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Prophylactic radiologic interventions to reduce postpartum hemorrhage in women with risk factors for placenta accreta spectrum disorder: a nationwide cohort study

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ABSTRACT

Objective: To quantify the association between prophylactic radiologic interventions and perioperative blood loss in women with risk factors for placenta accreta spectrum disorder (PAS)

Methods: We conducted a retrospective nationwide cohort study of women with risk factors for placenta accreta spectrum disorder who underwent planned cesarean section in 69 Dutch hospitals between 2008 and 2013. All women had two risk factors for PAS: placenta previa/anterior low-lying placenta and a history of cesarean section(s). Women with and without ultrasonographic signs of PAS were studied as two separate groups. We compared the total blood loss of women with prophylactic radiologic interventions, defined as preoperative placement of balloon catheters or sheaths in the internal iliac or uterine arteries, with that of a control group consisting of women without prophylactic radiologic interventions using multivariable regression. We evaluated maternal morbidity by the number of red blood cell (RBC) units transfused within 24 h following childbirth (categories: 0, 1–3, >4), duration of hospital admission, and need for intensive care unit (ICU) admission.

Results: A total of 350 women with placenta previa/anterior low-lying placenta and history of cesarean section(s) were included: 289 with normal ultrasonography, of whom 21 received prophylactic radiologic intervention, and 61 had abnormal ultrasonography, of whom 22 received prophylactic intervention. Among women with normal ultrasonography without prophylactic intervention ($n = 268$), the median blood loss was 725 mL (interquartile range (IQR) 500–1500) vs. 1000 mL (IQR 550–1750) in women with intervention ($n = 21$); the adjusted difference in blood loss was 9 mL (95% confidence interval (CI) −315–513), $p = .97$). Among women with abnormal ultrasonography, those without prophylactic intervention ($n = 39$) had a median blood loss of 2500 mL (IQR 1200–5000) vs. 1750 mL (IQR 775–4000) in women with intervention ($n = 22$); the adjusted difference in blood loss was −1141 mL (95% CI −1694– −219, $p = .02$). Results of outcomes on maternal morbidity were comparable among women with and without prophylactic intervention.

Conclusion: These findings suggest that prophylactic radiologic interventions prior to planned cesarean section may help to limit perioperative blood loss in women with clear signs of placenta accreta spectrum disorder on ultrasonography, but there was no evidence of a difference within the subgroup without such ultrasonographic signs. The use of these interventions should be discussed in a multidisciplinary shared decision-making process, including discussions of potential benefits and possible complications.

Trial registration: Netherlands Trial Registry, https://onderzoekmetmensen.nl/en/trial/28238, identifier NL4210 (NTR4363)

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1. Introduction

Placenta accreta spectrum disorder (PAS) is characterized by abnormal attachment of the placenta to the myometrium. PAS is a high-risk condition in pregnancy that may lead to life-threatening postpartum hemorrhage (PPH) [1–6]. The incidence of PAS has increased with increasing cesarean section rates, making it the leading indication for emergency peripartum hysterectomy worldwide [2,7–11]. PAS covers placenta accreta (placenta attached to the myometrium), increta (placenta invades the myometrium), and percreta (placenta invades through the myometrium) [12–14]. Women with placenta previa and a history of one or more cesarean section(s) are at risk of PAS, because a defect in the endometrial-myometrial interface may lead to abnormal decidualization in the area of a previous uterine scar [15]. This risk increases markedly as the number of prior cesarean sections increases: 11% for second, 40% for third, and over 60% for fourth or higher order cesarean sections [16].

Current guidelines in the United States and the United Kingdom recommend a multidisciplinary approach and planned cesarean section at approximately 34–36 weeks for women at risk of PAS [17,18]. The most generally accepted mode of birth in women with PAS is planned cesarean followed by hysterectomy; however, in recent years, conservative surgery has been performed as an alternative approach, with the possibility of preserving fertility [19–22]. Intrapartum management strategies for women at risk of PAS primarily focus on preventing blood loss. Prophylactic radiologic interventions have been used under the assumption that they may limit bleeding. These interventions include preoperative placement of balloon catheters or sheaths in the internal iliac or uterine arteries by an interventional radiologist. Inflation of balloons or embolization directly after childbirth reduces blood flow to the uterus and may reduce perioperative blood loss. However, quantitative evidence on whether these interventions actually improve maternal outcomes is inconclusive [19,23–26]. Moreover, adverse effects can be severe, including vessel rupture and thromboembolism [27].

We aimed to quantify the association of prophylactic radiologic interventions with perioperative blood loss, maternal morbidity, and mortality among pregnant women with risk factors for PAS who underwent planned cesarean section and collect data on the safety of these interventions.

2. Material and methods

2.1. Women with risk factors for PAS

We performed a nationwide cohort study, the Transfusion strategies in women during Major Obstetric Hemorrhage study (TeMpOH-3), between June 1st, 2013, and June 1st, 2015, in the Netherlands [28]. We contacted all 87 hospitals with an obstetric unit in the Netherlands, of which 69 (79.3%) participated including all university hospitals ($n = 8$). The cohort comprised consecutive women with risk factors for PAS from these 69 hospitals who underwent planned cesarean section between January 1st, 2008, and January 1st, 2013. Women with a combination of the following two risk factors for PAS were included: placenta previa/anterior low-lying placenta and a history of cesarean section(s). These risk factors were chosen to enable the selection of women with suspected PAS independent of ultrasonography. During the study period, it was common clinical practice in the Netherlands that women with these risk factors were considered to be at risk of PAS irrespective of ultrasonographic signs of PAS. At that time, the diagnostic strategy for PAS was not standardized in the Netherlands and the accuracy of ultrasonography was presumed to be low. At that time, screening for PAS was performed during routine ultrasonography throughout pregnancy in all women. Since there was no national protocol for the management of women with risk factors for PAS, the planning of intrapartum management strategies was determined case-by-case by a multidisciplinary team. There was variation between the participating hospitals in which specialisms were represented in this team. The team could include obstetricians, oncologic gynecologists, (obstetric) anesthetists, neonatologists, urologists, and interventional radiologists. It was common clinical practice that women with risk factors for PAS were scheduled for a planned cesarean section followed by a hysterectomy when PAS was confirmed. Prophylactic radiologic interventions were not offered in all 69 participating hospitals; thus, we expected women with comparable clinical profiles to be present in both the intervention and control groups. Women who gave birth by emergency cesarean section, defined as cesarean section before the planned date, were excluded because the emergency setting was hypothesized to allow no time for prophylactic interventions. Women were selected from the databases of two national registries and the birth registries of participating hospitals [29,30]. Detailed information on the data collection process is presented in Appendix B.

Approval was obtained from the Medical Ethics Committee of the Leiden University Medical Center (P13.264) and the institutional review boards of all participating hospitals. A waiver of informed consent was granted because the study collected anonymized data. The study was registered in the Dutch Trial Register (NTR4363).

2.2. Data collection and definitions

A comprehensive medical chart review was performed. Well-trained medical students and research nurses collected the data. Afterward, we checked all data for completeness and inconsistencies, and whenever necessary, an on-site chart review was repeated. Definitions of the collected data are described in Appendix B. The anonymized data were stored in a database developed by the Department of Advanced Data Management of Leiden University Medical Center, the Netherlands.

2.3. Outcomes

The primary outcome was defined as total perioperative blood loss in milliliters (mL). Total blood loss is the sum of intra- and postoperative blood loss within 24 h following childbirth. In the Netherlands, the volume of blood loss postpartum is determined by weighing gauzes, cloths, and surgical swabs, and by measurements using suction systems in the operating theater. Additionally, we report the categorical variables postpartum hemorrhage $>$500 mL and $>$1000 mL (yes or no). We evaluated maternal morbidity by the number of red blood cell (RBC) units transfused within 24 h following childbirth (categories: 0, 1-3, $\geq$4), length of hospital stay (number of days the women were admitted after birth, including day of birth), and need for intensive care unit (ICU) admission. Hysterectomies may have been planned or unplanned in an effort to stop bleeding resulting from PAS; data on the indications for hysterectomy were not available.

2.4. Intervention

The prophylactic radiologic intervention was defined as the preoperative placement of balloon catheters in the internal iliac or uterine arteries or preemptive vascular access with sheaths in the common femoral artery to reduce the procedure time of the radiologic interventions if needed. This procedure was performed by an interventional radiologist in the operating theatre or angiography suite of hospitals. Since there was no national protocol in the Netherlands for these interventions, the choice for the type of prophylactic intervention was based on expert/center experience and availability. Through puncture of the bilateral common femoral arteries, sheaths and (if performed) occlusion balloons were inserted under local anesthesia. Following the procedure, women underwent cesarean section. The decision to perform intraoperative balloon inflation and/or embolization and their timing depended on the physician performing the cesarean section. We classified complications according to the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) classification system [31]. Women in the control group did not receive prophylactic radiologic intervention. All women received standard care for PPH according to local protocols based on guidelines from the Dutch Society of Obstetrics and Gynecology (NVOG).

2.5. Statistical analysis

The possible effects of the intervention may vary according to the severity of PAS. This might be associated with the presence of ultrasonographic findings of PAS. Therefore, we analyzed women with risk factors for PAS, with or without ultrasonographic signs of PAS, as two separate groups. These two groups are further named "Normal ultrasonography" and "Abnormal ultrasonography". Within these two groups, we present outcomes (mean or proportion) in each of the intervention groups, along with crude and adjusted differences or odds ratios and their respective 95% confidence intervals, as appropriate. We used univariable and multivariable linear regression models to calculate crude and adjusted differences in the volume of blood loss. Potentially confounding variables were the number of previous cesarean sections (continuous), history of severe PPH (yes/no), history of PAS or retained placenta (yes/no), and type of PAS (placenta percreta yes/no). From this list, we only observed differences in the de variable type of PAS (percreta yes/no) for those with as compared to those without the intervention. Therefore, we used a multivariable linear regression model adjusted only for placenta percreta yes/no. We used univariable linear regression models to calculate crude differences in length of stay in the hospital. Total blood loss, the primary continuous outcome, and length of stay in the hospital were not normally distributed and were therefore log-transformed. Unadjusted logistic regression models were used for the following outcomes: PPH $>$ 500 mL, PPH $>$ 1000 mL, number of red blood cell

(RBC) units transfused within 24 h, and need for ICU admission. We decided to present only unadjusted results for our secondary outcomes because of low cell numbers for the variable placenta percreta yes/no for these outcomes.

In case of missing data in the primary outcome "total blood loss", we considered intra-operative blood loss as total blood loss. We performed a sensitivity analysis after removing women with missing data on total blood loss and compared the results with those of the primary analysis. Women without any data on the volume of blood loss were excluded from data analyses.

We performed a subgroup analysis among women with "confirmed PAS" to assess the association between prophylactic radiologic interventions and predefined clinical outcomes in pregnancies that were ultimately established as having actually been complicated by PAS. Confirmed PAS was defined as intraoperative confirmation of diagnosis PAS by the managing obstetrician–gynecologist and/or histopathological confirmation of PAS by the pathologist. At the request of one of the reviewers, we performed a sensitivity analysis of our primary outcome total blood loss stratified by postpartum confirmed type of PAS (3 categories: No PAS, Accreta/increta, Percreta). Women with missing data on the type of PAS were not included in this analysis. Statistical analysis was carried out with SPSS version 25 (IBM, Armonk, NY, USA).

3. Results

3.1. Population and interventions

In the five-year study period, 519.143 women gave birth in the participating hospitals, 85% of all births in hospitals ($n = 609.253$) in the Netherlands from 2008–2013. A total of 630 women with risk factors for PAS were identified (Figure 1). Among these, 280 (44%) underwent emergency cesarean section and were therefore excluded. One woman was excluded because of missing data on the total blood loss. The study cohort included the remaining 350 women with risk factors for PAS who underwent a planned cesarean section. The baseline characteristics are presented in Table 1. Within the two groups (normal and abnormal ultrasonography), we did not observe differences in characteristics between those with and without prophylactic radiologic intervention, except for the type of PAS (percreta yes/no). The prophylactic intervention was performed in 21/289 women (7.3%) with normal ultrasonography versus 22/61 women (36.1%) with abnormal ultrasonography. In this cohort, the prophylactic intervention was performed in 21 hospitals: 7/43 prophylactic interventions (16.3%) in university hospitals and 36/43 (83.7%) in nonuniversity hospitals. In the intervention group in 37/43 women, both sheaths and balloon catheters were placed, and only sheaths were placed in six women. In 12/21 women (57%) with normal ultrasonography, the balloons were inflated during surgery after childbirth and in one woman after surgery. In 5/22 women (23%) with abnormal ultrasonography, the balloons were inflated during cesarean section and two after surgery. Embolization was performed in 2/22 women (9.1%) with abnormal ultrasonography.

3.2. Total blood loss

Median blood loss in women with normal ultrasonography without prophylactic intervention was 725 mL (IQR) 500–1500) and with intervention 1000 mL (IQR 550–1750). The difference in blood loss was +198 mL ((95% CI −197–782), $p = .39$) and the adjusted difference was negligible (+9 mL (95% CI −315–513), $p = .97$) (Figure 2).

In women with abnormal ultrasonography without prophylactic intervention median blood loss was 2500 mL (IQR 1200–5000) and with intervention 1750 mL (IQR 775–4000), respectively. The difference in blood loss was −1007 mL ((95% CI −1697–150), $p = .08$) and the adjusted difference was −1141 mL (95% CI −1694– −219, $p = .02$).

In five women the value of total blood loss was missing, and in these women, we considered intraoperative blood loss as the primary outcome. Sensitivity analysis without these five women showed similar results (Appendix Table A.1). Results of the sensitivity analysis of our primary outcome total blood loss stratified by postpartum confirmed type of PAS (3 categories: No PAS, Accreta/Increta, Percreta) are presented in Appendix Table A.2.

3.3. Secondary outcomes

Results of secondary outcomes were comparable among women with and without prophylactic radiologic interventions (Table 2). There were no maternal deaths.

3.4. Subgroup analysis

In 83 women (23.7% of the total study population), the diagnosis PAS was confirmed during the operation and/or postoperatively by histopathology. Their characteristics are shown in Appendix Table A.3. Median

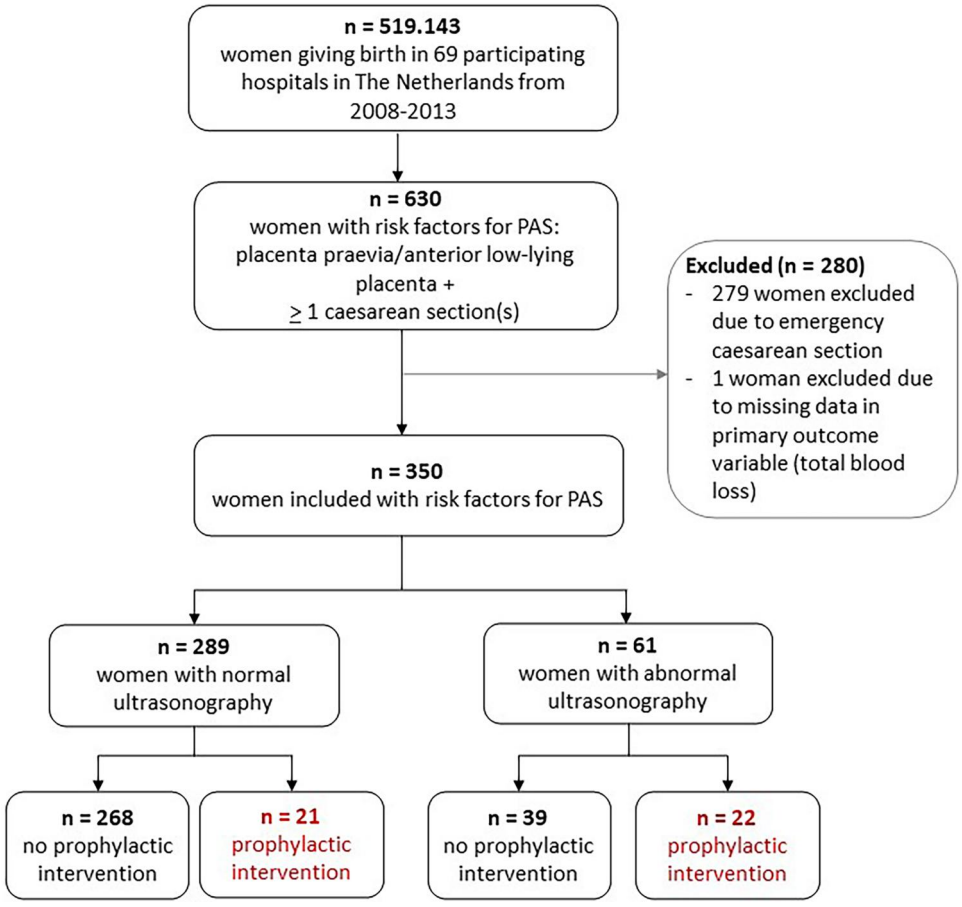

Figure 1. Study flowchart.

blood loss in women with confirmed PAS without prophylactic intervention was 3500 mL (IQR 1625–6750) and 2500 mL (IQR 800–4000) with intervention. The difference in blood loss was −996 mL (95% CI −1898–525, $p = .16$) and the adjusted difference was −1271 mL (95% CI −2056–122, $p = .07$) (Figure 2 and Table 2).

3.5. Complications related to the prophylactic radiologic intervention

Adverse effects of the prophylactic radiologic intervention occurred in 5/43 women (11.6%, CIRSE grade 1-3)) (Appendix Table A.4). The major complication rate (CIRSE grade 3-6) was 1/43 (2.3%). This woman developed a thrombus that required thrombectomy (CIRSE 3). Four women had minor complications (CIRSE 1).

4. Discussion

4.1. Main findings

In this nationwide cohort of women undergoing planned cesarean section, prophylactic radiologic interventions were associated with lower volumes of perioperative blood loss among those with ultrasonographic signs of PAS and among those with confirmed PAS, but not among women without ultrasonographic signs of PAS. One of the 43 women (2.3%) with prophylactic radiologic intervention developed a major complication that required additional intervention.

4.2. Strengths and limitations

We performed an observational study of potential intrapartum management strategies for a relatively rare but serious obstetric complication. A strength of this study was its relatively large sample. Another strength was that we studied women with and without ultrasonographic signs of PAS in two separate groups. At the time of our study, the role of ultrasound in prenatal diagnosis of PAS was limited. We expected that the more severe cases more often had abnormal ultrasonography and that the possible effect of the intervention would vary according to the severity of PAS. There was interhospital variation of practice. Because the prophylactic intervention was not offered in all 69 participating hospitals, there are

Table 1. Characteristics of the study population according to risk of PAS.

	Women with risk factors for PAS			
	Normal ultrasonography		Abnormal ultrasonography	
	No prophylactic intervention ($n = 268$)	Prophylactic intervention ($n = 21$)	No prophylactic intervention ($n = 39$)	Prophylactic intervention ($n = 22$)
Characteristic	*median (IQR)*			
Age (y)	35.0 (32.0–38.0)	35.0 (31.5–38.5)	34.0 (31.0–38.0)	36.0 (32.0–38.3)
BMI (kg/m^2)	24.6 (21.5–27.9)	26.6 (23.1–36.3)	24.2 (22.1–28.6)	25.4 (21.1–27.1)
unknown	70 (26.1%)	8 (38.1%)	7 (17.9%)	4 (18.2%)
Gestation at birth (weeks^{+days})	38^{+1} (37^{+1}–38^{+6})	37^{+2} (36^{+5}–38^{+2})	37^{+4} (36^{+6}–38^{+1})	36^{+3} (34^{+1}–38^{+0})
Obstetric history	*No. (%)*			
Previous cesarean section				
0[a]	N.A.	N.A.	2 (5.1%)	1 (4.5%)
1	243 (90.7%)	18 (85.7%)	27 (69.2%)	14 (63.6%)
2	18 (6.7%)	3 (14.3%)	4 (10.3%)	2 (9.1%)
>2	6 (2.2%)	0	0	1 (4.5%)
unknown	1 (0.4%)	–	6 (15.4%)	4 (18.2%)
History of PAS	7 (2.6%)	0	8 (20.5%)	3 (13.6%)
unknown	1 (0.4%)	–	–	–
History of retained placenta	3 (1.1%)	0	6 (15.4%)	3 (13.6%)
History of PPH (>1000 mL)	35 (13.1%)	1 (4.8%)	11 (28.2%)	6 (27.3%)
unknown	-	-	2 (5.1%)	-
Type of hospital				
University	38 (14.2%)	1 (4.8%)	20 (51.3%)	5 (22.7%)
Nonuniversity	230 (85.8%)	20 (95.2%)	19 (48.7%)	17 (77.3%)
Peripartum				
Hysterectomy	21 (7.8%)	4 (19.0%)	15 (38.5%)	6 (27.3%)
unknown	1	–	–	–
Postpartum				
Confirmed PAS	35 (13.1%)	6 (28.6%)	29 (74.4%)	13 (59.1%)
unknown	3 (1.1%)	–	1 (2.6%)	–
Type of PAS				
accreta/increta	30 (11.2%)	2 (9.5%)	25 (64.1%)	8 (36.4%)
percreta	4 (1.5%)	4 (19.0%)	4 (10.3%)	4 (18.2%)
unknown	4 (1.5%)	–	1 (2.6%)	1 (4.5%)

[a]Two women with uterine surgery in medical history and one woman with no gynecologic/obstetric medical history.
BMI: Body Mass Index; ICU: intensive care unit; PPH: postpartum hemorrhage; PAS: Placenta accreta spectrum disorder; IQR: interquartile range.

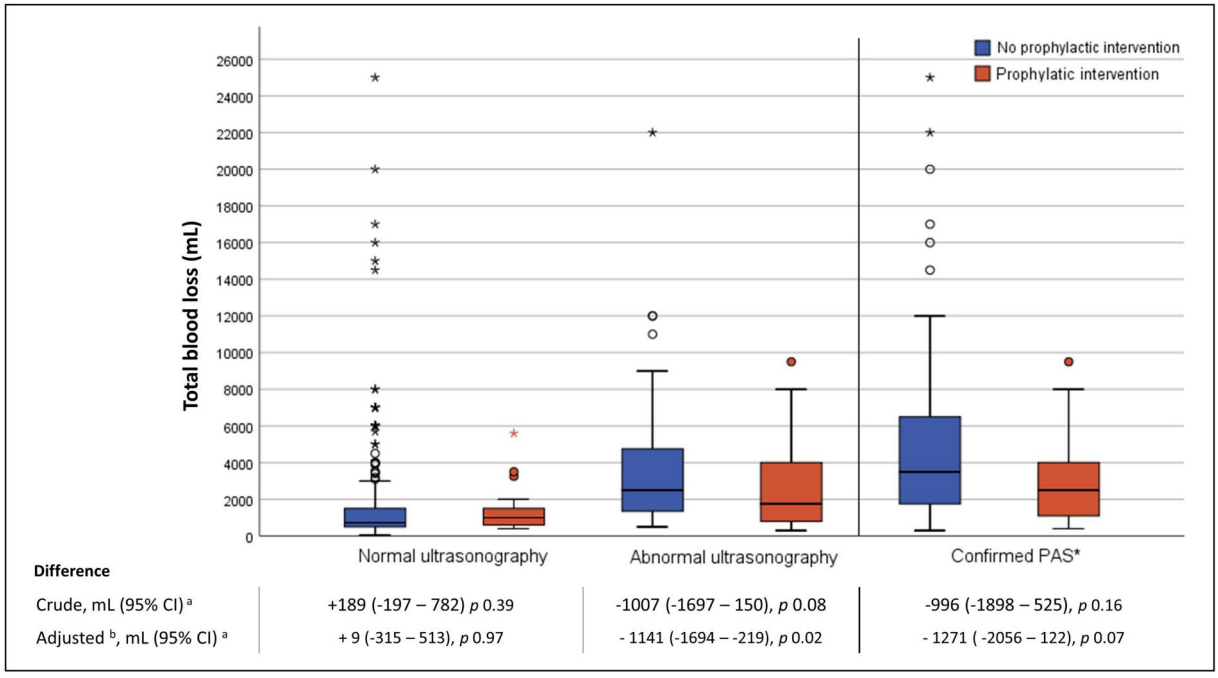

Figure 2. Primary outcome: Blood loss (mL): boxplot (median, IQR) and crude and adjusted differences between groups. [a]The outcome variable is log transformed, we interpreted the exponentiated regression coefficients. These values correspond to changes in the ratio of the expected geometric means of the original outcome variable. [b]Adjusted for placenta percreta (yes/no). *Results of subgroup analysis. PAS: Placenta accreta spectrum disorder; CI: confidence interval.

women with severe PAS who were not offered the prophylactic intervention. This variation in policy for women with similar severity of PAS enables the possibility to compare women with and without the intervention among those with similar severities. A limitation is that hysterectomy could not be studied as an outcome because in women with risk factors for PAS, a planned hysterectomy is often performed to prevent excessive bleeding. From the medical records, it was not possible to distinguish between planned and emergency hysterectomies.

The results may have been affected by residual confounding, despite adjustment for PAS severity as the main source of confounding. Yet, this residual confounding will most likely lead to an underestimation of the effect of the intervention because women with severe PAS are more likely to receive prophylactic radiologic interventions. Another source of bias may be differences in management between hospitals; however, we expect this potential bias to be limited because hospitals follow national guidelines.

When balloon catheters/sheaths are placed prophylactically before a planned cesarean section, inflation of the balloons or embolization may not be necessary. In the present study, balloons were inflated in 17/43 women (40%), and embolization was performed in 2/43 women (5%), with an underestimation of the effect if all the balloons had been inflated. On the other hand, the perioperative decision to not inflate the balloons could have been made because there was a less severe condition observed than expected. In these 'mild' cases of PAS, it is unlikely that the use of balloons would have reduced blood loss.

4.3. Interpretation

Previous studies have shown conflicting results regarding the efficacy of prophylactic radiologic interventions to reduce peripartum blood loss in women with risk factors for PAS. Two single-centre randomized controlled trials (RCT) evaluating the use of prophylactic balloon catheters in women with PAS have been published. Salim et al. (2015) randomly assigned women with risk factors for PAS based on ultrasonographic imaging to prophylactic placement of balloon catheters in the internal iliac arteries ($n = 13$) or no prophylactic intervention ($n = 14$). The mean blood loss was 1600 mL in both groups; calculated blood loss >2500 mL: relative risk (RR) 0.81 (95% CI 0.37–1.76) [27]. Chen et al. (2020) performed an RCT in 100 women with ultrasonographic signs of PAS. In the intervention group ($n = 50$) mean blood loss was 2630 mL (±1585) versus 2221 mL (±1694) in the control group ($n = 50$); estimated blood loss ≥2500 ml: RR 1.42 (95% CI 0.62–3.22) [32]. In accordance with our findings, several observational studies showed a

Table 2. Secondary outcomes.

	Women with risk factors for PAS								Confirmed PAS[a]			
	Normal ultrasonography				Abnormal ultrasonography							
	Women, No (%)				Women, No (%)				Women, No (%)			
	No prophylactic intervention (n = 268)	Prophylactic intervention (n = 21)	*Crude OR (CI)*[b]	*p*	No prophylactic Intervention (n = 39)	Prophylactic intervention (n = 22)	*Crude OR (CI)*[b]	*p*	No prophylactic intervention (n = 64)	Prophylactic intervention (n = 19)	*Crude OR (CI)*[b]	*p*
PPH >500 mL	168 (62.7%)	16 (76.2%)	1.9 (0.7–5.4)	.22	37 (94.9%)	19 (86.4%)	0.3 (0.1– 2.2)	.26	60 (93.8%)	17 (89.5%)	0.6 (0.1–3.4)	.53
unknown	–	–			–	–			–	–		
PPH >1000 mL	94 (35.1%)	10 (47.6%)	1.7 (0.7–4.1)	.25	34 (87.2%)	14 (63.6%)	0.3 (0.1–0.9)	.04	54 (84.4%)	14 (73.7%)	0.5 (0.2–1.8)	.29
	–	–			–	–			–	–		
Number of RBC units transfused within 24h												
0	210 (78.4%)	15 (71.4%)	0.7 (0.3–1.8)	.44	14 (35.9%)	12 (54.5%)	2.1 (0.7–6.0)	.19	17 (26.6%)	7 (36.8%)	1.6 (0.5–4.7)	.41
1-3	25 (9.3%)	5 (23.8%)	3.0 (1.0–9.0)	.05	8 (20.5%)	3 (13.6%)	0.6 (0.1–2.5)	.48	14 (21.9%)	6 (31.6%)	1.6 (0.5–5.0)	.41
≥ 4	32 (11.9%)	1(4.8%)	0.4 (0.0–2.8)	.34	16 (41.0%)	7 (31.8%)	0.6 (0.2–1.9)	.43	32 (50%)	6 (31.6%)	0.5 (0.2–1.3)	.15
unknown	1	–			1	–			1	–		
ICU admission	27 (10.1%)	2 (9.5%)	0.9 (0.2–4.2)	.93	6 (15.4%)	7 (31.8%)	2.5 (0.7–8.7)	.15	21 (32.8%)	7 (36.8%)	1.1 (0.4–3.3)	.81
unknown	1	–			1	–			2	–		
	Median (IQR)		*Crude, days (CI)*[b,c]	*p*	*Median (IQR)*		*Crude, days (CI)*[b,c]	*p*	*Median (IQR)*		*Crude days (CI)*[b,c]	*p*
Length of stay in hospital (days)	4.0 (4.0–5.0)	5.0 (4.0–6.0)	0.3 (-0.4–1.1)	.38	5.0 (4.0–8.0)	5.0 (4.0– 7.0)	-0.5(-1.7–1.0)	.46	6.0 (5.0–8.0)	5.0 (4.0–7.0)	-0.7 (-1.8–0.7)	.30
unknown	1	–			–	–			–	–		

[a]Results of subgroup analysis.
[b]We only present unadjusted results for our secondary outcomes because of low cell numbers for the variable placenta percreta yes/no for these outcomes.
[c]The outcome variable is log transformed, we interpreted the exponentiated regression coefficients. These values correspond to changes in the ratio of the expected geometric means of the original outcome variable.
ICU: intensive care unit; RBC: red blood cell; PPH: postpartum hemorrhage; PAS: Placenta accreta spectrum disorder; OR: odds ratio; CI: confidence interval; IQR: interquartile range.

reduced total blood loss, but confidence intervals are mostly wide, indicating a lack of precision [33–38]. Other observational studies did not show any improvement in maternal outcomes after prophylactic radiologic interventions [39–43].

Our results show a blood loss reduction of 1140 mL by prophylactic radiologic interventions in women with ultrasonographic signs of PAS. This could be the true causal effect since we do not consider confounding, selection bias, or measurement error as reasonable alternative explanations. In addition, in the subgroup analysis of women with clinically and/or pathologically confirmed PAS, we found a difference in blood loss of one liter between the intervention and control groups. Also, in our sensitivity analysis stratified by type of PAS, we found a difference in blood loss of 900 ml in women with placenta accreta/increta and three liter in women with placenta percreta. In women without ultrasonographic signs of PAS, there was no evidence of a difference in total blood loss in women with and without prophylactic interventions. This comparison might be affected by confounding by indication. Although we adjusted for confounding by disease severity (percreta yes/no) the assignment of the prophylactic intervention could have been influenced by other clinical parameters, resulting in a control group with women with less severe disease. This might have caused an underestimation of the effect.

Key in defining optimal intrapartum management strategies is the identification of women with risk factors for PAS prior to birth. In the past decade, the diagnostic accuracy of ultrasonographic imaging of PAS has gradually improved. The role of Magnetic Resonance Imaging (MRI) in prenatal diagnosis of PAS remains a topic of debate [44–46]. In the present study, women were identified with risk factors for PAS based on placenta previa in combination with previous cesarean section(s) with or without ultrasonographic signs of PAS. We used abnormal ultrasonography as a proxy for disease severity. As shown in Figure 2, the two groups (normal and abnormal ultrasonography) differ in terms of primary outcome blood loss: there seems to be a trend toward more blood loss in the abnormal ultrasonography group. However, in the normal ultrasound group, some extreme outliers were observed. This underlines the difficulty of prenatal diagnosis of PAS at the time of our study. The use of prophylactic radiologic interventions needs to be discussed in a multidisciplinary shared decision-making process, including a discussion of possible side effects. In the present study, adverse effects, mostly mild were observed in five women (11.6% of the intervention group); in one woman, an additional intervention (thrombectomy) was required.

PAS is a heterogeneous clinical condition, and the efficacy of prophylactic radiologic interventions varies by clinical condition. For the improvement of future research on the efficacy and safety of prophylactic radiologic interventions in women suspected of PAS, improved ultrasonographic expertise and standardization of definitions for PAS are needed. The efficacy of prophylactic radiologic interventions for each of the different clinical conditions and different interventions is best assessed in multiple RCTs. However, given the rare occurrence of PAS performing large trials is challenging. Collecting real-world observational data, such as the International Network of Obstetric Survey Systems (INOSS), would be of great value to learn from current clinical practice how to improve outcomes in women at high risk of PAS. For a global perspective, it is also important to consider management strategies for PAS that are available in low- and middle-income countries [47].

5. Conclusions

Prophylactic radiologic interventions might reduce perioperative blood loss in women with clear signs of PAS on ultrasonography compared with no prophylactic intervention, but not in women without such signs. Improvement in antepartum diagnosis of PAS could help to identify women who could benefit from these interventions. Current study results can help clinicians during the shared decision-making process when discussing potential benefits and possible complications.

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Author contributions

Concept, design, and obtained funding: VH, DH, JvdB, KB, JD, JvR, and JZ. Statistical analysis: LB, SF, AP, DH, JvdB, TvdA. Drafting of manuscript: LB, SF, JvdB, and DH. Interpretation of data and critical review of the manuscript: All authors.

Ethical approval

Institutional ethics committee approval (reference number: P13.264) was obtained on January 21st 2014, by the Medical Ethics Research Committee of Leiden University Medical Center and from the institutional review board of each study center.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Data availability statement

The data that support the findings of this study are available from the corresponding author, JvdB, upon reasonable request.

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