Can IVIM MRI be used to differentiate patients with placenta accreta spectrum disorders?

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Abstract

Objective The primary aim was to investigate whether the parameters from IVIM can be used to differentiate patients with PAS disorders complicating placenta previa. A second aim was to determine whether these parameters can be used to differentiate different categories of PAS disorders complicating placenta previa.

Methods All the patients had placenta previa, including 16 patients with placenta accreta, 51 patients with increta, 8 patients with percreta and 24 patients without PAS disorders between 28+0 and 39+6 weeks. All women underwent MRI examination including an IVIM sequence at 1.5T scanner. The perfusion fraction(f), pseudodiffusion coefficient (D*) and standard diffusion coefficient(D) were calculated.

Results Women with PAS disorders had a higher perfusion fraction ($P<0.05$) than women without the disease. Multiple comparisons showed perfusion fraction in patients without PAS disorders was significantly lower than in patients with placenta accreta and percreta($P<0.05$), but was not lower than in patients with increta($p>0.05$). Conclusion Patients with placenta accreta and percreta differ in placental perfusion fraction from women with increta and without PAS disorders. The perfusion fraction can be used as a reliable index to evaluate placenta perfusion fraction.

Background

The term placenta accreta spectrum disorders adopted by FIGO refer to a spectrum disorders including both abdominal adherence (placenta accreta) and abnormal invasion (placenta increta and percreta). The incidence of PAS disorders increased rapidly in recent years. Placenta previa and previous cesarean section represent the two major risk factors for PAS disorders. Recent cohort studies have shown that maternal mortality and morbidity are reduced when women with PAS disorders managed by multidisciplinary care team.

MRI sensitivity and specificity in diagnosing PAS disorders varied between 75–100% and 65–100% respectively [1]. The diagnostic value of MRI highly depends on observer's experience. IVIM offers a quantitative and objective technique to measure maternal placental perfusion and no contrast agent is used. Prenatal assessment of placental perfusion would be of considerable value for the diagnosis of PAS disorders and allows for delivery planning in an attempt to reduce delivery complications and predict clinical outcome.

IVIM has been widely applied recently mainly for the liver, pancreas, kidney and prostate analysis[2–7]. The placenta is a highly vascularized organ containing a high blood fraction and a large perfusion component, so it is appropriate for evaluation with IVIM. In a few small previous studies, placenta perfusion in normal pregnancy, pregnancies affected by intrauterine growth restriction and preeclampsia-complicated pregnancies, IVIM was adopted. [8–10].

In a preliminary study, we found a decreased perfusion fraction in women with placenta accreta and increta [11]. But we did not include patients with placenta percreta nor explored the diagnostic value of the perfusion fraction. The aim of this study was to investigate whether the parameters from IVIM could be used to differentiate patients with PAS disorders complicating placenta previa and the second aim was to determine whether these parameters can be used to differentiate different categories of PAS disorders complicating placenta previa.

Methods

The ethical review aboard of our hospital approved the study and informed consent was obtained from each woman participating in the study. Between Jan 2016 and Oct 2018, 206 gravid patients in the third trimester of pregnancy were referred for prenatal MRI, dedicated to placental evaluation; all patients were at risk for underlying PAS disorders due to the presence of placenta previa (n = 187), with(n = 137) or without(n = 50) suspicious imaging findings on routine second trimester sonographic examination. Only single pregnancy with a living fetus and a gestation length between 28+0 and 39+6 weeks were included. Women with chronic hypertensions, pre-existing renal disease, diabetes mellitus (n = 11) were excluded. Women with inadequate surgical records (n = 75) or severe artifact(n = 2) were also excluded. 99 patients completed the MR examination and formed our study group. The specific tomography of placental invasion was established in the operating room according to clinical and anatomical criterion. The final degree of placental invasion was established either by placental villi alterations from placental sample or from maternity records of the women's general practitioners. For patients who had total or subtotal hysterectomy, histologic criteria for PAS were based on chorionic villi attachment to the myometrium. Placenta accreta was defined as the placenta adhered firmly to the endometrium without invasion and showed non-self-controlled bleeding when detached, placenta increta was defined as the placenta deeply implanted in the myometrium and required curettage to remove invasive tissue, placenta percreta was defined as the placenta villi penetrated through the uterine serosa or the surrounding anatomical structures.

Imaging techniques

MR imaging was performed on a 1.5T scanner (Magnetom Area, Siemens, Erlanger, Germany) using the integrated whole-body transmit-receive coil. IVIM sequence with 8 different b-values (0,50,100,150,200,250,500,800s/m^2)was obtained perpendicular to the placenta. 40 slices, each of 5.5mm thickness were collected. The matrix was 192×120, and the FOV was 390×304mm. Acquisition time for this sequence was typically 8 minutes and 37 seconds.

Region of interest

Evaluation of the IVIM sequence was performed with research software (MITK diffusion). Two independent blinded observers, with 3 and 10 years of experience in obstetric imaging, respectively, carried out the measurement of IVIM. In patients without PAS disorders, ROIs were placed in the middle

part of the placenta including as large parts of the placenta as possible, but excluding areas with infarcts, hemorrhage or other artifactual signal loss. The same ROIs were draw on the slice above and below the middle slice. In patients with PAS disorders, the ROI were placed in the regions of placental adhesion according to the maternity record after surgery, and the same ROIs were draw on the slice above and below the middle slice. To avoid the flow artifacts in large vessels, ROI should locate at least 2cm from the insertion of the umbilical cord. Values of D, D* and f were then calculated by averaging over 3 ROIs totally.

Statistics

Inter-rater reliability of the f, D, D* values between 2 radiologists was assessed by the intra-class correlation coefficient. Physical and sociodemographic factors for PAS disorders were investigated by using the chi-square, student's t-test or the Mann-Whitney u test to compare patients with PAS disorders to those without. The IVIM parameters were compared using Mann-Whitney u test or Kruskal-Walls test. Receiver operating characteristic curve was used to determine the cutoff of f value with the best sensitivity and specificity for distinguishing patients with PAS disorders from patients without the disease. P values<0.05 were considered statistically significant. All analyses were performed using IBM SPSS statistics 20.

Results

99 pregnant women with satisfied raw images remained in the analysis (Figure 1). Intra-class correlation coefficient between 2 radiologists of f, D and D* values were 0.892, 0.775 and 0.541 respectively. The mean maternal age was 31.92±4.31 years(range22 –41 years), the mean gestational age at examination was 34□4□weeks(range 28—39weeks). All medical records were received postpartum, 16 patients were diagnosed as placenta accreta when the placenta attaches onto the myometrium, 51 patients were diagnosed as placenta increta when the placenta penetrated into the myometrium, 8 patients were diagnosed as placenta percreta when the placenta penetrated through the uterine serosa, and 24 patients were without PAS disorders. The methods of delivery included 50 cases of cesarean section, 45 cases of prophylactic distal abdominal aorta balloon occlusion and cesarean section, 2 cases of natural birth, 2 cases of total hysterectomy and 1 case of partial hysterectomy. Table 1 presents the maternal characteristics of the study participants. Numbers of previous cesarean section was greater in patients with PAS disorders than in patients without the disease ($p<0.05$). The blood loss during delivery in patients with PAS disorders was greater ($p<0.05$), and more patients with PAS disorders required transfusion ($p<0.05$). When compared with patients with PAS disorders, f and D* values were significantly lower in patients without the disease ($p<0.05$), while D values showed no statistical significance between the 2 groups ($p>0.05$). Figure 1 shows a comparison of the placental perfusion fraction between the 2 groups. Based on the receiver operating characteristic curve analysis, the area under the curve was o.659 with a sensitivity of 64% and specificity of 71%, the best cutoff of f value was 31.91% (fig 2). Multiple comparisons showed f values in patients without PAS disorders were significantly lower than f values in patients with placenta accreta and percreta ($p<0.05$), but were not significantly lower than in patients with

increta(p>0.05). Difference from the 4 groups in D and D* values was not statistically significant (Table 2). Figure 3 shows a comparison of the placental perfusion fraction between the 4 groups.

Discussion

PAS disorders are a growing obstetric issue and seem to parallel the increasing cesarean delivery rate. The incidence of placenta accreta was 1 in 533 pregnancies for the period of 1982–2002, which contrasts sharply with 1 in 4027 pregnancies in the 1970s and 1 in 2510 pregnancies in the 1980s [12,13]. The most commonly described risk factors for PAS disorders were previous cesarean delivery and placenta previa. Placenta previa in particular has been shown to be a significant risk factor for PAS disorders, associated with a 9.3% incidence of abnormal placentation in one series, with higher risk in women have undergone prior cesarean deliveries [14]. According to Yu's report, the incidence of placenta previa was 10.96% in one center in China, the average incidence of placenta accreta in patients with both prior cesarean delivery and placenta previa was 2.08‰[15]. In our study, the study participants were patients with placenta previa and were suspected of having PAS disorders from results from ultrasonography. More patients with PAS disorders had previous cesarean deliveries, which was in accordance with the previous reports.

MRI has been applied increasingly for the prenatal diagnosis of PAS disorders in recent years. A recent systematic review found that the sensitivity and specificity of MRI in diagnosing accreta placentation varies widely from 75% and 100% and 65% and 100%, respectively [16]. Irrespective of the imaging modality used, the PAS disorders remain undiagnosed before delivery in half to two thirds of cases from recent population studies [17–19]. In a series from specialists diagnostic units in the USA, around one third of cases of PAS disorders were not diagnosed during pregnancy [20]. However, when recognized prenatally, a multidisciplinary team approach has been shown, with dedicated care plan and surgical expertise, to reduce maternal morbidity, from multiple retrospective cohort studies [21–23].

MRI is now being used increasingly often in pregnancy, because it is non-invasive and has high soft-tissue contrast. In addition to information on morphology, it can also provide physiological information which is limited in evaluations from ultrasonography. Application of MRI in today's obstetrics mainly includes the identification of fetuses and mothers at high risk, quantification of placental function and prediction of clinical outcome. Functional MRI is capable of assessing placental function and potentially improves diagnosis of pregnancy complications. DWI is commonly used for fetal imaging. IVIM is a derivative of DWI that attempts to distinguish between diffusion and perfusion of fluids. IVIM is appropriate for highly vascularized organ containing high blood fraction and a large, anisotropic perfusion components, like the placenta. It has been used mainly in pregnancies complicated by PE and IUGR. In the previous study, we found a decreased perfusion fraction in patients with placenta accreta and increta. However, the exact physiologic alterations of the placental function in patients with PAS disorders have not been fully understood.

Considering the potential artifacts caused by respiratory or cardiac motion [18], it is believed that acceptable reproducibility of a parameter ensures the reliability in repeated measurement before it can be put into clinical use [24,25]. The reproducibility of imaging parameters of f and D values was good when scanning within free-breathing IVIM in our study. The results showed that the interobserver agreement of f and D was excellent, while the interobserver agreement of D* was poor. Similar to previous findings, D* demonstrated the worst interobserver agreement. It was partially attributed to intrinsic inhomogeneous perfusion alteration, low signal-to-noise ratio in abdominal DWI, and the limitation in current nonlinear least square fitting method [24,26].

The diffusion coefficient reflects cellular and interstitial characteristics of the tissue. Our study showed that D value did not differ between patients with PAS disorders and patients without the disease. This maybe because tissue diffusion did not change in the region where the placenta adhered to the myometrium abnormally.

In our study, f value was significantly higher in patients with PAS disorders. During normal pregnancy, extravillous trophoblast cells invade the maternal decidua and inner third of the myometrium, then they penetrate and remodel maternal blood vessels in the uterine decidua into dilated, compliant uterioles that are irresponsive to maternal vasomotor control. This process facilitates the maternal blood flow to the placenta. Histological studies demonstrated an increase in the number of partially or non-remodeled spiral arteries in placenta accreta, even in the presence of abundant extravillous trophoblast, and abnormal EVT invasion into radial and arcuate arteries deep within the myometrium [27,28]. These changes may explain the hypervascular nature of the placental bed in abnormally invasive placenta, which was also verified by a dynamic enhanced MRI study of the placenta [29]. So the perfusion fraction also increased in patients with PAS disorders in our study. Secondly, we expected to find a best cutoff of f value to differentiate patients with PAS disorders from patients without the disease. The area under the curve was just 0.659 with a sensitivity of 64% and a specificity of 71%.

To explore the reason, we further divided patients with PAS disorders into patients with placenta accreta, patients with increta and patients with percreta. We found an increase of perfusion fraction in patients placenta accreta, then a slight decrease in patients with increta, and last another increase in patients with percreta. The f values were significantly lower in patients without PAS disorders than in patients with placenta accreta and percreta, but were not significantly lower than in patients with increta. Pathologically, in placenta accreta, the placenta villi embedded directly onto the myometrium in the absence of the decidua. We assumed that the spiral arterial remodeling is only mildly reduced, while more maternal blood in the myometrium bathe the fetal villi, so the perfusion fraction increased in placenta accreta. In placenta increta, the chorionic villi are found deeper into the myometrium, the spiral arteries remodeling is further reduced, the placental perfusion is thus balanced in this stage. So the perfusion fraction is similar to that in normal placenta. In placenta percreta, the placenta villi penetrate the uterine serosa, although the reduced spiral arteries remodeling persists, higher numbers of small vessels close to the placental-myometrium junction could be detected in conjunction with vessel wall infiltration of larger arteries of the radial, arcuate system, deep to the myometrium [27], so the perfusion fraction increased

again in placenta percreta. In consequence, it's imprudent to simply use perfusion fraction to differentiate patients with PAS disorders from patients without the disease. Since the perfusion fraction did not show statistical difference between patients with placenta increta and patients without PAS disorders, it is possible to confuse the two entities solely rely on perfusion fraction.

The study has several limitations. First, this is a retrospective study, not a prospective one. We mainly measured the areas of placenta invasion according to the description of maternity record instead of measurement of the entire placenta. From our previous experience, IVIM parameters did not show statistical difference between the site where placenta separated from uterine wall normally in the patients with placenta accreta and the regions of placenta in patients without placenta accreta [11]. Chen et al [30] also argued that future studies can focus on only abnormal of high risk areas adjacent to the cesarean scar instead of the entire placenta which may produce more predictive results, as more homogeneous regions adjacent to abnormal areas may skew the data. Second, our study population mainly included patients already had high risk of PAS disorders after ultrasonography, so the results may be biased as MRI is not a method used for screening.

Conclusions

perfusion fraction can be used as a reliable index to quantitatively assess placental perfusion in patients with PAS disorders. The perfusion fraction increased in patients with PAS disorders complicating placenta previa, mainly in patients with placenta accreta and percreta.

Abbreviations

IVIM introvoxel incoherent motion

MRI magnetic resonance imaging

PASplacenta accreta spectrum

FIGO International federation of gynecology and obstetrics

ROI region of interests

Declarations

Ethics and Consent to participate

Written informed consent was obtained from each of the patient.

- The ethical review aboard of Sichuan Provincial People's Hospital approved the study and informed consent was obtained from each woman participating in the study

- Consent to publish

Written informed consent was obtained from each of the patient.

- Availability of data and materials

Data supporting the results reported in the article can be found in the database of Sichuan Provincial People's Hospital.

- Competing interests

The authors declare that they have no competing interest Funding

- Funding

Not applicable

- Authors' Contributions

Conception and design of this manuscript was carried out by TL, HP, administrative support was carried out by HP, provision of study materials or patients was carried out by TL, JM, MH, KL collection and assembly of data was carried out by TL, KL, MH, Data analysis and interpretation was carried out by HP, and manuscript writing ant the final approval of manuscript was carried out by all authors.

All authors have read and approved the final version of this manuscript.

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Tables

Table 1 Physical and sociodemographic features of patients studied

	Patients without PAS disoders	Patients with PAS disoders	P value
Number	24(24.24%)	75(75.76%)	
Age(years)	31.88±3.81	31.93±4.48	0.147
Less than 35	20(20.20%)	51(51.52%)	
35 or older	4(4.04%)	24(24.24%)	
Gestational age At examination (weeks)	33.5(4)	34(4)	0.825
Gestational age At the time of delivery (weeks)	37(2)	37(1)	0.241
Number of Previous caesarean Section			
0	11(11.11%)	15(15.15%)	
1	12(12.12%)	46(46.46%)	
2 or more	1(1.01%)	14(14.14%)	0.021
Previous uterine Dilation and Curettage			
No	2(2.02%)	16(16.16%)	
Yes	22(22.22%)	59(59.60%)	0.226
Blood lost(ml)	500(200)	800(600)	0.001
Transfusion	6(13.64%)	12(27.27%)	0.003
No	21(21.21%)	40(40.40%)	
Yes	3(3.03%)	35(35.35%)	
Amount of transfusion(ml)	0(0)	0(800)	0.002
f (%)	29.39(5.59)	34.12(9.8)	0.019
D ($10^{-3}mm^2/s$)	1.68(0.13)	1.7(0.13)	0.915
D*($10^{-3}mm^2/s$)	20.37(10.22)	24.84(8.94)	0.044

Table 2 Multiple comparsion between different groups of three parameters (n=44)

Group	n	f (%)	D($10^{-3}mm^2/s$)	D*($10^{-3}mm^2/s$)
Patients without PAS disorders	24(24.24%)	29.39(5.59)	1.68(0.13)	20.37(10.22)
Patients with Placenta accreta	16(16.16%)	37.73(18.17)	1.70(0.23)	24.84(14.35)
Patients with Placenta increta	51(51.52%)	32.32(8.56)	1.70(0.12)	23.35(9.19)
Patients with Placenta percreta	8(8.08)	36.01(13.27)	1.66(0.11)	29.31(7.26)
P value		0.016	0.794	0.160

Figures

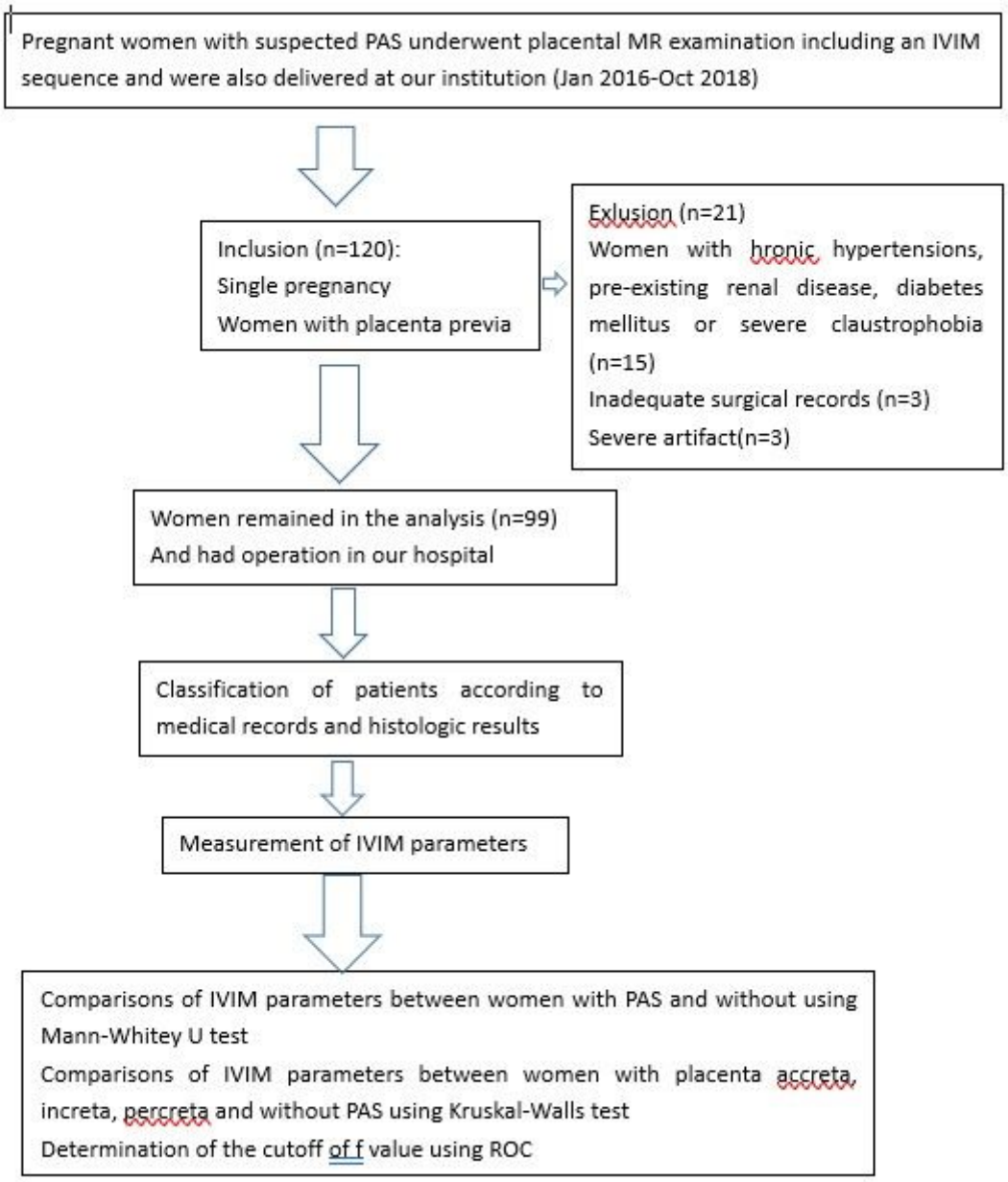

Figure 1

Flowchart of the study design

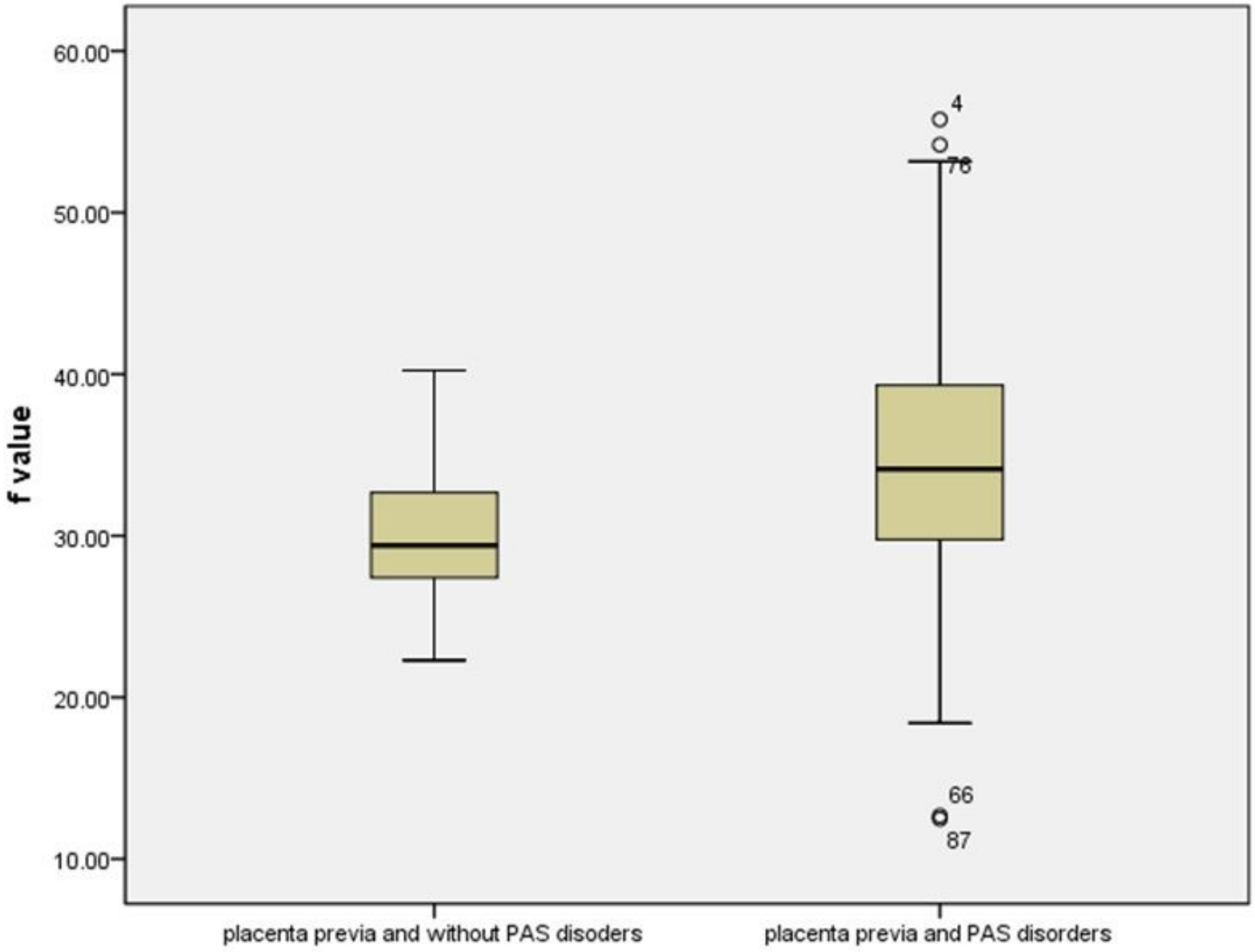

Figure 2

variation of f value. Box plot represented the distribution of f value in patients without PAS and with PAS.

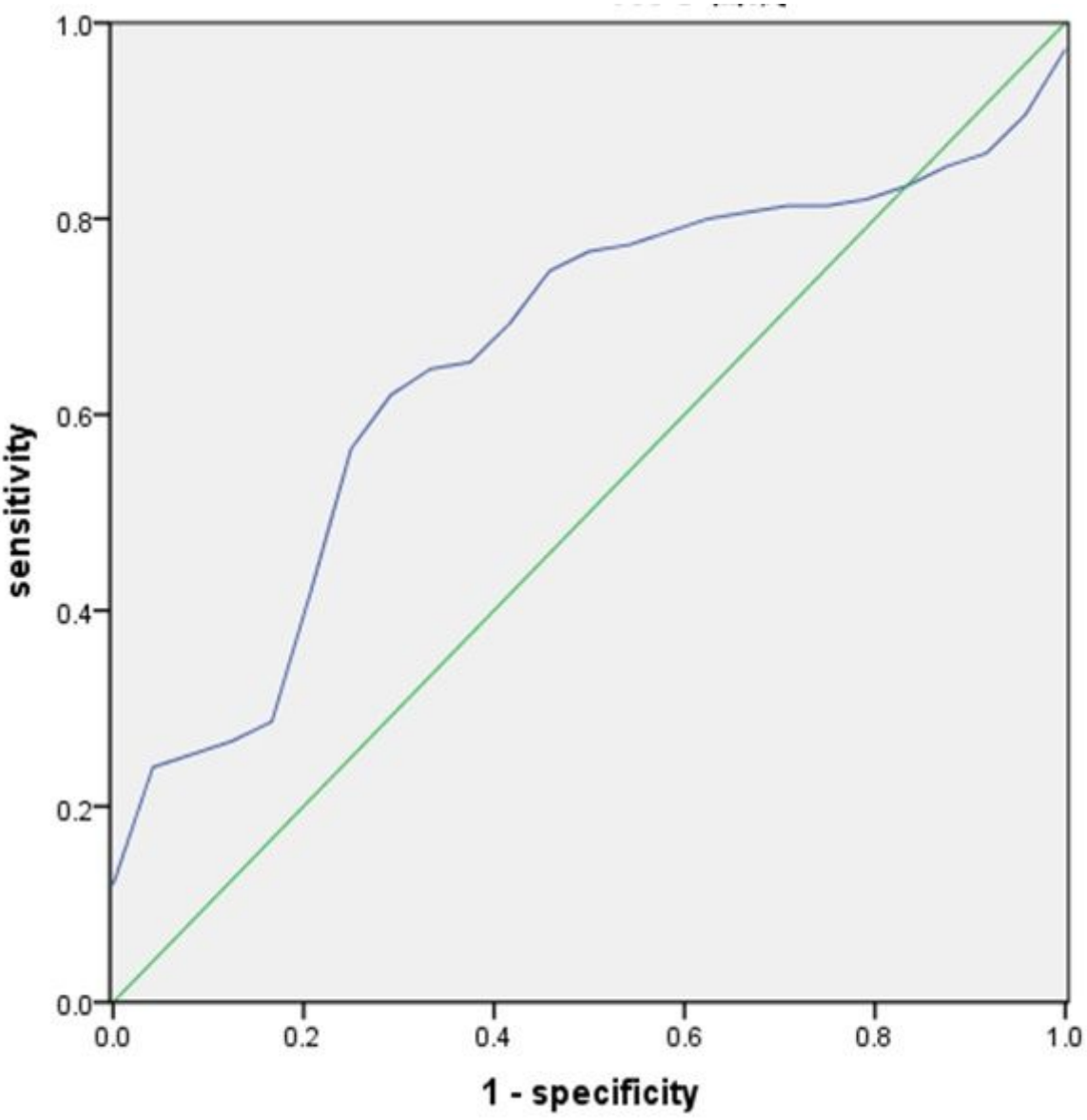

Figure 3

ROC curve of f value.

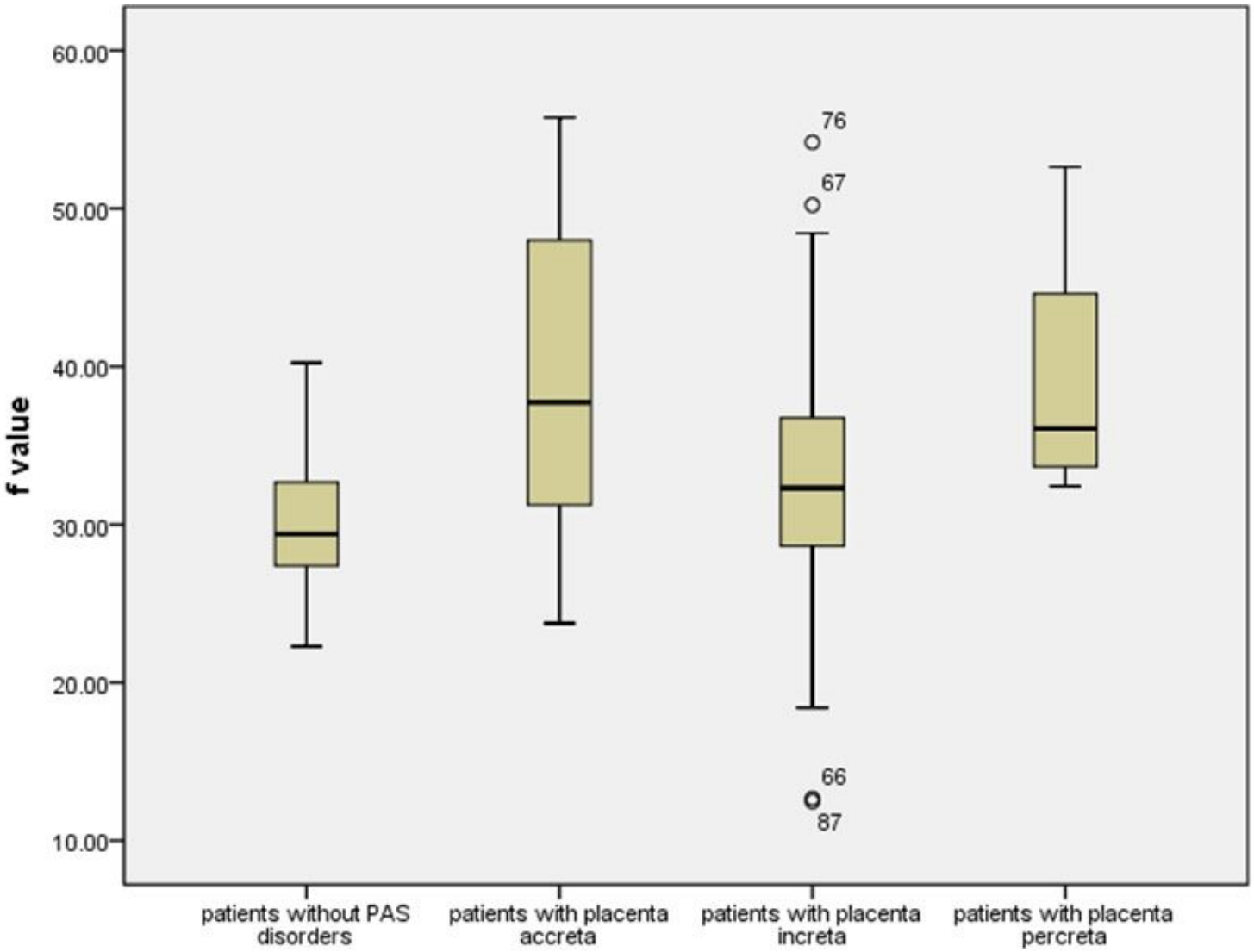

Figure 4

variation of f value. Box plot represented the distribution of f value in patients with placenta accreta, increta, percreta and without PAS.