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Original Research

Association between Placental Thickness and Intraoperative Hemorrhage in Patients with Suspected Placenta Accreta Spectrum and Placenta Previa: A Retrospective Cohort Study

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Abstract

Background: Placenta accreta spectrum (PAS) can easily lead to life-threatening hemorrhage. However, the association between placental thickness (PT) and massive bleeding remains unclear. Thus, this study investigated the association between PT and massive bleeding to determine which patients with suspected PAS and placenta previa were more likely to experience intraoperative hemorrhage. **Methods**: This retrospective cohort study was conducted between January 2018 and December 2020 at a general tertiary care hospital in Chongqing, China. Covariates included demographic, clinical, and ultrasonographic characteristics. Logistic regression analysis was used to explore the association between PT and massive bleeding. A sensitivity analysis was conducted by detecting trends in the association between PT quartile and massive bleeding risk. **Results**: PT was associated with a risk of massive intraoperative bleeding. The sensitivity analysis yielded a similar result using the minimally adjusted model (p for trend = 0.001), and minimal changes were observed using the crude and fully adjusted models (p for trend = 0.001 and 0.037, respectively). The risk of major bleeding was significantly higher in the fourth quartile (Q4) *versus* first quartile (Q1) group (odds ratio = 2.26, p = 0.034). A linear relationship was observed between PT and the risk of massive bleeding. **Conclusions**: PT was independently and linearly associated with the risk of massive bleeding. The risk of intraoperative hemorrhage was significantly higher in the higher PT (Q4) than lower PT (Q1) group. **Clinical Trial Registration:** The study was registered at Chinese Clinical Trial Registry (https://www.chictr.org.cn), registration number: ChiCTR2100044798.

Keywords: placental thickness; massive bleeding; placenta accreta spectrum; placenta previa; cesarean section

1. Introduction

Placenta accreta spectrum (PAS), an abnormal placental attachment induced by the invasion of placental villi into the myometrium, is a life-threatening severe obstetric disease [1–3]. Placenta previa covers the endocervical os. In China, the frequency of PAS associated with placenta previa increases annually, with the risk of a second cesarean delivery reaching as high as 3.4% in some cases [4].

The risk of intraoperative bleeding in PAS with placenta previa is substantially higher than that in placenta previa alone. According to Bailit *et al.* [5], the median estimated intraoperative blood loss of PAS is 2000 mL, reaching 8000 mL in emergency surgeries. Several models have been developed to predict significant intraoperative bleeding and massive blood transfusions in obstetric patients [6–10]. However, these models are mainly based on patients with placenta previa, and the risk variables derived from them are inconsistent [11]. A few studies linked massive bleeding with PAS to the post-placental clear space, cross-border blood vessels in the region of sub-placental vascularity, interruption or disappearance of the bladder line, and the presence of the cervical blood sinus [4,12].

Study has associated placental thickness (PT) in the lower uterine segment with PAS [13]. Predictive models for PAS include PT as a risk factor [14]. Another study suggested that PT exceeding 5 cm may be associated with intraoperative bleeding >2000 mL in patients with PAS; however, the authors concluded that it was not an independent risk factor [4]. Whether an increased PT is associated with severe intraoperative bleeding in patients with PAS and placenta previa remains unclear, and research to date on this topic is limited. Therefore, this study investigated the relationship between PT and the risk of major bleeding in patients with PAS and placenta previa to determine which patients were at greater risk of intraoperative major bleeding.

2. Materials and Methods

2.1 Subjects

This retrospective cohort study was conducted at the First Affiliated Hospital of Chongqing Medical University (no. 2021–059). Our local ethics committee approved the study and waived the requirement for informed consent owing to its retrospective nature. Here we reviewed the clinical data (extracted from the medical records) of consecutive patients with PAS and placenta previa who underwent a cesarean section (CS) between January 2018 and December 2020. Ultimately, 317 patients were included in the analysis. All reports followed the Guidelines for Strengthening the Reporting of Observational Epidemiological Studies.

The preoperative diagnosis of PAS is mainly based on the Placenta Accreta Spectrum Ultrasound Scoring System (PASUSS) [4,14] and the International Federation of Gynecology and Obstetrics (FIGO) diagnostic criteria [15]. In 2019, the diagnosis of PAS relied primarily on the PASUSS. In this study, PAS was confirmed by postoperative pathology if pathological examination was performed intraoperatively by the surgeon. Patients with PAS but no other prenatal disorders who underwent CS met the inclusion criteria. Patients with multiple pregnancies or hematologic disorders or for whom inadequate data were available were excluded. Patients with placental pathologies were also excluded.

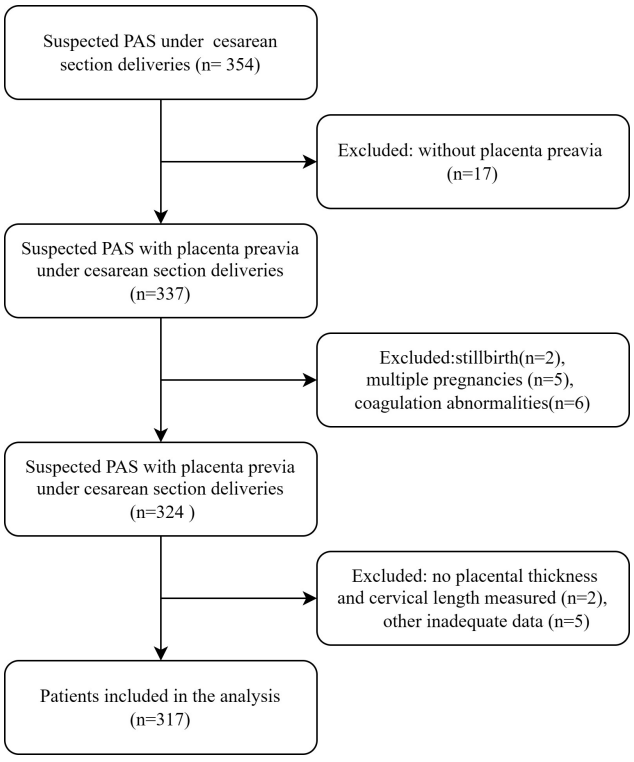

Fig. 1. Flowchart of the study population. PAS, placenta accreta spectrum.

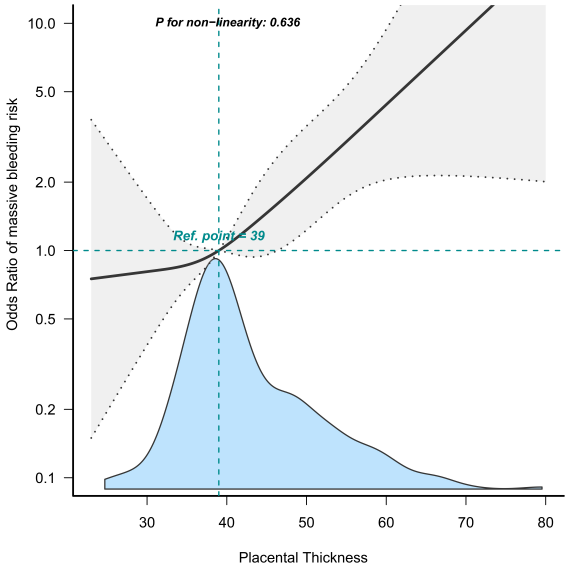

Fig. 2. Relationship between placental thickness and risk of massive bleeding.

2.2 Treatment Methods

The prevention of hemorrhage and measures to stop bleeding during CS were performed according to standard procedures. The surgeon selected whether to use abdominal aortic balloon placement before cesarean delivery depending on the patient's previous medical history and ultrasound findings. We developed a policy of prophylactic interruption of abdominal aortic balloon catheter placement followed by placental separation and uterine preservation during cesarean delivery whenever possible. The decision to remove the adherent placenta and apply a local suture in the placental bed or leave the placenta *in situ* and perform a hysterectomy was made after delivery of the newborn depending on the operative findings. The triple-P procedure was used in some patients to preserve the uterus whenever possible. If the placenta could not be removed or the balloon occlusion failed to control the hemorrhage, a subtotal hysterectomy was performed. Excising part of the placenta, manually detaching the placenta, ligating the bleeding artery, placing a ∞-shaped suture, or performing uterine tamponade, uterine artery embolization, or a hysterectomy were employed as required [16]. If the uterine contractions were poor, oxytocin, methylergonovine, or carboprost was selectively administered.

2.3 Outcome Measures and Definitions

The primary outcome indicator was the amount of intraoperative bleeding. Intraoperative blood loss was calculated based on pre-and postoperative hemoglobin values [17]. Women with a calculated blood loss $\geq$1000 mL were included in the massive bleeding group, while those with a calculated blood loss $<$1000 mL were categorized into the non-massive bleeding group [18].

Table 1. Baseline characteristics of patients

Variables	Total (n = 317)	Q1 (n = 68)	Q2 (n = 70)	Q3 (n = 90)	Q4 (n = 89)	*p*-value
Age (year), Mean ± SD	32.9 ± 4.3	33.1 ± 4.5	33.4 ± 4.9	32.4 ± 4.1	33.0 ± 3.8	0.545
Height (centimeter), Mean ± SD	157.9 ± 4.8	157.6 ± 5.3	158.1 ± 4.7	157.6 ± 5.1	158.1 ± 4.3	0.864
Weight (kg), Mean ± SD	68.4 ± 8.8	68.0 ± 9.1	68.8 ± 8.6	67.8 ± 8.3	68.9 ± 9.3	0.814
Gravidity, Mean ± SD	3.9 ± 1.7	3.4 ± 1.5	4.0 ± 1.8	3.9 ± 1.9	4.0 ± 1.7	0.128
Previous CS, n (%)						0.418
0	74 (23.3)	19 (27.9)	14 (20)	25 (27.8)	16 (18)	
1	194 (61.2)	40 (58.8)	47 (67.1)	49 (54.4)	58 (65.2)	
2	48 (15.1)	8 (11.8)	9 (12.9)	16 (17.8)	15 (16.9)	
≥3	1 (0.3)	1 (1.5)	0 (0)	0 (0)	0 (0)	
Curettage, n (%)						0.126
0	69 (21.8)	21 (30.9)	15 (21.4)	18 (20)	15 (16.9)	
1	84 (26.5)	10 (14.7)	20 (28.6)	25 (27.8)	29 (32.6)	
2	81 (25.6)	18 (26.5)	13 (18.6)	29 (32.2)	21 (23.6)	
≥3	83 (26.2)	19 (27.9)	22 (31.4)	18 (20)	24 (27)	
Gestational age (week), Mean ± SD	36.3 ± 1.6	36.1 ± 2.0	36.4 ± 1.1	36.9 ± 1.1	35.9 ± 1.8	<0.001
Diabetes, n (%)	83 (26.2)	22 (32.4)	20 (28.6)	24 (26.7)	17 (19.1)	0.276
Hypertension, n (%)	11 (3.5)	7 (10.3)	1 (1.4)	1 (1.1)	2 (2.2)	0.013
Suspected PAS, n (%)						<0.001
No PAS	18 (5.7)	16 (23.5)	2 (2.9)	0 (0)	0 (0)	
Accreta	103 (32.5)	24 (35.3)	19 (27.1)	41 (45.6)	19 (21.3)	
Increta	170 (53.6)	27 (39.7)	43 (61.4)	44 (48.9)	56 (62.9)	
Percreta	26 (8.2)	1 (1.5)	6 (8.6)	5 (5.6)	14 (15.7)	
Cervical canal length (mm), Mean ± SD	32.6 ± 5.2	34.7 ± 4.7	32.1 ± 4.2	33.0 ± 6.2	30.8 ± 4.7	<0.001

SD, standard deviation; CS, cesarean section; Q1, the first quartile; Q2, the second quartile; Q3, the third quartile; Q4, the fourth quartile; PAS, placenta accreta spectrum.

Measurements were performed only on transabdominal and transvaginal images obtained in the longitudinal plane [19]. The PT was measured at the thickest portion by an obstetric ultrasound-specialized radiologist with 5 years of post-fellowship experience. If the placental cord insertion was centric or eccentric by 2 cm, the PT was measured in the sagittal view in the area of placental cord insertion. When the placental cord insertion was marginal or velamentous, the maximum PT in the longitudinal plane was calculated linearly. The PT was measured the day before or the day of surgery. PT is also expressed in quartiles, where Q1 represents the first quartile, Q2 represents the second quartile, etc.

2.4 Collection of Clinical Characteristics

The patients' clinical characteristics were collected by review of their medical records during hospitalization for CS, including age, weight, height, gestational weeks, gravidity, curettage, previous number of CS, intraoperative estimated blood loss, incidence of transfusion, incidence of intensive care unit (ICU) admission, incidence of hysterectomy, operation time, and hospitalization duration. Furthermore, neonatal outcomes were assessed.

All ultrasound-related indicators including PT and cervical canal length were extracted from the latest preoperative obstetric ultrasound reports.

2.5 Statistical Analysis

Those for whom PT was unmeasured were excluded, while missing values for indicators such as cervical canal length were interpolated using the mean values. Continuous data are presented as mean ± standard deviation or median depending on normality. Normality was examined using the Shapiro-Wilk test. The *t*-test was used for normally distributed continuous variables. Categorical data are presented as number of cases and the corresponding percentages. Categorical and continuous data that were not normally distributed were analyzed using Pearson's chi-squared test, Fisher's exact test, or the Mann-Whitney U test as appropriate. Values of $p < 0.05$ were considered statistically significant.

Subsequently, smooth curve fitting was performed to determine the association between the risk of massive bleeding and PT. A univariate analysis was performed to assess candidate variables as risk factors for massive bleeding; associations between potential risk factors and outcomes are shown as odds ratio (OR) and 95% confidence interval (CI). We simultaneously show the results of unadjusted and minimally adjusted analyses (age, weight, height, and gestational age) and those from fully adjusted analyses (age, weight, height, gestational age, previous CS, gravidity, cervical canal length, and intra-aortic balloon occlusion). Moreover, a sensitivity analysis was performed

Table 2. Intraoperative and postoperative data.

Variables	Total (n = 317)	Q1 (n = 68)	Q2 (n = 70)	Q3 (n = 90)	Q4 (n = 89)	*p*-value
Blood loss (mL), Median (IQR)	611.0 (436.0, 1124.0)	546.0 (412.8, 1009.0)	566.0 (412.0, 1089.0)	573.0 (423.2, 1008.0)	1024.0 (554.0, 1578.0)	<0.001
IABO, n (%)	168 (53.0)	21 (30.9)	40 (57.1)	45 (50)	62 (69.7)	<0.001
Blood transfusion, n (%)	78 (24.6)	11 (16.2)	15 (21.4)	12 (13.3)	40 (44.9)	<0.001
Blood transfusion (Unit), Median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 3.0)	<0.001
Plasma, n (%)	55 (17.4)	4 (5.9)	12 (17.1)	8 (8.9)	31 (34.8)	<0.001
Cryoprecipitate, n (%)	18 (5.7)	1 (1.5)	5 (7.1)	2 (2.2)	10 (11.2)	0.029
Autologous blood collection, n (%)	43 (13.6)	4 (5.9)	9 (12.9)	7 (7.8)	23 (25.8)	<0.001
Postoperative transfusion, n (%)	60 (18.9)	6 (8.8)	18 (25.7)	10 (11.1)	26 (29.2)	<0.001
Uterine gauze stuffing, n (%)	45 (14.2)	6 (8.8)	5 (7.1)	12 (13.3)	22 (24.7)	0.006
Intrauterine balloon tamponade, n (%)	111 (35.0)	28 (41.2)	16 (22.9)	35 (38.9)	32 (36)	0.097
Uterine artery embolization, n (%)	25 (7.9)	2 (2.9)	5 (7.1)	4 (4.4)	14 (15.7)	0.01
Uterine bondage, n (%)	141 (44.5)	25 (36.8)	33 (47.1)	41 (45.6)	42 (47.2)	0.542
Cervical lift suture, n (%)	226 (71.3)	51 (75)	48 (68.6)	59 (65.6)	68 (76.4)	0.349
Triple-P procedure, n (%)	58 (18.3)	8 (11.8)	14 (20)	19 (21.1)	17 (19.1)	0.459
Placenta left *in situ*, n (%)	21 (6.6)	2 (2.9)	2 (2.9)	7 (7.8)	10 (11.2)	0.113
Hysterectomy, n (%)	11 (3.5)	0 (0)	5 (7.1)	1 (1.1)	5 (5.6)	0.028
ICU admission, n (%)	12 (3.8)	0 (0)	4 (5.7)	2 (2.2)	6 (6.7)	0.088
Operation time (min), Median (IQR)	74.0 (53.0, 98.0)	66.0 (50.5, 86.0)	68.5 (55.0, 90.0)	62.5 (48.5, 91.0)	91.0 (69.0, 117.0)	<0.001
Hospitalization time (day), Median	6.0 (5.0, 7.0)	6.0 (4.0, 7.0)	6.0 (5.0, 7.0)	5.0 (4.0, 7.0)	7.0 (5.0, 9.0)	<0.001
Neonatal sex, n (%)						0.259
male	169 (53.3)	39 (57.4)	33 (47.1)	54 (60)	43 (48.3)	
female	148 (46.7)	29 (42.6)	37 (52.9)	36 (40)	46 (51.7)	
Neonatal weight (g), Mean ± SD	2880.9 ± 471.3	2874.9 ± 601.3	2864.5 ± 339.4	3039.9 ± 398.6	2737.6 ± 473.7	<0.001

IABO, Intra-Abdominal Balloon Occlusion; ICU, intensive care unit; IQR, Interquartile range; SD, standard deviation; Q1, the first quartile; Q2, the second quartile; Q3, the third quartile; Q4, the fourth quartile.

to detect trends in the association between PT quartile and massive bleeding risk. A subgroup analysis of the PAS categories was conducted using a stratified logistic regression model. All analyses were performed using R statistical software (R 4.1.2, http://www.R-project.org; the R Foundation) and a free statistics analysis platform.

3. Results

3.1 Patients' Baseline Characteristics

During the study period, 337 patients with suspected PAS with placenta previa underwent cesarean deliveries at the institution. A total of 317 patients were included in the analysis (Fig. 1). Of them, 133 (41.9%) experienced massive intraoperative bleeding. Moreover, 78 (24.6%) required a transfusion of two or more blood product units (fresh-frozen plasma and/or red blood cells), 12 (3.8%) were admitted to the ICU, 11 (3.5%) required a hysterectomy, and 25 (7.9%) underwent angiographic embolization. The baseline clinical and ultrasonic characteristics of the intra-and postoperative indicators are presented in Tables 1,2. Among the PT group, a significant difference was noted in gestational age, cervical canal length, and PAS category. Bleeding, the probability of blood component transfusion, surgical duration, and hospitalization duration differed between the PT groups. A linear association was observed between the likelihood of massive bleeding and PT (Fig. 2).

3.2 Univariate Logistic Regression Analysis

The risk of massive intraoperative bleeding increased proportionally with PT (**Supplementary Table 1**). Univariate analysis indicated that cervical canal length, previous CS, and gestational age were associated with massive intraoperative bleeding.

3.3 Multivariate Logistic Regression and Sensitivity Analysis

In the crude model, PT was associated with high bleeding risk. Moreover, similar results were obtained using the minimally and fully adjusted models. In the sensitivity analysis, PT was a categorical variable (quartile), and the same trend was observed. In the fully adjusted model, a higher PT (Q4) was associated with a 126% increased risk of major bleeding compared to a lower PT (Q1) (OR: 2.26; $p = 0.034$) (Table 3).

Table 3. Relationship between PT and massive bleeding risk in the different models.

Index	Non-adjusted Model		Model I		Model II	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
PT	1.06 (1.03–1.09)	<0.001	1.06 (1.03–1.09)	<0.001	1.04 (1.01–1.07)	0.008
PT quartile						
Q1	1 (Reference)		1 (Reference)		1 (Reference)	
Q2	1.6 (0.79–3.25)	0.193	1.7 (0.83–3.49)	0.149	1.08 (0.49–2.37)	0.843
Q3	1.2 (0.61–2.37)	0.6	1.39 (0.69–2.81)	0.36	0.87 (0.4–1.88)	0.721
Q4	3.88 (1.98–7.62)	<0.001	3.86 (1.95–7.65)	<0.001	2.26 (1.07–4.8)	0.034
p for trend		<0.001		<0.001		0.037

As all Variance Inflation Factor (VIF) values were <5, we confirmed the absence of multicollinearity. PT, placental thickness; OR, odds ratio; CI, confidence interval; CS, Cesarean section; IABO, Intra-Aortic Balloon Occlusion.

Model I: Adjust for age, weight, height, and gestational age;

Model II: Adjust for age, weight, height, and gestational age, previous CS, gravidity, cervical canal length, IABO.

Table 4. Relationship between PT and risk of massive bleeding in different disease categories.

Subgroup	Variable	No. total	No. event (%)	OR (95% CI)	*p*-value	*p* for interaction
No PAS	PT	18.0	0 (0)	1 (0–Inf)	1.0	0.524
Accreta	PT	103.0	5 (4.9)	0.92 (0.79–1.08)	0.312	
Increta	PT	170.0	103 (60.6)	1.03 (1–1.07)	0.091	
Percreta	PT	26.0	25 (96.2)	1.06 (0.83–1.34)	0.655	

PT, placental thickness; OR, odds ratio; CI, confidence interval.

3.4 Results of Subgroup Analyses

Stratified analyses of the association between PT and massive intraoperative bleeding are presented in Table 4. The relationship between PT and massive intraoperative bleeding risk did not differ significantly among the subgroups based on disease category. The effect of PT on massive intraoperative bleeding was stable in all subgroups. The multiplicative interactions among the various groups regarding the risk of massive incident intraoperative bleeding were not significant.

4. Discussion

This retrospective cohort study included 317 patients with suspected PAS and placenta previa and examined the independent association between PT and intraoperative hemorrhage. Our study found that an increasing PT was associated with an increased risk of massive bleeding in patients with PAS placenta previa who underwent CS. We found that PT was significantly increased in patients with massive bleeding. To the best of our knowledge, this is the first study to report the association between PT and massive bleeding in patients with PAS and placenta previa.

Curve fitting revealed that intraoperative bleeding increased as PT increased. The relationship between PT and intraoperative hemorrhage was linear. In the subgroup analyses, the correlation between PT and the risk of major bleeding was not statistically different. This further suggests that the risk of major bleeding is related to the PAS type, with higher PT values predicting a higher PAS grade. When it can be accurately determined preoperatively, PT can assist in determining the risk of intraoperative hemorrhage.

Massive bleeding is the major cause of preventable peripartum mortality. As much as 70–93% of these deaths are deemed preventable [20]. A rapid diagnosis and early multidisciplinary management can improve the maternal prognosis. The early identification of the risk of hemorrhage facilitates appropriate preoperative countermeasures such as cross-matching, establishing extensive venous access, and autologous blood recovery [21,22]. Most cases of massive bleeding during CS are caused by placental abnormalities. These risk factors include maternal history and placental characteristics observed on ultrasonography [23]. The clinical features included maternal age, gestational age <37 weeks, preoperative bleeding, number of prior CS, PAS, a sponge-like appearance of the cervix, grade of lacunae, presence of a hypoechoic layer, depth of the placenta invading the uterine muscle wall, and an anterior placenta. Most of these features are used to diagnose PAS.

However, different PAS scores are associated with different bleeding risks. Wang *et al.* [4] showed that the risk of intraoperative hemorrhage in PAS is associated with the post-placental clear space, cross-border blood vessels in the region of sub-placental vascularity, interruption or disappearance of the bladder line, and presence of the cervical blood sinus. These ultrasound features are specific to some

patients with PAS and not universal. An experienced sonographer may obtain these indicators; however, subjective factors cannot be excluded [13]. When diagnosed with suspected PAS, a more objective indicator for predicting the risk of major bleeding is needed.

Many studies have used PT to predict fetal and maternal health [24,25]. The condition of the placenta can be a predictor of many events that occur in the mother and fetus [26]. Another study demonstrated a correlation between the PT and neonatal weight [27]. Li *et al*. [28] showed a correlation between PT and PAS. A threshold of 4.5 cm can help screen for patients with placenta previa and risk factors for PAS. There was a trend toward an increased PT in patients with different PAS types. PT was significantly greater in the penetrating PAS group than in the other two types. This may be related to an increased number of lacunae in the placenta. When more severe placental implantation occurs, lacunae of varying sizes develop within the placenta, thereby increasing the PT. The proportion of intra-placental lacunae increases with the degree of placental implantation. An increase in PT suggests a significantly higher likelihood of implantation or penetration. The underlying cause of an abnormally thick PT in women with PAS is unclear. However, this may be related to poor vascularization of the lower uterus and cervix as well as placental implantation in the cesarean scar, which limits placental migration [29]. One study showed that antenatally measured PT has a linear correlation with blood loss in patients with PAS [30]. Our study confirmed this finding. An increased PT suggests increased placental implantation and invasion into the myometrium and corresponding vessels. This may affect uterine contractions and complicate surgical hemostasis when the placenta peels off.

This study has some limitations. Moreover, it is limited by factors that limit all retrospective designs such as confounders and selection bias. The study was retrospective; therefore, PT was not measured prospectively. All ultrasound-related metrics were obtained by reviewing the patients ultrasound reports; therefore, some of the ultrasound metrics were not presented in the ultrasound reports, such as intraplacental hypoechogenicity. Therefore, relevant indicators were not included in the regression model, which may have been a confounding factor affecting the final results.

5. Conclusions

In conclusion, an increased PT in the lower uterine segment is associated with intraoperative hemorrhage in patients with PAS and placental previa. Preoperatively, an increased PT can provide an indicator for the assessment of intraoperative bleeding risk. The risk of intraoperative hemorrhage was significantly higher in the higher PT (Q4) than lower PT (Q1) group. A thickened PT seems to be a warning sign of massive bleeding during surgery for PAS with placenta previa.

Availability of Data and Materials

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Author Contributions

FH participated in the design of the study, data collection and analysis, and manuscript drafting. JW and KW designed the study and drafted and revised the manuscript. TY, WW, YX, QLX, QJX, and JZ acquired and interpreted the data and followed the patients. QJX and JZ performed the data analysis and interpretation. All authors have read and approved the final version of the manuscript. All authors contributed to the editorial revision of the manuscript and agreed to take responsibility for all aspects of this work.

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Ethics Committee of First Affiliated Hospital of Chongqing Medical University (approval number: 2021–059). All procedures were performed in accordance with the principles of the Declaration of Helsinki. The Ethics Committee of the First Affiliated Hospital of Chongqing Medical University waived the requirement for informed consent. The medical records used in this study were obtained from previous diagnoses and treatments. Exemption from informed consent will not adversely affect the rights or health of the subjects. The participants' privacy and personal identities were protected.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/j.ceog5102030.

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