

Development and external validation of a perioperative prediction model for high hidden blood loss after proximal femoral nail antirotation in older patients with intertrochanteric fractures

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Article

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Abstract

Background

Hidden blood loss (HBL) is a frequent and clinically important complication after proximal femoral nail antirotation (PFNA) for intertrochanteric fractures. A practical model that combines perioperative predictors and is externally validated may improve individualized blood management.

Methods

This retrospective prediction model study included a development cohort of 186 older patients who underwent PFNA and an independent external validation cohort of 84 patients from Xianning First People's Hospital between 2021 and 2023. High HBL was defined as $HBL > 650$ mL based on an X-tile-derived cutoff. A main perioperative model was developed using predictors available before and during surgery, with least absolute shrinkage and selection operator screening and multivariable logistic regression. Internal validation was performed using 1000 bootstrap resamples. Model performance was assessed using discrimination, calibration, Brier score, decision curve analysis, and external validation. A supplementary preoperative model using only preoperatively available variables was also constructed.

Results

High HBL occurred in 99 of 186 patients (53.2%) in the development cohort and 27 of 84 patients (32.1%) in the external validation cohort. The final perioperative model included preoperative anticoagulant use, preoperative albumin, and operation time. In the development cohort, the model achieved an apparent AUC of 0.715 (95% CI, 0.640–0.790) and a bootstrap optimism-corrected AUC of 0.698. In the external validation cohort, the AUC was 0.894 (95% CI, 0.826–0.963), with a Brier score of 0.165, calibration intercept of -1.806, and calibration slope of 1.026. Because the validation cohort had a lower event rate, an exploratory intercept-only recalibration was performed; this reduced the mean predicted risk from 53.4% to 32.1%, improved the Brier score from 0.165 to 0.121, and preserved the AUC at 0.894. The supplementary preoperative model showed moderate discrimination, with an external AUC of 0.839.

Conclusions

A simple perioperative model incorporating anticoagulant use, preoperative albumin, and operation time showed good external discrimination for high HBL after PFNA. The model may support individualized perioperative blood management, although local recalibration and multicenter prospective validation are required before broad clinical implementation.

1. Introduction

Intertrochanteric fractures are among the most common fragility fractures in older adults and represent a major source of disability, perioperative complications, and mortality. As the population ages, the clinical burden of trochanteric and subtrochanteric fractures continues to increase [1, 2]. Surgical fixation is generally preferred for most patients because it enables early mobilization and reduces complications related to prolonged bed rest. Proximal femoral nail antirotation (PFNA) is widely used for intertrochanteric fractures because of its minimally invasive characteristics and favorable biomechanical properties [1].

Despite the limited visible blood loss observed during PFNA, many patients experience a clinically relevant postoperative decrease in hemoglobin. This discrepancy is largely explained by hidden blood loss (HBL), which refers to blood sequestered in tissue compartments, the fracture gap, and the medullary cavity, as well as blood loss associated with hemolysis and third-space redistribution. HBL has long been recognized as a major contributor to perioperative blood loss in orthopedic surgery [4]. In intertrochanteric fracture surgery, HBL may lead to postoperative anemia, delayed rehabilitation, transfusion exposure, cardiovascular events, and prolonged hospitalization.

Previous studies have identified multiple risk factors for HBL after intertrochanteric fracture fixation, including fracture instability, advanced age, anticoagulant use, anesthesia method, bone mineral density, comorbid diseases, and laboratory indices [7–12]. For example, Cui et al. reported that bone density, fracture type, anesthesia, age, and anticoagulant exposure were associated with perioperative HBL [7]. Lou et al. developed a nomogram for perioperative HBL after PFNA and reported high AUC values in training and validation cohorts [8]. Several Chinese retrospective studies also found that age, fracture severity, hypertension, diabetes, and anticoagulant therapy were associated with increased HBL after PFNA [9–12]. However, many previous models relied on internal random splitting, lacked independent external validation, or focused exclusively on preoperative variables.

From a clinical decision-making perspective, preoperative and perioperative prediction scenarios should be clearly distinguished. A preoperative model can support early risk stratification before entering the operating room, whereas a perioperative model that incorporates both preoperative and intraoperative information may provide more accurate estimation immediately after surgery and guide postoperative blood management. Therefore, the present study aimed to develop and externally validate a simple perioperative prediction model for high HBL after PFNA in older patients with intertrochanteric fractures. A supplementary preoperative model was constructed separately to explore the potential value of risk assessment using only preoperatively available variables.

2. Methods

2.1 Study design and patients

This retrospective prediction model study was conducted in accordance with the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) principles [14]. The development cohort consisted of 186 older patients with intertrochanteric fractures treated with PFNA at Renmin Hospital, Hubei University of Medicine. An independent external validation cohort of 84 patients

was collected from Xianning First People's Hospital between 2021 and 2023 using the same eligibility criteria and outcome definition. The study was approved by the Ethics Committee of Shiyan People's Hospital Affiliated with Hubei University of Medicine (No. 2026-S430), and the development cohort and the external validation cohort from Xianning First People's Hospital (No. 2026-S513), approval covered both the development and external validation datasets.

The inclusion criteria were: (1) age of 60 years or older; (2) fresh, closed intertrochanteric fracture confirmed by radiography or computed tomography; (3) treatment with standard PFNA internal fixation; and (4) complete perioperative hemoglobin and hematocrit data for HBL assessment.

The exclusion criteria were: pathological fracture, multiple fractures or major combined injuries, preoperative transfusion, known bleeding disorders, severe coagulation abnormality, severe hepatic or renal dysfunction, and incomplete key clinical data.

2.2 Outcome definition

The outcome was high hidden blood loss. Total blood loss was calculated according to the Gross method using perioperative hematocrit changes [5], and patient blood volume was estimated using the Nadler formula [6]. HBL was calculated as total blood loss minus visible blood loss plus transfused blood volume when applicable. Based on an X-tile-derived threshold, high HBL was defined as $HBL > 650$ mL and coded as 1; $HBL \leq 650$ mL was coded as 0.

The use of a clinically interpretable binary outcome was intended to support bedside risk stratification. Because threshold selection may influence event rate, calibration, and clinical utility, the $HBL > 650$ mL cutoff should be interpreted in the context of the present dataset and requires additional prospective validation.

2.3 Candidate predictors

Candidate variables included age group (≥ 75 years vs < 75 years), Evans-Jensen fracture type (unstable vs stable), hypertension, anesthesia method (general vs spinal), time from injury to surgery (> 48 h vs ≤ 48 h), preoperative hemoglobin group (< 110 g/L vs ≥ 110 g/L), sex, body mass index (BMI), diabetes mellitus, osteoporosis, preoperative anticoagulant use, preoperative albumin, and operation time. The main perioperative model was allowed to include variables available before and during surgery. The supplementary preoperative model excluded intraoperative variables and was restricted to preoperatively available information.

2.4 Model development and internal validation

All 186 patients in the development cohort were used for model development to avoid loss of statistical power caused by random splitting of a relatively small dataset. LASSO logistic regression was used as an exploratory shrinkage and variable screening step. Clinically plausible variables identified by LASSO and univariable analysis were then evaluated using multivariable logistic regression. To improve parsimony and reduce overfitting, the final main model was restricted to a small number of predictors with clear perioperative interpretability.

The final main perioperative model included preoperative anticoagulant use, preoperative albumin, and operation time. Internal validation was performed using 1000 bootstrap resamples. Apparent AUC, mean optimism, and optimism-corrected AUC were reported. A visual nomogram was constructed from the final logistic regression equation.

2.5 External validation and model performance

External validation was performed by applying the final model coefficients from the development cohort to the independent external validation cohort without refitting. Discrimination was quantified using the area under the receiver operating characteristic curve (AUC) with 95% confidence intervals. Calibration was assessed using calibration intercept, calibration slope, grouped calibration plots, and Brier score. Clinical utility was evaluated using decision curve analysis (DCA) [15].

Because the event rate differed between the development and external validation cohorts, an exploratory calibration-in-the-large update was performed as a sensitivity analysis. This analysis updated only the model intercept while retaining the original predictor coefficients. The recalibrated model was not considered a replacement for the original external validation result; instead, it was used to determine whether risk overestimation was mainly attributable to baseline event-rate differences.

2.6 Supplementary preoperative model

To assess whether preoperative risk stratification might still be clinically useful before surgery, a supplementary model was developed using only preoperatively available variables. This model included osteoporosis, preoperative anticoagulant use, and preoperative albumin. Its discrimination, calibration, and clinical utility were evaluated in the same manner as the main perioperative model. DeLong testing was used to compare the AUCs of the main perioperative and supplementary preoperative models.

2.7 Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation, and categorical variables are presented as number and percentage. Between-group comparisons were performed using t tests, chi-square tests, or Fisher exact tests as appropriate. Logistic regression results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). A two-sided P value < 0.05 was considered statistically significant. Analyses were performed using R software.

3. Results

3.1 Patient characteristics

The study included 270 patients: 186 in the development cohort and 84 in the independent external validation cohort from Xianning First People's Hospital. High HBL occurred in 99 patients (53.2%) in the development cohort and 27 patients (32.1%) in the external validation cohort. The external validation cohort differed from the development cohort in fracture type, anesthesia method, sex distribution, BMI, diabetes mellitus, and preoperative anticoagulant use (Table 1). These differences indicate clinically relevant case-mix heterogeneity between the cohorts.

Table 1
Baseline characteristics of the development and external validation cohorts.

Variable	Development cohort (n = 186)	External validation cohort (n = 84)	P value
Age > = 75 years	116 (62.4%)	62 (73.8%)	0.089
Unstable fracture type	98 (52.7%)	32 (38.1%)	0.037
Hypertension	87 (46.8%)	46 (54.8%)	0.278
General anesthesia	80 (43.0%)	18 (21.4%)	0.001
Injury-to-surgery time > 48 h	93 (50.0%)	40 (47.6%)	0.817
Preoperative Hb < 110 g/L	78 (41.9%)	32 (38.1%)	0.645
Male sex	113 (60.8%)	30 (35.7%)	< 0.001
BMI, kg/m ²	22.87 +/- 0.97	23.19 +/- 1.31	0.045
Diabetes mellitus	26 (14.0%)	42 (50.0%)	< 0.001
Osteoporosis	126 (67.7%)	46 (54.8%)	0.055
Preoperative anticoagulant use	100 (53.8%)	18 (21.4%)	< 0.001
Preoperative albumin, g/L	36.03 +/- 1.32	35.49 +/- 2.64	0.079
Operation time, min	59.94 +/- 5.69	63.33 +/- 15.51	0.054
Values are n (%) or mean +/- SD. High HBL was defined as HBL > 650 mL according to the X-tile-derived cutoff. BMI, body mass index; Hb, hemoglobin.			

Within the development cohort, patients with high HBL had a higher rate of preoperative anticoagulant use, lower preoperative albumin, and longer operation time than patients with low HBL (Table 2). No significant differences were observed for age group, fracture type, hypertension, anesthesia method, injury-to-surgery time, preoperative hemoglobin group, sex, BMI, or diabetes mellitus in the development cohort.

Table 2
Baseline characteristics by HBL status in the development cohort.

Variable	High HBL (n = 99)	Low HBL (n = 87)	P value
Age > = 75 years	63 (63.6%)	53 (60.9%)	0.818
Unstable fracture type	55 (55.6%)	43 (49.4%)	0.491
Hypertension	45 (45.5%)	42 (48.3%)	0.812
General anesthesia	40 (40.4%)	40 (46.0%)	0.537
Injury-to-surgery time > 48 h	49 (49.5%)	44 (50.6%)	1.000
Preoperative Hb < 110 g/L	42 (42.4%)	36 (41.4%)	1.000
Male sex	58 (58.6%)	55 (63.2%)	0.621
BMI, kg/m ²	22.82 +/- 0.85	22.92 +/- 1.08	0.520
Diabetes mellitus	10 (10.1%)	16 (18.4%)	0.157
Osteoporosis	61 (61.6%)	65 (74.7%)	0.080
Preoperative anticoagulant use	63 (63.6%)	37 (42.5%)	0.006
Preoperative albumin, g/L	35.78 +/- 1.32	36.31 +/- 1.25	0.005
Operation time, min	61.39 +/- 5.68	58.28 +/- 5.26	< 0.001
Values are n (%) or mean +/- SD. HBL, hidden blood loss; BMI, body mass index; Hb, hemoglobin.			

3.2 Development of the main perioperative model

The main perioperative model retained three predictors: preoperative anticoagulant use, preoperative albumin, and operation time. In the multivariable logistic regression model, preoperative anticoagulant use was associated with increased odds of high HBL (OR, 2.488; 95% CI, 1.338–4.707; P = 0.004). Higher preoperative albumin was associated with lower odds of high HBL (OR per 1 g/L, 0.786; 95% CI, 0.615–0.997; P = 0.050). Longer operation time was independently associated with high HBL (OR per 1 min, 1.103; 95% CI, 1.043–1.169; P < 0.001) (Table 3).

Table 3
Multivariable logistic regression models.

Predictor	Beta	OR	95% CI	P value
Main perioperative				
Preoperative anticoagulant use	0.912	2.488	1.338–4.707	0.004
Preoperative albumin, per 1 g/L	-0.241	0.786	0.615–0.997	0.050
Operation time, per 1 min	0.098	1.103	1.043–1.169	< 0.001
Supplementary preoperative				
Osteoporosis	-0.619	0.539	0.275–1.035	0.066
Preoperative anticoagulant use	0.798	2.221	1.215–4.105	0.010
Preoperative albumin, per 1 g/L	-0.324	0.724	0.567–0.913	0.008
The main perioperative model included variables available before and during surgery. The supplementary preoperative model excluded operation time. OR, odds ratio; CI, confidence interval.				

The final model equation was: $\text{logit}(P) = 2.486590 + 0.911675 \times \text{anticoagulant} - 0.241000 \times \text{preoperative albumin} + 0.097609 \times \text{operation time}$. The predicted probability was calculated as $P = 1/[1 + \exp(-\text{logit}(P))]$. A nomogram was generated to facilitate bedside application (Fig. 2).

3.3 Discrimination, calibration, and clinical utility

In the development cohort, the main perioperative model achieved an apparent AUC of 0.715 (95% CI, 0.640–0.790), with a Brier score of 0.214. Bootstrap validation with 1000 resamples yielded a mean optimism of 0.017 and an optimism-corrected AUC of 0.698. In the external validation cohort, the model achieved an AUC of 0.894 (95% CI, 0.826–0.963), with sensitivity of 96.3%, specificity of 75.4%, positive predictive value of 65.0%, and negative predictive value of 97.7% at the Youden-derived threshold (Table 4 and Fig. 3).

Table 4
Performance of the main perioperative and supplementary preoperative models.

Model	Cohort	n/events	AUC (95% CI)	Brier	Calibration intercept	Calibration slope	Bootstrap- corrected AUC
Main model	Development	186/99	0.715 (0.640– 0.790)	0.214	0.000	1.000	0.698
Main model	External	84/27	0.894 (0.826– 0.963)	0.165	-1.806	1.026	-
Main model + intercept update	External	84/27	0.894 (0.826– 0.963)	0.121	0.005	1.026	-
Preop supplement	Development	186/99	0.679 (0.602– 0.757)	0.225	0.000	1.000	0.660
Preop supplement	External	84/27	0.839 (0.755– 0.923)	0.205	-1.494	2.387	-
The original external validation result should be interpreted as the primary validation result. The intercept-updated model was an exploratory calibration-in-the-large sensitivity analysis in the external validation cohort and did not replace the original model. Preop supplement denotes the supplementary preoperative model. AUC, area under the receiver operating characteristic curve.							

Calibration in the development cohort was acceptable by construction, with calibration intercept close to 0 and slope of 1. In the external validation cohort, the model retained a calibration slope close to 1 (1.026), suggesting that predictor effects were generally preserved. However, the calibration intercept was – 1.806 and the mean predicted risk was 53.4%, whereas the observed event rate was 32.1%, indicating a calibration-in-the-large problem and overestimation of absolute risk in the external cohort (Fig. 4). DCA showed that the main model provided greater net benefit than treat-all and treat-none strategies over threshold probabilities of approximately 0.23–0.77 in the development cohort and 0.05–0.61 in the external validation cohort (Fig. 5).

3.4 External recalibration sensitivity analysis

Given the lower event rate in the external validation cohort, an exploratory intercept-only recalibration was conducted. After intercept updating, the mean predicted risk decreased from 53.4% to 32.1%, matching the observed event rate in the external cohort. The Brier score improved from 0.165 to 0.121, and the calibration intercept improved from – 1.806 to 0.005, while the calibration slope remained 1.026 and the AUC remained unchanged at 0.894 (Table 4 and Supplementary Fig. 1). The estimated intercept update was – 1.766.

3.5 Supplementary preoperative model

The supplementary preoperative model included osteoporosis, preoperative anticoagulant use, and preoperative albumin. Its apparent AUC in the development cohort was 0.679 (95% CI, 0.602–0.757), and

the bootstrap optimism-corrected AUC was 0.660. In the external validation cohort, the supplementary preoperative model achieved an AUC of 0.839 (95% CI, 0.755–0.923), with a Brier score of 0.205, calibration intercept of -1.494, and calibration slope of 2.387. DeLong testing showed that the AUC difference between the main perioperative model and the supplementary preoperative model was not significant in the development cohort ($P = 0.274$), but was significant in the external validation cohort ($P = 0.028$).

4. Discussion

This study developed and externally validated a simple perioperative prediction model for high HBL after PFNA in older patients with intertrochanteric fractures. The final model incorporated three readily available variables: preoperative anticoagulant use, preoperative albumin, and operation time. The model showed moderate discrimination after bootstrap internal validation and strong discrimination in the independent external validation cohort. A supplementary preoperative model also demonstrated acceptable external discrimination, although it was inferior to the perioperative model in the validation cohort.

The clinical value of this study lies in the distinction between preoperative and perioperative prediction. A purely preoperative model is useful for early planning, but it cannot account for intraoperative complexity. In contrast, a perioperative model can be used immediately after surgery to identify patients who require closer hemoglobin monitoring, active anemia management, transfusion preparedness, and individualized postoperative blood management. The inclusion of operation time is therefore methodologically appropriate for a perioperative model, but it should not be interpreted as a preoperative predictor.

Preoperative anticoagulant use was the strongest binary predictor in the main model. This finding is consistent with several previous studies reporting that antiplatelet or anticoagulant exposure is associated with greater perioperative HBL in intertrochanteric fracture patients [7, 9, 10]. Mechanistically, anticoagulant exposure may reduce hemostatic reserve at the fracture site and increase oozing into soft-tissue spaces and the medullary cavity. Although perioperative antithrombotic management is necessary to prevent thromboembolic events, patients with preoperative anticoagulant exposure may require more intensive postoperative hemoglobin surveillance.

Preoperative albumin was inversely associated with high HBL. Albumin is a marker of nutritional reserve, inflammatory burden, and physiological resilience. Lower albumin may reflect frailty, impaired endothelial integrity, reduced tissue repair capacity, and greater vulnerability to postoperative anemia. In the present study, albumin was retained in both the perioperative and preoperative models, suggesting that nutritional status may be relevant to HBL risk stratification.

Operation time was independently associated with high HBL. Longer operation time may reflect more complex fracture reduction, repeated manipulation, greater soft tissue trauma, prolonged intramedullary instrumentation, and increased medullary cavity bleeding. This result is clinically intuitive and supports the importance of efficient surgical workflow, careful reduction, and standardized technique. It also explains why the perioperative model outperformed the preoperative model in external validation.

Several previous studies have reported the importance of fracture instability, age, comorbidities, and bone quality for HBL [7–12]. In the present development cohort, these variables were not retained in the final perioperative model after shrinkage and multivariable assessment. This discrepancy may be explained by sample size, case-mix differences, coding definitions, and correlations among predictors. For example, operation time may partially mediate the effect of fracture complexity, whereas albumin may capture part of the frailty and nutritional burden associated with age and comorbid disease. Therefore, the absence of a variable from the final model should not be interpreted as proof of no biological relevance.

External validation revealed a clinically important calibration-in-the-large issue. Although the model showed high external AUC and a calibration slope close to 1, it overestimated absolute risk because the external validation cohort had a substantially lower event rate than the development cohort. This pattern suggests that the model preserved patient ranking but required recalibration of baseline risk for the validation setting. The intercept-only recalibration improved the Brier score and calibration intercept without changing AUC, supporting the interpretation that the main transportability issue was baseline risk miscalibration rather than predictor instability. This finding should be viewed as a limitation of direct implementation rather than a failure of discrimination, and it indicates that local recalibration is necessary before using the model to estimate absolute risk in new clinical settings.

The decision curve analysis suggested that the main perioperative model may offer clinical net benefit across a range of thresholds. In practical terms, the model may help identify patients who would benefit from targeted postoperative monitoring, early repeat hemoglobin testing, individualized transfusion preparedness, optimization of anticoagulant management, and consideration of antifibrinolytic or anemia-management strategies when clinically appropriate. However, treatment decisions should not rely exclusively on the nomogram; they should be integrated with symptoms, hemodynamics, postoperative hemoglobin trajectory, and clinician judgment.

4.1 Limitations

This study has several limitations. First, it was retrospective and may be affected by selection bias and residual confounding. Second, the sample size was modest, especially in the external validation cohort, and the confidence intervals around some estimates remain relatively wide. Third, although independent external validation was performed, the original model overestimated absolute risk in the validation cohort; therefore, the recalibrated results should be interpreted as exploratory and the model should undergo further multicenter validation and local recalibration before routine implementation. Fourth, the high-HBL cutoff was derived from the available data and may require confirmation in independent cohorts. Fifth, potentially relevant variables such as intraoperative blood pressure, exact anticoagulant type and discontinuation interval, tranexamic acid use, drainage, postoperative anticoagulant regimen, and long-term outcomes were not fully incorporated. Sixth, the model requires electronic or bedside calculation and should be prospectively tested for whether it improves clinical decisions and patient outcomes.

5. Conclusion

A parsimonious perioperative prediction model based on preoperative anticoagulant use, preoperative albumin, and operation time showed good external discrimination for high hidden blood loss, defined as HBL > 650 mL, after PFNA in older patients with intertrochanteric fractures. The model may support individualized postoperative blood management. A supplementary preoperative model can provide preliminary risk stratification, but the perioperative model performed better in external validation. Because absolute risk was overestimated in the external cohort, local recalibration and prospective multicenter validation are recommended before broad clinical use.

Declarations

Ethics approval and consent to participate: This study was approved by the Ethics Committee of Shiyan People's Hospital Affiliated with Hubei University of Medicine (No. 2026-S430). The ethics approval covered both the development cohort and the external validation cohort from Xianning First People's Hospital (No. 2026-S513). The study was conducted in accordance with the Declaration of Helsinki. Consent procedures followed institutional requirements for retrospective clinical data research.

Consent for publication: Not applicable.

Availability of data and materials: The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Author contributions: Zhuolin Lei, Han Yu, and Haojie Ren contributed equally to this work. Hong Cao and Zhuolin Lei conceived the study. Haojie Ren and Han Yu contributed to data curation and formal analysis. Zhuolin Lei drafted the manuscript. Hong Cao supervised the project and critically revised the manuscript. All authors reviewed and approved the final manuscript.

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Figures

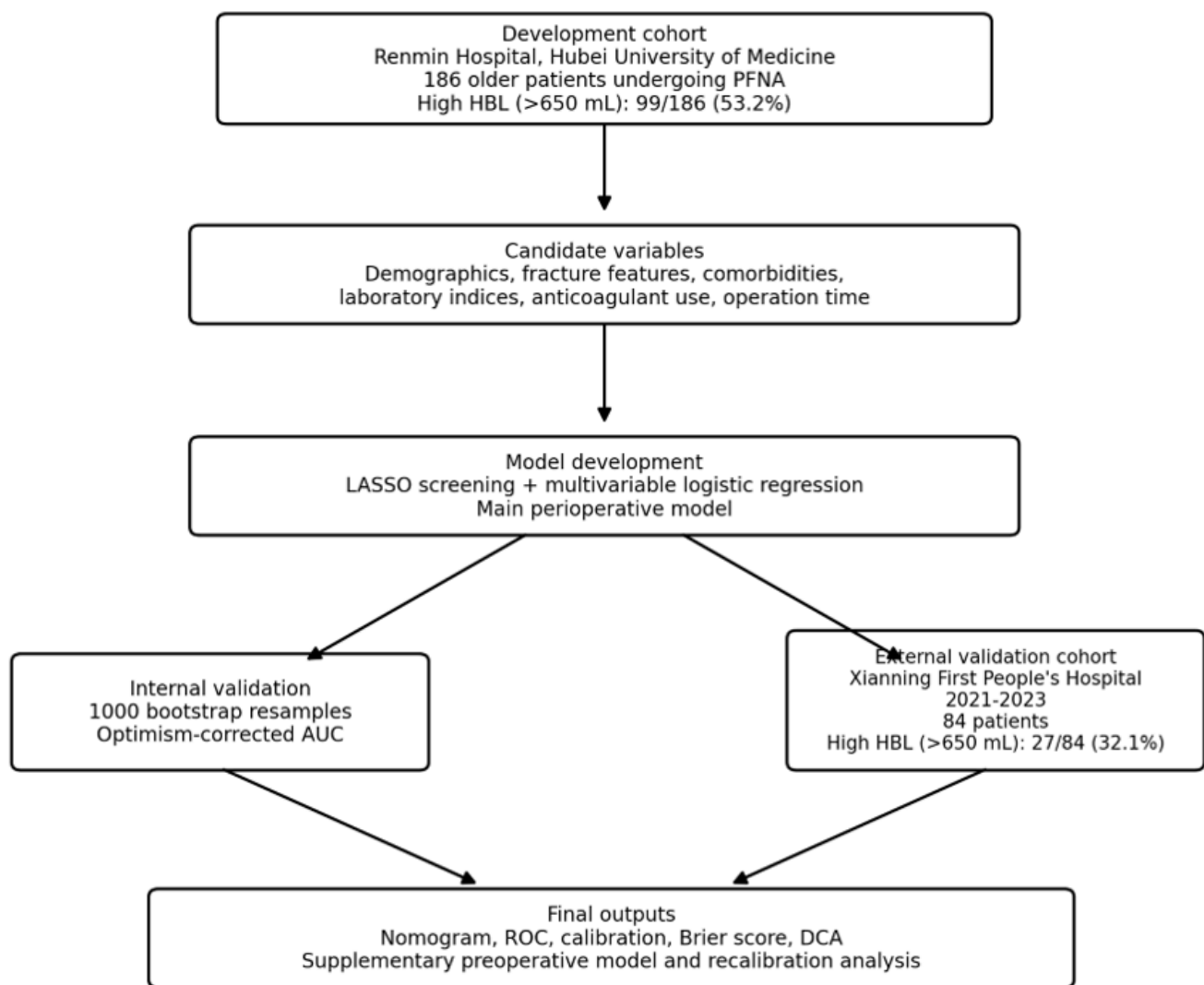


Figure 1

Study flow diagram for model development, internal validation, external validation, and sensitivity analysis.

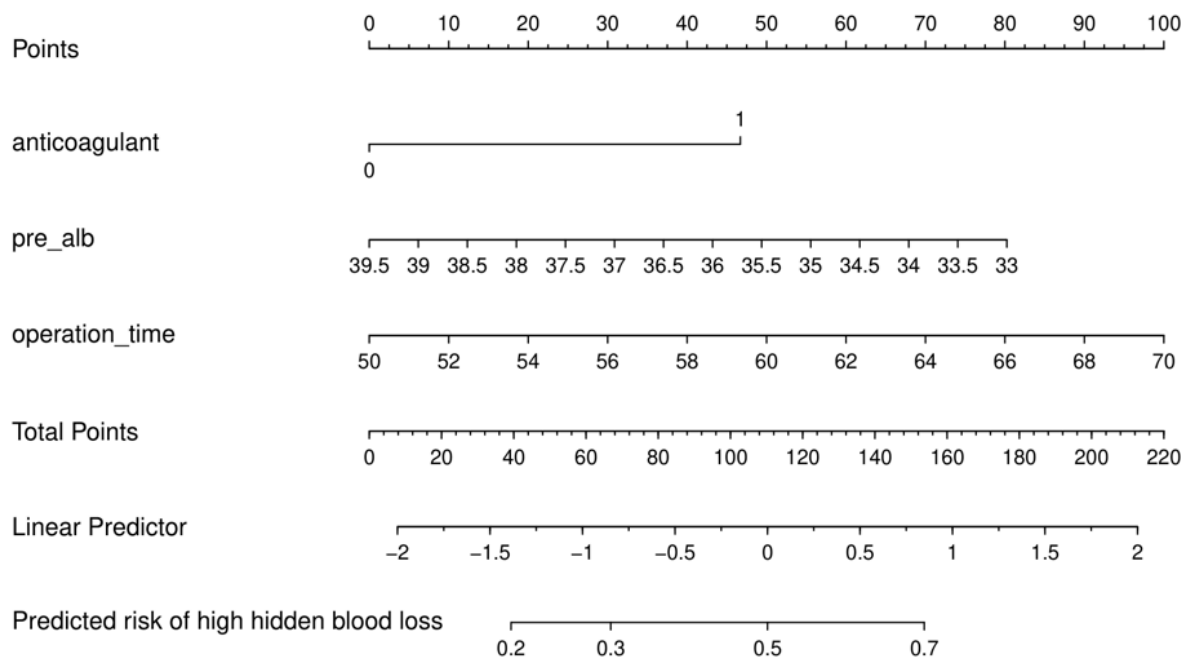


Figure 2

Nomogram of the main perioperative model for predicting high hidden blood loss (HBL >650 mL) after PFNA.

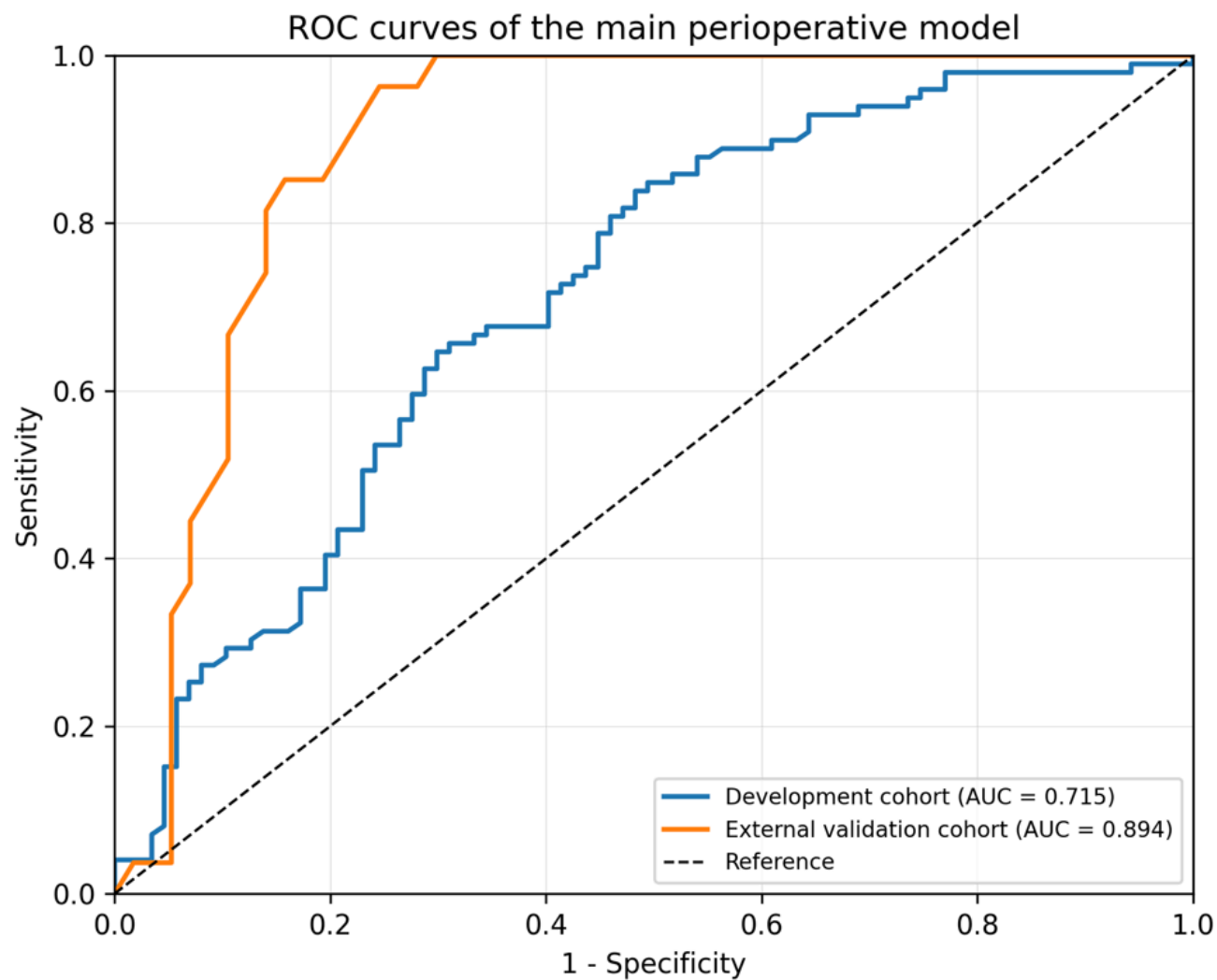


Figure 3

ROC curves of the main perioperative model in the development and external validation cohorts.

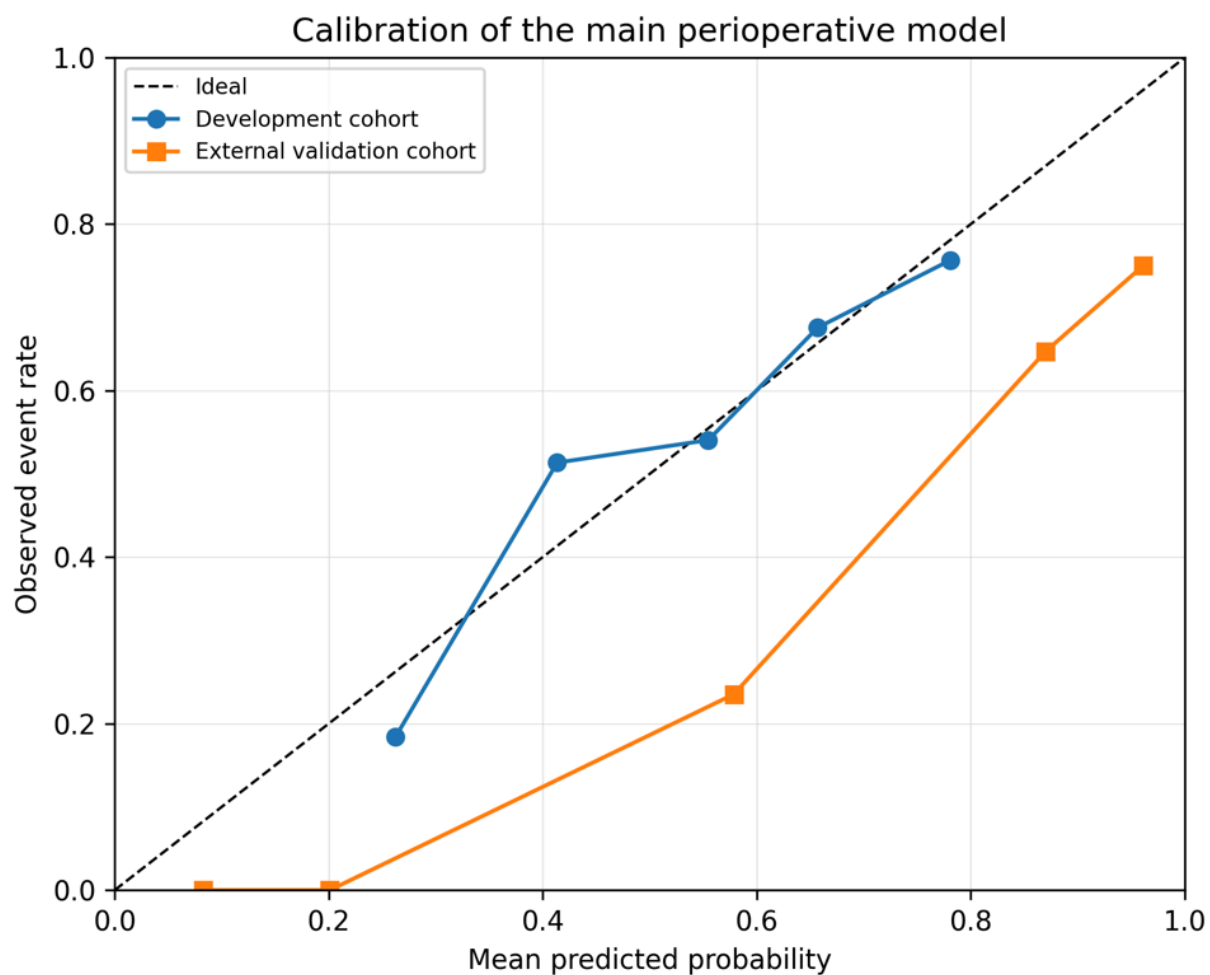


Figure 4

Calibration curves of the main perioperative model in the development and external validation cohorts. The original external validation curve demonstrates absolute risk overestimation before recalibration.

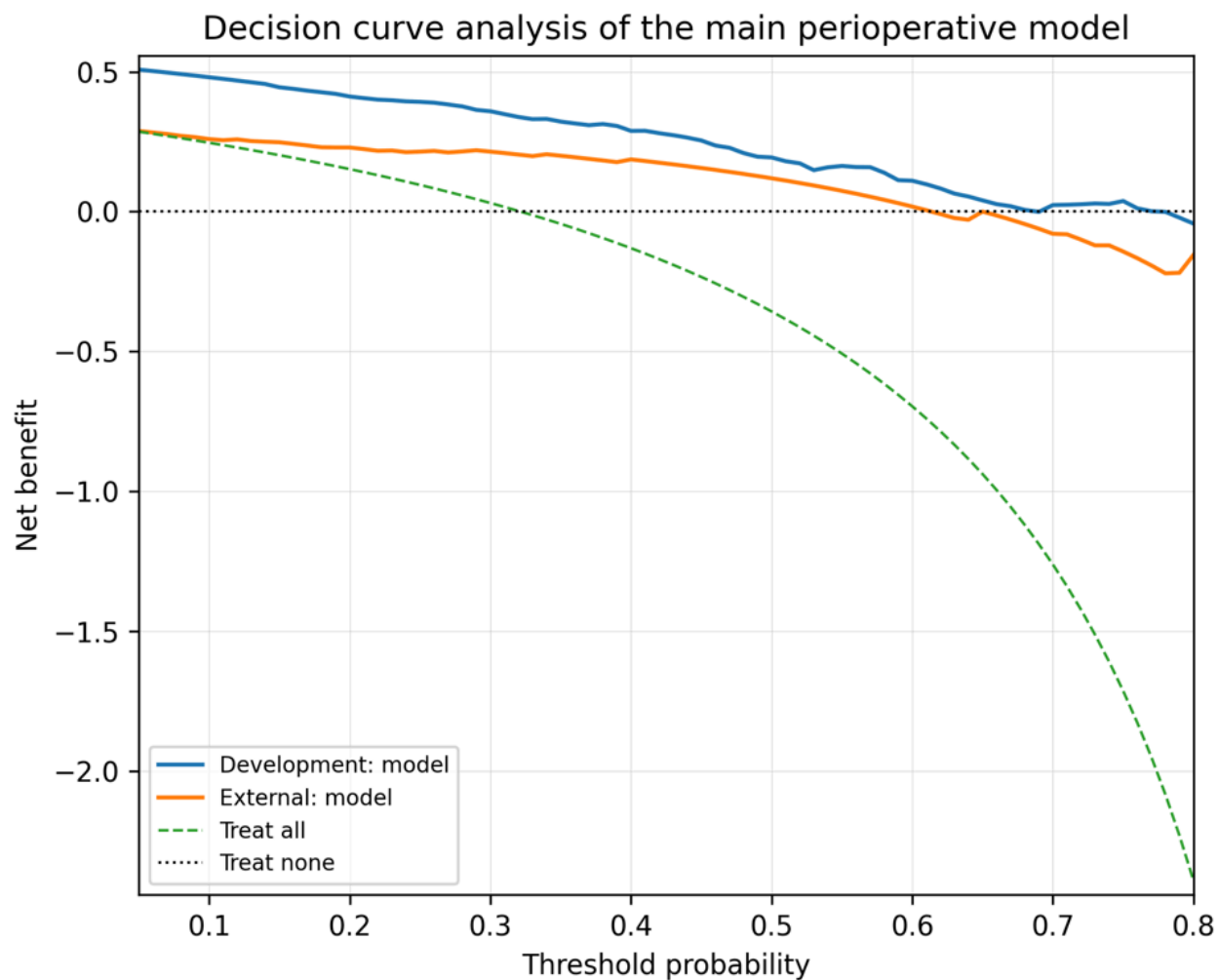


Figure 5

Decision curve analysis of the main perioperative model.

Supplementary Files

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