Factors Influencing Prolonged Intensive Care Unit Length of Stay after Craniotomy for Intracranial Tumor in Children: A 10-year Analysis from a University Hospital

Sunisa Sangtongjaraskul[1], Surunchana Lerdsirisopon[2], Vorrachai Sae-phua[3], Sukanya Kanta[4], Lalida Kongkiattikul[5]

Received on: 31 January 2023; *Accepted on:* 04 February 2023; *Published on:* 28 February 2023

Abstract

Background: Postoperative intensive care unit (ICU) admission is routinely practiced in pediatric and adult craniotomy. This study aims to identify the factors associated with an ICU stay of more than one day (prolonged ICU stay, PIS) after pediatric brain tumor surgery.

Methods: Medical records of children who underwent craniotomy for brain tumor during a 10-year period were reviewed and analyzed. Perioperative variables were examined and compared between the one-day ICU stay (ODIS) and PIS groups.

Results: A total of 314 craniotomies performed on 302 patients was included. Patients requiring postoperative ICU care for more than a day represented 37.9% of the sample. Significant factors found in the multivariate analysis affecting prolonged ICU length of stay included operative time ≥360 minutes (adjusted odds ratio [AOR], 2.438; 95% confidence interval [CI]: 1.223–4.861; $p = 0.011$), presence of an endotracheal (ET) tube (AOR, 7.469; 95% CI: 3.779–14.762; $p < 0.001$), and external ventricular drain (EVD) at ICU admission (AOR, 2.512; 95% CI: 1.458–4.330; $p = 0.001$).

Conclusion: While most children undergoing a craniotomy for brain tumor need a postoperative ICU care of ≤1 day, slightly more than a one-third in our study stayed longer. The prediction of a PIS can be beneficial for optimal resource utilization, increasing ICU bed turnover rate, reduction of operation cancellation, and improved preparation for parent expectations.

Keywords: Brain tumor, Craniotomy, Length of stay, Pediatric intensive care unit, Postoperative complications.

Indian Journal of Critical Care Medicine (2023): 10.5005/jp-journals-10071-24418

Highlights

The prediction of PIS after craniotomy for intracranial tumor in children might be beneficial for optimal resource utilization. Anesthetic technique and intraoperative events did not relate to the ICU length of stay. The independent factors associated with prolonged ICU length of stay were the operative time ≥360 minutes, presence of ET tube, and EVD in placed at ICU admission.

Introduction

Brain tumors are the most common solid tumor in children with an incidence of 6.06 per 100,000 children.[1] Incidence of postoperative complications after brain tumor surgery ranges from 7.4 to 14.3% depending on the definition.[2,3] Postoperative ICU admission for at least one day is routinely practiced in pediatric and adult craniotomy for close monitoring, early detection, and treatment of complications.[4–6] The pediatric ICU in general hospitals admit both medical and surgical patients of which about 20% were neurocritical care patients.[7] Pediatric ICU beds are often limited while ICUs need specialized trained personnel and complex equipment. The cost of ICU care is one of the largest expenditures of a hospital due to the consumption of significant resources such as expensive medication and monitoring. Predicting ICU length of stay can be helpful in optimal resource allocation with respect to both beds and personnel. It also can reduce unintentional cancellation of operations due to the lack of postoperative ICU capacity.[6]

Numerous studies have reported factors associated with prolonged ICU length of stay after craniotomy in adult patients.[5,8,9] Studies in children are limited with some studies did not explore specific in cases of pediatric brain tumor.[4,10,11] This study aims to identify the factors associated with an ICU stay of more than one day after pediatric brain tumor surgery. Additionally, postoperative complications and patient outcomes are also reviewed in this study.

[1,3]Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; Department of Anesthesiology, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

[2]Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

[4]Department of Anesthesiology, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

[5]Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Corresponding Author: Sunisa Sangtongjaraskul, Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; Department of Anesthesiology, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand, Phone: +66935569556, e-mail: sunisa.sa@chula.ac.th

How to cite this article: Sangtongjaraskul S, Lerdsirisopon S, Sae-phua V, Kanta S, Kongkiattikul L. Factors Influencing Prolonged Intensive Care Unit Length of Stay after Craniotomy for Intracranial Tumor in Children: A 10-year Analysis from a University Hospital. Indian J Crit Care Med 2023;27(3):205–211.

Source of support: Nil

Conflict of interest: None

Methods

The medical records of patients aged 0–15 years who underwent craniotomy for intracranial tumor between April 2010 and March 2020 at King Chulalongkorn Memorial Hospital, Bangkok, Thailand were analyzed. Inclusion criteria were all craniotomies for intracranial tumor resection/biopsy and elective/emergency conditions. Children with incomplete medical records were excluded. The study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB no. 904/64). The consent was waived due to the retrospective nature. Patient data were kept confidential.

The ICU length of stay was defined as the interval from the end of surgery to the date of ICU discharge. The patients were divided into two groups based on ICU length of stay: ODIS and PIS. The ODIS group defined as a 1-day ICU stay included overnight admission. The length of stay in the ODIS group might range from a few hours for a late evening admission to 24 hours for an early morning admission. The PIS group was defined as having an ICU stay of more than 1 day. In our institution, the pediatric ICU is a 10-bed medical and surgical unit with almost 600 admissions per year. Pediatric craniotomy patients are routinely admitted to ICU postoperatively. Some children with a body weight of more than 25 kg might be admitted to the adult neurosurgical ICU. In general, discharge criteria from either pediatric or neurological ICU depend on decision of the neurosurgeons and the pediatric intensivists such as patients' status, comorbidities, and the presence of neurological complications which need closely monitoring.

We collected preoperative data including patient characteristics, American Society of Anesthesiologists (ASA) classification, concomitant diseases (i.e., cardiac, respiratory, or hematologic diseases), presence of hydrocephalus or lower cranial nerve (CN IX, X, XI or XII) dysfunction, ET tube *in situ*, history of re-craniotomy for tumor resection, undergoing multiple neurosurgical procedures during the same admission, urgency of surgery, type of craniotomy (biopsy/resection), size and location of tumor (supratentorial/infratentorial), and histology of tumor. The size of the tumor was defined by the largest cross-sectional diameter of the tumor in millimeters measured from preoperative brain imaging. The intraoperative variables included anesthetic technique (inhalation/total intravenous anesthesia [TIVA]/combined), total dosage of fentanyl, patient positioning, presence of cardiovascular instability or difficult airway event, steroid/mannitol/antiepileptic drug (AED) administration, presence of hypothermia (body temperature: <35°C), hyperglycemia (blood sugar: >200 mg/dL), estimated blood loss (EBL), presence of blood transfusion, total volume of fluid and blood components administered, and duration of surgery. Cardiovascular instability was described as hypotension (decrease in mean arterial pressure of more than 20% from baseline) with or without vasopressor/inotropic agent required and/or bradycardia required atropine. The postoperative variables collected at ICU admission included ICU admission after working hours, ET tube *in situ*, EVD placement, fever (body temperature >38.3°C), hyperglycemia (blood sugar: >200 mg/dL), and dysnatremia (serum sodium: <135 and >145 mEq/L).

The incidence of ICU readmission within 72 hours was also studied. The clinical outcomes of the patients analyzed were length of ICU and hospital stay, discharge status, and postoperative complications including intracerebral hemorrhage (ICH) with or without re-craniotomy, infection, electrolyte disturbances (diabetes insipidus [DI], cerebral salt wasting [CSW], or syndrome of inappropriate antidiuretic hormone secretion [SIADH]), and others (hydrocephalus, seizure).

Statistical Analysis

All statistical analyses were performed using SPSS software version 22.0. Categorical variables were represented as numbers and percentages. Continuous variables were represented with mean and standard deviation (mean $\pm$ SD) or median and interquartile range using the 25 and 75 percentiles (IQR: Q1–Q3) depending on the normality of the distribution. Normality was tested by the Kolmogorov–Smirnov test. The comparison between two categorical variables used either Chi-square test or Fisher's Exact test. Continuous variables were compared by an independent sample *t*-test or Mann–Whitney *U*-test. The variables associated with PIS ($p \leq 0.05$) by the univariate analysis were included in the multivariate logistic regression which used the forward stepwise (Wald) method to identify associated factors. Adjusted odds ratio and 95% CI were reported. The receiver operating characteristic (ROC) curve analysis was performed to validate the multivariate model. A *p*-value of <0.05 was selected as the significance threshold.

Results

During the study period, 307 children underwent craniotomies for intracranial tumor. Five patients were excluded due to incomplete medical data. Eleven patients underwent a second or third craniotomy in the same hospitalization for a total of 314 craniotomies from 302 patients included in the analysis. The median age was 8 (4–12) years old. The overall median ICU and hospital length of stay were 1 (1–2) days and 18 (11–28) days. Postoperative complications were reported in 55.41% of patients. One hundred and nineteen patients (37.90%) stayed in the ICU for more than one day after craniotomy (PIS group). Factors including age, body weight, tumor size, ASA physical status, preoperative hydrocephalus, ET tube *in situ*, and undergoing multiple neurosurgical procedures during the same admission were statistically different between the groups (Table 1). The neurosurgical procedures in the same admission were ventriculoperitoneal shunt, subdural hygroma drainage, or re-craniotomy for ICH or tumor resection. Patient age in the PIS group was significantly higher than the ODIS group ($p = 0.014$) (Fig. 1). Body weight was also significantly higher in the PIS group compared to the ODIS group ($p = 0.046$).

The intraoperative and postoperative variables are shown in Table 2. Anesthetic techniques and total dosage of fentanyl administration did not show statistically significant differences between the ODIS and PIS groups ($p = 0.061$ and $p = 0.288$, respectively). In the univariate analysis, intraoperative hypothermia, hyperglycemia, EBL, blood transfusion, volume of blood components, crystalloid, colloid administration, and the duration of surgery were found to be significantly higher in the PIS group than the ODIS group. Additionally, ICU admission after working hours, presence of ET tube or EVD placement, fever, hyperglycemia, and dysnatremia at ICU admission was also significantly higher in the PIS group. In the multivariate logistic regression analysis, an operative time ≥360 minutes, presence of an ET tube, and EVD at ICU admission were statistically significant factors associated with a PIS (Table 3). The ROC curve analysis of this model had an area under the curve (AUC) of 0.757 (95% CI: 0.700–0.814) (Fig. 2).

Table 1: Preoperative patients characteristics of ODIS and PIS groups

Variables	*ODIS (n = 195)*	*PIS (n = 119)*	*p-value*
Sex			0.335
Male	117 (60.00)	64 (53.78)	
Female	78 (40.00)	55 (46.22)	
Age (year)	8.00 (3.00–11.00)	10.00 (6.00–13.00)	**0.014**
BW (kg)	23.00 (16.20–41.00)	27.40 (19.00–46.00)	**0.046**
ASA Physical status			**0.005**
I-II	187 (95.90)	103 (86.55)	
III-IV	8 (4.10)	16 (13.45)	
Concomitant diseases			
Respiratory diseases	14 (7.18)	8 (6.72)	1.000
Cardiac disease	1 (0.51)	3 (2.52)	0.154
Hematologic disease	37 (18.97)	20 (16.81)	0.739
Preoperative lower cranial nerves dysfunction	9 (4.62)	7 (5.88)	0.817
Preoperative hydrocephalus	101 (51.79)	82 (68.91)	**0.004**
ET tube *in situ*	3 (1.54)	14 (11.76)	<**0.001**
Prior re-craniotomy	59 (30.26)	32 (26.89)	0.610
Multiple neurosurgical procedures during the same admission	41 (21.03)	44 (36.98)	**0.003**
Emergency surgery	8 (4.10)	8 (6.72)	0.447
Location of tumors			0.157
Supratentorial	127 (65.13)	72 (60.50)	
Infratentorial	68 (34.87)	45 (37.82)	
Both	0 (0.00)	2 (1.68)	
Tumor size (mm)	43.23 (±19.55)	49.05 (±21.81)	**0.015**
Type of craniotomy			0.732
Biopsy	13 (6.67)	6 (5.04)	
Tumor resection	182 (93.33)	113 (94.96)	
Pathology			0.460
Gliomas: astrocytoma, glioblastoma, etc.	53 (27.18)	35 (29.41)	
Ependymomas	20 (10.25)	13 (10.92)	
Embryonal tumors: medulloblastoma, ATRT	42 (21.54)	15 (12.61)	
Craniopharyngioma and tumors of the sellar region	25 (12.82)	15 (12.61)	
Germ cell tumors: teratoma, germinoma, etc.	16 (8.21)	14 (11.76)	
Others	39 (20.00)	27 (22.69)	

Data are presented as number (%), mean ± SD or median (Q1–Q3). Bold values denote statistically significant difference ($p < 0.05$); ATRT, Atypical teratoid/rhabdoid tumor; mm, millimeters.

Postoperative complications and clinical outcomes are shown in Table 4. Readmission of ICU within 72 hours was found in five children which did not show statistical difference between the groups. Two patients were diagnosed with DI, two patients had postoperative seizure from obstructed EVD, and one patient had ICH required re-craniotomy. The hospital length of stay was longer in the PIS group than the ODIS group [16 (10–22) days, and 24 (15–35) days, respectively]. Postoperative complications including ICH with or without re-craniotomy, infections (central nervous system infection, surgical site infection (SSI), pneumonia, urinary tract infection, septicemia, and infected of unknown origin), electrolytes disturbances (DI, CSW, or SIADH), and other complications (seizure, hydrocephalus, pleural effusion, etc.) were found to be significantly higher in the PIS group (Table 4). Patients who required hospital transfer for further treatment or died were higher in the PIS group ($p = 0.012$).

Discussion

The present study revealed that 119 patients (37.90%) required postoperative ICU care for more than a day. These results are in keeping with the study by Spentzas et al. who reported 29.52% of their population required a stay of >24 hours.[4] The median ICU length of stay after craniotomy of 1 (1–2) day was comparable to the previous study.[4] Age, body weight, tumor size, ASA physical status, preoperative hydrocephalus, ET tube *in situ*,

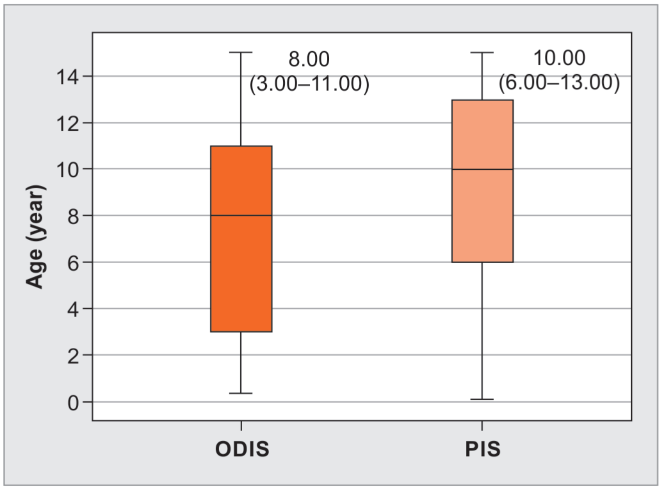

Fig. 1: The median age of patients were significantly higher in the PIS group than the ODIS group ($p = 0.014$). Values are presented as median (Q1–Q3)

underwent multiple neurosurgical procedures during the same admission, the intraoperative hypothermia, hyperglycemia, EBL, blood transfusion, volume of blood components, crystalloid, and colloid administration, the duration of surgery, time of ICU admission after working hours, presence of an ET tube or EVD in placed at ICU, fever, hyperglycemia, and dysnatremia at ICU admission were significantly different between the ODIS and PIS groups. Only the operative time $\geq$360 minutes, the presence of ET tube and EVD in placed at ICU admission were the independent factors associated with a prolonged ICU length of stay from the multivariate regression model. The validation of this model was deemed good based on the area under the ROC curve of 0.757 with 95% CI: 0.700–0.814.

Younger age was found associated with a prolonged ICU length of stay after pediatric craniotomy for tumor resection in a previous study.[4] In contrast, our study reported that the median age in the PIS group was statistically higher than in the ODIS group ($p = 0.014$). We did not find any studies with similar results in the literature. We speculate that neurosurgeons tend to provide

Table 2: The comparison of intraoperative and postoperative variables between the two groups

Variables	*ODIS (n = 195)*	*PIS (n = 119)*	*p-value*
Intraoperative variables			
Positioning			0.053
Supine	111 (56.93)	59 (49.58)	
Prone	65 (33.33)	49 (41.18)	
Lateral	19 (9.74)	8 (6.72)	
Multiple positions	0 (0.00)	3 (2.52)	
Anesthetic techniques			0.061
Inhalation	174 (89.23)	100 (84.03)	
TIVA (propofol)	0 (0.00)	3 (2.52)	
Combined inhalation with propofol	21 (10.77)	16 (13.45)	
Dose of fentanyl (mcg/kg/hr)*	0.64 (±0.32)	0.60 (±0.33)	0.288
Intraoperative difficult airway event	2 (1.03)	3 (2.52)	0.371
Intraoperative cardiovascular instability	30 (15.38)	29 (24.37)	0.067
Steroid administration	163 (83.59)	101 (84.87)	0.886
Mannitol administration	71 (36.41)	48 (40.34)	0.565
Antiepileptic drug administration	103 (52.82)	61 (51.26)	0.879
Intraoperative hypothermia	24 (12.31)	30 (25.21)	**0.005**
Intraoperative hyperglycemia	3 (1.61)	7 (6.09)	**0.047**
EBL (ml/kg)	8.81 (4.55–15.02)	11.43 (5.00–21.28)	**0.004**
Blood transfusion	98 (50.26)	76 (63.87)	**0.025**
Volume of blood transfusion (ml/kg)	0.00 (0.00–7.57)	5.93 (0.00–10.40)	**0.005**
Crystalloid (ml/kg)	38.63 (28.00–51.20)	50.00 (36.50–64.00)	<**0.001**
Colloid (ml/kg)	0.00 (0.00–0.00)	0.00 (0.00–7.50)	**0.010**
Urine output (ml/kg)	18.14 (9.44–25.87)	19.70 (12.07–30.00)	0.086
Duration of surgery (min)	230.00 (185.00–301.00)	290.00 (225.00–375.00)	<**0.001**
Postoperative variables at ICU admission			
ICU admission after working hours	124 (63.59)	95 (79.83)	**0.004**
ET tube *in situ*	14 (7.18)	51 (42.86)	<**0.001**
EVD placed	51 (26.15)	61 (51.26)	<**0.001**
Fever (>38.3°C)	16 (8.21)	4 (3.36)	0.142
Hyperglycemia	68 (36.76)	38 (33.04)	0.596
Dysnatremia	39 (20.10)	29 (24.37)	0.455

Data were expressed as number (%), mean ± SD, median (Q1–Q3). Bold values denote statistically significant difference ($p < 0.05$). *ml/kg/hours of operative time less invasive surgery in smaller children which might require less intensive care postoperatively. This would need confirmation in a future study.

A previous study in adults found TIVA was associated with shorter ICU stays after elective craniotomy.[6] TIVA seems to be more suitable for patients with brain surgery compared to inhalation technique in terms of intracranial pressure reduction and higher cerebral perfusion pressure. However, the anesthetic techniques were not significantly associated with ICU length of stay in our study. Notably, all three children with TIVA were in the PIS group. It might be due to the fact that anesthesiologists often provide TIVA to children with large lesions and at high risk of intracranial hypertension.

Table 3: Multivariate logistic regression analysis of the factors influencing PIS in pediatric craniotomy

Factors	*AOR*	*95% CI*	*p-value*
Operative time ≥360 min	2.438	1.223–4.861	**0.011**
ET tube *in situ* at ICU admission	7.469	3.779–14.762	**<0.001**
Postoperative EVD	2.512	1.458–4.330	**0.001**

Bold values denote statistically significant difference ($p < 0.05$)

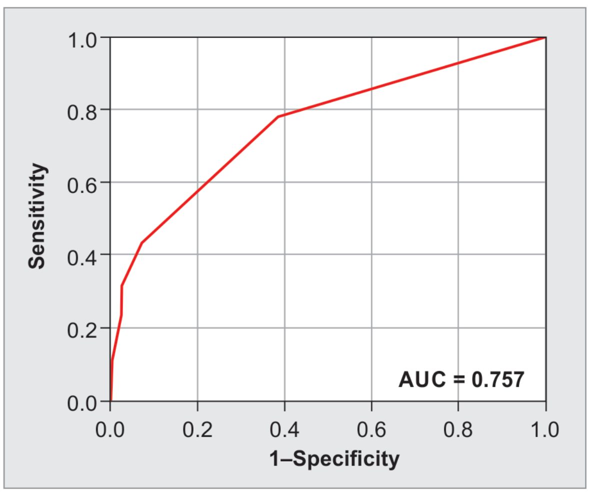

Fig. 2: Receiver operating characteristic curve of the multivariate logistic regression model to predict prolonged ICU stay after pediatric craniotomy for intracranial tumor. The area under the curve is 0.757 with 95% confidence interval 0.700–0.814 ($p < 0.001$)

The duration of anesthesia and operation was also one of the predictors of ICU length of stay after craniotomy.[6] The prolonged surgery might indicate a more invasive procedure or a complex surgery.[12] It is consistent with our study that surgery of more than 6 hours was the one of predictive factors for prolonged ICU length of stay. The duration of craniotomy for longer than 5 hours was also associated with postoperative pulmonary complications.[13]

Our study revealed that postoperative EVD was an independent factor of prolonged ICU length of stay. Postoperative EVD is a common therapy after intracranial tumor resection. EVD is used to monitor intracranial pressure and drain excess cerebrospinal fluid (CSF) or residual blood.[14] EVD system management require well-trained nurses and physicians, to monitor CSF drainage and dress the insertion site correctly for CSF leak detection.[15] Common complications related to EVD are meningitis, under/over drainage, and dislodgment.[16] Patients with EVD are often admitted to an ICU. At our hospital, most patients with EVD are admitted to ICU and transferred to the ward when clinically stable. Weaning from EVD before removing or converting to permanent CSF diversion is performed in the ward.

The most substantial predictive factor for prolonged ICU length of stay in our study was ET tube *in situ* on ICU arrival, which increased the probability of ICU stay of more than a day by 7.47 times compared to extubated children. This is consistent with findings from previous studies.[4,5,8] Intubated patients need a mechanical ventilator (MV) and intensive care such as tracheal suction and feeding via nasogastric tube. Our study showed that the duration of MV requirements were significantly longer in the PIS group compared to the ODIS group (164.36 ± 416.87 and 10.84 ± 4.92 hours, respectively.) Moreover, patients with unsuccessful extubation from the operating room might expect damage to the adjacent structures including the lower CN and brain stem.

In our results, it was not unexpected to find significantly greater EBL, volume of blood components, crystalloid, and colloid administration associated with prolonged ICU length of stay. Spentzas et al. also reported that EBL was a predictor of an ICU stay of more than 1 day in pediatric brain tumor surgery.[4] Our multivariate model did not demonstrate that these factors were predictive of a prolonged ICU length of stay. The literature also revealed that other predictive factors such as tumor severity score (assessed from midline location, mass effect, and midline shift),[4,5] tumor type,[8] diabetes patients,[9] blood transfusion requiement,[9] older adult patients,[9] and re-exploration surgery[10] were associated with prolonged ICU length of stay after craniotomy.

Table 4: Postoperative complications and clinical outcomes of the patients

Outcomes	*ODIS (n = 195)*	*PIS (n = 119)*	*p-value*
Readmission of ICU within 72 hours	2 (1.03)	3 (2.52)	0.371
Hospital length of stay (day)	16.00 (10.00–22.00)	24.00 (15.00–35.00)	**<0.001**
Postoperative ICH ± surgery	4 (2.05)	11 (9.24)	**0.009**
Postoperative infection: SSI, pneumonia	33 (16.92)	40 (33.61)	**0.001**
Postoperative electrolyte disturbance	48 (24.62)	46 (38.66)	**0.012**
Other postoperative complications: seizure, hydrocephalus	57 (29.23)	55 (46.22)	**0.003**
Discharge status			**0.012**
Home	194 (99.49)	112 (94.12)	
Refer for further care	1 (0.51)	4 (3.36)	
Death	0 (0.00)	3 (2.52)	

Data were expressed as number (%), median (Q1–Q3). Bold values denote statistically significant difference ($p < 0.05$)

The overall incidence of postoperative complications after craniotomy for intracranial tumor was 55.41%, which is comparable to the study by Mishra et al.[10] Postoperative electrolyte disturbances, especially abnormal serum sodium levels, was one of the most common complications in our study. Craniotomy for craniopharyngioma or tumors of the sellar region are commonly associated with postoperative dysnatremia which needs close monitoring of fluid balance and electrolytes in the ICU. Postoperative ICH was not frequent in our study (4.78%), similar to findings from a previous study in adults.[6] Almost half of our ICH patients required reoperation for hematoma removal, which required a longer ICU stay. Moreover, the likelihood of PISs also increases in cases of other postoperative complications such as infection, seizure, and hydrocephalus. All three children who died from medical conditions such as septicemia, pneumonia, and status epilepticus were in the PIS group. The poorer discharge status and longer hospital stay were significantly associated with a prolonged ICU length of stay.

An interesting issue is the need for postoperative ICU after craniotomy for brain tumor when compared to the cost of care and the rare life-threatening complications that can occur. Among selective elective craniotomy patients, the postoperative care at stepdown unit or neurosurgical ward was safe and increasingly reported in the adult literature.[9,17] Gabel et al.[18] studied elective craniotomy for brain tumor in children and reported that 90.15% (55 of 61) were safe initial admissions to wards postoperatively without transfer to ICU. This study also found that key factors related to transfer into ICU after initial admission to ward were primitive neuroectodermal tumor and repeat craniotomy in the same admission. The authors concluded that children undergoing elective craniotomy for brain tumor resection might be considered a candidate for postoperative admission to a non-ICU level ward. It would be beneficial in terms of overall cost savings and limited ICU resources. This issue was not covered in our study and needs to be investigated in future research.

The strength of our study is its focus on pediatric craniotomy for intracranial tumor which can help identify predictive factors for ICU length of stay for this population. A key limitation is the design, which is a retrospective, single institute study which might affect the analysis due to inherent bias and incomplete medical records. All our predictive factors could not be optimized before surgery due to these factors occurring in postoperative period. However, the results found could help physicians inform parents with children in the identified risk categories for postoperative care preparation. Lastly, although we reviewed the data in the 10-year period, the sample size was still relatively small for the statistical analysis. A prospective, multicenter center with larger sample sizes could provide a better ability to identify prognostic factors or create the prognostic scores for prediction of ICU length of stay in these populations.

Conclusion

This study found that most children undergoing craniotomy for brain tumors need only postoperative ICU care of $\leq$1 day. Independent factors associated with prolonged ICU length of stay were operative time $\geq$360 minutes, presence of ET tube, and EVD in placed at ICU admission. The prediction of PIS might be beneficial for optimal resource utilization, increasing ICU bed turnover rate, reduction of operation cancellation, and better preparation and understanding for parents of the children undergoing surgery. Identification of protocols to reduce or shorten these extended stays among patients with these characteristics should be the next step for inquiry.

Orcid

Sunisa Sangtongjaraskul https://orcid.org/0000-0002-2088-8444
Surunchana Lerdsirisopon https://orcid.org/0000-0003-2360-4088
Vorrachai Sae-phua https://orcid.org/0000-0002-7067-9755
Sukanya Kanta https://orcid.org/0000-0002-8760-1890
Lalida Kongkiattikul https://orcid.org/0000-0002-4150-039X

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