Article published online: 2023-04-05

Effectiveness of Preoperative Red Cell Preparation and Intraoperative Massive Transfusion in Brain Tumor Operation

Thara Tunthanathip[1] Sakchai Sae-heng[1] Thakul Oearsakul[1] Anukoon Kaewborisutsakul[1] Chin Taweesomboonyat[1]

[1] Division of Neurosurgery, Department of Surgery, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

Indian J Neurosurg 2024;13:134–143.

Address for correspondence Thara Tunthanathip, MD, PhD, Division of Neurosurgery, Department of Surgery, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand (e-mail: tsus4@hotmail.com).

Abstract

Background Excessive requests for preoperative packed red cell (PRC) preparation have been noted, resulting in waste of blood products and higher costs in brain tumor surgery. The objectives of the present study were as follows: (1) the primary objective was to assess the effectiveness index of blood preparation and utilization; (2) the secondary objective was to explore factors associated with intraoperative PRC transfusion; and (3) the third objective was to identify the prevalence and analyze risk factors of massive transfusion.

Methods A retrospective cohort study was done on patients who had undergone brain tumor operations. The effectiveness indexes of preoperative PRC preparation and intraoperative utilization were calculated as follows: the crossmatch to transfusion (C/T) ratio, transfusion probability (Tp), and transfusion index (Ti). Additionally, factors associated with intraoperative PRC transfusion and massive transfusion were analyzed.

Results There were 1,708 brain tumor patients and overall C/T, Tp, and Ti were 3.27, 45.54%, and 1.10, respectively. Prevalence of intraoperative PRC transfusion was 44.8%, and meningioma, intraosseous/skull-based tumor, and tumor size were linked with massive transfusion.

Conclusion Unnecessary preoperative blood component preparation for brain tumor surgery was noticed in routine practice. Exploring intraoperative transfusion variables has been challenged in optimizing crossmatch and actual use.

Keywords
- massive transfusion
- intraoperative transfusions
- brain tumor
- blood transfusion

Introduction

In the case of a brain tumor, surgical management is the primary therapeutic option for tissue diagnosis, tumor removal, or intracranial pressure reduction. Blood component preparation is one of the preoperative processes that may be ordered before surgery. However, an overabundance of requests for blood preparation has been observed in prior studies, particularly packed red cells (PRCs).[1–4] Chotisukarat et al found that the crossmatch to transfusion (C/T) ratio was 4.3% in 1,018 individuals who had elective neurosurgery operations.[3] Additionally, Saringcarinkul and Chuasuwan also studied 377 patients who had undergone neurosurgical operations and reported a high C/T ratio of 6.6.[4]

The unexpected vigorous bleeding during tumor resection was a concern for neurosurgeons because the event has been

article published online
April 5, 2023

DOI https://doi.org/10.1055/s-0043-1768066.
ISSN 2277-954X.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

associated with mortality.[5,6] Therefore, the request for more units of preoperative blood products for the patient's safety has been observed.[3,4] Nevertheless, the unnecessary blood products that were prepared led to the loss of resources and an increase in the amount of labor done in blood banks. Hence, the preoperative preparation of blood ought to optimize the potential benefit from the tradeoff between unexpectedly massive blood losses and blood waste.

According to the literature review, a few publications have addressed the risk factors of intraoperative transfusions in brain tumor surgery. Skull base tumor, meningioma, children with an age younger than 4 years, operative time longer than 270 minutes, and preoperative hemoglobin lower than 12.2 g/dL were associated with intraoperative PRC transfusion from prior studies.[7–9] However, various preoperative factors need to be further investigated to enable the establishment of a guideline or the blood component preparation protocol for balancing between preoperative crossmatch blood products and utilization.[4] Hence, the objectives of the present study were as follows: (1) the primary objective was to assess the effectiveness index of blood preparation and utilization; (2) the secondary objective was to explore factors associated with intraoperative transfusion that could be considered to set blood preparation protocol for brain tumor operation in the future; and finally, (3) the third objective was to identify the prevalence and analyze risk factors of massive transfusion.

Methods

Study Design and Study Population

A retrospective cohort study was done by reviewing medical records among brain tumor patients who had undergone cranial operations between January 2014 and January 2019. Exclusion criteria were unavailable crossmatch and transfusion data, unavailable preoperative imaging, unavailable preoperative details, and no definite diagnosis from the pathological report. Preoperative clinical characteristics, laboratory results, and treatment outcome were collected from electronics-based medical records. Preoperative magnetic resonance imaging scans were reviewed for tumor characteristics as follows: tumor size, tumor volume, number of tumors, lateralization, location, and midline shift. In addition, the tumor classification and the World Health Organization (WHO) grading were collected based on the official reports by the pathologist.

The main objective was to describe the effectiveness of blood utilization according to the C/T ratio, transfusion probability (Tp), and transfusion index (Ti) as follows:

A C/T ratio was defined as the number of units cross-matched/number of units transfused[10,11] and a C/T ratio of 2.0 or below suggested that blood utilization was effective.[12]

Tp was defined as the number of patients transfused/number of patients cross-matched $\times$ 100. A Tp of 30% or higher indicated successful blood utilization.

Ti was defined as the number of units transfused/number of patients cross-matched. A value of 0.5 or more was thought to show the effectiveness of blood being used.

For the third objective, the massive transfusion was defined as a patient who received more than 4 units of PRC within 1 hour or more than 10 units of PRC within 24 hours.[13,14]

Ethical Considerations

A human research ethics committee of the Faculty of Medicine, Prince of Songkla University approved the present study (REC 64–477–10–1). Because of the retrospective study design, patients were not required to provide informed consent. However, patients' identity numbers were encoded before analysis.

Statistical Analysis

Following the study objectives, proportion and percent were used to describe the results of the categorical variables, whereas mean and standard deviation (SD) were used to define continuous variables. Moreover, the C/T ratio, Tp, and Ti were calculated according to the definitions. Therefore, binary logistic regression was used for estimating factors associated with intraoperative transfusion. In addition, factors affecting massive transfusion were analyzed using binary logistic regression with univariate and multivariable analysis. In detail, the predictors were explored using binary logistic regression analysis, and the candidate variables with *p*-values of 0.10 were identified for multivariable analysis to generate the final model. Hence, multivariable analysis was performed with a backward elimination procedure. Finally, the model that had the lowest Akaike information criterion (AIC) was chosen as the final model. All *p*-values less than 0.05 were considered statistically significant, and the variance inflation factor (VIF) was used to detect multicollinearity in the final model, with a VIF value of 10 or above indicating multicollinearity.[15] Statistical analysis was performed using R version 4.4.0 software (R Foundation, Vienna, Austria).

Results

Baseline Clinical Characteristics

A total of 1,719 patients underwent screening; however, 11 individuals were excluded according to the exclusion criteria. As a result of this, the remaining 1,708 patients were examined. ►**Table 1** presents the clinical features and there was a male dominance in the study population. The mean age was 47.6 (SD 17.2) years and the mean body mass index (BMI) was 23.5 (SD 4.4) kg/m^2. The majority of the American Society of Anesthesiologists (ASA) classification was ASA class 3 in 85.6%, while the emergency operation was observed in 6.8% of the present cohort.

For preoperative hematologic laboratories, anemia (hemoglobin less than 10 g/dL) was found at 5.0%, and the mean neutrophil-lymphocyte (NL) ratio was 5.2 (SD 8.0). Craniotomy was the main operation in 56.5%, whereas decompressive craniectomy with tumor removal was

Table 1 Baseline characteristics of the present cohort ($N = 1,708$)

Characteristics	*N* (%)
Sex	
Male	733 (42.9)
Female	975 (57.1)
Mean age, y (SD)	47.6 (17.2)
Age, y	
0–15	137 (8.0)
> 15–30	108 (6.3)
> 30–40	194 (11.4)
> 40–50	450 (26.3)
> 50–50	451 (26.4)
> 60	368 (21.5)
Underlying disease	
Hypertension	270 (15.8)
Diabetes mellitus	182 (10.7)
Dyslipidemia	188 (11.0)
Liver disease	28 (1.6)
Renal failure	37 (2.2)
Preoperative seizure	157 (9.2)
Preoperative current medication	
Antiplatelet	21 (1.2)
Clexane	7 (0.4)
Warfarin	2 (0.1)
Mean body mass index, kg/m^2	23.5 (4.4)
American Society of Anesthesiologists classification	
1	3 (0.2)
2	238 (13.9)
3	1,462 (85.6)
4	5 (0.3)
Preoperative laboratory (SD)	
Mean hematocrit, %	12.8 (1.6)
Mean hemoglobin, g/dL	39.0 (10.1)
Mean white blood cell count, $\times 10^3$/μL	10.1 (5.0)
Mean neutrophil, %	67.2 (16.1)
Mean lymphocyte, %	24.6 (12.5)
Mean neutrophil-to-lymphocyte ratio	5.2 (8.0)
Mean platelet count, $\times 10^3$/μL	290.7 (90.5)
Mean prothrombin time ratio	0.98 (1.87)
Mean international normalized ratio	1.08 (1.23)
Tumor characteristics	
Mean diameter of tumor, cm (SD)	3.7 (1.6)
Mean tumor volume, mL (SD)	34.8 (40.4)
Mean preoperative midline shift, cm (SD)	0.31 (0.48)
Midline shift group, cm	
< 0.5	1,229 (72.0)
≥ 0.5	479 (28.0)
Tumor location	
Supratentorial location	1,451 (85.0)
Infratentorial location	257 (15.0)
Intraventricular tumor	47 (2.8)
Pineal tumor	33 (1.9)
Intraosseous/Skull-based tumor	44 (2.6)
Neurosurgical operation	
Craniotomy	965 (56.5)
Craniectomy	113 (6.6)
Suboccipital or rectosigmoid approach	228 (13.3)
Endoscopic transsphenoidal approach	250 (14.6)
Burr hole with biopsy	152 (8.9)
Emergency operation	116 (6.8)
Estimated blood loss, mL	773.2 (1137.0)
Tumor classification	
Meningioma	550 (32.2)
Glioma	377 (22.1)
Pituitary adenoma	241 (14.1)
Schwannoma	81 (4.7)
Metastasis	141 (8.3)
Lymphoma	111 (6.5)
Medulloblastoma	21 (1.2)
Craniopharyngioma	38 (2.2)
Neuroblastoma	10 (0.6)
Germinoma	22 (1.3)
Other	111 (6.5)
WHO grade	
I	963 (56.4)
II	161 (9.4)
III	91 (5.3)
IV	493 (28.9)
Outcome	
Intraoperative transfusion	766 (44.8)
Massive transfusion	79 (4.6)

Abbreviations: SD, standard deviation; WHO, World Health Organization.

found in 6.6% of total cases. In addition, an endoscopic transsphenoidal approach and burr hole with biopsy was performed in 14.6 and 8.9%. For pathological diagnosis, meningioma was the most common brain tumor that was resected in 32.2%. In detail, 90.4% of meningiomas were WHO grade I, while WHO grade II and III meningiomas were found in 8.4 and 1.3%. For gliomas, WHO grade IV gliomas (glioblastoma) were found in 45.6%, whereas WHO grade III, II, and I gliomas were found in 21.5, 24.4, and 8.5%, respectively.

Effectiveness Index of Preoperative Blood Preparation

Almost all patients (98.4%) had preoperative crossmatch preparation ordered for a total of 6,068 PRC units, but 45.5% (766/1,682) of total preparations were used during the operation. ►**Table 2** shows the C/T ratio, Tp, and Ti of PRC by tumor classification and operation. Overall, C/T ratio, Tp, and Ti were 3.27, 45.54%, and 1.10, respectively. According to tumor classification, all tumors had a C/T ratio greater than 2.0, but meningioma had nearly the effective threshold of this indicator. Surgery of pituitary adenoma and lymphoma had a high C/T ratio and Tp less than 30%, which means that the blood preparations for these tumors were ineffective.

All of the operations had a C/T ratio that was greater than 2.0, and almost all of them, with the exception of the endoscopic transsphenoidal and tumor biopsy operations, had a Tp that was lower than 30%. This demonstrated that the preoperative PRC preparations for these procedures were unsuccessful.

Factors Associated with Intraoperative Transfusion

The prevalence of intraoperative PRC transfusion was 44.8% in the present study. According to the secondary objective, factors significantly related to intraoperative PRC transfusion were being female, younger age, lower BMI, ASA classification, preoperative hematocrit, hemoglobin, platelet count, NL ratio, tumor diameter, tumor volume, tumor classification, WHO grade, intraventricular tumor, intraosseous/skull-based tumor, type of operation, and estimated blood loss by univariate analysis. By

Table 2 Crossmatch to transfusion ratio, transfusion probability, and transfusion index of packed red cells by tumor classification and operation

Tumor classification/ operation	Preoperative preparation		Intraoperative utilization		C/T ratio	Tp (%)	Ti
	Patient with crossmatch (*n*)	Total crossmatch (units)	Patient received transfusion (*n*)	Total transfusion (units)			
Total	1,682	6,068	766	1,855	3.27	45.54	1.10
Tumor classification							
Meningioma	550	2,166	360	1,073	2.02	65.45	1.95
Glioma	368	1,374	138	272	4.95	37.50	0.74
Pituitary adenoma	240	728	60	90	8.09	25.00	0.38
Schwannoma	81	306	36	64	4.78	44.44	0.79
Metastasis	141	509	52	64	7.95	36.88	0.45
Lymphoma	97	279	12	18	15.50	12.37	0.19
Medulloblastoma	20	69	14	24	2.88	70.00	1.20
Craniopharyngioma	38	142	19	31	4.58	50.00	0.82
Neuroblastoma	10	30	4	13	2.31	40	1.30
Germinoma	21	73	10	13	5.62	47.62	0.62
Other	116	420	61	181	2.32	52.59	1.56
Operation							
Craniotomy	958	3,701	510	1,251	2.96	53.24	1.31
Craniectomy	112	426	69	207	2.06	61.61	1.85
Suboccipital/ retrosigmoid approach	227	824	184	217	3.80	81.06	0.96
Endoscopic transsphenoidal approach	249	745	58	104	7.16	23.29	0.42
Burr hole with biopsy	136	373	11	16	23.31	8.09	0.12

Abbreviations: C/T ratio, crossmatch to transfusion ratio; Ti, transfusion index; Tp, transfusion probability.

multivariable analysis with backward elimination method, age, BMI, ASA classification, estimated blood loss, and type of operations are significantly associated with intraoperative PRC transfusion, as shown in ►**Table 3**. Additionally, the final model's factors all had VIF values under 10.

Prevalence and Factors Associated with Massive Transfusion

In this study, massive transfusion was observed in 79.4% of total cases and meningioma, increased diameter of tumor, intraosseous/skull-based tumor, and craniotomy were

Table 3 Binary logistic regression analysis for intraoperative transfusion

	Univariate analysis		Multivariable analysis	
Factor	Odds ratio (95%CI)	*p*-Value	Odds ratio (95%CI)	*p*-Value
Gender				
Male	Ref			
Female	1.94 (1.59–2.36)	< 0.001		
Age, y	0.98 (0.97–0.99)	< 0.001	0.98 (0.97–0.99)	< 0.001
Body mass index, kg/m^2	0.94 (0.92–0.96)	< 0.001	0.91 (0.88–0.94)	< 0.001
Underlying disease				
Hypertension[a]	1.05 (0.81–1.36)	0.69		
Diabetes mellitus[a]	1.00 (0.74–1.37)	0.95		
Dyslipidemia[a]	0.96 (0.71–1.31)	0.83		
Liver disease[a]	0.92 (0.43–1.95)	0.83		
Renal failure[a]	1.16 (0.60–2.24)	0.63		
Preoperative seizure[a]	0.96 (0.69–1.33)	0.81		
Preoperative current medication				
Antiplatelet[a]	0.92 (0.38–2.19)	0.85		
Warfarin[a]	1.23 (0.77–19.69)	0.88		
Clexane	0.49 (0.09–2.53)	0.39		
American Society of Anesthesiologists classification				
1–2	Ref		Ref	
3–4	0.60 (0.45–0.80)	< 0.001	1.87 (1.28–2.38)	< 0.001
Preoperative hematologic laboratory				
Hematocrit, %	0.88 (0.86–0.90)	< 0.001		
Hemoglobin, g/dL	0.66 (0.61–0.70)	< 0.001		
Platelet count, $\times 10^3$/μL	1.002 (1.001–1.003)	< 0.001		
White blood cell count, $\times 10^3$/μL	1.01 (0.99–1.03)	0.11		
Neutrophil/lymphocyte ratio	1.01 (1.003–1.028)	0.01		
Partial thromboplastin time ratio	0.86 (0.60–1.24)	0.44		
International normalized ratio	0.96 (0.83–1.10)	0.58		
Preoperative hemoglobin level, g/dL				
≥ 10	Ref		Ref	
< 10	5.82 (3.35–10.10)	< 0.001	13.46 (6.99–25.91)	< 0.001
Tumor location				
Supratentorial tumor	Ref			
Infratentorial tumor	1.15 (0.88–1.50)	0.29		
Intraventricular tumor[a]	2.02 (1.11–3.66)	0.02		
Pineal tumor[a]	1.68 (0.84–3.38)	0.14		
Intraosseous/Skull-based tumor[a]	2.19 (1.17–4.08)	0.01		
Tumor volume, mL	1.016 (1.012–1.019)	< 0.001		
Diameter of tumor, cm	1.41 (1.32–1.50)	< 0.001		

Table 3 (*Continued*)

	Univariate analysis		Multivariable analysis	
Factor	**Odds ratio (95%CI)**	***p*-Value**	**Odds ratio (95%CI)**	***p*-Value**
Preoperative midline shift, cm	1.62 (1.31–2.01)	< 0.001		
Emergency operation[a]	0.96 (0.65–1.40)	0.84		
Estimated blood loss, ml	1.003 (1.002–1.004)	< 0.001		
Estimated blood loss level-, mL				
< 500	Ref		Ref	
500–1,000	4.59 (3.60–5.85)	< 0.001	4.44 (3.36–5.87)	< 0.001
> 1,000	53.93 (34.55–84.32)	< 0.001	56.04 (34.55–90.89)	< 0.001
Neurosurgical operation				
Craniotomy	Ref		Ref	
Craniectomy	1.39 (0.93–2.08)	0.09	1.02 (0.61–1.71)	0.92
Suboccipital/rectosigmoid approach	0.95 (0.71–1.27)	0.76	1.43 (0.99–2.06)	0.053
Endoscopic transsphenoidal approach	0.27 (0.19–0.37)	< 0.001	0.72 (0.47–1.09)	0.12
Burr hole with biopsy	0.07 (0.03–0.13)	< 0.001	0.23 (0.11–0.47)	< 0.001
Tumor classification				
Meningioma	Ref			
Glioma	0.30 (0.23–0.40)	< 0.001		
Pituitary adenoma	0.17 (0.12–0.24)	< 0.001		
Schwannoma	0.42 (0.26–0.67)	< 0.001		
Metastasis	0.30 (0.21–0.45)	< 0.001		
Lymphoma	0.06 (0.03–0.11)	<0.001		
Medulloblastoma	1.05 (0.41–2.66)	0.90		
Craniopharyngioma	0.52 (0.27–1.02)	0.058		
Neuroblastoma	0.35 (0.09–1.26)	0.10		
Germinoma	0.44 (0.18–1.03)	0.06		
Other	0.58 (0.39–0.87)	0.009		
Meningioma[a]	3.50 (2.83–4.34)	< 0.001	1.75 (1.28–2.38)	< 0.001
Glioma[a]	0.64 (0.51–0.81)	< 0.001		
Pituitary adenoma[a]	0.35 (0.26–0.48)	< 0.001		
Schwannoma[a]	0.98 (0.62–1.54)	0.98		
Metastasis[a]	0.69 (0.48–0.99)	0.04		
Lymphoma[a]	0.13 (0.07–0.24)	< 0.001		
Medulloblastoma[a]	2.48 (0.99–6.19)	0.05		
Craniopharyngioma[a]	1.23 (0.64–2.35)	0.51		
Neuroblastoma[a]	0.81 (0.23–2.91)	0.75		
Germinoma[a]	1.02 (0.44–2.38)	0.95		
WHO grade				
IV	Ref			
III	0.65 (0.39–1.09)	0.10		
II	1.49 (1.03–2.14)	0.03		
I	2.14 (1.71–2.68)	< 0.001		

Abbreviations: CI, confidence interval; WHO, World Health Organization.
[a]Data show only "yes group" while reference groups (no group) are hidden.

candidate factors significantly related to the event of the massive transfusion by univariate analysis, as shown in ►**Fig. 1**. Therefore, multivariable analysis with the backward elimination procedure was performed and found that meningioma, intraosseous/skull-based tumor, and diameter of tumor were all strongly linked to intraoperative PRC transfusion with lowest AIC, as shown in ►**Fig. 2**. Furthermore, the VIF for every factor included in the final model was less than 10.

Discussion

Preoperative PRC preparation was overrequested in the present study, according to various indicators. As a result, more than half of all preparations were not employed that preferred the unnecessary crossmatch and over workload in the routine clinical practice. These findings were consistent with those of previous studies. Based on operation, the C/T ratio, Tp, and Ti of craniotomy with tumor removal were 5, 20%, and 0.5, respectively. Moreover, the endoscopic transsphenoidal approach had the C/T ratio, Tp, and Ti of 11, 7%, and 0.4, respectively, whereas those for the tumor biopsy had a C/T ratio, Tp, and Ti of 12, 8%, and 0.2, respectively.[3] According to the findings of tumor classification, surgery of meningiomas had effective indexes. The concordance results were similar to what had been shown in the Saringcarinkul and Chuasuwan study, which reported the Tp of patients with meningiomas was 49%.[4] However, pituitary adenoma had an imbalance between PRC preparations and utilization in the present study, which could be explained by concerns about the operation being close to internal carotid injury and can result in unexpected massive bleeding during the operation. The endoscopic transsphenoidal approach is the common operation for pituitary adenoma, while tumor biopsy is usually performed for cases of lymphoma. However, vascular complication is uncommon. From the literature review, intraoperative internal carotid injury has been reported in 0.12 to 1.1%,[16,17] and intraoperative bleeding was reported in 12.3% of neuronavigation-guided biopsy patients.[18] Therefore, the type and screen procedure processes check patient blood for ABO-Rh groups and unusual antibodies that might make donor blood incompatible may be an alternative resolution to reduce unnecessary cross-matches in low probability cases of requiring blood products.[19]

As a result, the ineffectiveness of preoperative PRC preparation and utilization was observed that potentially

Variable		N	Odds ratio	p
Age		1708	1.00 (0.99, 1.02)	0.660
Gender	Male	733	Reference	
	Female	975	1.63 (0.89, 3.05)	0.122
Diameter_gr	<3.5 cm	787	Reference	
	3.5-5 cm	534	3.79 (1.55, 10.66)	0.006
	>5 cm	387	16.94 (7.26, 46.72)	<0.001
MLS_gr	<0.5 cm	1229	Reference	
	>=0.5 cm	479	1.21 (0.69, 2.15)	0.504
ASA_gr	ASA1-2	241	Reference	
	ASA3-4	1467	1.47 (0.67, 3.69)	0.371
Antiplatelet_drug	No	1687	Reference	
	Yes	21	1.15 (0.06, 6.70)	0.898
Intraosseous_Skullbased_tumor	No	1664	Reference	
	Yes	44	4.85 (1.73, 12.23)	0.001
Intraventricular_tumor	No	1661	Reference	
	Yes	47	0.96 (0.14, 3.75)	0.958
Pineal_tumor	No	1675	Reference	
	Yes	33	5.72 (0.77, 27.40)	0.046
Supratential_tumor	No	257	Reference	
	Yes	1451	0.39 (0.18, 0.91)	0.023
Meningioma	No	1157	Reference	
	Yes	551	3.39 (1.62, 7.47)	0.002
WHO_gr	I	963	Reference	
	II	161	0.84 (0.35, 1.85)	0.687
	III	91	1.15 (0.25, 3.86)	0.837
	IV	493	0.76 (0.29, 1.94)	0.560
Craniotomy	No	743	Reference	
	Yes	965	2.29 (1.19, 4.66)	0.017
BMI		1708	0.98 (0.91, 1.04)	0.445
Pre_Hb		1708	1.10 (0.89, 1.44)	0.561
Pre_Hct		1708	0.98 (0.91, 1.02)	0.762
NL_ratio		1708	1.00 (0.96, 1.02)	0.863
Pre_INR		1708	0.82 (0.06, 1.09)	0.887

Fig. 1 The odds ratio plot of various factors using univariate analysis.

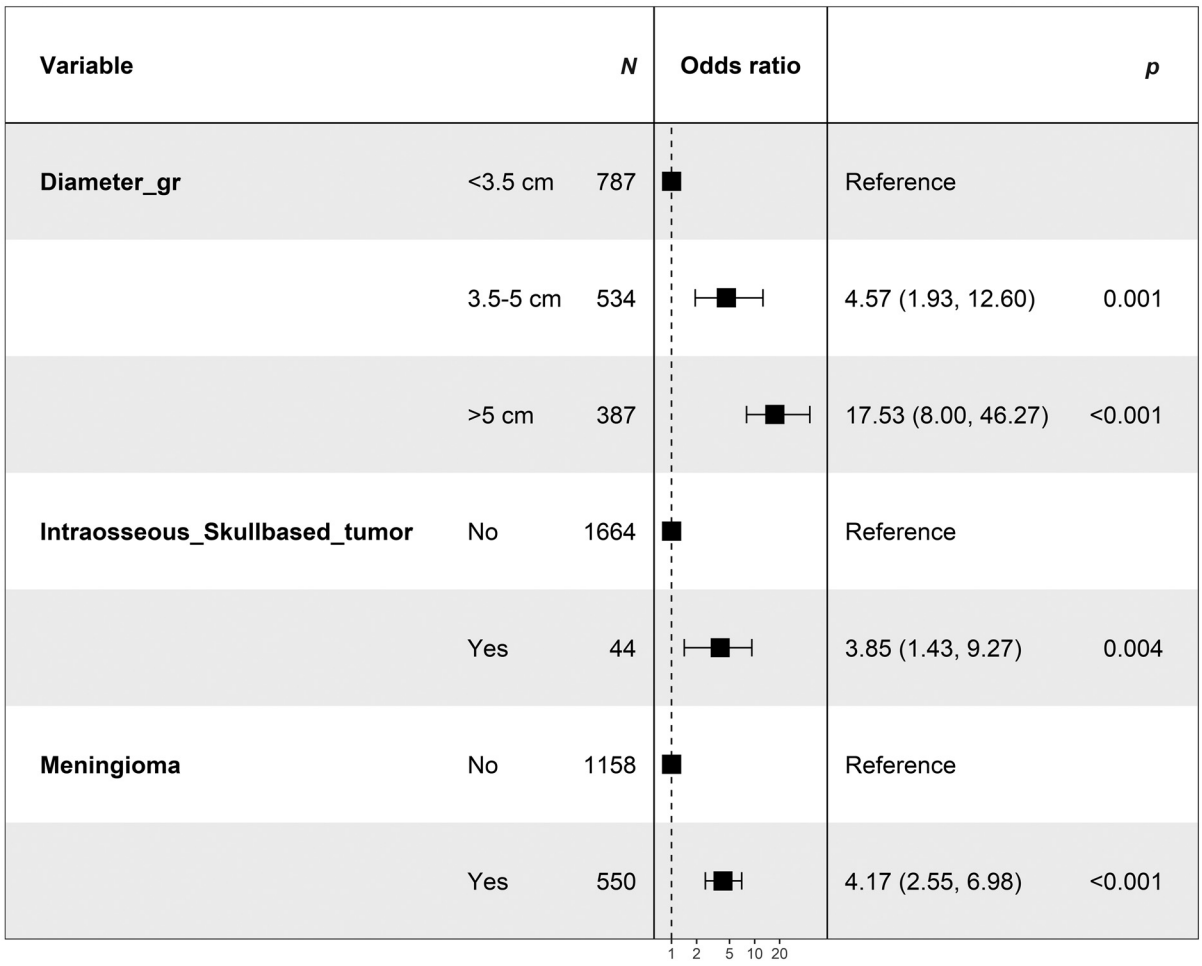

Fig. 2 The odds ratio plot of factors associated with massive transfusion using multivariable analysis.

led to unnecessary costs and the workload of a blood bank. Balancing between preoperative crossmatch and actual transfusion has been challenged. Currently, no standard guideline exists for crossmatch protocol or the Maximum Surgical Blood Order Schedule (MSBOS) in brain tumor operation. There are several methods for contributing to the guideline or MSBOS, for example, nomogram and machine learning (ML).[20–22] In the past, prior studies calculated MSBOS by the following equation ($1.5^{*}Ti$)[3,4] or consensus according to the procedures from prior studies.[23,24] In addition, Hu et al developed a nomogram predicting a transfusion in patients undergoing total knee arthroplasty from various predictors with multivariable analysis and reported the area under the curve ranged from 0.839 to 0.884 for the predictability.[25] ML is a sophisticated computer technology that learns from data to discover patterns and make predictions.[26,27] Liu et al used ML to predict PRC transfusion in mitral valve surgery and found that the accuracy of prediction was 86.8%.[26] In addition, Huang et al predicted PRC transfusion using various algorithms of ML and reported that the random forest algorithm had the best performance of prediction with 82.35%.[27] Therefore, predicting the PRC transfusion in patients with brain tumors by novel methods has been challenged. To create a predictive model in clinical prediction tools, feature selection is a critical step, and one technique of feature selection may be to investigate the significant factors associated with PRC transfusion using multivariable analysis.[28,29]

Younger age and low BMI were the significant factors related to intraoperative PRC transfusion in the present study. Similarly, Vassal et al found that in brain tumor patients who were younger than 4 years the risk of intraoperative transfusion was explained by tolerance blood loss in children less than adults. Hemorrhagic shock in children was more common than in adults from prior studies.[30] Additionally, previous studies reported that skull-based surgery and meningioma are potential factors linked with blood transfusion.[8,9] These were in concordance with our findings which shows that intraosseous/skull-based tumor and meningioma were associated with both intraoperative transfusion and massive blood loss. Although meningioma is a benign tumor, hypervascularity and numerous feeding vessels are common findings of this tumor.[31] The sunburst flow void was found in 96.5% of the cases, whereas the serpentine flow void was found in just 3.5% of meningiomas.[32] Intraosseous tumor removal and skull-based surgery are complex procedures that frequently

bleed from various vessels, including branches of the carotid artery in the basilar skull, the diploic vein in the cranial vault, and bridging veins near to the superior sagittal sinus during craniotomy.[1,33,34]

As per the authors' knowledge, the present study is the first study that mentioned predictors linked to intraoperative transfusion for brain tumor surgery that may be used to create the clinical prediction tools and MSBOS in the future. However, there were certain limitations in the present study that should be acknowledged. The current study was a retrospective cohort analysis, which might have resulted in bias from confounding variables.[35] Nevertheless, we attempted to adjust and control bias using multivariable analysis in the present study. Additionally, the incidence of intraoperative massive bleeding and transfusion has been reported in the range of 3 to 8% for cranial operations. Multicenter trials should be conducted in the future to address the increased occurrence of this complication for testing the predictive model's performance and will be useful in making guidelines. Finally, our hospital did not follow an autologous blood transfusion protocol during routine practice.[36] The present study's findings may help physicians identify high-risk operations and plan for autologous blood transfusions during surgery, which will reduce PRC transfusion and utilization ratios.[37,38]

Conclusion

Unnecessary preoperative blood component preparation for brain tumor surgery was noticed in routine practice. Exploring factors that are strongly associated with intraoperative transfusion and massive bleeding has posed a challenge in optimizing between crossmatch and actual use; moreover, those will be developed into a crossmatch guideline in the future.

Conflict of Interest
None declared.

References

1 Kisilevsky A, Gelb AW, Bustillo M, Flexman AM. Anaemia and red blood cell transfusion in intracranial neurosurgery: a comprehensive review. Br J Anaesth 2018;120(05):988–998
2 Boutin A, Chassé M, Shemilt M, et al. Red blood cell transfusion in patients with traumatic brain injury: a systematic review and meta-analysis. Transfus Med Rev 2016;30(01):15–24
3 Chotisukarat H, Akavipat P, Sookplung P, et al. Effectiveness index of preoperative blood preparation for elective neurosurgery at Prasat Neurological Institute. Thai J Anesthesiol 2017;43:232–240
4 Saringcarinkul A, Chuasuwan S. Maximum surgical blood order schedule for elective neurosurgery in a university teaching hospital in Northern Thailand. Asian J Neurosurg 2018;13(02): 329–335
5 Barbosa RR, Rowell SE, Sambasivan CN, et al; Trauma Outcomes Group. A predictive model for mortality in massively transfused trauma patients. J Trauma 2011;71(2, Suppl 3):S370–S374
6 Akaraborworn O, Chaiwat O, Chatmongkolchart S, et al. Prediction of massive transfusion in trauma patients in the surgical intensive care units (THAI-SICU study). Chin J Traumatol 2019;22(04): 219–222
7 Vassal O, Desgranges FP, Tosetti S, et al. Risk factors for intraoperative allogeneic blood transfusion during craniotomy for brain tumor removal in children. Paediatr Anaesth 2016;26 (02):199–206
8 Lagman C, Sheppard JP, Beckett JS, et al. Red blood cell transfusions following resection of skull base meningiomas: risk factors and clinical outcomes. J Neurol Surg B Skull Base 2018;79(06):599–605
9 Neef V, König S, Monden D, et al. Clinical outcome and risk factors of red blood cell transfusion in patients undergoing elective primary meningioma resection. Cancers (Basel) 2021;13(14): 3601
10 Raghuwanshi B, Pehlajani NK, Sinha MK, Tripathy S. A retrospective study of transfusion practices in a Tertiary Care Institute. Indian J Anaesth 2017;61(01):24–28
11 Zewdie K, Genetu A, Mekonnen Y, Worku T, Sahlu A, Gulilalt D. Efficiency of blood utilization in elective surgical patients. BMC Health Serv Res 2019;19(01):804
12 Ejaz A, Frank SM, Spolverato G, Mavros M, Kim Y, Pawlik TM. Variation in the use of type and crossmatch blood ordering among patients undergoing hepatic and pancreatic resections. Surgery 2016;159(03):908–918
13 Patil V, Shetmahajan M. Massive transfusion and massive transfusion protocol. Indian J Anaesth 2014;58(05):590–595
14 Chidester SJ, Williams N, Wang W, Groner JI. A pediatric massive transfusion protocol. J Trauma Acute Care Surg 2012;73(05): 1273–1277
15 Vatcheva KP, Lee M, McCormick JB, Rahbar MH. Multicollinearity in regression analyses conducted in epidemiologic studies. Epidemiology (Sunnyvale) 2016;6(02):227
16 Usachev D, Sharipov O, Abdali A, et al. Internal carotid artery injury in transsphenoidal surgery: tenets for its avoidance and refit-a clinical study. Brain Sci 2021;11(01):99
17 Al-Shami H, Alnemare AK. Inadvertent internal carotid artery (ICA) injury during transsphenoidal surgery: review of literature. Egypt J Neurosurg 2021;36:4
18 Taweesomboonyat C, Tunthanathip T, Sae-Heng S, Oearsakul T. Diagnostic yield and complication of frameless stereotactic brain biopsy. J Neurosci Rural Pract 2019;10(01):78–84
19 Chaudhary R, Agarwal N. Safety of type and screen method compared to conventional antiglobulin crossmatch procedures for compatibility testing in Indian setting. Asian J Transfus Sci 2011;5(02):157–159
20 Tunthanathip T. Translational Medicine in Neurosurgery. Bangkok, Thailand: Sahamit Pattana Printing; 2022
21 Wang J, Zhao Y, Jiang B, Huang X. Development of a nomogram to predict postoperative transfusion in the elderly after intramedullary nail fixation of femoral intertrochanteric fractures. Clin Interv Aging 2021;16:1–7
22 Mitterecker A, Hofmann A, Trentino KM, et al. Machine learning-based prediction of transfusion. Transfusion 2020;60(09): 1977–1986
23 Mcpherson RA, Pincus MR. Guidelines for ordering blood for elective surgery also referred to as maximum surgical blood order schedule (MSBOS). In: Mcpherson RA, Pincus MR, eds. Henry's Clinical Diagnosis and Management by Laboratory Methods. 24 ed. Missouri: Elsevier; 2021:1664–1665
24 Universiti Kebangsaan Malaysia. Guidelines on Blood and Blood Components Transfusion: Maximum Surgical Blood Order Schedule (MSBOS) For Elective Surgery. [Internet]. 2021. Accessed September 28, 2021, at: https://hctm.ukm.my/makmal/wp-content/uploads/2020/10/2-MSBOS-ed.5.pdf
25 Hu C, Wang YH, Shen R, et al. Development and validation of a nomogram to predict perioperative blood transfusion in patients undergoing total knee arthroplasty. BMC Musculoskelet Disord 2020;21(01):315

26 Liu S, Zhou R, Xia XQ, et al. Machine learning models to predict red blood cell transfusion in patients undergoing mitral valve surgery. Ann Transl Med 2021;9(07):530
27 Huang X, Wang Y, Chen B, et al. Ability of a machine learning algorithm to predict the need for perioperative red blood cells transfusion in pelvic fracture patients: a multicenter cohort study in China. Front Med (Lausanne) 2021; 8:694733
28 Tunthanathip T, Oearsakul T. Application of machine learning to predict the outcome of pediatric traumatic brain injury. Chin J Traumatol 2021;24(06):350–355
29 Taweesomboonyat C, Kaewborisutsakul A, Tunthanathip T, Saeheng S, Oearsakul T. Necessity of in-hospital neurological observation for mild traumatic brain injury patients with negative computed tomography brain scans. JHSMR 2020; 28:267–274
30 Gonzalez KW, Desai AA, Dalton BG, Juang D. Hemorrhagic shock. J Pediatr Intensive Care 2015;4(01):4–9
31 Lagman C, Ong V, Nguyen T, et al. The meningioma vascularity index: a volumetric analysis of flow voids to predict intraoperative blood loss in nonembolized meningiomas. J Neurosurg 2018;9(11):1–6
32 Wang C, Xu Y, Xiao X, Zhang J, Zhou F, Zhao X. Role of intratumoral flow void signs in the differential diagnosis of intracranial solitary fibrous tumors and meningiomas. J Neuroradiol 2016;43(05): 325–330
33 Sasaki K, Saito A, Nishijima Y, et al. Giant intraosseous meningioma associated with calvarial hyperostosis and subcutaneous invasion: case reports and literature review. Asian J Neurosurg 2021;16(03):589–594
34 Ishihara H, Ishihara S, Niimi J, et al. The safety and efficacy of preoperative embolization of meningioma with N-butyl cyanoacrylate. Interv Neuroradiol 2015;21(05):624–630
35 Kahlert J, Gribsholt SB, Gammelager H, Dekkers OM, Luta G. Control of confounding in the analysis phase - an overview for clinicians. Clin Epidemiol 2017;9:195–204
36 Tunthanathip T, Sae-Heng S, Oearsakul T, Kaewborisutsakul A, Taweesomboonyat C. Economic impact of a machine learning-based strategy for preparation of blood products in brain tumor surgery. PLoS One 2022;17(07):e0270916
37 Forgie MA, Wells PS, Laupacis A, Fergusson DInternational Study of Perioperative Transfusion (ISPOT) Investigators. Preoperative autologous donation decreases allogeneic transfusion but increases exposure to all red blood cell transfusion: results of a meta-analysis. Arch Intern Med 1998;158(06):610–616
38 Tunthanathip T. Malignant transformation in low-grade astrocytoma for long-term monitoring. J Cancer Res Ther 2022; 18(06):1616–1622