Am J Transl Res 2024;16(2):567-576
www.ajtr.org /ISSN:1943-8141/AJTR0152587

Original Article

Predictive value of coagulation function, alpha-fetoprotein and placental growth factor in patients with perilous placenta previa

Yuan Qiao[1*], Jin Xiao[1*], Tongqiang He[1], Rui Wang[2], Yehong Xu[2], Yang Wei[1], Jun Wang[1], Rui Hu[1], Zhibin Li[2]

[1]Obstetrics and Gynecology Intensive Care Unit, Northwest Women's and Children's Hospital, No. 1616 Yanxiang Road, Xi'an 710061, Shaanxi, China; [2]Department of Obstetrics, Northwest Women's and Children's Hospital, No. 1616 Yanxiang Road, Xi'an 710061, Shaanxi, China. [*]Equal contributors.

Received August 2, 2023; Accepted September 15, 2023; Epub February 15, 2024; Published February 28, 2024

Abstract: Objective: To analyze the predictive value of coagulation function, alpha-fetoprotein (AFP) and placental growth factor (PlGF) for postpartum hemorrhage in patients with perilous placenta previa (PPP). Methods: The clinical data of 104 PPP patients were retrospectively analyzed. The patients were divided into a hemorrhage group (n=68) and a non-hemorrhage group (n=36). A total of 55 healthy pregnant women were recruited as controls. The coagulation function, AFP and PlGF were compared between the three groups. Multivariate logistic regression was performed to determine independent risk factors for hemorrhage. Results: PT, TT, APTT, FIB and AFP were significantly higher while PlGF was lower in the PPP group than the control group (all P<0.05). Placental adhesion (OR 3.924, 95% CI 1.389-11.083, P=0.01), anterior placenta (OR 4.583, 95% CI 1.589-13.22, P=0.005), AFP (OR 0.208, 95% CI 0.068-0.635, P=0.006) and PlGF (OR 3.963, 95% CI 1.385-11.34, P=0.01) were independent risk factors for hemorrhage. Conclusion: Coagulation function, AFP and PlGF could predict postpartum hemorrhage in PPP patients.

Keywords: Coagulation function, alpha-fetoprotein, placental growth factor, perilous placenta previa, massive hemorrhage, prediction

Introduction

With the elevation of living standards, concerns about childbirth pain and advancements in reproductive technology have led to a significant increase in cesarean section rates [1]. This surge in cesarean deliveries has illuminated concerning associated complications, most notably placenta previa. Placenta previa is an obstetric condition where, after 28 weeks of gestation, the placenta situates at or below the uterus's lower segment, sometimes even obstructing the internal cervical orifice [4]. Alongside the rising cesarean rates, there's a noted increase in the incidence of perilous placenta previa (PPP) [2]. Data indicates a staggering postpartum hemorrhage rate exceeding 50% in PPP patients [3], a complication that gravely endangers both the mothers and the neonates.

Postpartum hemorrhage in such scenarios can precipitate shock, hemorrhagic anemia, hysterectomy, and even maternal mortality [4]. Concurrently, the fetus is not spared from the repercussions. Placental insufficiency resultant from PPP can lead to fetal hypoxia and distress, amplifying neonatal risks like respiratory distress syndrome, brain damage, and other associated complications [5]. PPP, commonly observed in women conceiving after a cesarean, is often coupled with placental implantation. This event, marked by placental villi invading the partial myometrial layer, can be a precursor to a series of life-threatening complications, from maternal hemorrhage and shock to uterine perforation and secondary infections [6].

Recent statistics have highlighted an alarming trend. The escalating cesarean section rates in

https://doi.org/10.62347/IVCJ9920

our nation have been directly proportional to the rising occurrences of PPP, introducing a complex clinical conundrum [7]. The aftermath of PPP can be profound: patients are susceptible to postpartum hemorrhage, a situation that can swiftly deteriorate, leading to maternal mortality. It is this potential hemorrhagic complication in PPP that underscores the urgency of early prediction. Recognizing the early signs, particularly through predictive indicators, equips clinicians with the ability to optimize treatment plans, mitigating the associated risks.

Furthermore, PPP's inherent risks are not confined to the immediate surgical period. The condition can precipitate bleeding episodes before, during, and post-operation, depleting essential coagulation factors, which in turn amplifies bleeding tendencies and compromises coagulation efficacy [8]. Alpha-fetoprotein (AFP), a fetal glycoprotein, has been under clinical scrutiny. Certain observations indicate that placental implantation can cause a surge in AFP concentrations, sometimes escalating to levels 2 to 5 times the standard range [9]. Placental growth factor (PlGF) is another pivotal entity. Expressed abundantly in placental tissues, PlGF orchestrates an array of vascular phenomena, from endothelial cell apoptosis and proliferation to vascular permeability and maturation [10]. Its role is pivotal during early gestation, aiding in the establishment and evolution of the uterine blood vessels [11]. Thus, assessing PlGF concentrations can offer valuable insights into maternal-fetal well-being.

Despite numerous advances in maternal and child healthcare, predicting postpartum hemorrhage in patients with PPP remains a challenge. Existing predictive tools, while highly valuable, exhibit certain limitations in terms of sensitivity, specificity, and clinical applicability. For example, ultrasound-based prediction methods and serum biomarker diagnostic tests have shown inconsistency in predictive results across different patient populations or have been limited by their high cost, technical difficulty, or timeliness issues. This leaves a gap in accurate and comprehensive prediction, thus highlighting the urgent need for novel, reliable and more efficient prediction tools.

Our study introduced coagulation, AFP and PlGF as potential predictors of postpartum hemorrhage in patients with PPP. Given the critical role of AFP and PlGF in placental physiology and their observed fluctuations in pathological states, they represent promising candidates for improving prediction accuracy. By utilizing these indicators, we hope not only to overcome the limitations of current tools, but also to provide clinicians with more accurate and feasible predictions that lead to early intervention.

Methods and materials

Sample collection

We conducted a retrospective study on 155 PPP patients who were admitted to the Northwest Women's and Children's Hospital between March 2020 and March 2023. For comparison, we also included 55 pregnant women, undergoing a normal pregnancy during the same period, as our control group. A flowchart illustrating our research methodology is presented in **Figure 1**. This study was approved by the Northwest Women's and Children's Hospital Ethics Committee (2023-052).

Inclusion and exclusion criteria

Inclusion criteria: The PPP group consisted of pregnant women who matched the diagnostic criteria for PPP [12], which includes: A singleton pregnancy reaching 28 weeks; A history of one or more cesarean sections; MRI or Doppler ultrasound verification of placental attachment to the uterus's lower segment, potentially obscuring the internal cervical orifice, and aligning with the prior uterine scar. For the control group, we considered healthy pregnant women with comprehensive clinical data.

Exclusion criteria: Pregnant women with the following conditions: multiple gestations; history of myomectomy; antepartum hypovolemic shock, coagulation disorders, multiple organ failure and other severe complications; severe hematologic diseases; severe immunologic diseases; and malignancies.

Sample screening and grouping

Upon applying our inclusion and exclusion criteria, we identified 104 suitable samples for the research group. Simultaneously, the control group comprised 55 pregnant women experi-

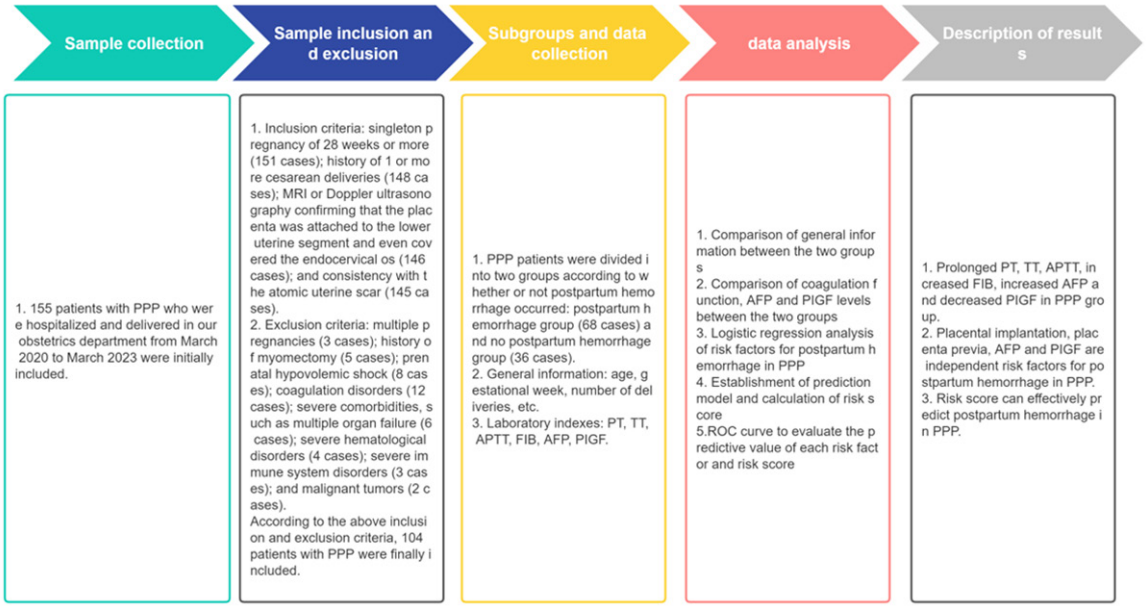

Figure 1. Flow chart of the prediction model for postpartum hemorrhage in patients.

encing standard pregnancies. The PPP group was further categorized into two sub-groups based on the presence or absence of postpartum hemorrhage: a postpartum hemorrhage group with 68 patients and a non-postpartum hemorrhage group with 36 patients.

Clinical data collection

We harvested patients' clinical data and pertinent laboratory metrics from their electronic pathology records and prenatal outpatient exam notes. This data encompassed attributes like age, average gestational age during delivery, parity, neonatal weight, nature of placental adhesion, placental implantation, placenta previa type, and cesarean section count. Laboratory metrics encapsulated indicators such as prothrombin time (PT), thrombin time (TT), activated partial thromboplastin time (APTT), fibrinogen (FIB), alpha-fetoprotein (AFP), and placental growth factor (PIGF) recorded a week before delivery.

Laboratory indicator detection

The Mindray C3510 coagulation analyzer (from Shenzhen Mindray Company) and its corresponding reagents determined coagulation-related metrics. The Roche 602 fully-automatic chemiluminescence device (by Roche) assessed AFP levels, while the enzyme-linked immunosorbent assay (sourced from Shanghai Enzyme Link, ml024102) measured serum PIGF levels.

Observation indicators

Primary observation indicators: The expression of coagulation function, AFP and PIGF between were compared between PPP patients and controls. Logistic regression analysis was performed to determine the risk factors associated with postpartum hemorrhage in PPP patients.

Secondary observation indicators: The baseline characteristics were compared between the PPP group and the control group. A risk prediction model was constructed for postpartum hemorrhage in PPP patients based on the β coefficients of significant risk factors. The predictive performance of the risk score model and individual risk factors were evaluated for PPP hemorrhage.

Statistical analysis

Graph Pad Prism 9.0 was used to visually process the data. Measurement data were represented by mean ± SD, and the intergroup comparisons was conducted using the independent sample t-test, represented by t; count data were represented by rate (%), and com-

Table 1. Baseline data

Factor	Control group (n=55)	Research group (n=104)	Chi-square	*P* value
Age ≥30 years	15	57	11.011	<0.001
Age <30 years	40	47		
Average gestational weeks ≥36 weeks	36	62	0.518	0.471
Average gestational weeks <36 weeks	19	42		
Parity (first pregnancy)	31	35	7.642	0.006
Parity (not first pregnancy)	24	69		
Newborn weight ≥3 kg	14	34	0.894	0.344
Newborn weight <3 kg	41	70		
Number of C-sections ≥2	44	94	3.384	0.065
Number of C-sections <2	11	10		

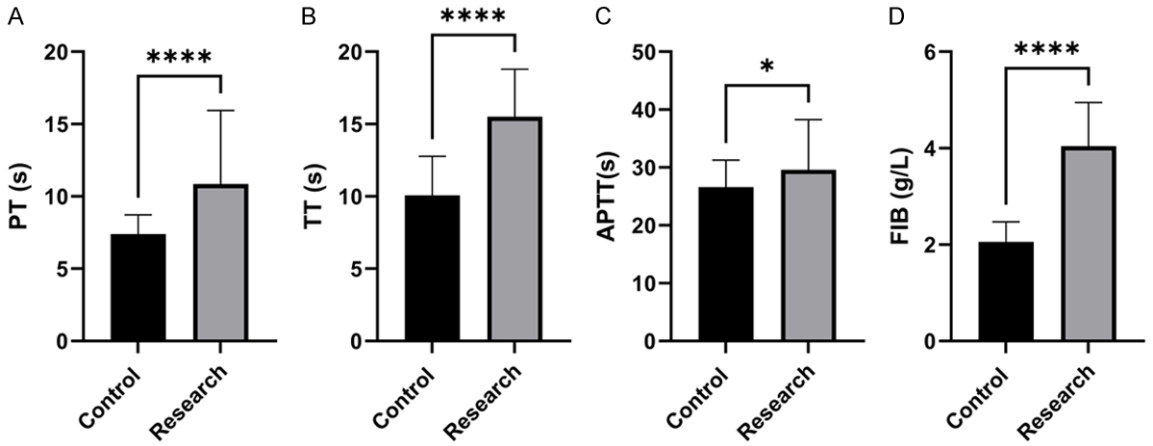

Figure 2. Levels of coagulation function in PPP patients. A. Comparing PT levels in peripheral blood between the research group and the control group. B. Comparing TT levels in peripheral blood between the research group and the control group. C. Comparing APTT levels in peripheral blood between the research group and the control group. D. Comparing FIB levels in peripheral blood between the research group and the control group. Note: PT, Prothrombin Time; TT, Thrombin Time; APTT, Activated Partial Thromboplastin Time; FIB, Fibrinogen; *P<0.05, ****P<0.0001.

pared using the chi-square test. Logistic regression was used to screen the risk factors for PPP hemorrhage, and the receiver operating characteristic (ROC) curve was used to verify their prediction performance. The Delong test was used to analyze the difference in the area under the ROC curve. When P<0.05, the data were statistically significant.

Results

Baseline data comparison

We first analyzed the baseline data differences between the research group and control group. The parameters like average gestational week at childbirth, newborn weight, and number of cesarean sections displayed no significant variations between the two groups (all P>0.05, **Table 1**). However, the proportion of women <30 years old (P<0.001) was significantly higher while the proportion of women with multipara (P=0.006) was significantly lower in the control group than in the PPP group.

Coagulation function of PPP patients

We observed that the coagulation function in PPP patients was notably diminished compared to the healthy controls. The research group exhibited significantly prolonged PT (P<0.001), TT (P<0.001), and APTT (P=0.018), while their FIB level (P<0.001) was elevated, as compared to the control group (**Figure 2**).

Expression levels of AFP and PlGF of PPP patients

AFP levels were significantly elevated in the research group compared to the control group

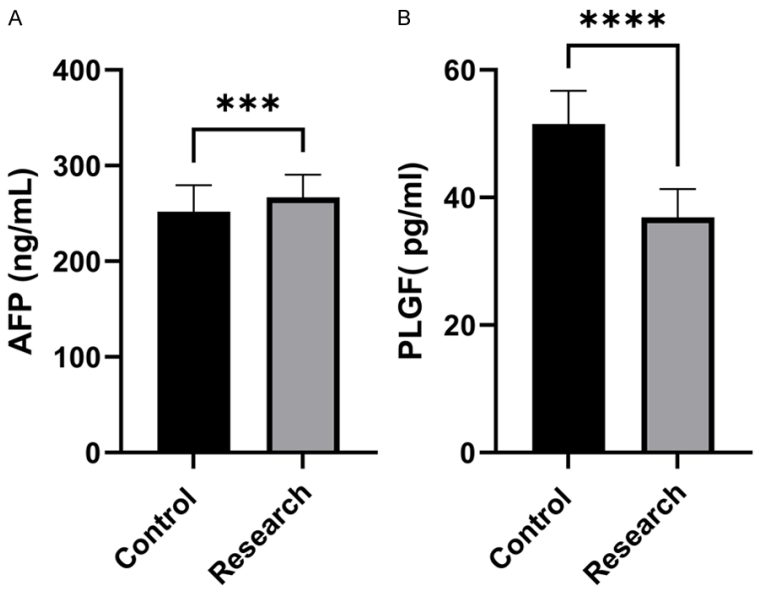

Figure 3. Levels of AFP and PLGF in PPP patients. A. Comparing AFP levels in peripheral blood between the research group and the control group. B. Comparing PLGF levels in peripheral blood between the research group and the control group. Note: AFP, Alpha-fetoprotein; PLGF, Placental Growth Factor; ***P<0.001, ****P<0.0001.

(P=0.001). Conversely, PIGF levels in PPP patients were reduced relative to healthy controls (P<0.001, **Figure 3**).

Determinants of postpartum hemorrhage in PPP patients

To understand the factors impacting postpartum hemorrhage in PPP, we categorized the patients into two groups: those who experienced postpartum hemorrhage (68 cases) and those who did not (36 cases). Our analysis revealed that placental adhesion (P=0.005), placental implantation (P=0.009), anterior placenta position (P=0.014), AFP (P<0.001), and PIGF (P<0.001) were significant determinants of postpartum hemorrhage among PPP patients (**Table 2**). We assigned scores to these significant variables (**Table 3**), performed multivariate logistic regression, and identified placental adhesion, anterior placenta, AFP, and PIGF as critical risk factors for postpartum hemorrhage in PPP (P<0.05, **Table 4**).

Predictive efficacy of the identified risk indicators for postpartum hemorrhage in PPP patients

To delve deeper into the predictive power of the identified risk factors for postpartum hemorrhage among PPP patients, we designed a risk assessment model. Based on the β coefficients, a risk equation was constructed as follows: placental adhesion1.367 + anterior placenta type1.522 + AFP (ng/mL) * -1.570 + PIGF (pg/mL) * 1.377. Notably, the risk scores in the hemorrhage group were substantially elevated compared to the non-hemorrhage group (P<0.001). ROC curve assessments further indicated that AFP, PIGF, and the Risk score all demonstrated substantial predictive capacity for major hemorrhage in PPP patients. Nonetheless, the DeLong test reflected no significant variance in their predictive capability for major hemorrhage in PPP patients (P>0.05, **Figure 4**; **Tables 5**, **6**).

Discussion

The pathogenesis of PPP (Perilous Placenta Previa) is still not fully understood to this day. Current theories suggest that abnormal or absent development of the basal decidua leads to abnormal placental implantation, enabling placental villi to invade or penetrate the myometrium and further invade adjacent organs and tissues [13, 14].

PT, APTT, TT, and FIB are commonly utilized coagulation indicators. Under normal circumstances, the coagulation and fibrinolysis systems maintain dynamic equilibrium [15]. PT chiefly demonstrates the function of extrinsic coagulation factors, while APTT primarily reveals intrinsic coagulation function [16]. Elevated PT and APTT values signify prolonged clotting time, impaired coagulation function, and increased bleeding risk [17, 18]. TT evaluates coagulation function by examining plasma fibrinogen's capacity to form fibrin polymers [19]. Prolonged TT indicates potential dysfunction in fibrinogen-to-fibrin conversion [20]. As the largest coagulation glycoprotein, FIB generates fibrin via thrombin and aids hemostasis [21]. Additionally, FIB facilitates platelet aggregation and thrombus formation. In late pregnancy, physiological hypercoagulability emerg-

Table 2. Comparison of clinical data between patients in the PPP bleeding group and patients without bleeding

Factor	Hemorrhage group (n=68)	Non-hemorrhage group (n=36)	Chi-square	*P* value
Age ≥30 years	35	22	0.883	0.347
Age <30 years	33	14		
Average gestational weeks ≥36 weeks	38	24	1.137	0.286
Average gestational weeks <36 weeks	30	12		
Parity (first pregnancy)	25	10	0.851	0.356
Parity (not first pregnancy)	43	26		
Newborn weight ≥3 kg	20	13	0.487	0.485
Newborn weight <3 kg	48	23		
Placental adhesion present	42	12	7.622	0.005
Placental adhesion not present	26	24		
Placental implantation present	15	1	6.722	0.009
Placental implantation not present	53	35		
Type of placenta previa - central	51	18	8.462	0.014
Type of placenta previa - marginal	13	10		
Type of placenta previa - partial	4	8		
Number of C-sections ≥2	61	33	0.104	0.746
Number of C-sections <2	7	3		
Prothrombin Time (PT, s)	10.72±5.35	10.82±5.13	0.088	0.930
Thrombin Time (TT, s)	15.31±3.19	15.89±3.47	0.851	0.396
Activated Partial Thromboplastin Time (APTT, s)	29.23±8.51	30.26±9.05	0.565	0.577
Fibrinogen (FIB, g/L)	4.07±0.98	3.99±0.75	0.453	0.651
Alpha-Fetoprotein (AFP, ng/mL)	258.48±18.80	282.44±24.08	5.599	<0.001
Placental Growth Factor (PLGF, pg/mL)	39.60±2.46	33.75±4.68	6.135	<0.001

Note: PT, Prothrombin time; TT, thrombin time; APTT, activated partial thromboplastin time; FIB, fibrinogen; AFP, alpha-fetoprotein; PLGF, placental growth factor; PPP, dangerous placenta previa.

Table 3. Scoring table

Factor	Score
Presence of placental adhesions	1
Absence of placental adhesions	0
Presence of placenta accreta	1
Absence of placenta accreta	0
Type of placenta previa - Central	1
Type of placenta previa - Marginal or Partial	0
AFP (ng/mL) ≥272	1
AFP (ng/mL) <272	0
PLGF (pg/mL) ≥38	1
PLGF (pg/mL) <38	0

Note: AFP, alpha-fetoprotein; PLGF, placental growth factor.

es, with compensatory fibrinolysis activation, raising fibrinolysis products and FIB levels, thereby preventing excessive bleeding during childbirth [22]. AFP signifies abnormal placental implantation, manifesting marked elevations in PPP, effectively indicating fetal status [23]. Placentally-expressed PlGF promotes placental vessel growth by stimulating trophoblast proliferation and differentiation, accurately reflecting placental function [24]. We analyzed coagulation function, AFP, and PlGF in PPP patients and controls before delivery. Results exhibited prolonged PT, TT, APTT, elevated FIB and AFP, and decreased PlGF in PPP patients versus controls, denoting poorer coagulation and increased bleeding risk in PPP patients. Elevated AFP and lowered PlGF in PPP patients result from defective placental implantation, potentially impairing placental blood flow.

Postpartum hemorrhage (PPH) is a primary consequence of PPP and poses a significant threat to both maternal and neonatal health. This complication represents a formidable challenge in obstetric care [13]. As indicated by

Table 4. Logistic regression analysis

Factor	B	Standard Error	Chi-square	*P*-value	OR	95% CI Lower	95% CI Upper
Placental adhesions	1.367	0.53	6.659	0.010	3.924	1.389	11.083
Placenta accreta	1.561	1.116	1.958	0.162	4.764	0.535	42.426
Type of placenta previa	1.522	0.54	7.934	0.005	4.583	1.589	13.22
AFP	-1.57	0.569	7.612	0.006	0.208	0.068	0.635
PLGF	1.377	0.536	6.589	0.010	3.963	1.385	11.34

Note: AFP, Alpha-fetoprotein; PLGF, placental growth factor.

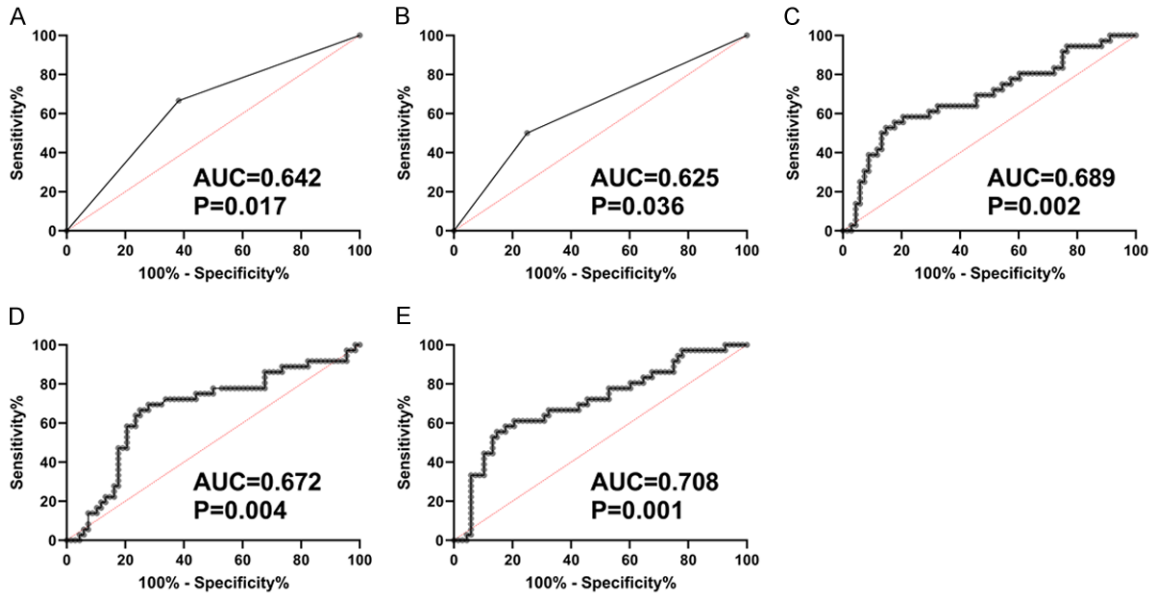

Figure 4. Area under the curve of risk factors and risk scores in predicting postpartum hemorrhage in PPP patients. A. ROC curve of placental adhesions in predicting postpartum hemorrhage in PPP patients. B. ROC curve of placenta implantation in predicting postpartum hemorrhage in PPP patients. C. ROC curve of AFP in predicting postpartum hemorrhage in PPP patients. D. ROC curve of PLGF in predicting postpartum hemorrhage in PPP patients. E. ROC curve of Risk score in predicting postpartum hemorrhage in PPP patients. Note: Alpha-fetoprotein (AFP), Placental Growth Factor (PLGF), and Receiver Operating Characteristic (ROC) curve.

data [25], nearly half of perinatal fatalities stem from postpartum hemorrhage. Historically, clinicians have evaluated the risk of PPH in PPP patients by considering variables such as maternal age, the number of cesarean deliveries, placenta previa type, and prior occurrences of placenta previa [26]. To enhance pregnancy outcomes, perinatal medicine has been actively seeking markers to anticipate the likelihood of PPH in PPP patients. Identifying these predictors can pave the way for timely interventions, treatments, and a subsequent reduction in PPH incidence rates. Through the logistic regression analysis, we identified placenta accreta, placenta previa type, AFP, and PIGF as pivotal risk factors associated with PPH in PPP patients.

Placenta accreta is characterized by the placenta's unusual adherence to the uterine wall, resulting in challenges or, at times, an inability to detach it. Any attempt by a physician to separate the placenta might compromise maternal blood vessels. Moreover, if complete placental detachment isn't achievable, it might necessitate a hysterectomy, further elevating the bleeding risk for the expectant mother [27]. A particularly hazardous type of placenta previa is the central type, where the placenta entirely obscures the cervical os. As childbirth progresses and the infant maneuvers through the cervix, there's a risk of premature placental detachment, inducing substantial hemorrhage [28]. Given the placenta's position obstructing the regular birth canal, a cesarean section may

Table 5. ROC parameter

Predictive Variable	Area Under the Curve	Confidence Interval	Sensitivity	Specificity	Youden's Index
Placental adhesions	0.642	0.545-0.740	66.67%	61.77%	28.43%
placenta Implantation	0.625	0.527-0.723	50.00%	75.00%	25.00%
AFP (ng/mL)	0.689	0.577-0.801	52.78%	85.29%	38.07%
PLGF (pg/mL)	0.672	0.557-0.786	66.67%	75.00%	41.67%
Risk score	0.708	0.600-0.817	55.56%	85.29%	40.85%

Note: AFP, Alpha-fetoprotein; PLGF, Placental Growth Factor.

Table 6. Pairwise sample regional differences under the ROC curve

Test Result Pair	Z-value	*P*-value	AUC Difference	Standard Error of Difference	95% CI	
					Lower	Upper
Placental adhesions - Type of placenta previa	0.231	0.817	0.017	0.316	-0.128	0.163
Placental adhesions - AFP	-0.684	0.494	-0.048	0.312	-0.186	0.090
Placental adhesions - PLGF	-0.996	0.319	-0.066	0.312	-0.196	0.064
Placental adhesions - Risk score	-0.910	0.363	-0.066	0.324	-0.209	0.076
Type of placenta previa - AFP	-0.916	0.360	-0.065	0.312	-0.205	0.075
Type of placenta previa - PLGF	-1.125	0.260	-0.083	0.314	-0.228	0.062
Type of placenta previa - Risk score	-1.107	0.268	-0.083	0.325	-0.231	0.064
AFP - PLGF	-0.303	0.762	-0.018	0.307	-0.134	0.098
AFP - Risk score	-0.520	0.603	-0.018	0.314	-0.086	0.050
PLGF - Risk score	0.000	1.000	0.000	0.318	-0.114	0.114

Note: AFP, Alpha-fetoprotein; PLGF, Placental Growth Factor.

be imperative, amplifying the maternal bleeding risk. Nevertheless, the role and underlying mechanisms of AFP and PIGF in massive PPH amongst PPP patients remain nebulous. We hypothesize that abnormal placental implantation, possibly at the cervical os or a lowered position in placenta previa scenarios, could perturb placental functionality and subsequently alter AFP concentrations.

Concluding our study, we formulated a risk prediction model and discerned that the risk scores for patients in the hemorrhage group significantly surpassed those of their non-hemorrhaging counterparts. We also plotted ROC curves for the risk score and all risk variables to forecast PPH in PPP patients. The resultant AUC for the risk score was an impressive 0.708. However, the Delong test indicated no statistically significant difference between the AUC of the risk score and PIGF. This suggests that solely examining PIGF as a predictor for PPH in PPP patients doesn't compromise prediction specificity or sensitivity.

In this study, we constructed a risk model for predicting postpartum hemorrhage in PPP patients through regression analysis. However, there are still limitations in our study. First, this study is a retrospective study, and whether the collection of samples based on chronological order affects the results still needs further experiments to verify. Secondly, as a single-center study, it is unclear whether our model is generalizable needs more experiments to verify. We hope to carry out more experiments in future research to perfect our research conclusions.

In conclusion, the risk model constructed by logistic regression predicts postpartum hemorrhage in PPP patients with no difference from placenta accreta, type of placenta previa, AFP, and PIGF, and they can all be used as observational indicators to predict postpartum hemorrhage.

Disclosure of conflict of interest

None.

Address correspondence to: Zhibin Li, Department of Obstetrics, Northwest Women's and Children's Hospital, No. 1616 Yanxiang Road, Xi'an 710061, Shaanxi, China. Tel: +86-0298-9550197; E-mail: lzhbzyzh@163.com

References

[1] Antoine C and Young BK. Cesarean section one hundred years 1920-2020: the good, the bad and the ugly. J Perinat Med 2020; 49: 5-16.

[2] Maskey S, Bajracharya M and Bhandari S. Prevalence of cesarean section and its indications in a tertiary care hospital. JNMA J Nepal Med Assoc 2019; 57: 70-73.

[3] Sandall J, Tribe RM, Avery L, Mola G, Visser GH, Homer CS, Gibbons D, Kelly NM, Kennedy HP, Kidanto H, Taylor P and Temmerman M. Short-term and long-term effects of caesarean section on the health of women and children. Lancet 2018; 392: 1349-1357.

[4] Jauniaux E, Gronbeck L, Bunce C, Langhoff-Roos J and Collins SL. Epidemiology of placenta previa accreta: a systematic review and meta-analysis. BMJ Open 2019; 9: e031193.

[5] Jain V, Bos H and Bujold E. Guideline no. 402: diagnosis and management of placenta previa. J Obstet Gynaecol Can 2020; 42: 906-917, e901.

[6] Zhu L, Lu J, Huang W, Zhao J, Li M, Zhuang H, Li Y, Liu H and Du L. A modified suture technique for the treatment of patients with pernicious placenta previa and placenta accreta spectrum: a case series. Ann Transl Med 2021; 9: 1140.

[7] Wang N, Shi D, Li N and Qi H. Clinical value of serum VEGF and sFlt-1 in pernicious placenta previa. Ann Med 2021; 53: 2041-2049.

[8] Han M, Li X, Ren D and Liu F. Application effect of sevoflurane in the cesarean section of pregnant women with pernicious placenta previa and its influence on maternal hemodynamics. Am J Transl Res 2021; 13: 2997-3003.

[9] Tao E, Ye D, Long G, Hu Y, Fu Q, Yuan T and Jiang M. Severe neonatal anemia affected by massive fetomaternal hemorrhage: a single-center retrospective observational study. J Matern Fetal Neonatal Med 2022; 35: 3972-3978.

[10] Trapiella-Alfonso L, Alexandre L, Fraichard C, Pons K, Dumas S, Huart L, Gaucher JF, Hebert-Schuster M, Guibourdenche J, Fournier T, Vidal M, Broutin I, Lecomte-Raclet L, Malaquin L, Descroix S, Tsatsaris V, Gagey-Eilstein N and Lecarpentier E. VEGF (vascular endothelial growth factor) functionalized magnetic beads in a microfluidic device to improve the angiogenic balance in preeclampsia. Hypertension 2019; 74: 145-153.

[11] Albonici L, Benvenuto M, Focaccetti C, Cifaldi L, Miele MT, Limana F, Manzari V and Bei R. PlGF immunological impact during pregnancy. Int J Mol Sci 2020; 21: 8714.

[12] Kingdom JC, Hobson SR, Murji A, Allen L, Windrim RC, Lockhart E, Collins SL, Soleymani Majd H, Alazzam M, Naaisa F, Shamshirsaz AA, Belfort MA and Fox KA. Minimizing surgical blood loss at cesarean hysterectomy for placenta previa with evidence of placenta increta or placenta percreta: the state of play in 2020. Am J Obstet Gynecol 2020; 223: 322-329.

[13] Fu M, Bu H, Fang Y, Wang C, Zhang L, Zhang Y, Sun X, Li M, Jin C, Xu Y and Chen L. Parallel loop binding compression suture, a modified procedure for pernicious placenta previa complicated with placenta increta. Front Surg 2021; 8: 786497.

[14] Ma Y, You Y, Jiang X and Lin X. Use of nitroglycerin for parallel transverse uterine cesarean section in patients with pernicious placenta previa and placenta accrete and predicted difficult airway: a case report and review of literature. Medicine (Baltimore) 2020; 99: e18943.

[15] Brake MA, Ivanciu L, Maroney SA, Martinez ND, Mast AE and Westrick RJ. Assessing blood clotting and coagulation factors in mice. Curr Protoc Mouse Biol 2019; 9: e61.

[16] Harrold IM and Oladipo O. Elevated PT and aPTT. Clin Chem 2018; 64: 1790-1791.

[17] Frans G, Meeus P and Bailleul E. Resolving DOAC interference on aPTT, PT, and lupus anticoagulant testing by the use of activated carbon. J Thromb Haemost 2019; 17: 1354-1362.

[18] Zhang L, Ye J, Luo Q, Kuang M, Mao M, Dai S and Wang X. Prediction of poor outcomes in patients with colorectal cancer: elevated preoperative prothrombin time (PT) and activated partial thromboplastin time (APTT). Cancer Manag Res 2020; 12: 5373-5384.

[19] Wada H, Ichikawa Y, Ezaki M, Matsumoto T, Yamashita Y, Shiraki K, Shimaoka M and Shimpo H. The reevaluation of thrombin time using a clot waveform analysis. J Clin Med 2021; 10: 4840.

[20] Apipongrat D, Police P, Lamool R, Butthep P and Chantkran W. Validation of high concentrated thrombin time assay for unfractionated heparin monitoring. J Clin Lab Anal 2022; 36: e24695.

[21] Xue L, Tao L, Li X, Wang Y, Wang B, Zhang Y, Gao N, Dong Y, Xu N, Xiong C, Zhou T, Liu Z, Liu H, He J, Li K, Geng Y and Li M. Plasma fibrinogen, D-dimer, and fibrin degradation product as biomarkers of rheumatoid arthritis. Sci Rep 2021; 11: 16903.

[22] Zhang EJ, Su SF, Gao S, Liu RX, Yue WT, Liu JH, Xie SH, Zhang Y and Yin CH. Association between coagulation function indicators and placental abruption among preeclampsia-eclampsia pregnant women. Zhonghua Yu Fang Yi Xue Za Zhi 2023; 57: 905-911.

[23] Glowska-Ciemny J, Szymanski M, Pankiewicz J, Malewski Z, von Kaisenberg C and Kocylowski R. Influence of selected factors on serum AFP

levels in pregnant women in terms of prenatal screening accuracy - literature review. Ginekol Pol 2023; 94: 158-166.
[24] Verlohren S, Brennecke SP, Galindo A, Karumanchi SA, Mirkovic LB, Schlembach D, Stepan H, Vatish M, Zeisler H and Rana S. Clinical interpretation and implementation of the sFlt-1/PlGF ratio in the prediction, diagnosis and management of preeclampsia. Pregnancy Hypertens 2022; 27: 42-50.
[25] Zou L, Wang P, Song Z, Wang X, Chen X, Zhang M and Zhang D. Effectiveness of a fetal magnetic resonance imaging scoring system for predicting the prognosis of pernicious placenta previa: a retrospective study. Front Physiol 2022; 13: 921273.
[26] Zhu L and Xie L. Value of ultrasound scoring system for assessing risk of pernicious placenta previa with accreta spectrum disorders and poor pregnancy outcomes. J Med Ultrason (2001) 2019; 46: 481-487.
[27] Zhou Y, Song Z, Wang X, Zhang M, Chen X and Zhang D. Ultrasound-based nomogram for postpartum hemorrhage prediction in pernicious placenta previa. Front Physiol 2022; 13: 982080.
[28] Hou Y, Zhou X, Shi L, Peng J and Wang S. Influence factors and pregnancy outcomes for pernicious placenta previa with placenta accreta. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2020; 45: 1074-1081.