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Comprehensive assessment of risk factors and development of novel predictive tools for perioperative hidden blood loss in intertrochanteric femoral fractures: a multivariate retrospective analysis

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Abstract

Objectives To identify independent risk factors for perioperative hidden blood loss (HBL) in intertrochanteric femoral fractures (ITFs) and to develop a predictive model.

Methods We enrolled 231 patients with ITFs who underwent proximal femoral nail antirotation (PFNA) surgery at the Orthopedics Department of Northern Jiangsu People's Hospital, Jiangsu Province, China, from January 2021 to December 2023. Hidden blood loss was calculated using the OSTEO formula, and independent risk factors were screened using the Least Absolute Shrinkage and Selection Operator (LASSO) logistic regression. A nomogram prediction model was subsequently constructed based on multivariate logistic regression.

Results The LASSO regression identified eight key predictive factors: sex, body mass index (BMI), Admission serum calcium (mmol/L), American Society of Anesthesiologists (ASA) physical status classification, fracture type (Evans), hypertension, preoperative blood transfusion, and preoperative hemoglobin (HGB, g/L). The nomogram model demonstrated excellent predictive performance in both the training and validation sets, with area under the curve (AUC) values of 0.947 and 0.902, respectively. Calibration curves and decision curve analyses further confirmed the strong agreement between model predictions and actual observations, as well as the net clinical benefit.

Conclusions The nomogram model facilitates an intuitive and quantitative assessment of the risk of perioperative hidden blood loss in patients with ITFs, providing robust support for clinical decision-making.

Keywords Hidden blood loss (HBL), Intertrochanteric fractures (ITFs), PFNA, Nomogram

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Introduction

The escalating incidence of intertrochanteric fractures (ITFs) has emerged as a pressing public health concern amidst the rapid global population aging. Recent epidemiological projections indicate that the global burden of hip fractures is expected to rise to approximately 4.5 million cases by 2050, with Asia, particularly China, predicted to account for nearly half of these new cases [1, 2]. This projection arises from a complex interplay between demographic shifts and fracture incidence rates. ITFs, characterized by their high mortality and morbidity, pose a formidable threat to patients' quality of life and place considerable strain on healthcare resources. Notably, ITFs exhibit a markedly higher 1-year postoperative mortality rate of 17.47% compared to the 9.83% rate in femoral neck fractures, which far exceeds the average mortality in the general population, highlighting the severity of these injuries [3, 4].

Within the comprehensive treatment paradigm for ITFs, perioperative hidden blood loss (HBL) remains an underappreciated yet crucial aspect that warrants urgent attention. Proximal femoral nail antirotation (PFNA) surgery, while effective in minimizing intraoperative overt blood loss, still results in significant overall perioperative blood loss, averaging 937 ml, with a staggering 81.96% being hidden blood loss. This underscores the non-negligible impact of HBL on postoperative recovery [5, 6]. Despite extensive research into the risk factors for perioperative hidden blood loss in ITF patients, the clinical utilization of these findings remains limited.

Consequently, the development of a scoring system that accurately assesses the probability of perioperative HBL across diverse ITFs patient populations is crucial. Nomograms, as predictive tools, have exhibited high accuracy and ease of interpretation in individual patient applications, underscoring their utility in complex medical decision-making scenarios. However, research on perioperative HBL, specifically in patients undergoing PFNA surgery, remains insufficient. To bridge this gap, the current study aims to develop a novel and streamlined risk model for HBL. This model is intended to precisely identify high-risk patients, facilitating targeted interventions to mitigate the risk of perioperative complications and, ultimately, enhance overall treatment outcomes and patient prognosis [7].

Methods

Patient selection

This study enrolled 231 patients with intertrochanteric fractures (ITFs) who underwent proximal femoral nail antirotation (PFNA) surgery at the Department of Orthopedics, Northern Jiangsu People's Hospital, from January 2021 to December 2023. The sample size was determined based on rigorous G Power statistical analysis to ensure adequate statistical power ($1\text{-}\beta = 0.80$) for detecting potential associations between independent variables and hidden blood loss (HBL) while controlling for a Type I error rate ($\alpha = 0.05$). Effect size estimates were derived from previous similar studies. The study protocol was reviewed and approved by the Institutional Review Board of the Northern Jiangsu People's Hospital (approval number: 2023ky214). The study methodology strictly adhered to relevant guidelines and regulations. Due to the retrospective nature of the study and the complete anonymity of all data, the Institutional Review Board waived the requirement for informed consent. Patients were rigorously screened according to strict inclusion criteria, including definitive clinical and radiological diagnoses, primary PFNA surgery, absence of prior ipsilateral fracture or surgery history, normal coagulation function, and complete medical records. These criteria were established to maintain homogeneity among the study participants and enhance data reliability. The exclusion criteria were designed to minimize potential factors and included perioperative massive hemorrhage, infection, chronic anemia, multiple fractures, pathological fractures, neoplastic diseases, severe hematological disorders, and any surgical contraindications.

Standardized perioperative management

To ensure patient safety and uphold research quality, a standardized perioperative management protocol was implemented. This included prophylactic anticoagulation therapy (e.g., low molecular weight heparin 4000 IU/day) prophylactic antibiotic treatment with second-generation cephalosporin via intravenous infusion, and standard PFNA surgical procedures conducted by experienced orthopedic teams under fluoroscopic guidance. Blood transfusion decisions adhered strictly to a restrictive transfusion strategy, aligning with internationally recognized guidelines, and were considered only when preoperative hemoglobin levels fell below 7 g/dL [8, 9].

Data collection

Demographic data, such as age, sex, and body mass index, along with surgical details and perioperative hematological parameters (RBC, HGB, PLT, and HCT), coagulation indices (TT, APTT, PT, and PT-INR), preadmission albumin levels (g/L), admission serum calcium (mmol/L), preoperative blood transfusion, and comorbidity status were systematically collected to ensure data integrity and accuracy.

Calculation of hidden blood loss

The OSTEO formula [10] was employed to calculate HBL, estimating blood volume based on patient gender and height while accounting for both uncompensated and compensated red blood cell losses to accurately assess postoperative blood loss. Given the standardized red blood cell content in transfusions, one unit of RBC was estimated at approximately 150 mL. Total blood loss was calculated using a hematocrit (Hct) level of 35%. By comparing total blood loss with overt blood loss, we established the HBL calculation method and determined a cutoff value of 1000 mL for assessing the risk level of perioperative HBL.

Statistical methods

The collected data set was randomly divided into training and validation groups at an 8:2 ratio, with variables compared between groups. Non-normally distributed data were presented as medians (interquartile ranges). Univariate analyses utilized chi-square or Fisher's exact tests for categorical variables and *t* tests or Mann–Whitney *U* tests for continuous variables. In the training cohort, least absolute shrinkage and selection operator (LASSO) logistic regression was applied for multivariate screening to identify independent risk factors influencing perioperative HBL and to construct the prediction model. Model performance was evaluated using receiver operating characteristic (ROC) curves and calibration plots, with the area under the ROC curve (AUC) ranging from 0.5 (no discrimination) to 1 (perfect discrimination). Decision curve analysis (DCA) was also conducted to ascertain the net benefit threshold of the prediction model. Results with p values <0.05 were considered statistically significant. All statistical analyses were performed using R software (version 4.2.2) and SPSS 27.

Results

Baseline characteristics of the patients

A total of 231 patients with intertrochanteric fractures with proximal PFNA were enrolled and randomly divided into two groups: a training cohort ($n=185$) and a validation cohort ($n=46$). The clinical baseline characteristics of the two groups were comparable, as detailed in Table S1.

In the training cohort, our observations indicated that 97 patients (52.4%) exhibited hidden blood loss (HBL), while the remaining 88 patients (47.6%) did not exhibit this phenomenon. Table S2 provides comprehensive information regarding demographic characteristics, laboratory indices, complications, and surgical variables associated with the two patient cohorts. Patients predisposed to HBL were notably older ($P<0.031$). Besides, according to the Evans classification, a higher fracture classification in patients signifies a more severe condition ($P<0.02$). In addition, the utilization of blood products was significantly higher in the HBL group, with a notable difference observed (75% vs. 25%, $P<0.001$). Furthermore, patients in the HBL group exhibited decreased levels of serum albumin ($P<0.042$), reduced red blood cell counts ($P<0.006$), and hemoglobin concentrations ($P<0.023$). It is worth noting that the incidence of hypertension was relatively low among patients who experienced HBL, comprising only 27% of this patient cohort.

Risk factor screening

By utilizing LASSO regression for variable selection, followed by cross-validation, we identified eight crucial predictors for constructing a multivariate logistic regression model. These predictors include sex, body mass index (BMI, kg/m^2), admission serum calcium concentration (mmol/L), ASA classification, fracture type (Evans classification), hypertension, history of preoperative blood transfusion, and preoperative hemoglobin level (HGB, g/L). To assess the predictive accuracy of these factors, we plotted the corresponding Receiver Operating Characteristic (ROC) curves. It is noteworthy that the Area Under the Curve (AUC) values for all variables were statistically significantly higher than 0.5. Among these, fracture type, history of preoperative blood transfusion, and preoperative hemoglobin levels demonstrated particularly notable AUC values, exceeding the threshold of 0.6 and, in some instances, reaching as high as 0.8 (Fig. 1).

Nomogram development and validation

Based on the results of the multivariate logistic regression analysis (Table S3), we constructed a nomogram prediction model (Fig. 2). In this model, a patient's risk score is calculated by summing the scores of individual risk variables, where each variable is assigned a specific value according to its position on the vertical axis of the nomogram corresponding to each risk indicator. Then, the probability of perioperative hidden blood loss for each patient is obtained from the 'Total Points' axis of the nomogram.

ROC curve analysis (Fig. 3) demonstrated the model's exceptional predictive performance, with an AUC of 0.947 (95% CI 0.917–0.976) in the training set, suggesting a high degree of accuracy. Comparable results were observed in the validation set, with an AUC of 0.902 (95% CI 0.812–0.991), further confirming the model's robustness. Calibration curves (Fig. 4A, B) provided further evidence of the strong concordance between predicted and observed outcomes. Moreover, decision curve analysis (Fig. 4C, D) highlighted the substantial net benefit of the model in both cohorts, emphasizing its utility in guiding precise interventions, optimizing resource allocation and improving patient outcomes, compared to the "treat all" or "treat none" strategies.

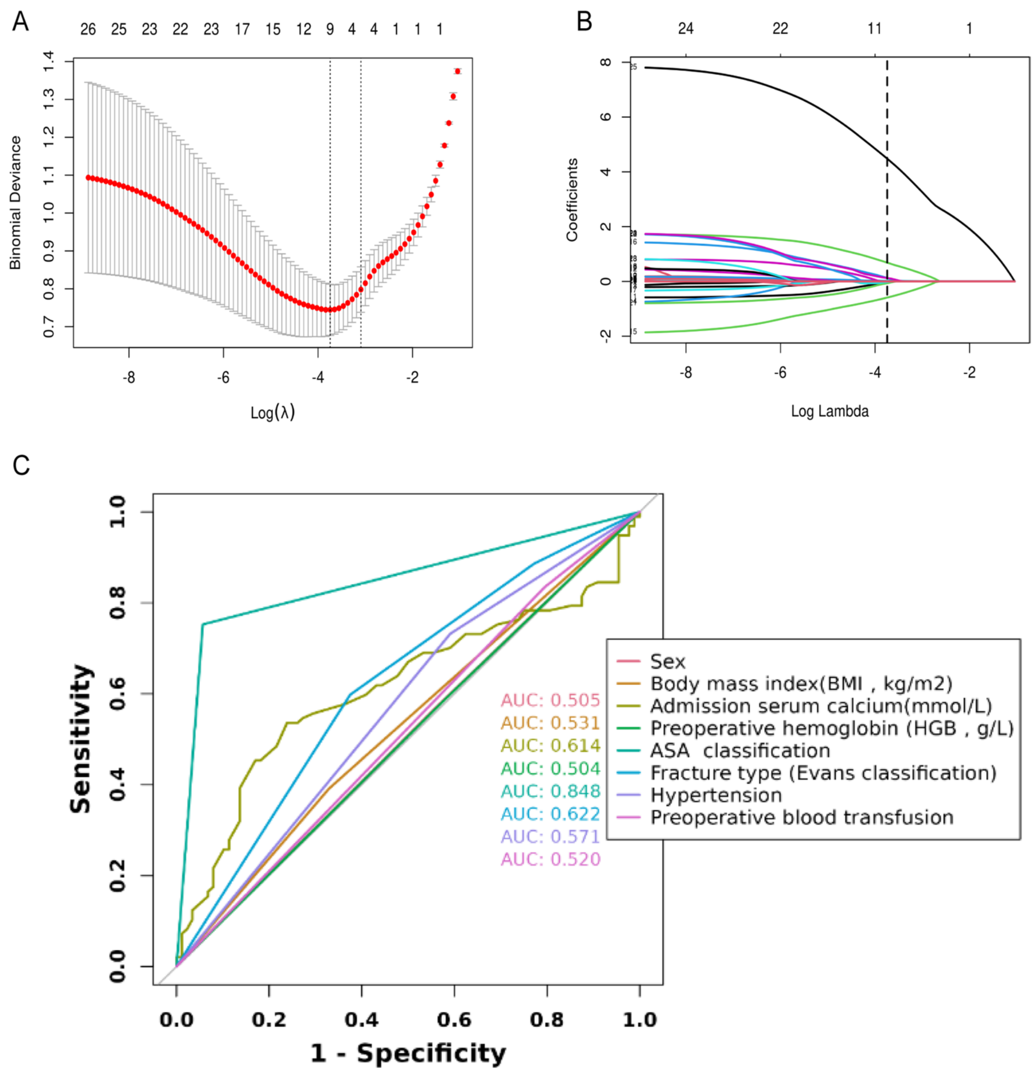

Fig. 1 Optimize the screening variables by the LASSO regression. **A** Lasso regression cross-validation plot. **B** Lasso regression coefficient path plot. **C** ROC curve analysis of 8 candidate diagnostic indicators

Discussion

In recent years, the incidence of ITFs has surged dramatically, with epidemiological studies clearly indicating a significant rise in mortality rates associated with these fractures [11]. Despite numerous studies focusing on perioperative mortality and blood loss risk assessment in ITFs, there remains a notable lack of precise models specifically designed to predict perioperative blood loss risk in patients. Our study aims to fill this gap and facilitate clinical decision-making.

In this research, we meticulously developed a nomogram model comprising eight key predictive factors: sex, body mass index (BMI, kg/m^2), admission serum calcium (mmol/L), ASA classification, fracture type (Evans classification), hypertension, preoperative blood transfusion, and preoperative hemoglobin (HGB, g/L). Unlike traditional models that solely incorporate variables with *P* values less than 0.05 in multivariate logistic regression, our approach comprehensively considered the clinical relevance and effect sizes of each variable. Some variables, although not statistically significant ($P > 0.05$), were included due to their important clinical implications and underwent rigorous internal validation. Comprehensive assessments using the area under the receiver operating characteristic curve (AUC), calibration curves, and decision curve analysis (DCA) revealed the superior predictive performance and significant clinical utility of our nomogram model. This model enables clinicians to accurately identify patients at high risk of perioperative blood loss, facilitating timely and effective early interventions.

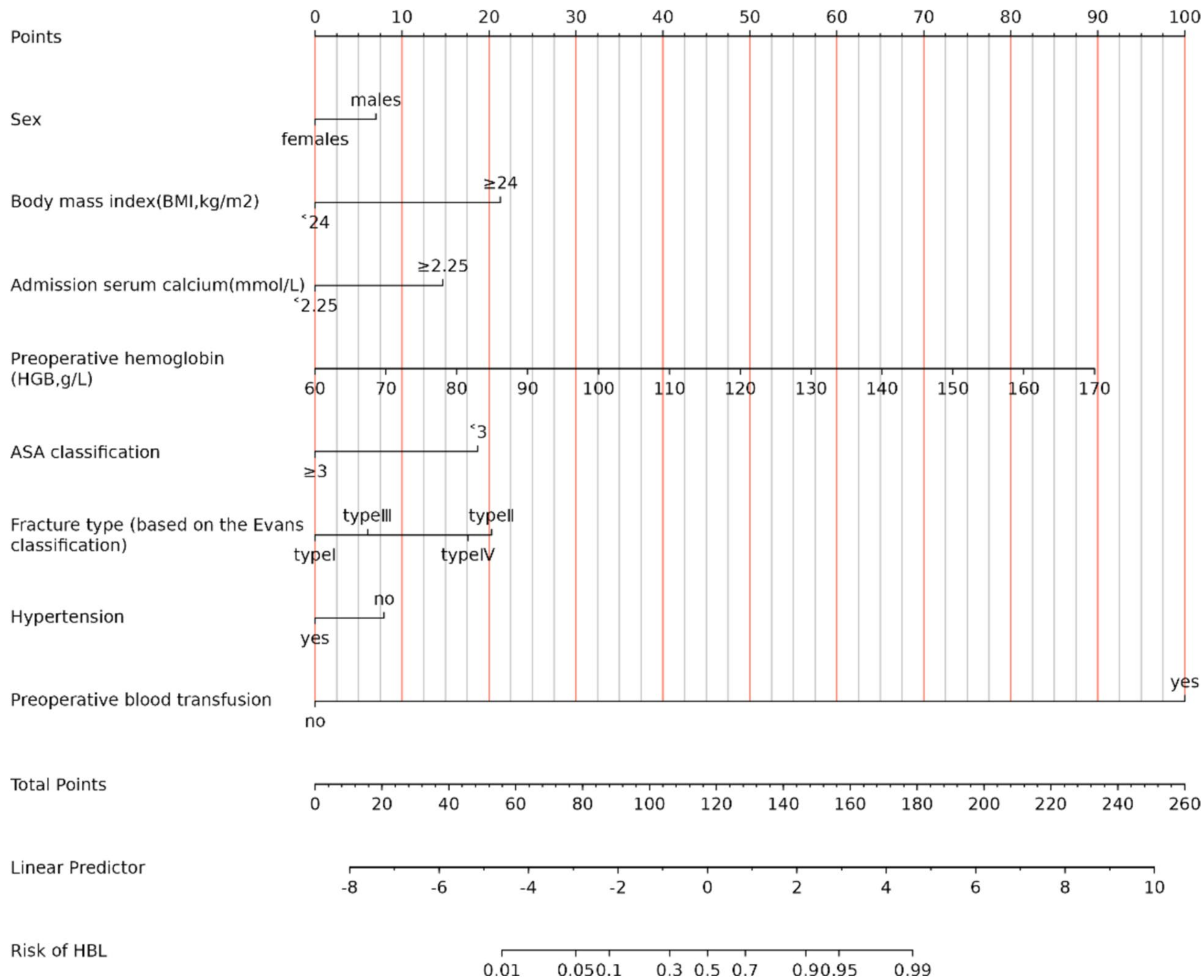

Fig. 2 Nomogram for predicting the risk factors for perioperative HBL in intertrochanteric femoral fractures

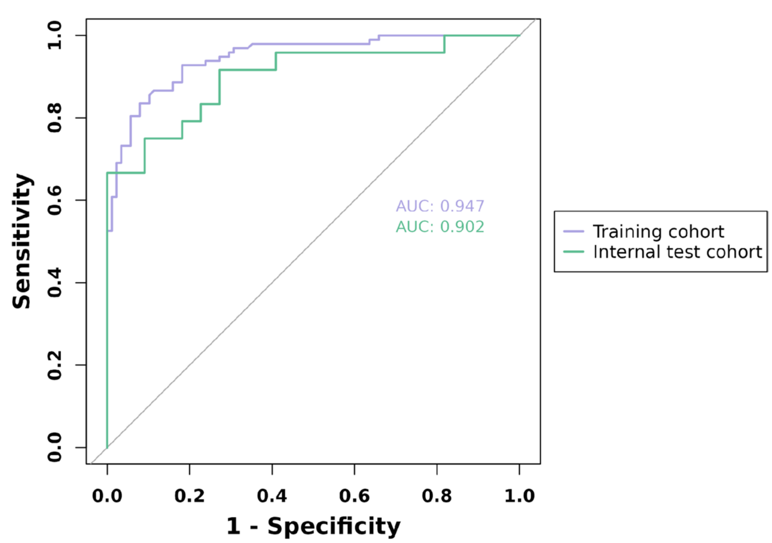

Fig. 3 ROC curves of the nomogram prediction mode

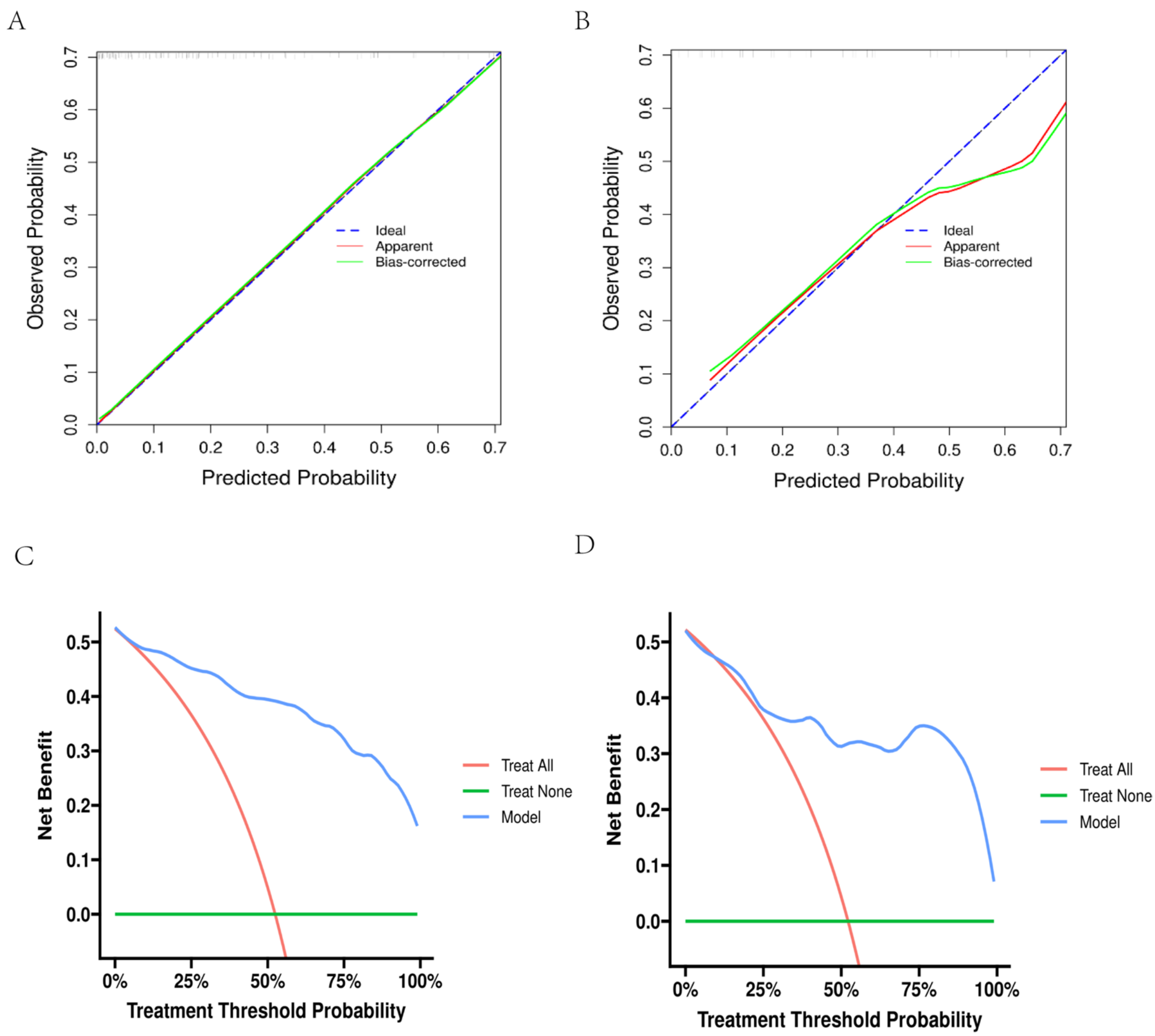

Fig. 4 Validation process of the nomogram prediction mode. **A** Calibration curve of training cohort. **B** Calibration curve of internal test cohort. **C** Decision curve analysis of training cohort. **D** Decision curve analysis of internal test cohort

Currently, there is disagreement in the literature regarding sex differences in perioperative hidden blood loss [12]. Our study findings indicate that females are at a higher risk of hidden blood loss compared to males (OR = 0.59; 95% CI 0.19–1.70; P = 0.339). Potential biological mechanisms underlying this gender disparity may include significant bone loss post-menopause in females, leading to increased hidden blood loss post-fracture surgery, and a higher prevalence of obesity among elderly females. BMI, a critical indicator of obesity, indirectly reflects the overall health status of patients. Higher BMI is associated with reduced surgical tolerance, potentially increasing surgical complexity, prolonging operative time, and exacerbating intraoperative soft tissue damage [13]. In our nomogram, patients with BMI ≥ 24 were assigned a higher weight (approximately 21), underscoring the importance of BMI in predicting perioperative blood loss. Therefore, when formulating perioperative blood management strategies, special consideration should be given to gender differences and patients with abnormal BMI.

The ASA physical status classification serves as an essential tool for assessing preoperative health status and surgical risk, providing a scientific basis for surgical decision-making [14, 15]. Patients with higher ASA scores often have multiple comorbidities and poorer prognoses, which may further exacerbate the risk of blood loss. In addition, fracture type (OR = 3.37, 95% CI 0.63–26.25; P = 0.166) and preoperative HGB levels (OR = 1.06; 95% CI 1.02–1.11; P < 0.004) have been established as strong independent predictors of ITFs [16, 17]. Intertrochanteric fractures, compared to other types of hip fractures, typically cause more significant hemoglobin decline due to the rich vascular supply in the intertrochanteric region and the containment effect of the joint capsule in femoral neck fractures [18]. Following intertrochanteric fractures, substantial blood from the fracture site infiltrates surrounding tissue spaces. Unstable fractures imply greater mobility of fracture fragments, complicating surgical procedures, such as intramedullary nailing, where pressure changes during reaming may lead to the release of fat particles from the bone marrow into the vascular system, triggering hemolysis [19, 20].

Notably, our study found that patients without hypertension were assigned a higher weight (approximately 7.5) in the final nomogram compared to those with hypertension, contrasting previous research findings. We hypothesize that this discrepancy may be attributed to structural changes in the vessel wall caused by prolonged hypertension, such as thickening, stiffening, and reduced elasticity, making the vessels less prone to rupture upon trauma. In addition, effective blood pressure control through medication or lifestyle modifications in hypertensive patients may mitigate the risk of tissue damage and bleeding [21–23]. Furthermore, serum calcium, a crucial regulator in the coagulation cascade, significantly influences bleeding risk. Calcium ions play a vital role in the timely formation and stabilization of fibrin polymerization sites. Altered calcium levels can impair platelet function and cause vasoconstriction dysfunction, leading to increased bleeding tendency and thrombosis promotion [24, 25]. Literature reports suggest an average increase of 166.5 ml in postoperative blood loss and a significant rise in transfusion requirements in hypocalcemic patients [26]. However, in our study, patients with serum calcium levels $\geq$ 2.25 mmol/l were assigned a higher weight (approximately 15), potentially related to increased bone resorption and abnormal calcium metabolism in intertrochanteric fracture patients due to immobilization and prolonged bed rest. Currently, research on the relationship between perioperative hypocalcemia, postoperative blood loss, and prognosis remains scarce, posing additional challenges in managing perioperative calcium levels.

However, our study also has limitations. First, being a retrospective study based on data from a single-center hospital system, potential selection bias cannot be fully eliminated. Future studies should include data from multiple institutions for multi-center and external validation to enhance the generalizability and reliability of the findings. Second, due to data accessibility constraints, certain variables potentially influential in perioperative blood loss among intertrochanteric fracture patients, such as dynamic changes in bone density and specific intramedullary nail sizes, were not included in this study. The inclusion of these variables would further refine the predictive model and improve its accuracy.

Conclusion

Our study identified sex, BMI, admission serum calcium, ASA classification, fracture type (Evans classification), hypertension, preoperative blood transfusion, and preoperative hemoglobin as predictors of perioperative HBL in patients with TIFs treated with proximal femoral nail against rotation (PFNA). We developed and validated a multivariate logistic regression model, as well as a nomogram. The model was validated to have superior predictive performance and is expected to facilitate the development of perioperative blood management strategies for patients with intertrochanteric fractures treated with PFNA in clinical practice.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40001-024-02244-1.

Additional file 1.

Author contributions

L.L. Writing-original draft, Data curation, Formal analysis, Conceptualization. L.X.: Writing-review and editing, Data curation. X. W. Validation, Supervision. C.X. Writing-review & editing. J.D. Formal analysis, Methodology, Conceptualization. L.H.Formal analysis, Conceptualization, Project administration.

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Data availability

The data presented in this study are available in article and supplementary material. Further inquiries can be directed to the corresponding authors.

Declarations

Ethics approval and consent to participate

The present study protocol was reviewed and approved by the Institutional Review Board of Northern Jiangsu People's Hospital (approval No. 2023ky214).

Competing interests

The authors declare no competing interests.

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