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INTERVENTIONAL

The effect of prophylactic balloon occlusion in patients with placenta accreta spectrum: a Bayesian network meta-analysis

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Abstract
Objectives Placenta accreta spectrum (PAS) can induce severe life-threatening obstetric hemorrhage. Herein, we conducted a Bayesian network meta-analysis of previous studies to evaluate the relative benefits of different prophylactic balloon occlusion (PBO) procedures.
Methods PubMed, Embase, Cochrane Library, and Web of Science were searched from inception to July 2021. Blood loss volume, blood transfusion volume, and hysterectomy rate were regarded as the primary endpoints. The data were pooled using a Bayesian network and traditional pairwise meta-analysis.
Results Fifty-nine articles with a total sample size of 5150 patients were included. Compared with no PBO (non-PBO) intervention, PBO of the abdominal aorta (PBOAA, mean difference(MD) − 1.02, 95% credible interval (CrI) − 1.4 to − 0.67), common iliac artery (PBOCIA, MD − 0.84; 95%CrI − 1.36 to − 0.06) and internal iliac artery (PBOIIA, MD − 0.42; 95%CrI − 0.72 to − 0.13) significantly lowered blood loss volume, with PBOAA being more effective than PBOIIA (MD − 0.60; 95%CrI − 1.05 to − 0.17). PBOAA and PBOIIA also significantly decreased blood loss volume (MD − 2.33; 95%CrI − 3.74 to − 0.94, MD − 1.57; 95%CrI − 2.77 to − 0.47 respectively) and hysterectomy rate (OR 0.31; 95%CrI 0.16 to 0.54, OR 0.53; 95%CrI 0.29 to 0.92 respectively). PBOAA has the highest probability of being more effective in reducing the blood loss volume, blood transfusion volume, and hysterectomy rate.
Conclusions Performing PBOAA, PBOCIA, or PBOIIA in PAS patients is an effective way to minimize blood loss volume, while PBOAA and PBOIIA also reduce blood transfusion volume and hysterectomy rate. PBOAA is a notably more effective strategy to reduce blood loss volume than PBOIIA.
Key Points
• *PBOAA, PBOCIA, and PBOIIA procedures can significantly reduce the blood loss volume compared to non-PBO intervention in PAS patients, of which PBOAA was more effective than the PBOIIA procedure.*
• *PBOAA and PBOIIA could significantly reduce the blood transfusion volume and hysterectomy rate in contrast to the non-PBO intervention in patients with PAS.*
• *According to our statistical treatment ranking, PBOAA was statistically superior in reducing blood transfusion volume, blood transfusion volume, and hysterectomy rate than other PBO procedures.*

Keywords Balloon occlusion · Hysterectomy · Placenta accreta · Postpartum hemorrhage

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Abbreviations

CI	Confidence interval
CrI	Credibility interval

DIC	Deviance information criterion
MD	Mean difference
OR	Odds ratios
PAS	Placenta accreta spectrum
PBO	Prophylactic balloon occlusion
PBOAA	Prophylactic balloon occlusion of the abdominal aorta
PBOCIA	Prophylactic balloon occlusion of the common iliac artery
PBOIIA	Prophylactic balloon occlusion of the internal iliac arteries
PBOUA	Prophylactic balloon occlusion of the uterine artery

Introduction

Placenta accreta spectrum (PAS) is a generalized term for placenta abnormally and firmly adhered to the uterine wall, which is associated with significant maternal morbidity as well as mortality and is a leading cause of severe obstetric hemorrhage or even peripartum hysterectomy [1]. Depending on the invasiveness of the placental chorionic villi, there are three major pathological subtypes: placenta accreta, placenta increta, and placenta percreta. A history of previous cesarean section is considered a major risk factor for PAS. Due to the rising global cesarean section rate, the morbidity of PAS has also increased from 0.8/1000 deliveries in the 1980s to 3/1000 deliveries during recent years [2].

Existing research shows that PAS has the highest emergency hysterectomy rate among all risk factors of postpartum hemorrhage and 90% of PAS patients will require blood transfusions (with 40% of patients even requiring massive transfusion). The average blood loss volume in patients with placenta increta or percreta has been reported to be up to 3000 ml and even exceeding 5000 ml in around 20% of patients [3–5]. Given the severity of PAS, further research and new interventional techniques are warranted to better manage and reduce bleeding, blood transfusion, and hysterectomy rates.

In the last few decades, endovascular interventional management strategies for bleeding control have been on the rise, such as prophylactic balloon occlusion (PBO). PBO can reduce the distal pulse pressure in the occluded arteries and reduce blood perfusion to the uterus, minimizing intraoperative bleeding. Based on the position of the balloon occlusion, PBO can be classified into different subtypes: prophylactic balloon occlusion of the abdominal aorta (PBOAA), common iliac artery (PBOCIA), internal iliac artery (PBOIIA), and uterine artery (PBOUA). However, the efficacy of PBO remains controversial, and there is no clear consensus on which artery should be chosen for occlusion intervention. There are only a few meta-analyses in the existing literature, and all of them are pairwise designs that compare non-PBO to PBOAA or PBOIIA. To this date, there is no comprehensive network meta-analysis to compare these four kinds of PBO interventions simultaneously.

To that end, we employed a Bayesian network meta-analysis to investigate the effectiveness of different PBO procedures for controlling PAS-related hemorrhage. The primary endpoints included blood loss volume, blood transfusion volume, and incidence of hysterectomy. The secondary endpoints comprised of the timing of balloon occlusion, radiation doses, and PBO-related complications.

Materials and methods

Search strategy

The literature was retrieved from PubMed, Embase, Cochrane Library, and Web of Science by Mesh terms and free keywords from the time of inception to July 2021. The following Mesh terms and free keywords were used in literature search: “placenta accreta,” “placenta increta,” “placenta percreta,” “placental abnormalities,” “prophylactic,” “balloon,” “catheter,” “occlusion,” “abdominal aorta,” “iliac artery,” “uterine artery,” and “endovascular”. The retrieved articles were imported into the Endnote X8 software and subsequently extracted by first screening the titles and abstracts. After preliminary screening, nonconforming literature was excluded by reading the full text, while the final remaining articles were selected for this study.

Inclusion and exclusion criteria

Studies that meet the following criteria included the following: (1) Studies comparing outcomes of patients with PAS who underwent PBO procedure before cesarean section versus those who did not; (2) Studies reporting on at least one outcome of our primary or secondary endpoints; (3) Studies published in English from inception to July 2021.

Studies with the following criteria excluded the following: (1) Studies not reporting a control group, without a clear confirmation of PAS, or reporting the use of PBO procedure in emergency setting; (2) case report, review articles, editorials, letters, and conference abstracts; (3) duplicated reports; (4) incomplete data and undetermined outcome endpoints.

Data extraction

Data extraction was performed independently by two reviewers. Disagreements were solved by discussion and following a third reviewer’s opinion. The main data extracted included: First author, year of publication, country of publication, patient characteristics, treatment methods, primary and secondary endpoints, and quality assessment. If the included studies did not provide standard deviations, the standard deviations were recalculated using the formula that was suggested in the Cochrane Handbook [6].

Quality evaluation

The quality assessment was completed by two independent researchers using the Newcastle–Ottawa Quality Assessment Scale. According to this scale, a study can be awarded a maximum of nine stars; four stars for study selection, two stars for comparability, and three stars for outcome sections. However, this scale does not provide a threshold score for distinguishing a good from a poor study. Publication bias was assessed using the comparison-adjusted funnel plots.

Statistical analysis

Firstly, we did a traditional pairwise meta-analysis for all available direct evidence using RevMan-5.4 software (the Cochrane Collaboration). Heterogeneity between studies was estimated using the chi-squared test (significant when the p value < 0.1) and the I^2 test (substantial heterogeneity when I^2 value $> 50\%$). If studies showed a significant heterogeneity ($I^2 > 0.5$, $p < 0.1$), a random-effects model was used to analyze the pooled effect sizes; if no significant heterogeneity ($I^2 < 0.5$, $p > 0.1$) was detected, a fixed-effects model was used. The mean difference (MD) and 95% confidence interval (95% CI) were calculated for continuous variables; odds ratios (OR) and 95% CI were calculated for dichotomous variables.

A Bayesian network meta-analysis was then performed using R-3.5 software (R Foundation for Statistical Computing) via the gemtc package. The statistical heterogeneity in the entire network was assessed based on the value of the heterogeneity parameter (I^2). The posterior distribution results were reported using its median (MD or OR), accompanied by the 95% credibility intervals (95% CrIs). The model's overall fit was assessed by calculating the ratio value of the posterior mean residual deviance with a random effect model and the number of independent data points [7; 8]. The consistency was evaluated by comparing the fit of consistency and inconsistency models using deviance information criteria (differences < 5 are considered consistency fitting) [9].

A network meta-regression analysis for the information of procedures operators (interventional radiologists or vascular surgeons) was conducted to address heterogeneity or confounding in the entire network. For each outcome, we evaluated the probability that each intervention is the first best, second best, third best, etc., based on the rank order of this intervention in each iteration of the Markov chain. $p \leq 0.05$ was considered statistically significant.

Results

As shown in Fig. 1, a total of 1010 articles were identified initially, 942 of which were excluded based on the title and abstract. The full texts of the remaining 68 articles were read. After re-excluding 9 articles, 59 articles were finally included in the network meta-analysis. The flow diagram of study selection is shown in Fig. 1.

Study characteristics

Fifty nine studies were incorporated in this network meta-analysis, including 5150 PAS patients undergoing cesarean section. Among them, 2913 patients underwent the PBO procedure, and the remaining 2237 patients did not undergo any PBO procedure. Of those patients who underwent the PBO procedure, 1605 were included in the PBOIIA management group, 137 were included in the PBOCIA management group, 1112 were included in the PBOAA management group, and 59 were included in the PBOUA management group. Apart from one study [10], the other 21 studies [11–31] reported radiation doses of less than 100 mGy. PBO procedure–related complications were reported in 65 (2.2%) patients. Artery thrombosis, a most common balloon-related vascular complication, was reported in 37 (1.2%) patients. Other PBO-related complications included dissection of an artery (4 patients), groin hematoma (7 patients), abdominal aortic dissection leading to death (1 patient), balloon rupture (2 patients), pseudoaneurysm in the common femoral artery (3 patients), balloon migration (1 patient), buttock claudication (1 patient), and lower limb paraesthesia (2 patients). The characteristics of the patients in the included studies are shown in Table 1.

Bayesian network meta-analysis

The network evidence maps of eligible comparisons are displayed in Supplementary Fig. 1.

Blood loss volume

A total of 55 articles compared the blood loss volume between the PBO group and the non-PBO group. PBOAA (MD – 1.02; 95%CrI – 1.4 to – 0.67), PBOCIA (MD – 0.84; 95%CrI – 1.36 to – 0.06), and PBOIIA (MD – 0.42; 95%CrI – 0.72 to – 0.13) significantly lowered the blood loss volume compared to the non-PBO treatment (Table 2). Moreover, PBOAA procedures encountered significantly less blood loss volume than those who underwent PBOIIA (MD – 0.60; 95%CrI – 1.05 to – 0.17). From the treatment

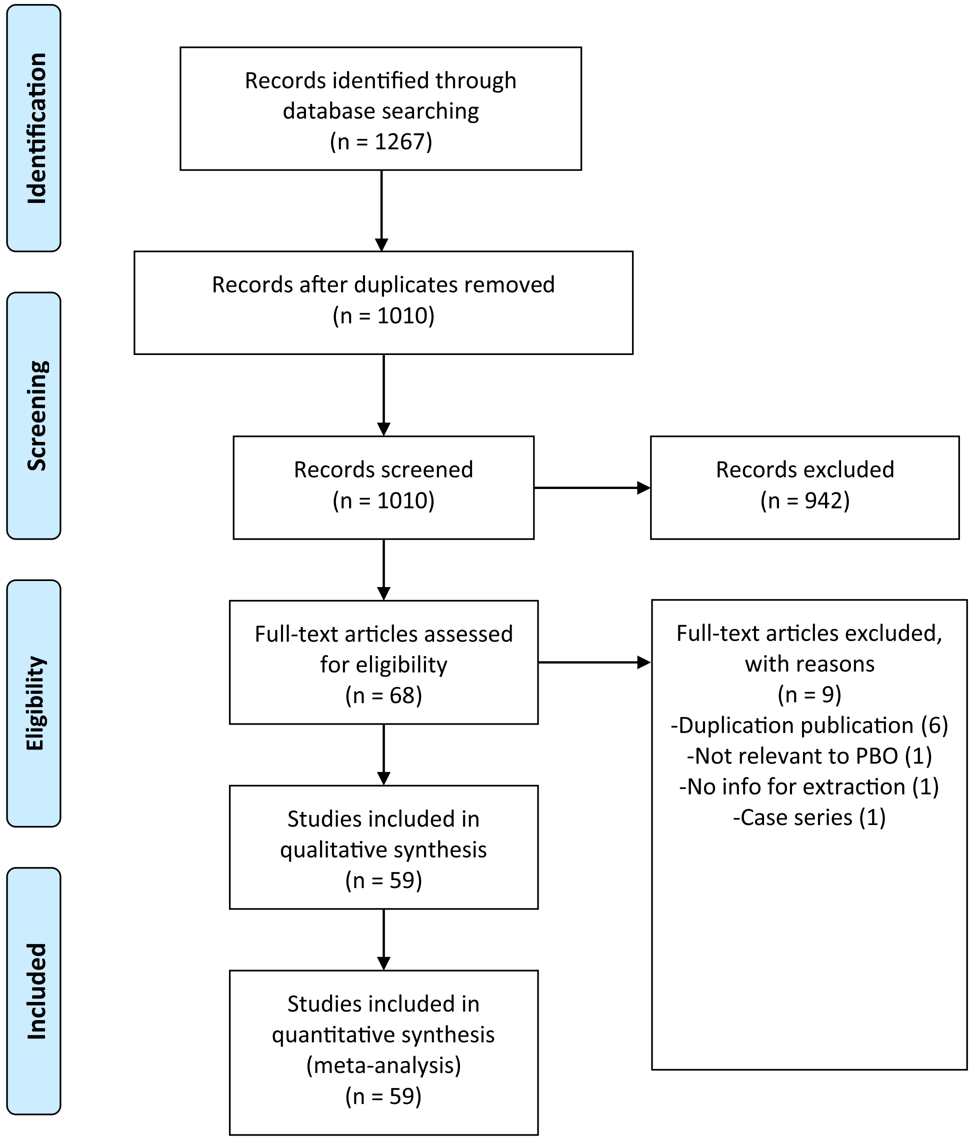

Fig. 1 The flow diagram of study selection

ranking gram (Fig. 2), PBOAA had the highest probability (46%) to be the best treatment for reducing blood loss volume.

Blood transfusion volume

Forty-six studies involving 4161 patients compared the blood transfusion volume between the PBO group and the non-PBO group. In contrast to the non-PBO group, the PBOAA (MD − 2.33; 95%CrI − 3.74 to − 0.94) and PBOIIA (MD − 1.57; 95%CrI − 2.77 to − 0.47) treatment groups had a notably lower blood transfusion volume (Table 2). However, there was no significant difference among the PBOIIA, PBOCIA, PBOAA, and PBOUA subgroups ($p > 0.05$). According to the treatment ranking gram (Fig. 2), PBOAA was ranked first in the probability of reduced blood transfusion volume.

Hysterectomy

Excluding the studies that had patients undergoing a planned cesarean hysterectomy after the PBO procedure, 42 studies compared the hysterectomy rate between the PBO and non-PBO groups. PBOAA (OR 0.31; 95%CrI 0.16 to 0.54) and PBOIIA groups (OR 0.53; 95%CrI 0.29 to 0.92) showed a reduced hysterectomy rate compared to the non-PBO group (Table 2). No significant difference was observed among the PBOIIA, PBOCIA, and PBOAA groups ($p > 0.05$). According to the treatment ranking gram (Fig. 2), PBOCIA had the highest probability to be the best treatment, followed by PBOAA. But considering that the difference between PBOCIA and non-PBO groups was not statistically significant (OR 0.23; 95%CI 0.04 to 1.2; $p > 0.05$), we concluded that it was PBOAA that ranked first as the intervention with statistically the lowest risk of hysterectomy.

Table 1 Characteristics of the included studies

Study	Country	Study design	Interventions	Sample size, *n*	Age, year	Mean occlusion time and radiation doses	Balloon-related complication
Bodner, L. J 2006	USA	Retro	G1: non-PBO G2: PBOIIA	G1: 22 G2: 6	G1: 35.3 ± 3.9 G2: 35.3 ± 7.6	NR	NR
Cher, H. T 2007	Singapore	Retro	G1: non-PBO G2: PBOIIA	G1: 14 G2: 11	G1: 35.0 ± 3.9 G2: 32.0 ± 2.5	84.1 (36–156) min	No
Shrivastava, V 2007	USA	Retro	G1: non-PBO G2: PBOIIA	G1: 50 G2: 19	G1: 34 ± 6.4 G2: 33 ± 4.7	NR	IIA thrombosis (1); IIA dissection (1); femoral artery thrombosis (1)
Ballas, J 2012	Canada	Retro	G1: non-PBO G2: PBOUA	G1: 58 G2: 59	G1: 33.2 ± 6.3 G2: 32.6 ± 5.8	NR	Femoral artery thrombosis (1); catheter site hematoma (1)
Panici, P. B 2012	Italy	Pros	G1: non-PBO G2: PBOAA	G1: 18 G2: 15	G1: 27.5 ± 1.7 G2: 29.4 ± 1.9	32 (25–39) min	No
Cali, G 2014	Italy	Pros	G1: non-PBO G2: PBOIIA	G1: 23 G2: 30	G1: 33.9 ± 4.0 G2: 34.3 ± 4.5	NR	No
Darwish, H. S 2014	Egypt	Retro	G1: non-PBO G2: PBOIIA	G1: 12 G2: 30	G1: 33.5 ± 3.5 G2: 33.8 ± 3.8	NR	No
Broekman, E. A 2015	Netherlands	Retro	G1: non-PBO G2: PBOIIA	G1: 26 G2: 42	G1: 34.1 ± 3.7 G2: 32.6 ± 4.3	NR	No
Salim, R 2015	Israel	RCT	G1: non-PBO G2: PBOIIA	G1: 14 G2: 13	G1: 37.2 ± 5.6 G2: 34.4 ± 4.3	NR	Buttock claudication (1)
Vinas, M. T 2015	UK	Retro	G1: non-PBO G2: PBOIIA	G1: 11 G2: 19	G1: 35.0 ± 5.1 G2: 36.1 ± 5.1	NR	IIA thrombosis (1)
Chen, M 2016	China	Retro	G1: non-PBO G2: PBOAA	G1: 20 G2: 23	G1: 31.3 ± 5.0 G2: 31.2 ± 5.1	37.0 (25–55) min 52.9 (33–71)mGy	No
Omar, H. R 2016	USA	Retro	G1: non-PBO G2: PBOCIA (3) + PBOIIA (11)	G1: 28 G2: 14	G1: 33.1 ± 6.0 G2: 32.7 ± 3.9	NR	Groin hematoma (1)
Wu, Q 2016	China	Retro	G1: non-PBO G2: PBOAA	G1: 38 G2: 230	G1: 30.4 ± 4.0 G2: 29.5 ± 3.6	23.6 ± 7.8 min 5.1 ± 3.0 mGy	Vein thrombosis (2)
Al-Hadethi, S 2017	Australia	Retro	G1: non-PBO G2: PBOCIA	G1: 27 G2: 25	G1: 34 ± 5.1 G2: 23 ± 5.0	NR	Artery thrombosis (2)
Cui, S 2017	China	Retro	G1: non-PBO G2: PBOAA	G1: 31 G2: 38	G1: 31.0 ± 4.4 G2: 31.2 ± 5.3	NR 3.3 ± 1.1 mGy	IIA thrombosis (1)
Fan, Y 2017	China	Pros	G1: no-nPBO G2: PBOIIA	G1: 89 G2: 74	G1: 32.0 ± 0.4 G2: 32.6 ± 0.6	NR 10.2 ± 1.5 mGy	IIA thrombosis (1)
Feng, S 2017	China	Retro	G1: non-PBO G2: PBOIIA	G1: 11 G2: 30	G1: 32.5 ± 5.7 G2: 31.1 ± 5.6	NR	No
Wang, Y. L 2017	China	Pros	G1: non-PBO G2: PBOAA	G1: 33 G2: 10	G1: 33.3 ± 3.9 G2: 31.0 ± 4.8	< 50 min	No
Xie, L 2017	China	Retro	G1: non-PBO G2: PBOAA	G1: 41 G2: 30	G1: 30.7 ± 4.9 G2: 32.1 ± 4.9	24.5 (9–52) min < 50 mGy	Hematoma in right common femoral artery (1)
Zeng, C 2017	China	Retro	G1: non-PBO G2: PBOAA	G1: 38 G2: 48	G1: 33.1 ± 5.2 G2: 32.3 ± 5.3	NR	Femoral artery thrombosis (1)
Zhu, B 2017	China	Retro	G1: non-PBO G2: PBOAA	G1: 37 G2: 42	G1: 31.6 ± 3.6 G2: 31.8 ± 5.2	NR	Abdominal aortic dissection to death (1)
Blumenthal, E 2018	USA	Retro	G1: non-PBO G2: PBOAA	G1: 19 G2: 16	G1: 33.9 ± 3.5 G2: 34.7 ± 4.5	66.5 (3–156) min	Groin hematoma (1)
Dai, M. J 2018	China	Retro	G1: non-PBO G2: PBOIIA	G1: 22 G2: 20	G1: 32.1 ± 2.2 G2: 32.3 ± 5.6	NR	Artery thrombosis (1)
Duan, X 2018	China	Retro	G1: non-PBO G2: PBOAA	G1: 23 G2: 22	G1: 31.7 ± 8.5 G2: 32.1 ± 6.9	20.5 ± 6.2 min 4.1 ± 3.2 mGy	No

Table 1 (continued)

Study	Country	Study design	Interventions	Sample size, *n*	Age, year	Mean occlusion time and radiation doses	Balloon-related complication
Gulino, F. A 2018	Italy	Pros	G1: non-PBO G2: PBOIIA	G1: 21 G2: 16	G1: 36.5 ± 5.1 G2: 36.2 ± 6.2	NR	NR
Li, K 2018	China	Retro	G1: non-PBO G2: PBOAA G3: PBOCIA G4: PBOIIA	G1: 87 G2: 33 G3: 42 G4: 37	G1: 33.4 ± 4.3 G2: 35.1 ± 6.4 G3: 35.2 ± 5.6 G4: 33.2 ± 5.4	G2: 40.9 ± 13.4 min 7.6 ± 3.2 mGy G3: 43.1 ± 14.9 min 14.0 ± 4.0 mGy G4: 59.0 ± 16.5 min 34.9 ± 10.6 mGy	No
Li, N 2018	China	Retro	G1: non-PBO G2: PBOAA	G1: 32 G2: 24	G1: 33.3 ± 3.4 G2: 33.8 ± 5.1	23.8 (5–50) min	No
Mei, Y 2018	China	Retro	G1: nonP-BO G2: PBOIIA	G1: 20 G2: 20	G1: 32.1 ± 6.2 G2: 33.9 ± 4.9	About 30 min 20 – 45 mGy	No
Ono, Y 2018	Japan	Retro	G1: non-PBO G2: PBOCIA	G1: 28 G2: 29	G1: 34.5 ± 3.6 G2: 33.7 ± 3.8	41.8 ± 15.0 min 29.4 ± 25.0 mGy	No
Picel, A. C 2018	USA	Retro	G1: non-PBO G2: PBOIIA	G1: 61 G2: 90	G1: 33.2 ± 6.0 G2: 33.3 ± 5.7	NR 52.7 ± 64.7 mGy	dissection of CIA (1); balloon rupture on inflation (1); hematoma (3); pseudoaneurysm in common femoral artery (2); thrombosis of external iliac artery (1)
Sun, W 2018	China	Retro	G1: non-PBO G2: PBOAA	G1: 12 G2: 19	G1: 35.0 ± 3.4 G2: 31.9 ± 5.2	25.6 (6–80) min 4.2 ± 1.5 mGy	Thrombosis of IIA (1)
Chen, M 2019	China	Retro	G1: non-PBO G2: PBOIIA	G1: 31 G2: 83	G1: 31.9 ± 4.7 G2: 32.3 ± 5.1	NR	No
Fratto, V. M 2019	USA	Retro	G1: no-nPBO G2: PBOAA(7) + PBOIIA(29)	G1: 87 G2: 36	G1: NR G2: NR	NR	No
McGinnis, J. M 2019	UK	Retro	G1: non-PBO G2: PBOIIA	G1: 12 G2: 12	G1: 32.4 ± 3.4 G2: 34 ± 6.1	NR	No
Mei, Y 2019	China	Retro	G1: PBOAA G2: PBOIIA	G1: 74 G2: 100	G1: 35.0 ± 3.4 G2: 31.9 ± 5.2	G1: 18 (8–29) min 1.85 (1–2.9) mGy G2: 25 (13–30) min 25 (18–31) mGy	No
Wei, Y 2019	China	Retro	G1: PBOIIA G2: PBOAA	G1: 71 G2: 52	G1: 33.1 ± 4.2 G2: 32.4 ± 5.2	G1: 6.69 ± 1.24 min 2.26 ± 0.56 mGy G2: 6.63 ± 1.31 min 2.29 ± 0.55 mGy	NR
Zheng, Z. R 2019	China	Retro	G1: non–PBO G2: PBOAA	G1: 68 G2: 102	G1: 31.6 ± 5.2 G2: 32.3 ± 5.3	25 (5–59) min 3.2 (0.2–71) mGy	Venous thrombosis (1); artery thrombosis (7)
Chen, M 2020	China	RCT	G1: non-PBO G2: PBOIIA	G1: 50 G2: 50	G1: 33.3 ± 4.0 G2: 32.5 ± 4.6	NR	No
Cho, S. B 2020	Korea	Retro	G1: non-PBO G2: PBOIIA	G1: 25 G2: 17	G1: 34.8 ± 3.3 G2: 34.5 ± 2.9	45.8 (32.2–63.8) mGy	No
Dai, M 2020	China	Pros	G1: non-PBO G2: PBOIIA	G1: 27 G2: 73	G1: 32.6 ± 4.1 G2: 33.5 ± 5.0	8.0 ± 2.1 h 31.3 ± 5.4 mGy	Artery thrombosis (3)
Lee, A. Y 2020	USA	Retro	G1: non-PBO G2: PBOAA(12) + PBOIIA(16)	G1: 143 G2: 28	G1: 33.9 ± 5.0 G2: 33.2 ± 5.6	About 30 min; 5.1 ± 3.0 mGy for PBOAA; 29.4 ± 25 mGy for PBOIIA	No
Ma, Y 2020	China	Retro	G1: non-PBO G2: PBOIIA	G1: 30 G2: 34	G1: 34.4 ± 4.7 G2: 34.5 ± 5.0	NR	NR

Table 1 (continued)

Study	Country	Study design	Interventions	Sample size, *n*	Age, year	Mean occlusion time and radiation doses	Balloon-related complication
Mei, Y 2020	China	Retro	G1: PBOAA G2: PBOIIA	G1: 15 G2: 17	G1: 33.3 ± 4.9 G2: 33.1 ± 3.2	G1: 27.4 ± 5.1 min 1.9 ± 0.4 mGy G2: 27.7 ± 4.2 min 22.4 ± 3.4 mGy	No
Mironov, N. R 2020	USA	Retro	G1: non-PBO G2: PBOIIA	G1: 24 G2: 10	G1: NR G2: 34.1 ± NR	NR	No
Papillon-Smith 2020	Canada	Retro	G1: non-PBO G2: PBOIIA	G1: 32 G2: 47	G1: 34.1 ± 4.6 G2: 35.3 ± 6.5	NR	pseudo-aneurysm of common femoral artery (1); balloon migration (1); dissection of the femoral artery (1); balloon rupture (1)
Peng, W 2020	China	Retro	G1: non-PBO G2: PBOIIA G3: PBOCIA	G1: 296 G2: 252 G3: 38	G1: 32.7 ± 4.6 G2: 32.7 ± 4.5 G3: 32.7 ± 4.8	< 35 min	Thrombosis in PBOAA group (7); Thrombosis in PBOCIA group (1);
Peng, Y 2020	China	Retro	G1: non-PBO G2: PBOIIA	G1: 56 G2: 48	G1: 33.5 ± 4.5 G2: 32.1 ± 3.9	NR	Thrombosis of IIA (1)
Riazanova, O. V 2020	Russia	Retro	G1: non-PBO G2: PBOAA	G1: 12 G2: 16	G1: 35.3 ± 2.9 G2: 35.3 ± 6.1	18.1 (15.5–20.5) min	deep venous thrombosis (1); femoral artery thrombosis (1)
Tokue, H 2020	Japan	Retro	G1: PBOIIA G2: PBOAA	G1: 32 G2: 28	G1: 34 ± 4.3 G2: 35.1 ± 4.9	G1: 103.2 ± 3.7 min 24.9 ± 5.7 mGy G2: 76.9 ± 31.9 min 18.2 ± 4.2 mGy	No
Yu, S. C. H 2020	China	RCT	G1: non-PBO G2: PBOIIA	G1: 20 G2: 19	G1: 36.1 ± 5.1 G2: 34.8 ± 4.9	NR	No
Zhu, H 2020	China	Retro	G1: non-PBO G2: PBOAA	G1: 23 G2: 25	G1: 31.3 ± 6.4 G2: 32.7 ± 4.9	16.1 ± 6.4 min	lower limb paraesthesia (2)
Ahmed, H. A 2021	Qatar	Retro	G1: non-PBO G2: PBOIIA	G1: 34 G2: 33	G1: 34 ± 5.0 G2: 34 ± 3.6	NR	deep vein thrombosis (1)
Fan, Y 2021	China	Retro	G1: non-PBO G2: PBOIIA	G1: 56 G2: 72	G1: 32.2 ± 0.5 G2: 33.1 ± 0.7	11.9 ± 2.0 mGy	No
Huo, F 2021	China	Retro	G1: non-PBO G2: PBOAA	G1: 16 G2: 17	G1: 34.4 ± 4.8 G2: 32.8 ± 4.5	39.70 ± 58.08 min	NR
Liu, Y 2021	China	Retro	G1: non-PBO G2: PBOAA	G1: 106 G2: 168	G1: 32.3 ± 4.9 G2: 31.6 ± 4.4	< 10 mGy	Artery thrombosis (1)
Nieto-Calvache, A. J 2021	Colombia	Retro	G1: non-PBO G2: PBOIIA G3: PBOAA	G1: 37 G2: 30 G3: 46	G1: NR G2: NR G3: NR	G2: 28.5 (20.5–38.5) min G3: 22 (5–30) min	G2: right common Femoral vein thrombosis (2); G3: common femoral artery thrombosis (2); external iliac artery thrombosis (1)
Rosner-Tenerowicz, A 2021	Poland	Retro	G1: non-PBO G2: PBOIIA	G1: 14 G2: 15	G1: 34.7 ± 4.87 G2: 34.0 ± 5.04	NR	NR
Savukyne, E 2021	Italy	Retro	G1: non-PBO G2: PBOIIA	G1: 47 G2: 19	G1: 34.0 ± 4.1 G2: 33.2 ± 3.5	NR	No
Zhou, X 2021	China	Retro	G1: non-PBO G2: PBOIIA	G1: 25 G2: 58	G1: 32.5 ± 4.3 G2: 32.3 ± 4.2	36.4 (20–45)mGy	Popliteal artery thrombosis (1);

Abbreviations: G, group; NR, not report; PBO, prophylactic balloon occlusion; PBOAA, prophylactic balloon occlusion of the abdominal aorta; PBOCIA, prophylactic balloon occlusion of the common iliac artery; PBOIIA, prophylactic balloon occlusion of the internal iliac artery; PBOUA, prophylactic balloon occlusion of the uterine artery; Retro, retrospective; Pros, prospective; RCT, randomized controlled trial

Occlusion time and radiation doses

Seven studies compared the timing of balloon occlusion and radiation doses between PBOIIA and PBOAA. Bayesian network meta-analysis could not be performed in this case, so we just performed a traditional pairwise meta-analysis (see later).

Quality assessment

The corresponding Newcastle–Ottawa Quality Assessment results were presented in Supplementary Table 1. The quality scores of studies ranged from six to nine stars with a median of seven stars.

Heterogeneity, model fit, and inconsistency

The Brooks-Gelman-Rubin plots showed that the model had a sufficient convergence in the entire network (Supplementary Fig. 2). Global I^2 was used to evaluate heterogeneity which was 1% for blood loss volume, 2% for blood transfusion volume, and 7% for hysterectomy. The model fit was estimated by comparing the posterior mean residual deviance with the number of data points, and the results were similar (Supplementary Table 2). The DICs values were analogous between consistency and inconsistency models, suggesting that the data was therefore consistent.

Traditional pairwise meta-analysis

In addition, we conducted a standard pairwise meta-analysis to complement the Bayesian network meta-analytical results. The results are shown in Table 3. In brief, PBOAA, PBOIIA, and PBOUA procedures significantly reduced the blood loss volume as well as blood transfusion volume when compared to the non-PBO intervention. Similar to the results of Bayesian network analysis, PBOAA procedures significantly reduced the blood loss volume than those who underwent PBOIIA (MD − 0.73; 95%CI − 1.43 to − 0.02). PBOCIA only displayed a notable reduction in the hysterectomy rate, as compared with the non-PBO intervention. Taken together, the findings of our Traditional pairwise meta-analysis were almost similar to those of our network meta-analysis. Furthermore, the random effect model results matched the fixed-effect model's (Supplementary Table 3), suggesting that our results possess high consistency overall.

As for the balloon occlusion time and radiation doses, PBOAA was associated with a shorter occlusion duration (MD − 7.41; 95%CI − 11.78 to − 3.04) and a lower radiation dose (MD − 16.77; 95% CI − 29.57 to − 3.98) when compared to PBOIIA procedure.

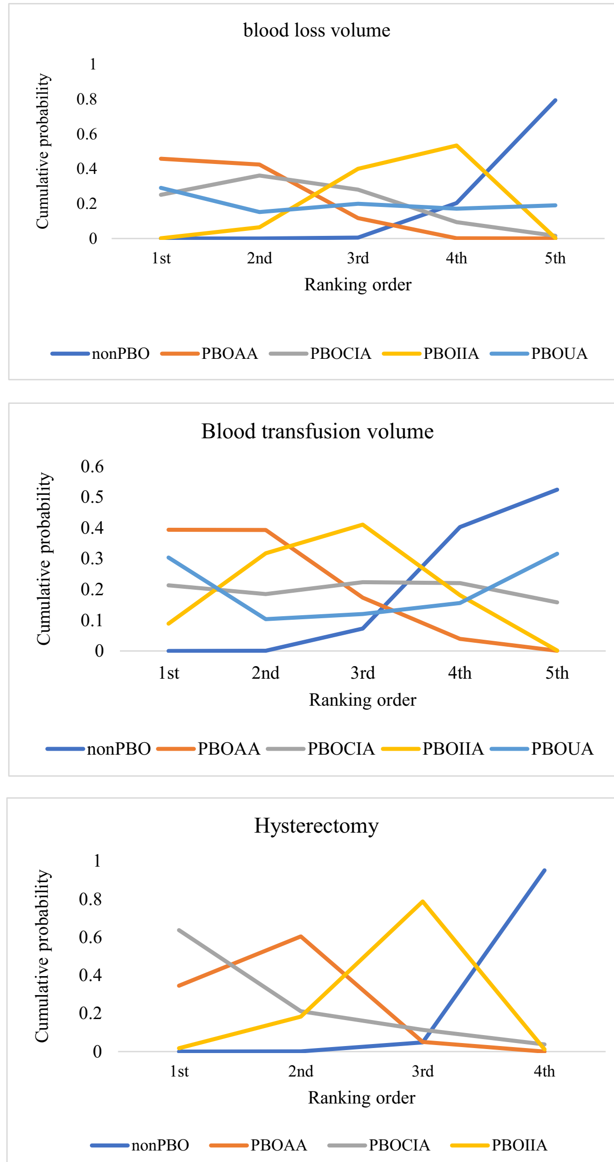

Fig. 2 Ranking grams of cumulative ranking probabilities for blood loss volume, blood transfusion volume, and hysterectomy

Meta-regression analyses

The meta-regression analysis for the information of procedures operators (interventional radiologists or vascular surgeons) did not alter the outcomes regarding the blood loss volume, blood transfusion volume, and hysterectomy (Supplementary Table 4).

Publication bias

The comparison-adjusted funnel plots were used to evaluate the publication bias. Visual estimation of the funnel plot revealed no significant asymmetry in the endpoints of blood

Table 2 Results of Bayesian network-analysis. For blood loss volume and blood transfusion volume, mean difference lower than 0 favors the row-defining treatment. For hysterectomy, odds ratio lower than 1 favors the row-defining treatment. Statistically significant results are in boldface

Blood loss volume				
non-PBO				
−1.02 (−1.4, −0.67)	PBOAA			
−0.84 (−1.36, −0.06)	0.18 (−0.63, 0.99)	PBOCIA		
−0.42 (−0.72, −0.13)	**0.60 (0.17, 1.05)**	0.42 (−0.41, 1.27)	PBOIIA	
−0.67 (−2.22, 0.86)	0.35 (−1.25, 1.93)	0.17 (−1.57, 1.92)	−0.28 (−1.85, 1.31)	PBOUA
Blood transfusion volume				
non-PBO				
−2.33 (−3.74, −0.94)	PBOAA			
−1.49 (−4.85, 2.19)	0.90 (−2.62, 4.58)	PBOCIA		
−1.57 (−2.77, −0.47)	0.70 (−0.97, 2.40)	−0.20 (−3.84, 3.34)	PBOIIA	
−1.19 (−7.11, 4.61)	1.13 (−4.97, 7.24)	0.21 (−6.75, 7.06)	0.34 (−5.70, 6.43)	PBOUA
Hysterectomy				
non-PBO				
0.31 (0.16, 0.54)	PBOAA			
0.23 (0.041, 1.2)	0.73 (0.13, 4.3)	PBOCIA		
0.53 (0.29, 0.92)	1.7 (0.85, 3.7)	2.4 (0.42, 13)	PBOIIA	

loss volume, blood transfusion volume, and hysterectomy rate (Supplementary Fig. 3), which means there was no obvious publication bias.

Discussion

Surgical management of PAS remains a clinical challenge. Endovascular interventional radiology techniques performed before surgery have been used extensively to treat postpartum hemorrhage, especially the PBO procedures. Placement of a balloon catheter in either the distal abdominal aorta, bilateral common iliac artery, internal iliac artery or uterine artery of PAS patients to temporarily reduce uterine blood flow would minimize bleeding and provide a clearer surgical field for obstetricians. However, there are different PBO techniques for PAS that vary considerably depending on the hospital and surgeon. To this date, the ideal PBO procedure remains up for debate, and there is a strong need for conformity.

Our study is the first comprehensive network meta-analysis of different PBO procedures in PAS patients undergoing a cesarean section. Herein we uncovered that in contrast to the non-PBO treatment, performing PBOIIA, PBOCIA, or PBOAA is associated with significantly reduced blood loss volume, blood transfusion volume, and lower hysterectomy

Table 3 Results of pairwise meta-analysis. For blood loss volume and blood transfusion volume, mean difference lower than 0 favors the row-defining treatment. For hysterectomy, odds ratio lower than 1 favors the row-defining treatment. Statistically significant results are in boldface

Blood loss volume				
non-PBO				
−1.05 (−1.47, −0.64)	PBOAA			
−0.74 (−2.53, 1.05)	0.23 (−0.58, 0.13)	PBOCIA		
−0.39 (−0.52, −0.26)	**0.73 (0.02, 1.43)**	**1.6 (1.20, 2.02)**	PBOIIA	
−0.67 (−0.77, −0.58)	NA	NA	NA	PBOUA
Blood transfusion volume				
non-PBO				
−2.53 (−4.05, −1.01)	PBOAA			
−0.32 (−10.58, 9.95)	−1.52 (−6.07, 3.02)	PBOCIA		
−1.64 (−2.29, −0.99)	0.10 (−3.89, 4.09)	−0.71 (−1.76, 0.34)	PBOIIA	
−1.2 (−1.89, −0.51)	NA	NA	NA	PBOUA
Hysterectomy				
non-PBO				
0.37 (0.21, 0.63)	PBOAA			
0.21 (0.08, 0.52)	2.46 (0.24, 24.82)	PBOCIA		
0 .77 (0.58, 1.03)	1.02 (0.39, 2.67)	**4.18 (1.04, 16.84)**	PBOIIA	

rate in PAS patients. Interestingly, PBOAA had a better effect of reducing blood loss than PBOIIA procedures (mean reduction 600 ml). The poorer performance of PBOIIA than PBOAA may be due to the extensive collateral circulation between the arteries in the pelvis. Through the collateral circulation, the branches originating from other blood vessels (including external iliac artery or femoral artery) can quickly compensate for the occluded arteries of the uterus [32], which causes PBOIIA may not completely block the uterine blood supply. PBOAA had the highest probability of being the best treatment in reducing blood loss volume, blood transfusion volume, and lower hysterectomy rate.

Interventional procedures routinely necessitate the use of X-rays which are associated with an increased risk of harm to the fetus development. However, according to the International Commission on Radiological Protection (ICRP), the fetal teratogenic risk does not increase if the radiation dose is less than 100 mGy. Of the 22 included studies that mentioned radiation doses, 21 had radiation doses below 100 mGy. Since catheterization into the abdominal aorta is easier than the common iliac artery, internal iliac artery, or uterine artery; the procedural time for PBOAA was the shortest; and the radiation doses were the lowest accordingly. Our meta-analysis confirmed that PBOAA was associated with lower radiation doses compared to that of PBOIIA and no radiation-related neonatal complications were reported in these studies.

Artery thrombosis is one of the most notable and common vascular complications related to PBO procedures. The risk of thrombosis is generally associated with the hypercoagulability of maternity blood, vascular intimal injury when inserting the balloon catheter, and the blocking time of balloon occlusion [33]. One previous study pointed out that the balloon occlusion time should not be too long to avoid thrombotic complications and PBOAA should be intermittently inflated for a maximum duration of 40 min, whereas PBOIIA balloons be intermittently inflated for a maximum duration of 4 h [17]. Similarly, a too-long balloon occlusion duration might also lead to limb ischemia necrosis or even the multiple organ dysfunction syndromes [11]. Thus, if there is a need to prolong the balloon occlusion time, it is necessary to deflate the balloon intermittently for 10–15 min to restore the blood supply. This meta-analysis presented that PBOAA has a shorter occlusion duration than PBOIIA.

Previous meta-analyses focused mainly on a specific PBO management, for instance, occlusion of the internal iliac artery or abdominal aorta [34–36]. The studies of He, Q. (2019) [35] and Chen, L. (2019) [34] showed that the use of PBOAA was associated with reduced blood loss volume, blood transfusion volume, and hysterectomy rate. In comparison, Nankali, A. (2021) [32] concluded that PBOIIA was only associated with reduced blood loss volume and hysterectomy rate, with no significant difference in blood transfusion volume. Other studies have also summarized the role of interventional radiology treatment modalities in the management of PAS, including the use of PBO procedures, but there was no quantitative analysis of the outcomes [37–39].

Only two meta-analyses analyzed the efficacy of different balloon occlusion procedures for hemorrhage control in PAS [40; 41]. The study of Shahin, Y 2018 [40] showed that interventional radiology significantly reduced blood loss and red blood cell transfusions, with no difference in unplanned hysterectomy. In addition, the subgroup analysis suggested that PBOAA was related with the lowest blood loss volume, blood transfusion volume, and hysterectomy rate during a cesarean section while PBOIIA correlated with decreased blood loss volume and blood transfusion volume only. The other meta-analysis [41], which included 13 studies, revealed significantly lower intraoperative blood loss in patients with PBO procedures than non-PBO procedures, with no statistical difference in other outcomes. However, this author made a general synthetic analysis with high heterogeneity ($I^2 = 98\%$), and no further subgroup analysis was conducted on the other different types of occlusion artery.

Our Bayesian network meta-analysis study possessed low global heterogeneity: 1% for blood loss volume, 2% for blood transfusion volume, and 7% for hysterectomy. More importantly, we also conducted a traditional pairwise meta-analysis that yielded consistent results compared to our Bayesian network meta-analysis. These results further affirmed the robustness of our findings.

Nevertheless, our study has some limitations: firstly, we observed high heterogeneity for direct pairwise meta-analysis in blood loss volume and blood transfusion volume ($I^2 > 50\%$). We tried to lower the heterogeneity using a sensitivity analysis by removing studies one at a time and reanalyzing them but were unsuccessful. We speculate that it may originate at the obstetrician, patient characteristics assessments, and blood loss volume estimation level. Moreover, most studies did not detail the area and depth of placental implantation of PAS patients, which may also be one of the sources of heterogeneity. Secondly, although we compared four different PBO procedures, most of the included studies focused on PBOAA or PBOIIA. The limited number of PBOCIA or PBOUA studies might affect the robustness of our findings, especially in their respective outcomes. Thirdly, for the outcome of hysterectomy rate, some studies had no event rates. Thus, the corresponding CrIs were very wide, resulting in increased uncertainty. Finally, limited by the small number of RCT studies, we only included 3 RCT studies in our analysis. If analyzing using more RCT, it can strengthen the evidence grade.

In conclusion, our Bayesian network meta-analysis indicated that PBOAA and PBOIIA could significantly reduce the blood loss volume, blood transfusion volume as well as hysterectomy rate in contrast to the non-PBO intervention in patients with PAS. PBOAA was more effective in reducing blood loss volume, fetus radiation dose, and balloon occlusion duration compared with PBOIIA. There were few studies in the literature-reported PBOCIA and PBOUA procedures. These limited researches showed that PBOCIA could only significantly reduce the blood loss volume compared with non-PBO intervention. What's more, according to our statistical treatment ranking, PBOAA was statistically superior in reducing blood transfusion volume, blood transfusion volume and hysterectomy rate than other PBO procedures.

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Declarations

Guarantor The scientific guarantor of this publication is Xuebin Zhang.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors has significant statistical expertise.

Informed consent Approval from the institutional animal care committee was not required because this is a meta-analysis based on published studies.

Ethical approval Institutional Review Board approval was not required because this is a meta-analysis based on published studies.

Methodology
• Bayesian network meta-analysis.

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