

Supplementary Table 1. Number of cases per center included in the analysis.

Center	Frequency	Percent
Liege, Belgium	12	3.6
Berlin, Germany	57	16.9
Oxford, England	73	21.6
Brussels, Belgium	8	2.4
Helsinki, Finland	16	4.7
Poznan, Poland	32	9.5
Prague, Czech Republic	8	2.4
Vienna, Austria	12	3.6
Stockholm, Sweden	15	4.4
Nancy, France	13	3.8
Utrecht, Netherlands	5	1.5
Houston, USA	18	5.3
Rotterdam, Netherlands	10	3.0
Naples, Italy	33	9.8
Copenhagen, Denmark	26	7.7
Total	338	100.0

Supporting information S1. Material and methods.

Selection of study groups

So far, different definitions of severe postpartum hemorrhage have been proposed. Possible thresholds for estimated total blood loss include >1000 mL,^{1,2} >1500 mL,³ >2000 mL,⁴ or >2500 mL⁵ within 24 hours of birth. Other parameters include transfusion of ≥ 4 units,³ ≥ 5 units⁵ or ≥ 8 units⁶ of blood; or a decrease in hemoglobin levels ≥ 4 g/dL.³ As centers in different countries may differ in their local protocols for the administration of red blood cell concentrates and postpartum hemoglobin levels need to be collected in a standardized manner, which was not implemented in this retrospective evaluation, we chose not to base our analyses on these measures. To produce analyses that are independent from diverging recommendations and to take into account that the study comprises cases from 15 referral centers on different continents, we chose to define the thresholds of severe blood loss based on the 75th and 90th percentiles of the cohort itself.

Statistical analysis

To identify the factors associated with high and extraordinarily high blood loss, we compared pregnancies with blood loss until 3500ml and more than 3500ml by univariate and multivariate analyses. In a second step, pregnancies with blood loss until 5500ml and more than 5500ml were compared. A random-intercept multilevel logistic regression model served to control for the intraunit correlation of the outcome.

The following factors were included in the model as dependent variables:

- Number of previous cesarean deliveries
- Presence of placenta previa
- Antenatal PAS diagnosis (antenatally suspected vs unsuspected PAS)
- IS-PAS grades of invasion 2 - 6⁷
- Degree of urgency of delivery, defined as:
 - immediate threat to life of woman or fetus (“crash” or “emergent”)
 - maternal or fetal compromise which is not immediately life-threatening (“urgent” or “within 30 minutes”)
 - needing early delivery but no maternal or fetal compromise

- at a time suitable to both the woman and maternity team (“elective” or “scheduled”)

- Experience of the surgeon: specialist in PAS vs gynecologist/obstetrician with no particular training in PAS (definition: an expert is a person with significant experience in PAS and a high level of knowledge and/or skills relating to the condition)⁸
- Operative management
 - Type of management (planned hysterectomy, unplanned hysterectomy, focal resection, placenta left in situ with uncomplicated resorption, placenta in situ followed by planned or unplanned delayed hysterectomy)
 - Position of the uterine incision (fundal, lower transverse, transverse above placenta)
- Measures to support uterine contraction/aid blood clotting
 - Oxytocin (prophylactic administration: before increased blood loss occurred, therapeutic administration: after increased blood loss occurred)
 - Tranexamic acid (prophylactic administration: before increased blood loss occurred, therapeutic administration: after increased blood loss occurred)
 - Prostaglandin F2 α / E2 / E1 (prophylactic administration: before increased blood loss occurred, therapeutic administration: after increased blood loss occurred)
 - Intrauterine balloon (prophylactic administration: before increased blood loss occurred, therapeutic administration: after increased blood loss occurred)
- Perioperative occlusion of uterine blood supply
 - Pelvic arterial embolization
 - Intravascular balloon
 - Uterine artery ligation
 - Internal iliac artery ligation

Quantitative co-variables with linear associations were entered in the model as continuous. We assessed the variability of the blood loss between maternity units by the inter-unit variance in multilevel logistic regression models, through definition of the 15 centers as the second level variable. In a first step, the influence on peripartum blood loss was calculated for each first level variable separately (univariate analysis). In analyses comparing planned management approaches, planned hysterectomy was the reference category for operative management as this is the most commonly used, definitive immediate treatment of placenta accreta spectrum.⁹ Crude odds ratios with 95% confidence interval (95% CI) were calculated for all results. In a

second step, a multivariate regression analysis was carried out, including variables that had been identified as having a significant effect in univariate analysis ($p \leq 0.05$). This applied to the following variables: operative management, PAS Grading, grade of surgeon, urgency of CD. Management variables such as the administration of uterotonics, tranexamic acid, or vascular occlusion were excluded from multivariate analyses when used only therapeutically, i.e. after high blood loss had already occurred. They would have been included, when used prophylactically. Multivariate analyses yielded adjusted odds ratios with 95% confidence interval (95% CI). The proportion of missing values was $\leq 5\%$ for all variables. For most categorical predictor variables, the option with the least assumed blood loss was chosen as the reference category. For adjunctive measures (measures to support uterine contraction/aid blood clotting, perioperative occlusion of uterine blood supply), the renunciation of the use of the measure was used as the reference category (e.g. “no oxytocin”). Analyses were conducted using SPSS® v26 (IBM®, Coppel, TX, USA).

References of Supporting information S1.

1. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 183: Postpartum Hemorrhage. *Obstet Gynecol.* 2017;130(4):e168-e186.
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Supporting information

Appendix S2. Material and methods.

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