Outcomes of prospectively-collected consecutive cases of antenatal-suspected placenta accreta

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Abstract

Background: Accurate diagnosis of placenta accreta is tentative before surgery. This study developed a predictive score for antenatal diagnosis of placenta accreta through mathematical modeling using clinical signs.

Methods: Antenatal cases of suspected placenta accreta were collected prospectively in a single-site tertiary delivery center. Women with clinical signs of placenta accreta (placenta previa, number of previous cesarean deliveries and/or ultrasound suspicion of placenta accreta) were included. The diagnosis of accreta was confirmed surgically. The primary endpoint was the proportion of surgically-diagnosed placenta accreta among all suspected cases. Logistic regression modeling was performed to assess preoperative risk factors for placenta accreta. The risk score was tested on a receiver operator characteristic curve to identify subjects with placenta accreta and the optimum cut-point was chosen.

Results: Over nine years, 92 suspected accreta cases were identified from 46623 deliveries (0.2%). The diagnosis was confirmed at surgery in 52/92 cases (56%) and there were no maternal deaths. Blood transfusion requirements were greater in patients with placenta accreta versus patients without placenta accreta (median 7 [range 0–25, interquartile range 3–10] versus 0 [0–6, 0–2] units of blood, \( P < 0.0001 \)). Area under the curve of the receiver operator characteristic curve was 0.846, with contribution from three variables (placenta previa, number of previous cesarean deliveries and ultrasound suspicion), each with a \( P \) value <0.05. From the ROC curve a cut-point with 100% sensitivity and specificity 25% (95% CI 12.69%–41.20%) was achieved, compared with 86.6% sensitivity (95% CI 74.21%–94.41%) and 60.0% specificity (95% CI 43.33%–75.14%) using ultrasound alone.

Conclusions: Combining diagnostic features associated with placenta accreta through mathematical modeling has better positive predictive value than ultrasound alone.

Keywords: Placenta accreta; Anesthesia; Hemorrhage; Modeling; Risk

Introduction

The rate of cesarean delivery is climbing, along with that of repeat cesarean delivery, resulting in a rising incidence of placenta accreta. With the latter, highly vascular placental trophoblastic tissue results in severe hemorrhage with substantial maternal and fetal morbidity. Hemorrhage has become more frequent and more dramatic in recent years. Current recommended management is to anticipate cesarean hysterectomy, except where the diagnosis is uncertain.

Risk factors for placenta accreta are well-described and include placenta previa, previous cesarean delivery, multiparity, previous curettage, uterine anomalies, and advanced maternal age. Diagnosis using ultrasound (US) has a high sensitivity, but may be wrong. Magnetic resonance imaging (MRI) may improve diagnostic accuracy but may not identify anterior placental adherence. In the absence of specific markers, diagnosis of actual placenta accreta is either surgical (adherent placenta) or pathological. In a clinical setting, in order not to miss a single case of accreta, use of risk factors such as placenta previa and US findings leads to over-diagnosis. This may result in unnecessary elective preterm delivery, transfer to tertiary care.
centers, intensive care unit (ICU) booking, general anesthesia and possibly elective cesarean hysterectomy.

Previously, we described protocol-guided management in a prospective series of placenta accreta cases. The current study was designed to improve the rate of diagnosis through a combination of parameters, thereby improving triage of patients with antenatally-suspected placenta accreta such that delivery timing, location and anesthesia planning could be directed to cases of true placenta accreta with potential for hemorrhage. We report on the outcome of 92 antenatally-suspected cases of placenta accreta, one of the largest case series in the literature.

**Methods**

This prospective, observational derivation study was conducted in a single-site tertiary referral center with a reported incidence of placenta accreta of 0.1%. Institutional Review Board approval was obtained with waiver of informed consent because of the non-interventional observational nature of the study. Data on cases of antenatally-suspected placenta accreta were collected prospectively from September 2002 until July 2011, including 28 cases previously reported.

All women with either placenta previa and/or at least one previous cesarean delivery were evaluated with detailed US over and above routine US performed during pregnancy. Women who did not have placenta previa and had no uterine scar were excluded. In cases of placenta previa US was transvaginal and in other cases was transabdominal. The grade of suspicion for placenta accreta on US was binary (high or low). US criteria suggestive of a high risk of placenta accreta included any one of the following: placental lacuna, obliteration of the echo lucent area between the uterus and placenta, myometrium thickness <1 mm, and interruption of the posterior bladder–uterine border. In cases where US did not show these specific signs but placenta accreta could not be excluded (e.g. the placental–myometrial border was not clear, or there were small lacunae alone), the risk was considered low. Patients who had no suspicious signs on US yet had placenta previa and uterine scar were also categorized as low risk. MRI was not routinely performed.

All cases of antenatally-suspected placenta accreta were scheduled for elective preterm cesarean delivery at or before 36 weeks of gestation. Unexpected antepartum bleeding was managed with immediate or expedited cesarean delivery, depending on the severity of bleeding and gestational age. A multidisciplinary team was assigned and followed a pre-established multidisciplinary protocol. General anesthesia with rapid-sequence induction and opioid/inhalational/muscle relaxant maintenance was planned; however, the anesthesiologist was at liberty to choose a combined spinal–epidural technique if preferred. Before surgery, two intravenous catheters (one 7 Fr) were inserted and a rapid-infusion system, cross-matched blood (4 units) and fresh frozen plasma (4 units) were prepared. An ICU bed was booked for postoperative care.

The diagnosis of placenta accreta was confirmed by the surgeon during surgery according to adherent placenta or visual signs such as the proportion of placental surface involved, depth of invasion, invasion of other pelvic organs and bleeding. Pathological confirmation was not routinely used. Elective cesarean hysterectomy was not performed. Hysterectomy was performed in cases of surgical visual diagnosis of placenta increta/percreta following uterine exposure before uterine incision and delivery of the fetus and placenta, or in clinical situation of hemorrhage or failed placental separation. The plan for hemorrhage control included ligation of the internal iliac vessels. Intravascular balloons were not used. Follow-up was for 24 h after surgery and subsequent relevant data were retrieved from patient files.

The primary study endpoint was the proportion of surgically-diagnosed placenta accreta among antenatally-suspected cases. To avoid bias, the operating surgeons were blinded to the primary study outcome to avoid the unlikely possibility that this could impact their diagnosis made at surgery. Secondary endpoints included gestational age at delivery, hysterectomy, transfusion requirement, type of anesthesia, Apgar scores and maternal complications.

A plot of the risk score (probability index, \( P \)) to estimate the predicted risk of placenta accreta for specific patients with antenatally-suspected placenta accreta, enabled plotting of the cumulative degree of risk as a function of the combined presence or absence of the various individual risk factors. The risk score is a relative probability where higher scores indicate greater likelihood of placenta accreta. Using the receiver operator characteristic (ROC) curve as a guide, the optimum cut-point was chosen. The ROC curve is summarized by the area under the curve (AUC) which describes the diagnostic accuracy for determining risk of placenta accreta. The curve is a plot of the sensitivity versus the false positive rate (1-specificity) as its cut-point value is varied.

**Statistical analysis**

In order to estimate an AUC of 0.8 with a 95% confidence interval half-width of 0.1, it was calculated that 92 subjects would be required if the sample of women with antenatally-suspected placenta accreta were expected to contain approximately 50% with a confirmed diagnosis of placenta accreta at surgery among all antenatally-suspected cases. Data analysis was performed using SPSS 19.0 (SPSS Inc. Chicago, IL, USA) and SAS® v9.2 (SAS Institute, Cary, NC, USA). Antenatally-
suspected cases of placental accreta confirmed at surgery were compared with those in whom placenta accreta was not found. Discrete variables (presence of placenta previa, US grading, mode of anesthesia and surgical management) are presented as a count and percentage and were compared using the Chi-square test. Continuous variables are presented as a mean ± standard deviation (SD) and were compared using the independent samples t-test, or are presented as median, range and interquartile range (IQR) and were compared using the Mann–Whitney two-sample test. No imputation of missing data was performed. A P value of 0.05 was considered statistically significant and nominal P values are presented.

Logistic regression modeling was performed to assess preoperative risk factors for placenta accreta. Variables with \( P < 0.05 \) were identified and entered into a multivariate model. The variables designated to remain in the model were those preoperative risk factors for placenta accreta which remained statistically significant when entered together and that maximized the predictive power \( (\text{AUC of the ROC curve}) \) of the model such that the AUC of the resulting ROC curve was at least 0.8. The risk score was created from the logistic regression model, ranging from 0 to 1, and is a linear function of the model coefficients.

Results

During the nine-year study period there were 46623 deliveries. We identified 92 cases of antenatally-suspected placenta accreta \( (0.2\%) \). The diagnosis of placenta accreta was confirmed surgically in 52 cases \( (56\%) \). There were no cases of unsuspected placenta accreta at cesarean delivery and there were no maternal deaths. Preoperative study screening procedures thus identified all patients with risk factors who had surgically-diagnosed placenta accreta during the study period. Patient characteristics including the rate of potential risk factors leading to preoperative suspicion of placenta accreta are presented in Table 1.

Surgery was performed at \( 34.6 ± 3.2 \) weeks of gestation in women with placenta accreta and \( 35.6 ± 2.2 \) weeks of gestation in patients without placenta accreta \( (P = 0.116) \). Fifty-nine \( (64.1\%) \) cesarean deliveries were performed on the planned date, with no difference between the patients with and without placenta accreta. Hysterectomy was performed in 45 \( (86.5\%) \) women with placenta accreta. One patient \( (2.5\%) \) without placenta accreta had hysterectomy performed because of uterine atony and massive hemorrhage despite no intraoperative evidence of placenta accreta.

General anesthesia was performed in 50 \( (96.2\%) \) patients with and 29 \( (72.5\%) \) without placenta accreta. Blood transfusion requirement was greater in the patients who underwent hysterectomy versus those without hysterectomy \( (0 \ [0–25] \text{ vs. } 0 \ [0–9] \text{ units of packed red cells respectively, } P < 0.0001) \). Maternal and neonatal outcomes are summarized in Table 2.

A combination of placenta previa, number of previous cesarean deliveries together with US resulted in increased sensitivity compared to US alone (Table 3). Placenta previa \( \text{(yes/no)} \), number of previous cesarean deliveries \( \text{(continuous)} \), and US suspicion of placenta accreta \( \text{(yes/no)} \) were the independent variables selected and entered into the logistic regression model. Variables such as maternal age and antepartum bleeding which have been found in other studies to be risk factors for placenta accreta were not entered into the model as they did not improve prediction.

The regression model coefficients were then used to derive the risk score \( \text{(termed probability index)} \) as \( P = e^{Y}/(1 + e^{Y}) \), where \( Y \) is the log of the odds of having placenta accreta, and is a linear function of the independent factors. Significant interactions between placenta previa and number of previous cesarean deliveries raised the AUC to 0.846, therefore our goal was attained.

The ROC curve depicting the ability of the risk score to identify subjects with placenta accreta is presented together with the respective area under the curve \( (\text{AUC}) \) and 95% Wald confidence interval in Fig. 1. The derived model was:

\[
Y = -8.2862 + (6.5184 \times R) + (2.3313 \times N) + (2.7272 \times H) - (2.1151 \times N \times R)
\]

**Table 1** Patient characteristics and risk factors for placenta accreta

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Placenta accreta ( n = 52 )</th>
<th>Not placenta accreta ( n = 40 )</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.6 ± 4.1</td>
<td>35.0 ± 4.6</td>
<td>0.68</td>
</tr>
<tr>
<td>Gravidity</td>
<td>6 [2–17, 4–9]</td>
<td>5 [2–13, 3.25–8.0]</td>
<td>0.31</td>
</tr>
<tr>
<td>Parity</td>
<td>4 [0–12, 2–6]</td>
<td>3 [0–13, 2–6.75]</td>
<td>0.46</td>
</tr>
<tr>
<td>Previous dilatation and curettage</td>
<td>32 (61.5%)</td>
<td>21 (52.5%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Previous cesarean delivery</td>
<td>2.5 ± 1.5</td>
<td>1.6 ± 1.3</td>
<td>0.003</td>
</tr>
<tr>
<td>Antenatal vaginal bleeding</td>
<td>31 (59.6%)</td>
<td>20 (50%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Placenta previa</td>
<td>46 (88.5%)</td>
<td>28 (70%)</td>
<td>0.027</td>
</tr>
<tr>
<td>Ultrasound signs of placenta accreta</td>
<td>45 (86.5%)</td>
<td>16 (40%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are mean ± SD. Median [range, IQR], or number (%).
where \( R \) = placenta previa (1 = yes, 0 = no), \( N \) = number of previous cesarean deliveries, and \( H \) = US suspicion (1 = high, 0 = low).

A plot of the risk score (probability index, \( P \)) to estimate the predicted risk of a specific subject is presented in Fig. 2. From the ROC curve we chose two different cut-points: one at 100% sensitivity, and our optimal cut-point with the most advantageous balance between sensitivity and specificity to match our required aims for magnitude of sensitivity. To select the optimum cut-point, we examined the ROC curve visually, to estimate where the highest point on ROC curve appeared. We looked for a point with sensitivity above the 86% sensitivity of using US alone, but with the highest possible specificity. We then used the table of numbers to choose a specific cut-point. The table of numbers consists of 92 pairs (1 per subject) called sensitivity-specificity pairs. Any point we chose visually on the ROC curve has a sensitivity-specificity pair in the table. These cut-points represent two different clinical approaches; either the desire to not miss a single case of placenta accreta (100% sensitivity), even at the risk of false positives, or alternatively an optimal balance of identifying as many cases of actual placenta accreta as possible with the anesthetic challenge of unanticipated hemorrhage whilst minimizing the false positive rate. The probability level for the first cut-point (having 94% sensitivity) is 0.208, and the probability for the 100% sensitivity cut-point is 0.174.

Table 2  Maternal and neonatal outcomes

<table>
<thead>
<tr>
<th></th>
<th>Placenta accreta (( n = 52 ))</th>
<th>Not placenta accreta (( n = 40 ))</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRBC transfusion, (number of units)</td>
<td>7 [3–10]</td>
<td>0 [0–2]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Massive transfusion (&gt;8 units of PRBC)</td>
<td>26 (50%)</td>
<td>0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>150 [120–150]</td>
<td>60 [40–60]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tracheal extubation immediately after surgery</td>
<td>23 (44.2%)</td>
<td>39 (97.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Admission to the intensive care unit</td>
<td>37 (71.2%)</td>
<td>9 (22.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Length of hospital stay (day)</td>
<td>8 [6–8]</td>
<td>6.5 [5–6.5]</td>
<td>0.001</td>
</tr>
<tr>
<td>Apgar score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 min</td>
<td>8 [6–8]</td>
<td>9 [6–9]</td>
<td>0.09</td>
</tr>
<tr>
<td>5 min</td>
<td>9 [9–9]</td>
<td>9 [9–9]</td>
<td>0.16</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>2.6 ± 0.6</td>
<td>2.7 ± 0.5</td>
<td>0.82</td>
</tr>
</tbody>
</table>

Data are median [IQR], number (%) or mean ± SD; PRBC: packed red blood cells.

Table 3  Sensitivity, specificity, positive and negative predictive value using models of categorization for predicting suspected placenta accreta

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (95% CI)</th>
<th>Positive predictive value (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Negative predictive value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound alone</td>
<td>86.6% (74.2–94.4%)</td>
<td>73.8% (60.9–84.2%)</td>
<td>60.0% (43.3–75.1%)</td>
<td>77.4% (9.6–41.1%)</td>
</tr>
<tr>
<td>Combination of three parameters; maximal sensitivity cut-off</td>
<td>100% (93.2–100%)</td>
<td>72.1% (59.9–82.3%)</td>
<td>25.0% (12.7–41.2%)</td>
<td>87.5% (2.7–32.4%)</td>
</tr>
<tr>
<td>Combination of three parameters; optimal cut-off</td>
<td>94.2% (84.1–98.8%)</td>
<td>63.4% (52.1–73.8%)</td>
<td>52.5% (36.1–68.5%)</td>
<td>100%</td>
</tr>
</tbody>
</table>

Fig. 1  Receiver operating characteristic (ROC) curve, summarized by the area under the curve (AUC), which describes the diagnostic accuracy for determining placenta accreta (AUC = 0.85, 95% CI: 0.758–0.933). The curve is a plot of the sensitivity versus the false positive rate (1-specificity) as its cut-point value is varied.
likelihood that the suspicion is correct. Her clinical predictors can be plotted on the nomogram, similar to that used to plot body mass index, to identify whether she is above (considered to have placenta accreta) or below (considered not to have placenta accreta) the cut-point. For example, for a woman with no placenta previa, two previous cesarean deliveries and low US suspicion, the predictive model is:

\[ Y = -8.2862 + (6.5184 \times 0) + (2.3313 \times 2) + (2.7272 \times 0) = 3.6236. \]

Therefore, she has a probability index \( P = 0.027 \), so the likelihood of placenta accreta is extremely low. Therefore, we could model, with a level of certainty represented by the position on the nomogram, whether the patient should be treated as having or not having placenta accreta. If the patient is above the cut-point line she should be managed as having placenta accreta and if below she can be managed as not having placenta accreta.

**Discussion**

This series of antenatally-suspected cases of placenta accreta is the largest prospectively collected to date, and included all patients in whom placenta accreta was suspected before surgery using clinical data corroborated with US findings.

To require assessment for placenta accreta in our model, the patient would fit clinical criteria whereby placenta accreta cannot be excluded. Through use of the nomogram, using the 100% sensitivity cut-point, all women with placenta accreta could be correctly included among those suspected of having placenta accreta, assuming the nomogram can be validated. An example of use of the model with the 100% cut-point is that 10 out of 92 patients could be advised that they are likely to be true negatives and therefore would not need to be exposed to general anesthesia, preterm delivery and other implications of potential placenta accreta; this is a numerical example of the potential value of our approach. The trade-off for this 100% sensitivity is that 30 of 40 women without placenta accreta would also require strategies for massive hemorrhage, as specificity is only 25%. For a procedure where assessments are done before surgery, such as suspected appendicitis, a false positive rate is inevitable and a grey zone of unclear diagnosis is inevitable.\(^\text{18}\) The different cut-points were presented because each institution will have a specific goal in mind. For example, a center performing all placenta accreta surgery in the main operating rooms, or performing routine cesarean hysterectomy may desire to identify true negatives, enabling the focus of treatment on those women who have placenta accreta. In
contrast, an institution attempting placental separation in every case will want to have no false negatives.

A distinctive aspect to the data presented in our study is that all cases of placenta accreta were collected prospectively. This enables a unique look at the population of antenatally-suspected cases of placenta accreta, many of whom do not actually have placenta accreta. In previous studies reporting placenta accreta, the starting point for data collection was the surgical and/or pathological diagnosis. Risk factors reported have been identified using logistic regression in these retrospectively-diagnosed cases of placenta accreta. Our study confirms with prospective data that these factors are important. Because of retrospective retrieval of data previously, those patients who did not have placenta accreta were not included. Prospective collection of placenta accreta cases has been done using US identification but without the addition of other predictors (placenta previa, cesarean delivery).

We identified placenta previa and prior cesarean delivery as major predictors of placenta accreta and this is consistent with previous retrospectively-collected data. Comparing US alone with a combined tool of US and clinical predictors improved the sensitivity of the diagnosis in our cohort. Clinical suspicion alone (bleeding, placenta previa, previous cesarean delivery) enables identification of up to 50% of placenta accreta cases. Among patients without placenta previa the risk is only 4.7% for ≥6 previous cesarean deliveries. Factors such as maternal age, parity, previous curettage and antenatal bleeding that were used to predict placenta accreta in other retrospective studies did not contribute to the model in our cohort.

Sonographic criteria for antenatal diagnosis of placenta accreta and their sensitivity/specificity vary even when using similar criteria. US criteria suggestive of placenta accreta include placental lacuna (sensitivity 79%, positive predictive value 92% between 15 and 40 weeks of gestation), obliteration of the echolucent area located between the uterus and the placenta (low diagnostic and predictive sensitivity false-positive rate nearly 50%), myometrium thickness <1 mm (sensitivity 100%, specificity 72% and positive predictive value 72%), and interruption of the posterior bladder–uterine border (sensitivity 13%, specificity 98% and positive predictive value 87%).

However, transabdominal US is less efficient at detecting posterior or fundal implantation and further hampered in obesity and following previous cesarean delivery. Recently, threedimensional US has been employed to neovascular components, providing relevant information for hemostasis.

This is a proof of concept study. It is important to highlight this model so that others may improve or validate it and the nomogram is not complete for clinical decision-making until validation has been performed. Ideally, such a study would include hundreds of cases of placenta accreta so a model could be derived and validated for widespread use. Our model is useful in our institution with our high level of suspicion. However as placenta accreta is rare, albeit with increasingly prevalence, generalization of our model is limited by the size of the cohort. Since no single center will have sufficient numbers to both derive and validate such a model, collaboration will likely be the optimum way to produce a reliable predictive model.

The cut-points associated with a high likelihood of accreta were defined post-hoc in this study, a method associated with high likelihood of type I error. Moreover, the sample population was an enriched group that included all women with a priori suspected placenta accreta. As such, the proportion of true positives was very high relative to the proportion of true negatives and the model performance may be less suitable for another population. The presence of placenta accreta is not binary and this is not addressed in our model. Gradations of severity may factor into delivery planning. The false negative cases on US may represent a population with more circumscribed placental invasion. More detailed consideration of US findings may enable better grading of the US risk level entered into the model in the future. Women not at risk of placenta accreta because they have no cesarean scar, no placenta previa and no US signs are not considered at risk of placenta accreta, even though placenta accreta may exist also among this population. Another limitation of our study is that diagnosis of placenta accreta was made by the surgeon and not always confirmed pathologically. Regarding anesthesia, our local practice was to perform general anesthesia for all cases of placenta accreta. The anesthesiologist may have identified discriminating features to choose to perform a neuraxial technique but this was not reported.

Antenatally-suspected placenta accreta requires preparations for major hemorrhage. However, use of a more structured model based on routine easily reproducible diagnostic factors, could enable some women to be detached from the group at risk, directing management efforts including preterm delivery and massive hemorrhage preparations to those women for whom massive hemorrhage is most likely.

Disclosure

No external funding and no competing interests are declared.

References


