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Blood transfusion in pediatric intracranial tumor surgery

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Abstract

Background Pediatric central nervous system tumors are the most common solid tumors in children and leading cause of cancer-related morbidity and mortality. Various factors may influence the practice of blood transfusion during this tumor diagnosis. The primary aim of this study was to determine the factors that may influence intraoperative blood transfusion in pediatric patients undergoing surgery for intracranial tumors and to predict patients who may require blood transfusion.

Methods A retrospective study was performed in all pediatric patients younger than 15 years who underwent craniotomy for brain tumor removal from January 2018 to December 2023 in our institution. Preoperative, intraoperative and postoperative data were collected from medical and store anesthesia records. The predictors of intraoperative blood transfusion were determined using multivariate logistic regression.

Results A total of 138 patients were enrolled in the study, of whom 62 (44.9%) required intraoperative blood transfusion. In multivariate regression analysis age < 4 years and operating time > 490 min were determined as independent variables in terms of need for intraoperative blood transfusion. It was determined that the need for transfusion was higher in patient who were operated on urgently and patients with comorbidities ($p = 0.023$, $p = 0.005$).

Conclusion In conclusion, the findings obtained in this study suggest that age and surgical duration are independent risk factors for intraoperative blood transfusion in pediatric patients undergoing surgery for intracranial tumors. Particularly, in younger patients and prolonged surgeries, closer monitoring and awareness may enhance early detection, leading to the prevention of complications.

Keywords Pediatric neuroanesthesia, Volatil anesthesia, Blood transfusion

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Introduction

Pediatric central nervous system (CNS) tumors are the second most common malignancies in childhood and the most frequent solid tumors in children. In the United States, the incidence of primary brain and other CNS tumors in children and adolescents is approximately 5.67 per 100,000 individuals per year [1]. Supratentorial tumors are more commonly observed in infants and children up to 3 years of age and in those older than 10 years, while infratentorial tumors are more prevalent in children aged 4 to 10 years [2]. In younger children, embryonal tumors such as medulloblastoma and atypical teratoid/rhabdoid tumors have a higher incidence. In contrast, older individuals more frequently encounter tumors of glial origin. The symptoms and signs observed in patients depend on several factors, including the tumor's location, the child's age, and the tumor's growth rate [2, 3].

Anemia is one of the most common medical complications that occur during surgical procedures [4]. In general, studies encompassing all brain surgery procedures have reported an allogenic transfusion rate ranging from 1.7–5.4%. [4, 5] The reported incidence of transfusions for specific patient populations undergoing intracranial neurosurgery ranges from 10 to 95%. The risks associated with allogenic blood transfusion are significant, especially in children, where these risks have been particularly well-documented [7]. Transfusion-related complications include infectious diseases, allergic reactions, transfusion-related lung injury, and hemolytic reactions [8]. Allogenic blood transfusion may increase morbidity and mortality in the surgical population [9].

Prospective studies have shown that restrictive transfusion strategies are as effective as liberal approaches and, in certain instances, may offer superior outcomes [9–13]. However, in recent years, restrictive transfusion strategies have gained prominence worldwide due to clinical studies demonstrating significant transfusion-related risks and the escalating costs associated with transfusions.

The primary aim of this study was to identify the factors influencing intraoperative blood transfusion in pediatric patients undergoing surgery for intracranial masses and to predict which patients may require a blood transfusion.

Materials and methods

All pediatric patients with brain tumor operated at Dicle University Hospital between January 2018 and December 2023 were included in this retrospective and cross-sectional study. Ethical approval was received from the ethics committee of Dicle University Faculty of Medicine (dated March 20, 2024 number 99). Written and verbal informed consent for participation was obtained from all participants in the study. Between the specified dates, patients undergoing surgery for pediatric brain tumors were assessed based on the American Society of Anesthesiologists (ASA) classification, perioperative hemodynamic data, the need for intraoperative blood transfusion, the use of inotropes during surgery, the type of anesthesia administered, the anesthetic agents used, the postoperative status of patients (intubated or extubated), the duration of stay in the intensive care unit (ICU), whether a central venous catheter (CVC) was inserted, and the presence of CVC complications or malrotation. Additionally, radiological images and pathology records were reviewed. Patients aged ≥ 15 years and those undergoing brain surgery for reasons other than brain tumors were not included in the study.

All surgical procedures were performed under general anesthesia. The choice between inhalation and intravenous anesthesia induction technique was made by the attending anesthesiologist based on the presence of signs of intracranial hypertension in the patient. Following endotracheal intubation, general anesthesia was maintained with intravenous infusion of remifentanil (0.02–0.2 μg/kg/min) and propofol (Propofol, Fresenius Kabi, Sweden) (6–12 mg/kg/h) or sevoflurane (Sevoflurane Liquid 100%, Queenborough) at a concentration < 1 MAC. Routine intraoperative monitoring included electrocardiography, noninvasive arterial blood pressure, capnography, pulse oximetry, body temperature, and urinary output through a catheter. Following the induction of general anesthesia, an arterial catheter and a central venous line were placed.

Demographic data including age, sex, body weight, along with ASA classification, preoperative hemoglobin levels, coagulation parameters, and the localization of the intracranial mass (supratentorial or infratentorial based on tumor histology) were recorded. Intraoperative data such as the duration and year of operation, intraoperative position, intraoperative inotrope use, blood transfusion, and placement of CVC and arterial catheter were recorded. All patients were transferred to the ICU for postoperative follow-up. During the postoperative period, whether the patients were intubated or extubated, postoperative hemoglobin and hematocrit values, duration of ICU stay, and length of hospitalization were recorded.

Statistical analysis

SPSS 16.0 software for Windows (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Continuous data are expressed as mean and standard deviation, and categorical data are expressed as frequency and percentage. The categorical data of the groups were compared using the Chi-square and Fisher's exact tests. The Kolmogorov-Smirnov test was used to determine whether

the numerical data were normally distributed. The Student's t-test was used to analyze data with a normal distribution, while the Mann–Whitney U test was used to analyze no normally distributed data. In all comparisons, $p<0.05$ was considered significant.

Results

A total of 140 patients were included in the study. The records of one patient could not be obtained, and one patient was excluded from the study because of postoperative transfer, and the study was completed with 138 patients. Patients were divided into two groups according to the need for blood transfusion: Group 1 and Group 2. Group 1 consisted of 62 (44.9%) patients who received transfusion. Group 2 consisted of 76 (55.1%) patients who did not need transfusion (Fig. 1).

Univariate analysis

The groups were compared in terms of demographic data, preoperative laboratory values, intraoperative hemodynamic data, and other characteristics. Demographic data showed that mean age and body weight were lower in Group 1 than Group 2 ($p=0.006$ for both data), and the incidence of comorbidities was higher in Group 1 ($p=0.005$). There was no statistically significant difference between the two groups in terms of sex and ASA classification (Table 1). There was no statistically significant difference in tumor size between the groups. (Table 1).

Comparison of the groups in terms of emergency and elective surgical procedures showed that the need for transfusion was significantly higher in patients undergoing emergency surgery than patients undergoing elective surgery ($p=0.023$). Transfusion was not required for 42.8% (59 patients) of patients undergoing elective surgery. Comparison of groups in terms of preoperative laboratory values showed that preoperative hemoglobin levels were significantly lower in Group 1 than Group 2 ($p=0.027$). The duration of anesthesia and surgery was longer in Group 1 than Group 2 ($p=0.001$). Analysis of the groups in terms of inotrope use showed that all patients requiring intraoperative inotropes were in

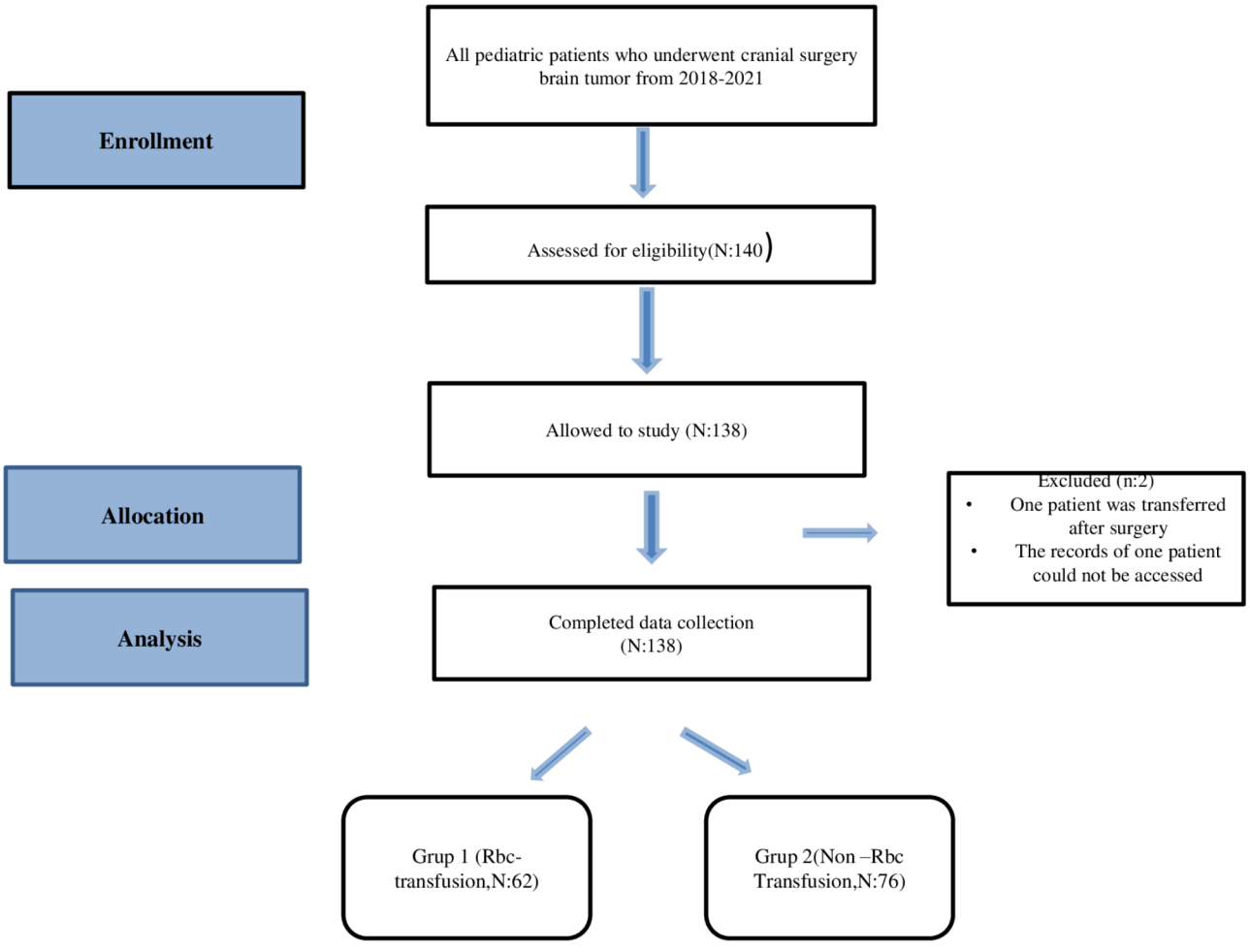

Fig. 1 Patient enrollment flowchart

Table 1 Demographic data of patients

Parameters	Group 1 (RBC-Transfusion, *n*:62)		Group 2 (Non-RBC Transfusion *n*:76)		*p* value
	Mean	**SD**	**Mean**	**SD**	
Age (y)	5.82	4.57	7.89	4.89	**0.006**
Weight	22.69	15.03	29.33	15.43	**0.006**
Hemoglobin (g/L)	11.56	1.32	12.36	1.63	**0.027**
Hematocrit (%)	35.94	3.9	37.34	4.31	0.15
Tumor size(mm)	41.8	11.9	39.2	9.5	0.157
Intensive care hospitalization period	22.21	17.13	18.33	14.38	0.3
Anesthesia duration	578.52	235.66	452.95	200.58	**0.001**
Surgery duration	545.82	227.78	421.15	191.36	**0.001**
Preoperative SpO^2	97.95	1.5	98.12	2.11	0.1
Intraoperative SpO^2	99.18	1.39	99.09	1.03	0.85
Postoperative SpO^2	98.62	2.04	98.51	1.31	0.93
Preoperative heart rate (bpm/min)	113.08	20.7	107.45	18.72	0.09
Intraoperative heart rate (bpm/min)	107.05	19.04	100.84	19.66	0.07
Postoperative heart rate (bpm/min)	116.39	26.45	96.47	19.06	**< 0.001**
Preoperative MAP (mmHg)	72.48	11.12	75.37	11.23	0.13
Intraoperative MAP (mmHg)	67	8.81	72.71	10.51	**< 0.001**
Postoperative MAP (mmHg)	65.19	9.28	71.48	9.81	**0.001**
	Frequency	**Percent**	**Frequency**	**Percent**	
Gender					0.15
Male	37	26.8	36	26.1	
Female	25	18.1	40	29	
ASA classification					0.054
1	8	5.8	19	13.9	
2	34	24.8	38	27.7	
3	15	10	19	13.9	
4	4	2.9	0	0	
Surgery type					**0.023**
Emergency	25	18.1	17	12.3	
Elective	37	26.8	59	42.8	
Comorbitidy					**0.005**
Yes	13	9.4	4	2.9	
No	49	35.5	72	52.2	
Anesthetic agent					0.25
Sevoflurane	21	15.2	19	13.8	
TIVA	41	29.7	57	41.3	
Inotrop using					**0.025**
Yes	4	2.9	0	0	
No	58	42.1	76	100	
Postoperative					**0.004**
Extubated	10	7.2	29	21	
Intubated	52	37.7	47	34.1	
Mortality					0.053
Nonsurvivor	8	5.8	3	2.2	
Survivor	54	39.1	73	52.9	
Patient positions					0.48
Supine	28	20.3	39	28.3	
Prone	30	21.7	28	20.3	
Sitting	2	1.4	5	3.6	
Lateral	2	1.4	4	2.9	
Central venous catheter					0.17
No catheter	10	7.2	21	15.2	
Right jugular vein	45	32.6	45	32.6	

Table 1 (continued)

Parameters	Group 1 (RBC-Transfusion, *n*:62)		Group 2 (Non-RBC Transfusion *n*:76)		*p* value
	Mean	SD	Mean	SD	
Left jugular vein	3	2.2	4	2.9	
Right infraclavicular vein	1	0.7	5	3.6	
Femoral vein	3	2.2	1	0.7	
Central venous catheter malposition					0.22
Yes	7	5.1	4	2.9	
No	54	39.1	72	52.2	

SPO2:Oxygen saturation, MAP; Mean arterial pressure, ASA: American Society of Anesthesiologist

Table 2 Tumor histopathology between transfusion and non transfusion groups[20]

HISTOPATHOLOGY	Total n:138(%)	RBC-Transfusion n:62(%)	Non-RBC Transfusion n:76(%)	*p* value
Gliomas	40(29)	20(32.25)	20(26.31)	0.444
Ependymomas	13(9.4)	8(12.9)	5(6.57)	0.206
Choroid plexus papilloma	11(8)	2(3.22)	9(11.84)	0.063
Embryonal tumors(Medulloblastoma, ATRT)	19(13.8)	10(16.12)	9(11.84)	0.467
Pineoblastoma	2(1.4)	2(3.22)	0	0.115
Cranıal and paraspınal nerve tumors (Schwannoma, Neurofibroma, Perineuroma, Paraganglioma)	3(2.2)	1(1.61)	2(2.63)	0.683
Meningioma	1(0.7)	1(1.61)	0	0.266
Mesenchymal and non mesenchymal tumors (Hemangioma and Vascular Malformations, Hemangioblastoma, Ewing Sarcoma)	11(8)	3(4.83)	8(10.52)	0.220
Chondroosseous tumors	3(2.2)	1(1.61)	2(2.63)	0.683
Germ cell tumors(Germinom, Teratom, Koryosarkom, Yolk Sac Tümör)	2(1.4)	1(1.61)	1(1.31)	0.884
Tumors of the sellar region(Kraniofarenjiom)	8(5.8)	4(6.45)	4(5.26)	0.766
Others (Leptomeningeal Kist, Araknoid Kist, Abse, Dermoid, Epidermoid, Kolloid Kist, Kist Hidatik)	25(18.1)	9(14.51)	16(21.05)	0.321

Table 3 Predictive factors for intraoperative blood transfusion for brain tumor removal in multivariate logistic regression

			95% Confidence Interval	
Predictor	***p*-value**	**Odds ratio**	**Lower**	**Upper**
Age ≤ 4	**0.027**	2.927	11.294	7.586
Duration of surgery > 490 min	**0.016**	3.063	12.268	7.650
Preoperative Hgb < 13	0.148	2.636	0.7094	9.797

Group 1 ($p=0.025$). Analysis of the patients in terms of postoperative ICU discharge status showed that most of the intubated patients (52 patients, 37.7%) were in Group 1 ($p=0.004$) (Table 1). There was no statistically significant relationship between tumor histopathology and the need for intraoperative blood transfusion.(Table 2).

Comparison of groups in terms of intraoperative heart rate and mean arterial pressure (MAP) showed that patients in Group 1 had higher postoperative heart rates ($p<0.001$) and lower intraoperative and postoperative MAP values ($p<0.001$ and $p=0.001$, respectively) than Group 2 (Table 1).

Multivariate analysis

Multivariate analysis showed that age≤4 years and surgery duration>490 min were independent risk factors associated with intraoperative blood transfusion requirement ($p=0.027$ and $p=0.016$, respectively) (Table 3). Having a preoperative hemoglobin value<13 g/dL was not an independent risk factor for blood transfusion ($p=0.148$). The receiver operating characteristic curve analysis for predicting intraoperative blood transfusion need using this model yielded an area under the curve of 0.768 (95% CI=0.692–0.839) (Fig. 1).

Discussion

The results of the present study, which investigated factors influencing intraoperative blood transfusion in pediatric patients undergoing surgery for intracranial masses, indicated that 44.9% of the patients required intraoperative blood transfusion. Patient age of 4 years or younger and operation duration exceeding 490 min were identified as independent risk factors for intraoperative blood transfusion in this surgical population.

In the relevant literature, Vassal et al. conducted a retrospective study over three years, assessing the outcomes of 110 pediatric patients who underwent brain tumor resection. The authors emphasized that a patient

age of less than 4 years, an operation duration of more than 270 min, and a preoperative hemoglobin concentration of less than 12.2 g/dL were key factors associated with allogenic blood transfusion [14] In a retrospective study evaluating 297 pediatric brain tumor cases, Zhang et al. reported that age, preoperative hemoglobin level, duration of anesthesia, tumor size, unclear tumor margin, intraoperative vasopressor infusion, and tumor grade were independent predictors of RBC transfusion [15]. Hsu et al. evaluated 99 adult patients operated for intracranial meningioma and reported that larger tumor size and prolonged operation time increased the risk of severe bleeding [16]. Rajagopalan et al. conducted a retrospective study in 2019, categorizing and examining 456 adult patients who underwent intracranial tumor surgery. They divided the patients into four groups based on the amount of bleeding. The results identified female sex, hypertension, tumor size greater than 5 cm, and operation time exceeding 300 min as risk factors for bleeding [17]. The results obtained in this study align with the existing literature concerning the evaluated parameters. However, although preoperative hemoglobin levels were significantly lower in patients who received transfusions, preoperative hemoglobin was not identified as an independent risk factor for blood transfusion, contrary to previous findings. This discrepancy may be due to the high cutoff value set for hemoglobin levels (< 13 g/dL).

Although the safety of blood product administration has significantly improved in recent years, risks associated with blood transfusions still remain. These risks include allergic reactions, transmission of infectious agents, acute hemolytic reactions, lung injury, and immunomodulation [7]. In a retrospective study conducted in 2011, Laurent et al. examined the relationship between blood transfusion and 30-day morbidity and mortality in 10,100 patients. The authors concluded that intraoperative blood transfusion in surgical patients with severe anemia is associated with increased morbidity and mortality [8]. In a retrospective study involving a large patient cohort over a 5-year period, Rolston et al. emphasized that complications, including bleeding, were more common in cranial surgeries. They also found that receiving more than 4 units of blood transfusion was significantly associated with postoperative complications [6]. Data related to postoperative mobility were not available in the present study. We did not find a significant relationship between mortality and blood transfusion. This may be because of the fact that subgroup analysis could not be performed based on the amount of transfusion. The necessary data for this analysis were not available in the hospital information system.

Another result was that the need for blood transfusions was higher in emergency cases. This expected finding was consistent with the existing literature. Similar to the present study, Cohen et al. examined 8,924 adults undergoing cranial surgery in their article published in 2017 and reported that patients undergoing emergency surgery required almost twice as many blood transfusions [18].

Piastra et al. investigated the relationship between age and blood transfusion in pediatric cases. They examined 43 patients aged ≤ 1 year who underwent brain tumor surgery and were admitted to the pediatric ICU. The authors reported that the mean age was significantly lower in patients who experienced intraoperative blood loss exceeding their preoperative blood volume [19]. Similarly, in the present study, the mean age of the group receiving transfusion was significantly lower than the other group, and patient age ≤ 4 years was identified as an independent risk factor for blood transfusion.

The present study has certain limitations that warrant consideration. The primary limitation is the lack of intraoperative blood loss and transfused blood volume data in the hospital records. Additionally, the study's retrospective and single-center design limits its generalizability. There is a need for prospective, multicenter studies on this subject. Finally, due to the retrospective nature of this study, the target hemoglobin level for making transfusion decisions was not fully standardized within our population. The decision to transfuse was influenced by factors such as intraoperative blood loss, hemodynamic status, urinary output, and blood clotting parameters.

Conclusions

In conclusion, the findings obtained in this study suggest that age and surgical duration are independent risk factors for intraoperative blood transfusion in pediatric patients undergoing surgery for intracranial masses. Particularly, in younger patients and prolonged surgeries, closer monitoring and awareness may enhance early detection, leading to the prevention of complications.

Abbreviations

CNS	Central Nervous System
ASA	American Society of Anesthesiologists
ICU	Intensive Care Unit
CVC	Central Venous Catheter
MAP	Mean Arterial Pressure

Supplementary Information

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Supplementary Material 1

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Author contributions
All authors contributed to the study's conception and design. The first draft of the manuscript was written by HTS,ÖO, OU, and SS, and all authors commented on previous versions of the manuscript. Material preparation: HTS and FÇ. Data collection: FŞ and KA. Analysis was performed by HTS and BA. Review and editing: SS, BG, and RTT. All authors read and approved the final manuscript.

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Data availability
All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate
This study was initiated after obtaining approval from the Ethics Committee of Dicle University Faculty of Medicine Non-Interventional Clinical Research dated March 20, 2024 (number 99). Written and verbal informed consent for participation was obtained from all participants in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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