Factors Affecting Delayed Extubation After Intracranial Surgery in Siriraj Hospital

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ABSTRACT

Background: The time to extubation in neurosurgical patients depends on a number of various factors, including patient, surgical and anesthetic factors.
Objective: To determine the factors influencing the time to extubation in neurosurgical patients.
Methods: This study is a prospective study including all patients who underwent intracranial surgery from October 2008 to April 2009 at Siriraj Hospital. We excluded patients who were under the age of 18 years, intubated or had undergone tracheostomy prior to the surgery and had a history of difficult intubation. Demographic data and various factors expected to involve the extubation were collected and analyzed.
Results: There were 171 (89.1%) patients suitable for the early extubation and 21 (10.9%) patients remained in the intubated condition. A univariate analysis revealed 10 factors influencing failure of the extubation, including age >65 years, ASA physical status > class II, Glasgow coma score (GCS) <13, emergency surgical condition, anesthetic time >300 minutes, estimated blood loss >700 ml, use of cerebral protective technique, total propofol dosage >1,000 mg, total fentanyl dosage >50 mcg/hour, and a completed operation time after 4 pm. In a multivariate analysis, the delayed extubation was associated with 3 factors, including GCS <13, emergency surgical condition and estimated blood loss >700 ml.
Conclusion: The incidence of the early extubation in neurosurgical patients who underwent intracranial surgery was 89.1%. Factors associated with an increased risk of delayed extubation included low Glasgow coma score, emergency surgical status and a large amount of intra-operative blood loss.

Keywords: Early extubation, intracranial surgery, neuroanesthesia

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Early extubation and rapid awakening in patients who undergo intracranial surgery has several benefits, including early detection of post-operative surgical complications[1], less catecholamine release[2] and decreased expense of intensive care unit (ICU) admission. However, systemic hypertension in the emergence period is major disadvantage of an early extubation which may cause intracranial complications such as bleeding and brain edema[3]. Moreover, hypercarbia or hypoxia in a hypoventilated patient is a problem which must be recognized during the transfer period to ICU. Therefore, in fact, a decision about an early extubation depends on many individual factors.[4,5]

Many factors associated with velocity of recovery and period of extubation have been studied. Short acting anesthesia agents, for instance, Remifentanyl[6] and Sevoflurane[7] often facilitate early extubation in neurosurgical patients. On the other hand, intracranial surgery of tumors larger than 30 mm in size was related to retardation of awakening.[8] A utilization of neuroprotective agents, particularly barbiturates, perhaps causes cardiovascular and respiration depression resulting in delayed recovery.[9]

A previous study of Srirojanakul and colleagues indicated two major factors associated with failure of early extubation among patients who encountered intracranial surgery which included prolonged anesthetic time more than 300 minutes and estimated intra-operative blood loss of more than 500 ml.[10] Since this study was a retrospective study, insufficient data seemed to be an important pitfall. Thus, we have designed a novel prospective study for more accurate data collection and identification of factors which could predict delay extubation.

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MATERIALS AND METHODS

This study is a prospective study conducted from October 2008 to April 2009 at Siriraj Hospital. All patients gave their informed consent. Exclusion criteria included age <18 years, patients who underwent an intubation or tracheostomy prior to the surgery and those with a history of difficult intubation. Demographic data and other factors which were expected to be involved in an extubation were recorded, including age (<65 or >65 years), ASA physical status (class 1-2 or higher than class 2), Glasgow coma score (GCS) (<13 or 13-15)[11], types of the operations (tumor, vascular, trauma, stroke, others), operative status (elective or emergency operation), total anesthetic time (≤300 or >300 minutes[10]), estimated total intraoperative blood loss (≤700 or >700 ml), body temperature at the end of the surgery (≤35 or >35°C), use of neuroprotective technique (yes or no), total propofol dosage (≤1,000 or >1,000 mg), total fentanyl dosage (≤50 or >50 mcg/hour), surgical approaches (craniotomy, craniectomy or transphenoidal approach), finished operation time (before or after 4 pm.) and locations of lesions (supratentorial or infratentorial). We were concerned about the time that the operation finished because in our hospital, we usually have a shift change of attending anesthesiologist staff over the operating rooms after 4 pm, which may result in a difference in decision making for an extubation.

"Early extubation" was defined as the patients who were extubated within 6 hours after the operation finished.[12,13]

According to sample size determination, data from the previous study showed early extubation in 57 percent of patients who underwent intracranial surgery.[10] A sample size was considered to have 90% power, an accepted variation of 0.07 and a significance level of α = 0.05. The result of the calculated sample size totaled 192 patients.

Statistical analysis was performed with SPSS Version 11.5 for Windows. Descriptive statistics were used to examine the demographic data. Categorical variables were analyzed by using Chi-square or Fisher Exact Test. Results of univariate analysis were reported as crude odds ratio (OR) and 95% confidence interval (95%CI). Potential confounders or predictors were subsequently entered into a final multivariate model. Multiple logistic regression analysis was used to test for associations between potential factors reporting in adjusted odds ratio (AOR) and 95% CI. Differences were considered to be statistically significant if the *p*-value was less than 0.05. The cut-off point of amount of estimated intra-operative blood loss and total propofol dosage were determined by using the area under the curve (AUC) of a Receiver-Operating-Characteristic (ROC) analysis.

All materials and methods used in the study were approved by the Siriraj Institutional Review Board (SIRB).

RESULTS

One hundred and ninety-two patients were enrolled in the study. Early extubation occurred in 171 patients (89.1%), whereas 21 patients (10.9%) underwent ongoing intubation. Of the total cases, immediate extubation in the operating room occurred in 162 patients (84.4%). Unfortunately, one patient who was early extubated was reintubated in the ICU due to insufficient respiration at 2 hours after the extubation. None of the patients was excluded from the study. The demographic data was shown in Table 1.

With regard to an univariate analysis, 10 adverse factors predicting a failure of early extubation included age >65 years, ASA physical status >class II, Glasgow coma score <13, emergency surgery, anesthetic time > 300 minutes, estimated intra-operative blood loss >700

TABLE 1. Demographic data.

Data	Results
Gender, numbers (%)	
Male	84 (43.7%)
Female	108 (56.3%)
Age, years	
Mean ± SD	48.48 ± 14.4
Range (min - max)	18-85
ASA physical status, numbers (%)	
Class 1-2	157 (81.8%)
Class ≥ 2	35 (18.2%)
Glasgow coma score	
Mean ± SD	14.8 ± 0.8
Range (min - max)	9-15
Type of surgery, numbers (%)	
Tumor resection	152 (79.2 %)
Vascular surgery	22 (11.4 %)
Neurotrauma surgery	4 (2.1%)
Stroke surgery	1 (0.5%)
Other surgery	13 (6.8%)
Operative status, numbers (%)	
Elective surgery	181 (94.3%)
Emergency surgery	11 (5.7%)
Anesthetic time, minutes	
Mean ± SD	296.0 ± 112.1
Range (min - max)	87-735
Estimated blood loss, ml	
Mean ± SD	635.0 ± 1,513.0
Range (min - max)	10 - 19,000
Temperature, °C	
Mean ± SD	36.3 ± 0.7
Range (min - max)	33.6-38.6
Brain protection, number (%)	
No	103 (53.6%)
With propofol	86 (44.8%)
With thiopenthal	3 (1.6%)
Approach, number (%)	
Craniotomy/craniectomy	167 (87.0%)
Transphenoidal	25 (13.0%)
Propofol infusion dose, mg	
Median	500
Range (min - max)	80-2,000
Thiopenthal infusion dose, mg	
Median	600
Range (min - max)	300 - 2,000
Fentanyl infusion dose, µg/hour	
Mean ± SD	50.6 ± 17.6
Range (min - max)	16-128
Time of finished operation, number (%)	
Before 4 P.M.	137 (71.4%)
After 4 P.M.	55 (28.6%)
Location of tumors (Total 152), number (%)	
Supratentorial	104 (68.4%)
Infratentorial	48 (31.6%)

ml, use of neuroprotective technique, total propofol dosage >1,000 mg, total fentanyl dosage >50 mcg/hour and an operation which finished after 4 pm.

Multiple logistic regression analysis was used to determine the influence of the various covariates on the early and delayed extubation groups (Table 2). Three independent factors were as follows: Glasgow coma score <13 (AOR 20.16, 95%CI 2.13 - 190.90, p = 0.009); emergency surgery (AOR 10.12, 95%CI 1.04 - 98.10, p = 0.046); estimated blood loss >700 ml (AOR 7.26, 95%CI 1.70 - 31.04, p = 0.007).

As can be seen from Table 2, the patients who had supratentorial and infratentorial masses, of which the total number was 152, might be effected by the time to extubation. Therefore, we included the location of tumors as one predictor. However, this factor was not statistically significant.

Comparison between median, 25th and 75th percentile values of estimated intra-operative blood loss and total propofol infusion dosage were presented in Table 3. None of them are within the normal distribution range (Fig 1 and 2).

DISCUSSION

Incidence of the early extubation in this study was 89% which was much different from the former study of Srirojanakul et al (57.7%).[10] One possible reason might be a result of a difference in the time of data collection. Our study collected data during 2008 - 2009, whereas that of the study of Srirojanakul and colleagues was collected during 2004 - 2005. From this finding we may infer an increase of experience of neurosurgeons over the years which could be seen from the reduction of mean anesthetic time (from 352 minutes of the study of Srirojanakul et al to 296 minutes of our study).

Three main factors, including patient, surgical and anesthetic factors were assumed to influence the early

TABLE 2. Univariate and multivariate analysis of factors associated with time to the extubation.

Factors	Extubation time		Crude analysis		Adjusted OR	
	≤ 6 hours	> 6 hours	p-value	OR (95%CI)	p-value	OR (95%CI)
Age						
≤ 65 years	151 (91%)	15 (9%)		1		1
> 65 years	20 (76.9%)	6 (23.1%)	0.04*	3.0 (1.0,8.6)	0.177	2.9 (0.6, 14.0)
ASA physical status						
Class 1-2	144 (91.7%)	13 (8.3%)		1		1
> Classes 2	27 (77.1%)	8 (22.9%)	0.03*	3.2 (1.2,8.6)	0.482	1.8 (0.4, 8.9)
GCS						
13-15	168 (90.8%)	17 (9.2%)		1		1
< 13	3 (42.9%)	4 (57.1%)	0.003*	13.1 (2.7,63.8)	0.009*	20.2 (2.1, 190.9)
Operative status						
Elective	165 (91.2%)	16 (8.8%)		1		1
Emergency	6 (54.5%)	5 (45.5%)	0.003*	8.5 (2.3,31.3)	0.046*	10.1 (1.0, 98.1)
Anesthetic time						
≤ 300 minutes	111 (94.9%)	6 (5.1%)		1		1
> 300 minutes	60 (80%)	15 (20%)	0.002*	4.6 (1.7,12.5)	0.12	3.4 (0.7, 16.3)
Estimated blood loss						
≤ 700 ml	144 (94.1%)	9 (5.9%)		1		1
> 700 ml	27 (69.2%)	12 (30.8%)	<0.001*	7.1 (2.7,18.5)	0.007*	7.3 (1.7, 31.0)
Temperature						
> 35^{o}c	143 (88.3%)	19 (11.7%)		1		
≤ 35^{o}c	2 (50%)	2 (50%)	0.07	7.5 (1.0,56.6)	-	-
Brain protection						
No	98 (95.1%)	5 (4.9%)		1		1
Yes	73 (82%)	16 (18%)	0.008*	4.2 (1.5,12.2)	0.151	2.9 (0.7, 12.9)
Propofol infusion dose						
≤ 1,000 mg	158 (91.3%)	15 (8.7%)		1		1
> 1,000 mg	13 (68.)4%	6 (31.6%)	0.009*	4.9 (1.6,14.6)	0.358	2.2 (0.4, 12.2)
Approach						
Cranio/craniectomy	147 (88%)	20 (12%)		1		
Transphenoidal	24 (96%)	1 (4%)	0.3	0.3 (0.03,2.3)	-	-
Fentanyl dose						
≤ 50 (μg/hour)	94 (83.9%)	18 (16.1%)		1		1
> 50 (μg/hour)	77 (96.3%)	3 (3.8%)	0.007*	0.2 (0.05,0.7)	0.126	0.3 (0.07, 1.4)
Time of finished operation						
Before 4 P.M.	127 (92.7%)	10 (7.3%)		1		1
After 4 P.M.	44 (80%)	11 (20%)	0.02*	3.1 (1.2,7.9)	0.366	0.5 (0.1, 2.3)
Location of tumors						
Supratentorial	96 (92.3%)	8 (7.7%)		1		
Infratentorial	43 (89.6%)	5 (10.4%)	0.5	1.4 (0.4,4.5)	-	-

*Statistically significant

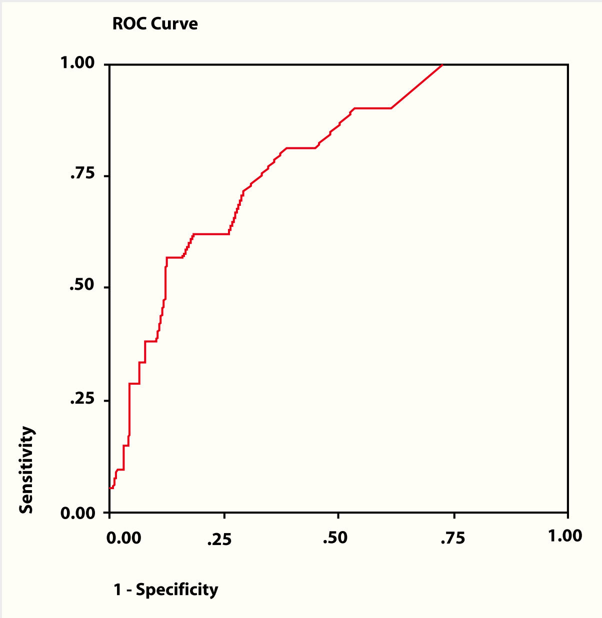

Fig 1. ROC curve of intra-operative blood loss.

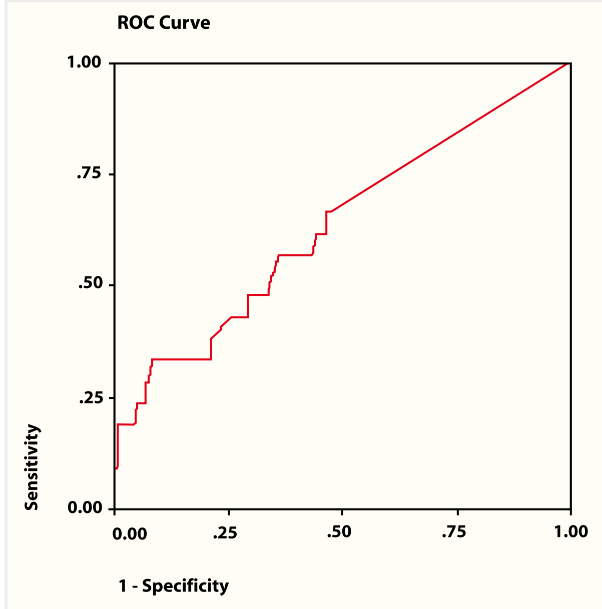

Fig 2. ROC curve of propofol dosage.

extubation. The patient factors were age >65 years and ASA physical status >2 which were not significantly associated with the extubation time, whereas GCS <13 which also included the patients with either moderate or severe brain injury[11] was independently associated with the delayed extubation (p value = 0.003), since the patients with low GCS were often intubated before the operation. However, only 7 patients who had GCS <13 were included in our study.

Subsequently, many surgical factors, including operative status, intra-operative blood loss, surgical approach and location of lesions were assumed to impinge upon the time of extubation. Emergency operative status was a significant factor of the delayed extubation, because the patients who require emergency procedure probably have severity of the intracranial lesions greater than those of the patients who underwent elective surgery. Estimated intra-operative blood loss >700 ml, which is the cut-off point of a ROC analysis, was associated with the delayed extubation while in the Srirojanakul study[10], intra-operative blood loss >500 ml was a predictive factor of the delayed extubation. The difference between the results of both studies probably occurred as a result of the wide range in estimated volume of intra-operative blood loss, ranging from 10 to 19,000 ml of our study and 20 to 9,600 ml in the study of Srirojanakul et al. This difference eventually led to the different cut-off point. Our study confirmed that the surgical approach and location of the lesion were not the predicting factors affecting the extubation time. Bruder et al suggested that the patients should not

TABLE 3. Median estimated intraoperative blood loss and median total propofol infusion dose in the groups of early extubation and delayed extubation.

Factors	Median (25th, 75th percentile)	
	Early extubation	Delayed extubation
Estimated blood loss (ml)	300 (150, 550)	900 (425, 1450)
Propofol infusion dose (mg)	500 (215, 812.5)	770 (242.5, 1800)

be extubated if cranial nerves, especially IX, X and XII have injuries or for a large tumor resection.[1] Nevertheless, our study demonstrated that neither supratentorial nor infratentorial tumor resection influenced the extubation time, even in resection of an infratentorial tumor adjacent to such cranial nerves.

Numerous anesthetic factors were studied to find out which were the factors influencing early extubation in our neurosurgical patients. We emphasized total anesthesized time, body temperature, brain protection technique, quantity of propofol and fentanyl given and the finishing time of the operation. Protracted duration of anesthesia directly resulted in delayed recovery.[14] In the same manner, anesthetic time longer than 5 to 6 hours brought about slow recovery in neurosurgical patients.[5,10] However, we could not demonstrate a significant effect of an anesthetic time longer than 300 minutes on the extubation time. Additionally, a body temperature less than 35.5°C did not influence the extubation time. Only 4 patients in our study had a body temperature less than 35.5°C. A rare incidence of hypothermia among the patients occurred because we have routinely utilized a forced-air warming mattress for heat loss prevention during every neurosurgical procedure.

Anesthetic drugs were assumed to be the factors that cause delayed recovery in patients with general anesthesia. Inhalation and intravenous anesthetic agents including barbiturates and opioids have been implicated in delayed emergence.[9,15,16] Nowadays, short-acting agents that provide rapid recovery with early extubation are in popular use by anesthesiologists. One recent randomized prospective study of Bhagat and colleagues revealed the use of low dose anesthetics successfully resulting in the early emergence.[4] Interestingly, Llacer et al used remifentanyl, short-acting opioids resulting in the extubation time earlier than that produced by fentanyl.[6] However, opioids other than fentanyl were not used in our neurosurgical patients. Therefore, a variety of opioids was not considered in our study. Use of fentanyl dosage of more than 50 mcg/hour did not affect the time of extubation. Propofol, an anesthetic agent with a neuroprotective effect[17], has been recently increasingly used for intracranial surgery in our institute. In the same way, the amount of propofol infusion did not cause the delayed extubation. This result of our study could be comparable to a prospective, randomized study of Talke et al. They proposed the use of three anesthetic techniques, including propofol infusion, isoflurane inhalation, and a combination of them (once the dura was closed, isoflurane was discontinued and propofol simultaneously started) which were not different in the early post-operative recovery variables.[18]

Finally, we assumed that the finishing time of the operation after 4 pm. was a factor involved in the delayed extubation due to the shift change of anesthesiologists. However, the result of this factor was not statistically significant for the time to extubation.

The limitations of this study were fundamentally derived from the individual decisions of anesthesiologists. Although most of the patients were able to extubate within 6 hours after the operations, post-operative monitoring of the respiratory, cardiovascular and neurological systems were actually required for prevention of further complications.

CONCLUSION

The incidence of the early extubation in the neurosurgical patients who underwent intracranial surgery in our study was 89.1%. The major factors associated with increased risk of the delayed extubation included Glasgow coma score <13, emergency surgical status and estimated blood loss >700 ml.

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