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Original Article

Correlation between perioperative red blood cell transfusion strategy and 3-month neurological outcomes in patients undergoing craniotomy for traumatic brain injury

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Abstract: Objective: To investigate the correlation between perioperative red blood cell (RBC) transfusion trigger thresholds and 3-month neurological outcomes in patients undergoing craniotomy for traumatic brain injury (TBI). Methods: A total of 113 patients were retrospectively enrolled and stratified into two groups according to hemoglobin (Hb) level: a restrictive transfusion group (Hb < 80 g/L) and an liberal transfusion group (Hb < 90 g/L). Transfusion exposure and clinical outcomes were compared between the two groups, and multivariate logistic regression as well as inverse probability of treatment weighting (IPTW) were adopted for statistical analysis. Results: The restrictive group had lower transfusion rate and transfusion volume (both $P < 0.05$). The incidence of adverse neurological functional outcomes (defined as Glasgow Outcome Scale-Extended score, GOSE score ≤ 4) at 3 months postoperatively was lower in the restrictive group. Multivariate logistic regression analysis indicated that the restrictive transfusion strategy was marginally associated with a lower risk of adverse outcomes (OR=0.40, P=0.053). The IPTW analysis yielded a consistent trend without statistical significance (P=0.110). There was no statistically significant difference in the incidence of complications. Conclusion: The restrictive transfusion strategy can reduce transfusion exposure and is correlated with a favorable trend in neurological functional prognosis. Further studies are still required to validate these findings.

Keywords: Traumatic brain injury, craniotomy, perioperative period, erythrocyte transfusion strategy, neurological function

Introduction

Traumatic brain injury (TBI) is one of the leading global causes of mortality and disability. The primary goal of perioperative management is to maintain adequate cerebral perfusion pressure and cerebral oxygenation, thereby attenuating the development and progression of secondary brain injury [1]. According to the 2019 Global Burden of Disease (GBD) systematic analysis, there were approximately 27.16 million new TBI cases and 48.99 million prevalent cases worldwide in 2019, with around 7.08 million years lived with disability (YLDs), indicating a persistently high long-term disease burden [2]. The World Health Organization has reported that injuries (e.g., caused by traffic accidents and falls) account for approximately 4.4 million annual deaths, nearly 8% of all global mortality, and TBI contributes substantially to injury-related death and disability [3].

Against this background, perioperative anemia and transfusion management have become an unavoidable clinical challenge. Anemia reduces blood oxygen-carrying capacity and elevates the risk of cerebral hypoxia. Although red blood cell (RBC) transfusion can increase arterial oxygen content, it may also raise the risk of transfusion-related adverse events such as volume overload and acute lung injury, as well as induce unfavorable inflammatory and immune responses [4, 5]. Accordingly, the optimal perioperative RBC transfusion trigger threshold remains

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an ongoing controversy among neurosurgical and neurocritically ill patients.

In recent years, randomized controlled trials focusing on acute brain injury have yielded critical evidence to address this clinical dilemma. The HEMOTION trial compared liberal versus restrictive transfusion strategies in patients with TBI, while the TRAIN trial assessed transfusion protocols based on different hemoglobin (Hb) thresholds in a broader population with acute brain injury [6, 7]. Overall, current evidence cannot consistently confirm that adopting a higher Hb threshold yields definite functional benefits, and liberal transfusion strategies are generally associated with greater transfusion exposure [8, 9]. In real-world clinical practice, transfusion decisions are not determined by Hb threshold alone. For patients undergoing craniotomy, perioperative transfusion strategies are further influenced by intraoperative blood loss, coagulation function, radiological injury severity, and surgical modality. Real-world evidence comparing the two widely applied transfusion thresholds (Hb < 80 g/L and Hb < 90 g/L) in TBI patients undergoing craniotomy remains scarce. Therefore, this study adopted a single-center retrospective cohort design to compare transfusion exposure, changes in laboratory parameters, and 3-month postoperative neurological outcomes between restrictive (Hb < 80 g/L) and liberal (Hb < 90 g/L) transfusion strategies. Multivariate logistic regression and propensity score weighting were applied to verify the robustness of the findings, aiming to provide evidence for individualized perioperative transfusion decision-making in clinical practice.

Materials and methods

Study design and participants

This single-center retrospective cohort study consecutively enrolled adult patients who underwent craniotomy for traumatic brain injury (TBI) between January 2024 and December 2025. Participants were stratified according to the perioperative red blood cell (RBC) transfusion trigger threshold: the restrictive transfusion group (n=70, transfusion triggered at Hb < 80 g/L) and the liberal transfusion group (n=43, transfusion triggered at Hb < 90 g/L). The study flowchart is shown in **Figure 1**. This study was approved by the Ethics Committee of The First People's Hospital of Jiashan.

Sample size estimation was performed using the formula for comparing proportions between two independent groups:

$$n_1 = \frac{\left[Z_{\frac{\alpha}{2}} \cdot \sqrt{\left(1+\frac{1}{k}\right) \cdot \bar{P}(1-\bar{P})} + Z_{\beta} \cdot \sqrt{\frac{P_1(1-P_1)+P_2(1-P_2)}{k}}\right]^2}{(P_1 - P_2)^2}$$

$$\bar{P} = (P_1 + kP_2)/(1+k)$$

The two-sided significance level was set at $\alpha=0.05$, statistical power at $1-\beta=0.80$, and the sample size ratio of the liberal group to the restrictive group $k=43/70\approx0.614$. Assuming the 3-month incidence of adverse neurological outcomes was 26% in the restrictive transfusion group and 52% in the liberal transfusion group, the calculated required sample size was approximately 69.92 cases for the restrictive transfusion group and 42.95 cases for the liberal transfusion group. After rounding, 70 and 43 cases were enrolled respectively.

Inclusion criteria: (1) Age ≥ 18 years; (2) Intracranial injury confirmed by admission imaging and receipt of craniotomy including hematoma evacuation or decompressive craniectomy (brain CT images of patients with intracranial injury are shown in **Figure 2**); (3) At least one perioperative routine blood test and coagulation function examination; (4) Complete clinical data available for 3-month follow-up.

Exclusion criteria: (1) Complicated with active hematological diseases or a history of severe coagulation disorders; (2) Receipt of special perioperative interventions that substantially affected cerebral oxygenation; (3) Unavailable key variables precluding statistical analysis.

Definition of perioperative RBC transfusion strategy and group allocation: The perioperative RBC transfusion trigger threshold was defined as the primary exposure variable. Group allocation was determined based on documented transfusion thresholds in anesthesia documents, ICU medical orders, clinical progress notes, and the hospital transfusion management system, with consistency verified by the Hb level measured prior to the first RBC transfusion.

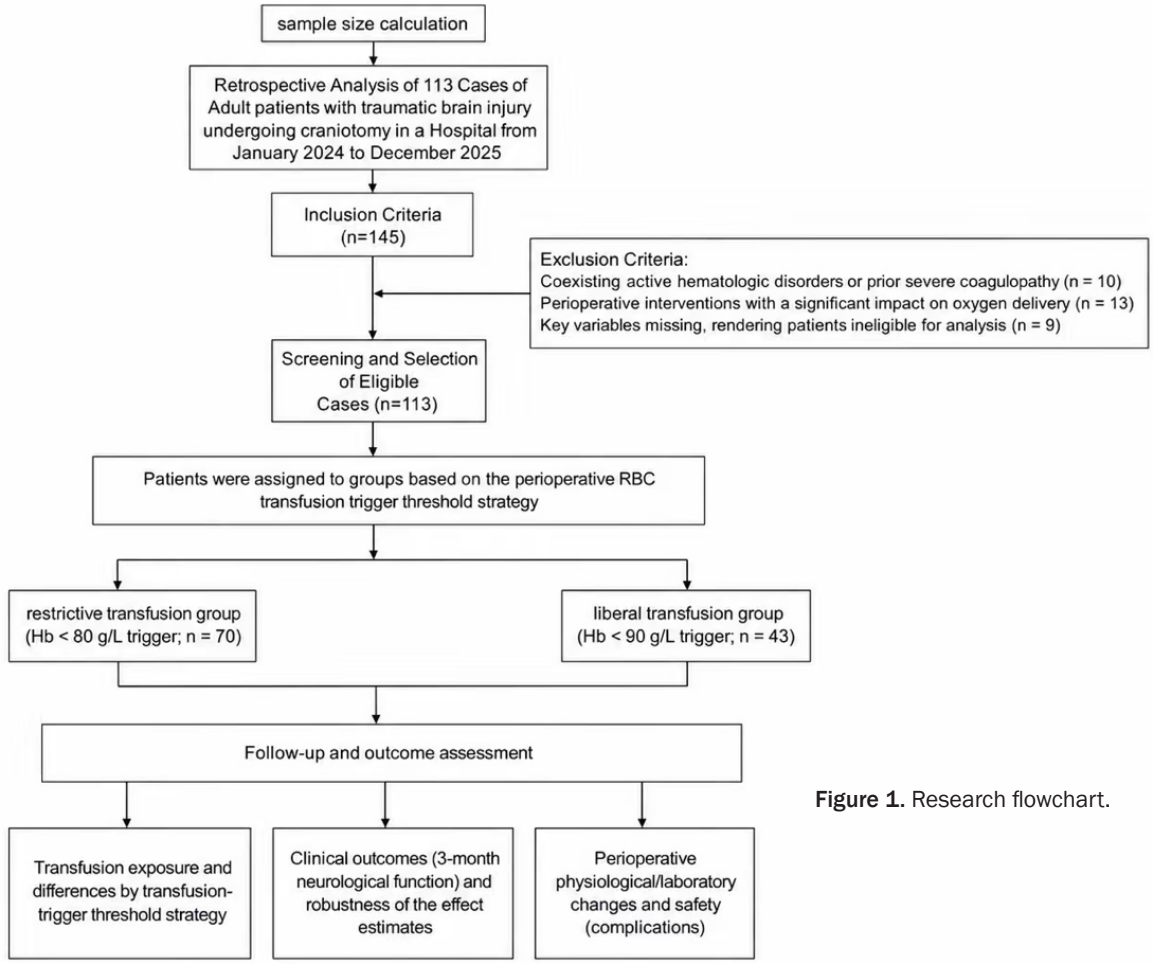

Figure 1. Research flowchart.

Grouping criteria were defined as follows: In the restrictive transfusion group, RBC transfusion was considered when perioperative medical records adopted Hb < 80 g/L as the primary transfusion trigger.

In the liberal transfusion group, RBC transfusion was considered when perioperative medical records adopted Hb < 90 g/L as the primary transfusion trigger.

In clinical practice, transfusion decisions were not determined by Hb threshold alone, but comprehensively evaluated according to active bleeding status, hemodynamic stability, and risk of cerebral hypoxia. For patients with inconsistent recorded information or overlapping transfusion strategies, classification was conducted following the principle of recorded threshold priority combined with verification of the initial pre-transfusion Hb level, and relevant conditions were described in the strategy compliance analysis. To minimize grouping bias, grouping based on medical records was further verified using the Hb value before the first RBC transfusion. Nevertheless, since clinical transfusion decisions were affected by multiple confounding factors, a certain degree of misclassification bias was inevitable.

Strategy compliance evaluation: A compliance evaluation was conducted to reflect the real-world implementation of the two transfusion strategies. For patients receiving RBC transfusion, the initial trigger Hb was defined as the most recent Hb measurement immediately before transfusion initiation; if multiple tests were available within the same time window, the value closest to transfusion start time was adopted.

An initial trigger Hb < 80 g/L was defined as consistent with the restrictive strategy, and an initial trigger Hb < 90 g/L as consistent with the

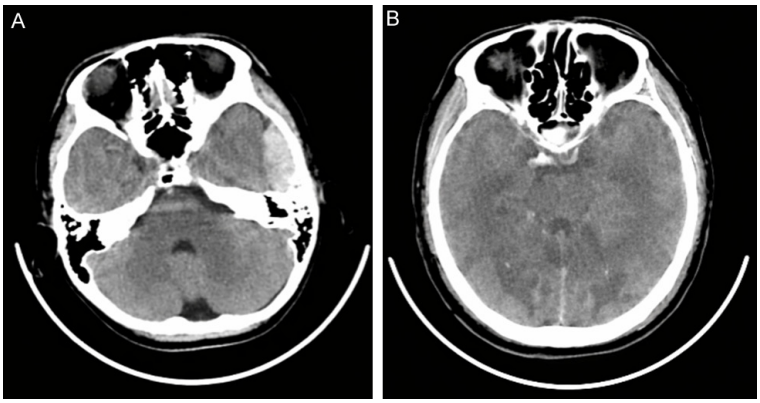

Figure 2. Brain CT scans in patients with intracranial injury. A: Patients with epidural hematoma. B: Patients with combined subdural and intracerebral hematoma.

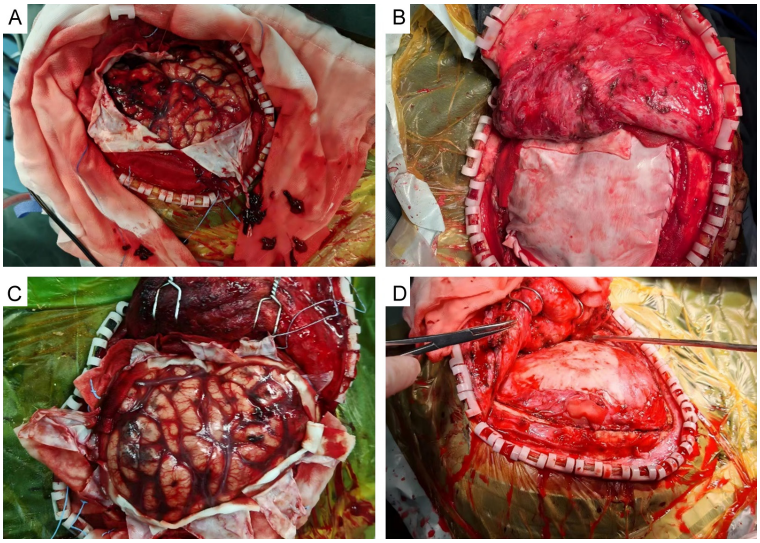

Figure 3. Subdural hematoma removal surgery. A: Incised meninges in patients with combined subdural hematoma and intracerebral hematoma. B: Meningeal suture after subdural hematoma removal surgery. C: Surgical field status after subdural hematoma removal surgery. D: State of bone flap removal after subdural hematoma removal surgery.

liberal strategy. Transfusion administered when the initial trigger Hb exceeded the corresponding threshold was recorded as above-threshold transfusion, with clnical indications documented, such as active bleeding, hemodynamic instability, or elevated risk of cerebral hypoxia.

Compliance indicators were only used to describe clinical implementation features and were not applied to redefine group allocation.

Definition of perioperative period: The perioperative period in this study was defined as 24 hours preoperatively to 72 hours postoperatively, or the time point prior to hospital discharge, death, or reoperation, whichever occurred first. Perioperative RBC transfusion exposure included all RBC transfusions administered during surgery and within 72 hours after operation.

Perioperative management and surgical procedures

All patients received standardized perioperative management for TBI, including maintenance of hemodynamic stability, intracranial pressure control, correction of coagulation disorders and acidosis, and sedation, analgesia and mechanical ventilation when necessary [1]. Surgical approaches were determined by attending neurosurgeons according to preoperative imaging manifestations and intraoperative conditions. The procedure of subdural hematoma evacuation is illustrated in **Figure 3**.

Outcome measures

Specimen collection and laboratory detection: (1) Routine blood parameters (Hb, platelet count): A total of 2 mL peripheral venous blood was collected into EDTA-K2 anticoagulant tubes and detected within 2 hours using an automated hematology analyzer (Sysmex XN-1000). (2) Lactate: Arterial blood was collected with heparin anticoagulation and examined immediately via a blood gas analyzer (Radiometer ABL800 FLEX). (3) Coagulation function (fibrinogen, D-dimer): Sodium citrate-anticoagulated plasma was adopted. Detection was performed on an automatic coagulation analyzer (STA-R Max). Fibrinogen was measured by the Clauss method, and D-dimer was measured by immunoturbidimetry (STA-Liatest D-Di).

Primary outcomes: Unfavorable neurological outcome at 3 months postoperatively: An Extended Glasgow Outcome Scale (GOSE) score ≤ 4 was defined as unfavorable neurological outcome, a cutoff widely adopted in TBI studies [10].

Secondary outcomes: Secondary outcomes included 3-month mortality; perioperative transfusion exposure (RBC transfusion rate and transfusion volume); in-hospital complications (infection, acute kidney injury [AKI], rebleeding, reoperation for hemostasis, venous thromboembolism [VTE], etc.); healthcare resource utilization (duration of mechanical ventilation, ICU stay length, total hospital stay length); and serial laboratory parameters (Hb, lactate, fibrinogen, platelet count, D-dimer). AKI was diagnosed in accordance with the KDIGO guidelines [11].

Injury severity and radiological indicators: Admission Glasgow Coma Scale (GCS), Injury Severity Score (ISS), admission oxygen saturation (SpO_2 < 90%), pupillary light reflex grading, pupillary abnormality, midline shift, Marshall CT classification, and Rotterdam CT score were recorded. The ISS was used to assess the overall severity of the patient's trauma; the imaging classification was reviewed by two physicians, and any discrepancies were resolved by a third physician [12, 13].

Data sources: Data regarding complications, transfusion and mortality were extracted from electronic medical records, transfusion management system, ICU medical orders and discharge summaries.

Follow-up and GOSE assessment: The primary endpoint was unfavorable neurological outcome (GOSE score ≤ 4) at 3 months postoperatively. The follow-up window was set at 90 ± 14 days after surgery. GOSE assessment was preferentially based on outpatient revisit records; if unavailable, telephone follow-up was performed for evaluation. GOSE scoring was conducted according to standardized structured interview guidelines [10]. For patients with multiple follow-up records, the assessment closest to postoperative day 90 was adopted.

Statistical analysis

All statistical analyses were performed using SPSS 29.0. Normally distributed continuous variables were expressed as mean ± standard deviation and compared by independent samples t-test; non-normally distributed continuous variables were presented as median (interquartile range) and compared by the Mann-Whitney U test. Categorical variables were expressed as case numbers (percentages) and analyzed using the χ^2 test or Fisher's exact test, as appropriate.

The primary outcome adopted logistic regression to assess the association between transfusion strategies and adverse outcomes, with clinically relevant confounding factors included in the analysis. Propensity score was calculated, and stabilized inverse probability of treatment weighting (IPTW) was conducted with weight truncation. Standardized mean difference was used to evaluate intergroup baseline balance. Extreme weights were winsorized at the 1st and 99th percentiles to improve the stability of the estimates. A two-tailed *P* value < 0.05 was considered statistically significant.

Complete case analysis was adopted. Patients with missing primary endpoint (3-month GOSE) data were excluded from the final analysis. Cases with missing key covariates incorporated into multivariate logistic regression and propensity score models were excluded according to the exclusion criteria. Missing values of non-key variables were not imputed and only described descriptively. Strategy compliance indicators, including initial trigger Hb and above-threshold transfusion proportion, were only used to characterize real-world clinical practice and did not alter the original group allocation.

Results

Comparison of baseline characteristics

The two groups were generally comparable in terms of age, sex, admission GCS score, Injury Severity Score (ISS), admission hypoxia, pupillary response, radiographic severity (Marshall/Rotterdam scale), concomitant head trauma, surgical type, intraoperative blood loss, and the proportion of decompressive craniectomy (all P > 0.05, **Table 1**).

Comparison of transfusion rate and transfusion volume

The perioperative RBC transfusion rate in the restrictive transfusion group was lower than

Table 1. Comparison of baseline characteristics between the two groups of patients

Variable	Restrictive transfusion group (n=70)	Liberal transfusion group (n=43)	Statistical value ($t/\chi^2/Z$/Fisher)	P
Age (years)	47.7±12.2	48.8±13.4	-0.427	0.670
Male	45/70 (64.3%)	31/43 (72.1%)	0.425	0.514
ISS score	27.5 (18.0-32.0)	27.0 (19.0-35.0)	-1.014	0.311
Admission GCS	7.0 (5.0-10.0)	8.0 (5.0-9.5)	0.325	0.746
Severe TBI (GCS ≤ 8)	41	27	0.061	0.805
Admission hypoxia (SpO_2 < 90%)	5	4	/	0.729
Abnormal pupils	23	19	1.019	0.313
Pupillary light reflex			1.472	0.479
0	10	8		
1	13	11		
2	47	24		
Midline shift ≥ 5 mm	38	32	3.766	0.052
Marshall CT classification	4.0 (3.0-5.0)	5.0 (4.0-5.0)	-0.917	0.332
Rotterdam CT score	4.0 (3.0-4.0)	4.0 (3.0-4.0)	-1.638	0.081
Comorbid with extracranial injury	29	18	0.000	1.000
Surgical type			2.766	0.429
Craniotomy (Other)	27	15		
Decompression + Evacuation	16	14		
Evacuation (EDH)	11	3		
Evacuation (SDH)	16	11		
Intraoperative blood loss (mL)	548.5 (328.0-801.0)	577.0 (424.0-913.5)	-1.153	0.250
Decompressive craniectomy	16	14	0.836	0.360

TBI, traumatic brain injury; SpO_2, oxygen saturation; ISS, Injury Severity Score; GCS, Glasgow Coma Scale; EDH, epidural hematoma; SDH, subdural hematoma.

that in the liberal transfusion group (P < 0.001). In the whole cohort analysis (including patients who did not receive transfusions), the RBC transfusion volume in the restrictive transfusion group was lower than that in the liberal transfusion group (P < 0.001, **Table 2**).

Comparison of Hb levels at different time points

There were no statistically significant differences in preoperative Hb levels between the two groups (all P > 0.05). The minimum Hb level at 24 h postoperatively and Hb level at 72 h postoperatively in the restrictive transfusion group were lower than those in the liberal transfusion group (all P < 0.05, **Figure 4**).

Comparison of peak lactate levels at 24 h and 72 h postoperatively

The peak lactate levels before surgery were similar between the two groups (P > 0.05). Regarding postoperative indicators, the peak lactate levels at 24 h and 72 h postoperatively in the restrictive transfusion group were lower than those in the liberal transfusion group, and the differences were statistically significant (all P < 0.05, **Figure 5**).

Comparison of coagulation and platelet parameters

There were no statistically significant differences in fibrinogen levels, platelet counts, or D-dimer levels between the two groups before surgery (all P > 0.05). At 24 h and 72 h postoperatively, fibrinogen levels and platelet counts in the restrictive transfusion group were higher than those in the liberal transfusion group (all P < 0.05). Conversely, D-dimer levels in the restrictive transfusion group were lower than those in the liberal transfusion group (all P < 0.05, **Figure 6**).

Comparison of 3-month neurological outcomes and mortality

The incidence of unfavorable neurological outcome at 3 months was lower in the restrictive

Table 2. Comparison of blood transfusion rates and volume between the two groups

Variable	Restrictive transfusion group (n=70)	Liberal transfusion group (n=43)	Statistical value ($t/\chi^2/Z/$ Fisher)	P
Red blood cell transfusion (Yes)	24	30	12.056	< 0.001
Red blood cell transfusion volume (unit, including those who did not receive transfusion)	0.0 (0.0-2.0)	3.0 (0.0-4.5)	-4.143	< 0.001

RBC, red blood cells.

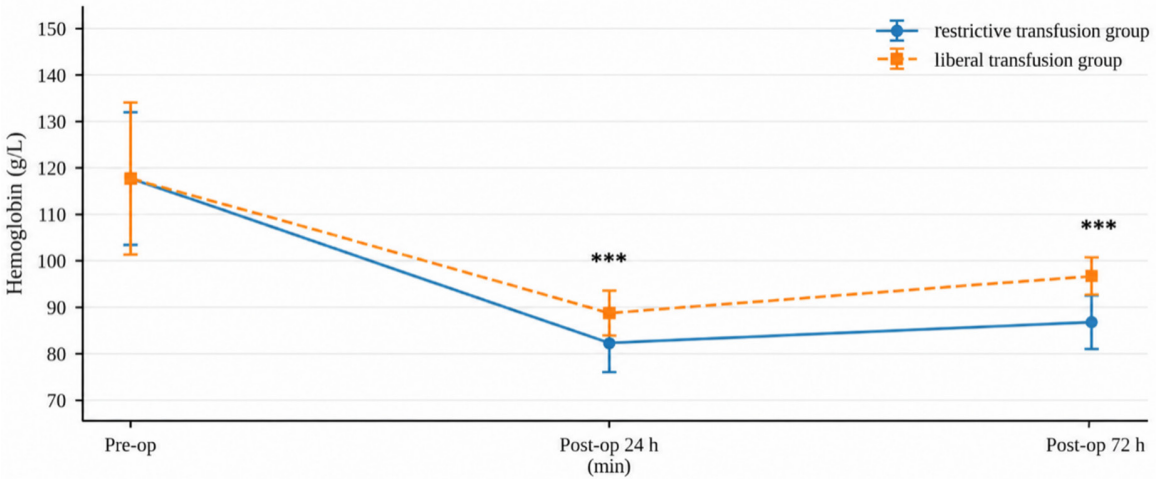

Figure 4. Comparison of Hb levels at different time points. Note: Compared with the liberal transfusion group, ***P < 0.05.

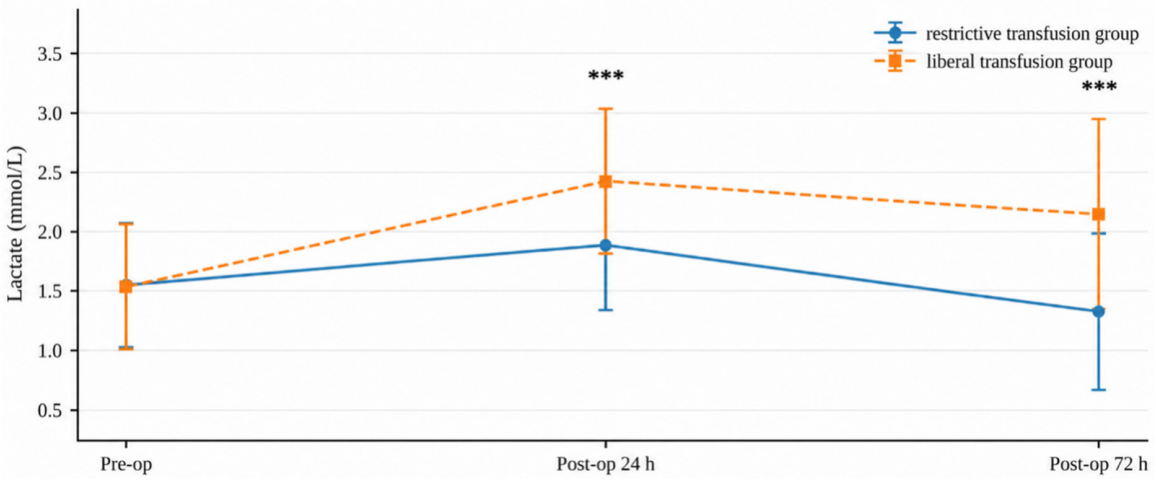

Figure 5. Comparison of peak lactate at different times. Note: Compared with the liberal transfusion group, ***P < 0.05.

transfusion group than that in the liberal transfusion group (P < 0.05). Regarding 3-month mortality, the restrictive transfusion group showed a lower trend, but the difference between the groups did not reach statistical significance (P > 0.05, **Figure 7**).

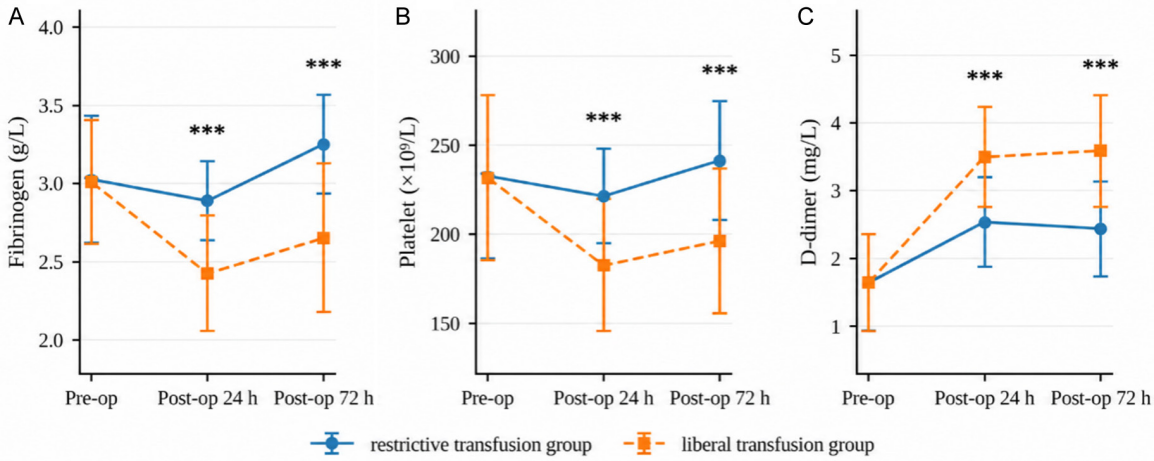

Figure 6. Comparison of coagulation and platelet indicators. A: Changes in fibrinogen levels in the two groups. B: Changes in platelet counts in the two groups. C: Changes in D-dimer levels in the two groups. Note: Compared with the liberal transfusion group, $^{***}P < 0.05$.

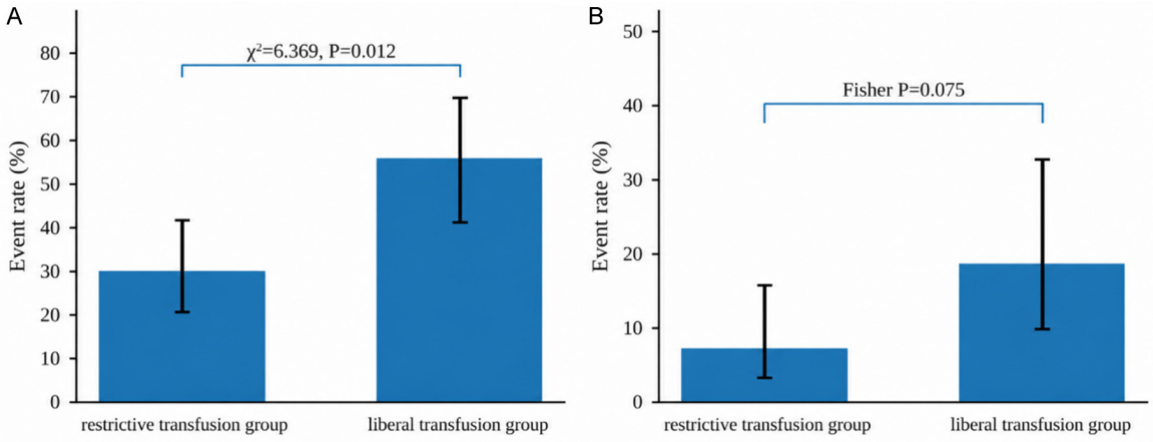

Figure 7. Comparison of 3-month neurological outcomes and mortality. A: Comparison of 3-month neurological outcomes. B: Comparison of 3-month mortality rates.

Comparison of complications

There were no statistically significant differences between the two groups in nosocomial infections, AKI, rebleeding/reoperational hemostasis, VTE, use of vasopressors, and persistently elevated lactate (all $P > 0.05$, **Table 3**).

Multivariate and propensity score weighted analysis

In the uncorrected model, restrictive transfusion strategy was associated with a reduced risk of adverse neurological outcomes at 3 months (OR=0.34, 95% CI 0.15-0.75, P=0.007). After including factors such as age, admission GCS score, pupillary abnormalities, Rotterdam CT score, intraoperative blood loss, and decompressive craniectomy, the association remained consistent in direction, but the effect size weakened, showing a marginally significant trend (OR=0.40, 95% CI 0.16-1.01, P=0.053). In the IPTW analysis, after stabilizing the weights and truncating 1-99%, the association between restrictive strategies and the risk of adverse outcomes remained consistent, but did not reach statistical significance (OR=0.53, 95% CI 0.24-1.16, P=0.110). The IPTW analysis without stabilization showed a consistent trend (OR=0.54, 95% CI 0.31-0.93, P=0.026). Considering the sensitivity of different weighting methods to extreme values, this difference suggests that the model estimation is somewhat

Table 3. Comparison of complications between the two groups

Variable	Restrictive transfusion group (n=70)	Liberal transfusion group (n=43)	Statistical value ($t/\chi^2/Z$/Fisher)	P
Days of mechanical ventilation	4.0 (2.0-6.0)	7.0 (3.0-8.5)	Z=-2.963	0.003
Days of ICU stay	5.9 (4.1-8.0)	7.8 (5.0-10.2)	Z=-2.147	0.032
Total days of hospitalization	13.3 (9.8-16.3)	14.8 (11.9-17.6)	Z=-1.789	0.074
Infection in the hospital	15	5	χ^2=1.148	0.284
Acute kidney injury	8	8	χ^2=0.615	0.433
Rebleeding or reoperation for hemostasis	2	5	/	0.103
Postoperative need for vasopressors	25	15	χ^2=0.000	1.000
Continuous increase in lactate (24 hours)	17	13	χ^2=0.226	0.634
VTE event	2	4	/	0.199

VTE, venous thromboembolism.

Table 4. Association analysis between blood transfusion strategies and 3-month adverse neurological function outcomes

Model/Analysis	The OR of restrictive strategies for adverse outcomes (95% CI)	P
Simplified Model	0.34 (0.15-0.75)	0.007
Multifactor Logistic (adjusted for age, GCS, pupil, Rotterdam, blood loss, craniectomy)	0.40 (0.16-1.01)	0.053
IPTW (stabilized + 1%/99% censored)	0.53 (0.24-1.16)	0.110
IPTW (unstabilized)	0.54 (0.31-0.93)	0.026

IPTW, inverse probability of treatment weighting.

dependent on the sample structure and weight distribution. See **Table 4**.

Discussion

This study focused on patients undergoing craniotomy for TBI, a population characterized by marked perioperative bleeding burden and fluctuating coagulation status. We compared a restrictive transfusion strategy initiated at a hemoglobin (Hb) threshold of < 80 g/L with a liberal transfusion strategy initiated at Hb < 90 g/L. The results demonstrated that the restrictive strategy significantly reduced RBC transfusion exposure. In terms of clinical outcomes, the restrictive transfusion group exhibited a lower incidence of unfavorable neurological outcome at 3 months in the unadjusted analysis. Although the directional association remained consistent across analyses, it failed to reach statistical significance. Such discrepancies may be attributable to differences in model construction and weight processing methods.

Despite marginal discrepancies in statistical significance, all models yielded consistent directional effects, indicating that the restrictive transfusion strategy was potentially associated with a lower risk of adverse outcomes. These findings suggest a trend toward better functional outcomes with the restrictive strategy, which should be interpreted with caution, and definitive causal inference cannot be drawn solely from the present results. No significant between-group differences were observed in the incidence of major complications, including infection, AKI, rebleeding/reoperative hemostasis, and VTE. Collectively, our findings supported that a more conservative transfusion threshold reduced unnecessary blood transfusion without increasing the burden of major complications, and provided a directional signal of potential functional benefits.

In addition, patients in the restrictive strategy group exhibited shorter duration of mechanical ventilation and ICU stay length. The underlying mechanism may be related to the reduction of transfusion-related adverse events. Previous studies have confirmed that RBC transfusion can increase volume overload and systemic inflammatory response, which may induce or exacerbate transfusion-related acute lung injury and transfusion-associated circulatory overload, thereby prolonging mechanical ventilation [14]. By minimizing unnecessary transfusion,

the restrictive strategy may lower the risk of such pulmonary complications, facilitate the recovery of respiratory function, and shorten ICU stay.

The HEMOTION and TRAIN trials have provided pivotal evidence regarding transfusion thresholds in patients with acute brain injury [6, 7]. Overall, available randomized controlled trial evidence does not support that adopting a higher Hb transfusion threshold yields definitive functional benefits, whereas a liberal transfusion strategy increases transfusion exposure [6, 7]. In a cohort of TBI patients, Robertson et al. evaluated erythropoietin administration alongside different transfusion thresholds, and found that maintaining a higher Hb level failed to improve neurological recovery, suggesting a potential increased thrombotic risk [14]. Consistent with the overall findings of those previous studies, our perioperative cohort also demonstrated a favorable result in functional outcomes with the restrictive strategy, implying that a liberal Hb threshold should not be routinely adopted by default in patients undergoing TBI craniotomy.

An increasing number of studies have attempted to incorporate physiological parameters into transfusion decision-making, rather than relying solely on a single Hb threshold [15, 16]. From a pathophysiological perspective, although elevated Hb increases arterial oxygen content, cerebral oxygen supply is modulated by multiple factors, including cerebral autoregulation, microcirculatory perfusion, blood viscosity, and oxygen utilization efficiency [16]. Accordingly, a higher Hb level does not necessarily translate into improved cerebral tissue metabolism. In our study, the restrictive group exhibited a lower minimum Hb level at 24 hours postoperatively accompanied by a lower peak lactate concentration. This phenomenon suggests that tissue perfusion and oxygen metabolism are not adversely compromised under a relatively lower Hb state. Potential mechanisms include improved microcirculatory perfusion, enhanced oxygen utilization efficiency, and alleviated metabolic disturbance induced by transfusion-related adverse reactions.

Furthermore, transfusion-related adverse events are common in perioperative critically ill and surgical patients, with TACO and TRALI posing well-documented clinical risks [17]. Reducing unnecessary transfusion theoretically decreases the risk of such complications, which is in line with the core principle of patient blood management (PBM): avoiding non-indicated transfusion while meeting basic physiological demands [18].

Accumulated evidence indicates that reduced transfusion exposure is correlated with a more favorable coagulation and fibrinolytic phenotype [19]. Patients undergoing TBI craniotomy present dynamic and bidirectional coagulation disturbances, with a predisposition to both hemorrhage and hypercoagulability-related microthrombosis. Previous systematic reviews have reported discrepancies in clinical outcomes and transfusion-related adverse events across different transfusion strategies [20-22]. In the present study, the restrictive group had higher fibrinogen levels and platelet counts, as well as lower D-dimer levels, without an increased risk of rebleeding or reoperation for hemostasis. These results imply a potential association between the restrictive strategy and improved coagulation profile. Nevertheless, these observational correlations are susceptible to confounding factors such as injury severity and hemostatic interventions, and a causal relationship cannot be established. Future studies incorporating the dosage of other blood products, detailed hemostatic management, and dynamic high-resolution coagulation monitoring may help clarify the underlying mechanistic pathways.

Prognosis of TBI is strongly correlated with injury severity, and radiological grading plays a vital role in risk stratification. The Marshall CT classification and Rotterdam CT score are well-validated radiological tools for evaluating intracranial injury burden and prognostic risk [12, 13]. Although decompressive craniectomy effectively controls intracranial pressure, its impact on long-term functional outcomes is complex, and it may also alter perioperative bleeding risk and transfusion requirements [8, 9]. We incorporated key indicators of injury severity and surgical characteristics into the multivariate regression and propensity score model to minimize indication bias in between-group comparisons. Given the heterogeneity of surgical subtypes, further stratified analysis and interaction analysis based on larger sample sizes are warranted to identify the optimal transfusion th-

reshold across different surgical approaches and radiological risk levels.

With the widespread application of multimodal monitoring in neurocritical care, parameters such as intracranial pressure (ICP) and brain tissue oxygen tension ($PbtO_2$) provide direct physiological evidence for assessing cerebral oxygen insufficiency [23, 24]. The OXY-TC trial and subsequent systematic reviews suggested that multimodal monitoring may affect certain clinical outcomes, while notable heterogeneity exists across published studies [25, 26]. Therefore, transfusion decision-making based merely on a fixed Hb threshold cannot fully accommodate inter-individual variability. For patients with hypoxia, elevated ICP or abnormal cerebral oxygenation, timely correction of anemia and close dynamic re-evaluation are recommended. By contrast, for patients with stable perfusion, normal lactate levels and no evidence of cerebral oxygen deficit, aggressive targeting of higher Hb levels only increases transfusion exposure without generating clear clinical benefits. Based on our findings, a rational perioperative strategy should integrate Hb concentration with perfusion and metabolic biomarkers. When available, cerebral oxygenation monitoring should be referenced to shift transfusion decision-making from single threshold-based management to physiological status-guided individualized care.

Several limitations of this study should be acknowledged. As a retrospective observational study, indication bias and residual confounding factors could not be completely eliminated. In addition to multivariate regression, we adopted propensity score weighting and performed 1-99% percentile censoring on extreme weights to improve the robustness of results. However, the influence of unmeasured or difficult-to-quantify confounding factors cannot be excluded, including the duration of intraoperative hypotension, cerebral perfusion pressure, storage time of blood products, heterogeneity in hemostasis and transfusion management, and incomplete documentation of perioperative complications. Moreover, this was a single-center study with a relatively small sample size and a limited number of outcome events, which may lead to insufficient statistical power. Transfusion decisions are affected by active bleeding and hemodynamic instability; thus, indication bias and group misclassification are inevitable. In addition, we did not perform stratified analysis according to the timing of transfusion (preoperative, intraoperative, and postoperative), which may exert distinct impacts on long-term prognosis. Further large-sample, multicenter prospective studies or rigorous target trial simulation analyses are required to validate our conclusions.

Consistent directional associations were observed across the unadjusted model, multivariate regression, and propensity score-weighted analysis, despite fluctuations in statistical significance. This phenomenon is common in observational studies and can be explained by the following factors: (1) Substantial indication bias in perioperative transfusion decision-making; (2) Limited sample size restricting model stability; (3) IPTW weight distribution being sensitive to extreme values, with different weight stabilization approaches affecting effect estimation. Therefore, our results should be interpreted based on the consistency of effect direction rather than relying solely on the statistical significance of a single *P* value.

Conclusion

In patients undergoing craniotomy for TBI, a restrictive transfusion strategy with a threshold of Hb < 80 g/L reduces RBC transfusion exposure, shows a consistent favorable trend in neurological functional outcomes in multi-model analyses, and does not increase the risk of major complications. Given the retrospective design and potential residual confounding factors in this study, our findings need further validation in large-sample, multicenter prospective studies.

Disclosure of conflict of interest

None.

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