Magnetic Resonance Imaging–Based Radiomics Nomogram to Predict Intraoperative Hemorrhage of Placenta Previa

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Abstract

Objective Placenta previa (PP) is associated with intraoperative and postpartum hemorrhage, increased maternal morbidity and mortality. We aimed to develop a magnetic resonance imaging (MRI)-based nomogram to preoperative prediction of intraoperative hemorrhage (IPH) for PP.

Study Design A total of 125 PP pregnant women were divided into a training set (n = 80) and a validation set (n = 45). An MRI-based model was built for the classification of patients into IPH and non-IPH groups in a training set and a validation set. Multivariate nomograms were built according to radiomics features. Receiver operating characteristic (ROC) curve was used to assess the model. Predictive accuracy of nomogram were assessed by calibration plots and decision curve analysis.

Results In multivariate analysis, placenta position, placenta thickness, cervical blood sinus, and placental signals in the cervix were significantly independent predictors for IPH (all ps < 0.05). The MRI-based nomogram showed favorable discrimination between IPH and non-IPH groups. The calibration curve showed good agreement between the estimated and the actual probability of IPH. Decision curve analysis also showed a high clinical benefit across a wide range of probability thresholds. Area under the ROC curve was 0.918 (95% confidence interval [CI]: 0.857–0.979) in the training set and 0.866 (95% CI: 0.748–0.985) in the validation set by the combination of four MRI features.

Conclusion The MRI-based nomograms might be a useful tool for the preoperative prediction of IPH outcomes for PP. Our study enables obstetricians to perform adequate preoperative evaluation to reduce blood loss and cesarean hysterectomy.

Keywords

► placenta previa
► magnetic resonance imaging
► intraoperative hemorrhage
► nomogram

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Placenta previa (PP) is characterized by the abnormal placenta overlying the lower uterine segment, and it is known as one of the most serious obstetric complications. The incidence of PP is approximately 3.5 to 4.6 per 1,000 pregnancies. The incidence of PP and placenta accreta is increasing due to spontaneous abortion, cesarean section, and other uterine surgical history (myomectomy or ablation). The exact pathophysiology of PP is not exactly known. PP is divided into four types according to the distance between the placenta and the cervix: low-lying placenta, marginal placenta, partial placenta, and complete PP. PP is commonly diagnosed by ultrasound sonography or magnetic resonance imaging (MRI) in the third trimester. Ultrasound is the preferred procedure for evaluating placental position and placenta accreta but is limited in some cases, such as patients with abdominal fat hypertrophy and posterior placenta. MRI was used widely in recent years, which can clearly define the position of placenta, evaluate the morphology of the cervical canal and the surrounding placental tissue in more detail, and give doctors more detailed preoperative evaluation. MRI has a wide field of view and high-contrast resolution to describe the characterization of placental anatomy. MRI is an effective imaging modalities for guiding management of PP. Due to the high incidence of intraoperative hemorrhage (IPH) and postpartum hemorrhage, need for blood transfusion and hysterectomy, which is considered a severe complication of pregnancy, and even death. In addition, women with PP has a serious threat on fetal health, such as delivery premature, fetal distress, neonatal intensive care unit (NICU) admission, stillbirth, and neonatal death. In recent years, more scholars combined clinical data and imaging examination to predict the risk of IPH in patients with PP. Choi and Yangyu, respectively, developed a model based on clinical and ultrasonic signs to predict IPH and the possibility of hysterectomy in patients with PP. Most current ultrasound models related to the risk of placenta accreta or hysterectomy. Before cesarean section, obstetricians are more concerned about the difficulty of operation and the possible amount of bleeding during cesarean section.

Our hospital is a treatment center for high-risk pregnant women, and most of the pregnant women with PP around our hospital were referred to our hospital for delivery. Through the treatment of a large number of pregnant women with PP, we have accumulated some experience in treatment. A well-planned multidisciplinary team approach could reduce IPH and minimize the potential risks of maternal mortality. Thus, an accurate prenatal diagnosis and evaluation of PP is imperative. Hence, in this study, we sought to develop an MRI signature nomogram to predict IPH in patients with PP.

**Key Points**
- MRI is an important method for preoperative assessment of the risk of placenta previa.
- MRI-based nomogram can assess the risk of intraoperative bleeding of placenta previa.
- MRI is helpful for more comprehensive evaluation of placenta previa and adequate preoperative preparation.

**Materials and Methods**

**Patients Selection**

The Ethical Committee of the affiliated Suzhou hospital of Nanjing Medical University approved the experimental protocol. Given the retrospective study and anonymous patient data, the requirement for informed consent was waived. All methods were performed in accordance with relevant guidelines and regulations. A total of 125 consecutive patients with PP who were treated from May 2015 to December 2019 were enrolled in our study, according to the following inclusion criteria: (1) all pregnant women received regular prenatal examinations and delivered in our hospital; (2) PP was confirmed by pelvic MRI before cesarean section, regardless of the presence or absence of placenta accreta; and (3) availability of clinical characteristics. Patients excluded are those unable to undergo MRI (n = 51), marginal PP (n = 92), and delivery in other hospitals (n = 67). Finally, a total of 125 patients were enrolled in the study. All cases were cesarean section; emergent cesarean section was required when a pregnant woman has massive bleeding or obvious uterine contractions. In our study, 120 pregnant women had scheduled cesarean section and 5 cases had emergent cesarean section. Archived clinical data, such as age at the time of delivery, body mass index (BMI), gestational age by MRI, amount of blood transfusion, operative time, and cesarean hysterectomy were extracted from reviewing the medical records.

**Standard of Reference**

Severe postpartum hemorrhage may occur in PP patients after removal of the placenta in cesarean section. Intraoperative blood loss is an important indicator of the severity of PP. Normal parturient can tolerate 1,000 mL of blood loss, when the volume of blood loss is more than 2,000 mL, the parturient may be in a state of shock, which will seriously threaten the life of parturient. We need a multidisciplinary (urinary surgery department, gastrointestinal surgery department, vascular interventional department, anesthesiology department, intensive care unit, etc.) approach to rescue the mother and fetus and referring to previous studies, so the cutoff value of IPH was set at 2,000 mL in our study. In this study, blood loss was measured by using weighed swabs, which is more precise than methods using visual estimation. The IPH group was defined as cesarean section with massive intraoperative bleeding (≥2,000 mL). The non-IPH group was defined as cesarean section with minor intraoperative bleeding (<2,000 mL).
Magnetic Resonance Imaging Data Acquisition
Before cesarean delivery, all patients were performed pelvic MRI using a 3.0 T MRI system (Siemens Medical Solutions, Erlangen, Germany). The imaging protocol included three-plane (sagittal, coronal, and axial) T1-weighted and T2-weighted images of the pelvis. MRI images were retrospectively interpreted by three experienced radiologists on reading PP MRI. MRI findings suggestive of IPH of PP included placenta position, placenta thickness, bladder line, placenta pit, cervical blood sinus, cervical form, and placental signals in the cervix. The signs of PP were analyzed by MRI; an MRI model was constructed by using only the typical features extracted from the MRI. To obtain placental thickness, we need to find the most complete cervical morphology in the sagittal slice of pelvic MRI. The tangent line a was traced on the maternal side of the placenta at the thickest part of the placenta, and the parallel line b of a was traced on the fetal side of the placenta, then the vertical distance between the two lines was the placental thickness (Fig. 2A, blue line). We established a high-risk table for MRI features of IPH, and radiologists evaluated MRI image according to the figure (Fig. 2). Any disagreement in the process of interpretation was resolved by the senior radiologist. For convenience of clinical application, an MRI-based nomogram was constructed from the logistic regression model to predict the risk of IPH.

Data Analysis and Statistics
The nomogram construction, calibration plots and decision curve analysis were done with R software (https://www.r-project.org/). Other statistical analysis was performed using SPSS 23.0 statistics software (SPSS, Inc., Chicago, IL) and a two-sided p-value < 0.05 was considered significant. The differences in continuous variables were analyzed by Kruskal-Wallis test, whereas the differences in the categorical variables were assessed by Pearson’s χ² test or Fisher’s exact test. Univariate and multivariate logistic regression analysis was performed to identify independent factors associated with IPH > 2,000 mL. Multivariate logistic regression model was used to construct the nomograms. Feature selection and model construction were only performed on the training cohort and the validation cohort only for evaluating the model performance. The characteristics (area under the receiver operating characteristic curve [AUC], sensitivity, specificity, positive predictive value, negative predictive value, and accuracy) of MRI signs in the models were tested by SPSS 23.0.

Results
Clinical Characteristics of the Patients
Among the 125 patients, we analyzed 30 patients with IPH > 2,000 mL and 95 patients without. The clinical characteristics of patients in the training set, validation set, IPH, and non-IPH group were listed in Tables 1 and 2. The frequency of IPH in the training and validation sets was similar (23.750 vs. 24.444%, χ² = 0.008, p = 0.930). The training and validation sets were similar in terms of the baseline clinical characteristics (p > 0.05). Statistical differences were found between IPH and non-IPH group in gravidity, parity, gestational age at delivery, amount of blood transfusion, operative time, IPH, placenta accreta, cesarean hysterectomy, and NICU admission (p < 0.05). There were no statistically significant differences in amount of predelivery bleeding, preterm labor, and infection in the puerperium between IPH and non-IPH group (p > 0.05).
Performance of the Radiomics Signature
There was a significant difference in radiomics signatures between IPH and non-IPH patients in the training set \( (p < 0.05) \) and validation set \( (p < 0.05) \), which indicates the radiomics signatures were related to the IPH \( (\text{Table 2}) \). The univariate and multivariate model was constructed using the radiomics signature in the training cohort. On univariable analyses, placenta position, placenta thickness, bladder line, placental pit, cervical blood sinus, cervical form, and placental signals in the cervix on MRI emerged as predictors of IPH \( (p < 0.05) \). All of these covariates were included in a multivariable logistic regression model. Placenta position, placenta thickness, cervical blood sinus, and placental signals in the cervix on MRI emerged as predictors for the outcome of IPH on multivariable analysis \( (p < 0.05; \text{Table 3}) \).

Performance of the Nomogram
Based on the above multivariate analysis results, the nomogram was constructed. In \( \text{Fig. 3} \), the nomogram shows the impact on the probability of IPH contributed by placenta position, placenta thickness, cervical blood sinus, and placental signals in the cervix. By determining the score from all variables on a total point scale, probabilities of IPH \( (\text{IPH} > 2,000 \text{mL}) \) could be determined by drawing a vertical line to the total score \( (\text{Fig. 3}) \).

Receiver Operating Characteristic Curve Analysis and Internal Validation
The discriminatory ability of the nomogram for predicting IPH was investigated by receiver operating characteristic curves \( (\text{Fig. 4 A and B}) \). The combination of four MRI features model yielded an AUC of 0.918 (95% confidence interval [CI]: 0.857–0.979) in the training set, with an accuracy of 87.9%, and an AUC of 0.866 (95% CI: 0.748–0.985) in the validation set, with an accuracy of 85.3%. The sensitivity and specificity were 80.3 and 89.5% in the training set and 77.8 and 86.1% in the validation set \( (\text{Table 4}) \).

Two calibration plots were constructed to measure the fit between the predicted rate and the actual outcome. The calibration curve of the nomogram showed good calibration in the training and validation sets. A perfect model would demonstrate a 1:1 relationship between predicted and observed values, resulting in a perfect 45-degree slope. Our models for predicting the presence of IPH exhibited excellent
### Table 1 Clinical characteristics of pregnant women with placenta previa

| Parameter                        | Training set (n = 80) | Validation set (n = 45) | p-Value |
|----------------------------------|-----------------------|-------------------------|---------|
|                                  | IPH (n = 19)          | Non-IPH (n = 61)        |         |
| Age at delivery (y)             | 32.95 ± 2.95          | 31.26 ± 4.35            | 0.119   |
| BMI before delivery (kg/m²)     | 27.71 ± 4.20          | 25.94 ± 2.91            | 0.099   |
| Gravidity                       | 4.00 ± 1.60           | 3.13 ± 1.20             | 0.013   |
| Parity                          | 2.32 ± 0.58           | 1.85 ± 0.57             | 0.003   |
| GA at delivery (wk)             | 34.91 ± 1.07          | 35.60 ± 1.20            | 0.001   |
| GA by MRI (wk)                  | 34.75 ± 2.28          | 33.71 ± 2.41            | 0.099   |
| Previous uterine surgery        |                       |                         |         |
| Cesarean section                | 14 (73.68%)           | 32 (52.46%)             | 0.102   |
| Dilatation and curettage        | 6 (31.58%)            | 12 (19.67%)             | 0.278   |
| Myomectomy                      | 2 (10.53%)            | 5 (8.20%)               | 0.754   |
| Previous placenta previa        | 1 (5.26%)             | 1 (1.64%)               | 0.377   |
| Amount of predelivery bleeding (mL) | 215.31 ± 56.34    | 242.87 ± 67.06          | 0.109   |
| Preterm labor                   | 10 (52.60%)           | 18 (29.51%)             | 0.065   |
| Amount of blood transfusion (mL) | 2,682.89 ± 674.21    | 877.05 ± 540.41         | <0.001  |
| Operative time                  | 121.21 ± 44.30        | 57.36 ± 19.81           | <0.001  |
| IPH (mL)                        | 3,814.73 ± 1,289.12   | 877.05 ± 540.41         | <0.001  |
| Placenta accreta                | 14 (73.68%)           | 17 (27.87%)             | <0.001  |
| Cesarean hysterectomy           | 1 (5.26%)             | 0 (0.00%)               | <0.001  |
| Infection in the puerperium     | 1 (5.26%)             | 3 (4.92%)               | 0.952   |
| Birth weight (g)                | 2,907.89 ± 379.06     | 2,762.30 ± 340.18       | 0.117   |
| Apgar Score 1st minute          | 9.58 ± 0.77           | 9.82 ± 0.53             | 0.128   |
| Apgar Score 5th minute          | 9.68 ± 0.67           | 9.90 ± 0.30             | 0.186   |
| Neonatal outcome                |                       |                         |         |
| NICU admission                  | 13 (68.42%)           | 25 (40.98%)             | 0.037   |

Abbreviations: GA, gestational age; IPH, intraoperative hemorrhage; MRI, magnetic resonance imaging; NICU, neonatal intensive care unit.

### Table 2 Clinical characteristics of the training and validation sets for magnetic resonance imaging

| Parameter                        | Training set (n = 80) | Validation set (n = 45) | p-Value |
|----------------------------------|-----------------------|-------------------------|---------|
|                                  | IPH (n = 19)          | Non-IPH (n = 61)        |         |
| Placenta position                |                       |                         | <0.001  |
| Anterior                         | 17 (89.47%)           | 24 (39.34%)             | 9 (81.82%) |
| Posterior                        | 2 (10.53%)            | 37 (60.66%)             | 2 (18.18%) |
| Placenta thickness               | 5.55 ± 1.122          | 4.32 ± 1.342            | 0.001   |
| Bladder line                     |                       |                         | <0.001  |
| Complete                         | 7 (36.84%)            | 50 (81.97%)             | 4 (36.36%) |
| Incomplete                       | 12 (63.16%)           | 11 (18.03%)             | 7 (63.64%) |
| Placenta pit                     |                       |                         | <0.001  |
| Yes                              | 12 (63.16%)           | 8 (13.11%)              | 7 (63.64%) |
| No                               | 7 (36.84%)            | 53 (86.89%)             | 4 (36.36%) |
| Cervical blood sinus             |                       |                         | <0.001  |
| Yes                              | 13 (68.42%)           | 4 (6.56%)               | 7 (63.64%) |
| No                               | 6 (31.58%)            | 57 (93.44%)             | 4 (36.36%) |
| Cervical form                    |                       |                         | <0.001  |
| Complete                         | 7 (36.84%)            | 54 (88.52%)             | 4 (36.36%) |
| Incomplete                       | 12 (63.16%)           | 7 (11.48%)              | 7 (63.64%) |
| Placental signals in the cervix  |                       |                         | <0.001  |
| Yes                              | 13 (68.42%)           | 5 (8.20%)               | 7 (63.64%) |
| No                               | 6 (31.58%)            | 56 (91.80%)             | 4 (36.36%) |

Abbreviation: IPH, intraoperative hemorrhage.
### Table 3 Univariate and multivariate regression analyses of the indicators for intraoperative hemorrhage in the training cohort

| Indicators                        | Univariate |         |         |         |         | Multivariate |         |         |         |
|----------------------------------|------------|---------|---------|---------|---------|--------------|---------|---------|---------|
|                                  | OR         | 95% CI  | p-Value | OR      | 95% CI  | p-Value      | OR      | 95% CI  | p-Value |
| Placenta position                | 5.181      | 2.038–13.857 | 0.003   | 3.026   | 1.001–7.447 | 0.012 |
| Placenta thickness               | 2.238      | 1.300–3.850  | 0.004   | 3.546   | 1.437–8.749  | 0.016 |
| Bladder line                     | 3.012      | 0.953–7.823  | 0.021   | 2.776   | 0.405–7.010  | 0.298 |
| Placental pit                    | 4.818      | 1.487–15.612 | 0.009   | 0.705   | 0.082–6.090  | 0.751 |
| Cervical blood sinus             | 5.169      | 1.365–19.572 | 0.016   | 7.519   | 1.654–15.626 | 0.019 |
| Cervical form                    | 3.560      | 1.023–12.393 | 0.046   | 0.580   | 0.053–3.341  | 0.656 |
| Placental signals in the cervix  | 7.361      | 2.29–23.664  | 0.001   | 10.913  | 1.934–19.935 | 0.001 |

Abbreviations: CI, confidence interval; OR, odds ratio.

**Fig. 3** Nomogram for the prediction of intraoperative hemorrhage (IPH) in patients with placenta previa. For example, a patient with complete placenta previa, magnetic resonance imaging (MRI) showed that the placenta was mainly located in the anterior wall of the uterus, placenta thickness was 7 cm, cervical blood sinus and placental signals were visible in the cervix. The corresponding points for the four MRI features (placenta position, anterior = 26 points [black line]; placenta thickness, 7 cm = 30 points [yellow line]; cervical blood sinus, yes = 18 points [green line]; placental signals in the cervix, yes = 22 points [blue line]) yielding a total of 96 points, which indicates the probability of IPH (≥2,000 mL) is 0.67 [red line].

**Fig. 4** Receiver operating characteristic curve for prediction of risk of intraoperative hemorrhage (IPH) by different magnetic resonance imaging (MRI) features. (A) MRI model reached area under the receiver operating characteristic curve (AUC) of 0.918, with a sensitivity of 0.803 and a specificity of 0.895 by the combination of four MRI features (red line) in training set. (B) MRI model reached AUC of 0.866, with a sensitivity of 0.778 and a specificity of 0.861 by the combination of four MRI features (red line) in validation set.
calibration (Fig. 5A and B). The decision curve analysis for evaluating the clinical utility of the predictive model were plotted, which showed favorable performance of the radiomics nomogram in the training and validation sets. This reflected greater benefit for the PP patients by MRI-based nomogram in the prediction of IPH (IPH > 2,000 mL), if the threshold probability was greater than 0.07 (Fig. 6).

**Discussion**

Multiple spontaneous abortions and intrauterine procedures may damage the endometrium, and placental villi can penetrate the myometrium, leading to placenta accreta. Previous cesarean section is an independent risk factor for PP and placenta accreta. The normal placenta is attached to the decidua basalis of the uterus, and the placenta can be removed smoothly after delivery. PP has a higher risk of placenta accreta, in which placental villi may directly to the myometrium with potentially deeper invasion into the uterine wall or surrounding organs. When the placenta inserted into the myometrium is removed, the local myometrium is missing and leads to massive bleeding. The damage of myometrial by the placental accreta is responsible for maternal bleeding and potential fetal compromise. PP often leads to uncontrolled bleeding during childbirth or postpartum, which can cause serious consequences, even life-threatening. About 40 to 60% of the peripartum hysterectomies are due to placenta accreta. The IPH group had a higher NICU admission, mainly due to cesarean sections at a smaller gestational age in IPH group. Therefore, prenatal diagnosis of placenta accreta and prediction of intraoperative blood loss can help clinicians make adequate preoperative preparation, develop appropriate surgical procedures, and avoid serious complications. For example, if pregnant women with PP have a high risk of IPH, we can make a detailed surgical plan through multidisciplinary consultation before surgery, prepare sufficient blood products and rescue drugs, and cesarean section was performed by experienced obstetricians at the appropriate gestational age. Therefore, the aim of our study was to investigate the role of MRI for the PP diagnosis and the clinical prediction in IPH.

Although ultrasound is an important method for the diagnosis of PP, MRI has been used more and more in the diagnosis and treatment of PP in recent years, which fully demonstrates its value in the evaluation of intraoperative blood loss of PP. MRI is complementary to ultrasound, and it is important for the accurate diagnosis of PP and placenta accreta. MRI is a better way to predict placental accreta spectrum in patients with PP independently from ultrasound finding. Patients with PP may have more intraoperative bleeding due to the intense bleeding of the uterus during delivery of the placenta, especially those with the placenta located entirely in the lower uterine segment. Placenta accreta can cause the placenta and uterine wall contact closely; postpartum placenta is not easy to peel and affect the uterine contraction, resulting in uterine blood sinus cannot be closed and postpartum hemorrhage.
In MRI images, the typical shadowing characteristics of placenta accreta include thinning of the myometrium, placental penetration into the uterine wall, and uneven placental signals. Interruption of myometrium signal and placental invasion into pelvic tissues and organs are the most direct manifestations of placenta accreta in MRI. However, due to the thinning of myometrium in the third trimester of pregnancy, the above features are lack of sensitivity and difficult to visualize, so they are rarely used in clinical diagnosis.

In this study, indirect signs (placenta position, placenta thickness, bladder line, and placenta pit, etc.) were combined with the imaging characteristics of PP for overall analysis, which was beneficial to improve the reliability of clinical diagnosis. Our study demonstrated that placental position, placental thickness, cervical blood sinus, and placental signals in the cervix were independent predictors in predicting the risk of IPH. The intraplacental blood sinuses may be an overgrowth of the placenta and inserted into the myometrium. Our study found that placental signal in the cervix (odds ratio [OR] = 10.913) and cervical blood sinus (OR = 7.519) are the two major MRI signs at high risk of intraperitoneal bleeding, because it may indicate placenta accreta in the cervix. Anterior to the lower segment of the uterus is the bladder, left and right ureters, and posterior to the rectum, which presents a great challenge to the operation of hemostasis in the cervix. An increase in the thickness of the placenta usually indicates that the placenta’s blood supply is abundant, even implanted in the uterine wall. The anterior placenta is another risk factor for intrapartum bleeding, especially in pregnant women with a history of cesarean section. The placenta is easily implanted and can even penetrate the bladder, causing intrapartum bleeding and bladder damage.

Our study indicated that MRI-based nomogram could provide a noninvasive way to predict the risk of IPH in PP, which was confirmed by calibration and decision curve analyses. Our study showed that combining multiple MRI features has higher diagnostic value than a single feature, with high AUCs in the training and validation set. In terms of predicting IPH during cesarean section of PP, our study only used MRI indicators to achieve similar predictive efficacy as previous studies that combined clinical general data and MRI data. According to The International Federation of Gynecology and Obstetrics diagnostic criteria, 48 pregnant women with placenta accreta were found in our study subjects. If a pregnant woman has a high risk score, abdominal aorta, common iliac artery balloon occlusion, and other procedures may be selected for cesarean section. Our hospital is a critical maternal treatment center, our team has accumulated a wealth of clinical experience in the treatment of PAS patients, and the medical team has performed adequate...
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Conflict of Interest
None declared.

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