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Management and outcomes of women with placenta accreta spectrum grade 3: an INOSS multicountry multiperiod population-based study

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Abstract

Background Management and outcomes in women with placenta accreta spectrum grade 3 are rarely reported from population-based studies. The objective of this study is to describe profiles, management, and outcomes, of women with placenta accreta spectrum (PAS) grade 3 from three multiperiod studies.

Methods This analysis used data from three multiperiod population-based cohort studies from the United Kingdom (UK) (May 2010–April 2011), France (November 2013–October 2015), and Italy (September 2014–August 2016) to compare the management and outcomes of women with grade 3 PAS. The main outcome measures were postpartum hemorrhage (PPH) ≥ 3000 mL, blood transfusion ≥ 4 units, and other severe maternal complications (death, damage to bowel or urinary tract).

Results This study included 39 women with PAS grade 3 in the UK, 51 in France, and 34 in Italy, a total of 124 women. PAS was suspected before birth in 59% of the UK cases, 88% in France, and 82% in Italy ($P < .01$). Conservative management was attempted only in the UK (38%) and in France (61%). PPH ≥ 3000 mL occurred in 54% of the UK women, 25% in France, and 12% in Italy ($P < .01$); 67% in the UK, 47% in France, and 41% in Italy received blood transfusion ≥ 4 units ($P = .06$). The final (immediate and secondary) hysterectomy rate differed significantly between the three countries: 69% in the UK, 57% in France, 100% in Italy ($P < .01$).

Conclusion Maternal outcomes in women with grade 3 PAS varied between the three periods and countries, alongside the evolution in prenatal screening and peri-operative management.

Trial registration For the UK: reference number: RP-PG-0608-10038. For France: reference number: AOR12156. For Italy: reference number: Port. PRE-839/13

Keywords Placenta accreta, Post-partum hemorrhage, Population-based study

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Background

Placenta accreta spectrum (PAS), caused by abnormal invasion of the chorionic villi into the myometrium [1], is usually classified into three grades according to the depth of placental invasion. Its most invasive form is grade 3 (also known as placenta percreta): the placenta invades the uterine serosa or the urinary bladder or other pelvic tissue/organs.[2] This grade is associated with the highest level of severe maternal morbidity [3, 4] and accounts for 7–29%[5–8] of PAS cases. Its reported prevalence ranges from 0.21 to 0.84 per 10,000 deliveries [5–8].

Despite its severity, the morbidity and management of grade 3 PAS are understudied, probably because its rarity makes it difficult to assemble adequate numbers of women. The available literature includes only three previous series – one of which is quite dated - focused on grade 3 PAS; these single-center, retrospective studies were limited by the questionable generalizability of their findings to the broader population [3, 9, 10]. Defining the optimal management for these women thus remains challenging, especially, the choice between the two principal strategies: cesarean hysterectomy and conservative management [11, 12]. Moreover, PAS management may include additional interventions that can take place either before surgery — preoperative ureteral catheters, preoperative intravascular balloon catheter — or during or after surgery — uterine sutures or pelvic vessel ligation and prophylactic artery embolization [13–16]. None of these procedures are evidence-based for this condition but their implementation has varied over time.

We therefore conducted an international observational comparative analysis between different time periods and countries illustrating different management policies. Three International Network of Obstetrics Survey Systems (INOSS) members conducted separate population-based studies of PAS from three periods: the United Kingdom (UK) in 2010–2011, France in 2013–2015, and Italy in 2014-2016 [5, 6, 17–19]. Together they coordinated this study to analyze population-based data on this form of PAS. Although the management of PAS has evolved since the study period in each country, their combined analysis may help to understand the differences in outcomes according to the management historically used in each country. Indeed, the outcome do not rely only on a treatment such as conservative treatment or cesarean hysterectomy but depends on many factors such as care organization, prenatal diagnosis of PAS and adjuvant therapies.

Our objective was to conduct a comparative analysis of management and outcomes in women with grade 3 PAS in studies conducted in the UK, France, and Italy at various time periods.

Methods

Study design

This analysis of three population-based studies of women with grade 3 PAS compared management and outcomes from the UK, France, and Italy [5, 6, 17–19].

Data sources

UKOSS (UK)

The UKOSS (UK Obstetric Surveillance System for rare disorders of pregnancy) is a prospective database with rolling inclusion in every UK maternity hospital of uncommon pregnancies conditions (fewer than 1 case in 2000) that are significant causes of maternal morbidity and/or mortality over a given period [20]. Women with a diagnosis of PAS were identified nationally from May 2010 to April 2011. Women were included as having PAS if they met any of the following criteria: (1) placenta accreta/increta/percreta diagnosed histologically after hysterectomy or post-mortem, or (2) an abnormally adherent placenta, requiring active management, including conservative management where the placenta is left in situ. Women who had a manual placental removal with minimal or moderate difficulty but required no additional active management were excluded. Active management was defined by the need for some other manipulation to remove the placenta that resulted in its partial or piecemeal removal with clear documentation that the clinician did not feel it was fully removed. The UKOSS data on PAS cases have previously been published [5, 17].

At the time of data collection, the national recommendations for PAS issued in 2005 left the choice of delivery management for PAS to the team's choice [20].

PACCRETA (France)

The PACCRETA was a prospective population-based study conducted in 176 maternity hospitals in 12 French regions between November 1, 2013, and October 31, 2015. From a source population of 520,114 births, i.e., 30% of the national total, all women with PAS were included in the immediate postpartum period (i.e., after live- or stillbirth after 22 weeks of gestation). PAS was defined by at least one of the following criteria: (1) manual removal of the placenta partially or totally impossible and no cleavage plane between part or all of the placenta and the uterus, (2) massive bleeding from the implantation site after forced placental removal in the absence of another cause of postpartum hemorrhage (PPH), (3) histological confirmation of PAS on a hysterectomy specimen, and (4) signs of PAS at laparotomy in women with suspected PAS on prenatal imaging. The study protocol and a descriptive analysis of the PAS cases have been published [6, 19].

At the time of data collection, national recommendations for PAS had been issued in 2004 and did not

prioritize either conservative treatment or cesarean hysterectomy [21].

ItOSS study (Italy)

As part of ItOSS (Italian Obstetric Surveillance System) [21], a prospective population-based study was conducted in six Italian regions from September 2014 to August 2016 (covering 49% of national births). It included all women with PAS, defined as "vaginal delivery with difficult, incomplete manual removal of placenta and blood transfusion within 48 hours or cesarean … with difficult removal of placenta assessed to be abnormally invasive." Trained clinicians in each participating maternity unit used electronic data collection forms to report cases prospectively. A descriptive analysis of the PAS cases has been published [18].

At the time of data collection, there were no national recommendations on PAS.

Case definition

For this analysis, we included all women with a diagnosis of grade 3 PAS reported in each of the three databases. In women with hysterectomies, grade 3 was defined histologically by a pathology analysis of the uterus showing the presence of villous tissue within or breaching the uterine serosa with or without invading pelvic tissues/organs. For women with conservative management, it was defined by clinical assessment during surgery showing abnormal macroscopic findings on the uterine serosal surface and placental tissue invading through the surface of the uterus with or without invasion of any other organ in agreement with FIGO definition [2].

Data collection

From each database, we collected individual data on (i) maternal characteristics — age, body mass index (BMI), country of birth, nationality or ethnic group, depending on the information available, to describe women's geographical/minority background, parity, prior PPH, number of previous cesarean deliveries; any prior uterine surgery (combined into a variable that also included myomectomy, cavity breach, dilatation and curettage, previous surgical termination of pregnancy, and evacuation of retained products of conception); (ii) characteristics of pregnancy: single or multiple, placental location prior to delivery; prenatal suspicion of any PAS, gestational age at delivery; (iii) additional preoperative intervention for women with prenatal suspicion of any PAS: preoperative ureteral catheters or preoperative intravascular balloon catheter; (iv) surgical management of PAS: conservative management or cesarean hysterectomy, and type of anesthesia. Conservative management was defined as the placenta left in situ, either completely or partially, in women who did not have a cesarean hysterectomy; (v) additional interventions: uterine sutures or pelvic vessel ligation, artery embolization (prophylactic or for PPH treatment) and methotrexate; (vi) maternal outcomes evaluated by median estimated total blood loss (EBL); EBL ≥ 1,500 mL; EBL ≥ 3000 mL; red blood cell (RBC) transfusion; blood transfusion ≥ 4 units of RBCs; platelet transfusion, fresh frozen plasma transfusion, administration of fibrinogen, recombined activated factor VII, tranexamic acid, use of cell saver, maternal admission to the intensive care unit, post-delivery infection, damage to the bowel or urinary tract (combined into one category), and maternal death. Women in France who did not have a PPH did not have any blood loss value entered; the estimated blood loss for French women without a PPH was imputed to be 500 mL, as above this threshold a PPH would have been recorded in the data collection form [19]. Post-delivery infection and damage to the surrounding organs were extracted from free-text responses to the question of "did woman have any other morbidity?" in the UK. In the French and Italian data, post-delivery infection was reported by specific questions. Neonatal outcomes included neonatal intensive care unit admission, and perinatal death.

Statistical analysis

We calculated the incidence of grade 3 PAS per 10,000 maternities with its binomial 95% confidence interval according to the number of maternities from each country or region during the study period. We described the women's characteristics, management, and outcomes in each country, with numbers and percentages for categorical variables and means and standard deviations (SD) for continuous variables. We tested the differences between countries with Pearson's Chi2 test or Fisher's exact test for categorical variables, as appropriate.

We conducted two secondary analyses in order to overcome the heterogeneity of some practices between countries and further explore delivery management strategies and associated outcomes. First, in order to overcome the heterogeneity of prenatal screening practices between countries, we analyzed outcomes according to prenatal screening, i.e. separately in women with prenatally suspected PAS and in women without prenatally suspicion of PAS. Second, to further homogenize the clinical contexts compared between countries, we conducted an analysis in the subpopulation of women with a PAS suspected antenatally and managed by cesarean hysterectomy.

The data were analyzed with R Studio (1.3.1093).

Results

Our study population included 39 women with PAS grade 3 in the UK, 51 in France, and 34 in Italy, a total of 124 women, with corresponding estimated incidences per 10,000 maternities of 0.5 (95% CI 0.3–0.6) in the UK,

Table 1 Study populations by country

	United Kingdom[5]	France[6]	Italy[20]
Inclusion Period	05/2010–04/2011	11/2013–10/2015	09/2014–08/2016
Maternities* (n)	798,634	520,114	458,995
PAS confirmed (n)	134	249	130
PAS grade 3 (n, % of PAS cases)	39, 29%	51, 20%	34, 26%
PAS grade 3 incidence (per 10 000 pregnancies regardless of plurality, 95% CI)	0.5, 0.3–0.6	1.0, 0.7–1.2	0.7, 0.5-1.0

*: pregnancies regardless of plurality

1.0 (95% CI 0.7–1.2) in France, and 0.7 (95% CI 0.5-1.0) in Italy (Table 1).

The proportion of women with prior uterine surgery (cesareans excluded) differed between the three countries (15% in the UK, 32% in France, and 50% in Italy, $P<.01$ for global test) (Table 2).

The proportion of women with PAS suspected before delivery was lower in the UK than in France and Italy where it was suspected for a high proportion of women before delivery (59% versus 88% and 82% respectively, $P<.01$ for global test) (Table 3). Among the women with prenatally suspected PAS, a preoperative intravascular balloon catheter was used less frequently in France than in Italy (7% versus 85%, $P<.01$; data not collected in the UK). In the UK, manual removal of the placenta was attempted for half the women (49%), but only 16% in France and 18% in Italy ($P<.01$ for global test). Cesarean hysterectomies were performed for 62% in the UK and 39% in France, compared with all women in Italy (100%) ($P<.01$ for global test). Among women with initial conservative management, the proportion with secondary hysterectomies was similar in the UK and France (25% and 30% respectively, $P=.76$) (Table 3). Overall, the proportion of women who finally had a hysterectomy differed between the three countries: it was smallest in France (59%), intermediate in the UK (69%), and highest in Italy (100%) ($P<.01$ for global test) (Table 3).

The proportion of women with estimated blood loss ≥ 3000 mL differed between the three countries: it was highest in the UK (54%), intermediate in France (25%), and lowest in Italy (12%, $P<.01$ for global test). Post-delivery infection was reported in 30% of the women in France and in no women in either the UK or Italy ($P<.01$ for global test). The proportion of women with damage to the bowel or urinary tract was similar in all three countries: 19% in the UK, 18% in France, and 18% in Italy ($P=.95$ for global test). Infant outcomes did not differ significantly between these countries (Table 4).

The secondary analysis stratified according to prenatal screening showed the same patterns of differences in outcomes between countries (supplemental Tables 1,2,3). In women with prenatally suspected PAS (23 women in the UK, 45 in France, and 28 in Italy) the proportion of EBL ≥ 3000 mL was 48% in the UK, 26% in France, and 11% in Italy ($P<.01$ for global test). In women with no prenatal suspicion of PAS (16 women in the UK, 6 in France and 6 in Italy) the proportion of EBL ≥ 3000 ml was 63% in the UK, 33% in France and 17% in Italy ($p=.12$ for global test).

The other secondary analysis restricted to women with prenatally suspected PAS and managed with cesarean hysterectomy again provided similar patterns of

Table 2 Characteristics of women with PAS Grade 3 in the UK, France, and Italy

		UK *n* (%) *n* = 39	France *n* (%) *n* = 51	Italy *n* (%) *n* = 34	*P*
Age (years) (median, IQR)*		35 [33–38]	35 [32–40]	35 [32–39]	
	≥ 35	24 (62)	24 (47)	18 (53)	0.39
BMI (kg/m^2) (median, IQR)		26 [22–30]	26 [22–30]	25 [22–28]	
	≥ 30	9 (24)	14 (29)	5 (15)	0.34
	Missing	1	2	0	
Migrant or minoritized ethnic background†		9 (23)	19 (39)	2 (6)	-
Missing		0	4	3	
Parity*	0	1 (3)	1 (2)	2 (6)	
	1	9 (23)	10 (20)	9 (26)	0.77
	≥ 2	29 (74)	40 (78)	23 (68)	
Prior PPH*		5 (13)	8 (16)	1 (3)	0.18
Number of previous cesareans*	0	2 (5)	3 (6)	2 (6)	
	1	15 (39)	21 (41)	12 (35)	
	2	9 (23)	12 (24)	13 (38)	0.77
	≥ 3	13 (33)	15 (29)	7 (21)	
Prior uterine surgery‡ (CD excluded)*		6 (15)	16 (32)	17 (50)	< 0.01
Prior uterine surgery‡ (CD included)*		38 (97)	49 (96)	33 (97)	0.93
In Vitro Fertilization		1 (3)	1 (2)	1 (3)	0.54
Multiple pregnancy*		0 (0)	0 (0)	1 (3)	0.26
Gestational hypertensive disorders		0 (0)	1 (2)	2 (6)	0.52
Preterm premature rupture of membranes		1 (3)	4 (8)	0 (0)	0.23
Placenta location prior to delivery	Normal	9 (23)	4 (8)	3 (10)	
Low-lying		2 (5)	6 (13)	0 (0)	0.05
	Previa	28 (72)	38 (79)	28 (90)	
	Missing	0	3	3	

Data are reported as numbers (percentages) unless otherwise stated

IQR: interquartile range, BMI: body mass index, PPH: post-partum hemorrhage, CD: cesarean delivery

*: no missing data for any country; †: non-White for UK, non-French nationality for France, non-Italian place of birth for Italy

‡: including myomectomy, cavity breach, dilation and curettage, previous surgical termination of pregnancy, and evacuation of retained products of conception

Table 3 Mode of birth and management of women with PAS Grade 3 in the UK, France, and Italy

		UK *n* (%) *n* = 39	France *n* (%) *n* = 51	Italy *n* (%) *n* = 34	*P*
Prenatal suspicion of PAS*†		23 (59)	45 (88)	28 (82)	< 0.01
Transfer to a referral center		0 (0)	24 (47)	NA	< 0.01
GA at delivery (median, IQR)*		36 [34–37]	36 [35–40]	35 [34–36]	-
< 37 weeks		24 (67)	35 (67)	28 (82)	0.27
Type of primary anesthesia	Regional	NA	23 (45)‡	20 (87)‡	
	General	NA	28 (55)	3 (13)	< 0.01
	Missing data	NA	0	11	
Cesarean delivery*		36 (92)	51 (100)	34 (100)	0.04
In women with prenatal suspicion of PAS		*n* = 23	*n* = 45	*n* = 28	
Preoperative ureteral catheters		NA	23/45 (51)	8/20 (40)	0.30
Missing		NA	0/45	8/28	
Preoperative intravascular balloon catheters		NA	3/45 (7)	17/20 (85)	< 0.01
Missing		NA	0/45	8/28	
Attempt to remove placenta at delivery*		19 (49)	8 (16)	6 (18)	< 0.01
Prophylactic artery embolization		NA	11 (22)	19 (56)	< 0.01
Cesarean hysterectomy*		19 (62)	21 (41)	34 (100)	< 0.01
Conservative management: placenta left in situ*		20 (51)	30 (59)	0 (0)	-
Hysterectomy after placenta left in situ*		5/20 (25)	9/30 (30)	0/0 (0)	0.76
The final hysterectomy (immediate or secondary)*		24 (69)	30 (59)	34 (100)	< 0.01

Data are reported as numbers (percentages) unless otherwise stated

PAS: placenta accreta spectrum; GA: gestational age; NA: not available

*: no missing data for any country

†: prenatal suspicion of PAS but not necessarily of type 3

‡: Regional anesthesia was converted to general anesthesia for 12 women in France and none in Italy

differences of outcomes between countries (supplemental Tables 4,5,6).

Discussion

Main findings

This comparative study conducted in three countries in multiple time periods showed that maternal outcomes differed between the three population-based cohorts of women with PAS grade 3. Findings suggest that this may result from differences in prenatal screening and perioperative management (surgery and additional interventions). Italian women, the most recent population, appeared to have the fewest severe PPH-related outcomes, and UK women, the oldest population, the most severe outcomes. Nevertheless, in Italy all women with PAS grade 3 were managed by cesarean hysterectomy while in the UK and in France a conservative management was more commonly attempted, leaving 31% of women with their uterus in the UK and 41% in France.

Strengths and limitations

One strength of this study is its design. Data come from three population-based studies whereas most previous studies about grade 3 PAS were case reports [22–24] or case series based on single-center registries [3, 9, 25]. Our study provided one of the largest specific samples of grade 3 PAS: 124 women in total; these population-based data came from all types of hospitals — expert centers and others. Another strength of this study is its different time periods. These three time periods allow to provide a comprehensive overview of national practices and their impact on outcomes. This information remains valuable for inform current practice and our findings serve as a baseline for future studies. Indeed, there is a clear need for new prospective population-based studies to further investigate potential differences between countries in the context of current practices.

Regarding the identification criteria, variability between studies cannot be ruled out, despite the inclusion criteria being broadly similar. As these studies were conducted by different teams, the methods for collecting data for some outcomes were not consistent (infections, for instance).

One other limitation is the absence of histopathological analysis of the uterus for women with a conservative treatment. The FIGO classification, which includes both histological and clinical criteria, has recently come under scrutiny, especially in cases of clinical diagnosis alone [1, 26]. In this study, we included women who received only conservative treatment, so a potential overdiagnosis of grade 3 PAS for these women cannot be excluded. However, a histopathological analysis of the uterus was

Table 4 Maternal and neonatal outcomes for women with PAS grade 3 in the UK, France, and Italy

	UK *n* (%) *n* = 39	France *n* (%) *n* = 51	Italy *n* (%) *n* = 34	*P*
Maternal outcomes				
Total EBL (mL) (median, IQR)*	3000 [1500–8000]	1200 [500–2750]	1500 [1000–2000]	-
Min-Max	300-24000	500–9000	700–4500	
EBL ≥ 1500 mL (%)*	31 (79)	19 (39)	18 (53)	< 0.01
EBL ≥ 3000 mL (%)*	21 (54)	13 (25)	4 (12)	< 0.01
Packed RBCs transfused*	28 (72)	34 (67)	26 (76)	0.62
Number of packed RBCs transfused (median, IQR)*	8 [6–14]	6 [3-10.7]	2.5 [1.3-4]	< 0.01
Packed RBCs transfused ≥ 4	26 (67)	24 (47)	14 (41)	0.06
Platelet units transfused*	13 (33)	8 (16)	1 (3)	< 0.01
Fresh frozen plasma transfused*	20 (41)	29 (57)	7 (21)	< 0.01
Fibrinogen*	10 (26)	19 (37)	2 (6)	< 0.01
Recombined activated factor VII*	3 (8)	1 (2)	0 (0)	0.14
Tranexamic acid*	NA	22 (43)	5 (15)	< 0.01
Use of cell saver	8 (31)	7 (14)	1 (3)	0.02
Missing	13	2	0	
Any uterine suture or pelvic vessel ligation*†	11 (28)	8 (16)	4 (12)	0.16
Maternal transfer to ICU*	31 (80)	21 (41)	11 (32)	< 0.01
ICU length of stay (days) (median, IQR)*	2[1–3]	2 [1–2]	1[1–2]	0.23
Maternal death*	0 (0)	1 (2)‡	0 (0)	0.49
Post-delivery infection	0 (0)	15 (30)	0 (0)	< 0.01
Missing	0	1	0	
Damage to bowel or urinary tract*	6 (19)	9 (18)	6 (18)	0.95
Neonatal outcomes				
In utero fetal death*	2 (5)	2 (4)	0 (0)	0.56
Among live births				
Neonatal ICU admission	18 (50)	28 (56)	15 (63)	0.38
Missing	1	0	11	
Neonatal death	1 (3)	0 (0)	1 (3)	0.48
Missing	1	2	0	

Data are reported as numbers (percentages) unless otherwise stated

EBL: estimated blood loss, ICU: intensive care unit, RBCs: red blood cells, IQR: interquartile, NICU: neonatal intensive care units; NA: not available

*: no missing data for any country

†: B-Lynch or other uterine suture and/or uterine ligation and/or pelvic vessel ligation

‡: A woman with a body mass index of 41.5 and prenatally suspected placenta accreta had an emergency cesarean hysterectomy at 32 weeks of gestation because of preeclampsia and bleeding, followed by a pelvic arterial embolization because of diffuse bleeding with coagulopathy. After 2 days, she died of multiorgan failure

performed for 73% of the women in the entire study population, and a secondary analysis including only women who underwent primary hysterectomy yielded results like those of the total population.

Interpretation

Baseline characteristics of women are not likely to explain differences in outcomes between countries as they did not significantly differ between countries, except for some that were more prevalent in Italy, the country were PPH-related outcomes were actually the least prevalent.

Advances in knowledge, awareness, management of PAS and in organization care across the three time periods may be one explanation for the differences observed in outcomes in these three countries as suggested in previous investigations [4, 9, 27–29].

One striking difference between studies relates to the prenatal diagnosis rate, which is lower in the UK compared to France and Italy, corroborating the increase in prenatal diagnosis rates over time [26, 30]. More severe outcomes, in particular massive hemorrhage, have been reported in women with PAS not suspected prenatally, and more frequent attempts to remove the placenta [29–31]. Of note, the high maternal morbidity found in the UK population in our study is similar to that reported in large series of women with PAS managed with cesarean hysterectomy during the same time period [32–35]. The median EBL ranged from 2300 mL to 4510 mL in those reports, compared to 3000 mL in the UK PAS grade 3 population in our study [32–35].

The findings of our secondary analysis showed that differences in outcomes between countries persisted in subgroups where prenatal diagnosis was homogenized suggests the implication of other factors, beyond differences in prenatal screening practices. Indeed, maternal morbidity in the UK cohort may have been exacerbated by inappropriate delivery management still used during the study period. Attempts to remove the placenta, known to cause high risk of heavy bleeding, were performed in 49% of women in the UK (vs. 16% in France and 18% in Italy) [8]. Similarly, methotrexate use was not uncommon in the UK (33% vs. 0% in France) while this treatment is no longer recommended currently [36–39]. In contrast, in Italy the management was the most standardized than in the other countries. In Italy, all women had cesarean hysterectomies, a country with the highest rate of all-causes peripartum hysterectomy in Europe [40]. Some centers, especially in Southern Italy — the geographical area with the highest incidence of PAS — have developed expertise in PAS management by planned cesarean hysterectomy. Typically, all prenatally suspected PAS cases are referred to these centers, although data on transfer were not available in our analysis for Italy, in contrast with the United Kingdom, where no women were transferred to a referral center [20]. This provides a framework to minimize blood loss during cesarean hysterectomy: active management involving prophylactic preoperative procedures such as preoperative ureteral and intravascular balloon catheters, regional anesthesia,

cesarean deliveries, and uterine and placental embolization before hysterectomy. Prophylactic embolization was facilitated by setting up the surgical suite in the embolization room. Other teams have published this staged procedure (cesarean, embolization, and hysterectomy) for PAS management with preliminary results showing lower maternal morbidity than with a cesarean hysterectomy without embolization [41–44].

Still other publications have shown that management in expert centers is associated with lower morbidity in women with PAS [9, 28]. Notably, the median EBL in the Italian population in this study (1500 mL) is similar to that reported in a recent series of PAS grade 2 or 3 cases from an expert center in the USA (ranging from 1350 mL to 2100 mL) [9, 28].

Although conservative management has been associated with significant lower blood loss than cesarean hysterectomy in previous reports [4, 45], in this study, severe maternal morbidity was found to be slightly more frequent in France, where conservative management was quite frequently attempted, than in Italy where all women underwent cesarean hysterectomy. However, comparing different surgical treatments whether within a specific population or through cross-country comparison, remains challenging because of baseline characteristics of women and other components of care that likely differ between the two approaches. More generally, and adopting another perspective, the available evidence including the present study may be interpreted as the fact that, in women with PAS, the management most frequently implemented in each country may be that associated with the lowest maternal morbidity there. A randomized study may be the only method to assess the best treatment in cases of grade 3 PAS. However, considering the strong impact of the medical organization and the level of excellence necessary for cesarean hysterectomy procedure, the results of this randomized study may be difficult to generalize. Finally, a highly standardized cesarean hysterectomy procedure may well be associated with less morbidity but still leads to permanent infertility.

Conclusion

This prospective study of population-based data from three multiperiod studies showed that maternal outcomes in women with grade 3 PAS varied between the three periods and countries, alongside the evolution in prenatal screening, peri-operative management and organization of care for these women. Our findings may serve as a baseline for future prospective population-based studies to further investigate differences between countries in the context of current practices.

Abbreviations

EBL Estimated Blood Loss
PAS Placenta Accreta Spectrum
BMI Body Mass Index
PPH Post-Partum Hemorrhage
CD Cesarean Delivery

Supplementary Information

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Supplementary Material 1

Author contributions

Please note that Catherine Deneux-Tharaux and Gilles Kayem contributed equally to this work and should be considered as co-final authors. Anne Pinton made statistical analysis and interpretation of data, and drafted the work and made the correction of the manuscript and approved the final version to be published and agreed to be accountable for all aspects of the works. Sara Ornaghi made substantial contributions to the acquisition of data for the work and revising it critically and approved the final version to be published and agreed to be accountable for all aspects of the works. Loïc Sentilhes made substantial contributions to the interpretation of data for the work and revised it critically for important intellectual content and approved the final version to be published and agreed to be accountable for all aspects of the works. Marian Knight made substantial contributions to the acquisition of data for the work and revising it critically and approved the final version to be published and agreed to be accountable for all aspects of the works. Serena Donati made substantial contributions to the interpretation of data for the work and revised it critically for important intellectual content and approved the final version to be published and agreed to be accountable for all aspects of the works. Gilles Kayem and Catherine Deneux-Tharaux made contributions to the conception and design of the work, interpretation of data, and revised it critically and approved the final version to be published and agreed to be accountable for all aspects of the works.

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Data availability

For the UK, this article presents independent research funded by the National Institute for Health Research (NIHR) under the 'Beyond maternal death: Improving the quality of maternity care through national studies of "near-miss" maternal morbidity' program (program grant RP-PG-0608-10038). Marian Knight is an NHR senior investigator. The views expressed in this publication are those of the author(s), and not necessarily those of the NHS, the NIHR, or the Department of Health. The funder had no role in the study design, data collection and analysis, decision to publish, or preparation of the article.For France, PACCRETA was funded by the French Health Ministry under its Clinical Research Hospital Program (grant number: AOR12156) and by the Angers University Hospital. The fundershad no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.For Italy, the study was approved by the Committee of the Italian National Institute of Health (Port. PRE-839/13). The study was funded by the Italian Ministry of Health/CCM. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Declarations

Ethical approval and consent to participate

For the UK, this study was approved by the London Research Ethics Committee (ref. 10/H0717/20). The need for consent to participate was also waived by the ethics committee that approved this study. Data ware fully anonymized before being accessed and analyzed. For France, PACCRETA The appropriate ethics committees (Consultative Committee on the Treatment of Data on Personal Health for Research Purposes – reference no. AOR12156; 12/19/2013, and the Committee for the Protection of People Participating in Biomedical Research – reference CPP 13–017; 05/28/2013), and the National Data Protection Authority (CNIL no. DR-2013-427; 12/20/2013) approved the study. The need for consent to participate was also waived by the ethics committee that approved this study. Data ware fully anonymized before being accessed and analyzed. For Italy, the study was approved by the Committee of the Italian National Institute of Health (Port. PRE-839/13). The need for consent to participate was also waived by the ethics committee that approved this study. Data ware fully anonymized before being accessed and analyzed.

Consent for publication

Not applicable.

Consent to publish

All authors consent to the publication of this manuscript.

Competing interests

The authors declare no competing interests.

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