (6.3)	12 (7.9)	7 (4.7)	0.248
Cardiac arrest	1 (0.3)	0	1 (0.7)	0.313
Anesthesia-related adverse events				
Reintubation	5 (1.7)	0	5 (3.3)	0.023[a]
Difficult intubation	1 (0.3)	1 (0.7)	0	0.320
Pulmonary aspiration	3 (1.0)	1 (0.7)	2 (1.3)	0.554

Data presented as number (%) or median (min, max) as appropriate.
[a]$p < 0.05$ considered statistically significant.

Table 3 Intraoperative major complications, short-term (in hospital) and long-term outcomes

	With major complication[a]	Without major complication	*p*-Value
Short-term outcome	$n = 40$	$n = 262$	
Intensive care unit stay (days)	4.5 (1, 9.75)	1.0 (0, 6)	0.020[c]
Ventilator day (days)	8.5 (5.25, 13)	4.0 (2, 9)	0.003[c]
Length of hospital stay (days)	16.5 (11, 24.5)	11 (7.25, 19)	0.004[c]
At hospital discharge			
Improved	32 (80.0)	237 (90.5)	0.035[c]
Disable	3 (7.5)	16 (6.1)	
Death	5 (12.5)	9 (3.4)	
Long-term outcome	$n = 33$	$n = 231$	
Good outcome[b]			
Three months	22/33 (66.7)	184/231 (79.7)	0.092
Six months	23/31 (74.2)	187/218 (85.8)	0.097
Twelve months	23/31 (74.2)	188/217 (86.6)	0.069

Data presented as number (%) or median (min, max) as appropriate.
[a]The complications include delayed ischemic neurologic deficits and/or intraoperative aneurysm rupture.
[b]Good outcome defined as Glasgow Outcome Scale 4 and 5 (4 = moderate disability: such a patient is able to look after himself, to get out. However, some previous activities are now no longer possible by reason of either physical or mental deficit, 5 = good recovery: the capacity to resume normal occupational and social activities, although there may be minor physical or mental deficits).

There is a scarcity of publications comparing the long-term outcomes of patients with and without postoperative major complications. In this study, there was no significant difference in the long-term outcome between the two groups at 3 months, 6 months, and 1 year after surgical clipping, which might be due to a minimal number of complications. In a previous study,[33] most patients who survived and were discharged continued to improve even though the immediate postoperative outcome was not favorable.

However, it is important to acknowledge the limitations of this study. As a single-center and retrospective study, there may have been inadequate information and the reported complications may have been underestimated. We also did not have any information about patients who did not have surgeries. To gain a more comprehensive understanding of related complications, further comparative studies across multiple centers are needed, taking into account all relevant factors. In addition, potential strategies to prevent these complications should also be explored.

Conclusion

Considering that the reintubation rate was high in the ultra-early surgery cases (< 24 hour), extubation in these cases should be weighed between risks and benefits, and if there were any doubts, the extubation should be postponed.

Ethical Approval
This study was approved by the Siriraj Institutional Review Board of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (SI 520/2020). All methods were performed in accordance with the Declaration of Helsinki and the international ethical guidelines for human biomedical research.

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Conflict of Interest
None declared.

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