# Chapter 10
# Prediction and Risk Reduction of Clinical Outcomes of Placenta Accreta Spectrum

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## Introduction

Placenta accreta spectrum (PAS), previously termed adherent or invasive placental disorder, is a major obstetric condition that may lead to detrimental maternal outcomes [1, 2]. The magnitude of PAS has been substantially potentiated in the current century in response to the rising trend of cesarean deliveries worldwide [3]. Therefore, PAS has no longer become a rare incidence, and obstetricians'/gynecologic surgeons' exposure to PAS management experience has expended over time. Although the rising rate of PAS cases has been overwhelming to obstetric practice and health systems, it has enhanced our understanding of these disorders and encouraged extensive research to promote early diagnosis and facilitate evidence-based clinical decisions [4].

In the last few decades, our understanding of PAS has considerably developed, including our awareness of PAS risk factors [5]. Recognition of risk factors, accompanied by emerging imaging expertise, has led to robust strategies of antenatal characterization and early diagnosis of PAS [6]. More recently, evolving clinical studies proposed risk stratification systems of women with presumed diagnosis of PAS to predict their peripartum outcomes and contribute to counseling, decision-making, and management planning [7].

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In this chapter, we will primarily focus on clinical predictors of clinical outcomes in women with presumed PAS during pregnancy, with special emphasis on their role in risk stratification and management decision prior to delivery.

## PAR-A (Placenta Accreta Risk–Antepartum) and PAR-P (Placenta Accreta Risk–Peripartum) Scores

### *Score Development*

PAR-A and PAR-P scores were introduced to the literature in 2020 [7]. The scores were originally developed using an international database, which was created for the purpose of that study. The database comprises antenatal, peripartum, and postpartum data of 727 women, recruited from 11 tertiary centers, with presumed PAS, which was confirmed at birth. The two scores were created using machine learning algorithms and were tested internally using a testing subset of the data [7].

### *Score Components*

Both scores were designed to predict significant morbidity in women with PAS, primarily PAS-associated massive blood loss (≥ 2500 mL). Other predicted outcomes include maternal admission to intensive care unit (ICU) after birth and prolonged postpartum hospitalization. PAR-A score considers antenatally determined factors only in predicting these outcomes. Therefore, the score can be calculated shortly after diagnosis is suspected in order to stratify maternal risk of significant adverse maternal outcomes. The most contributing factors to PAR-A score are number of previous cesarean deliveries, Asian ethnicity, parity, centrally situated placentas, and prenatal hemoglobin level (Fig. 10.1). PAR-P score combines both antenatal and intrapartum factors to predict the same outcomes. Unlike PAR-A score which serves as a tool for risk stratification and counseling, PAR-P score enables testing of different management scenarios of the same patient in priori to predict clinical outcomes. Accordingly, PAR-P score may be used to decide an individualized management plan and endorse alternative strategies based on intraoperative findings prior to delivery. Diagnostic modality, parametrial invasion, intrapartum diagnosis of PAS, bladder invasion, and uterine incision away from placental site yield the highest impact on PAR-P score (Fig. 10.2) [7].

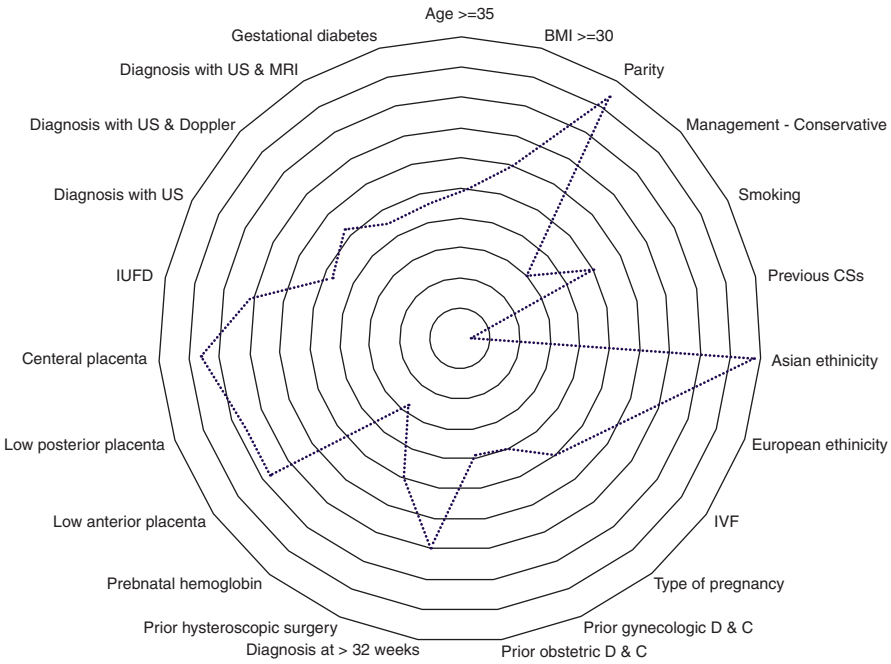


**Fig. 10.1** Magnitude of contribution of antepartum characteristics to PAR-A score. * *BMI* body mass index, *CS* cesarean section, *IVF* in vitro fertilization, *D&C* dilation and curettage, *IUFD* intrauterine fetal death, *US* ultrasound, *MRI* magnetic resonance imaging

## *Score Performance*

In the primary study, PAR-A score predicted PAS-associated massive blood loss, prolonged hospitalization, and admission to ICU with an area under curve (AUC) of 0.84, 0.81, and 0.82, respectively [7]. Recently, PAR-A score was externally validated through a prospective multicenter study, that was conducted by six PAS-specialized centers. Results were comparable to the original study; AUC of PAS-associated massive blood loss was 0.85 (95% confidence interval [CI] 0.74–0.95), and 0.88 (95% CI 0.81–0.95) for ICU admission [8]. PAR-P score yielded AUC of 0.86, 0.90, and 0.86 for PAS-associated massive blood loss, prolonged hospitalization, and admission to ICU, respectively, as reported by the original study [7].

## *Score Applicability*

Unlike traditional statistics, machine learning-based scores are complex and do not rely on straight, and fully interpretable calculations. Therefore, clinical implementation of these scores requires software applications that run the algorithm of the

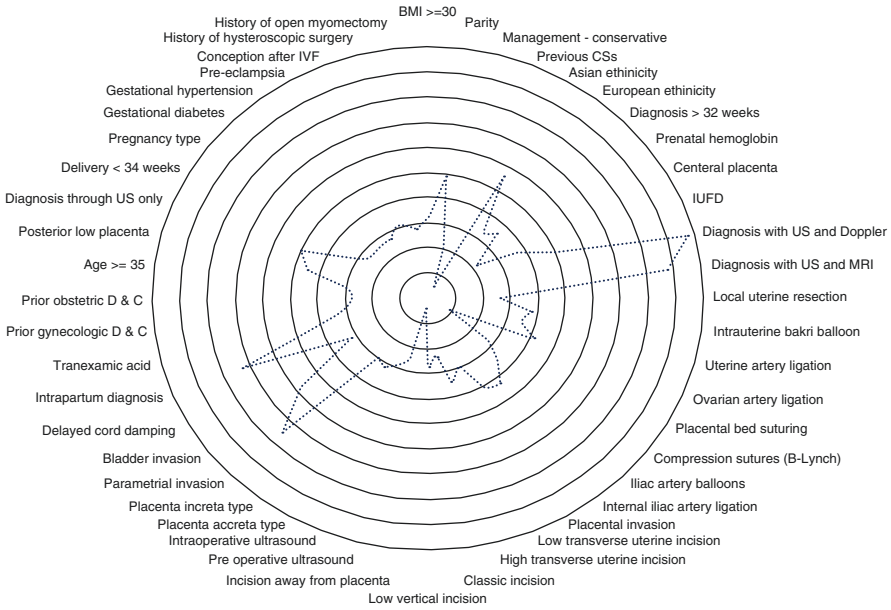


**Fig. 10.2** Magnitude of contribution of antepartum characteristics to PAR-P score. * *BMI* body mass index, *CS* cesarean section, *IVF* in vitro fertilization, *D&C* dilation and curettage, *IUFD* intrauterine fetal death, *US* ultrasound, *MRI* magnetic resonance imaging

created model and produce a final result. A tool was developed by SilverAxon® (SilverAxon For artificial intelligence-based medical software, Egypt), in collaboration with PAR score research team [9]. Patient and disease features are provided through the software interface to calculate the output, which presents as a score from 1 to 12 depending on probability, sensitivity, and specificity of prediction of adverse outcomes, i.e., massive blood loss and admission to ICU, and is plotted on the corresponding area receiver operating characteristic (ROC) curve (Fig. 10.3).

Interpretation of the score should be made carefully since it focuses primarily on sensitivity and specificity. According to basic statistical understanding, sensitivity indicates high score ability to recognize women who would develop the outcome (complications). In other words, high sensitivity of, e.g., massive blood loss indicates that the risk of this complication is unlikely missed and that most women developing the complication are recognized. Similarly, low sensitivity conveys that many patients who would develop massive blood loss are likely not diagnosed. On the other hand, high specificity denotes that development of the complication is highly likely, while low specificity means that most diagnosed patients are not actually at risk [10]. In practice, clinicians should cautiously consider whether they would prioritize high sensitivity, high specificity, or a balanced point of both depending on the nature of the condition. Sensitivity may be superior to specificity in serious and life-threatening conditions since the score should miss as few cases as possible, while specificity may be superior when overdiagnosis could be associated

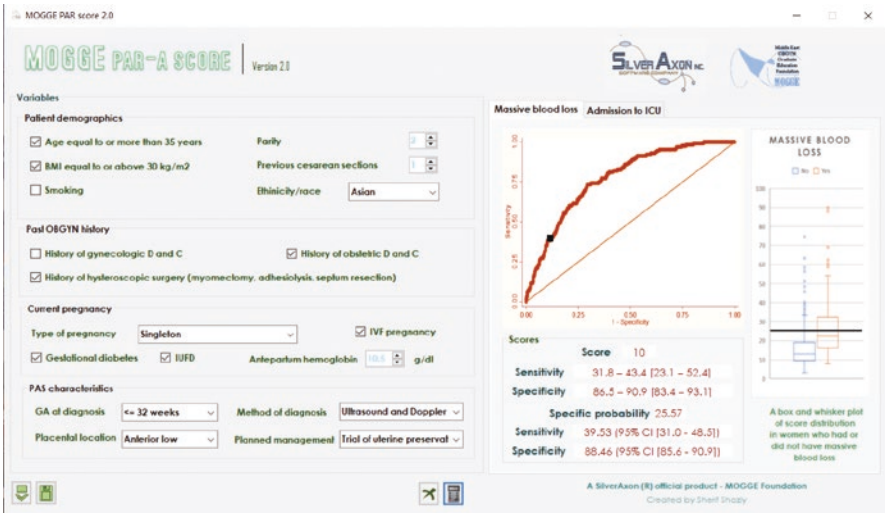


**Fig. 10.3** PAR-A score calculator

with significant sequences such as unnecessary interventions or high costs. In PAS patients, both parameters are important. Nevertheless, sensitivity is more critical. Overall, this information may assist risk stratification, which subsequently supports decision-making on managing facility, preparation for delivery, decision for hospitalization, and possible need for additional measures, e.g., interventional radiology.

## *Disadvantages and Limitations*

Since these scores were developed using retrospective databases, they acquire the same inherent limitations of these studies. Specifically, retrospective studies reveal associations between variables and the outcome, which do not necessarily indicate causality. For example, administration of tranexamic acid slightly contributes to worse outcomes according to PAR-P score [7] while clinically, administration of tranexamic acid should reduce the amount of blood loss in obstetric surgeries [11]. Whereas this should be true among women with PAS as well, administration of tranexamic acid may indicate significant or ongoing blood loss, which triggers its administration, rather than being a risk factor for massive bleeding.

In fact, these concerns are common with machine learning models, which commonly use retrospective studies to provide sufficiently large databases for machine learning algorithms. Interestingly, data scientists do not necessarily consider that as a limitation. Unlike conventional statistics, machine learning does not investigate or highlight inference between a variable and an outcome. Instead, it builds models that use all complex interactions between all variables, including unrecognized ones, to predict an outcome. Thus, it does not necessarily define understandable or

recognizable direct associations and should not be used for this propose. Indeed, they are meant to analyze the whole clinical scenario including all linked patient variables [12].

Finally, institutional auditing of these scores may be necessary since estimation of blood loss and admission to ICU may be influenced by institutional methods and protocols, respectively, and score interpretation may be adjusted based on internal outcomes.

## Conservative Management of PAS (CON-PAS) Score

### *Score Development*

CON-PAS score is a new scoring system that was designed to predict probability of success of uterus-preserving procedures in women with PAS prior to delivery [13]. The score was generated using the subset of women who underwent uterine preservation from the Placenta Accreta Spectrum International Database (PAS-ID), which was originally created to produce PAR scores [14]. Data from 587 women was included to develop this score using logistic regression approach [13].

### *Score Components*

Composition of this score is similar to PAR-P score, where both antenatal and intraoperative factors are considered. Consequently, it predicts success of uterus-preserving procedures as per anticipated clinical scenarios at the time of surgery. The most contributing factors to this score are possibility of local uterine resection, number of previous cesarean deliveries, and type of uterine incision. In general, feasibility of local uterine resection and uterine incision away from placenta site contributes the most to uterine preservation success, while increasing number of previous cesarean deliveries and classic uterine incision are associated with increased risk of failed uterine preservation (Fig. 10.4).

### *Score Performance*

According to the original study, AUC of this model in predicting success of uterine preservation was 0.91. The score was internally validated using a subset of data that was not involved in score creation (validation cohort) and AUC for this cohort was 0.90 [13]. Unpublished results on external validity of CON-PAS score, based on the

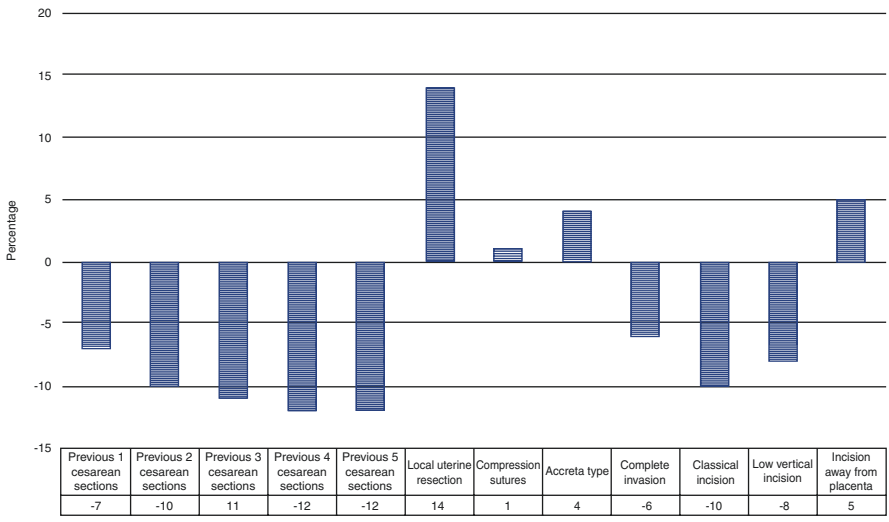


**Fig. 10.4** Factors included in CON-PAS score and their magnitude of contribution

same database used to validate PAR-A score, showed that AUC of this prospective cohort was 0.94.

## *Score Applicability*

The score was built using traditional logistic regression models. However, a software is available to determine probability of procedure success and plot the score in comparison to reference score ranges in women who had successful versus unsuccessful uterine preservation procedures (MoggeSoft®); (MoggeSoft For medical software, Egypt) [15].

Although the score seems to be a unique tool to counsel women and determine whether they are good candidates for uterine preservation, some of the information used to calculate CON-PAS is only determined intraoperatively. Accordingly, it may be used to determine potential probability of success if certain criteria are met or not met during surgery. Thereby, a decision may be altered based on intraoperative assessment in correspondence to previously calculated scores. For example, the score may indicate high probability of treatment success if local uterine resection or incision away from placental site can be achieved. Otherwise, hysterectomy should be better performed. Obviously, using the score in such a way may be complex, yet beneficial in certain scenarios. Also, some intraoperative findings may be anticipated through prenatal and intraoperative imaging.

### *Disadvantages and Limitations*

Similar to PAR score, the score emerged from a retrospective study. Nevertheless, the score is more transparent and simple compared to machine learning-based scores. Therefore, association between variables and score outcome is interpretable. As mentioned earlier, practical applicability of CON-PAS score may not be straightforward since it consider alternative plans based on intraoperative findings. In addition, PAS-ID, the original database, originated from centers that possess long experience in uterine preservation, and results should not be generalized to less experienced centers, even if calculated scores are reassuring.

## Conclusion

Recently, novel scores have been proposed to predict perioperative outcomes in women with PAS. Specifically, PAR scores are designed to calculate risk of adverse outcomes at time of cesarean delivery, while CON-PAS score predicts the chance of uterine preservation success. These types of scores have not previously available and their potential implementation is new to the field of PAS management. Wide application of these scores may enhance their validity as a tool that aids patient counseling, decision-making, and management planning.

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