





COMMENTARY

Developing a database for multicenter evaluation of placenta accreta spectrum

Thorsten Braun^{1,2}  | Heleen J. van Beekhuizen³  | Maddalena Morlando⁴  |
Olivier Morel⁵ | Vedran Stefanovic⁶  | on behalf of the International Society for Placenta
Accreta Spectrum (IS-PAS)*

¹Department of Obstetrics, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin, Germany

²Department of Experimental Obstetrics, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin, Germany

³Department of Gynecological Oncology, Erasmus MC Cancer center, Rotterdam, The Netherlands

⁴Obstetrics and Gynecology Unit, Department of Woman, Child and General and Specialized Surgery, University of Campania “Luigi Vanvitelli”, Naples, Italy

⁵Womens’ Unit, Nancy Regional and University Hospital Center (CHRU), Université de Lorraine, Nancy, France

⁶Department of Obstetrics and Gynecology, Fetomaternal Medical Center, Helsinki University Hospital and University of Helsinki, Finland

Correspondence

Thorsten Braun, Department of Obstetrics, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, 13353 Berlin, Germany.
Email: thorsten.braun@charite.de

Abstract

Studies of rare, but complex clinical conditions require multicenter cooperation. The International Society for Placenta accreta spectrum (IS-PAS) have established a secure web-based database to analyze pregnancies complicated by PAS. By repeated in-person meetings of the IS-PAS, a core dataset was established. Then, a custom-made, secure online database, capable of receiving strictly anonymized patient-related textual and imaging data and allowing statistical queries was designed, tested, amended and implemented. Between 2008 and 2019, 14 IS-PAS centers across Europe and one center in the USA contributed data for all their PAS cases, containing pregnancy data for a total of 442 pregnant women. Data were analyzed by a designated data analysis sub-group of the IS-PAS. Center characteristics are presented. Based on experiences with previous versions, our new online database now allows an all-encompassing data collection. It has shown its usefulness in the current analysis project.

KEYWORDS

abnormally invasive placenta, case reporting form, online database, placenta accreta spectrum

Placenta accreta spectrum (PAS) describes a placenta that does not separate spontaneously after delivery of the fetus and cannot be detached without causing massive and potentially life-threatening

blood loss.^{1,2} The incidence of PAS has been shown to be rising worldwide,^{3,4} most likely due to the increasing rates of cesarean delivery, which is also the major risk factor for PAS in subsequent pregnancies. PAS is one of the most dangerous conditions of pregnancy, as it is significantly associated with maternal morbidity and mortality.⁵

Abbreviations: PAS, placenta accreta spectrum; IS-PAS, international society for placenta accreta spectrum.

*See Appendix.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2021 The Authors. *Acta Obstetrica et Gynecologica Scandinavica* published by John Wiley & Sons Ltd on behalf of Nordic Federation of Societies of Obstetrics and Gynecology (NFOG).

Given the heterogeneous definition of this condition used in the literature, the lack of correlation among ultrasound signs, clinical presentation and histopathologic diagnoses, the retrospective design of the available studies, and a sample size limited to case reports, case series and small cohort studies, good quality evidence on PAS is still lacking.^{6,7}

The International Society for Placenta Accreta Spectrum (IS-PAS) (www.is-pas.org; formerly International Society for Abnormally Invasive Placenta) is a registered not-for-profit association of about 50 clinicians and basic science researchers from 17 countries. The aim of the IS-PAS is to promote excellence in all aspects of health-care relating to PAS, including research, clinical diagnosis, management, and education, especially with a view to prevention.

Since its first meeting, the need for prospective data and larger cohorts to provide accurate evidence on PAS was clear. By repeated in-person meetings of the IS-PAS, held in clinical centers across Europe, a core dataset was established. In 2012, a first version (paper-based case reporting form) was established, based on the UK Obstetric Surveillance System (UKOSS) collecting form modified for the needs of the study group. In 2016, a custom-made, secure online database FetView (FetView; Zeitgeist Health SE), capable of receiving strictly anonymized patient-related textual and imaging data and allowing statistical queries, was designed, tested, amended and implemented. It is currently in use, allowing the construction of the IS-PAS international registry.

The case reporting form is available as Figure S1. The IS-PAS Grading⁸ used in this case reporting form was proposed by FIGO 2018³ before the FIGO classification for the clinical diagnosis of placenta accreta spectrum disorders was published⁹ (Table 1). A core group was established consisting of five IS-PAS members from four centers which conducted data extraction and data cleaning for quality approach.

Fourteen European and one non-European center (USA) provided cases retrospectively treated between 2008 and 2014 and prospectively treated from 2014 to 2019. Our database allows for the registration of antenatally suspected PAS cases via ultrasound or MRI; this explains how G1 cases with normal placentation are entered into the registry. A perinatal clinical and pathological confirmation of PAS facilitates further classification of our cases according to the FIGO grading system.⁹ The classification of the cases into grades alleviates the problem that limits the utility of available literature in matters of PAS, namely, the binary analysis for a disorder that presents as a spectrum of severity. Local Ethical Committee/IRB approval and Data Use Agreements were obtained by each center according to local policies (Table S2). Selected characteristics of the contributing centers (dated from 2019) are shown in Table S3.

All the contributing centers are specialized in PAS management,⁶ with between 1950 and 9405 deliveries (mean 5179) in 2019. Cesarean section (C-section) rates ranged between 17.0% and 50.4% (mean 29.0%). The respective national C-section rates also varied considerably, ranging between 16.7% and 45.3% (mean 25.1%). Mean numbers of PAS cases in 2019 were 11 per center (range 4–55). All suspected PAS cases were examined by an obstetrician with

Key message

The International Society for Placenta accreta spectrum (IS-PAS) focused on improving the diagnosis and treatment of PAS. Successful development of an online database made it possible to set up the first international multi-center study on PAS and analyses of a number of clinically relevant questions will be published.

specific expertise in PAS management and in almost all centers, management was multidisciplinary (93%). A gynecologic oncologist was reported to be present or on standby during cesarean section in 50% of centers but and in 31% of centers only in rare cases or never. In 12.5% of the centers, cystoscopy was always performed, in 47% only in selected cases (eg example with suspected bladder invasion) and in 18.8% of the centers never. Ureteric stents were placed in each PAS case in only 18.7% of the centers, in 43.8% of the centers only in selected cases with suspected bladder wall invasion, and in 37.5% of centers ureteric stents were never placed before surgery. An interventional radiology suite was available in almost all centers (93.7%). Magnetic resonance imaging (MRI) was always performed preoperatively in 56.2% of the centers in cases with suspected PAS and in 37.5% of centers only in selected cases. The timing of delivery in PAS cases without any bleeding during pregnancy varied. The timing of elective cesarean section varied between 34⁺⁰ and 39⁺⁰ weeks of gestation (mean 35⁺⁰ weeks). A feedback session with the team was always arranged after discharge in 75% of centers. A special team for PAS treatment in the case of non-elective surgery was available 24 hours, 7 days per week in 62.5% of the centers. Antenatal steroids for fetal maturation were electively administered after 35⁺⁰ weeks of gestation in 50% of the centers.

Based upon the FIGO classification at the time of recruitment, a total of 442 cases (410 grades 2–6) were enrolled into the study. The majority of cases ($n = 382$ of 442) were entered between 2013 and 2019. The case distribution regarding the PAS grading is shown in Figure 1 and Table S4.

There are several topics where evidence-based recommendations due to lack of conclusive relevant studies could not be formulated, therefore our recommendations of the IS-PAS guidelines were often based on expert consensus.⁶ As a large range of information has now been collected and is based on the recommendations previously published by the society, a core group decided to try to document the following questions better by analyzing the IS-PAS database:

- Determinants for neonatal outcomes
- Respective diagnostic value of ultrasound and MRI
- Reasons for high blood loss
- Impact of body mass index (BMI)
- Impact of management strategy: hysterectomy, conservative approach, focal resection

TABLE 1 The clinical grading system for Placenta accreta spectrum used in the present IS-PAS database was proposed by FIGO in 2018,³ before the “clinical diagnosis of placenta accreta spectrum disorders classification” was published by FIGO in 2019⁹

FIGO clinical class			IS-PAS grading	
CLASS	Clinical findings	Histopathology findings	GRADE	
Not graded	Normal placental separation	Normal placenta	1	At cesarean or vaginal delivery: complete placental separation at third stage; not Placenta accreta spectrum
1	No separation with oxytocin and gentle cord traction; attempts at manual removal result in heavy uterine bleeding from the placental implantation site requiring mechanical or surgical procedures At laparotomy, the uterus shows no obvious bulge or distension, no placental tissue seen extruding, and minimal to no neovascularity	Microscopic examination of the placental bed samples from hysterectomy specimen shows extended areas of absent decidua between villous tissue and myometrium with placental villi attached directly to the superficial myometrium The diagnosis cannot be made on just delivered placental tissue nor on random biopsies of the placental bed	2	At cesarean delivery or laparotomy: no placental tissue seen invaded through the serosal surface of the uterus; only partial separation with synthetic oxytocin and gentle controlled cord traction, manual removal of placenta required for remaining tissue AND parts of placenta thought to be abnormally adherent by a senior, experienced clinician At vaginal delivery; manual removal of placenta required AND parts of placenta thought to be abnormally adherent by a senior, experienced clinician
2	At laparotomy, abnormal macroscopic findings over the placental bed: bluish/purple coloring, distension (placental “bulge”) Significant amounts of hypervascularity (dense tangled bed of vessels or multiple vessels running parallel craniocaudally in the uterine serosa) No placental tissue seen to be invading through the uterine serosa Gentle cord traction results in the uterus being pulled inwards without separation of the placenta (so-called dimple sign)	Hysterectomy specimen or partial myometrial resection of the increta area shows placental villi within the muscular fibers and sometimes in the lumen of the deep uterine vasculature (radial or arcuate arteries)	3	At cesarean delivery or laparotomy: no placental tissue seen invaded through the serosal surface of the uterus; no signs of any separation with synthetic oxytocin and gentle controlled cord traction, manual removal of placenta required AND the whole placental bed thought to be abnormally adherent by a senior, experienced clinician At vaginal delivery: manual removal of placenta required AND the whole placental bed thought to be abnormally adherent by a senior, experienced clinician
3a	Limited to the uterine serosa At laparotomy, abnormal macroscopic findings on uterine serosal surface (as above) and placental tissue seen to be invading through the surface of the uterus No invasion into any other organ, including the posterior wall of the bladder (a clear surgical plane can be identified between the bladder and uterus)	Hysterectomy specimen showing villous tissue within or breaching the uterine serosa	4	At cesarean delivery or laparotomy: placental tissue seen to have invaded through the serosal surface of the uterus but NOT passing into any surrounding structures (including the posterior wall of the urinary bladder); a clear surgical plane can be identified between the bladder and uterus to allow nontraumatic reflection of the urinary bladder at hysterectomy
3b	With urinary bladder invasion At laparotomy, placental villi are seen to be invading into the bladder but no other organs Clear surgical plane cannot be identified between the bladder and uterus	Hysterectomy specimen showing villous tissue breaching the uterine serosa and invading the bladder wall tissue or urothelium	5	At cesarean delivery or laparotomy: placental tissue seen to have invaded through the serosal surface of the uterus AND invaded into the urinary bladder ONLY (consequently, a clear surgical plane cannot be identified between the bladder and uterus to allow nontraumatic reflection of the urinary bladder at hysterectomy)
3c	With invasion of other pelvic tissue/organs Placental villi are seen to be invading into the broad ligament, vaginal wall, pelvic sidewall or any other pelvic organ (with or without invasion of the bladder)	Hysterectomy specimen showing villous tissue breaching the uterine serosa and invading pelvic tissues/organs (with or without invasion of the bladder)	6	At cesarean delivery or laparotomy: placental tissue seen to have invaded through the serosal surface of the uterus AND invaded into the pelvic side wall or any organ other than the urinary bladder, with or without invasion into the urinary bladder

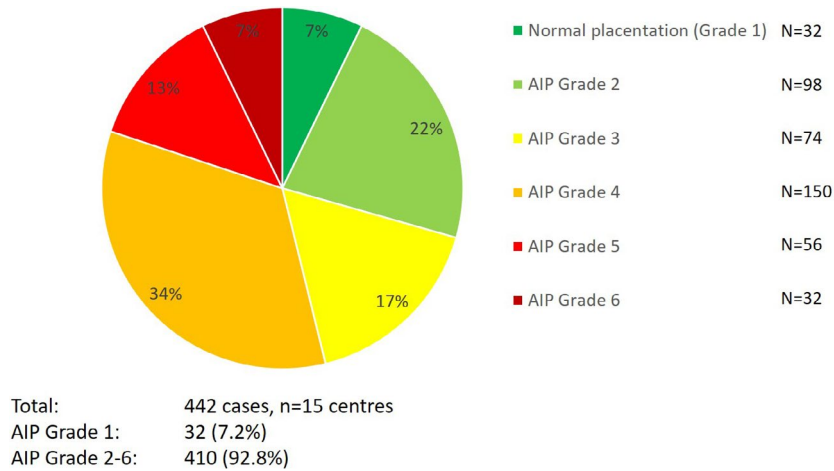


FIGURE 1 PAS case grading distribution [Color figure can be viewed at wileyonlinelibrary.com]

Authorship was based on the International Committee of Medical Journal Editors' recommendations.¹⁰ For reporting data, the STROBE¹¹ methodology was recommended. After completing the first drafts of papers within the authors' writing groups, data and manuscripts were presented to all IS-PAS members for evaluation, discussion and final approval.

Missing data are a limitation of this study. Indeed, it was found that certain categories of information, in particular those about antenatal imaging and neonatal outcome, were less exhaustive for the gynecologists and obstetricians who were responsible for filling in the database. This led to completeness discrepancy between different data categories and will be specifically discussed in the corresponding manuscripts.

One of the main limitations of the IS-PAS cohort is that it includes only patients from specialized referral centers and it is not possible to evaluate the global incidence of PAS. That could have been a very interesting analysis, considering the wide differences in national cesarean section rates between the different participating countries (ranging from 16.7% in Finland to 45.3% in Poland). However, as previously emphasized, this international case collection also offers the major advantage of providing data from teams with different practices. The variety of team organization, management techniques and the number of cases is more important here than in the other recent large PAS cohort study, that is, the PACCRETA study, in which only French centers participated and in which the practices described were limited to the conservative management vs cesarean hysterectomy.¹²

Even before entering into the analysis of the various clinical questions which will be developed subsequently, the construction of this cohort itself provides very interesting information as to the great differences in practices and organization in Europe. It is evident from Table S3 that the IS-PAS centers are heterogeneous in their characteristics, and although they all are required to meet certain standards before joining the society, variations regarding the diagnosis and management of PAS cases in each center persist. More effort is therefore needed to test which of the defined criteria are essential for a participating center. For example, although all centers included in this registry are recognized as specialized PAS

centers, 38% of them do not have cell salvage availability on site. Interventional radiology is also not always available and in some of the centers there is no 24-hour designated specialist or systematic feedback session.

The discrepancy of national recognition of specialized PAS departments is mirrored in the lack of national guidelines for PAS management for 50% of the IS-PAS centers. It would be exciting to compare the impact of different practices and organizations on diagnostic and care performance, for the first time based upon a simultaneous case report in a unique database; of course keeping in mind that it is not a controlled trial.

ACKNOWLEDGMENTS

We thank David Dostal, FetView, Zeitgeist Health SE, Prague, Czech Republic, for his great in setting up and managing the database.

CONFLICT OF INTEREST

None.

ORCID

Thorsten Braun <https://orcid.org/0000-0002-1989-9920>

Heleen J. van Beekhuizen <https://orcid.org/0000-0001-8899-7412>

Maddalena Morlando <https://orcid.org/0000-0002-1304-7575>

Vedran Stefanovic <https://orcid.org/0000-0001-5230-1698>

REFERENCES

1. Jauniaux E, Collins S, Burton GJ. Placenta accreta spectrum: pathophysiology and evidence-based anatomy for prenatal ultrasound imaging. *Am J Obstet Gynecol*. 2018;218:75-87.
2. Chantraine F, Langhoff-Roos J. Abnormally invasive placenta – AIP. Awareness and pro-active management is necessary. *Acta Obstet Gynecol Scand*. 2013;92:369-371.
3. Jauniaux E, Chantraine F, Silver RM, Langhoff-Roos J. Diagnosis FPA, Management Expert Consensus P. FIGO consensus guidelines on placenta accreta spectrum disorders: epidemiology. *Int J Gynaecol Obstet*. 2018;140:265-273.
4. Morlando M, Sarno L, Napolitano R, et al. Placenta accreta: incidence and risk factors in an area with a particularly high rate of cesarean section. *Acta Obstet Gynecol Scand*. 2013;92:457-460.

5. Fitzpatrick KE, Sellers S, Spark P, Kurinczuk JJ, Brocklehurst P, Knight M. The management and outcomes of placenta accreta, increta, and percreta in the UK: a population-based descriptive study. *BJOG*. 2014;121:62-70; discussion 1.
6. 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.
7. Jauniaux E, Bhide A, Kennedy A, et al. FIGO consensus guidelines on placenta accreta spectrum disorders: prenatal diagnosis and screening. *Int J Gynaecol Obstet*. 2018;140:274-280.
8. 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.
9. Jauniaux E, Ayres-de-Campos D, Langhoff-Roos J, et al. FIGO classification for the clinical diagnosis of placenta accreta spectrum disorders. *Int J Gynaecol Obstet*. 2019;146:20-24.
10. JCMJE. Defining the Role of Authors and Contributors International Committee of Medical Journal Editors 2020. <http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>
11. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370:1453-1457.
12. Kayem G, Deneux-Tharoux C, Sentilhes L, group P. PACCRETA: clinical situations at high risk of placenta ACCRETA/percreta: impact of diagnostic methods and management on maternal morbidity. *Acta Obstet Gynecol Scand*. 2013;92:476-482.

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)¹¹ who contributed PAS cases and who are not listed as authors:

Ammar Al Naimi, Department of Obstetrics and Gynecology, Buergerhospital – Dr Senckenberg Foundation, and Department of Obstetrics and Gynecology, University Hospital of the Goethe University of Frankfurt, Frankfurt, Germany.

Charline Bertholdt, Université de Lorraine, CHRU-NANCY, Pôle de la Femme, F-54000 Nancy, France and Université de Lorraine, Inserm, IADI, F-54000 Nancy, France.

Pavel Calda, Department of Obstetrics and Gynaecology First Faculty of Medicine Charles University and General University Hospital in Prague, Prague, Czech Republic.

Kinga M. Chalubinski and Petra Pateisky, Department of Obstetrics and Gynecology, Division of Obstetrics and Feto-Maternal Medicine, Medical University of Vienna, Vienna, Austria.

Fredric Chantraine and Philippe Petit, Department of Obstetrics and Gynecology, Centre Hospitalier Universitaire de Liège, site CHR Citadelle, Liège, Belgium.

Sally Collins, Nuffield Department of Women's and Reproductive Health, University of Oxford, and the Fetal Medicine Unit, John Radcliffe Hospital, Oxford, UK.

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, Texas, USA.

Lene Gronbeck, Department of Obstetrics, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark.

Wolfgang Henrich, Andreas Nonnenmacher, Alexander Schwickert and 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.

Pasquale Martinelli, MD Department of Neuroscience, Reproductive Sciences and Dentistry, University Federico II Naples, Naples, Italy.

Mina Mhallem Gziri, Department of Obstetrics, Cliniques Universitaires Saint-Luc, Brussels, Belgium.

Jorma Paavonen and Minna Tikkanen, Department of Obstetrics and Gynecology, Helsinki University Hospital and University of Helsinki, Finland.

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.

Gita Strindfors, Department of Obstetrics and Gynecology, South General Hospital (Södersjukhuset), Stockholm, Sweden.

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.