



# Peak Systolic Velocity of Subplacental Blood flow as Prenatal Diagnosis of Placenta Accreta Spectrum in Patients With Anterior Placenta Previa

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## Abstract

**Objectives:** Placenta accreta spectrum (PAS) is a serious complication of pregnancy with maternal and fetal morbidity and mortality. Ultrasonography is a useful application in the prenatal diagnosis of PAS disorders. The main scope of this study was to assess the peak systolic velocity (PSV) of subplacental blood flow and its correlation with the clinical description of PAS disorders.

**Materials and Methods:** In this cross-sectional study, 60 pregnant women with persistent anterior placenta previa in the third trimester of pregnancy were examined by color Doppler and grayscale ultrasonography for the diagnosis of PAS disorders. The PSV and resistive index (RI) of the subplacental blood flow were measured by spectrum Doppler in the anterior wall of the inferior uterine segment. Eventually, the patients were followed up until delivery and the correlation between PSV, RI, and PAS disorders was assessed post-surgery.

**Results:** A total of 26 (43.3%) out of 60 patients was diagnosed with PAS disorders. In cases with PAS disorders, the PSV of the subplacental blood flow was significantly higher (AUC = 0.94, 95% CI = 0.89-1.00) compared to the not affected ones. In addition, the PSV of  $\geq 43.65$  cm/sec with 100% specificity was determined as the optimal cut-off for the prenatal diagnosis of PAS disorders. Finally, the RI of subplacental blood flow showed no significant difference between the two groups (AUC = 0.551, 95% CI = 0.398-0.705).

**Conclusions:** Overall, the measurement of the PSV of the subplacental blood flow in patients with anterior placenta previa can increase the accuracy of the ultrasound diagnosis of PAS disorders.

**Keywords:** Placenta accrete spectrum disorders, Peak systolic velocity, Resistive index

## Introduction

Placenta accreta spectrum (PAS) disorder, as a general term, is attributed to the abnormal invasion of the placenta into the uterus. It is classified into placenta accreta, increta, and percreta due to the depth of the trophoblastic invasion into the uterine myometrium. In addition, PAS disorders are assumed as the serious complications of pregnancy with life-threatening morbidities such as severe hemorrhage, massive blood transfusion, hysterectomy, preterm labor, and either maternal or neonatal mortality (1-4). According to some studies (5-7), placenta previa is the most important risk factor for PAS disorders in patients with a previous cesarean section (CS). In recent decades, the frequency of PAS disorders is markedly elevating due to the increasing rate of cesarean delivery (8). Prenatal screening and PAS diagnosis are considered useful for consulting with patients and their families about abnormal placental adhesion and probable morbidities. Hence, the morbidity and mortality of affected patients can be reduced by providing a scheduled pregnancy termination in a tertiary center (2,9).

Color Doppler ultrasonography (US) and B-mode grayscale US are the primary prenatal diagnostic tools of PAS disorders. The sensitivity of color Doppler and the grayscale US in the detection of placenta accreta, increta, and percreta were 90.6%, 93%, and 81.3%, respectively. Concomitantly, the specificity was 97.1%, 98.4%, and 98.9%, respectively (10). Previously, the specific value of US in the prenatal diagnostic of PAS disorders was around 90% (5,11-14).

The pathogenesis of PAS disorders is mostly attributed to the insufficient decidualization, the abnormal invasion of trophoblastic cells into the myometrium, and the remodeling defect of maternal vessels in the previous uterine scar region (13,15,16). The neovascularization and abnormal vasodilation of the placental bed are considered as the characteristic features of PAS disorders (4,17). In cases with PAS disorders, the proliferation of large vessels and an increase in the number of vessels can result in excessive uteroplacental circulation and abnormal placental blood flow. Given that the unusual uteroplacental vasculature can represent high peak



systolic velocity (PSV) and low resistive index (RI) in the spectrum Doppler (18,19), it can be detected by the color Doppler US (14,20). Although histopathological findings post-surgery are the gold standard in the diagnosis of PAS disorders, there are some interfering factors as follows (8).

In some cases, the fibers of the myometrium appear in the normal placenta as well. In many cases, the pathological diagnosis of placenta percreta is impossible as a result of thin and disappearing myometrial tissues. Consequently, the clinical description is vital for the diagnosis of PAS disorders in many cases (8). Considering the above-mentioned explanations, the aim of this study was to measure PSV and RI in subplacental arteries by spectrum Doppler US regarding increasing the diagnostic accuracy of PAS disorders (18,20,21).

### Materials and Methods

The present cross-sectional study was performed on 60 pregnant women with anterior placenta previa or low-lying placenta (less than 2 cm distance between placental edge and internal os) in the third trimester of pregnancy ( $\geq 28$  weeks), who referred to the maternity unit of Al-Zahra hospital of Tabriz University of Medical Sciences from September 2018 to October 2019. Demographic data were gathered, including maternal age, parity, the number of previous CS, and the like.

### Inclusion Criteria

- Pregnant women with consistent anterior placenta previa or low-lying placenta in the third trimester of pregnancy ( $\geq 28$  weeks);
- Willingness to participate in the study.

### Exclusion Criteria

- Maternal hypertension (all types),
- overt diabetes mellitus,
- intrauterine growth retardation,
- autoimmune disease,
- unwillingness to participate in the study.

### Procedure

A transabdominal ultrasound was initially utilized to confirm placenta previa. In addition, cases with low-lying placenta suspicion were examined by transvaginal ultrasound to evaluate the distance between the placental edge and internal os. Two fellowships in Maternal-Fetal Medicine diagnosed PAS disorders utilizing color Doppler and B-mode grayscale transabdominal ultrasound (a Philips ultrasound device, Affinity 70, USA; equipped with 2-6 MHTZ transducer). The ultrasound criteria of PAS disorders were considered in the B-mode grayscale ultrasound examination as follows (10,18,20,22-28):

- Abnormal placental lacunae (multiple irregular hypochoic spaces within the placenta);
- Loss of a clear zone (the loss of the retroplacental

complex between the placenta and myometrium);

- Myometrial thinning (the thinning of myometrium in the retro placental area  $< 1$  mm);
- Bladder wall interruption (the loss or interruption of the bright bladder wall);
- Placental bulge (the abnormal protrusion of placental tissue into the bladder);
- The color Doppler ultrasound was further applied to detect the following criteria (14,19,28);
- Subplacental or uterovesical hypervascularity (hypervascularity observed in the subplacental area/ between the myometrium and the bladder);
- Bridging vessels (vessels that extend from the placenta into the bladder).

At the inferior uterine segment, the PSV and RI of the blood flow in the several points of subplacental clear vessels were measured by the spectrum Doppler (the angle of insonation  $< 15^\circ$ , sample volume = 2 mm). The maximum PSV was reported as well. The RI of the uterine artery on each side was estimated by placing the sample volume in one centimeter downstream of the cross between the uterine and external iliac arteries. In addition, the average bilateral RIs was recorded to find any probable correlation between the PSV and RI of the subplacental blood flow in cases with PAS disorders (29). Further, patients with no symptoms were followed weekly until delivery and those with vaginal bleeding or labor pain were admitted to our hospital. Furthermore, pregnancy was terminated at 34-35 weeks + 6 days in asymptomatic patients who were diagnosed as PAS disorders. In cases with placenta previa and no signs of PAS disorders, pregnancy termination was scheduled at 36-37 weeks + 6 days. Moreover, patients were categorized into cases with and without PAS disorders post-surgery. The surgical team was not informed about PSV results. Finally, the diagnosis was performed based on clinical and histopathological evidence provided by the surgical team or in hysterectomy cases, respectively.

### Statistical Analysis

Values were summarized as mean  $\pm$  SD or median (IQR), as well as frequency and percentages for continuous and categorical variables, respectively. Categorical variables were compared using the  $K^2$  test or Fisher exact test, as appropriate. Moreover, the Kolmogorov-Smirnov test was used to examine the normality of data distribution. A receiver operating characteristic curve analysis was also performed using a Youden index to determine the optimal cut-off point of the maximum PSV for predicting PAS. All participant's data were used to calculate positive and negative predictive values for the test. Eventually, Pearson's correlation analysis was utilized to assess the correlation between the mean RI of the subplacental blood flow. SPSS, version 25 (SPSS Inc., Chicago, IL) was used for all statistical analyses and  $P < 0.05$  were considered statistically significant.

## Results

Eighty patients with anterior placenta previa or low-lying placenta were enrolled in this experiment although 13 and 7 patients were excluded because of not meeting the inclusion criteria and delivery in other centers, respectively. In general, 26 (43.3%) out of 60 patients undergoing a cesarean section (CS) in our hospital were confirmed to have PAS disorders. The details of diagnosis include accreta ( $n=8$ , 30.7%), increta ( $n=14$ , 53.8%), and percreta ( $n=4$ , 15.3%). The diagnosis was confirmed based on either the clinical evidence provided by the surgical team or histopathological evidence in the cases with hysterectomy. The demographic information of patients with and without PAS disorders is summarized in Table 1. At the time of ultrasound examination, the median gestational age of patients without PAS disorders, accreta, increta, and percreta were 34 (IQR=32.1-34.8), 35 (IQR=34.2-35.8), 32.2 (IQR=30.8-34.3), and 34.5 (IQR=30.7-37.2) weeks, respectively. At the time of pregnancy termination, the median gestational age of patients without PAS disorders, accreta, increta, and percreta were also 34 (IQR=32-34), 35 (IQR=34-35), 33 (IQR=31-34), and 34 (IQR=30-36) weeks, respectively. It should be mentioned that the gestational age of cases with PAS disorders was lower compared to not affected patients at the time of pregnancy termination ( $P=0.013$ ). In the demographic criteria, the maternal age did not differ significantly in the two groups ( $P=0.628$ ). In this study, 83.3% of cases with placenta previa had previous CS and the rate of CS in patients with and without PAS disorders did not differ significantly ( $P=0.819$ ). Additionally, the rate of vaginal bleeding in the third trimester was higher in cases with PAS disorders compared to not affected cases ( $P=0.036$ ).

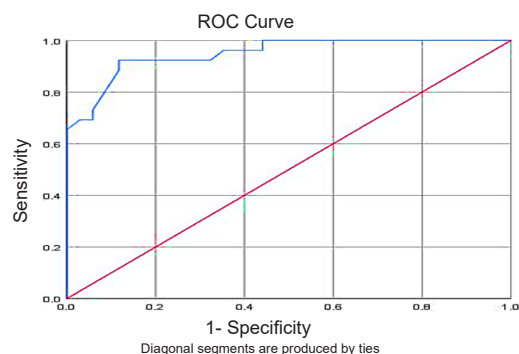
The details of pregnancy termination in cases with PAS disorders are non-separated placenta and hemorrhage in 12 cases (46.1% of PAS) that resulted in the hysterectomy. By pathological examinations, percreta and increta were diagnosed in 4 and 8 cases. In addition, several techniques such as the local excision of the uterus wall at the site of placenta penetration, the ligation of uterine and utero-

ovarian arteries, hypogastric artery, and intrauterine packing were performed in 6 cases with placenta increta (23% of PAS). Further, the hemorrhage of 8 patients with placenta accreta (30.7% of PAS) was controlled by suturing the bleeding area and placing an intrauterine pack.

The PSV analysis of the subplacental blood flow in cases with and without PAS disorders was described with receiver operating characteristic curve (ROC) curve (Figure 1). There was a significant association between the maximum PSV of the subplacental blood flow and the diagnosis of PAS disorders (AUC=0.94, 95% CI=0.89-1.00).

By applying the Youden index for estimating the optimal cut-off of PSV, the velocity of 43.65 cm/s was estimated optimal for the diagnosis of PAS disorders. Furthermore, the maximum PSV  $\geq 43.65$  cm/s had 100% specificity and 72% sensitivity in the diagnosis of PAS disorders. Additionally, positive and negative predictive values were estimated at 94.7% and 80.5%, respectively. The details of measured PSV in patients with and without PAS disorders are presented in Table 2. According to the Youden index, the maximum PSV of the subplacental blood flow  $\leq 32.3$  cm/s has 100% sensitivity and 52.9% specificity (the state of highest specificity) for ruling out PAS disorders.

The ROC curve analysis of RI of the subplacental blood



**Figure 1.** ROC Curve for Predicting PAS Disorders Based on the Maximum Peak Systolic Velocity of Subplacental Blood Flow. Note. PAS: Placenta accrete spectrum; CI: Confidence interval; PSV: Peak systolic velocity; AUC: Area under curve (AUC = 0.94, 95% CI: 0.89–1.00).

**Table 1.** Demographic Information of Patients With and Without PAS Disorders

Criteria	Patients		P Value
	With PAS Disorder	Without PAS Disorder	
Maternal age (y)	33.8±4.6	33.2±5.2	0.628*
Parity status, No. (%)	Para = 0	1 (3.8%)	2 (5.8%)
	Para = 1	11 (42.3%)	20 (58.8%)
	Para $\geq 2$	14 (53.8%)	12 (35.2%)
Previous CS, No. (%)	0	4 (15.4%)	6 (17.6%)
	1	14 (53.8%)	17 (50%)
	$\geq 2$	8 (30.7%)	11 (32.3%)
Vaginal bleeding	17 (65.4%)	12 (35.3%)	0.036**
Pregnancy termination (wk)	34.9 (34.2-36.7)	36.5 (35.9-37)	0.013***

PAS: placenta accreta spectrum; CS: cesarean section.

\* D'Agostino's K<sup>2</sup> test,  $P<0.05$ ; \*\* Fisher exact test,  $P<0.01$ ; \*\*\* Mann-Whitney U test,  $P<0.001$ .

**Table 2.** The Maximum PSV of Subplacental Blood Flow in Patients With and Without PAS Disorders

PSV (cm/s)	Patients With PAS Disorders			Patients Without PAS Disorder n=34 (%)
	Percreta n=4 (%)	Increta n=14 (%)	Accreta n=8 (%)	
≥43.65	4 (100%)	12 (85.7%)	2 (25%)	0
<43.65	0	2 (14.3%)	6 (75%)	34 (100%)

PAS: Placenta accrete spectrum; PSV: Peak systolic velocity.

flow in cases with and without PAS disorders showed that this criterion (AUC = 0.551 and 95% CI = 0.398-0.705) had no diagnostic value in PAS disorders (Figure 2).

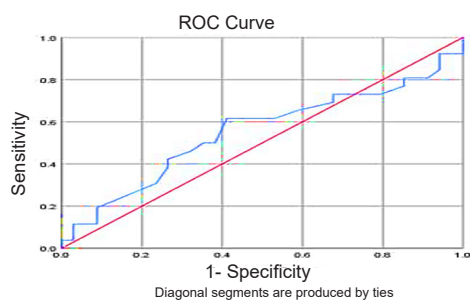
In patients with PAS disorders, there was no significant correlation between the averages of RI measured in bilateral uterine arteries and the RI of the subplacental blood flow ( $P=0.509$ ). Moreover, no significant correlation was achieved between the averages of RI measured in bilateral uterine arteries and the maximum PSV of the subplacental blood flow ( $P=0.082$ ). Grayscale and color Doppler findings for the diagnosis of PAS disorders are listed in Table 3.

## Discussion

Ultrasound is a useful tool in the prenatal diagnosis of PAS disorders. The importance of PAS disorders and their timely diagnosis regarding reducing maternal and neonatal morbidity and mortality pave the way for increasing the

specificity of diagnosis by pinpointing accurate criteria. Accordingly, hysterectomy and unnecessary prophylactic measures can be hampered by preventing the overdiagnosis and the incidence of iatrogenic preterm labor.

In the present study, 83.3% of cases with placenta previa had previous CS and the rate of CS in patients with and without PAS disorders did not differ significantly. A higher rate of third trimester vaginal bleeding in cases with PAS disorders compared to not affected ones can be essentially assumed as a symptom with the prognostic value in PAS disorders. In addition, the lower median of gestational age in cases with PAS disorders compared to not affected ones is related to either earlier elective or emergency pregnancy termination in most cases with vaginal bleeding or labor pain. Further, the frequency of PAS disorders in cases with placenta previa was as high as 43.3% (31%, 54%, and 15% for accrete, increta, and percreta, respectively). A comprehensive review study (1) announced 0.17% as the total prevalence of PAS disorders (63%, 15%, and 22% for accrete, increta, and percreta, respectively). Regardless of the higher prevalence of accreta rather increta, the higher percentage of increta cases in our study can be attributed to the higher CS in the enrolled patients compared to the general population. Similar to previous experiments, the percentage of hysterectomy in cases with PAS disorder was 46.1% (21,30). In cases with abnormal placenta penetration, the velocity of the subplacental blood flow at the inferior uterine segment was higher than those with the normal placenta. Similarly, the increased velocity of the subplacental blood flow robust the probability of placenta penetration into myometrium. The PSVs  $\geq 43.65$  cm/s were measured in 100%, 85.7%, and 25% of cases



**Figure 2.** ROC Curve for Predicting PAS Disorders Based on the RI of Subplacental Blood Flow.

Note. PAS: Placenta accrete spectrum; CI: Confidence interval; RI: Resistive index (AUC = 0.551, 95% CI = 0.398-0.705).

**Table 3.** Ultrasound Findings in Patients With and Without PAS Disorders

Ultrasound sign <sup>a</sup>	Patients (n)		Sensitivity (%)	Specificity (%)	AUC	95% CI
	With PAS Disorders	Without PAS Disorders				
Abnormal lacunae	19	5	73.1	85.3	0.792	0.669-0.914
Loss of clear zone	18	1	69.2	97.1	0.83	0.751-0.947
Myometrial thinning	17	1	65.4	97.1	0.812	0.691-0.933
Bladder wall interruption	10	1	38.5	97.1	0.678	0.534-0.821
Bridging vessels	10	1	38.5	97.1	0.678	0.534-0.821
Uterovesical hypervascularity	22	7	84.6	79.4	0.820	0.707-0.933
PSV $\geq 43.65$	18	0	72	100	0.949	0.898-1.00

PAS: Placenta accrete spectrum; PSV: Peak systolic velocity; AUC: Area under curve; CI: Confidence interval.

<sup>a</sup> Ultrasound findings were presented as observation or lack of observation (yes/no). Sensitivity and specificity were calculated to yes/no findings of ultrasound criteria.



with placenta percreta, increta, and increta, respectively. The PSV of subplacental blood flow never transcended 43.65 cm/s in cases with normal placenta penetration. Hence, PSV  $\geq 43.65$  cm/s with 100% specificity and 72% sensitivity can be assumed as a worthwhile criterion in diagnosing and scaling the placenta invasion into the myometrium. Therefore, preoperative planning can be scheduled based on the ultrasound diagnosis in order to reduce the complications. The abnormal placenta penetration was diagnosed only in 8 cases with PSV  $< 43.65$  cm/s. Furthermore, placenta increta was diagnosed in 2 cases and the other 6 cases were affected by placenta accreta. It should be noted that the PSV of the subplacental blood flow decreased below 43.65 cm/s in none of the cases with placenta percreta. In a study on cases with anterior placenta previa, Zhang et al showed that the subplacental peak blood velocity of  $\geq 41$  cm/s had 87% sensitivity and 78% specificity in the diagnosis of placenta abnormal penetration (18). In this study, PAS disorders were diagnosed in no cases with PSV  $\leq 32.35$  cm/s thus, it can be assumed as an excluding marker for placental invasion. The RI of the subplacental blood flow did not significantly differ in groups with and without PAS disorders.

Among other ultrasound markers, utero-vesical hypervascularity was the solo marker with the highest sensitivity (84.6%). All four bridging vessels, bladder wall interruption, the loss of the clear zone, and myometrial thinning markers ranked equally in the specificity (97.1%). In previous studies, the highest sensitivity in the diagnosis of accreta and increta was attributed to myometrial thinning. In the diagnosis of percreta, utero-vesical hypervascularity and the loss of the clear zone showed the highest sensitivity. Moreover, the exophytic focal mass in cases with percreta and bladder wall interruption in cases with accreta and increta achieved the highest specificity (10). Although it was previously reported that the average of RI in uterine arteries of cases with PAS disorder was lower than non-affected ones (31), no correlation was observed between the average RI of uterine arteries and neither the RI or PSV of the subplacental blood flow in patients with a PAS disorder. Accordingly, further research with a higher sample volume is needed to evaluate such a correlation.

### Conclusions

In general, the spectrum Doppler by providing complementary data can increase the ultrasound accuracy in detecting PAS disorders. In patients with placenta previa, the measurement of PSV of the subplacental blood flow can increase the diagnostic accuracy of PAS disorders.

### Conflict of Interests

Authors declare that they have no conflict of interests.

### Ethical Issues

The Ethical Committee of Tabriz University of Medical Sciences approved the experiment (IR.TBZMED.REC.1398.372). According to written consent, all included patients were informed about the procedure of ultrasonography.

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