ORIGINAL RESEARCH ARTICLE

Maternal and neonatal outcomes in planned versus emergency cesarean delivery for placenta accreta spectrum: A multinational database study

Maddalena Morlando[1,2] 🔟 | Alexander Schwickert[3] 🔟 | Vedran Stefanovic[4] 🔟 |
Mina M. Gziri[5] 🔟 | Petra Pateisky[6] | Kinga M. Chalubinski[6] | Andreas Nonnenmacher[3] |
Olivier Morel[7,8] 🔟 | Thorsten Braun[3,9] 🔟 | Charline Bertholdt[7,8] 🔟 |
Heleen J. Van Beekhuizen[10] 🔟 | Sally L. Collins[11,12] 🔟 | on behalf of the International Society
for Placenta Accreta Spectrum (IS-PAS)*

[1]Department of Neuroscience, Reproductive Sciences and Dentistry, University of Naples Federico II, Naples, Italy

[2]Department of Woman, Child and of General and Specialized Surgery, University "Luigi Vanvitelli", Naples, Italy

[3]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Obstetrics, Berlin, Germany

[4]Department of Obstetrics and Gynecology, Fetomaternal Medical Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland

[5]Department of Obstetrics, Cliniques Universitaires Saint-Luc, Brussels, Belgium

[6]Department of Obstetrics and Gynecology, Division of Obstetrics and Feto-Maternal Medicine, Medical University of Vienna, Vienna, Austria

[7]Women's Division, Nancy Regional and University Hospital Center (CHRU), Université de Lorraine, Nancy, France

[8]Diagnosis and International Adaptive Imaging (IADI), Inserm, Université de Lorraine, Nancy, France

[9]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität

Abstract

Introduction: Placenta accreta spectrum (PAS) is a condition often resulting in severe maternal morbidity. Scheduled delivery by an experienced team has been shown to improve maternal outcomes; however, the benefits must be weighed against the risk of iatrogenic prematurity. The aim of this study is to investigate the rates of emergency delivery seen for antenatally suspected PAS and compare the resulting outcomes in the 15 referral centers of the International Society for PAS (IS-PAS).

Material and methods: Fifteen centers provided cases between 2008 and 2019. The women included were divided into two groups according to whether they had a planned or an emergency cesarean delivery. Delivery was defined as "planned" when performed at a time and date to suit the team. All the remaining cases were classified as "emergency". Maternal characteristics and neonatal outcomes were compared between the two groups according to gestation at delivery.

Results: In all, 356 women were included. Of these, 239 (67%) underwent a planned delivery and 117 (33%) an emergency delivery. Vaginal bleeding was the indication for emergency delivery in 41 of the 117 women (41%). There were no significant differences in terms of blood loss, transfusion rates or major maternal morbidity between planned and emergency deliveries. However, the rate of maternal intensive therapy unit admission was increased with emergency delivery (45% vs 33%, *P* = .02). Antepartum hemorrhage was the only independent predictor of emergency delivery (aOR: 4.3, 95% confidence interval 2.4-7.7). Emergency delivery due to vaginal bleeding was more frequent with

- -

Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of 'Experimental Obstetrics', Berlin, Germany

[10]Department of Gynecological Oncology, Erasmus MC Cancer center, Rotterdam, the Netherlands

[11]Nuffield Department of Women's and Reproductive Health, University of Oxford, Oxford, UK

[12]Fetal Medicine Unit, John Radcliffe Hospital, Oxford, UK

Correspondence
Alexander Schwickert, Charité – Universitätsmedizin Berlin, Klinik für Geburtsmedizin , Augustenburger Platz 1, 13353 Berlin, Germany.
Email: alexander.schwickert@charite.de

false-positive cases (antenatally suspected but not confirmed as PAS at delivery) and the milder grades of PAS (accreta/increta). The rate of infants experiencing any major neonatal morbidity was 25% at 34[+1] to 36[+0] weeks and 19% at >36[+0] weeks.

Conclusions: Emergency delivery in centers of excellence did not increase blood loss, transfusion rates or maternal morbidity. The single greatest risk factor for emergency delivery was antenatal hemorrhage. When adequate expertise and resources are available, to defer delivery in women with no significant antenatal bleeding and no risk factors for pre-term birth until >36[+0] weeks can be considered to improve fetal outcomes. Further studies are needed to investigate this fully.

K E Y W O R D S
abnormally invasive placenta, gestational age, maternal morbidity, neonatal morbidity, placenta accreta spectrum

Key message

Emergency delivery in a specialist center did not increase maternal morbidity. When adequate expertise and resources are available, with no bleeding or risk factors for pre-term birth, delivery at >36[+0] weeks' can be considered.

1 | INTRODUCTION

Placenta accreta spectrum (PAS) is a potentially life-threatening condition for the mother that often results in severe blood loss and peripartum hysterectomy.[1,2] Ensuring early prenatal diagnosis of such cases allows careful planning of delivery in a specialized center with an experienced multi-disciplinary team. This has been shown to decrease maternal morbidity.[3,4] A planned rather than emergency delivery is also associated with a reduction in bleeding and emergency procedures.[3-8] Many centers base their timing of delivery on an elegant decision analysis published in 2010[9] which suggested that the optimal delivery for women with placenta previa was 34 weeks. The flaw with extrapolating this model to PAS, however, is that the risk of bleeding used to formulate it, was based on 400 women with placenta previa only. Many accoucheurs have since anecdotally reported that previa complicated by severe PAS appears to be less likely to bleed than a normal previa. This is biologically plausible, as a deeply invaded placenta covering the internal cervical os is potentially less likely to separate. However, planning delivery at later gestational ages potentially increases the risk of emergency delivery, which may increase the risk of maternal morbidity. In the recent evidence-based guideline, the International Society for PAS (IS-PAS) suggested expectant management until after 36 weeks' gestation for asymptomatic women with no obvious risk factors for preterm delivery, whereas planned delivery at around 34 weeks' gestation was advised for women with a history of previous preterm birth, recurrent vaginal bleeding or preterm rupture of membranes.[10] Of note, this was based on expert opinion, as the current literature does not provide any robust evidence specific to PAS on the optimal management strategy to balance maternal and neonatal morbidity. The few previous studies that have examined perinatal outcomes have been limited by small sample sizes and heterogeneous, often vague diagnostic criteria for PAS.

The aim of this study was to use cases from the IS-PAS database to investigate (1) the rate of emergency delivery observed at different gestations according to the severity of the PAS, (2) the differences in both maternal and neonatal morbidity between planned and emergency delivery according to gestation and (3) whether there were any factors which predicted the risk of emergency delivery.

2 | MATERIAL AND METHODS

This is a cohort study based on cases recorded in the IS-PAS FetView database; 14 European and one non-European center (USA) provided cases retrospectively between 2008 and 2014 and prospectively collected data from 2014 to 2019.[11] All the women with an antenatal diagnosis of suspected PAS were included whether or not they were confirmed as PAS at delivery. Cases with no antenatal suspicion of PAS were excluded from this analysis as the planned date of delivery will have been dependent on non–PAS-related factors. As the main outcome being investigated was planned timing of cesarean delivery (CD), additional exclusion criteria were: pregnancy outcomes other than CD (spontaneous vaginal delivery, miscarriage [spontaneous delivery or in utero demise <22 weeks' gestation] and termination of pregnancy), missing data on timing of CD, multiple pregnancy and neonates with major congenital anomalies, as all of these factors may have affected the decision on timing. Prenatal suspicion of PAS was made in each center according to their local guidelines and practice (ultrasound, MRI or both). The severity was classified at delivery according to the IS-PAS grading system.[10-12] This system was adopted by the International Federation of Gynaecology and

Obstetrics (FIGO) in 2018[13] and formed the basis of the more recently published FIGO Clinical Classification system.[14] The publication by Braun et al[11] includes details on the exact classification and how it correlates with the current FIGO classification system.

The women included in the analyses were divided into two groups according to whether they had a planned or an emergency delivery. The delivery was defined as "planned" when it was performed at a time to suit the woman and maternity team (elective). It was classified as an "emergency" when it was performed for: (1) an immediate threat to life of the woman or the fetus; (2) maternal or fetal compromise which was not immediately life-threatening; (3) a reason requiring delivery soon but without maternal/fetal compromise (i.e. it needed to occur soon but could wait until "daylight hours"). Maternal mortality and morbidity data were collected: estimated blood loss, transfusion rates, lower urinary tract trauma, fistula formation, sepsis, admission to the Intensive Therapy Unit (ITU), etc.[3] Neonatal outcomes collected included: stillbirth, APGARs at 5 minutes, cord pH, respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, severe jaundice, severe infection, hypoxic ischemic encephalopathy, admission to the Neonatal Intensive Care Unit. These outcomes were defined by each center according to their individual guidelines. The maternal and neonatal outcomes were compared by gestation according to whether the delivery was planned or an emergency. To determine whether the rate of emergency delivery varied with the severity of PAS, the planned and emergency deliveries were also compared by recorded grade of PAS at delivery. Factors associated with emergency delivery such as severity of PAS, parity, position of placenta and occurrence of antepartum hemorrhage were also collected. Antepartum hemorrhage was defined as any kind of vaginal bleeding during pregnancy.

2.1 | Statistical analyses

The analysis was performed using all available data, following application of the exclusion criteria. The distribution of continuous variables was explored using histograms, skewness and kurtosis to identify any clear departure from a normal distribution. Data were described using mean (and standard deviation) where it was normally distributed, and median (and interquartile range) where it was not. Where data were normally distributed, they were analyzed using the *t* test and the Mann-Whitney *U* Test. Chi-square test or Fisher's Exact test, were used where the data were not normally distributed. A *P* value <.05 was considered significant. Univariate and multivariate analyses were used to identify the factors associated with emergency cesarean section. A multilevel logistic regression model served to control for possible variation between participating centers. Crude odds ratios with a 95% confidence interval (CI) were calculated for all results. A multivariate regression analysis was carried out, including variables that had been identified as having a significant effect in univariate analysis (i.e. *P* ≤ .05), and adjusted odds ratios with 95% CI were provided. SPSS® v26 (IBM®) was used for all statistical analyses.

2.2 | Ethical approval

All the centers obtained approval from their local Ethical Committee to share the data anonymously. Details of these can be found in the online Supporting Information contained in the second Commentary of this supplement.[11]

3 | RESULTS

In total, 442 women were included in the IS-PAS database; 86 of these women did not meet the inclusion criteria, leaving 356 women in this analysis (Figure 1). Among the 356 women included, 239 (67%) underwent a planned CD and 117 (33%) an emergency CD. Vaginal bleeding was the indication for emergency delivery in 41 of 117 women (41%). There were no differences between the two groups in terms of the main maternal characteristics except that the women who delivered as an emergency had a higher parity (*P* = .01) and lower body mass index (*P* = .02: Table 1).

The proportion of women experiencing antepartum hemorrhage was significantly higher in the group with an emergency delivery (66% vs 28%, *P* < .001). When multivariate analysis was performed, antepartum hemorrhage was the only significant independent predictor of emergency CD (adjusted odds ratio: 4.7, 95% CI 2.6-8.5, *P* < .001) (Table 2).

Emergency delivery occurred at significantly lower median gestational ages (34 vs 36 weeks, *P* < .001). Of the 356 women, 92 (26%) were delivered before 34^{+0} weeks, 65 (71%) as emergencies, 132 (37%) between 34^{+1} and 36^{+0} weeks. No significant differences were seen in the estimated blood loss, number of blood units transfused or incidence of major maternal morbidities between women who
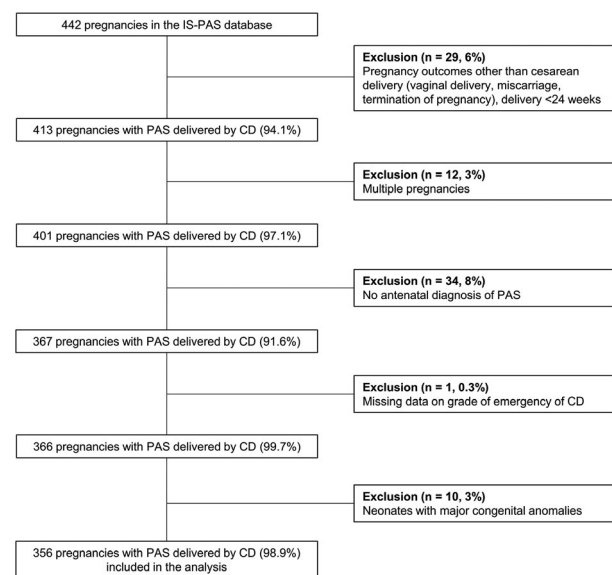

FIGURE 1 Selection of cases. IS-PAS, International Society for Placenta Accreta Spectrum; PAS, placenta accreta spectrum; CD, cesarean delivery

TABLE 1 Maternal characteristics and outcomes for women undergoing planned and emergency delivery

	Planned delivery (n = 239)	Emergency delivery (n = 117)	P value	Missing data (%)
Antepartum characteristics				
Age[a]	35 (31–38)	34 (31–38)	.66	2 (0.6)
Parity[a]	2 (1–2)	2 (1–3)	**.01**	0
Previous cesarean sections[a]	1 (1–2)	2 (1–3)	.07	0
Previous D&C[a]	0 (0–1)	0 (0–1)	.51	
Placenta previa[b]	219 (92)	109 (93)	.61	0
Ethnicity[c]			.42	22 (6)
African, Caribbean and African-American	13 (5)	5 (4)		
East Asian	2 (1)	2 (2)		
South Asian	14 (6)	3 (3)		
European, Middle Eastern, and Latin American	193 (81)	102 (87)		
BMI at booking[a]	25.5 (23.2–28.7)	24.6 (22.3–28.3)	**.02**	17 (5)
Antepartum hemorrhage[b]	67 (28)	77 (66)	**<.001**	0
Gestational age of first episode of antepartum hemorrhage (weeks)[a]	28 (26–32)	29 (24–33)	.44	0
Maternal outcomes				
Estimated blood loss[a]	2000 (1200–4000)	1550 (1000–3500)	.89	14 (4)
Blood units transfused[a]	2 (0–6)	2 (0–6)	.45	0
Maternal ITU admission[b]	78 (33)	53 (45)	**.02**	0
Gestational age at delivery (weeks)[a]	36 (35–37)	34 (32–36)	**<.001**	0
Major maternal morbidity[d]				
Renal failure[c]	0 (0)	1 (1)	.33	0
Bowel damage[c]	2 (1)	0 (0)	–	0
Urinary tract damage[c]	2 (1)	1 (1)	–	0
Bladder damage[b]	10 (4)	8 (7)	.31	0
Genitourinary fistula[c]	1 (0.4)	0 (0)	–	0
Cardiac arrest[c]	0 (0)	1 (1)	.33	0
Hemorrhagic shock[c]	1 (0.4)	1 (1)	.55	0
Wound infection[c]	0 (0)	2 (2)	.11	0
Thrombotic event[c]	2 (1)	2 (2)	.60	0
Sepsis[c]	1 (0.4)	0 (0)	–	0

Abbreviations: BMI, body mass index; D&C, dilation and curettage; ITU, intensive therapy unit.

Statistically significant p values (< .05) are written in bold.

[a]Data presented as median (IQR) and analyzed by Mann-Whitney U test.

[b]Data presented as n (%) and analyzed by Chi-square test.

[c]Data presented as n (%) and analyzed by Fisher's Exact test.

[d]Different morbidities in one mother are counted separately.

underwent planned versus emergency delivery. However, the rate of maternal Intensive Care Unit admission in women undergoing an emergency delivery was higher (45% vs 33%, P = .02). Even after grouping women with lower (2–3) and higher (4–6) grading of PAS, we found no significant differences in the main maternal outcomes (estimated blood loss and blood units transfused) in women with planned and emergency delivery, as it was in the overall population (Table S1). The rates of emergency delivery were similar among all six grades of PAS (Table 3). However, significantly higher rates of emergency delivery due to bleeding were reported in the lower grades of PAS (P = .03), indicating that the women at higher risk of emergency

delivery due to bleeding were the ones with either normal placentas (Grade 1) or milder grades of PAS (2/3/4).

Between 24^{+0} and 34^{+0} weeks' gestation, the babies delivered as emergencies were significantly smaller (P < 0.001), had higher 5 minute APGAR scores and spent longer in the Neonatal Intensive Care Unit (P < 0.001) compared with the babies who were planned to be delivered at that gestation (Table 4). Among women delivered before 34^{+0} weeks' gestation, there were no significant differences in the proportion of fetuses who received antenatal corticosteroids between the planned and the emergency group (75% vs 83%, P = .59). After 34^{+1} weeks' gestation, there were no significant differences

TABLE 2 Multilevel logistic regression analysis of risk factors for emergency cesarean delivery in pregnancies complicated with placenta accreta spectrum disorders

	Univariate		Multivariate	
	Crude OR (95% CI)	P values	Adjusted OR (95% CI)	P values
Gravidity	1.3 (1.1–1.5)	**.01**	1.2 (0.9–1.7)	.16
Parity	1.3 (1.1–1.6)	**.01**	1.1 (0.8–1.6)	.60
BMI at booking	0.9 (0.9–1.0)	**.02**	0.9 (0.9–1.0)	.06
Antepartum hemorrhage	5.0 (2.9–8.7)	**<.001**	4.7 (2.6–8.5)	**<.001**

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.

Statistically significant p values (< .05) are written in bold.

TABLE 3 Indication for delivery according to placenta accreta spectrum grade

	Grade 1 n = 26 (7%)	Grade 2 n = 56 (16%)	Grade 3 n = 58 (16%)	Grade 4 n = 135 (38%)	Grade 5 n = 52 (15%)	Grade 6 n = 29 (8%)	Total (n = 356)	P value
Planned delivery	19 (73)	40 (71)	38 (66)	90 (67)	33 (62)	19 (66)	239 (67)	.35
Emergency delivery	7 (27)	16 (29)	20 (34)	45 (33)	19 (38)	10 (37)	117 (33)	
Bleeding	3 (43)	8 (50)	7 (35)	19 (42)	2 (11)	2 (20)	41 (35)	.03
Labor and other reasons[a]	4 (57)	8 (50)	13 (65)	26 (58)	17 (89)	8 (80)	76 (65)	

Note: Data presented as n (%) and analyzed by Mann-Whitney U test. Data presented as n (%). Significant values in bold.

[a]The other possible reasons for emergency delivery stated are suspected ruptured uterus, maternal or fetal compromise.

seen between the planned and emergency outcomes except that the babies born as an emergency after 36^{+1} weeks were significantly smaller (P = .03). The rate of infants experiencing any major neonatal morbidity was 25% at 34^{+0} weeks and 19% at 36^{+0} weeks. There was one neonatal mortality; this baby was born at 34^{+4} weeks by emergency CD for fetal compromise. The baby was small for gestational age, weighing 1740 g at birth. There were no stillbirths.

4 | DISCUSSION

The major finding of this study is that in cases of antenatally suspected PAS, the estimated blood loss, transfusion rates and severe maternal morbidity for emergency delivery occurring in specialist centers are not significantly higher than those for planned delivery. Significantly more women were admitted to ITU in the emergency delivery cohort, but as ITU admission is a decision based on the facilities available, local protocols and preference of the surgical team, it is difficult to draw solid conclusions from this single metric in the absence of evidence of significant differences in transfusion rates and major morbidities. The only significant independent predictor of emergency CD was antepartum hemorrhage. Our results also demonstrated that emergency deliveries due to bleeding were significantly more likely to be diagnosed with either a normal placenta or a milder grade of PAS, suggesting that women at higher risk of emergency delivery due to bleeding might be the ones with the least aggressive invasion, representing the less surgically complex end of the PAS. This could explain the finding of similar blood loss and morbidity between planned and emergency cases. It is also biologically

plausible, as placentas deeply invading the pelvis would seem to be less likely to separate and therefore bleed significantly. This finding calls into question the often reported strategy of delivering PAS antenatally suspected to be very severe (FIGO grade 3 – percreta) earlier than milder ones to prevent maternal morbidity from an unscheduled emergency delivery.

When we compared the neonatal outcomes in women with planned vs emergency delivery within the same gestational range, there only differences were in the outcomes at gestations $<34^{+0}$ weeks. These outcomes were recorded at birth and did not translate to significant differences in major neonatal morbidity. This finding demonstrates that the most relevant factor affecting the neonatal outcome in women with PAS is gestational age at delivery, with better neonatal outcomes for higher gestational ages.

A guiding principle in the management of women with PAS is to achieve a scheduled delivery in order to reduce the probability of a woman needing emergent delivery, and therefore to improve maternal outcomes.[4] However, the desire to avoid an emergent delivery must be balanced against the risks of prematurity related to an earlier delivery. Different management strategies have been suggested by current guidelines, proposing a planned elective delivery for women with PAS ranging from 34^{+0} to 37^{+0} weeks,[10,15-18] further demonstrating that there is still a lack of evidence and expert consensus to recommend one gestational age over another (Table S2). The finding that in specialist centers for PAS the blood loss and maternal morbidity is not significantly different for emergent deliveries potentially pushes the balance of benefit in favor of later delivery in the interests of the neonate. We acknowledge that our findings are from highly experienced referral centers for the management of

TABLE 4 Neonatal outcomes by gestational age and planned or emergency delivery, from 24^{+0} to $\geq 36^{+1}$ weeks

	24^{+0} to 34^{+0} weeks			34^{+1} to 36^{+0} weeks			$\geq 36^{+1}$ weeks		
	Planned	Emergency	p value	Planned	Emergency	P value	Planned	Emergency	p value
Number of cases	27	65		99	33		113	19	
Birthweight in grams[a]	2315 (2143-2552)	1808 (1488-2100)	**<.001**	2550 (2415-2730)	2620 (2510-2840)	.38	3030 (2670-3305)	2860 (2540-2890)	**0.03**
5 min APGAR score[a]	9 (8-10)	8 (6-9)	**.02**	9 (7-10)	9 (7-10)	.40	9 (8-10)	10 (9-10)	0.17
Arterial pH[a]	7.31 (7.30-7.37)	7.30 (7.24-7.33)	.07	7.30 (7.26-7.34)	7.30 (7.26-7.35)	.67	7.29 (7.26-7.31)	7.27 (7.25-7.30)	0.27
Days in NICU[a]	0 (0-6)	12 (0-31)	**<.001**	0 (0-4)	0 (0-8)	.36	0 (0-0)	0 (0-0)	0.75
Major neonatal morbidities[b]									
Respiratory distress syndrome[c]	1 (6)	4 (24)	.18	11 (24)	3 (15)	.52	9 (17)	0 (0)	0.19
Severe jaundice (requiring phototherapy)[c]	1 (6)	4 (24)	.18	4 (9)	2 (10)	1.00	0 (0)	1 (8)	0.20
Severe infection (e.g. sepsis, meningitis)[c]	0 (0)	0 (0)	n/a	0 (0)	1 (5)	.30	0 (0)	0 (0)	n/a
IVH, NEC, neonatal encephalopathy, exchange transfusion[c]	0 (0)	0 (0)	n/a	0 (0)	0 (0)	n/a	0 (0)	0 (0)	n/a
Neonatal mortality									
Stillbirth	0 (0)	0 (0)	n/a	0 (0)	0 (0)	n/a	0 (0)	0 (0)	n/a
Neonatal death[c]	0 (0)	0 (0)	n/a	0 (0)	1 (5)	.30	0 (0)	0 (0)	n/a

Abbreviations: IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit. Statistically significant p values (< 0.05) are written in bold.

[a]Data presented as median (IQR) and analyzed by Mann-Whitney U test.

[b]each morbidity has been counted separately.

[c]data presented as n (%) and analyzed by Fisher's Exact test.

PAS and, therefore, the results of present study do not necessarily reflect the possible effect of this kind of delivery strategy in less experienced centers.

In a decision analysis published in 2010,[9] the optimal timing of delivery suggested for women with placenta previa and antenatal suspicion of PAS was 34 weeks. However, the main limitation of their study was that the risk of bleeding used to formulate the nine hypothetic management models included in the analysis was based on 400 women with placenta previa without PAS. Later data also suggested the possibility that women with placenta previa may be more likely to experience bleeding than those with PAS, and therefore, it may not be appropriate to extrapolate data from just placenta previa to those complicated by PAS.[19]

Gestational age at delivery was the most relevant factor influencing neonatal outcomes, further confirming that the advantages of avoiding emergency delivery with earlier intervention must be weighed against the neonatal risks of iatrogenic prematurity. Our data do not show a rise in maternal adverse outcomes in women undergoing an emergency delivery, with only an increased rate of ITU admission. This finding was not surprising, as similar results have already been reported in previous studies.[3-5] In our cohort, 26% of women with PAS had been delivered by 34^{+0} weeks of gestation, with >70% of those deliveries being an emergency. Of the 264 women remaining undelivered by 34^{+1} weeks, 33 (12.5%) experienced an emergency delivery before 36^{+0} weeks, with 99 (37.5%) being delivered electively. What remains unknown is why the decisions were made to deliver them electively and whether the emergency deliveries were scheduled for before or after 36 weeks. What was shown was the rate of infants experiencing any major neonatal morbidity decreased from 25% at 34^{+0} weeks to 19% at 36^{+0} weeks. Therefore, the decision to defer delivery until after 36 weeks in the absence of significant antenatal bleeding or other risk factors for pre-term labor suggested by the IS-AIP intrapartum guidelines[10] does not seem an unreasonable one.

Antepartum hemorrhage was the only significant independent predictor of emergency CD. We therefore support the recommendations from previous studies and guidelines, which advocate a management tailored to the individual woman's characteristics.[10]

In a previous study[20] limited by a small sample size, bleeding prior to 32 weeks' gestation was not associated with a significantly higher rate of emergent delivery compared with women without bleeding remote from term (60.0% vs 27.3%; P = .20). In our study, despite a wider cohort of women involved, there was no association between the gestational age of the first episode of antepartum hemorrhage and the occurrence of emergency delivery.

Despite the limitation due to small numbers in the higher grades of PAS, one key finding of this study is the trend towards higher rates of emergency delivery due to bleeding in the lower grades of PAS, showing that the women at higher risk of emergency delivery due to bleeding are the ones with milder grades of PAS. This finding is of relevant clinical value, as in milder cases with no invasion of adjacent organs and structures, a cesarean hysterectomy even in an emergency setting will be less likely to be extremely surgically complex,

and therefore less likely to increase maternal morbidity significantly. This finding might be explained by the fact that in higher grades of PAS, with diffuse placental invasion involving large areas of the placental attachment surface, the possibility of partial placental detachment and subsequent bleeding seems to be unlikely. Conversely, in lower grades of PAS, the coexistence of areas of normal adhesion together with areas of focal invasion is more likely, making the occurrence of focal placental detachment and subsequent bleeding more probable. Indeed, this speculation will need further evaluation in future studies.

Of note, 26 women (7%) with antenatal suspicion of PAS were found to be false-positives with no evidence of PAS during surgery. This false-positive rate is not high in comparison with previous reports[21] and it might reflect the high quality of care provided in the centers of excellence participating in this study. However, it once more highlights the need for an improvement in the antenatal diagnosis of PAS, in order to reduce the overtreatment of women without disease and to avoid the consequences of an iatrogenic premature delivery to their infants.

The strength of the present study is the wide population involved, with all the cases included managed in referral centers specialized in the management of PAS. One additional strength of this study is the use of a standardized definition of the intraoperative appearance of the PAS disease. This allowed a consistent definition of all the cases included in the database in terms of severity of the disease. Indeed, the heterogeneous definition used in former studies is the first challenge when dealing with PAS. The interpretation of the clinical evidence will vary according to the definitions used to diagnose PAS. To overcome all these limitations, in 2019 FIGO proposed a standardized clinical classification to describe and categorize the different aspects of PAS at the time of delivery.[14] The intraoperative classification adopted in the present study was the original grading system which the FIGO classification was developed from. Although very similar (grades 4, 5 and 6 are virtually identical to grades 3a, 3b and 3c) some of the definitions are different and therefore cannot be directly compared. This highlights how vital it is for future research to adopt a unique common classification to allow data comparison among different studies and centers.

One of the limitations of the present study is the retrospective collection of the data for cases occurring in 2008-2014. This might have introduced a selection bias and an observational bias in the data collected at that time. This limitation might have also impacted on the rate of missing information for some of the variables analyzed. For instance, the occurrence of any neonatal morbidity was not reported in 22 (6%) women in the study. Additionally, according to the actual form of the IS-PAS database, we were unable to provide any information about the amount/degree of bleeding before delivery, the number of bleeding episodes and the need for antepartum hospitalization, each of which may be a risk factor for an emergency delivery. Additional studies on such risk factors in women with PAS may be helpful and might be considered for future research. Furthermore, all participating

centers are in high-resource settings and have established PAS treatment teams; therefore, our results may not be generalizable to centers in low-income countries or without multidisciplinary team care. A final limitation due to the nature of the IS-PAS database in its current form, is the absence of a clear indication for emergency delivery in some cases, which might have led to an underestimation of the number of cases delivered due to hemorrhage. At the same time, the antenatally suspected disease severity was not reported in the database and we cannot exclude that this factor might have influenced the planned time of delivery for some cases.

5 | CONCLUSION

Emergency delivery in a center of excellence for PAS does not appear to increase maternal morbidity, but earlier delivery holds iatrogenic risks of prematurity for the neonate. The single greatest risk factor for emergency delivery is antenatal hemorrhage. Therefore, delivery at >36^{+0} weeks' gestation in women who have not bled and have no risk factors for pre-term birth could be considered. However, the findings from the present study should be interpreted with caution, as they are based on highly experienced referral centers for the management of PAS and therefore do not necessarily reflect the possible effect of this kind of delivery strategy in less experienced centers. Future research should be focused on the development of an accurate system to identify the women at lower risk of emergency delivery, whose infants might benefit from later delivery with no increase in maternal morbidity.

CONFLICT OF INTEREST
The authors have stated explicitly that there are no conflicts of interest in connection with this article.

ORCID
Maddalena Morlando https://orcid.org/0000-0002-1304-7575
Alexander Schwickert https://orcid.org/0000-0003-2360-6016
Vedran Stefanovic https://orcid.org/0000-0001-5230-1698
Mina M. Gziri https://orcid.org/0000-0003-3528-2389
Olivier Morel https://orcid.org/0000-0001-6359-1328
Thorsten Braun https://orcid.org/0000-0002-1989-9920
Charline Bertholdt https://orcid.org/0000-0001-9297-5363
Heleen J. Van Beekhuizen https://orcid.org/0000-0001-8899-7412
Sally L. Collins https://orcid.org/0000-0002-0648-7433

REFERENCES
1. Chantraine F, Nisolle M, Petit P, Schaaps J-P, Foidart J-M. Individual decisions in placenta increta and percreta: a case series. *J Perinat Med*. 2012;40:265-270.
2. Jauniaux E, Silver RM, Matsubara S. The new world of placenta accreta spectrum disorders. *Int J Gynaecol Obstet*. 2018;140:259-260.
3. Fitzpatrick K, Sellers S, Spark P, Kurinczuk J, Brocklehurst P, Knight M. The management and outcomes of placenta accreta, increta, and percreta in the UK: a population-based descriptive study. *BJOG*. 2014;121:62-71.
4. Eller AG, Porter TF, Soisson P, Silver RM. Optimal management strategies for placenta accreta. *BJOG*. 2009;116:648-654.
5. Al-Khan A, Gupta V, Illsley NP, et al. Maternal and fetal outcomes in placenta accreta after institution of team-managed care. *Reprod Sci*. 2014;21:761-771.
6. Shamshirsaz AA, Fox KA, Salmanian B, et al. Maternal morbidity in patients with morbidly adherent placenta treated with and without a standardized multidisciplinary approach. *Am J Obstet Gynecol*. 2015;212:218.e1-218.e9.
7. Silver RM, Fox KA, Barton JR, et al. Center of excellence for placenta accreta. *Am J Obstet Gynecol*. 2015;212:561-568.
8. Morlando M, Collins S. Placenta accreta spectrum disorders: challenges, risks, and management strategies. *Int J Womens Health*. 2020;12:1033-1045.
9. Robinson BK, Grobman WA. Effectiveness of timing strategies for delivery of individuals with placenta previa and accreta. *Obstet Gynecol*. 2010;116:835-842.
10. Collins SL, Alemdar B, van Beekhuizen HJ, et al. Evidence-based guidelines for the management of abnormally invasive placenta: recommendations from the International Society for Abnormally Invasive Placenta. *Am J Obstet Gynecol*. 2019;220:511-526.
11. Braun T, van Beekhuizen HJ, Morlando M, Morel O, Stefanovic V; IS-PAS. Developing a database for multicenter evaluation of placenta accreta spectrum. *Acta Obstet Gynecol Scand*. 2021;100(Suppl. 1): 7-11.
12. Collins SL, Stevenson GN, Al-Khan A, et al. Three-dimensional power Doppler ultrasonography for diagnosing abnormally invasive placenta and quantifying the risk. *Obstet Gynecol*. 2015;126:645-653.
13. Jauniaux E, Chantraine F, Silver RM, Langhoff-Roos J; for the FIGO Placenta Accreta Diagnosis and Management Expert Consensus Panel. FIGO consensus guidelines on placenta accreta spectrum disorders: epidemiology. *Int J Gynecol Obstet*. 2018;140:265-273.
14. Jauniaux E, Ayres-de-Campos D, Langhoff-Roos J, Fox KA, Collins S; FIGO Placenta Accreta Diagnosis and Management Expert Consensus Panel. FIGO classification for the clinical diagnosis of placenta accreta spectrum disorders. *Int J Gynaecol Obstet*. 2019;146:20-24.
15. Allen L, Jauniaux E, Hobson S, Papillon-Smith J, Belfort MA; FIGO Placenta Accreta Diagnosis and Management Expert Consensus Panel. FIGO consensus guidelines on placenta accreta spectrum disorders: nonconservative surgical management. *Int J Gynaecol Obstet*. 2018;140:281-290.
16. Jauniaux E, Alfirevic Z, Bhide AG, et al. Placenta praevia and placenta accreta: diagnosis and management. Green-top Guideline No. 27a. *BJOG*. 2019;126(1):e1-e48.
17. Hobson SR, Kingdom JC, Murji A, et al. No. 383-screening, diagnosis, and management of placenta accreta spectrum disorders. *J Obstet Gynaecol Can*. 2019;41(7):1035-1049.
18. American College of Obstetricians and Gynecologists, Society for Maternal-Fetal Medicine. Obstetric care consensus no. 7: placenta accreta spectrum. *Obstet Gynecol*. 2018;132:e259-e275.
19. Rac MWF, Wells CE, Twickler DM, Moschos E, McIntire DD, Dashe JS. Placenta accreta and vaginal bleeding according to gestational age at delivery. *Obstet Gynecol*. 2015;125:808-813.

20. Fishman SG, Chasen ST. Risk factors for emergent preterm delivery in women with placenta previa and ultrasound findings suspicious for placenta accreta. *J Perinat Med*. 2011;39:693-696.

21. D'Antonio F, Iacovella C, Bhide A. Prenatal identification of invasive placentation using ultrasound: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2013;42:509-517.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

APPENDIX 1

Members of the International Society for Placenta Accreta Spectrum (IS-PAS) who contributed PAS cases and are not listed as authors:

Pavel Calda, Department of Obstetrics and Gynecology First Faculty of Medicine Charles University and General University Hospital in Prague, Czech Republic. Fredric Chantraine, Department of Obstetrics and Gynecology, Centre Hospitalier Universitaire de Liège, site CHR Citadelle, Liège, Belgium. Johannes J. Duvekot, Department of Obstetrics and Gynecology, Division of Obstetrics and Prenatal Medicine, Erasmus MC, University Medical center Rotterdam, Rotterdam, The Netherlands. Karin Fox, Division of Maternal-Fetal Medicine, Dept of OB-GYN, Baylor College of Medicine, Houston, TX, USA. Lene Gronbeck, Department of Obstetrics, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark. Wolfgang Henrich, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Obstetrics, Berlin, Germany. Pasquale Martinelli, Department of Neuroscience, Reproductive Sciences and Dentistry, University Federico II Naples, Italy. Jorma Paavonen, Department of Obstetrics and Gynecology, Helsinki University Hospital and University of Helsinki, Finland. Philippe Petit, Department of Obstetrics and Gynecology, Centre Hospitalier Universitaire de Liège, site CHR Citadelle, Liège, Belgium. Marcus Rijken, Department of Obstetrics, Division Women and Baby, University Medical center Utrecht, Utrecht University, Utrecht, The Netherlands and Julius Global Health, The Julius center for Health Sciences and Primary Care, University Medical center Utrecht, Utrecht University, Utrecht, The Netherlands. Mariola Ropacka, Department of Perinatology and Gynecology, Poznan University of Medical Sciences, Poland. Minna Tikkanen, Department of Obstetrics and Gynecology, Helsinki University Hospital and University of Helsinki, Finland. Alexander Weichert, Practice for Prenatal Diagnosis, Bergmannstrasse, Berlin and Department of Obstetrics, Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin Institute of Health, Campus Virchow-Klinikum, Berlin, Germany. Katharina von Weizsäcker, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Obstetrics, Berlin, Germany.