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Perioperative Predictors of Extubation Failure and the Effect on Clinical Outcome After Infratentorial Craniotomy

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Background: The purpose of the study was to analyze the risk factors for failed extubation in subjects submitted to infratentorial craniotomy.


Material/Methods: Patients aged over 18 years who received infratentorial craniotomy for brain tumor resection were consecutively included in this study. Perioperative variables were collected and analyzed. Univariate analyses and multiple logistic regression were used to derive factors related to failed extubation. Patients had follow-up care until either out of hospital or death.

Results: Throughout the course of the study, 2118 patients were eligible and 94 (4.4%) suffered from extubation failure at some point during their hospital stay. Five factors were recognized as independent risk factors for postoperative failed extubation: craniotomy history, preoperative lower cranial nerve dysfunction, tumor size, tumor position, and maximum change in blood pressure (BP) during the operation. Failed extubation was related to a higher incidence rate of pneumonia, mortality, unfavorable Glasgow Outcome Scale score, longer stay in the neuro-intensive care unit (ICU) and hospitalization, and higher hospitalization costs compared with successful extubation.

Conclusions: History of craniotomy, preoperative lower cranial nerve dysfunction, tumor size, tumor position, and maximum change in BP during the operation were independent risk factors related to postoperative failed extubation in patients submitted to infratentorial craniotomy. Extubation failure raises the incidences of postoperative pneumonia, mortality, and higher hospitalization costs, and prolongs neuro-ICU and postoperative length of stay.

MeSH Keywords: **Airway Extubation • Infratentorial Neoplasms • Risk Factors**

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Background

Because of the potential risk of damage to cranial nerves and brain stem respiratory center during surgery, patients undergoing infratentorial craniotomy represent the special populations who have high risk of extubation failure after surgery. Failed extubation is associated with prolonged mechanical ventilation (MV), increased nosocomial pneumonia, longer stay in the intensive care unit (ICU), and increased postoperative mortality and morbidity [1–6]. Furthermore, extubation failure may lead to hypoxemia and result in worse neurodevelopmental outcomes in patients after craniotomy.

To date, a number of studies have reported the relationship between the parameters of airway protection, such as cough strength, secretion volume, and neurological function, and extubation outcome [7–9]. Little has been done to identify the perioperative factors predictive of the extubation outcome after infratentorial craniotomy. The aim of this prospective study was to distinguish the risk factors for failed extubation after infratentorial craniotomy. Knowing these may assist clinicians in making the extubation decision for such patients.

Material and Methods

Our study was approved by the Institutional Review Board of Beijing Tiantan Hospital, Capital Medical University, Beijing, China. Written informed consent was obtained from each patient.

Study design and patient population

This study was carried out at the neuro-ICU of Beijing Tiantan Hospital. All adult patients who had infratentorial craniotomy for brain tumor resection were consecutively enrolled. Patients were excluded if they underwent pre-operative tracheotomy or if extubation was not attempted during hospitalization.

Patients reintubated for re-operation within 72 h after extubation were also excluded for analysis.

Clinical practice

Anesthesia

All craniotomy procedures were performed under general balanced anesthesia with tracheal intubation, and all patients were transferred to the neuro-ICU for post-operative care. Typically, pre-medication with 1 to 3 mg of intravenous midazolam was given 30 min before induction. Anesthesia was induced with intravenous propofol 1.5–2.0 mg/kg and fentanyl 3–5 µg/kg or sufentanil 0.4–0.7 µg/kg. Tracheal intubation was performed after intravenous vecuronium 0.1 mg/kg or rocuronium 0.8 mg/kg. Anesthesia was maintained using sevoflurane 1.5–2% in 40% oxygen, propofol (target-controlled infusion [TCI] at 4–5 µg/mL), and 0.05–0.3 µg/kg/min. Neuromuscular blockade and opioid analgesics were given intermittently as needed. Propofol and remifentanyl were stopped at the time of dural closure. Sevoflurane was stopped when skin closure was started.

Extubation and reintubation

Near the end of operation, anesthesiologists and neurosurgeons in charge discussed together extubation according to the patients' condition. When they decided to extubate patients in the operating room (OR), neostigmine and atropine was given to reverse the residual neuromuscular blockade. Once the patient's spontaneous breathing recovered, a screening checklist (Table 1) was performed. Extubation was tried when the answer to all checklist items was yes.

When it was decided not to attempt extubation, the patients were transferred to the neuro-ICU with intubation and were supported with MV. Ventilation mode was synchronized intermittent mandatory ventilation plus pressure support (PS). The fraction of inspired oxygen (FIO₂) was 0.4. The tidal volume (V_T)

Table 1. Screening checklist used to determine the patient's suitability for extubation. The answer to all questions must be "yes" in order for extubation to be approved.

Question	Answer
1. Awake and alert with cerebral function adequate for patient co-operation or equivalent preoperative state of consciousness?	Yes/No
2. Hemodynamic stability (lack of vasopressor support and mean arterial pressure within 10–15% of baseline)?	Yes/No
3. Adequate recovery of muscle strength?	Yes/No
4. Normal tidal volumes, normocapnia (end-tidal carbon dioxide 30–45 mmHg), minimum pulse oximetry >95% with Fio ₂ 0.5?	Yes/No
5. Intact gag reflex and swallow function (presence of clearly audible cough during suctioning)?	Yes/No

Fio₂ – fraction of inspired oxygen.

was 6 to 8 mL/kg of body weight. The respiratory rate was 12 to 15/min and the PS level was 10 to 15 cmH₂O, and positive end-expiratory pressure was 3 to 6 cmH₂O. The MV mode was turned to PS only when the patient resumed spontaneous breathing.

The neurosurgeon in charge was notified once the patient had passed the spontaneous breathing trial. Extubation was attempted after the neurosurgeon and neuro-ICU physician reached agreement about the screening checklist (Table 1). Screening would be repeated the next morning if the initial screening was not passed. Tracheotomy would be performed by the neurosurgeon in charge if a patient's mental status decreased or airway protection ability was impaired.

Reintubation was performed if a patient met one of the following criteria: (1) mental status became worse (Glasgow Coma Scale [GCS] score ≤ 8 [10]); (2) spontaneous respiration rate became slow; (3) decreased oxygen saturation of $<90\%$ despite a FIO₂ of >0.5 ; or (4) increased signs of respiratory work.

Postoperative care

On arrival to the neuro-ICU, routine monitoring was applied, including a 5-lead electrocardiograph (ECG), oxygen saturation, noninvasive blood pressure monitor, capnograph, and rectal thermometer. A face mask was provided for patients who had been extubated. A warming blanket was used to maintain the patient's rectal temperature. Neurological examination was carried out every hour. All patients received a computed tomography (CT) scan after being transferred to ICU.

Shivering was treated with administration of intravenous meperidine 0.4 mg/kg. Intravenous infusion of urapidil 0.07 mg/kg was used to treat persistent systemic hypertension (systolic blood pressure [SBP] >140 mm Hg or 20% above preoperative base level).

Patients were transferred to ward the next morning after physiologic status became stable. Patients who were not extubated were not discharged. Patients with a tracheotomy were transferred after successful weaning from MV.

Data collection and definitions

Our investigators collected data prospectively by means of a standardized case report form.

Parameters collected before surgery included age; body mass index (BMI); gender; history of hypertension, diabetes, and craniotomy; American Society of Anesthesiologists (ASA) physical status [11]; lower cranial nerve dysfunction; tumor size; tumor location; cerebellar tonsillar herniation; and hydrocephalus. All patients admitted to our hospital underwent a routine

neurological examination, especially a lower cranial nerve (IX, X, XI, and XII) function test. The definition of lower cranial nerve dysfunction was one or more function disorder in nerves IX, X, or XII. Tumor size and location, preoperative cerebellar tonsillar herniation, or hydrocephalus were quantified by CT or magnetic resonance imaging (MRI) before operation. Tumor size was defined by the tumor maximum cross-sectional diameter, and the cut-off point was set at 30 mm according to a previous study [12]. Tumor location was classified as three types (brain stem tumors, tumors oppressing the brain stem, and tumors not oppressing the brain stem) according to the relationship between the brain stem and tumor.

Intraoperative parameters included fluid balance, duration of surgery, estimated blood loss, fluid administration, maximum change in blood pressure (BP), analgesics, and muscle relaxants. Maximum changes in BP were defined as the difference between highest and lowest mean arterial pressure (MAP) during surgery.

Parameters about clinical outcomes included postoperative mortality, pneumonia, Glasgow Outcome Scale (GOS) score at discharge, ICU length of stay (LOS), postoperative hospital LOS, and hospitalization costs. Pneumonia was defined by the National Nosocomial Infections Surveillance System definition [13]. GOS scores were divided as unfavorable (GOS 1–3) and favorable (GOS 4–5) by the five-category GOS score [14]. The ICU LOS was categorized as ≥ 24 and <24 hours.

The definition of failed extubation was the need for reintubation or tracheotomy within 72 hours following the scheduled extubation for any reasons other than reintubation or tracheotomy for reoperation.

Statistical analysis

Categorical data were represented by percentages. Continuous data needed for testing for normal distribution before further statistical examination were shown as mean and standard deviation (SD) or median with the 25th and 75th percentiles when applicable. The chi-square test was used to examine differences among categorical variables, except small sample size data, which were analyzed using Fisher's exact test. Analysis of continuous data was done with Student's t test for normally distributed variables and use of the Mann-Whitney U test for non-normally distributed variables. After multiple logistic regression analyses, univariate regression analyses were conducted to identify risk factors related to delayed extubation. Pre- and intra-operative factors were also analyzed as predictors of failed extubation, and factors with a p-value of less than 0.5 were included in multivariable analysis (stepwise forward logistic regression) to recognize the independent factors for failed extubation. A p-value of <0.05 was considered statistically

Table 2. the time to extubation attempt and outcome.

Extubation time	Successful (n=2024)	Failed (n=94)
OR	988	18 (1.8%)
Neuro-ICU	1036	76 (6.8%)
1 das	857	47 (5.2%)
2 das	137	6 (4.2%)
3 das	13	4 (23.5%)
4 das	7	3 (30.0%)
5 das	6	4 (40.0%)
6 das	7	5 (41.7%)
≥7 das	9	7 (43.8%)

OR – operating room; ICU – intensive care unit; das – days after surgery.

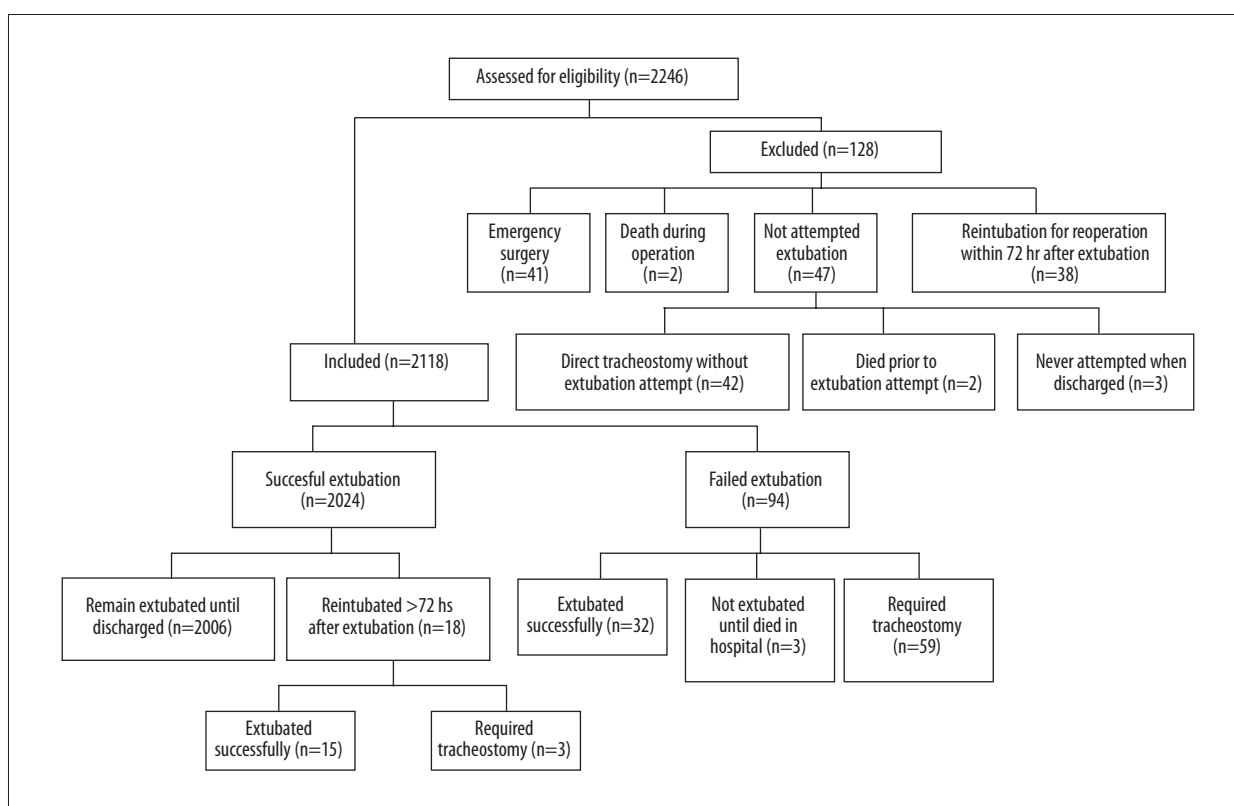


Figure 1. Flow of patient's through the trial.

significant. Statistical analysis was performed by use of SPSS statistical software (version 16.0; SPSS, Chicago, Illinois, USA).

Results

In the course of the study, 2246 patients were treated by elective craniotomy in our hospital. Of these patients, 2118 met the above inclusion criteria and were included in the study

(778 males/1340 females; mean age 45.5±13.4 years, age from 18 to 81 years; 1006 extubated in the OR and 1112 extubated in the neuro-ICU). Among the patients who were enrolled, 2024 were extubated successfully (95.6%, successful extubation group; 988 were extubated in the OR and 1036 in the neuro-ICU), and 94 suffered from extubation failure at some point during their hospital stay (4.4%, failed extubation group; 18 occurred in the OR and 76 in the neuro-ICU). The overall rate of failed extubation of this study was remarkably higher in the

Table 3. Demographic, preoperative and intraoperative characteristics of patients undergoing infratentorial craniotomy for brain tumour resection included in a study to identify the factors associated with failed extubation (n=2118).

Characteristic	Successful (n = 2024)		Failed (n = 94)		p Value
Age (years)	46	(37–55)	47	(36–55)	0.965
BMI (kg/m ²)	23.4	(21.2–25.9)	23.4	(19.0–26.4)	0.366
Males	778	(38.4)	42	(44.7)	0.225
History of hypertension	423	(20.9)	17	(18.1)	0.511
History of diabetes	83	(4.1)	4	(4.3)	0.941
History of craniotomy	124	(6.1)	16	(17.0)	<0.001
ASA physical status					0.022
Class 1/2	1673	(82.7)	69	(73.4)	
Class 3/4	351	(17.3)	25	(26.6)	
Lower cranial nerve dysfunction	414	(20.5)	47	(50.0)	<0.001
Tumor size ≥30 mm	357	(61.8)	38	(95.0)	0.001
Tumor location					<0.001
No brain stem oppression	440	(21.7)	6	(6.4)	
Brain stem oppression	1445	(71.4)	69	(73.4)	
Brain stem tumor	139	(6.9)	19	(20.2)	
Cerebellar tonsillar herniation	184	(9.1)	9	(9.6)	0.873
Hydrocephalus	607	(30.0)	24	(25.5)	0.356
Duration of surgery ≥6 h	816	(40.3)	55	(58.5)	0.016
Estimated blood loss ≥1000 ml	283	(14.0)	24	(25.5)	0.002
Fluids administration (ml/h)	698.7	(594.1–848.1)	653.8	(574.9–758.1)	0.009
Fluid balance(ml)	1700.0	(1250.0–2300.0)	1800	(1137.5–2100.0)	0.595
Maximum change in BP (mmHg)	39.3	(30.3–49.7)	41.3	(36.4–57.0)	<0.001
Analgesics					0.964
Fentanyl + remifentanyl	1490	(73.6)	69	(73.4)	
Sufentanyl + remifentanyl	534	(26.4)	25	(26.6)	
Muscle relaxants					0.200
Vecuronium	387	(19.1)	23	(24.5)	
Rocuronium	1637	(80.9)	71	(75.5)	

BMI – body mass index; ASA – American Society of Anesthesiologists; BP – blood pressure.

ICU than that in the OR. According to Table 2, rates of failing at the first attempt at extubation were remarkably higher on the third day after surgery than those on the first and second days. Of the 94 patients who failed extubation, extubation was attempted again in 25 patients and succeeded; 5 patients were extubated successfully after failing twice; and another 2 patients experienced extubation failure three times before it was finally successful. Besides, 59 patients received tracheotomy,

16 patients failed extubation two times, and another 2 patients failed three times and received a tracheostomy at last.

Figure 1 and Table 2 describe the patients' condition and provides some other information about this study.

Table 3 show the statistical test results analyzed by univariate analysis of the preoperative and intraoperative factors. Among

Table 4. Stepwise forward regression analysis to identify factors independently associated with failed extubation in patients undergoing infratentorial craniotomy for brain tumour resection (n=2118).

Factor	B	SE	Wald	Odds ratio (95% CI)	p Value
History of craniotomy	1.096	0.306	12.858	2.992 (1.644, 5.446)	<0.001
Preoperative lower cranial nerve dysfunction	0.963	0.222	18.856	2.620 (1.696,4.046)	<0.001
Tumor size ≥30 mm	0.828	0.329	6.325	2.289 (1.201, 4.365)	0.012
Tumor location					<0.001
No brain stem oppression			19.915		
Brain stem oppression	0.760	0.440	2.987	2.138 (0.903, 5.062)	
Brain stem tumor	1.899	0.495	14.704	6.681 (2.531, 17.637)	
Maximum change in BP (mmHg)	0.039	0.008	24.584	1.039 (1.024, 1.055)	<0.001

BP – blood pressure.

Table 5. Clinical outcomes following successful or failed postoperative extubation in patients undergoing infratentorial craniotomy for brain tumour resection (n=2118).

Variable	Successful (n=2024)	Failed (n=94)	p Value
Pneumonia	88 (4.3)	26 (27.7)	<0.001
Death	17 (0.8)	4 (4.3)	0.012
GOS score			<0.001
Unfavourable	55 (2.7)	18 (19.1)	
Favourable	1969 (97.3)	76 (80.9)	
ICU LOS			<0.001
≥24 h	114 (5.6)	30 (31.9)	
<24 h	1910 (94.4)	64 (68.1)	
Postoperative hospital LOS (days)	11 (8–14)	15 (11–19)	<0.001
Hospitalization costs (RMB)	43 969 (35 514–54 044)	56 628 (40 624–75 428)	<0.001

GOS – Glasgow Outcome scale; ICU – intensive care unit; LOS – length of stay; RMB – Chinese yuan.

these factors, five preoperative and five intraoperative factors were significantly associated with postoperative failed extubation (p<0.05). These factors included preoperative history of craniotomy, ASA physical status, lower cranial nerve dysfunction, tumor size, tumor location, duration of surgery, estimated blood loss, fluid administration, fluid balance, and maximum change in BP during the operation. These 10 parameters were then included in multiple logistic regression analyses, and 5 factors were recognized as independent risk factors for postoperative failed extubation: craniotomy history, preoperative lower cranial nerve dysfunction, tumor size, tumor position, and maximum change in BP during the operation (Table 4).

Analysis of the clinical outcomes for the successful extubation and failed extubation groups revealed that failed extubation was related to a higher incidence rate of pneumonia,

mortality, unfavorable GOS score, longer neuro-ICU and postoperative LOS, and higher hospitalization costs compared with successful extubation (p<0.05 for each comparison; Table 5).

Discussion

In patients submitted to infratentorial craniotomy, extubation is a major concern in clinical practice. Several studies have reported that patients after neurosurgery may have the risk of an increasing incidence of failed extubation, pneumonia, and longer MV [6,15–18]. However, as there is no uniform extubation criterion that can predict successful extubation, the decision to extubate relies almost exclusively on clinical judgment. To improve the quality of clinical practice, it is important to understand the risk factors related to extubation failure, which may

help to reduce mortality, morbidity, and cost [19]. The purpose of our study was to investigate the rate of and perioperative risk factors related to failed extubation for patients undergoing infratentorial craniotomy for tumor resection.

Extubation failure occurred in 4.4% of patients in our study. The rate is compatible with that described in a review by Brown and coworkers [20], who reported that extubation failure occurred in 6% of extubated patients. However, the incidence observed in the present study was higher than the range of 0.06% to 0.83% observed in general surgery [15,21,22], which may indicate that patients undergoing infratentorial craniotomy are a high-risk population for suffering postoperative extubation failure. Similar to our result, in a retrospective study including 145 patients undergoing infratentorial craniotomy, Cata et al. [21] reported that the incidence of endotracheal re-intubation was 0.83% within 24 hours after primary extubation in the OR and 6.25% within 48 hours after ICU admission. In addition, our extubation failure rate was lower than that presented in other studies in neurosurgical patients, which ranged between 8.2% and 16.8% [6,23–25]. Although the incidence rate of failed extubation in the high-risk population was low and avoided the negative consequences caused by extubation failure, 52.5% of patients suffering from delayed extubation (extubation was not attempted in the OR and patients were transferred to the neuro-ICU intubated), and delayed extubation may result in complications related to the airway. In addition, the differences among extubation failure rates in different studies may be related to the population being studied, the definition of extubation failure, and the surgical approach selected by surgeon in charge. Studies only focusing on patients admitted to the ICU may have a higher incidence of extubation failure than that reported for patients after general surgery.

As far as we know, this is the first study to identify the risk factors related to extubation failure following infratentorial craniotomy for tumor resection. In this study, history of craniotomy, lower cranial nerve dysfunction before surgery, tumor size, tumor position, and maximum change in BP during the operation were identified as independent risk factors associated

with extubation failure. These factors mainly related to lower cranial nerves and brain stem. The posterior fossa is a small space in the skull. The cranial nerves or respiratory center in the posterior fossa can be potential affected during surgery because of the small operating space. The normal integrity of the respiratory center relies on the full functionality of cranial nerves V, VII, IX, X, and XII. Impairment of cranial nerves IX, X, and XII can lead to swallowing dysfunction, which can result in silent aspiration and pneumonia. Dubey et al. [26] reported that 4.8% of patients undergoing infratentorial craniotomy suffer from cranial nerve palsy. In addition, immediate postoperative brain stem edema can directly affect the respiratory center and may lead to extubation failure after surgery [26].

It was interesting to find that history of craniotomy and maximum change in BP play an important role in predicting extubation failure after infratentorial craniotomy. History of craniotomy may increase the difficulty of the operation, and the cranial nerves and brain stem are more likely to be injured. The stimulation of the brain stem and cranial nerves can lead to sharp fluctuation in BP.

Long operation times are probably caused by complicated procedures and lead to more fluid administration, blood loss, and drug consumption, which accordingly increase the risk of brain edema, delayed recovery, and delayed extubation.

Conclusions

According to our study, history of craniotomy, preoperative lower cranial nerve dysfunction, tumor size, tumor position, and maximum change in BP during the operation were independent risk factors in connection with postoperative failed extubation in patients treated by infratentorial craniotomy.

Competing interests

The authors declare no conflict of interest in preparing this article.

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