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IMAGES IN OBSTETRICS AND GYNECOLOGY

Scoring system for the prediction of the severity of placenta accrete spectrum in women with placenta previa: a prospective observational study

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Abstract

Purpose The clinical outcomes are significantly different in accreta, increta, and percreta. There is currently no scoring system that can preoperatively distinguish its severity in an at-risk population. The aim of this study is to establish a scoring system for the prediction of the severity of placenta accrete spectrum (PAS) in women with placenta previa.

Methods A prospective observational study was conducted in patients with placenta previa who delivered at a Chinese tertiary care center between June 12, 2016 and June 30, 2018. Optimal scaling regression was performed to determine the parameters which really contribute to the prediction of PAS, and calculate percentage of contribution.

Results Among 392 cases with placenta previa, 79, 53, and 28 had been surgically and/or histologically confirmed as accreta, increta, or percreta, respectively. Seven parameters were scheduled for the estimated scores for PAS, and five of them were finally entered into the predictive model. Their percentage of contribution was as follows: placental lacunas (19%), vascularity at the uterus–bladder interface (17.5%), myometrial thickness and hypoechoic retroplacental zone (25.6%), bladder line (22.6%), and previous caesarean sections (15.3%). The thresholds of scores for the prediction of accreta, increta, and percreta yielded 2.25–6.2, 6.2–8.95, and ≧ 8.95, respectively, with the positive and negative predictive value, and false positive rates of the scoring system were 96.68%, 95.44%, and 3.32%, respectively.

Conclusions The scoring system can predict the severity of PAS in women with placenta previa. This will help identify the actual high-risk patients and improve their treatment.

Keywords Scoring system · Placenta accrete spectrum · Placenta previa · Accreta · Increta · Percreta

Introduction

Placenta accrete spectrum(PAS) is classified into accreta, increta, and percreta based upon the depth that villi invades the myometrium [1]; and it constitutes one of the major causes of serious complications, including maternal death. Its incidence has been increasing and it is well known that the incidence is significantly higher in patients with placenta previa. Although many studies have reported that accurate prepartum diagnosis can improve clinical outcomes [2–4], in clinical practice, the actual high-risk patients are those with deep implantation, such as with percreta and increta. A recent study also confirmed that severe morbidity in women with PAS was far higher for those with percreta than with accreta [5]. There is no method currently available that allows prediction of the severity of PAS before surgery, and can distinguish among accreta, increta, and percreta.

Over the past decades, numerous studies have been reported concerning the efficiency of clinical features for predicting PAS in at-risk women. These features usually included previous cesarean sections (CS) [6, 7] and several sonographic signs with an accuracy that varied greatly [1, 8–12]. An increasing number of researchers have found that a single parameter was of limited value in prediction, and have tried to develop a scoring system through a set of clinical features to assess the risk of PAS, with the area under the ROC curve up to 0.87–0.94 [13–17]. The purpose of these

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studies was to assess the relationship between clinical characteristics and the diagnosis of PAS, without distinguishing its detailed severity (accreta, increta, and percreta). However, there are two issues remaining to be addressed: the first one is how to determine the percentage of contribution of each parameter to the entire severity, and the second one is how to predict the severity of PAS. We therefore conducted this prospective study to develop a scoring system by weighing the selected clinical features, and thus to predict the severity of PAS in women with placenta previa.

Methods

Study design and participants

This was a prospective, single-center, observational cohort study with the purpose of predicting severity of PAS, conducted between June 12, 2016 and June 30, 2018. Patients aged 19–44 years who had sonographic confirmation of placenta previa after 28 weeks of gestation were the subjects of this study. We excluded those women who experienced an emergency referral and subsequent surgery due to massive vaginal bleeding without routine ultrasonographic examination in our hospital.

Estimated score scale for PAS

The parameters selected in our study were widely reported to be strongly associated with PAS. In addition to the previous history of cesarean section (CS), ultrasonographic parameters were included: placental lacunas, main uterine wall of placental attachment, vascularity at the uterus–bladder interface, myometrial thickness of the anterior wall and hypoechoic retroplacental zone, bladder line, and cervical length. An estimated scoring for PAS was established by seven parameters mentioned previously (Table 1). Placental lacunas were graded with reference to Finberg's [18] study as follows: level 1, none seen; level 2, 1–3 present, generally round and small, < 2 cm in size; level 3, 4–6 present, generally irregular, 2–4 cm; level 4, irregular lacunas involving major regions of the placenta or present throughout the placenta, ≥ 4 cm. Main uterine wall of placental attachment was graded as follows: level 1, posterior; level 2, lateral; level 2, anterior. Vascularity at the uterus–bladder interface was graded with reference to Adle's [19] study as follows: level 1, minimal or moderate flow, less than 10 vessels (usually less than 1 mm in diameter); level 2, increased flow, more than 10 small vessels and/or several main vessels were visualized; and level 3, interface filled with vessels or presence of bridge vessels. We always found a myometrial thickness < 1 mm after the disappearance of the hypoechoic retroplacental zone, so that they were combined into one parameter. It was graded as follows: level 1, myometrium ≥ 1 mm and zone clear; level 2, myometrium ≥ 1 mm and zone vague or lost; level 3, myometrium < 1 mm and zone lost. Bladder line was graded as follows: level 1, line clear and complete; level 2, line vague or irregular; level 3, line lost. Cervical length was graded as follows: level 1, > 3 cm; level 2, 1–3 cm; level 3, < 1 cm. With respect to myometrial thickness, we measured the thickness of the lower anterior at the horizon of internal cervix in the sagittal plane.

Ultrasonography was performed on Philips IU-Elite imaging machine (Philips Electronics NV, The Netherlands) or GE VOLUSON E8 imaging machine (General Electric Co., USA) equipment using 4–9-MHz transducers. In addition to grayscale imaging and transabdominal ultrasonography, color Doppler and transvaginal ultrasonography were used, especially with respect to vascularity and myometrial thickness. At least two experienced sonographers performed

Table 1 Estimated score scale for PAS

Variable	Level and its score			
	Level 1	Level 2	Level 3	Level 4
	Score = 0	Score = 1	Score = 2	Score = 3
Placental lacunas	None seen	1–3 present, round and < 2 cm	4–6 present, irregular, 2–4 cm	Irregular, ≧ 4 cm
Main uterine wall of placental attachment	Posterior	Lateral	Anterior	
Vascularity in uterus–bladder interface	Minimal or moderate flow	Increased flow	Interface filled with vessels or presence of bridge vessels	
Bladder line	Clear and complete	Line vague or irregular	Line lost	
Cervical length	> 3 cm	1–3 cm	< 1 cm	
Myometrial thickness and hypoechoic retroplacental zone	Myometrium ≧ 1 mm and zone clear	Myometrium ≧ 1 mm and zone vague or lost	Myometrium < 1 mm and zone lost	
Times of previous CS	0	1	2	≧ 3

the ultrasound scans. The last images before delivery were extracted as analysis data from the electronic archiving system. The estimated score scale was the sum of all variables, with the maximum score of 18.

Clinical procedures

As part of our study, the estimated scores of PAS were reported to the surgical team. Those with score of ≧ 4 are considered with a risk of PAS. If a woman shows a score of 4 or higher, it may suggest a high possibility of PAS (Fig. 1). Accordingly, the patient will undergo CS by experienced obstetricians and gynecologic oncologist and with a multidisciplinary team available, including radiologists for pelvic artery embolization. The bladder must be carefully separated away from the uterus before fetal delivery and a temporary occlusion of uterine blood flow by sponge forceps so as to reduce bleeding while removing of placenta and remolding of the uterus (Fig. 2A–D). If a woman shows a score of 3 or lower, it was taken that the probability of PAS is very low. The operation maybe conducted by experienced obstetricians. The gynecologic oncologist and other members of multidisciplinary team were available when needed, but not always involved in. Hysterectomy will be only performed in cases of failed hemostasis after all measures available, such as balloon tamponade, haemostatic sutures, uterine remolding and pelvic artery embolization.

Confirmation of level of PAS was made in all cases by experienced surgeons [15], and/or by histologic evidence in hysterectomy. If the placenta was removed spontaneously, the patient was categorized as without PAS. If the majority of the placenta could be removed manually and the residual placental diameter was less than 1 cm, this was defined as accreta [5]. If the removal required scissors [17], this was defined as increta or percreta. If placenta was found to have invaded the myometrium but not reached to the serosa, this was termed placenta increta; and if it invaded through the myometrium reached to or beyond the serosa, it was termed percreta. Patients were divided into four groups based on the implantation depth: without PAS, accreta, increta, and percreta.

Statistical analysis

All quantitative data were presented as median (interquartile range), and categorical data were presented as frequencies and percentages. Statistical analyses included univariate and multivariate analysis. Kruskal–Wallis test and Chi-square test were used in univariate analysis. The parameters of estimated score scale for PAS were analyzed by univariate analysis first, and were continued for multivariate analysis if these variables show significant difference. The optimal scaling regression model was employed in multivariate analysis to determine the parameters which really contributed to the prediction of PAS, and the percentage of contribution of each parameter to the entire severity. This model quantified the categorical variables and was more likely to avoid the bias caused by predetermined values of parameters. To make the scores easier to use in clinical practice, the levels of PAS and each parameter (including its grades) were then converted to 0–10 scores based on the results of the equation. The scoring system was thereby established. Positive predictive value (PPV), negative predictive value (NPV) and false positive rate were calculated. For statistical analyses we employed SPSS for Windows version 22.0, $p < 0.05$ was considered to be statistically significant.

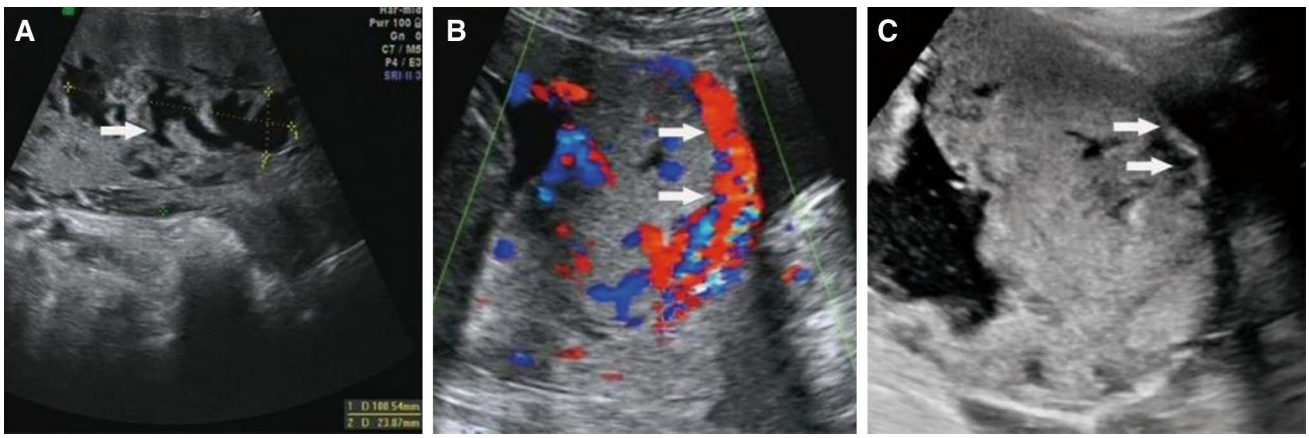

Fig. 1 Ultrasonographic images suggesting placenta accrete. A woman with placenta previa had two previous CS (0.79 point), the most lacuna size ≥ 4 cm (arrow, **a** 2.57 point), the uterus–bladder interface filled with vessels (arrows, **b** 1.99 point), myometrium and hypoechoic retroplacental zone lost (arrows, **c** 2.68 point) and obliteration of bladder line (arrows, **c** 1.58 point). The sum of these point yielded the score of 9.61 which is closest to percreta (> 8.7)

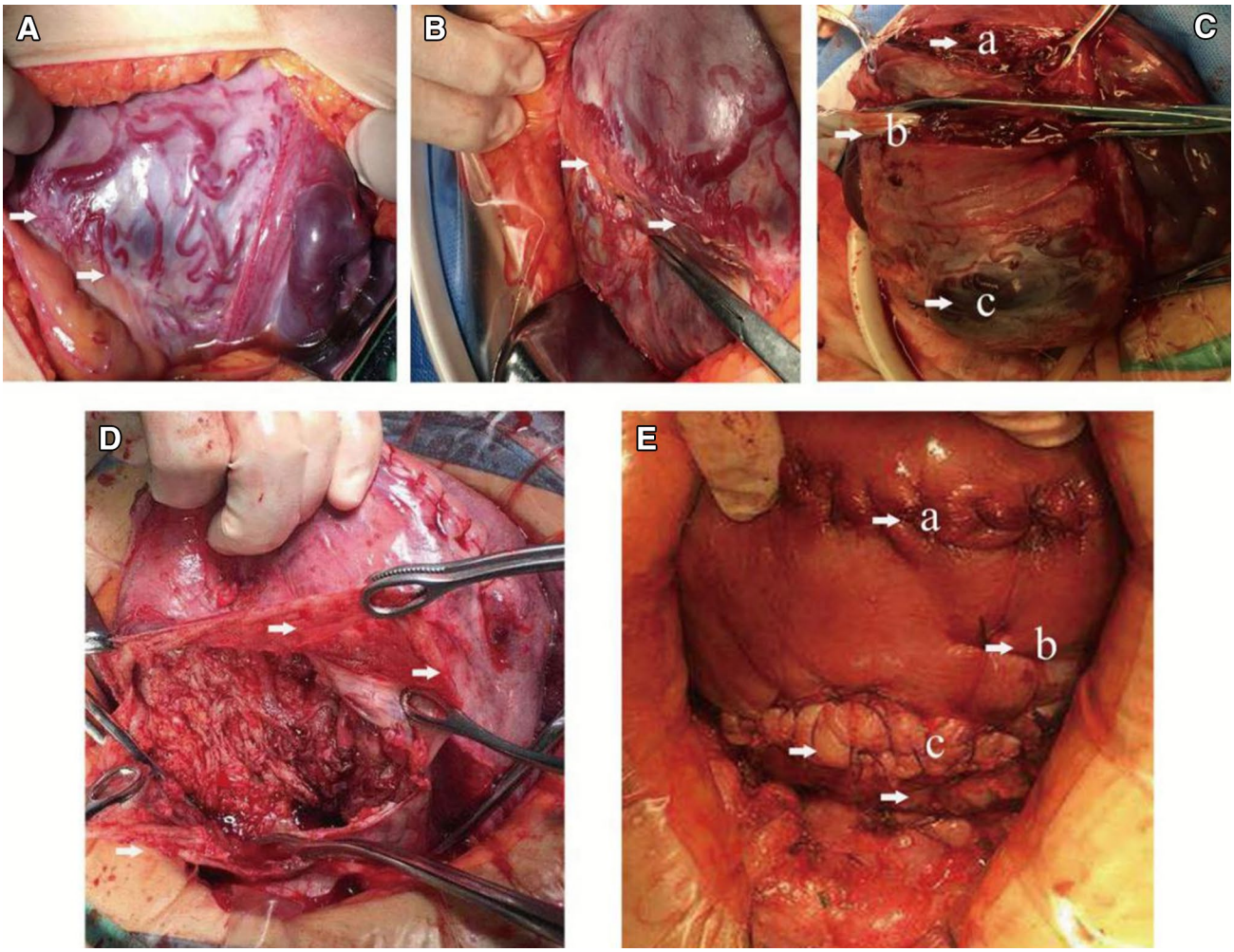

Fig. 2 Surgical procedure of woman with accrete. A woman who antenatally suspected percreta managed to obtain planned cesarean section with the experienced multidisciplinary surgical team. Images showing the vascularity seen between uterine and bladder (**A**). Arrows showing the starting point where the bladder dissected away from the uterus (arrows, **A**, **B**). The blood flow of uterus was blocked by an elastic band (d, **C**) after delivering. Then, a heavy bleeding from uterine incision (a, **C**) and placenta (b, **C**) was avoided, even in a woman with percreta (c, **C** placental invasion reached the serous of uterus). The uterine wall where the placenta invaded into (arrows, **D**) was very thin, after the removal of placenta. Uterus was preserved after uterine reconstruction (a, **E**, uterine incision, b, c, **E** reconstruction)

Results

During the study period, 409 women received a diagnosis of placenta previa out of 9408 deliveries at our center. Seventeen women who received an emergency surgery without routine ultrasonographic examination in our hospital were excluded, and 392 women included in the analysis finally. Table 2 showed the maternal characteristics. According to the clinical findings at the time of surgery and histological examination, 160 (40%) women were diagnosed with placenta accrete spectrum (PAS), including accreta in 79 (20%) cases, increta in 53 (13%) cases, and percreta in 28 (7%) cases. 250 (64%) women have one previous CS and 62 (16%) had two or more previous CS. Maternal age, the number of previous abortions and antenatal vaginal bleeding not differ significantly among the groups. There was a significant difference in gravidity, previous vaginal deliveries, previous CS between the groups.

In the univariate analysis, seven parameters which were possible predictors of PAS were listed in the Table 1. All seven of them showed a significant difference between groups. The results showed in Table 3, $p < 0.01$ for all comparisons.

In the multivariate analysis, two parameters, main uterine wall of placental attachment and cervical length, showed a $p > 0.05$. So they were considered that the value of predicting PAS was limited and therefore did not enter the final optimal scale regression analysis. All the other five variables

Table 2 Maternal characteristics of the groups

Variable	Without PAS ($n=232$)	Accreta ($n=79$)	Increta ($n=53$)	Percreta ($n=28$)	p
Maternal age[a]	31 (7)	30 (7)	32 (6)	32 (6.75)	0.169
Gravidity[a]	4 (3)[d,e]	4 (2)[g]	5 (2)[d]	6 (3)[e,g]	*< 0.01*
Previous vaginal deliveries[a]	1 (1)[c,d]	0 (1)[c]	0 (1)[d]	0 (0)	*< 0.05*
Previous cesarean sections[a]	0 (1)[c,d,e]	1 (0)[c,f,g]	1 (1)[d,f,h]	2 (1)[e,g,h]	*< 0.01*
Previous abortions[a]	2 (2)	2 (2)	2 (2)	2 (2)	0.233
Antenatal vaginal bleeding[b]	93 (57)	37 (23)	19 (12)	15 (9)	0.326

$p < 0.05$ was considered statistically significant (in italics)

[a]Values given as median (interquartile range), Kruskal–Wallis test

[b]Values given as *n* (%), Chi-square test; CS, cesarean section

Significant differences between: [c]without PAS and accreta; [d]without PAS and increta; [e]without PAS and precreta; [f]accreta and increta; [g]accreta and precreta; [h]increta and percreta

Table 3 Possible features related to PAS

Variable	Without PAS	Accreta	Increta	Percreta	p
Placental lacunas					*< 0.01*
1	202 (87.1)	13 (16.5)	3 (5.7)	1 (3.6)	
2	29 (12.5)	34 (43)	8 (15.1)	2 (7.1)	
3	1 (0.4)	28 (35.4)	33 (62.3)	8 (28.6)	
4	0 (0)	4 (5.1)	9 (17)	17 (60.7)	
Main uterine wall of placental attachment					*<0.01*
1	24 (10.3)	4 (5.1)	0 (0)	0 (0)	
2	69 (29.7)	13 (16.5)	0 (0)	0 (0)	
3	139 (59.9)	62 (78.5)	53 (100)	28 (100)	
Vascularity in uterus–bladder interface					*< 0.01*
1	200 (86.2)	14 (17.7)	2 (3.8)	3 (10.7)	
2	32 (13.8)	62 (78.5)	36 (67.9)	19 (67.9)	
3	0 (0)	3 (3.8)	15 (28.3)	6 (21.4)	
Bladder line					*< 0.01*
1	228 (86.7)	25 (9.5)	8 (3)	2 (0.8)	
2	4 (4)	51 (50.5)	34 (33.7)	12 (11.9)	
3	0 (0)	3 (10.7)	11 (39.3)	14 (50)	
Cervical length					*< 0.01*
1	171 (73.7)	42 (53.2)	41 (77.4)	16 (57.1)	
2	25 (10.8)	28 (35.4)	11 (20.8)	9 (32.1)	
3	36 (15.5)	9 (11.4)	1 (1.9)	3 (10.7)	
Myometrial thickness and hypoechoic retroplacental zone					*< 0.01*
1	212 (91.4)	20 (25.3)	6 (11.3)	0 (0)	
2	20 (8.6)	45 (57)	19 (35.8)	1 (3.6)	
3	0 (0)	14 (17.7)	28 (52.8)	27 (96.4)	
Times of previous CS					*< 0.01*
0	128 (55.2)	14 (17.7)	0 (0)	0 (0)	
1	104 (44.8)	58 (73.4)	8 (15.1)	4 (14.3)	
2	0 (0)	7 (8.9)	44 (83)	16 (57.1)	
≧ 3	0 (0)	0 (0)	1 (1.9)	8 (28.6)	

$p < 0.05$ was considered statistically significant (in italics)

Values given as frequency (percentage), Chi-square test

Table 4 Value of each quantified parameter is added together to generate placenta implantation score

Variable	Level of variable	Score		
		Importance of prediction[c] (%)	Calculated values[a]	Converted values[b]
Degree of implantation	Without PAS	100.0	− 0.76	0.00
	Accreta		0.51	4.50
	Increta		1.47	7.90
	Percreta		2.08	10.00
Placental lacunas	1	19.0	− 0.64	0.00
	2		− 0.26	0.22
	3		1.14	1.03
	4		2.63	1.90
Vascularity in uterus–bladder interface	1	17.5	− 0.81	0.00
	2		0.78	0.83
	3		2.55	1.75
Myometrial thickness and loss of hypoechoic retroplacental zone	1	25.6	− 0.69	0.00
	2		0.31	0.95
	3		1.99	2.56
Bladder line	1	22.6	− 0.68	0.00
	2		1.14	1.42
	3		2.23	2.26
Times of previous caesarean section	0	15.3	− 1.10	0.00
	1		0.19	0.51
	2		1.47	1.02
	3		2.76	1.53

[a]The values were calculated by optimal scaling regression

[b]The values of degree of implantation were converted to a 0–10 scale

were significantly associated with PAS ($p < 0.05$). As shown in Table 4, their proportions accounting for PAS risk are presented: placental lacunas accounted for 19%, vascularity at the uterus–bladder interface accounted for 17.5%, myometrial thickness and loss of hypoechoic retroplacental zone accounted for 25.6%, bladder line accounted for 22.6%, and previous CS accounted for 15.3%. We listed the values calculated by the equation and then converted to a ten-point system for clinical application. The cutoff values were 0, 4.5, 7.9, and 10 points are corresponded to the serious of PAS, respectively: without PAS, accreta, increta, and percreta. We assigned a total value of 1.9 points for placental lacunas, and 0, 0.22, 1.03, or 1.9 points for levels 1–4 of PAS, respectively. Vascularity at the uterus–bladder interface was assigned a total value of 1.75 points, and levels 1–3 were assigned 0, 0.83, or 1.75 points, respectively. Myometrial thickness and hypoechoic retroplacental zone were assigned a total value of 2.56 points, and showed the highest value of implantation prediction; levels 1–3 were assigned 0, 0.95, and 2.56 points, respectively. Bladder line was assigned a total value of 2.26 points, and levels 1–3 were assigned 0, 1.42, and 2.26 points, respectively. The number of CS accounted for 15.3% of the entire risk, and the converted predictive values were 0.51, 1.02, and 1.53 points for 1, 2, and 3 previous cesarean sections, respectively. The sum of the points for five variables yielded the predictive score of PAS. A higher score indicates a higher possibility of PAS and a higher possibility of severe PAS. The threshold scores for predicting without PAS, accreta, increta, and percreta were < 2.25, 2.25–6.2, 6.2–8.95, ≧ 8.95, respectively.

Table 5 presented the maternal and neonatal outcomes according to the levels of PAS. Clinical outcomes, including hemostatic strategies, transfusion, duration of surgery, length of hospital stay and neonatal 1- and 5-min Apgar score, are provided. There was no significant difference in length of hospital stay and neonatal Apgar score among the levels. All the other outcomes were significantly different among the levels. The rate of using of balloon tamponade, uterine artery embolization increased with the severity of PAS. All patients with increta and percreta underwent haemostatic sutures or uterine remolding. The surgery time in patients with increta and percreta is significantly increased. Patients with percreta had a large amount of intraoperative blood loss and blood transfusion than other levels. No woman died and only one patient underwent hysterectomy throughout the study period, who suffered placenta percreta.

As shown in Table 6, using the threshold scores, this scoring system yielded high positive predictive value (PPV

Table 5 Maternal and neonatal outcomes

Variable	Without PAS ($n=232$)	Accreta ($n=79$)	Increta ($n=53$)	Percreta ($n=28$)	p
Balloon tamponade[b]	170 (73.3)[d,e]	63 (79.7)[g]	48 (90.6)[d]	28 (100)[e,g]	*<0.01*
Uterine artery embolization[b]	24 (10.3)[c,d,e]	23 (29.1)[c]	15 (28.3)[d]	16 (57.1)[e]	*<0.01*
Haemostatic sutures or uterine remolding[b]	20 (8.6)[c,d,e]	34 (43)[c,f,g]	53 (100)[d,f]	28 (100)[e,g]	*<0.01*
Duration of surgery (min)[a]	65 (25)[c,d,e]	85 (55)[d,g]	95 (30)[d]	130 (77)[e,g]	*<0.01*
Intraoperative bleeding (ml)[a]	800 (550)[c,e]	1000 (800)[c]	1000 (1000)	1850 (950)[e]	*<0.01*
Transfusion (ml, included autologous blood)[a]	257 (650)[c,d,e]	650 (800)[c]	800 (703)[d]	1049 (1046)[e]	*<0.01*
Hysterectomy[b]	0 (0)	0 (0)	0 (0)	1 (3.5)	*<0.01*
Length of hospital stay (day)[a]	5 (1)	5 (1)	5 (1)	5 (1)	0.303
Apgar score[a]					
1 min	10 (2.75)	10 (2)	10 (1)	10 (1)	0.855
5 min	10 (2)	10 (1)	10 (0)	10 (1)	0.695

[a]Values given as median (interquartile range), Kruskal–Wallis test

[b]Values given as *n* (%), Chi-square test

Significant differences between: [c]without accreta and accreta; [d]without accreta and increta; [e]without accreta and percreta; [f]accreta and increta; [g]accreta and precreta; [h]increta and percreta

Table 6 Scoring thresholds and predictive values of scoring system

	Without PAS	Accreta	Increta	Percreta	Total
Thresholds of scores	<2.25	2.25–6.20	6.20–8.95	≥8.95	
PPV (%)	95.44	80.26	75.47	81.81	96.68
NPV (%)	98.68	94.30	96.17	97.30	95.44
False positive rates (%)	4.56	19.74	24.53	18.19	3.32

PPV positive predictive values, *NPV* negative predictive values

95.44% and 81.81%) for without PAS and percreta, and moderate (80.26% and 75.47%) for accreta and increta. Also, the system got a high negative predictive value (NPV = 5.44%) and a low false positive rates = 3.32%. Without PAS have showed a very low false positive rates of 4.56%.

Discussion

As one of the major tertiary referral centers in our province, many women who are suspected PAS are referred to our center which resulted in a higher rate of PAS in our institution. It is imperative to improve the diagnostic accuracy for improving clinical outcomes. To our knowledge, this is the first study that described a scoring system based on several clinical parameters for risk assessment of the severity of PAS. Women without PAS accounted for 95.44% of the low-score group (a score of <2.25), and in the high-score group (8.95–10), 81.81% patients were confirmed as percreta. In the moderate-score group (2.25–6.2 and 6.2–8.95), women who were confirmed as accreta and increta accounted for 80.26%, 75.47%, respectively. We herein demonstrated that women with placenta percreta and without PAS can be distinguished prepartumly from those who were increta and accreta.

There are limited reports in the literature of scoring systems for risk assessment of PAS. Our search yielded five articles [13–17], including two retrospective studies and three prospective studies in the last 5 years. These studies included women who were at risk of PAS, and their scoring systems were developed using several clinical features that were well recognized and of high predictive value with respect to PAS. In our study, the estimated scores for PAS (Table 1) were also established with reference to the studies mentioned previously. However, the aims of these studies were to predict the possibility of implantation without distinguishing the detailed severity of PAS.

A number of studies have reported that previous CS were significantly correlated with PAS, and the risk increased with increased number of CS [20, 21]. A multicenter observational study found that the incidence of placental implantation after the first, second, third, fourth, and fifth or more repeated cesarean deliveries was 0.24, 0.31, 0.57, 2.13, 2.33, and 6.74%, respectively [7]. We then adopted the number of CS as a parameter rather than an enrollment criterion in our study. Our results showed that not only the possibility but also the degree of PAS, increased with increasing CS.

In addition to the previous CS, ultrasonography with color Doppler and grayscale images is the widely acknowledged first-line modality for diagnosing invasive placenta [13, 15–17]. Therefore, color Doppler and grayscale images were both adopted for our study. Taken together with lack of widespread availability, and lack of radiologists with expertise and the costs in using to diagnose PAS, our study did not choose MRI as one of the parameters.

How to weigh each parameter and its levels remains a key event in developing a scoring system. Logistic regression model was used to weigh each parameter and ROC analysis to determine the cutoff values [13, 14], or weighting of parameter and cutoff values were predetermined [15–17]. The summation of all the values for each parameter then yielded the score. In contrast, we employed an optimal scaling regression to weigh the contribution of each parameter toward implantation, assigned a score for each parameter and its different levels mathematically. Since we found that the distances between parameters and their different levels were not exactly equal, this may present an alternative strategy that reflects their contributions to PAS.

Limitations of our study included, first, that it was a single-center study, although it entailed a large sample size and was a prospective study. Second, other risk factors for placental implantation were not included, such as prior fibroids, or endometrial or cervical surgeries. Third, the inclusion criteria were placenta previa patients, and we are not certain that the study would be appropriate for non-placenta previa patients. Last, we tested the accuracy of the predictive model based on the sample that was used to develop it. This may have led to overly optimistic predictions. Future research is therefore needed to validate the predictive model in independent samples.

In conclusion, a scoring system based on ultrasonographic findings and number of CS can be employed to identify the severity of PAS for women with placenta previa. This will help clinicians with counseling and scheduling deliveries in a more targeted fashion, and avoid the unnecessary waste of medical resources with the premise of improving clinical outcomes.

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Author contributions ZQC: project development and manuscript editing. LL and QLS: data collection and manuscript writing. DMY, XHW, PY, and YY: data analysis.

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Compliance with ethical standards

Conflict of interest We declare that we have no conflict of interest.

Ethical approval This study was reviewed prior to data collection and approved by the Institutional Review Board at Xinqiao Hospital of Third Military Medical University, no. 20160228-1, dated 12 June 2016; and was registered with the Chinese Clinical Trials Registry, URL: https://www.chictr.org.cn/index.aspx, number ChiCTR-OOC-16008372. All patients signed informed consent upon admission to obtain their blood or tissue specimens and hospital data for analysis and publication. (The Second Clinical Medical College of Army Medical University was renamed from the Xinqiao Hospital of Third Military Medical University in 2018.)

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