

Tranexamic acid-based prediction model for blood transfusion in traumatic brain injury: A retrospective case-control study

Ren Hu¹, Xiu-cun Wang² and Zhen Yan^{1*}

¹Department of Blood Transfusion, Affiliated Hospital of Xuzhou Medical University, China

²Department of Neurosurgery, Affiliated Hospital of Xuzhou Medical University, China

Abstract: Blood transfusion planning in traumatic brain injury (TBI) is ideal and pharmacotherapy such as tranexamic acid (TXA) may influence transfusion requirement. Within this retrospective, single-center case-control study, 259 TBI patients who were admitted from January 2022 to December 2024 were randomly allocated into training (70%) and validation (30%) datasets. Demographic, clinical, laboratory, surgical and pharmacologic variables-like TXA-were evaluated using univariable and multivariable logistic regression for independent predictors of transfusion. Surgery, tracheal intubation, longer hospital stay, lower hemoglobin and TXA administration were independent predictors of transfusion. The TXA nomogram had high discrimination (AUC 0.94 training; 0.93 validation), good calibration and clinical utility as demonstrated by decision curve analysis. Higher TXA use in transfused patients is likely due to confounding by indication, as patients were more ill and more likely to receive TXA. The inclusion of TXA in predictive models enhances personalized risk prediction of transfusion, but the model remains hypothesis-generating and requires external multicenter verification before being used clinically. This study is supportive of the development of pragmatic, pharmacology-driven tools for early risk stratification and precision transfusion planning in TBI.

Keywords: Blood transfusion; Risk prediction; Traumatic brain injury; Tranexamic acid

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INTRODUCTION

Traumatic brain injury (TBI) is an extreme worldwide public health problem and a frequent determinant of death and disability in hospitalized patients, with tens of millions of severe TBI recorded every year across the globe (Montgomery *et al.*, 2022). Transfusion of blood is typically an inevitable intervention in treating severe TBI, with the purposes to reestablish oxygenation of ischemic brain tissue and normalize coagulopathy (Florez-Perdomo *et al.*, 2023). Maintenance of hemoglobin has been demonstrated to reduce mortality in hemodynamically unstable patients. Planning transfusion strategy in TBI is a major clinical dilemma. Restrictive transfusion practices are likely to reduce complications such as TRALI and TACO but may not restore injured brain tissue with the high oxygen demands (Guglielmi *et al.*, 2024). Liberal transfusion practices such as those supported by American Association of Blood Banks (AABB) guidelines may exacerbate cerebral edema and inflammatory cascades (Russell *et al.*, 2022). Moreover, transfusion triggers also vary considerably across institutions, as it suggests the lack of individualized evidence-based guidelines for TBI patients (Turgeon *et al.*, 2024; Rakhit *et al.*, 2021).

Pharmacologic therapies in recent years have been highly promising as adjuncts to augment transfusion therapy for TBI patients (Anderson *et al.*, 2021; Nakae *et al.*, 2022). Tranexamic acid (TXA), an antifibrinolytic drug, is effective in bleeding control in trauma and neurosurgery

patients through the inhibition of fibrinolysis and strengthening of the clot (Bossers *et al.*, 2021; Wallen *et al.*, 2022; Hanley *et al.*, 2021). Through hemorrhage reduction, TXA can decrease allogenic blood transfusion needs, which correlate with increased morbidity, longer length of stay and higher healthcare costs (Huang *et al.*, 2022; Yokobori *et al.*, 2020). Hence, TXA is currently a key component of tailored transfusion approaches, balancing patient benefit against transfusion complications (Meer *et al.*, 2024; Prudovsky *et al.*, 2022).

The majority of predictive models for blood transfusion in TBI patients, although grounded in widespread evidence for TXA's hemostatic effect, take into account only demographics, lab values and surgery and exclude pharmacologic therapy. This exclusion reduces their clinical usefulness, as current neurotrauma practice is trending toward early and individualized pharmacologic treatments (Bossers *et al.*, 2021; Guyette *et al.*, 2021; Meer *et al.*, 2024). The inclusion of TXA in risk models for transfusion would allow increased predictive accuracy and allow clinicians to tailor interventions to individual patient needs, aligning with precision medicine approaches to TBI management (Sigmon *et al.*, 2023; Stitt and Spinella, 2024; Rowell *et al.*, 2020).

In addition, independent predictors of transfusion, both clinical and pharmacologic in nature, can be identified to optimize perioperative planning and minimize unnecessary exposure to blood products. This is in line with progressive standards of neurotrauma care that focus on evidence-based, patient-centered care to enhance both short- and

*Corresponding author: e-mail: 43548757@qq.com

long-term outcomes (Meyfroidt *et al.*, 2022; Wu *et al.*, 2022; Zhang *et al.*, 2024).

To address these gaps, we collected comprehensive demographic, clinical, laboratory, surgical and pharmacologic data, including TXA utilization, from TBI patients admitted to a tertiary center between 2022 and 2024. We employed univariable and multivariable analysis to identify independent predictors of transfusion and derive a TXA-containing prediction model. We hypothesized that inclusion of TXA in a predictive nomogram would enhance personalized risk estimation, knowing that administration of TXA is potentially confounded by indication (sicker injury patients at higher risk for receiving TXA). This internally validated model aims to provide clinicians with an evidence-based, quantitative method for precision transfusion planning, best pharmacologic utilization and improved neurocritical care outcomes.

MATERIALS AND METHODS

Study design and participants

This study was a single-center, retrospective, observational case-control study designed to identify predictors of blood transfusion in patients with traumatic brain injury (TBI). This study was conducted at the Affiliated Hospital of Xuzhou Medical University, a tertiary general hospital with an affiliated Department of Neurosurgery and an affiliated Neurocritical Intensive Care Unit (ICU) with high volume of severe neurotrauma. The observation period was from January 2022 through December 2024, during which all TBI patients were evaluated for enrollment. Complete clinical, laboratory, operative and pharmacologic data-like the administration of tranexamic acid (TXA)-were electronically extracted from the hospital database in a systematic way. This setting was an extensive source of data, where detailed evaluation of both traditional clinical parameters and pharmacologic interventions was possible.

By enrolling a well-characterized patient population at a single institution, the study aimed to minimize variability in treatment protocols and measurement of data, thereby maximizing internal validity. Yet, the single-center nature of the study itself underscores the importance of multicenter confirmation in the future to maximize generalizability of findings.

Inclusion and exclusion criteria

Patients were eligible to participate if they were 18 years or older, had traumatic brain injury (TBI) due to external trauma and had structural intracranial injury which was verified by cranial CT or MRI, i.e., hematoma, cerebral contusion, diffuse axonal injury, or primary brainstem injury. Additional conditions were hospital admission within 24 hours of the injury and receiving standardized medical or surgical therapy during hospitalization (Lee *et al.*, 2025). Exclusion factors included hospitalization for

fewer than 24 hours, primary hematologic or immunosuppressive diseases, or incomplete medical records, particularly lacking information on transfusion or pharmacologic therapies. Of 271 patients who were screened, 12 were excluded (5 were under the age of 18 years, 4 were admitted over 24 hours after injury and 3 were hospitalized for fewer than 24 hours). The analysis was completed on 259 patients.

The study was approved by the Affiliated Hospital of Xuzhou Medical University's Ethics Committee and conducted according to the Declaration of Helsinki. Informed consent was waived due to the retrospective nature of the study and patient identifiers were anonymized before analysis.

Data collection

Clinical data were extracted extensively from the electronic medical record system of the hospital to ensure accuracy and completeness. The records were checked and cross-checked independently by two experienced neurosurgical doctors and any differences were resolved by consensus with a senior researcher. This process minimized errors and ensured the reliability of the dataset. Demographics (age and sex), admission vital signs (blood pressure, heart rate, respiratory rate and body temperature) and comorbidities (renal disease, cardiovascular disease, liver disease, diabetes, hypertension) were information that were gathered. Neurologic status was assessed using Glasgow Coma Scale (GCS) score and pupillary light reflex. Injury-related characteristics included TBI type (hematoma, contusion/laceration, diffuse axonal injury, open/closed TBI, primary brainstem injury), cerebral herniation, skull fractures and multiple traumas. Clinical management (surgery, tracheal intubation, ICU admission and hospital length of stay) and complications such as bloodstream infections, heart failure, ARDS and MODS were also documented.

Tranexamic acid (TXA) administration was an important area of interest and was marked as a binary variable (Yes/No). Where available, additional data on dose, timing (prehospital, emergency department, intraoperative) and rate of infusion were collected to allow subgroup and sensitivity analyses. TXA was included a priori in multivariable models as a first-line pharmacologic predictor in order to determine its relationship to transfusion risk. TXA administration is known to be influenced by clinician judgment, which represents potential confounding by indication and this is addressed in the Results and Discussion. Other important laboratory parameters, including hemoglobin (Hb), C-reactive protein (CRP), prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (FIB), D-dimer and albumin, were also obtained. Admission and pre-transfusion or pre-surgical values were used to best reflect the peri-traumatic physiological status of each patient.

Study cohorts

After eligibility screening, patients were assigned randomly with a fixed random seed into training set (n = 181, 70%) and validation set (n = 78, 30%) for reproducibility. Baseline factors-demographics, injury severity, laboratory values and TXA administration-were compared and analyzed between the groups. There were no differences other than diffuse axonal injury (P = 0.046), allowing good balance and cohort validation for predictive modeling.

Statistical analysis

All statistical analysis was performed on SPSS version 26.0 and R version 4.3.2. Continuous data were described as mean $\pm$ SD or median with IQR and categorical data as counts and percentages (n, %). Between-group comparisons were established by independent t-tests or Mann-Whitney U tests for continuous data and chi-square or Fisher's exact tests for categorical data. A two-tailed P value of <0.05 was considered statistically significant.

To identify predictors of blood transfusion, univariate logistic regression was first done among demographic, clinical, laboratory and pharmacologic factors in the training cohort. Subsequently, those with P < 0.05 were included in a multivariable logistic regression model with tranexamic acid (TXA) included a priori due to its pharmacologic significance. Multicollinearity among predictors was identified using variance inflation factor (VIF <3) and tolerance (>0.2) to ensure model stability. A nomogram was then built from the final multivariable model to predict individualized risk of transfusion. Fit of the model was evaluated by discrimination using ROC curves and area under the curve (AUC), calibration by the Hosmer–Lemeshow test and calibration plots and value in clinical practice by decision curve analysis (DCA).

Also, subgroup and sensitivity analyses considered the effect of TXA timing, dose and route and interaction with type of surgery and baseline hemoglobin level and provided greater depth of understanding of drivers of transfusion risk.

RESULTS

Patient selection and baseline characteristics

Among 271 patients screened, 12 were excluded: 5 due to age <18 years, 4 due to admission >24 hours after injury and 3 due to hospital stay <24 hours. 259 patients were enrolled and allocated randomly to a training set (n = 181, 70%) and a validation set (n = 78, 30%). Among all the patients, 180 (69.5%) were male and 111 (42.9%) were more than 60 years old. Hematoma was the most common (74.5%) in cases of severity of injury, followed by contusion (44.4%), diffuse axonal injury (2.7%) and cerebral herniation (7.7%). TXA was applied in 42 patients (16.2%).

No statistically significant differences were observed between the training and validation cohorts for most of the baseline characteristics, except diffuse axonal injury (P = 0.046), determining overall balance and validity for subsequent modeling (Table 1).

Transfusion vs. Non-transfusion group comparisons

Clinical and physiological characteristics

In the training cohort, patients requiring transfusion experienced higher physiological stress and worse neurological status. They had significantly elevated heart rate, respiratory rate and temperature and more frequently had severe neurological impairment (GCS $\leq$ 8, no pupillary reflex). Measures of injury severity were also higher for the transfusion group (Table 2).

Interventions, pharmacologic treatment and outcomes

Transfused patients underwent more surgery, tracheal intubation and ICU admission and were hospitalized for longer periods. TXA was administered more frequently to transfused patients (27.6% vs. 9.6%, P = 0.002), as per clinicians' practice of giving TXA in more risky cases (Table 3).

Laboratory findings

Transfused patients had significantly lower hemoglobin and albumin levels and higher CRP and PT levels, suggesting greater blood loss and systemic inflammation (Table 4).

Multivariable logistic regression analysis

Multivariable analysis identified five independent predictors of transfusion: surgery, intubation of trachea, hospitalization, administration of TXA and hemoglobin.

Administration of TXA was independently associated with transfusion, reflecting both its therapeutic application and the severity of bleeding as a marker (Table 5).

Predictive nomogram and model performance

The nomogram predicting TXA and the other independent predictors showed excellent discrimination with AUC 0.94 (95% CI: 0.91–0.97) in the training and 0.93 (95% CI: 0.87–0.99) in the validation cohort. The model was well calibrated, indicating good concordance between observed and predicted outcomes and provided a net clinical benefit across a wide range of threshold probabilities as demonstrated by decision curve analysis. Sensitivity, specificity and predictive values were high in both cohorts uniformly, testifying to the clinical utility and reliability of the model (Table 6).

Calibration and clinical utility

Calibration plots showed close concordance of predicted and actual probabilities. Decision curve analysis also stated that the TXA-containing model provided greater net clinical benefit compared to "treat-all" or "treat-none" options (Figs. 1 and 2).

Table 1: Baseline characteristics of patients in training and validation cohorts

Variable	Total (n = 259)	Training (n = 181)	Validation (n = 78)	P-value
Age >60 years, n (%)	111 (42.9)	77 (42.5)	34 (43.6)	—
Male, n (%)	180 (69.5)	125 (69.1)	55 (70.5)	—
Hematoma, n (%)	193 (74.5)	135 (74.6)	58 (74.4)	—
Cerebral contusion, n (%)	115 (44.4)	80 (44.2)	35 (44.9)	—
Diffuse axonal injury, n (%)	7 (2.7)	6 (3.3)	1 (1.3)	0.046*
Cerebral herniation, n (%)	20 (7.7)	14 (7.7)	6 (7.7)	—
TXA administration, n (%)	42 (16.2)	33 (18.2)	9 (11.5)	—

Note: Values are n (%). Statistical significance defined as $P < 0.05$; Validation and training groups were fairly balanced as a whole and diffuse axonal injury alone differed significantly.

Table 2: Clinical and physiologic characteristics by transfusion status (Training Cohort)

Variable	Transfusion group	Non-transfusion Group	P-value
Heart rate (bpm)	87	79	0.007*
Respiratory rate (breaths/min)	18	17	0.016*
Body temperature (°C)	36.7	36.5	0.031*
GCS ≤ 8 , n (%)	82.8	58.5	<0.001*
Pupils without light reflex, n (%)	18.4	5.3	0.006*
Open craniocerebral injury, n (%)	14.9	5.3	—
Closed craniocerebral injury, n (%)	10.3	2.1	—
Cerebral herniation, n (%)	11.5	2.1	—

Note: Continuous variables are mean values; categorical variables are percentages. $P < 0.05$ was considered statistically significant.

Table 3: Interventions, pharmacologic treatment and outcomes

Variable	Transfusion group	Non-transfusion group	P-value
Surgery, n (%)	74.7	33.0	<0.001*
Tracheal intubation, n (%)	95.4	56.4	<0.001*
ICU admission, n (%)	83.9	46.8	<0.001*
Length of hospital stay, median (days)	24	12.5	<0.001*
TXA use, n (%)	27.6	9.6	0.002*

Note: Values are percentages unless stated otherwise. $P < 0.05$ considered statistically significant.

Table 4: Laboratory findings by transfusion status

Variable	Transfusion group	Non-transfusion group	P-value
Hemoglobin (g/L)	94.9 $\pm$ 19.7	123.2 $\pm$ 25.8	<0.001*
CRP (mg/L)	67.0	24.4	<0.001*
Prothrombin time (s)	12.2	11.2	<0.001*
Albumin (g/L)	34.1	39.4	<0.001*

Note: Values are mean $\pm$ SD. $P < 0.05$ considered statistically significant.

Table 5: Multivariable logistic regression analysis of independent predictors of blood transfusion

Variable	Adjusted OR (95% CI)	P-value	Interpretation
Surgery	8.43 (3.21-22.17)	<0.001*	Surgical patients more likely to require transfusion
Tracheal intubation	8.66 (1.89-39.58)	0.005*	Reflects severe injury requiring airway support
Length of hospital stay (days)	1.03 (1.01-1.07)	0.044*	Longer stay increases transfusion risk
TXA use	3.25 (1.05-10.06)	0.041*	Pharmacologic marker of high bleeding risk
Hemoglobin (per g/L)	0.95 (0.93-0.97)	<0.001*	Lower baseline Hb strongly predicts transfusion

Note: OR = odds ratio, CI = confidence interval. $P < 0.05$ was considered statistically significant.

Table 6: Predictive model performance in training and validation cohorts

Metric	Training cohort	Validation cohort
ROC AUC (95% CI)	0.94 (0.91-0.97)	0.93 (0.87-0.99)
Accuracy	0.89	0.83
Sensitivity	0.87	0.91
Specificity	0.91	0.77
Positive predictive value (PPV)	0.91	0.76
Negative predictive value (NPV)	0.87	0.92
Calibration (Hosmer-Lemeshow)	Good fit	Good fit
Decision curve analysis (DCA)	Net benefit across 10-90% thresholds	Net benefit across 10-90% thresholds

Note: ROC = receiver operating characteristic, AUC = area under the curve. Values represent excellent discrimination and clinical usefulness.

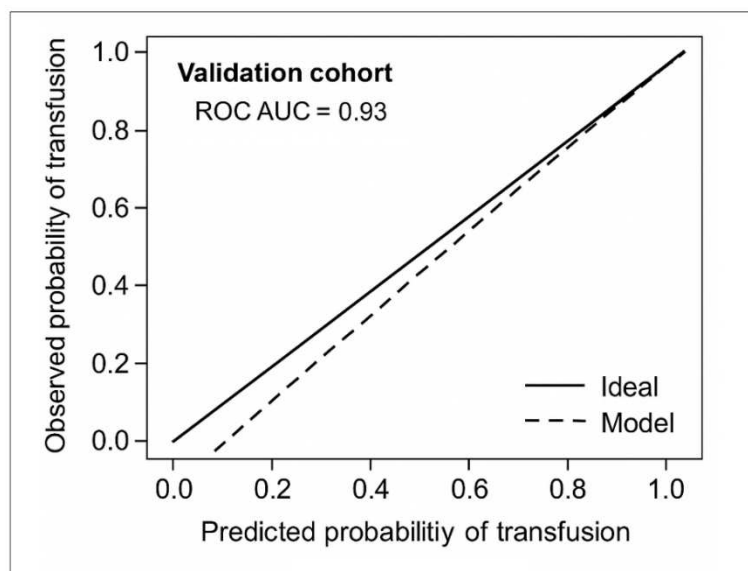


Fig. 1: Calibration curve for TXA-inclusive model of prediction in validation cohort; Diagonal dashed line is ideal calibration, and solid line is model-predicted probability of transfusion. The close proximity of the solid line to the diagonal indicates good model fit.

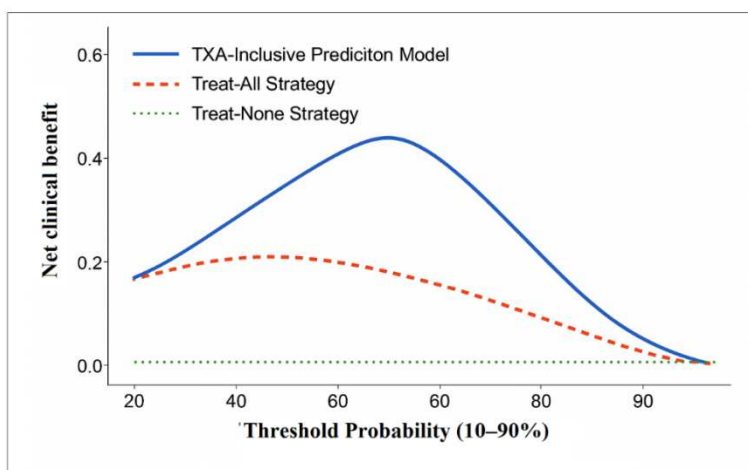


Fig. 2: Decision curve analysis of the TXA-inclusive prediction model in comparison to universal transfusion strategies; The TXA-inclusive model enjoys superior net clinical benefit to "Treat-All" and "Treat-None" strategies for the entire range of threshold probabilities (10–90%), indicating that it will prove useful for personalized transfusion decision-making.

Subgroup observations

Exploratory analyses revealed that those patients who were treated with TXA within three hours of presentation were marginally more likely to require a transfusion and this most likely reflects selection of TXA for more high-risk cases rather than causal effect. Those with both baseline low hemoglobin and TXA exposure had highest probability of transfusion, confirming additive predictive value of pharmacologic and hematologic factors.

DISCUSSION

TBI patients are usually in need of a blood transfusion for hemorrhage, anemia, or secondary cerebral hypoxia. Transfusion is lifesaving, but there remains controversy as to what ideal transfusion threshold should be. Liberal transfusion approach (e.g., 10 g/dL hemoglobin threshold) is known to restrict short-term neurological deterioration but is not consistently associated with superior long-term functional outcomes such as 6-month Glasgow Outcome Scale (GOS) score (Yuan *et al.*, 2024; Taccone *et al.*, 2024). There is an opposite effect for restrictive approach (e.g., Hb ≤ 7 g/dL) to decrease the transfusion complications of infection, thrombosis and acute kidney injury without increasing mortality or neurological deterioration. However, inappropriately low hemoglobin levels can augment cerebral hypoxia and over-transfusion can trigger inflammatory cascades that promote secondary brain injury (Ha, 2024; Rakhit *et al.*, 2021). There is no uniform guideline that recommends a universal transfusion threshold for TBI, with the strong need for individualized decision-making incorporating cerebral oxygenation, intracranial pressure, hemodynamics and pharmacologic treatment (Rathmell and Vacas, 2025).

Five independent predictors of transfusion were identified in this study: surgery, tracheal intubation, hospital stay, hemoglobin levels and the application of tranexamic acid (TXA) (Bossers *et al.*, 2021). Significantly, the addition of TXA as a pharmacological variable represents a new inclusion, as past prediction models effectively excluded drug treatment. The inclusion represents contemporary neurocritical care trends where hemostatic agents are increasingly being added to perioperative and trauma-induced bleeding control (Hollingworth *et al.*, 2024; Colomina Soler *et al.*, 2022). The model was robust with good discrimination (training AUC = 0.94, validation AUC = 0.93) and good calibration, implying its potential for early identification of high-risk TBI patients (Guo *et al.*, 2021; Li *et al.*, 2020).

Surgery was strongly associated with transfusion (OR = 8.43), as would also be seen from previous works reporting that surgeries such as decompressive craniectomy and hematoma evacuation increase intraoperative blood loss and transfusion levels. This is a reflection of the composite effects of surgical complexity, hemorrhage and use of anticoagulants (Wang *et al.*, 2022). Concurrently, tracheal

intubation (OR = 8.66) is an indicator of major neurologic impairment and multi-system trauma, both of which are associated with increased transfusion risk (Hassoun-Kheir *et al.*, 2020). Hospital length of stay was modestly associated with transfusion (OR = 1.03 per day), indicating multiple interventions, secondary hemorrhage and infections (Cao *et al.*, 2023; Wang *et al.*, 2024).

TXA use was independently associated with transfusion (OR = 3.25). Whereas TXA mechanistically reduces bleeding through the inhibition of fibrinolysis, such an association may be confounded by indication, since physicians selectively administer TXA to patients at higher perceived risk of hemorrhage (Li *et al.*, 2025; Lo *et al.*, 2024). As such, TXA is both a therapeutic action and a clinical marker for severity of bleeding. Hemoglobin was inversely correlated to transfusion (OR = 0.95), emphasizing the importance of dynamic Hb monitoring in transfusion decision-making. Furthermore, elevated heart rate and CRP in transfused patients suggest systemic inflammation and hypoperfusion in driving transfusion demand, as evidenced in prior trauma literature (Abdallah *et al.*, 2021; Yoon *et al.*, 2020).

Calibration plots demonstrated superb predicted vs. observed transfusion probability concordance and decision curve analysis (DCA) reiterated the net clinical benefit gain of the TXA-including model vs. "treat-all" or "treat-none" approaches at 20–80% thresholds. This reflects its promise of individualized transfusion planning and pharmacologic treatment. Including TXA increases clinical utility by adding drug dosing to transfusion risk prediction (Stitt *et al.*, 2024; Ahmadzia *et al.*, 2021).

Clinical applications: For the pharmacy and critical care staff, the model is a mathematical framework for dynamic transfusion monitoring of transfusion requirements, reducing TXA utilization and reducing unnecessary exposure to blood products. It allows for accurate transfusion strategies with the application of pharmacologic, lab and clinical markers in real-time patient management (Napolitano *et al.*, 2021; Kataria *et al.*, 2025).

Limitations: There are several limitations of this research. First, its single-center, retrospective design lowers external validity, necessitating multicenter investigations in the future for broadened utility. Second, the relatively modest number of subjects may limit robustness; greater numbers are needed for additional optimization. Third, dynamic parameters such as serial hemoglobin levels, evolving coagulation profiles and accurate TXA timing were not optimally captured, lowering in situ utility. Finally, unmeasured confounders such as institutional transfusion policies and surgeons' preferences likely impacted results. Future work should include prospective multicenter validation, incorporation of dynamic monitoring variables and use in real-time decision support systems to optimize

individualized transfusion care (Lee *et al.*, 2022; Eyth *et al.*, 2025).

CONCLUSION

Surgery, tracheal intubation, hospital length of stay, hemoglobin and TXA use were independent predictors of transfusion among patients with TBI. By integrating pharmacologic and clinical factors, the model provides a more comprehensive prediction of bleeding risk according to modern neurocritical care practice. The TXA-included model allows for earlier, tailored risk stratification, guiding individualized transfusion practice, optimizing blood product utilization and improving patient safety. External validation through large prospective multicenter studies is, however, required before routine clinical implementation.

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Not applicable.

Authors' contributions

Hu Ren and Wang Xiu-cun contributed to the conception and design of the study. Hu Ren was responsible for data collection, data curation and statistical analysis. Hu Ren drafted the manuscript. Wang Xiu-cun provided critical revisions for important intellectual content. Yan Zhen supervised the study, provided methodological guidance and served as the corresponding author. All authors reviewed and approved the final manuscript.

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Data availability statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical approval

The study was approved by the Ethics Committee of the Affiliated Hospital of Xuzhou Medical University (Approval No. XYFY2023-KL491) and conducted in accordance with the Declaration of Helsinki. Informed consent was waived due to the retrospective study design and all patient identifiers were anonymized before analysis.

Conflict of interest

The authors declare that they have no conflicts of interest relevant to this study.

REFERENCES

Abdallah AA, Sallam AA and Arafa MS (2021). Topical tranexamic acid in total knee arthroplasty: Does it augment the effect of the intravenous administration in patients with moderate-to-high risk of bleeding? A randomized clinical trial. *J. Knee Surg.*, **34**(14): 1570-8.

Ahmadzia HK, Luban NL, Li S, Guo D, Misztal A, Gobburu JV, Berger JS, James AH, Wolberg AS and van den Anker J (2021). Optimal use of intravenous tranexamic acid for hemorrhage prevention in pregnant women. *Am. J. Obstet. Gynecol.*, **225**(1): 85-e1.

Affan A, Zurada JM and Inanc T (2021). Adaptive individualized modeling from limited clinical data for precise anemia management. *IEEE Access*, **9**: 119466-75.

Anderson TN, Farrell DH and Rowell SE (2021). Fibrinolysis in traumatic brain injury: Diagnosis, management and clinical considerations. *Semin. Thromb. Hemost.*, **47**(5): 527-37.

Bossers SM, Loer SA, Bloemers FW, Den Hartog D, Van Lieshout EM, Hoogerwerf N, Van Der Naalt J, Absalom AR and Peerdeman SM (2021). Association between prehospital tranexamic acid administration and outcomes of severe traumatic brain injury. *JAMA Neurol.*, **78**(3): 338-45.

Cao MM, Zhang YW, Sheng RW, Gao W, Kang QR, Gao YC, Qiu XD and Rui YF (2023). General anesthesia versus regional anesthesia in the elderly patients undergoing hip fracture surgeries: A systematic review and meta-analysis of randomized clinical trials. *World J. Surg.*, **47**(6): 1444-56.

Colomina Soler MJ, Contreras L, Guilabert P, Koo Gómez M, Méndez E and Sabate Pes A (2022). Clinical use of tranexamic acid: Evidences and controversies. *Braz. J. Anesthesiol.*, **72**(6): 795-812.

Dong W, Tang Y, Zhou Y, Li J, Wu C, Liu Y, Yan Y, Peng Z and Zhao J (2025). Application and research progress of tranexamic acid in the perioperative period of posterior lumbar interbody fusion. *Front. Med.*, **12**: 1612281.

Eyth A, Borngaesser F, Rudolph MI, Paschold BS, Ramishvili T, Kaiser L, Tam CW, Wongtangman K, Eikermann G, Garg S and Karasick MH (2025). Development and validation of a risk model to predict intraoperative blood transfusion. *JAMA Netw. Open*, **8**(4): e255522.

Florez-Perdomo WA, Garcia-Ballesteras E, Martinez-Perez R, Agrawal A, Deora H, Joaquim AF and Quinones-Ossa GA (2023). Hemoglobin levels as a transfusion criterion in moderate to severe traumatic brain injury: A systematic review and meta-analysis. *Br. J. Neurosurg.*, **37**(6): 1473-9.

Gernsheimer TB, Brown SP, Triulzi DJ, Key NS, El Kassab N, Herren H, Poston JN, Boyiadzis M, Reeves BN, Selukar S and Pagano MB (2022). Prophylactic tranexamic acid in patients with hematologic malignancy: A placebo-controlled, randomized clinical trial. *Blood*, **140**(11): 1254-62.

Guo Y, Guo XM, Li RL, Zhao K, Bao QJ, Yang JC, Zhang Q and Yang MF (2021). Tranexamic acid for acute spontaneous intracerebral hemorrhage: A meta-analysis of randomized controlled trials. *Front. Neurol.*, **12**: 761185.

- Guyette FX, Brown JB, Zenati MS, Early-Young BJ, Adams PW, Eastridge BJ, Nirula R, Vercruyse GA, O'Keeffe T, Joseph B and Alarcon LH (2021). Tranexamic acid during prehospital transport in patients at risk for hemorrhage after injury: A double-blind, placebo-controlled, randomized clinical trial. *JAMA Surg.*, **156**(1): 11-20.
- Ha EJ (2024). Optimizing RBC transfusion strategies in traumatic brain injury: Insights on early resuscitation and cerebral oxygenation. *Korean J. Neurotrauma*, **20**(3): 137.
- Hanley C, Callum J and Jerath A (2021). Tranexamic acid and trauma coagulopathy: Where are we now? *Br. J. Anaesth.*, **126**(1): 12-7.
- Hassoun-Kheir N, Hussein K, Abboud Z, Raderman Y, Abu-Hanna L, Darawshe A and Bolotin G (2020). Risk factors for ventilator-associated pneumonia following cardiac surgery. *J. Hosp. Infect.*, **105**(3): 546-51.
- Hinson HE, Radabaugh HL, Li N, Fukuda T, Pollock J, Schreiber M, Rowell S and Ferguson AR (2024). Predicting progression of intracranial hemorrhage in the prehospital TXA for TBI trial. *J. Neurotrauma*, **41**(19-20): 2349-61.
- Hollingworth M, Woodhouse LJ, Law ZK, Ali A, Krishnan K, Dineen RA, Christensen H, England TJ, Roffe C, Werring D and Peters N (2024). The effect of tranexamic acid on neurosurgical intervention in spontaneous intracerebral hematoma: Data from 121 surgically treated participants from the tranexamic acid in intraCerebral hemorrhage-2 randomized controlled trial. *Neurosurgery*, **95**(3): 605-16.
- Kataria S, Juneja D and Singh O (2025). Redefining haemostasis: Role of rotational thromboelastometry in critical care settings. *World J. Crit. Care Med.*, **14**(2): 102521.
- Lee S, Kim M, Kwon SM, Kwon MY, Kim CH, Son NH and Kim JH (2025). Relationship between tranexamic acid use and safety in patients with acute brain injury: A systematic review and meta-analysis of mortality and thromboembolic events. *CNS Drugs*, **39**(7): 637-650.
- Lee SM, Lee G, Kim TK, Le T, Hao J, Jung YM, Park CW, Park JS, Jun JK, Le HC and Kim D (2022). Development and validation of a prediction model for need for massive transfusion during surgery using intraoperative hemodynamic monitoring data. *JAMA Netw. Open*, **5**(12): e2246637.
- Li M, Jiang W, Lin J, Du H, Shan J and Qin L (2025). Development and evaluation of a dynamic nomogram model for intraoperative blood transfusion decision-making. *Front. Med.*, **12**: 1566325.
- Li YY, Yu TS, Ho CN, Lai YC, Yew M, Yu CH and Hung KC (2025). Thromboembolic safety and clinical benefits of tranexamic acid beyond hemostasis in post-COVID-19 patients undergoing major arthroplasty: A STROBE-compliant retrospective study. *Med.*, **104**(36): e44317.
- Li Z, You M, Long C, Bi R, Xu H, He Q and Hu B (2020). Hematoma expansion in intracerebral hemorrhage: an update on prediction and treatment. *Front. Neurol.*, **11**: 702.
- Lo HC, Hsu SC, Soong RS and Huang SK (2024). Unraveling postoperative bleeding dynamics in laparoscopic Roux-en-Y gastric bypass: Insights from a single-center tranexamic acid study. *Obes. Surg.*, **34**(8): 3012-20.
- Meer MM, Mumtaz M, Farrukh Z, Ahmed B and Meer M (2024). Efficacy and safety of tranexamic acid in traumatic brain injury: A systematic review and meta-analysis of randomized controlled trials. *Cureus*, **16**(11): e73781.
- Montgomery EY, Barrie U, Kenfack YJ, Edukugho D, Caruso JP, Rail B, Hicks WH, Oduguwa E, Pernik MN, Tao J and Mofor P (2022). Transfusion guidelines in traumatic brain injury: A systematic review and meta-analysis of the currently available evidence. *Neurotrauma Rep.*, **3**(1): 554-68.
- Nakae R, Murai Y, Morita A and Yokobori S (2022). Coagulopathy and traumatic brain injury: Overview of new diagnostic and therapeutic strategies. *Neurol. Med. Chir.*, **62**(6):261-9.
- Napolitano LM (2021). Hemostatic defects in massive transfusion: an update and treatment recommendations. *Expert Rev. Hematol.*, **14**(2): 219-39.
- Prudovsky I, Kacer D, Zucco VV, Palmeri M, Falank C, Kramer R, Carter D and Rappold J (2022). Tranexamic acid: beyond antifibrinolysis. *Transfusion*, **62**:S301-12.
- Rakhit S, Nordness MF, Lombardo SR, Cook M, Smith L and Patel MB (2021). Management and challenges of severe traumatic brain injury. *Semin. Respir. Crit. Care Med.*, **42**(1): 127-44.
- Rathmell C and Vacas S (2025). Transfusion thresholds in patients with neurological injury: Balancing oxygen delivery and risk. *J. Neurosurg. Anesthesiol.*, **37**(3): 265-70.
- Rowell SE, Meier EN, McKnight B, Kannas D, May S, Sheehan K, Bulger EM, Idris AH, Christenson J, Morrison LJ and Frascione RJ (2020). Effect of out-of-hospital tranexamic acid vs placebo on 6-month functional neurologic outcomes in patients with moderate or severe traumatic brain injury. *JAMA*, **324**(10): 961-74.
- Russell R, Bauer DF, Goobie SM, Haas T, Nellis ME, Nishijima DK, Vogel AM and Lacroix J (2022). Plasma and platelet transfusion strategies in critically ill children following severe trauma, traumatic brain injury and/or intracranial hemorrhage: From the transfusion and anemia expertise initiative-control/avoidance of bleeding. *Pediatr. Crit. Care Med.*, **23**(Suppl 1): e14-24.
- Sigmon J, Crowley KL and Groth CM (2023). Therapeutic review: The role of tranexamic acid in management of traumatic brain injury, nontraumatic intracranial hemorrhage and aneurysmal subarachnoid hemorrhage. *Am. J. Health-Syst. Pharm.*, **80**(18): 1213-22.
- Stitt G, Spinella PC, Bochicchio GV, Roberts I, Downes KJ and Zuppa AF (2024). Population pharmacokinetic

- modelling and simulation of tranexamic acid in adult trauma patients. *Br. J. Clin. Pharmacol.*, **90**(8): 1932-41.
- Taccone FS, Bittencourt CR, Møller K, Lormans P, Quintana-Díaz M, Caricato A, Ferreira MA, Badenes R, Kurtz P, Søndergaard CB and Colpaert K (2024). Restrictive vs liberal transfusion strategy in patients with acute brain injury: The TRAIN randomized clinical trial. *JAMA*, **332**(19): 1623-33.
- Turgeon AF, Fergusson DA, Clayton L, Patton MP, Neveu X, Walsh TS, Docherty A, Malbouisson LM, Pili-Floury S and English SW (2024). Liberal or restrictive transfusion strategy in patients with traumatic brain injury. *N. Engl. J. Med.*, **391**(8): 722-35.
- Wang D, Lu Y, Sun M, Huang X, Du X, Jiao Z, Sun F and Xie F (2022). Pneumonia after cardiovascular surgery: Incidence, risk factors and interventions. *Front. Cardiovasc. Med.*, **9**: 911878.
- Wang L, Du Y, Huang N, Yin N, Du J, Yang J, Jiang L and Mao Y (2024). Clinical characteristics and anaesthetic management of severe scoliosis patients with spinal muscular atrophy: Case series. *Ann. Med. Surg.*, **86**(2): 643-9.
- Wu J, Moheimani H, Li S, Kar UK, Bonaroti J, Miller RS, Daley BJ, Harbrecht BG, Claridge JA and Gruen DS (2022). High dimensional multiomics reveals unique characteristics of early plasma administration in polytrauma patients with TBI. *Ann. Surg.*, **276**(4): 673-83.
- Yokobori S, Yatabe T, Kondo Y and Kinoshita K (2020). Efficacy and safety of tranexamic acid administration in traumatic brain injury patients: A systematic review and meta-analysis. *J. Intensive Care*, **8**(1): 46.
- Yoon JY, Park JH, Kim YS, Shin SJ, Yoo JC and Oh JH (2020). Effect of tranexamic acid on blood loss after reverse total shoulder arthroplasty according to the administration method: A prospective, multicenter, randomized, controlled study. *J. Shoulder Elbow Surg.*, **29**(6): 1087-95.
- Yuan X, Zhang S, Wan J, Chen C, Wang P, Fan S, Liu Y, Yang J, Hou J, You Q and Li X (2024). Efficacy of restrictive versus liberal transfusion strategies in patients with traumatic brain injury: A systematic review and meta-analysis of randomized controlled trials. *Ann. Intensive Care*, **14**(1):177.
- Zhang M and Liu T (2024). Efficacy and safety of tranexamic acid in acute traumatic brain injury: a meta-analysis of randomized controlled trials. *Am. J. Emerg. Med.*, **80**: 35-43.