

Original Article

Risk factors for postpartum hemorrhage in critically ill pregnant women with placenta previa and construction of a dynamic nomogram model

Xiaomeng Yang, Xuexue Che, Yao Li, Wenjing Liu, Jia Zhang, Jiao Han

Department of Obstetrical III, Baoji Maternal and Child Health Hospital, Baoji 721000, Shaanxi, China

Received September 29, 2024; Accepted January 7, 2025; Epub March 15, 2025; Published March 30, 2025

Abstract: Objective: To identify independent risk factors for postpartum hemorrhage (PPH) and to develop a dynamic nomogram model for early prediction and prevention of PPH. Methods: A retrospective analysis was conducted on clinical data from 372 pregnant women with placenta previa admitted to Baoji Maternal and Child Health Hospital between March 2022 and March 2024. Patients were categorized into a PPH group (blood loss ≥ 1500 mL, $n = 109$) and a non-PPH group (blood loss < 1500 mL, $n = 263$). Clinical data were collected from electronic medical records. The included cases were split into a training set ($n = 260$) and a validation set ($n = 112$) at a 7:3 ratio. Multivariate logistic regression were conducted to identify risk factors for PPH, and a nomogram predictive model was constructed based on the identified factors. The predictive performance of the model was assessed using ROC curve analysis, decision curve analysis (DCA), and calibration curves. Results: Multivariate logistic regression identified age ≥ 32.5 years ($P < 0.001$), number of cesarean sections ≥ 2 ($P = 0.037$), placental adhesion ($P < 0.001$), placental implantation ($P = 0.002$), partial placenta previa ($P = 0.004$), prior cesarean section with placenta previa ($P = 0.020$), and anemia ($P = 0.002$) as independent risk factors for PPH. The nomogram achieved an AUC of 0.880 in the training set and 0.840 in the validation set, indicating strong discrimination and predictive capability. ROC analysis showed that age, number of cesarean sections, and placental adhesion had high sensitivity and specificity for predicting PPH, supporting the model's clinical utility. Conclusion: The dynamic nomogram model developed in this study, based on factors such as age, number of cesarean sections, placental adhesion, placental implantation, placenta previa type, previous cesarean with placenta previa, and anemia, demonstrated excellent predictive performance for early identification of PPH risk.

Keywords: Postpartum hemorrhage, placenta previa, risk factors, retrospective study, nomogram prediction model

Introduction

Postpartum hemorrhage (PPH) is a leading preventable cause of maternal mortality worldwide, significantly impacting women's reproductive health [1, 2]. According to the World Health Organization (WHO), approximately 70,000 women die each year from PPH, accounting for 27% of all maternal deaths, with most cases occurring in low- and middle-income countries [3]. Although PPH is less prevalent in high-income countries, it remains a major cause of severe maternal complications and mortality [4]. Research indicates that PPH significantly prolongs hospital stays and increases medical costs [5]. Furthermore, multiple European studies confirm that, despite advanced

medical care, PPH remains a critical obstetric complication requiring significant attention [6].

PPH is influenced by various factors, including uterine atony, placental abnormalities (e.g., placental adhesion, implantation issues, and placenta previa), multiple cesarean sections, and maternal health conditions such as anemia and impaired glucose tolerance [7]. Although high-risk factors are theoretically associated with an increased likelihood of PPH, clinical practice demonstrates that women with high-risk factors or multiple low-risk factors can still experience smooth deliveries. This variability complicates prediction and prevention efforts [8]. Current methods for estimating PPH volume - such as the volumetric, area method, and weighing method - lack sufficient evidence to sup-

Postpartum hemorrhage in critically ill pregnant women with placenta previa

port universal recommendation. Consequently, guidelines in the United Kingdom, United States, and China recommend combining blood loss assessment with clinical symptoms to diagnose PPH [9].

Despite the development of numerous prediction models, including scoring tables, nomograms, and decision trees, many of these models fall short in predictive power, accuracy, and generalizability, particularly across different populations [10, 11]. Existing studies often identify individual risk factors for PPH but fail to integrate them into reliable predictive tools capable of effectively identifying high-risk women [12]. Additionally, limitations such as small sample sizes, inappropriate selection of predictive factors, and inadequate validation methods compromise the accuracy and clinical applicability of current models [13, 14].

This study aims to identify comprehensive risk factors for PPH through multivariate retrospective analysis and to develop and validate a dynamic nomogram for early prediction and prevention of PPH. In this single-center retrospective study, clinical data from PPH cases were divided into a modeling group and a validation group. The modeling group was used to identify high-risk factors and construct a predictive model, while the validation group was employed to assess the model's performance and reduce overfitting. The resulting prediction model is presented in the form of a scoring table.

Materials and methods

Sample size calculation

Based on the study by Fan et al. [15], the probability of PPH in patients with placenta previa is approximately 22.3%. Using the formula for sample size calculation $N = Z^2 \times [P \times (1-P)]/E^2$, with a 95% confidence level ($Z = 1.96$), a PPH incidence rate of 22.3% ($P = 0.223$), and a margin of error of 5% ($E = 0.05$), the required sample size is approximately 266 patients per group. Considering a 10% loss to follow-up or missing data, the adjusted sample size increases to approximately 293 patients per group. The final number of participants depended on clinical data availability and actual patient recruitment.

Study design

This retrospective cohort study aims to identify risk factors for PPH and develop a prediction model. The study adheres to STROBE reporting guidelines to ensure the scientific validity of the research design and reliability of results [16].

Study subjects

The study included 372 critically ill pregnant women with placenta previa admitted to Baoji Maternal and Child Health Hospital between March 2022 and March 2024. All participants were transferred to the Intensive Care Unit (ICU) for close monitoring prior to cesarean section or vaginal delivery. Placenta previa was diagnosed by experienced obstetric ultrasonographers using transvaginal ultrasound after 28 weeks of gestation, defined as the placenta partially or completely covering the internal cervical Os. This study was approved by the Ethics Committee of Baoji Maternal and Child Health Hospital, and all data were anonymized to protect patient privacy. The study strictly followed the ethical principles outlined in the Declaration of Helsinki [17].

Inclusion and exclusion criteria

Inclusion Criteria: 1. Admitted to the ICU prior to cesarean section or vaginal delivery. 2. Diagnosed with placenta previa by experienced obstetric ultrasonographers using transvaginal ultrasound after 28 weeks of gestation [18]. 3. Singleton pregnancy. 4. History of previous cesarean section.

Exclusion Criteria: 1. Fetal death during pregnancy. 2. Lack of relevant delivery information or incomplete medical records, preventing the retrieval of key data. 3. Significant bleeding before delivery. 4. Presence of severe cardiovascular or cerebrovascular diseases, liver or kidney dysfunction, or other major illnesses that may affect delivery or blood loss. 5. Gestational age less than 28 weeks, or fetal malformations or other abnormal conditions.

Definition of PPH

PPH was defined based on the "Guidelines for the Management and Prevention of PPH" published by the Chinese Medical Association of Obstetrics and Gynecology [18]. Blood loss was

Postpartum hemorrhage in critically ill pregnant women with placenta previa

assessed using a combination of gauze weighing and blood collection trays. Measurement started from the skin incision time for cesarean sections, at the onset of vaginal bleeding in emergency cesarean sections, or from the start of delivery in vaginal births, and continued until 24 hours postpartum. Blood loss was recorded by trained nurses every two hours. Patients were categorized into the PPH group (blood loss ≥ 1500 mL, $n = 109$) and the non-PPH group (blood loss < 1500 mL, $n = 263$).

Data collection and variable definitions

Clinical data were collected from the Baoji Maternal and Child Health Hospital electronic medical record system, including basic information (age, gravidity, gestational weeks at delivery, pre-pregnancy body mass index [BMI]), medical history (smoking history, alcohol consumption, anemia, impaired glucose tolerance, intrauterine infection, etc.), pregnancy and delivery-related factors (number of cesarean sections, placental position, placental adhesion, placental implantation, type of placenta previa, interval since last cesarean section, whether a prior cesarean section was accompanied by placenta previa), delivery and postpartum data (mode of delivery, amount of bleeding, newborn weight, gestational age at termination of pregnancy), and outcome indicators (occurrence of PPH).

Outcome measures

Primary outcome: Identification of independent risk factors for PPH using logistic regression analysis [6].

Secondary outcomes: Evaluation of the prediction model's performance, including discrimination, calibration (via calibration curves), and decision curve analysis (DCA). Metrics used for evaluation include sensitivity, specificity, accuracy, precision, F1 score, and the Youden index [19].

Statistical analysis

The dataset was randomly split into a training set and a validation set in a 7:3 ratio. Descriptive statistical analysis was performed on all variables. Continuous variables were expressed as mean \pm standard deviation or median (interquartile range), while categorical variables were expressed as frequencies and percentages.

Univariate analysis included t-tests or Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables, in order to identify factors significantly associated with PPH. Variables with $P < 0.05$ in univariate analysis were included in multivariate logistic regression, using a stepwise method to identify independent risk factors. A dynamic nomogram prediction model was then constructed based on the multivariate regression results. The model was developed using the training set data, and internal validation was performed with the validation set. Model performance was assessed using discrimination, calibration curves, and DCA. Correlation analysis was conducted using a correlation coefficient matrix to assess relationships among predictive factors and minimize multicollinearity. All statistical analyses were conducted using SPSS (version 26.0) for general statistics and R (version 4.3.2) for DCA, ROC, calibration curves, logistic regression, and nomogram construction, with a significance level set at $P < 0.05$.

Results

Baseline characteristics of patients

Among the 372 critically ill pregnant women with placenta previa, significant differences were observed in multiple baseline characteristics between the PPH group ($n = 109$) and the non-PPH group ($n = 263$). Specifically, the PPH group exhibited a higher prevalence of having two or more cesarean sections ($P < 0.001$), placental adhesion ($P < 0.001$), placental implantation ($P < 0.001$), partial placenta previa ($P < 0.001$) and an interval of less than three years since the last cesarean section ($P < 0.001$), all of which were more prevalent in the PPH group compared to the non-PPH group. Additionally, a history of placenta previa in prior cesarean sections ($P < 0.001$), anemia ($P = 0.003$), advanced maternal age ($P < 0.001$), and increased neonatal weight ($P = 0.022$) were all significantly higher compared to the non-PPH group (**Table 1**).

Comparison of baseline characteristics after model splitting

The study sample was randomly divided into a training set ($n = 260$) and a validation set ($n = 112$) in a 7:3 ratio. Comparisons of baseline characteristics between these sets revealed no

Postpartum hemorrhage in critically ill pregnant women with placenta previa

Table 1. Baseline characteristics of the included patients

Variable	PPH Group (n = 109)	Non-PPH Group (n = 263)	X ² /t/Z Value	P-Value
Smoking History			0.792	0.373
Yes	17	32		
No	92	231		
Alcohol Consumption			0.967	0.326
Yes	16	29		
No	93	234		
Number of Cesarean Sections			17.575	< 0.001
≥ 2	40	44		
< 2	69	219		
Placental Attachment Site			0.451	0.502
Primarily Anterior Wall	63	142		
Primarily Posterior Wall	46	121		
Placental Adhesion			26.812	< 0.001
Yes	90	142		
No	19	121		
Placental Implantation			31.57	< 0.001
Yes	27	13		
No	82	250		
Type of Placenta Previa			21.922	< 0.001
Marginal	9	47		
Partial	5	50		
Complete	95	166		
Interval Since Last Cesarean (years)			14.675	< 0.001
≥ 3	25	116		
< 3	84	147		
Placenta Previa in Prior C-Section			22.966	< 0.001
Yes	29	21		
No	80	242		
Intrauterine Infection			0.839	0.36
Yes	7	11		
No	102	252		
Impaired Glucose Tolerance			1.521	0.217
Yes	9	13		
No	100	250		
Anemia			8.668	0.003
Yes	32	42		
No	77	221		
Gestational Age at Termination			0.82	0.365
Full-term	57	151		
Preterm	52	112		
Age (years)	33.77 ± 3.25	30.54 ± 4.56	7.702	< 0.001
Gestational Weeks at Delivery (weeks)	37.00 (36.00-38.00)	37.00 (35.00-38.00)	1.121	0.255
Gravidity (times)	4.00 (3.00-4.00)	4.00 (3.00-4.00)	0.784	0.414
Newborn Weight (g)	2886.72 ± 434.67	3000.83 ± 432.68	-2.307	0.022
Pre-pregnancy BMI (kg/m ²)	23.54 ± 3.51	23.25 ± 2.91	0.757	0.45

Note: PPH: Postpartum Hemorrhage; BMI: Body Mass Index.

Postpartum hemorrhage in critically ill pregnant women with placenta previa

significant differences ($P > 0.05$), indicating good consistency between the training and validation groups (**Table 2**).

Comparison of baseline characteristics of PPH patients in the training set

Within the training set, significant differences were still observed between the PPH group ($n = 73$) and the non-PPH group ($n = 187$). The PPH group continued to exhibit higher rates of two or more cesarean sections ($P < 0.001$), placental adhesion ($P < 0.001$), placental implantation ($P < 0.001$), partial placenta previa ($P < 0.001$), an interval of less than three years since the last cesarean section ($P = 0.015$), a history of placenta previa in prior cesarean sections ($P < 0.001$), anemia ($P < 0.001$), advanced maternal age ($P < 0.001$), and increased neonatal weight ($P = 0.022$) compared to the non-PPH group (**Table 3**).

ROC analysis of nine characteristic factors in predicting PPH

The discriminatory ability of the nine characteristic factors for predicting PPH varied. Age demonstrated the highest area under the curve (AUC) of 0.739 (95% confidence interval [CI]: 0.678-0.800), indicating good discriminatory power, with a specificity of 69.52% and sensitivity of 71.23%, reflecting a relatively balanced performance. In contrast, neonatal weight exhibited a lower predictive power with an AUC of 0.578 (95% CI: 0.501-0.655), sensitivity of 52.05%, specificity of 60.96%, and a Youden index of 13.02%. Other factors, such as placental adhesion (AUC = 0.641, 95% CI = 0.584-0.698) and the type of placenta previa after cesarean section (AUC = 0.616, 95% CI = 0.561-0.670), also demonstrated some value in predicting PPH risk (**Figure 1; Table 4**).

Correlation analysis of PPH-related characteristic factors

Correlation analysis of the nine PPH-related characteristic factors revealed generally weak correlations among them. The strongest correlations were observed between placental implantation and placental adhesion ($r = 0.162$, $P = 0.006$), neonatal weight and age ($r = 0.163$, $P = 0.008$), and the type of placenta previa with a history of placenta previa in prior cesarean sections ($r = 0.153$, $P = 0.013$). However, all corre-

lation coefficients were below 0.3, indicating that the linear relationships among these characteristic factors were weak and insufficient for predicting PPH using linear models (**Figure 2**).

Logistic regression screening of independent risk factors influencing PPH

Multivariate logistic regression analysis was used to identify independent risk factors for PPH based on the nine characteristic factors (**Table 5**). The analysis revealed that parturients aged 32.5 years or older had a significantly increased risk of PPH ($P < 0.001$, odds ratio [OR] = 5.967). A history of two or more cesarean sections was also associated with a higher risk ($P = 0.037$, OR = 2.326). Other significant risk factors included placental adhesion ($P < 0.001$, OR = 4.579), placental implantation ($P = 0.002$, OR = 5.701), complete placenta previa ($P = 0.004$, OR = 2.236), and a history of placenta previa in prior cesarean sections ($P = 0.020$, OR = 3.351). Conversely, an interval of three or more years since the last cesarean section was associated with a reduced risk of PPH ($P = 0.037$, OR = 0.449) (**Table 6**).

Construction and internal validation of the dynamic nomogram model

A nomogram model was constructed based on multiple risk factors, including age, number of cesarean sections, placental adhesion, placental implantation, type of placenta previa, interval since last cesarean section, history of placenta previa, and anemia. The model formula is as follows: $\text{Logit} = -3.1903 + 1.7633 (\text{Age} \geq 32.5 \text{ years}) + 0.8716 (\text{Number of Cesarean Sections} \geq 2) + 1.5119 (\text{Presence of Placental Adhesion}) + 1.7289 (\text{Presence of Placental Implantation}) + 1.3801 \times (\text{Type of Placenta Previa: Marginal}) - 1.4666 \times (\text{Type of Placenta Previa: Partial}) - 0.8119 \times (\text{Post-Cesarean Interval} \geq 3 \text{ years}) + 1.1622 \times (\text{Placenta Previa in Prior C-Section}) + 1.2598 \times (\text{Presence of Anemia})$. In this model, placental adhesion, placental implantation, and the number of cesarean sections were strongly correlated with PPH, while age, type of placenta previa, and interval since the last cesarean section showed moderate correlations. A history of placenta previa and anemia had relatively weaker correlations with PPH (**Figure 3A**). Utilizing the DynNom package, a dynamic model was created. To evaluate its practical application, seven patients

Postpartum hemorrhage in critically ill pregnant women with placenta previa

Table 2. Comparison of baseline characteristics between the training set and validation set

Variable	Training Set (n = 260)	Validation Set (n = 112)	$\chi^2/t/Z$ Value	P-Value
Smoking History			0.007	0.934
Yes	34	15		
No	226	97		
Alcohol Consumption			0.288	0.591
Yes	33	12		
No	227	100		
Number of Cesarean Sections			0.214	0.644
≥ 2	57	27		
< 2	203	85		
Placental Position			0.153	0.696
Primarily Anterior Wall	145	60		
Primarily Posterior Wall	115	52		
Placental Adhesion			0.072	0.788
Yes	161	71		
No	99	41		
Placental Implantation			0.145	0.704
Yes	29	11		
No	231	101		
Type of Placenta Previa			0.379	0.827
Marginal	40	16		
Partial	40	15		
Complete	180	81		
Interval Since Last Cesarean (years)			0.016	0.898
≥ 3	98	43		
< 3	162	69		
Placenta Previa in Prior C-Section			0.098	0.754
Yes	34	16		
No	226	96		
Intrauterine Infection			0.693	0.405
Yes	11	7		
No	249	105		
Impaired Glucose Tolerance			0.033	0.857
Yes	15	7		
No	245	105		
Anemia			0.042	0.838
Yes	51	23		
No	209	89		
Gestational Age at Termination			0.02	0.887
Full-term	146	62		
Preterm	114	50		
PPH Status			0.625	0.429
Yes	73	36		
No	187	76		
Age (years)	31.40 \pm 4.64	31.70 \pm 4.02	0.629	0.53
Gestational Weeks at Delivery (weeks)	37.00 (36.00-38.00)	37.00 (35.00-38.00)	-0.012	0.991
Gravidity (times)	4.00 (3.00-4.00)	3.50 (3.00-4.00)	-0.127	0.895
Newborn Weight (g)	2970.70 \pm 445.45	2959.73 \pm 414.35	-0.229	0.819
Pre-pregnancy BMI (kg/m ²)	23.34 \pm 3.10	23.33 \pm 3.11	-0.022	0.983

Note: PPH: Postpartum Hemorrhage; BMI: Body Mass Index.

Postpartum hemorrhage in critically ill pregnant women with placenta previa

Table 3. Comparison of baseline characteristics of PPH and non-PPH patients within the training set

Variable	PPH Group (n = 73)	Non-PPH Group (n = 187)	$\chi^2/t/Z$ Value	P-Value
Smoking History			0.05	0.823
Yes	9	25		
No	64	162		
Alcohol Consumption			0.517	0.472
Yes	11	22		
No	62	165		
Number of Cesarean Sections			13.454	< 0.001
≥ 2	27	30		
< 2	46	157		
Placental Position			1.42	0.233
Primarily Anterior Wall	45	100		
Primarily Posterior Wall	28	87		
Placental Adhesion			17.684	< 0.001
Yes	60	101		
No	13	86		
Placental Implantation			27.024	< 0.001
Yes	20	9		
No	53	178		
Type of Placenta Previa			14.132	< 0.001
Marginal	6	34		
Partial	4	36		
Complete	63	117		
Interval Since Last Cesarean (years)			5.881	0.015
≥ 3	19	79		
< 3	54	108		
Placenta Previa in Prior C-Section			11.975	< 0.001
Yes	18	16		
No	55	171		
Intrauterine Infection			0.391	0.532
Yes	4	7		
No	69	180		
Impaired Glucose Tolerance			0.218	0.641
Yes	5	10		
No	68	177		
Anemia			16.481	< 0.001
Yes	26	25		
No	47	162		
Gestational Age at Termination			0.693	0.405
Full-term	38	108		
Preterm	35	79		
Age (years)	33.77 \pm 3.25	30.54 \pm 4.56	7.702	< 0.001
Gestational Weeks at Delivery (weeks)	37.00 (36.00-38.00)	37.00 (35.00-38.00)	1.121	0.255
Gravidity (times)	4.00 (3.00-4.00)	4.00 (3.00-4.00)	0.784	0.414
Newborn Weight (g)	2886.72 \pm 434.67	3000.83 \pm 432.68	-2.307	0.022
Pre-pregnancy BMI (kg/m ²)	23.54 \pm 3.51	23.25 \pm 2.91	0.757	0.45

Note: PPH: Postpartum Hemorrhage; BMI: Body Mass Index.

Postpartum hemorrhage in critically ill pregnant women with placenta previa

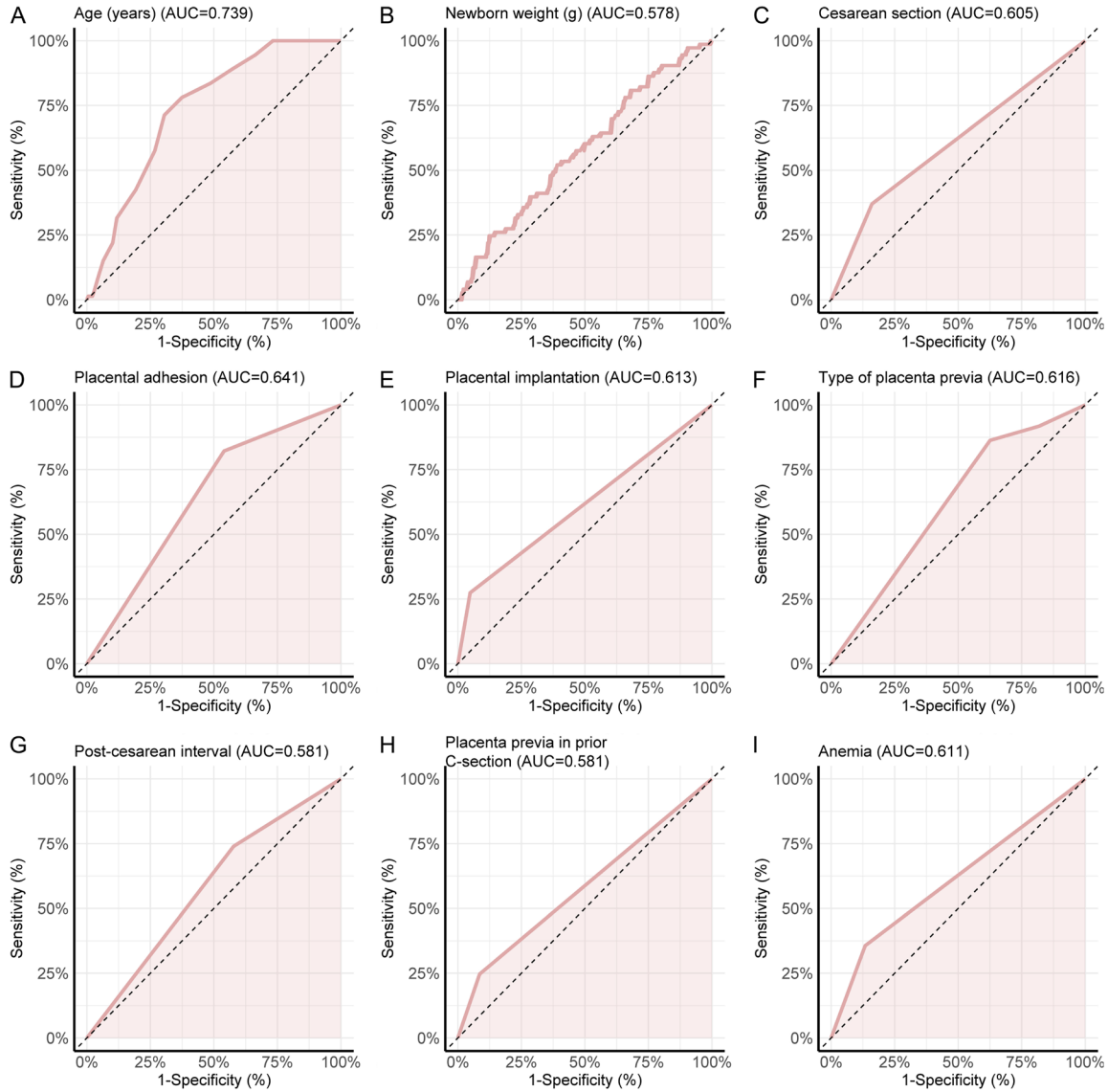


Figure 1. ROC curves of nine characteristic factors in predicting PPH. A. ROC curve for age (years). B. ROC curve for newborn weight (g). C. ROC curve for number of cesarean sections. D. ROC curve for placental adhesion. E. ROC curve for placental implantation. F. ROC curve for type of placenta previa. G. ROC curve for post-cesarean interval. H. ROC curve for Anemia. I. ROC curve for Placenta Previa in Prior C-Section. Note: PPH: Postpartum Hemorrhage; ROC: Receiver Operating Characteristic Curve.

Table 4. ROC parameters of nine characteristic factors in predicting PPH

Marker	AUC	95% CI	Specificity	Sensitivity	Youden Index	Cut-off	Accuracy	Precision	F1 Score
Age (years)	0.739	0.678-0.800	0.6952	0.7123	0.4075	32.5	0.7	0.7123	0.5714
Newborn Weight (g)	0.578	0.501-0.655	0.6096	0.5205	0.1302	2881.5	0.4154	0.4795	0.3153
Cesarean Section	0.605	0.543-0.666	0.8396	0.3699	0.2094	0.5	0.7077	0.3699	0.4154
Placental Adhesion	0.641	0.584-0.698	0.4599	0.8219	0.2818	0.5	0.5615	0.8219	0.5128
Placental Implantation	0.613	0.559-0.667	0.9519	0.274	0.2258	0.5	0.7615	0.274	0.3922
Type of Placenta Previa	0.616	0.561-0.670	0.3743	0.863	0.2373	1.5	0.5115	0.863	0.498
Post-Cesarean Interval	0.581	0.519-0.643	0.4225	0.7397	0.1622	-0.5	0.5115	0.7397	0.4596
Placenta Previa in Prior C-Section	0.581	0.527-0.634	0.9144	0.2466	0.161	0.5	0.7269	0.2466	0.3364
Anemia	0.611	0.551-0.672	0.8663	0.3562	0.2225	0.5	0.7231	0.3562	0.4194

Note: PPH: Postpartum Hemorrhage.

Postpartum hemorrhage in critically ill pregnant women with placenta previa

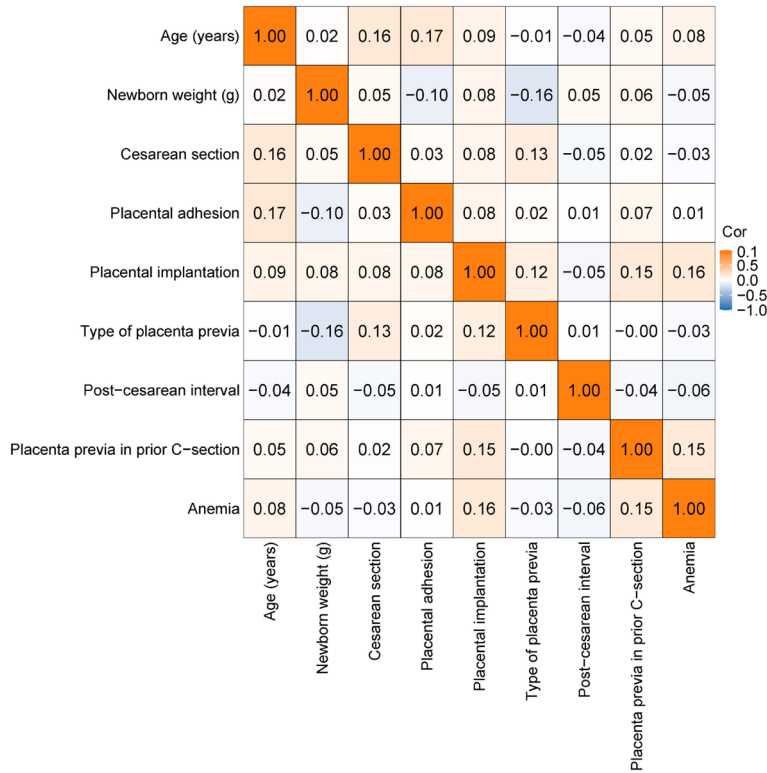


Figure 2. Correlation matrix of nine characteristic factors in predicting PPH. This heatmap displays the correlation coefficients (r) among nine characteristic factors related to PPH. The values along the diagonal represent perfect correlations of each factor with itself ($r = 1$). The color gradient indicates the strength and direction of the correlations, with blue representing positive correlations and red representing negative correlations. Note: PPH: Postpartum Hemorrhage.

were randomly selected from the validation set. This model allows clinicians to calculate the probability of PPH risk in real time based on specific patient characteristics (Figure 3B).

Internal validation of the nomogram model within the training set demonstrated good discrimination and calibration. Decision curve analysis (DCA) indicated that the model provided a high net benefit within a threshold probability range of 0-64% (Figure 4A). Calibration curve's goodness-of-fit testing yielded a chi-square value of $1.1216e-26$ ($P < 0.999$), suggesting ideal calibration in the training set (Figure 4B). ROC curve analysis showed an AUC of 0.880, demonstrating high discriminatory power and its ability to effectively distinguish between high- and low-risk patients (Figure 4C).

In the validation set, the model's performance remained robust, with DCA showing a high net

benefit within a threshold probability range of 0-69% (Figure 4D). Calibration curve testing in the validation set yielded a chi-square value of $2.1334e-24$ ($P < 0.999$), indicating good calibration (Figure 4E). The ROC curve in the validation set showed an AUC of 0.840, slightly lower than in the training set, but still demonstrating good predictive ability and discrimination (Figure 4F).

Discussion

This study conducted a retrospective cohort analysis to identify independent risk factors affecting PPH in critically ill pregnant women with placenta previa and constructed a dynamic nomogram prediction model based on these factors. The results demonstrated that age ≥ 32.5 years, number of cesarean sections ≥ 2 , placental adhesion, placental implantation, partial placenta previa, prior cesarean section with placenta previa, and anemia are significant independent risk factors for PPH. The nomogram model achieved an AUC of 0.880 in the training group and 0.840 in the validation group, indicating strong discrimination and predictive performance. Compared with the findings of Xu et al. [20], whose artificial neural network model achieved an AUC of 0.917, and Okunade et al. [21], whose antenatal risk prediction model in Nigeria achieved an AUC of 0.72, our dynamic nomogram model exhibited robust applicability and stability across different populations.

In a multicenter retrospective case-control study by Dang et al. [22], their nomogram model achieved an AUC of 0.839 in the validation set, which aligns closely with our validation AUC of 0.840, suggesting strong generalizability of nomogram models in diverse medical settings. Cao et al. [23] developed a nomogram model for patients with placenta previa and previous cesarean sections, achieving an AUC

Postpartum hemorrhage in critically ill pregnant women with placenta previa

Table 5. Assignment table

Variable	Factor Type	Assignment
Number of Cesarean Sections	X	$\geq 2 = 1$; $< 2 = 0$
Placental Adhesion	X	Yes = 1; No = 0
Placental Implantation	X	Yes = 1; No = 0
Post-Cesarean Interval	X	≥ 3 years = 1; < 3 years = 0
Placenta Previa in Prior C-Section	X	Yes = 1; No = 0
Anemia	X	Yes = 1; No = 0
Type of Placenta Previa	X	Marginal = 0; Partial = 1; Complete = 2
Age (years)	X	$< 32.5 = 0$; $\geq 32.5 = 1$
Newborn Weight (g)	X	$< 2881.5 = 0$; $\geq 2881.5 = 1$
PPH Status	Y	No = 0; Yes = 1

Note: Y: Dependent Variable; X: Independent Variable. PPH: Postpartum Hemorrhage.

Table 6. Multivariate logistic regression analysis

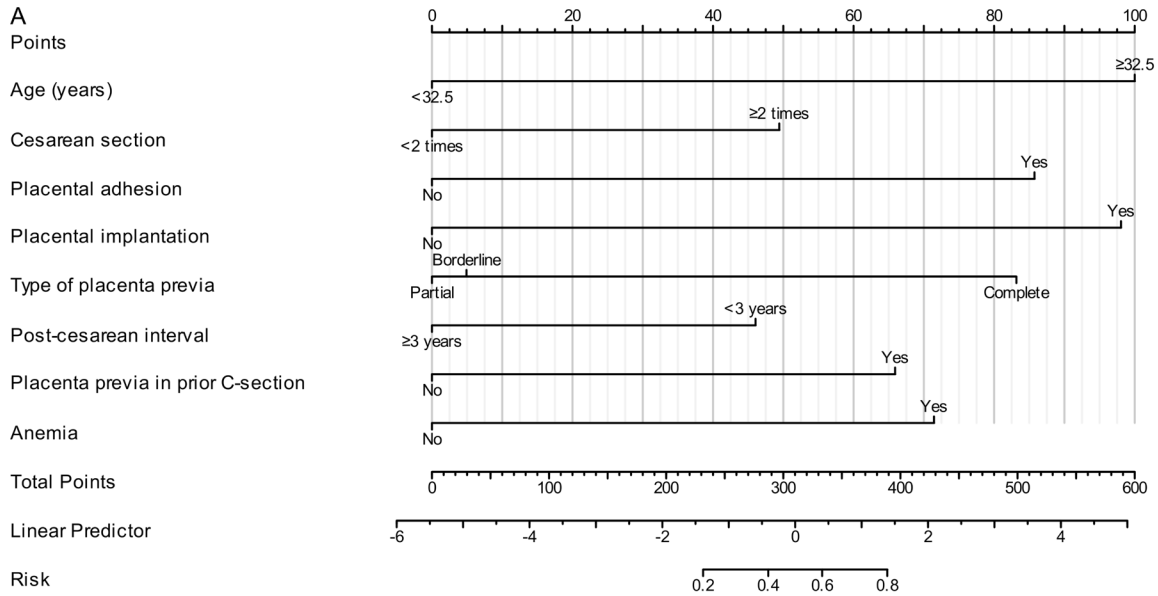
Variable	β	SE	P-Value	OR	Lower 95% CI	Upper 95% CI
Age (years)	1.786	0.374	< 0.001	5.967	2.922	12.782
Newborn Weight (g)						
Cesarean Section	0.844	0.405	0.037	2.326	1.048	5.177
Placental Adhesion	1.522	0.423	< 0.001	4.579	2.067	10.974
Placental Implantation	1.741	0.561	0.002	5.701	1.971	18.066
Type of Placenta Previa	0.805	0.283	0.004	2.236	1.325	4.049
Post-Cesarean Interval	-0.802	0.384	0.037	0.449	0.207	0.937
Placenta Previa in Prior C-Section	1.209	0.52	0.02	3.351	1.214	9.468
Anemia	1.316	0.435	0.002	3.73	1.602	8.91

of 0.863 in the validation set. Furthermore, Lu et al. [24] constructed a nomogram model combining MRI and ultrasound data, achieving an AUC of 0.918 in predicting PPH risk in patients with placenta previa.

Our study's findings align with multiple existing studies, deepening the understanding of PPH risk factors. Ma et al. [25] highlighted placenta previa and placenta accreta as major contributors to PPH, consistent with our findings on placental adhesion and implantation. Pettersen et al. [26] and Liu et al. [27] confirmed the increased risk of PPH with placental implantation and placenta previa, reinforcing our conclusions. Kawakita et al. [28] evaluated existing PPH risk assessment tools and found them to have moderate predictive capabilities, emphasizing the need for more precise prediction models like ours. Yang et al. [29] explored the impact of advanced maternal age on PPH risk, validating our findings regarding age. Zeng et al. [18] constructed a multifactorial nomogram model, showcasing the potential of such models in predicting PPH, similar to our approach.

When analyzing the grouped characteristic factors, we can categorize them into three groups: basic maternal information, pregnancy and delivery-related factors, and maternal health status. Firstly, age ≥ 32.5 years is a critical maternal characteristic. Older maternal age is associated with decreased uterine contractility and increased vascular fragility, both of which elevate the risk of hemorrhage [30]. As women age, their uterine elasticity diminishes, reducing muscle blood flow and increasing the likelihood of uterine atony, a significant contributor to PPH. Moreover, the decreased elasticity and increased fragility of vascular walls in older women make hemorrhage more challenging to control. Secondly, multiple cesarean sections and a history of placenta previa are key pregnancy and delivery-related factors. Multiple cesarean sections can result in uterine scar formation, increasing the risk of abnormal placental attachment, such as adhesion and implantation [26, 29]. Uterine scars alter the uterine structure and blood supply, creating favorable conditions for abnormal placental attach-

Postpartum hemorrhage in critically ill pregnant women with placenta previa



B Graphical Summary Numerical Summary Model Summary

95% Confidence Interval for Response

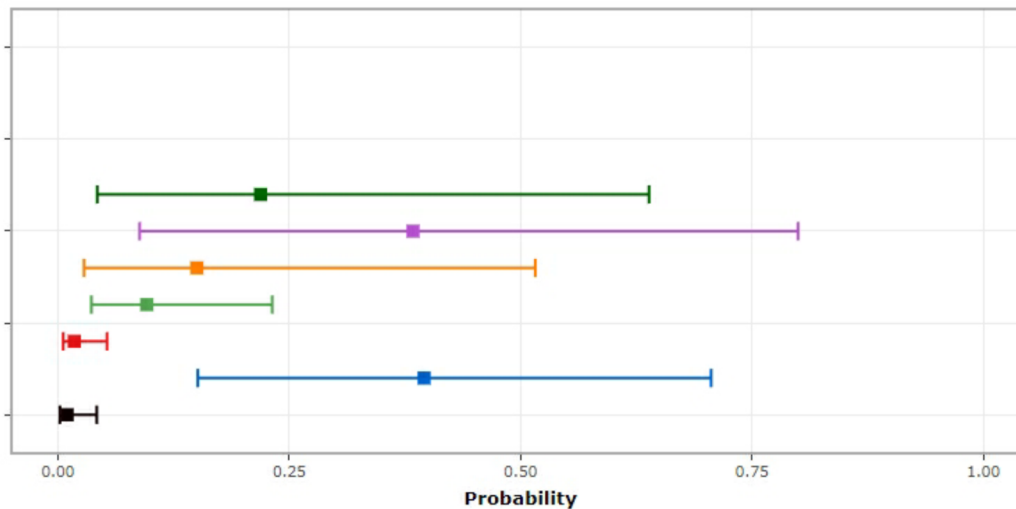


Figure 3. Nomogram model and its dynamic validation results. A. The nomogram model constructed based on multiple risk factors for assessing the risk of PPH. B. Validation results of the dynamic model constructed using the DynNom package. We randomly selected seven patients from the validation set for risk assessment, presenting their predicted probabilities and 95% confidence intervals. Note: PPH: Postpartum Hemorrhage.

ment, significantly increasing the risk of PPH. Additionally, an increased number of cesarean sections is associated with abnormal placental positions. Partial placenta previa, where the placenta partially covers the internal cervical Os, heightens the risk of bleeding during placental separation [31]. Lastly, anemia, as a key factor in maternal health status, contributes to reduced blood volume and hemoglobin reserves, exacerbating the risk of bleeding [28]. Anemic patients are less capable of effectively

transporting oxygen and maintaining tissue function, making them more susceptible to shock and multi-organ dysfunction during hemorrhage. Additionally, anemia can impair uterine contractility, further increasing hemorrhage risk. Analyzing these characteristic factors highlights their specific mechanisms in influencing PPH occurrence and underscores the clinical utility of the dynamic nomogram model. This model enables clinicians to assess bleeding risk prenatally, enabling them to formulate

Postpartum hemorrhage in critically ill pregnant women with placenta previa

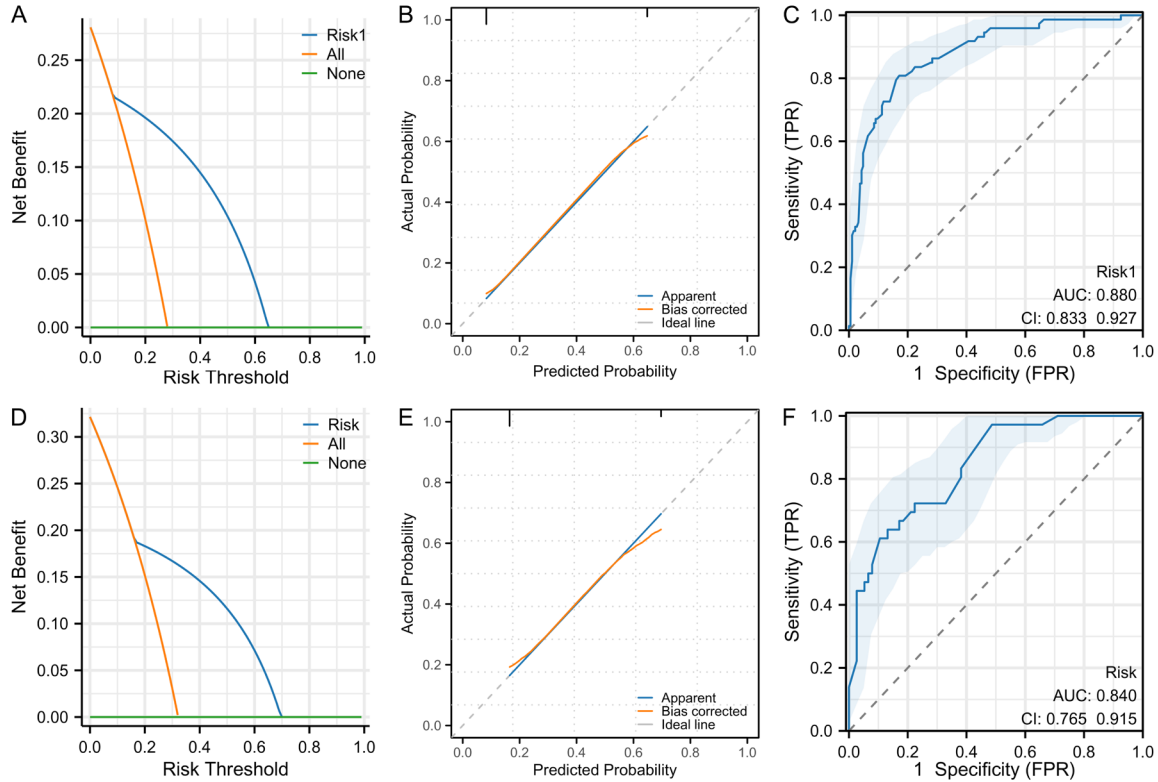


Figure 4. Internal validation of the nomogram model's decision curve analysis, calibration curves, and ROC curves. (A-C) Decision curve analysis (A), calibration curve (B), and ROC curve (C) of the model in the training group. (D-F) Decision curve analysis (D), calibration curve (E), and ROC curve (F) of the model in the validation group. Note: DCA: Decision Curve Analysis; ROC: Receiver Operating Characteristic; AUC: Area Under the Curve.

personalized prevention and intervention measures, optimize medical resource allocation, and reduce transfusion needs and related complications.

Despite the progress made in identifying PPH risk factors and constructing the prediction model, our study has several limitations. First, as a single-center retrospective study, there is a potential for selection bias and information bias, which may limit the generalizability of the results. Second, relying on electronic medical records may lead to data omissions and incomplete records, affecting the comprehensiveness of the variables. Additionally, the study did not consider some potential risk factors, such as genetic factors, biochemical markers, and lifestyle during pregnancy, which may influence the model's predictive ability.

Future research should adopt multicenter prospective designs covering different regions and medical settings to validate the model's applicability in a broader population. Integrating additional data dimensions, including genetic

information, biochemical indicators, and lifestyle factors, would enhance the model's comprehensiveness and precision. Moreover, integrating artificial intelligence and machine learning technologies could further optimize the model's predictive performance and practicality.

Conclusion

This retrospective cohort analysis successfully identified independent risk factors affecting PPH in critically ill pregnant women with placenta previa and constructed a dynamic nomogram prediction model based on these factors. The model demonstrated strong predictive performance in both the training and validation groups, with high discrimination and calibration. Applying the dynamic nomogram model aids clinicians in the early identification of high-risk pregnant women, enabling personalized prevention and intervention measures, improving maternal safety, and reducing PPH-related complications and mortality.

Postpartum hemorrhage in critically ill pregnant women with placenta previa

Disclosure of conflict of interest

None.

Address correspondence to: Jiao Han, Department of Obstetrical III, Baoji Maternal and Child Health Hospital, No. 2, East Section of Xinjian Road, Weibin District, Baoji 721000, Shaanxi, China. E-mail: 18729729252@163.com

References

- [1] Burki T. Understanding postpartum haemorrhage. *Lancet* 2023; 402: 601.
- [2] Bienstock JL, Eke AC and Hueppchen NA. Postpartum hemorrhage. *N Engl J Med* 2021; 384: 1635-1645.
- [3] Dol J, Hughes B, Bonet M, Dorey R, Dorling J, Grant A, Langlois EV, Monaghan J, Ollivier R, Parker R, Roos N, Scott H, Shin HD and Curran J. Timing of maternal mortality and severe morbidity during the postpartum period: a systematic review. *JBI Evid Synth* 2022; 20: 2119-2194.
- [4] Corbetta-Rastelli CM, Friedman AM, Sobhani NC, Arditi B, Goffman D and Wen T. Postpartum hemorrhage trends and outcomes in the United States, 2000-2019. *Obstet Gynecol* 2023; 141: 152-161.
- [5] Fein A, Wen T, Wright JD, Goffman D, D'Alton ME, Attenello FJ, Mack WJ and Friedman AM. Postpartum hemorrhage and risk for postpartum readmission. *J Matern Fetal Neonatal Med* 2021; 34: 187-194.
- [6] Maas DPMSM, Saes JL, Blijlevens NMA, Cnossen MH, den Exter PL, van der Heijden OWH, Kruis IC, Meijer K, Peters M, Schutgens REG, van Heerde WL, Nieuwenhuizen L and Schols SEM; RBiN study group. High prevalence of postpartum hemorrhage in women with rare bleeding disorders in the Netherlands: retrospective data from the RBiN study. *J Thromb Haemost* 2023; 21: 499-512.
- [7] Mende L, MacDonald J, Jolly D, Neher JO and Safranek S. Preventing postpartum hemorrhage. *Am Fam Physician* 2023; 107: 539-540.
- [8] Rood KM. Foreword: postpartum hemorrhage. *Clin Obstet Gynecol* 2023; 66: 342-343.
- [9] Giouleka S, Tsakiridis I, Kalogiannidis I, Mampoulos A, Tentas I, Athanasiadis A and Dagklis T. Postpartum hemorrhage: a comprehensive review of guidelines. *Obstet Gynecol Surv* 2022; 77: 665-682.
- [10] Faysal H, Araji T and Ahmadzia HK. Recognizing who is at risk for postpartum hemorrhage: targeting anemic women and scoring systems for clinical use. *Am J Obstet Gynecol MFM* 2023; 5: 100745.
- [11] Zheng W, Zhang H, Ma J, Dou R, Zhao X, Yan J and Yang H. Validation of a scoring system for prediction of obstetric complications in placenta accreta spectrum disorders. *J Matern Fetal Neonatal Med* 2022; 35: 4149-4155.
- [12] Xing Z, He Y, Ji C, Xu C, Zhang W, Li Y, Tan X, Zhao P, Wang Q and Zheng L. Establishing a perinatal red blood cell transfusion risk evaluation model for obstetric patients: a retrospective cohort study. *Transfusion* 2019; 59: 1667-1674.
- [13] Mattar G, Al Sahafi N, Al Hazmi L, Al Hazmi N, Abozeid HE and Sultan I. Evaluation of risk stratification and adherence to venous thromboembolism prophylaxis among hospitalized obstetric women: retrospective case file review at East Jeddah Hospital during 2018-2019. *Ann Thorac Med* 2022; 17: 94-101.
- [14] Ende HB, Domenico HJ, Polic A, Wesoloski A, Zuckerwise LC, McCoy AB, Woytash AR, Moore RP and Byrne DW. Development and validation of an automated, real-time predictive model for postpartum hemorrhage. *Obstet Gynecol* 2024; 144: 109-117.
- [15] Fan G, Yuan M, Niu H, Lu Y, Yang H and Liang X. Retraction of: the significance of thromboelastogram in predicting postpartum hemorrhage and guiding blood transfusion. *Clin Lab* 2023; 69: 1-2.
- [16] Ghaferi AA, Schwartz TA and Pawlik TM. STROBE reporting guidelines for observational studies. *JAMA Surg* 2021; 156: 577-578.
- [17] Brøgger H. The new declaration of Helsinki. *Tidsskr Nor Laegeforen* 2023; 143.
- [18] Zeng J, Mao L and Xie K. Establishment of risk nomogram model of postpartum hemorrhage after second cesarean section. *Int J Womens Health* 2024; 16: 1211-1218.
- [19] Obstetrics Subgroup, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association; Chinese Society of Perinatal Medicine, Chinese Medical Association. Guidelines for prevention and treatment of postpartum hemorrhage (2023). *Zhonghua Fu Chan Ke Za Zhi* 2023; 58: 401-409.
- [20] Xu L, Liu Z, Ma N, Chen J, Shen J, Chen X and Zhao C. Development and validation of an artificial neural network prediction model for postpartum hemorrhage with placenta previa. *Minerva Anestesiol* 2023; 89: 977-985.
- [21] Okunade KS, Ugwu AO, Adenekan MA, Olu-modeji A, Oshodi YA, Ojo T, Adejimi AA, Ademuyiwa IY, Adaramoye V, Okoro AC, Olowe A, Akinmola OO, John-Olabode SO, Adelabu H, Henriquez R, Decroo T and Lynen L. Development of antepartum risk prediction model for postpartum hemorrhage in Lagos, Nigeria: a prospective cohort study (predict-PPH study). *Int J Gynaecol Obstet* 2024; 166: 343-352.
- [22] Dang X, Zhang L, Bao Y, Xu J, Du H, Wang S, Liu Y, Deng D, Chen S, Zeng W, Feng L and Liu H. Developing and validating nomogram to pre-

Postpartum hemorrhage in critically ill pregnant women with placenta previa

- dict severe postpartum hemorrhage in women with placenta previa undergoing cesarean delivery: a multicenter retrospective case-control study. *Front Med (Lausanne)* 2022; 8: 789529.
- [23] Cao P, Ji L and Qiao C. Nomogram based on clinical characteristics and ultrasound indicators for predicting severe postpartum hemorrhage in patients with anterior placenta previa combined with previous cesarean section: a retrospective case-control study. *BMC Pregnancy Childbirth* 2024; 24: 572.
- [24] Lu Y, Zhou L, Wang X, Li Y, Chen D, Gu Y and Yue Y. Magnetic resonance imaging-based radiomics nomogram to predict intraoperative hemorrhage of placenta previa. *Am J Perinatol* 2024; 41: e2174-e2183.
- [25] Ma G, Yang Y and Fu Q. The incidence, indications, risk factors and pregnancy outcomes of peripartum hysterectomy at a tertiary hospital between 2013 and 2022. *Arch Gynecol Obstet* 2024; 310: 145-151.
- [26] Pettersen S, Falk RS, Vangen S and Nyfløt LT. Peripartum hysterectomy due to severe postpartum hemorrhage: a hospital-based study. *Acta Obstet Gynecol Scand* 2022; 101: 819-826.
- [27] Liu CN, Yu FB, Xu YZ, Li JS, Guan ZH, Sun MN, Liu CA, He F and Chen DJ. Prevalence and risk factors of severe postpartum hemorrhage: a retrospective cohort study. *BMC Pregnancy Childbirth* 2021; 21: 332.
- [28] Kawakita T, Mokhtari N, Huang JC and Landy HJ. Evaluation of risk-assessment tools for severe postpartum hemorrhage in women undergoing cesarean delivery. *Obstet Gynecol* 2019; 134: 1308-1316.
- [29] Yang Y, He J and Deng N. Factors associated with primary postpartum hemorrhage in elderly women undergoing repeated cesarean deliveries. *Int J Womens Health* 2021; 13: 1261-1267.
- [30] Zhou Y, Yin S, Sheng Q, Yang J, Liu J, Li H, Yuan P and Zhao Y. Association of maternal age with adverse pregnancy outcomes: a prospective multicenter cohort study in China. *J Glob Health* 2023; 13: 04161.
- [31] Lu X, Zhang H, Wu X, Chen X, Zhang Q, Song W, Jin Y and Yuan M. The value of the combined MR imaging features and clinical factors nomogram model in predicting intractable postpartum hemorrhage due to placenta accreta. *Medicine (Baltimore)* 2024; 103: e37665.