




Incidence and Perioperative Risk Factors of Delayed Extubation following Pediatric Craniotomy for Intracranial Tumor: A 10-Year Retrospective Analysis in a Thailand Hospital

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Abstract

Background The determination of extubation (early or delayed) after pediatric craniotomy for intracranial tumor should be carefully considered because each has its pros and cons. The aim of this study was to investigate the incidence of the delayed extubation in these patients. The secondary goal was to identify the perioperative factors influencing the determination of delayed extubation.

Methods This retrospective study was performed in pediatric patients with intracranial tumor who underwent craniotomy at a university hospital between April 2010 and March 2020. Preoperative and intraoperative variables were examined. The variables were compared between the delayed extubation and early extubation group.

Results Forty-two of 286 pediatric patients were in the delayed extubation group with an incidence of 14.69%. According to multivariate analyses, the risk factors that prompted delayed extubation were the intracranial tumor size ≥ 55 mm (adjusted odds ratio [AOR], 2.338; 95% confidence interval [CI], 1.032–5.295; $p = 0.042$), estimated blood loss (EBL) $\geq 40\%$ of calculated blood volume (AOR, 11.959; 95% CI, 3.457–41.377; $p < 0.001$), blood transfusion (AOR, 3.093; 95% CI, 1.069–8.951; $p = 0.037$), duration of surgery ≥ 300 minutes (AOR, 2.593; 95% CI, 1.099–6.120; $p = 0.030$), and completion of the operation after working hours (AOR, 13.832; 95% CI, 2.997–63.835; $p = 0.001$).

Conclusions The incidence of delayed extubation after pediatric craniotomy was 14.69%. The predictive factors were the size of tumor ≥ 55 mm, EBL $\geq 40\%$ of calculated blood volume, blood transfusion, duration of surgery ≥ 300 minutes, and completion of surgery after routine working hours.

Keywords

- ▶ craniotomy
- ▶ extubation
- ▶ intracranial tumor
- ▶ pediatric

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Introduction

The incidence of pediatric intracranial tumors ranges from 2.47 to 6.06 per 100,000 children.¹⁻³ The determination of extubation at the end of the pediatric craniotomy should be carefully discussed between the neurosurgeons and anesthesiologists. In previous studies, the incidence of delayed extubation after pediatric craniotomy for intracranial tumor was reported to be 14.3 to 40.6%, depending on the location of the tumors.⁴⁻⁶ The benefits of prediction in delayed extubation after craniotomy are intensive care unit (ICU) personnel and equipment allocation, reduced probability of reintubation immediately following extubation with more postoperative complications,⁷ and prediction of tracheostomy probability.⁶ There is no consensus on the protocol for extubation after pediatric craniotomy. Some authors have suggested extubation following pediatric craniotomy should be delayed if the tumor was large, with preoperative midline shift, surgical time exceeding 6 hours, damage to lower cranial nerves (LCNs; especially IX, X, XI, XII), and if the child had hypothermia at the end of surgery.⁸ To our knowledge, the factors associated with delayed extubation after craniotomy for intracranial tumors in pediatric patients have not been studied in Thailand. The primary aim of this study was to investigate the incidence of delayed extubation following craniotomy in them and the secondary aims were to identify the various perioperative factors responsible for delayed extubation, and the comparison of clinical outcomes between early and delayed extubation.

Materials and Methods

After approval from the Chulalongkorn University Institutional Review Board (IRB no.807/64), the authors performed a retrospective study by reviewing the medical records of pediatric patients (0–15 years old) with intracranial tumor (supratentorial as well as infratentorial tumor) who underwent craniotomy at the King Chulalongkorn Memorial Hospital between April 2010 and March 2020. The included craniotomies were tumor resection and biopsies. The few emergency craniotomies were also included. The exclusion criteria were children with a tracheal tube in situ, tracheostomy planned to be performed at the same time as the craniotomy, repeat operation within 7 days, and incomplete medical data. Delayed extubation was defined as retaining the endotracheal tube in the patient before leaving the operating room. The preoperative data included patients' demographic characteristics, American Society of Anesthesiologists classification, coexisting diseases (i.e., respiratory, cardiac, or hematologic diseases), urgency of surgery, undergoing planned multiple operation at the same hospitalization, the location of tumor (supratentorial/infratentorial or both), the tumor size, presence of hydrocephalus, and LCN (IX, X, XI, or XII) dysfunction. The size of tumor was defined as the largest cross-sectional diameter of the tumor in millimeters. The hydrocephalus was diagnosed by preoperative brain imaging (computed tomography or magnetic resonance imaging). LCN dysfunction was determined by preoperative neurological examination. The pathology of tumor was included in the

analysis. The intraoperative data included anesthetic technique, dose of fentanyl administered, ease of airway management, intraoperative cardiovascular instability, use of steroid/mannitol/antiepileptic drug, estimated blood loss (EBL), incidence of massive transfusion, total volume of fluid and blood components administered, the patient position, duration of surgery, body temperature during emergence phase, and completion of operation during or after working hours. The anesthesia induction was either inhalational or intravenous and maintenance of anesthesia was with inhalation, total intravenous anesthesia (TIVA), or combination of inhalation and TIVA in air or nitrous oxide (N₂O). Intermittent boluses of the muscle relaxant and fentanyl were administered as and when needed. Hypothermia was prevented by several warming devices (forced air warmed devices and/or circulating-water mattress) as routine practice for pediatric neuroanesthesia. Decision to extubate or not was left at the discretion of the anesthesiologist managing the patient depending upon various factors such as preoperative condition, presence/absence of hydrocephalus, size of the tumor, and intraoperative events like cardiovascular instability and massive blood transfusion. The intraoperative cardiovascular instability was defined as hypotension (a decrease in mean arterial pressure of more than 20% from baseline) with or without vasopressor/inotropic agent support or bradycardia requiring atropine. Blood volume was calculated as 90 mL/kg for neonates, 80 mL/kg for infants younger than 1 year of age, and 75 mL/kg for children age more than 1 year.⁹ Massive blood transfusion was defined as transfusion of blood components including packed red cells (PRCs), fresh frozen plasma (FFP), and platelet concentrate (PC) more than 100% of calculated blood volume during the operation.

In addition, we studied the incidence of reintubation within 72 hours in early extubation group and the time to extubation after the end of surgery in delayed extubation group. We also compared the duration of ICU stay, duration of hospitalization, discharge status, and airway status at discharge.

Statistical Analysis

The sample size was calculated using the data from an observational study (unpublished data) which had a 21% incidence of delayed extubation after pediatric craniotomy. A 5% type I error rate was incorporated into the equation yielding a sample size was determined to be 256 patients. Categorical variables were presented as number and percentage (%). The continuous variables with normal distribution were presented as mean and standard deviations (mean \pm SD). The medians with the 25 and 75 percentiles (Q1, Q3) represented the nonnormally distributed continuous variables. Univariate analysis was used to compare between two categorical variables with chi-square test or Fisher's exact test, and two continuous variables with an independent sample *t*-test or Mann-Whitney *U* test, as per the normality distribution of the variables. The variables associated with delayed extubation ($p \leq 0.05$) by univariate analysis were included in the multivariate logistic regressions with forward stepwise (Wald) method to identify the predictive factors. Adjusted odds ratio (AOR) and 95% confidence interval (CI) were reported. Finally, receiver

operating characteristic (ROC) curve analysis was performed to validate the multivariate model. A *p*-value of <0.05 was regarded as statistically significant. All statistical analyses were performed using SPSS software, version 22.0.

Results

During the study period, 286 children who underwent craniotomy for intracranial tumor were included in our analysis. There were 42 patients in the delayed extubation group, with an incidence of 14.69%. The incidence of reintubation within 72 hours in the early extubation group was 2.87% (7 of 244 patients). The causes of reintubation were postoperative seizure, the new onset hydrocephalus, and swelling of the brain. Two patients could not be extubated; one of them died in the hospital while the second one was referred to a community hospital (with tracheal tube in situ) for further management. For the remaining 40 patients, the mean time of extubation was 28.28 hours (12.96, 38.73).

The preoperative data of the patients are shown in ► **Table 1**. The mean age of the children was 8.10 ± 4.45 years. The age of the children in both groups was comparable. Six patients who had emergency surgery were included in the study. Two of them were in the delayed extubation group. The number of patients who had emergency craniotomy was not significantly different between the two groups. By contrast, the intracranial tumor size was significantly different between the two groups (43.34 ± 20.18 mm in the early extubation group, 56.19 ± 20.03 mm in the delayed extubation group; $p < 0.001$). The pathologies of the tumor are shown in ► **Table 2**. In the univariate analysis, ependymoma was associated with delayed extubation after craniotomy ($p = 0.028$). The majority of the factors related to delayed extubation occurred intraoperatively such as EBL, blood transfusion, massive blood transfusion, total volume of blood components (PRCs, FFP, and PC) administration, total volume of crystalloids and colloids administration, duration of surgery, and completion of operation after working hours (► **Table 3**). There were significantly more number of children in the early extubation group who received N_2O ($p = 0.02$). In the multivariate logistic regression analysis, the intracranial tumor size ≥ 55 mm, EBL $\geq 40\%$ of calculated blood volume, blood transfusion, duration of surgery ≥ 300 minutes, and completion of operation after working hours were the statistically significant factors related to delayed extubation (► **Table 4**). The ROC curve analysis of this model to predict delayed extubation had an area under the curve of 0.875 (95% CI: 0.825–0.926) (► **Fig. 1**).

The clinical outcomes between the two groups were significantly different (► **Table 5**). The patients in the delayed extubation group had a longer duration in the ICU and hospital stay ($p = 0.002$ and $p = 0.020$, respectively).

Discussion

The incidence of delayed extubation following pediatric craniotomy for intracranial tumor in this study was 14.69% which is comparable to 14.29% in the study by Spentzas et al.⁴ Goethe

et al reported a higher incidence of delayed extubation, 40.6%, in children with infratentorial tumor surgery.⁶ Infratentorial tumor resection has a high probability to injure the brain stem that can affect respiratory function and awakening as well as injure the LCN that can affect the airway protective reflexes. Additionally, patients with infratentorial tumor have a higher risk for respiratory failure and death after craniotomy.¹⁰ All these factors result in delayed extubation in children following posterior fossa tumor surgery. Our study showed that the incidence of delayed extubation in supratentorial and infratentorial tumor was 12.97 and 17.17%, respectively, which were comparable. Failure to demonstrate a higher incidence of delayed extubation in infratentorial surgery compared with supratentorial surgery may be due to a fewer number of infratentorial tumor patients or tumor not encroaching on the brain stem.

The validity of our multivariate logistic regression model to predict delayed extubation following pediatric craniotomy for intracranial tumor was high according to the area under the ROC curve. From anesthesia management point of view, preoperative predictive factors for delayed extubation after pediatric craniotomy would be more beneficial compared with the intraoperative factors. We studied if the preoperative factors were responsible for delayed extubation and observed the tumor size was the only preoperative predictive factor that was associated with delayed extubation, specifically when the largest diameter of the tumor size was more than 55 mm with an AOR of 2.338 ($p = 0.042$). The larger brain tumor is associated with more surgical bleeding, more brain edema, and brain tissue shift after tumor removal which probably influences the patient's sensorium and neurological status.¹¹ We observed that the anesthesiologists managing the case refrained from extubation at the end of surgery when the tumor size was more than 55 mm. This observation may be helpful for the anesthesiologists to inform the parents about the probability of their child remaining intubated after the surgery.

Though there are studies on the factors for delayed extubation in adults following infratentorial surgery,^{12,13} there are no systematically conducted studies in pediatric population on factors for delayed extubation following brain tumor resection (supratentorial/infratentorial). Ziai et al¹⁴ reported that benign tumors in adult patients were associated with longer duration of ICU stay and utilized significantly more ICU resources because there was more aggressive resection of the benign tumors compared with malignant tumors. Goethe et al⁶ reported that children less likely extubated immediately postoperatively are likely to have ependymoma (41.7%) or astrocytoma (25%). Our study tried to find the correlation between pathology of tumor and delayed extubation after craniotomy. Ependymoma did show a statistical significance in the univariate analysis, but it did not remain significant in the multivariate model. The fewer number of ependymomas in our study might have resulted in failure to achieve a statistically significant level in the multivariate analysis.

In our study, most factors on which anesthesiologists decided to keep trachea intubated were encountered during surgery. It is well known that intraoperative EBL is an independent factor associated with delayed extubation after

Table 1 Patients' demographic and clinical characteristics

Variables	Total (n = 286)	Early extubation (n = 244)	Delayed extubation (n = 42)	p-Value
Sex				0.173
Male	167 (58.39)	147 (60.25)	20 (47.62)	
Female	119 (41.61)	97 (39.75)	22 (52.38)	
Age (y)	8.10 ± 4.45	8.25 ± 4.44	7.21 ± 4.47	0.162
Body weight (kg)	26.15 (16.68, 43.85)	26.35 (17.9, 45)	21.50 (15.55, 40.23)	0.303
Location of tumors				0.233
Supratentorial	185 (64.69)	161 (65.98)	24 (57.14)	
Infratentorial	99 (34.61)	82 (33.61)	17 (40.48)	
Both	2 (0.70)	1 (0.41)	1 (2.38)	
Tumor size (mm)	45.24 ± 20.64	43.34 ± 20.18	56.19 ± 20.03	< 0.001 ^a
Preoperative lower cranial nerves dysfunction	16 (5.59)	11 (4.51)	5 (11.90)	0.068
Preoperative hydrocephalus	158 (55.24)	131 (53.69)	27 (64.29)	0.268
ASA physical status				1.000
I-II	280 (97.90)	239 (97.95)	41 (97.62)	
III-IV	6 (2.10)	5 (2.05)	1 (2.38)	
Coexisting respiratory diseases	17 (5.94)	15 (6.15)	2 (4.76)	1.000
Coexisting cardiac disease	4 (1.40)	3 (1.23)	1 (2.38)	0.472
Coexisting hematologic disease	47 (16.43)	43 (17.62)	4 (9.52)	0.279
Multiple operations during the same hospitalization	61 (21.32)	50 (20.49)	11 (26.19)	0.529
Emergency surgery	6 (2.1)	4 (1.6)	2 (4.7)	0.217

Abbreviations: ASA, American Society of Anesthesiologists; SD, standard deviation.

Note: Data were expressed as number (%), mean ± SD, median (Q1, Q3).

^aSignificant at $p < 0.05$.

craniotomy in adult patients.^{12,13} Most anesthesiologists would assess the blood loss, volume of blood products, and fluid administration before determining whether to extubate or not because there are higher risks of hemodynamic instability and volume overload during and after surgery notwithstanding good physiologic reserve in children. They are able to maintain blood pressure even after a loss of 25 to 40% of calculated blood volume.¹⁵ The present study demonstrated that $EBL \geq 40\%$ of calculated blood volume was an independent factor that could predict delayed extubation after pediatric craniotomy. Vassal et al¹⁶ also reported that the use of postoperative mechanical ventilation was significantly higher in transfused pediatric patient following craniotomy. In our study, it is notable that all three children with massive blood transfusion were kept intubated, but we could not show that massive blood transfusion was statistically significant predictive factor in the multivariate analysis. It is possible that delayed extubation may be the result of the interplay of various factors apart from massive transfusion.

A larger tumor usually is associated with longer duration of surgery and has more risks of damaging the adjacent structures such as the LCN and brain stem.¹⁷ The longer duration of surgery may also reflect a more extensive surgery and complicated procedure.¹² Previous study in adult craniotomies for infratentorial tumor found that the operative duration for ≥ 6 hours was the independent factor related to delayed extubation.¹³ In the present study, we demonstrated that the duration of surgery for ≥ 5 hours was an independent predictor of delayed extubation after pediatric craniotomy. Additionally, Sogame et al¹⁸ suggested that duration of surgery for ≥ 5 hours increases the risk for postoperative pulmonary complication after intracranial surgery in adults which would also increase the duration of ICU stay. We too observed children who had delayed extubation spent more time in the ICU as well as in the hospital, possibly from increased clinical or subclinical pulmonary complications.

We have no explanation as how N_2O facilitated early extubation. Even literature search did not throw any light on

Table 2 Pathology of tumor in early extubation and delayed extubation groups

Pathology	Total (n = 286)	Early extubation (n = 244)	Delayed extubation (n = 42)	p-Value
Gliomas: astrocytoma, glioblastoma, etc.	83 (29.02)	73 (29.92)	10 (23.81)	0.534
Ependymomas	31 (10.84)	22 (9.02)	9 (21.43)	0.028 ^a
Embryonal tumors: medulloblastoma, ATRT	48 (16.78)	42 (17.21)	6 (14.29)	0.806
Tumors of the sellar region: craniopharyngioma, pituitary adenoma	38 (13.28)	36 (14.75)	2 (4.76)	0.129
Germ cell tumors: teratoma, germinoma, etc.	23 (8.04)	19 (7.79)	4 (9.52)	0.757
Arachnoid cyst	14 (4.90)	13 (5.33)	1 (2.38)	0.701
Hematolymphoid tumors: lymphoma, histiocytosis, juvenile xanthogranuloma	7 (2.45)	7 (2.87)	0 (0.00)	0.599
Others	42 (14.69)	32 (13.11)	10 (23.81)	0.116

Abbreviation: ATRT, atypical teratoid/rhabdoid tumor.

Note: Data were expressed as number (%).

^aSignificant at $p < 0.05$.

Table 3 Univariate analysis of intraoperative factors in early extubation and delayed extubation groups

Variables	Total (n = 286)	Early extubation (n = 244)	Delayed extubation (n = 42)	p-Value
Positioning				0.415
Supine	157 (54.90)	138 (56.55)	19 (45.24)	
Lateral	23 (8.04)	18 (7.38)	5 (11.90)	
Prone	103 (36.01)	86 (35.25)	17 (40.48)	
Multiple positions	3 (1.05)	2 (0.82)	1 (2.38)	
Intraoperative difficult airway	5 (1.75)	3 (1.23)	2 (4.76)	0.158
Intraoperative cardiovascular instability	50 (17.48)	41 (16.80)	9 (21.43)	0.611
Anesthetic techniques				0.367
Inhalation	256 (89.51)	219 (89.75)	37 (88.10)	
TIVA	2 (0.70)	1 (0.41)	1 (2.38)	
Combination of inhalation and TIVA	28 (9.79)	24 (9.84)	4 (9.52)	
Nitrous oxide use	226 (79.02)	199 (81.56)	27 (64.29)	0.020 ^a
Dose of fentanyl (mcg/kg/h)	0.60 ± 0.30	0.59 ± 0.27	0.68 ± 0.45	0.253
Steroid use	240 (83.92)	205 (84.02)	35 (83.33)	1.000
Mannitol use	106 (37.06)	95 (38.93)	11 (26.19)	0.160
AED use	152 (53.15)	131 (53.69)	21 (50.00)	0.783
EBL (% of calculated blood volume)	11.93 (6.02, 24.16)	10.28 (5.56, 18.38)	26.10 (16.38, 54.63)	< 0.001 ^a
Blood transfusion	148 (51.75)	111 (45.49)	37 (88.10)	< 0.001 ^a
Massive blood transfusion	3 (1.05)	0 (0.00)	3 (7.14)	0.003 ^a
Volume of blood transfusion (mL/kg)	2.82 (0.00, 8.69)	0.00 (0.00, 7.21)	9.87 (5.18, 23.88)	0.002 ^a
Crystalloid (mL/kg)	46.23 ± 23.21	43.24 ± 19.94	63.60 ± 32.03	< 0.001 ^a
Colloid (mL/kg)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	5.59 (0.00, 15.36)	0.001 ^a
Urine output (mL/kg/h)	4.48 ± 2.66	4.53 ± 2.71	4.19 ± 2.35	0.443
BT at emergence < 35°C	7 (2.45)	7 (2.87)	0 (0.0)	0.599

(Continued)

Table 3 (Continued)

Variables	Total (n = 286)	Early extubation (n = 244)	Delayed extubation (n = 42)	p-Value
Duration of surgery (min)	275.64 ± 113.74	254.98 ± 87.07	395.62 ± 166.47	< 0.001 ^a
Completion of the operation after working hours	168 (58.74)	129 (52.87)	39 (92.86)	< 0.001 ^a

Abbreviations: AED, antiepileptic drugs; BT, body temperature; EBL, estimated blood loss; SD, standard deviation; TIVA, total intravenous anesthesia. Note: Data were expressed as number (%), mean ± SD, median (Q1, Q3).

^aSignificant at $p < 0.05$.

Table 4 Stepwise forward regression analysis of the predictive factors for delayed extubation in pediatric craniotomy

Factors	Adjusted odds ratio	95% confidence interval	p-Value ^a
Tumor sizes ≥ 55 mm	2.338	1.032–5.295	0.042
Estimated blood loss $\geq 40\%$ of calculated blood volume	11.959	3.457–41.377	< 0.001
Blood transfusion	3.093	1.069–8.951	0.037
Duration of surgery ≥ 300 min	2.593	1.099–6.120	0.030
Completion of the operation after working hours	13.832	2.997–63.835	0.001

^aSignificant at $p < 0.05$.

it. We speculate more number of patients with small tumors/biopsies received N₂O. However, this issue needs further exploration.

Time of completion of craniotomy was another determinant of early or delayed extubation. The anesthesiologists preferred to retain the tracheal tube among children whose surgery finished beyond the routine working hours. This is consistent with previous finding from a cervical spinal study in adult patients.¹⁹ Completion of surgery after working hours has its own risks; there will be fewer, lesser experi-

enced and more exhausted health care providers in the ICU. Therefore, the anesthesiologists like to leave patient intubated for mechanical ventilation for patient safety. Extubation protocol after pediatric craniotomy and scheduled arrangement for finishing the operation within the working hours should be developed to improve the patient's safety.

There were some limitations in our study. First, this was a single-institution retrospective study, which can be influenced by the inherent biases and local practices related to our medical personals' experience and team setting. The observations from our study cannot be generalized to all pediatric neurosurgical centers. Second, health care records of some patients documented only the largest diameter of the tumor instead of the tumor dimensions. It is possible that the tumor volumes or tumor size compared with the size of cranium may be a better predictor of extubation. Third, the various locations of tumor in the study might affect the predictive factors. Moreover, our study included emergency patients who may not be in good neurological condition to warrant immediate extubation following craniotomy irrespective of tumor site, size, and pathology. However, in our study, very few children were operated in emergency and they were in both groups. We strongly feel that their inclusion is unlikely to alter our results. Last, the sample size of this study was relatively small. We recommend a multicenter prospective study with a large sample size to develop an extubation protocol in these patients.

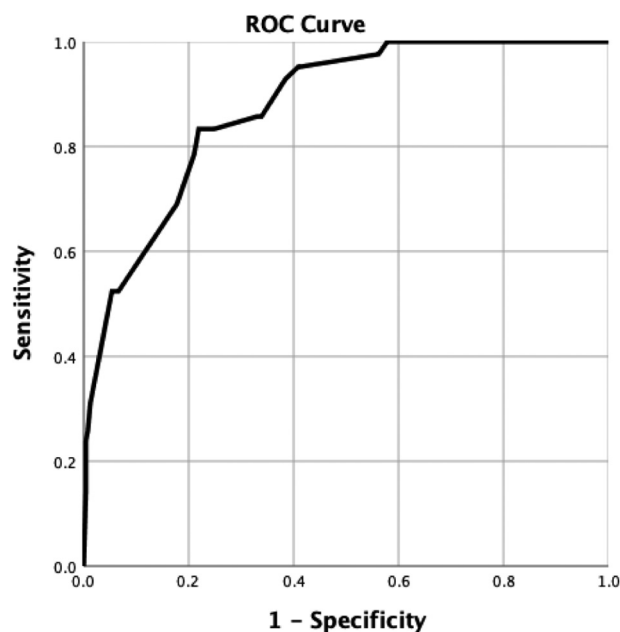


Fig. 1 Receiver operating characteristic curve of the multivariate logistic regression model to predict delayed extubation after pediatric craniotomy for intracranial tumor. The area under the curve was 0.875 with 95% confidence interval of 0.825–0.926.

Conclusions

This retrospective study demonstrated that the incidence of delayed extubation after pediatric craniotomy for intracranial tumor was 14.69%. The only preoperative predictive factor was the intracranial tumor size that was ≥ 55 mm. The intraoperative factors predicting delayed extubation were

Table 5 Clinical outcomes of the patients

Outcomes	Total (n = 286)	Early extubation (n = 244)	Delayed extubation (n = 42)	p-Value ^a
Duration of ICU stay (d)	1 (1, 2)	1 (1, 2)	2 (1.25, 7)	0.002
Duration of hospital stay (d)	17 (10, 27)	16 (10, 26)	22.5 (14.25, 36)	0.020
Discharge status				< 0.001
Home	281 (98.25)	243 (99.59)	38 (90.48)	
Refer for further care	4 (1.40)	1 (0.41)	3 (7.14)	
Death	1 (0.35)	0 (0.00)	1 (2.38)	
Airway status at discharge				0.001
Normal	278 (97.20)	240 (98.36)	38 (90.48)	
Endotracheal tube	2 (0.70)	0 (0.00)	2 (4.76)	
Tracheostomy	6 (2.10)	4 (1.64)	2 (4.76)	

Abbreviation: ICU, intensive care unit.

Note: Data were expressed as number (%), median (Q1, Q3).

^aSignificant at $p < 0.05$.

EBL more than 40% of calculated blood volume, blood transfusion, duration of surgery longer than 300 minutes, and completion of surgery after routine working hours. This information may be beneficial to the anesthesiologists who have to prepare the postoperative arrangements and to inform the parents about further care.

Conflict of Interest

None declared.

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