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INTERVENTIONAL

Endovascular interventional modalities for haemorrhage control in abnormal placental implantation deliveries: a systematic review and meta-analysis

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Abstract

Objectives To examine the evidence regarding the effectiveness and safety of endovascular interventional modalities for haemorrhage control in abnormal placentation deliveries.

Methods MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to July 2017. Blood loss volume was regarded as the primary endpoint. Other important results are described. Random and fixed effects models were used for the meta-analysis.

Results Of 385 studies identified, 69 (1,811 patients, mean age 32.9 years, range 23–39 years) were included. Mean gestational age at delivery was 35.1 weeks (range 27–38 weeks). Of 1,395 patients who underwent endovascular intervention, 587 (42%) had placenta accreta, 254 (18%) placenta increta and 313 (22%) placenta percreta. Prophylactic balloon occlusion of the internal iliac arteries (PBOIIA) was performed in 470 patients (33.6%), of the abdominal aorta (PBOAA) in 460 patients (33%), of the uterine artery (PBOUA) in 181 patients (13%), and of the common iliac arteries (PBOCIA) in 21 patients (1.5%). Primary embolization of the UA was performed in 246 patients (18%), of the pelvic collateral arteries in 12 patients (0.9%), and of the anterior division of the IIA in 5 patients (0.3%). Follow-up ranged from 0.5 to 42 months. Endovascular intervention was associated with less blood loss than no endovascular intervention ($p < 0.001$) with the lowest blood loss volume in patients who underwent PBOAA ($p < 0.001$). PBOAA was associated with a lower rate of hysterectomy ($p = 0.030$). Endovascular intervention did not result in increases in operative time or hospital stay.

Conclusions Endovascular intervention is effective in controlling haemorrhage in abnormal placentation deliveries. PBOAA was associated with a lower rate of hysterectomy and less blood loss than other modalities.

Key points

- *Endovascular intervention in abnormal placentation deliveries is effective in reducing blood loss.*
- *Endovascular intervention did not result in longer operative time or hospital stay.*
- *Prophylactic balloon occlusion of the abdominal aorta is superior to other modalities.*

Keywords Endovascular procedures · Balloon occlusion · Uterine artery embolization · Placenta accreta · Haemorrhage

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Abbreviations

MAP	Morbidly adherent placenta
PBOIIA	Prophylactic balloon occlusion of the internal iliac artery
PBOCIA	Prophylactic balloon occlusion of the common iliac artery
PBOAA	Prophylactic balloon occlusion of the abdominal aorta
PBOUA	Prophylactic balloon occlusion of the uterine artery
UA	Uterine artery
IIA	Internal iliac artery
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
OR	Odds ratio
MD	Mean difference
SD	Standard deviation
PRBC	Packed red blood cells

Introduction

Significant maternal morbidity and mortality can result from a morbidly adherent placenta (MAP) secondary to severe obstetric haemorrhage. Placental implantation abnormalities are classified as accreta, increta and percreta based on the depth of penetration of the chorionic villi, with placenta accreta being the most common but less severe implantation abnormality, and placenta percreta the least common but most severe abnormality. The incidence of placenta accreta ranges from 1 in 540 to 1 in 93,000 births with a tenfold increase since the 1950s due to the recent increase in the rate of caesarean deliveries [1]. MAP can be diagnosed before delivery using ultrasound and magnetic resonance imaging which enables early identification of women with this condition who are at high risk of haemorrhage.

Endovascular interventional modalities for haemorrhage control during caesarean section for placental implantation abnormalities are increasingly used. However, there is no consensus regarding the safety and effectiveness of these modalities. Prophylactic balloon occlusion of the internal iliac arteries (PBOIIA), common iliac arteries (PBOCIA), abdominal aorta (PBOAA) and uterine arteries (PBOUA) with or without embolization of the UA have been used. Other procedures include primary embolization of the UA, pelvic collaterals and anterior divisions of the IIA.

The objective of this study was to examine the evidence for the effectiveness and safety of endovascular interventional modalities for haemorrhage control in deliveries complicated by abnormal placentation. Blood loss volume was regarded as the primary endpoint. Secondary endpoints included blood transfusion, hysterectomy rate, mean fluoroscopic time, maternal and fetal radiation doses, length of hospital stay, operative time, balloon occlusion time and postoperative complications.

Material and methods

Search strategy

A systematic search of the medical databases MEDLINE, EMBASE, clinicaltrials.gov, and the Cochrane Central Register of Controlled Trials (CENTRAL) was performed. In addition, the reference lists of relevant articles were searched to identify articles missed by the electronic searches. The following MeSH terms and free keywords were used: 'prophylactic', 'iliac artery', 'balloon', 'catheter,' 'occlusion' ,'placental abnormalities', 'placenta accreta', 'placenta percreta', 'placenta increta', 'caesarean section', 'caesarean delivery', 'common iliac artery', 'abdominal aorta', 'uterine artery', 'embolisation', 'embolization', 'endovascular', 'haemorrhage', 'hemorrhage', 'control', 'intervention', 'interventional' and 'modality' . An expanded search was used using Boolean operators. The search was limited to studies published in English and involving humans. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) was used for the reporting of this study [2].

Inclusion criteria

The criteria for inclusion of studies in this systematic review were as follows: (1) studies of any design that reported outcomes of any endovascular intervention modality for control of haemorrhage in deliveries complicated by any placental implantation abnormality (increta, percreta, accreta, praevia, or low-lying placenta), including those that reported endovascular management of both intrapartum and postpartum haemorrhage; (2) studies including at least one of the outcome measures (primary or secondary endpoints) of this systematic review. and (3) studies published in English from inception until July 2017. A summary of these studies can be found in Table 1. Studies were excluded if data could not be extracted from the published report or if endovascular haemorrhage control had been performed during delivery for the purpose of termination of pregnancy.

Data extraction

The following data were recorded for each study: First author, year of publication, country of publication, patient characteristics (total number of patients, age, gestational age at delivery, parity and gravidity). The authors of the included studies were contacted when data were not available, as appropriate. Two independent reviewers extracted and checked the included studies. Disagreements between the reviewers were resolved by consensus.

Statistical analysis

Generic inverse variance was used for data analysis and to compare outcomes between the endovascular and control

Table 1 Characteristics of patients and included studies

Reference	Country	Type	No. of patients[a]	Age (years)	Gestation (weeks)	Gravidity	Parity	Prior caesarean section (*n*)	Prior placenta praevia (*n*)	Uterine surgery (*n*)	Placental abnormality (*n*)	Artery	Anaesthesia	Uterine artery embolization (*n*)	Transfusion, *n* (%)	Transfusion (units packed red blood cells)	Estimated blood loss (ml)	Length of stay (days)	Follow-up (months)
[3]	Australia	CR	1	33	34	3	NR	NR	NR	NR	Praevia percreta	AA	GA	NR	1 (100)	2	900	NR	NR
[4]	Canada	CR	2	33	33	6.5	3.5	2.5	NR	NR	Percreta (2)	Hypogastric	NR	NR	2 (100)	NR	2,350	8.5	NR
[5]	USA	CS	2	38.5	35	2.6	1	4	NR	2	Praevia accreta (2)	UA embolization	NR	2	2 (100)	9	3,650	NR	NR
[6]	USA	Pros	5	32.5	36.8	NR	NR	5	NR	3	Accreta (2), percreta (2), increta (1)	IIA (2), hypogastric (1), UA (2)	NR	0	4 (80)	5.5	5,025	8.5	NR
[7]	USA	CR	1	37	34	9	NR	NR	NR	NR	Increta	IIA	NR	0	1 (100)	3	1,500	8	17
[8]	USA	CS	5	30	37	5.2	2.8	12	NR	2	Accreta (2), percreta (1), praevia (1)	Hypogastric	NR	NR	3 (60)	11	2,240	NR	NR
[9]	UK	CR	1	34	38	NR	NR	1	NR	NR	Percreta	AA	GA	0	1 (100)	42	NR	NR	NR
[10]	Finland	Retro	7	33.9	37	NR	3.9	7	NR	NR	Praevia (5), accreta (2)	IIA	NR	0	NR	NR	4,500	NR	NR
[11]	Taiwan	CR	1	34	34	4	1	1	0	2	Percreta	CIA	NR	0	1 (100)	2	800	NR	NR
[12]	USA	CR	1	31	NR	2	1	NR	NR	0	Increta	UA embolization	LA	1	NR	NR	NR	NR	NR
[13]	USA	Retro	6	35.3	32.5	4.3	2.2	NR	NR	NR	Praevia accreta (3), praevia perceta (2), praevia increta (1)	IIA and IIA anterior divisions	NR	6	4 (67)	6.5	2,800	23	NR
[14]	USA	CR	1	37	37	3	2	1	1	NR	Praevia and accreta	IIA	Spinal	0	1 (100)	2	1,500	5	NR
[15]	USA	CR	1	27	27	3	3	3	NR	NR	Praevia accreta	IIA	Epi	NR	1 (100)	9	2,000	4	NR
[16]	France	Retro	6	30	NR	6	4	4	1	2	Accreta (4), increta (1), percreta (1)	UA embolization	NR	6	4 (84)	3	NR	NR	12.5
[17]	UK	CS	13	33	NR	NR	2	1	NR	NR	Praevia (8), accreta (4), percreta (1)	IIA	NR	7	9 (69)	8.7	6,415	NR	NR
[18]	USA	Retro	19	33	35.3	NR	NR	NR	NR	NR	Accreta (13), percreta (2), increta (4)	IIA and IIA anterior divisions	NR	NR	NR	10	2,700	5	NR
[19]	Singapore	Retro	11	32	36.2	3	2	1.5	NR	NR	Accreta (3), perceta (7), increta (1)	IIA	NR	NR	NR	NR	2,011	6.7	30
[20]	Taiwan	Pros	11	36	33.5	2	2.5	NR	NR	NR	Percreta (4) increta (3) accreta (4)	UA embolization	NR	11	NR	NR	3,090	NR	NR
[21]	Japan	CR	1	32	34	1	1	1	NR	NR	Praevia percreta	AA	NR	0	1 (100)	NR	3,200	NR	3
[22]	France	Retro	11	31.4	38	3.2	1.8	8	0	6	Accreta (11)	UA embolization	NR	11	7 (64)	NR	2,600	NR	26
			6	34.6	35	5.6	3.3	4	1	4	accreta (6)	UA embolization	NR	6	1 (17)	NR	700	NR	35
[23]	Israel	Retro	25	34.3	35.6	NR	NR	25	NR	NR	Accreta (25)	IIA	NR	23	NR	4	2,000	5.5	NR
[24]	Korea	CR	1	33	38	NR	NR	NR	NR	NR	Praevia increta	Hypogastric	GA	NR	NR	NR	800	6	NR
[25]	Brazil	CS	21	30.5	36	3.6	NR	1	NR	8	Accreta (10), percreta (7), increta (2), praevia (2)	IIA	NR	NR	13 (62)	1	NR	NR	NR
[26]	UK	CR	1	36	37	2	1	1	0	1	Percreta	IIA	spinal/GA	0	NR	NR	15,000		0.5
[27]	India	CS	6	30.67	NR	NR	NR	1	NR	NR	Praevia (6)	IIA	NR	0	0	0	1,117	12	NR
[28]	Korea	Retro	17	33.9	NR	2	1.5	5	5	3	Accreta (17)	UA embolization	NR	17	NR	NR	1,941	NR	30.7
[29]	Korea	Retro	8	31.5	37.5	NR	NR	NR	NR	NR	Accreta (8)	UA embolization	NR	8	1 (100)	21	NR	NR	NR
[30]	UK	Retro	13	31.6	38	NR	2	4	NR	NR	Accreta (4), praevia (6), low-lying placenta (3)	UA	Spinal/epidural/GA	1	5 (38)	4	800	NR	NR
[31]	France	CS	12	37.7	NR	4	2.5	9	NR	3	Accreta (4), increta (2), percreta (6)	Pelvic collateral arteries	NR	0	NR	12.5	1,000	NR	NR
[32]	New Zealand	CS	14	NR	35	4.5	NR	27	6	NR	Accreta (1), praevia (6), increta (1), undetermined (6)	IIA	GA	NR	8 (57)	8	3,861	NR	NR
[33]	USA	Retro	59	32.6	33.9	NR	NR	NR	2	NR	Accreta (24), percreta (35)	UA	NR	NR	46 (78)	5	2,165	7.6	NR
[34]	France	Retro	14	34	NR	NR	2.9	12	1	4	Accreta (10), percreta (4)	UA embolization	LA	14	7 (50)	5	2,242	NR	NR
[35]	Korea	Retro	40	34.7	NR	3.2	NR	7	10	NR	Accreta (40)	UA embolization	NR	40	35 (87.5)	3	NR	NR	NR
[36]	USA	CR	1	23	34	NR	NR	3	NR	NR	Praevia accreta	IIA	NR	0	1 (100)	4	4,500	NR	NR
[37]	China	Retro	10	31	30.4	3.5	NR	NR	NR	NR	Accreta (6), increta (4)	UA embolization	LA	10	NR	NR	NR	NR	11
[38]	UK	Retro	12	NR	NR	NR	NR	NR	NR	NR	Percreta (8), accreta (4)	UA	NR	NR	5 (42)	3	2,490	7	NR

Table 1 (continued)

Reference	Country	Type	No. of patients[a]	Age (years)	Gestation (weeks)	Gravidity	Parity	Prior caesarean section (*n*)	Prior placenta praevia (*n*)	Uterine surgery (*n*)	Placental abnormality (*n*)	Artery	Anaesthesia	Uterine artery embolization (*n*)	Transfusion, *n* (%)	Transfusion (units packed red blood cells)	Estimated blood loss (ml)	Length of stay (days)	Follow-up (months)
[39]	Italy	Pros	15	29.4	36	1.9	NR	15	NR	3	Accreta (13), increta (2)	AA	GA	0	7 (47)	0	950	3	NR
[40]	Hong Kong	Retro	6	37	35	4	2	2	NR	1	Accreta (3), percreta (3)	UA embolization	LA	6	0	0	5,500	14	6
[41]	Denmark	CS	15	34.9	33	3	2	1	0	0	Percreta (15)	IIA	Epi, GA	0	13 (87)	4	4,050	8	NR
[42]	Brazil	CS	13	36.5	NR	NR	NR	NR	NR	NR	Accreta (9), praevia (4)	IIA	NR	NR	5 (38)	2	NR	12.9	NR
[43]	UK	Retro	27	35.96	34	3.74	2.63	NR	NR	NR	Accreta (17), perceta (8), increta (2)	IIA	NR	8	14 (52)	NR	1,920	6	NR
[44]	Italy	CS	30	34.3	35.0	NR	NR	NR	NR	NR	Accreta perceta (18), increta (12)	Hypogastric	NR	NR	NR	1	933	6.8	NR
[45]	Egypt	CS	32	33.8	35.6	3.6	2	NR	NR	NR	Praevia accreta and percreta (32)	Hypogastric	NR	NR	27 (84)	3	1,900	21.9	NR
[46]	China	Pros	12	31	36	NR	NR	12	NR	12	Praevia accreta (7), praevia (4), percreta (1)	UA embolization	Epi	12	12 (100)	5	1,391	8.8	NR
[47]	Netherlands	Retro	42	32.6	37	NR	1	9	NR	NR	Praevia (42)	IIA	NR	NR	4 (10)	7	NR	NR	NR
[48]	China	Retro	13	32.8	32.2	NR	NR	NR	NR	NR	Accreta (1), increta (7), percreta (4), praevia (1)	CIA	NR	1	NR	NR	1,902	NR	NR
[49]	Canada	CS	10	34.7	36	3.8	1.7	2	NR	8	Increta (4), percreta (6)	IIA	NR	10	2 (20)	1	1,150	8.9	14
[50]	China	Retro	42	32.1	36.5	3.5	NR	2	NR	2	Accreta (37), percreta (5)	AA	GA	42	NR	1	586	5.5	6
[51]	Argentina	Retro	95	35	36	3	2	NR	NR	19	Accreta (20), perceta (36), increta (18), no praevia accreta (16)	UA	NR	90	45 (57)	NR	NR	4 and7	NR
[52]	Japan	CS	3	33.5	34.5	1	1	3	NR	NR	Accreta (3)	IIA	GA, Epi	0	2 (66)	4	1,500	15	NR
[53]	Japan	CR	1	34	37	2	2	1	NR	NR	Accreta	CIA	LA	0	1 (100)	12	5,020	8	NR
[54]	Germany	CS	3	34	31.5		2	2	NR	NR	Accreta (3)	CIA	NR	0	3 (100)	5	3,200	NR	NR
[55]	Israel	RCT	13	34.4	35.1	4.6	3.7	13	0	1	Accreta (12), percreta (1)	IIA	NR	0	11 (84)	5	1,600	6.6	4
[56]	China	Retro	45	31	35.3	NR	NR	42	NR	NR	Accreta (22), increta (20), percreta (3)	AA	GA, Epi	0	11 (24.4)	2	835	7.8	12
[57]	Germany	CS	3	34.5	32	3	NR	3	0	0	Accreta (1), increta (2)	CIA	NR	NR	1 (33)	1	933	NR	NR
[58]	Italy	Pros	50	33.2	35.5	3	2	44	NR	19	Praevia (23), accreta (21), percreta (6)	UA embolization	NR	50	NR	1	NR	4	6
[59]	Italy	Retro	12	35.66667	NR	3.5		2	NR	NR	Accreta (3), increta (1), percreta (1), praevia (7)	UA or anterior division of IIA embolization	NR	10	12 (100)	4	2,389	NR	42
[60]	USA	CR	1	39	36	9	2	1	0	1	Percreta	UA embolization	GA	1	NR	NR	1,000	7	2
[61]	Malaysia	Retro	13	32.8	NR	4	2.5	13	NR	3	Accreta (1), increta (6), percreta (2), praevia (4)	IIA	LA	2	7 (54)	2	1,261	5	NR
[62]	China	Retro	230	29.5	35.6	4.2	2	NR	NR	NR	Percreta (88), increta (112)	AA	LA	NR	NR	1	921	5.1	NR
[63]	China	Retro	18	30.8	35	3	1	NR	NR	NR	Accreta (10), percreta (3) Increta (5)	UA embolization	NR	18	NR	NR	1,372	NR	18
[64]	Italy	Retro	37	35	35	NR	NR	28	NR	NR	Accreta (14), percreta (20), increta (3)	IIA	Epi	4	24 (65)	4	2,052	4.5	NR
[65]	Korea	Pros	18	36.6	36.6	NR	NR	4	NR	NR	Praevia (18), otherwise undetermined	IIA and IIA anterior divisions	GA	8	14 (77.8)	6	1,950	9.9	NR
[66]	China	Retro	38	31.2	36.6	3.6	NR	1	NR	NR	Accreta (13), increta (12), percreta (13)	AA	Epi	12	NR	4	1,560.5	8.5	NR

Table 1 (continued)

Reference	Country	Type	No. of patients[a]	Age (years)	Gestation (weeks)	Gravidity	Parity	Prior caesarean section (*n*)	Prior placenta praevia (*n*)	Uterine surgery (*n*)	Placental abnormality (*n*)	Artery	Anaesthesia	Uterine artery embolization (*n*)	Transfusion, *n* (%)	Transfusion (units packed red blood cells)	Estimated blood loss (ml)	Length of stay (days)	Follow-up (months)
[67]	China	Retro	30	31.8	37	4	1	30	NR	NR	Accreta (9), increta (17), percreta (4)	IIA	GA	NR	14 (47)	0	1,000	5	NR
[68]	China	Retro	26	33	34.9	NR	NR	NR	NR	NR	Accreta (18), increta (7), percreta (1)	UA embolization	LA	26	NR	NR	2,080	NR	27
[69]	China	Pros	57	25.4	NR	NR	NR	NR	NR	NR	Accreta (57)	AA	GA	16	NR	1	450.4	5.7	6
	China	Pros	48	25.7	NR	NR	NR	NR	NR	NR	Accreta (48)	IIA	GA	14	NR	1.5	619	5.9	6
[70]	China	Retro	30	32	37	NR	3	25	NR	NR	Accreta/increta (25), percreta (5)	AA	GA, spinal epi	0	21 (70)	1	961	NR	NR
[71]	China	CR	1	25	33	3	2	1	NR	NR	Increta	IIA	LA	NR	1	9	4,200	NR	NR

CR case report, *CS* case series, *Pros* prospective, *Retro* retrospective, *RCT* randomized controlled trial, *GA* general anaesthesia, *LA* local anaesthesia, *Epi* epidural, *IIA* internal iliac artery, *CIA* common iliac artery, *AA* abdominal aorta, *UA* uterine artery, *NR* not reported

[a] Number of patients who underwent endovascular intervention

groups using odds ratios (OR) for dichotomous variables and weighted mean differences (MD) for continuous variables with their corresponding standard errors and 95% confidence intervals (CI). In studies reporting the medians and interquartile ranges, the medians were taken to be representative of the means, and the interquartile ranges were converted into standard deviations by dividing by 1.35 [72]. Standard deviations and 95% CIs were also converted to standard errors using a standard formula [72]. A sensitivity analysis was performed to assess the contribution of each study to the pooled treatment effect by excluding each study one at a time and recalculating the pooled treatment effect for the remaining studies. Treatment effect was considered significant if the p value was <0.050. Heterogeneity between studies was tested using both the chi-squared test (significant if the p value was <0.100) and the I^2 test (with substantial heterogeneity defined as values >50%). When studies showed significant heterogeneity, a random effects model was used to calculate the pooled effect sizes. A fixed-effects model was used when heterogeneity was insignificant. Review Manager version 5.0 (The Cochrane Collaboration 2008) was used for data analysis [73].

Risk of bias, publication bias and quality of included studies

Risk of bias of all the articles was assessed using the Cochrane Collaboration's tool for assessing risk of bias [72] and the Jadad scoring system [74] for controlled trials (Supplementary Table 1) and the Newcastle-Ottawa quality scale for cohort and case-controlled studies [75] (Supplementary Tables 2 and 3, respectively). Publication bias was assessed using the funnel plot technique. Blood loss volume and hysterectomy rate effect sizes were plotted against their standard errors.

Outcome measures

The primary endpoint was estimated blood loss volume. Secondary endpoints were total number of units of packed red blood cells (PRBC) transfused, number of patients transfused, hysterectomy rate, mean fluoroscopic time, maternal and fetal radiation doses, fetal complications including Apgar score, length of hospital stay, operative time, balloon occlusion time, and postoperative complications related to surgery or to the endovascular procedure.

Results

Literature search

The search identified 385 potentially eligible publications of which 300 were excluded on title and abstract. The full articles of the remaining 85 studies were collected and evaluated. Of

these 85 studies, 69 met the inclusion criteria and were included in the systematic review [3–71] (Table 1), and 16 were excluded [1, 76–90]. The reasons for exclusion are summarized in the PRISMA flow diagram presented in Fig. 1.

Characteristics of patients and trials

The analysis included 69 studies and 1,811 patients, of whom 1,395 (77%) underwent endovascular management for haemorrhage. Of the 69 studies, 16 [18, 19, 22, 33, 44, 47, 48, 55, 62, 63, 65–70] were controlled and the remainder were cohort studies (prospective or retrospective), case series or case reports. Of the 1,395 patients who underwent endovascular intervention, 13 were randomized in one trial [55], 938 were included in retrospective studies, 215 were included in case series or case report,s and 229 were included in prospective cohort or non-randomized controlled studies. Mean (range) patient age was 32.9 years (23 years [36] to 39 years [60]). Mean gestational age at delivery was 35.1 weeks (27 weeks [15] to 38 weeks [9, 22, 24, 30]), gravidity 3.7 (1–9), and parity 2.2 (1–4). Of the 1,395 patients, 587 (42%) had placenta accreta, 254 (18%) placenta increta, and 313 (22%) placenta percreta. PBOIIA was performed in 470 patients (33.6%), PBOAA in 460 patients (33%), PBOUA in 181 patients (13%), and PBOCIA in 21 patients (1.5%). Primary embolization of the UA was performed in 246 patients (18%), of the pelvic collateral arteries in 12 patients (0.9%), and of the anterior division of the IIA in 5 patients (0.3%). Mean body mass index ranged from 21 to 28.2 kg/m^2. In studies which reported previous uterine surgery, 415 patients (30%) had previous caesarean section and 76 (5%) had other uterine surgery including uterine curettage (0.8%). Mean fluoroscopy times and fetal radiation doses ranged from 0.04 min [50] to 38 min [59] and from 0.04 mGy [21] to 61 mGy [6], respectively. Mean maternal radiation doses ranged from 30.6 mGy [68] to 1,759 mGy [31]. Balloon inflation times ranged from 5 min [65] to 300 min [64]. Follow-up periods ranged from 0.5 months [26] to 42 months [59]. Other characteristics of the patients and studies are summarized in Table 1.

Methodological quality of included studies

This meta-analysis included studies that varied in methodological quality. Salim et al. [55] reported adequate sequence

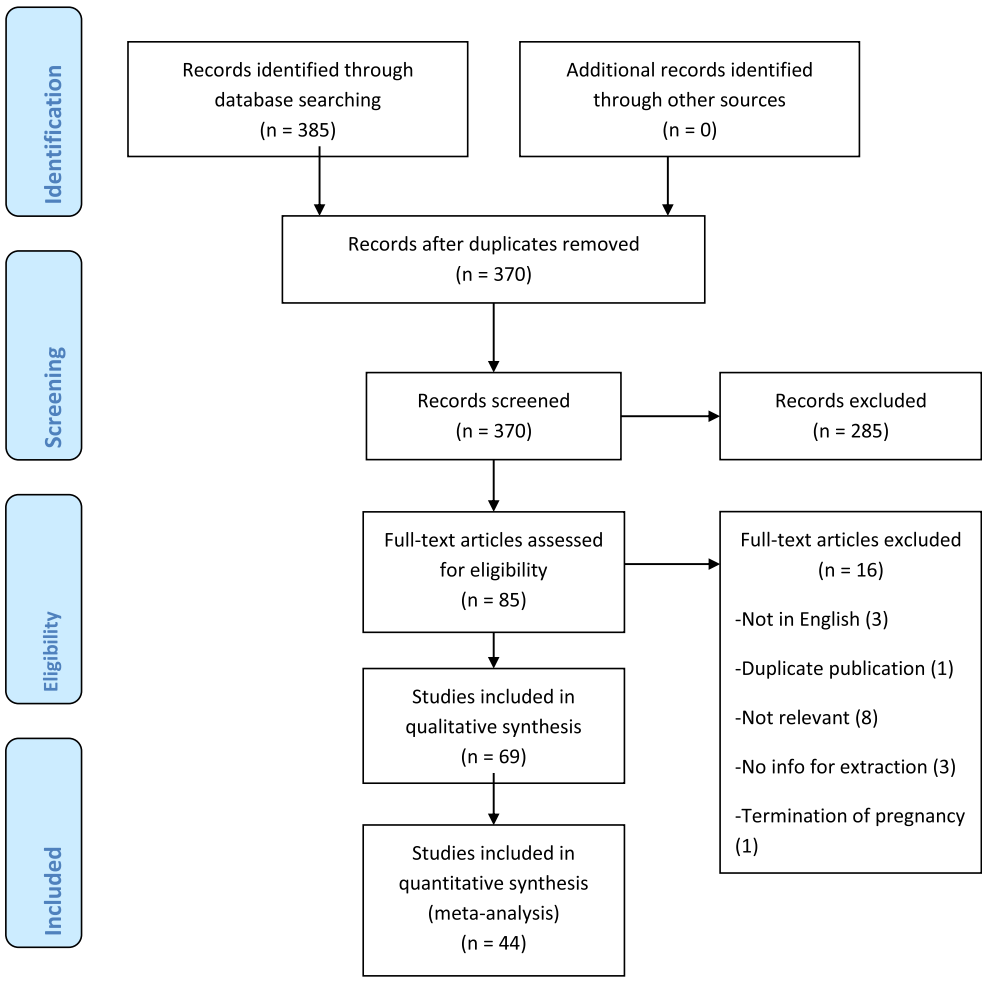

Fig. 1 PRISMA study flow diagram summarizing the literature search, and inclusion and exclusion criteria

generation and appropriate allocation to groups, but the study was open and other sources of bias could not be excluded. Wang et al. [69] performed a nonrandomized open controlled trial with adequate loss to follow-up reporting but with no sequence generation and inadequate group allocation. Furthermore, both studies were single-centre with a small sample size scoring 3 and 1 on the Jadad scale, respectively (Supplementary Table 1). The remaining 67 studies were retrospective and scored 3–7 on the Newcastle-Ottawa quality scale for cohort and case-controlled studies (Supplementary Tables 2 and 3, respectively). The retrospective aspect of these studies might have resulted in selection and information (misclassification) bias. Overall, the methodological quality of the included studies in this meta-analysis was moderate.

Quantitative synthesis (meta-analysis)

Cumulative blood loss volume

The mean blood loss volume from all endovascular procedures ranged from 586 ml [50] to 15,000 ml [26]. Blood loss volumes following PBOIIA were reported in 25 studies [8, 10, 13, 15, 17–19, 23, 25, 27, 32, 36, 41, 43–45, 47, 49, 55, 61, 64, 65, 67, 69]. The mean cumulative blood loss volume was 1,263 ml (95% CI 1,030 to 1,497.5 ml). Blood loss volumes following PBOAA were reported in seven studies [39, 50, 56, 62, 66, 69, 70]. The mean cumulative blood loss volume was 865.5 ml (613.6 to 1,117.4 ml). Mean blood loss volumes following PBOCIA [11, 48, 54, 57] and PBOUA [30, 33, 38] were 1,650 ml (827.5 to 2,473 ml) and 1,141 ml (265.3 to 2,016.8 ml), respectively. Blood loss volumes following UA embolization were reported in seven studies [20, 22, 28, 40, 46, 56, 63]. The mean blood loss volume was 2,273.4 ml (980.5 to 3,566.4 ml).

Endovascular intervention versus no endovascular intervention

Blood loss volume Overall, 14 studies [18, 19, 33, 39, 44, 47, 48, 55, 62, 65–68, 70] compared endovascular intervention with no endovascular intervention as control (Fig. 2). Endovascular intervention for haemorrhage control significantly reduced blood loss volume compared with no endovascular intervention (MD −893.24 ml, 95% CI −1,389.4 to −397 ml, $p < 0.001$). Seven studies [18, 19, 44, 47, 55, 65, 67] compared PBOIIA with no endovascular intervention. PBOIIA significantly reduced blood loss following delivery compared with no endovascular intervention (MD −232.11 ml, 95% CI −392 to −72.2 ml, $p = 0.004$) with no heterogeneity. In a subgroup analysis (Fig. 3) of PBOIIA for caesarean section [19, 47, 55, 65, 67] and caesarean hysterectomy [18, 44] for deliveries complicated by placental anomalies, only the latter was associated with a significant reduction in blood loss (MD −310 ml, 95% CI −565.3 to −55.6 ml, $p = 0.020$).

PBOAA was compared with no intravascular intervention as control in four studies [39, 62, 66, 70]. PBOAA significantly reduced blood loss volume (MD −1,391.7 ml, 95% CI −2,153 to −630 ml, $p < 0.001$) with significant heterogeneity ($I^2 = 94\%$, $p < 0.001$). PBOUA [33] and PBOCIA [48] significantly reduced blood loss volume compared with the control (MD −672 ml, 95% CI −768.9 to −575 ml and −2,544 ml, 95% CI −3,153.3 to −1,934.7 ml, respectively, $p < 0.001$). Embolization of the UA reduced blood loss compared with the control in one study [68], but not significantly (MD −720 ml, 95% CI −2,426.6 to 986.7 ml, $p = 0.410$).

Blood transfusion The number of PRBC units transfused was reported in 11 studies [18, 19, 33, 39, 44, 47, 55, 62, 66, 67, 70]. Overall, patients who underwent endovascular intervention for haemorrhage control had fewer PRBC units transfused than those who did not (MD −1.54 units, 95% CI −2.27 to −0.81 units, $p < 0.001$; Fig. 4). PBOAA reduced the number of PRBC units transfused (MD −1.68 units, 95% CI −3.03 to −0.34 units, $p = 0.010$). PBOIIA and PBOUA also reduced the number of PRBC units transfused compared with no endovascular intervention (PBOIIA MD −1.45 units, 95% CI −2.40 to −0.49 units, $p = 0.003$; PBOUA −1.54 units, 95% CI −2.27 to −0.81 units, $p < 0.001$; Fig. 4).

Operative time Operative time was reported in nine studies [18, 19, 44, 47, 55, 62, 66, 67, 70]. Operative time was shorter in patients who underwent endovascular intervention than in those who did not, but not significantly (MD −4.21 min, 95% CI −19.6 to 11.2 min, $p = 0.590$; Supplementary Fig. 1).

Hysterectomy rate The unplanned caesarean hysterectomy rates in patients who underwent endovascular intervention and in those who did not were compared in eight studies [39, 55, 62, 65–68, 70]. Overall, the hysterectomy rates were not significantly different between the two groups (OR 0.63, 95% CI 0.25 to 1.57, $p = 0.320$; Fig. 5). However, patients who underwent PBOAA were less likely to have hysterectomy (OR 0.27, 95% CI 0.08 to 0.89, $p = 0.030$; Fig. 5).

Length of hospital stay Supplementary Fig. 2 summarizes the pooled data from ten studies comparing the length of hospital stay between patients who underwent endovascular intervention and those who did not [18, 19, 33, 39, 44, 55, 62, 65–67]. There was no significant difference between the two groups (MD −0.55 days, 95% CI −2.15 to 1.06 days, $p = 0.500$).

Complications of surgical and endovascular procedures

The most common surgical complication was bladder injury requiring repair (86 patients). In 14 patients admission to the

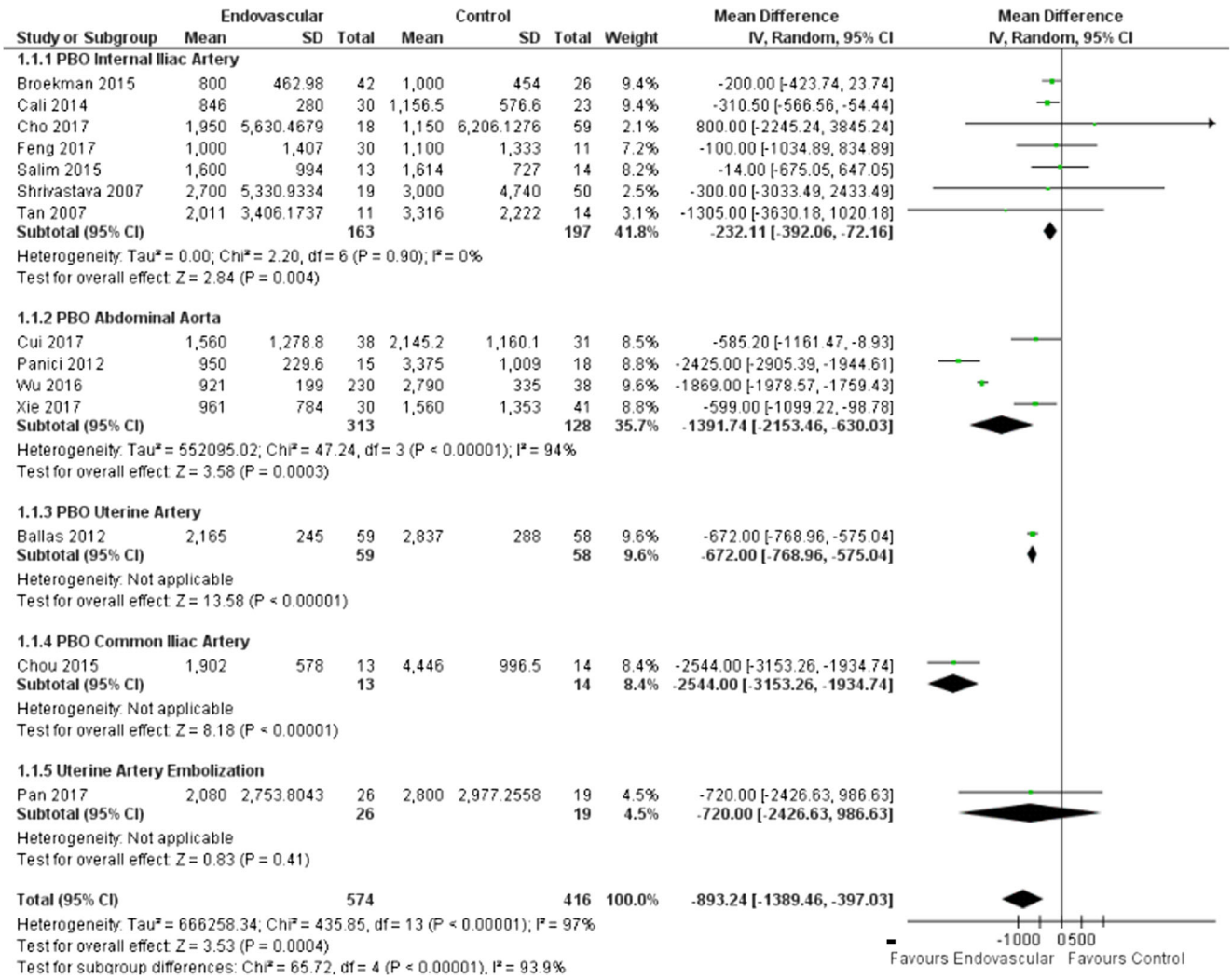

Fig. 2 Forest plot comparing blood loss volume (in millilitres) between the endovascular and control groups. Small squares represent mean differences for each of the included studies. The 95% confidence intervals (*CI*) for individual studies are represented by the horizontal lines and the pooled effects by diamonds. *PBO* prophylactic balloon occlusion, *SD* standard deviation, *IV* inverse variance

intensive care unit was required. Ureteric injury was reported in 3 patients and disseminated intravascular coagulopathy in 23 patients. Other surgical complications included vesicovaginal or vesicouterine fistula formation (3 patients), reoperation (5 patients), rebleeding requiring further endovascular intervention or surgical ligation (5 patients), endometritis (6 patients), and surgical wound-related complications (30 patients). Of patients who underwent PBOIIA or PBOCIA, 10 developed intermittent lower limb or buttock claudication and 16 had arterial thrombosis. Balloon rupture occurred in 1 patient and balloon migration in 3 patients. Two patients developed access vessel pseudoaneurysm. Of patients who underwent UA embolization, 43 developed post-embolization syndrome (fever and lower abdominal pain) which was self-limiting, and 2 patients had uterine necrosis requiring hysterectomy. Overall, including all procedures, 10 patients developed groin haematoma.

Fetal complications

Neonatal birth weights ranged from 1,650 g [20] to 3,500 g [24]. An Apgar score of <7 at 1 minute was reported in ten neonates [3, 66–68]. An Apgar score of <7 at 5 minutes was reported in three neonates [3, 55]. Three fetal deaths were reported in one study [51] due to maternal complications following caesarean section before 24 weeks gestation. In one patient, intrauterine death was confirmed prior to surgery.

Evaluation of publication bias

Funnel plots for studies assessing endovascular intervention versus no endovascular intervention with blood loss volume and hysterectomy rate as outcome measures showed asymmetry on visual inspection (Fig. 6 and Supplementary Fig. 3, respectively) with gaps suggesting that few studies with negative results have been published.

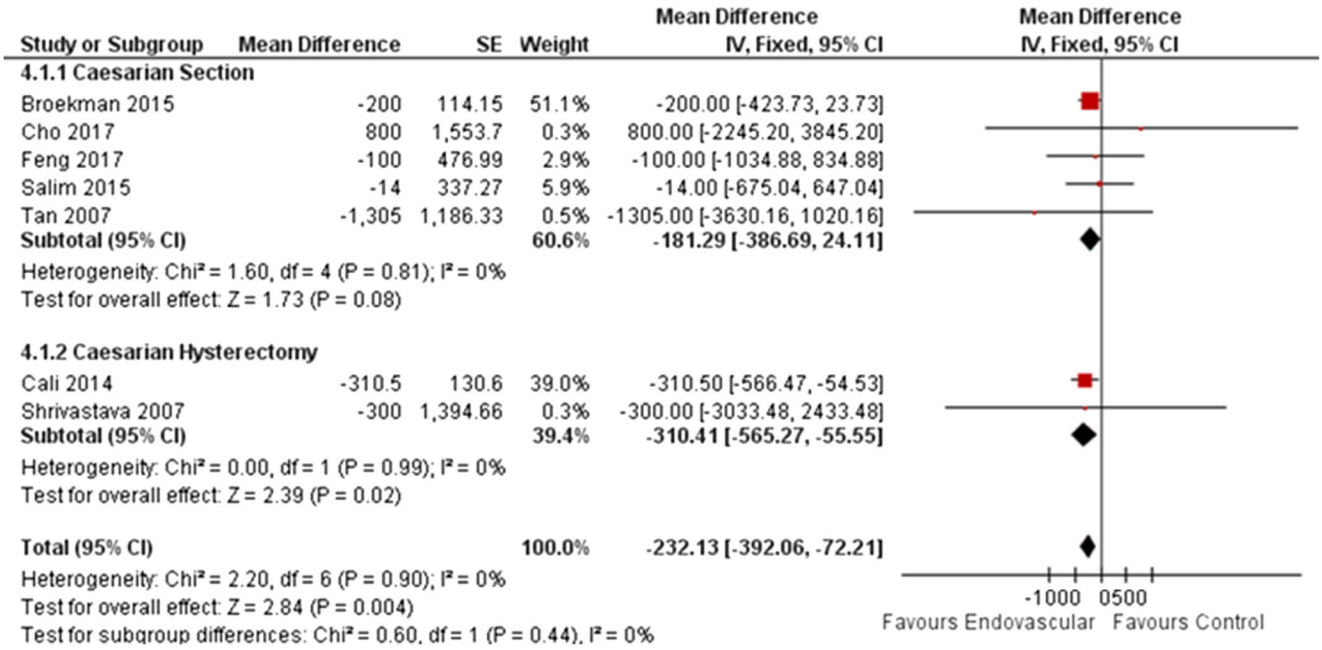

Fig. 3 Forest plot illustrating subgroup analysis of PBOIIA comparing blood loss volume between the endovascular and control groups. *SE* standard error. For further details see Fig. 2 legend

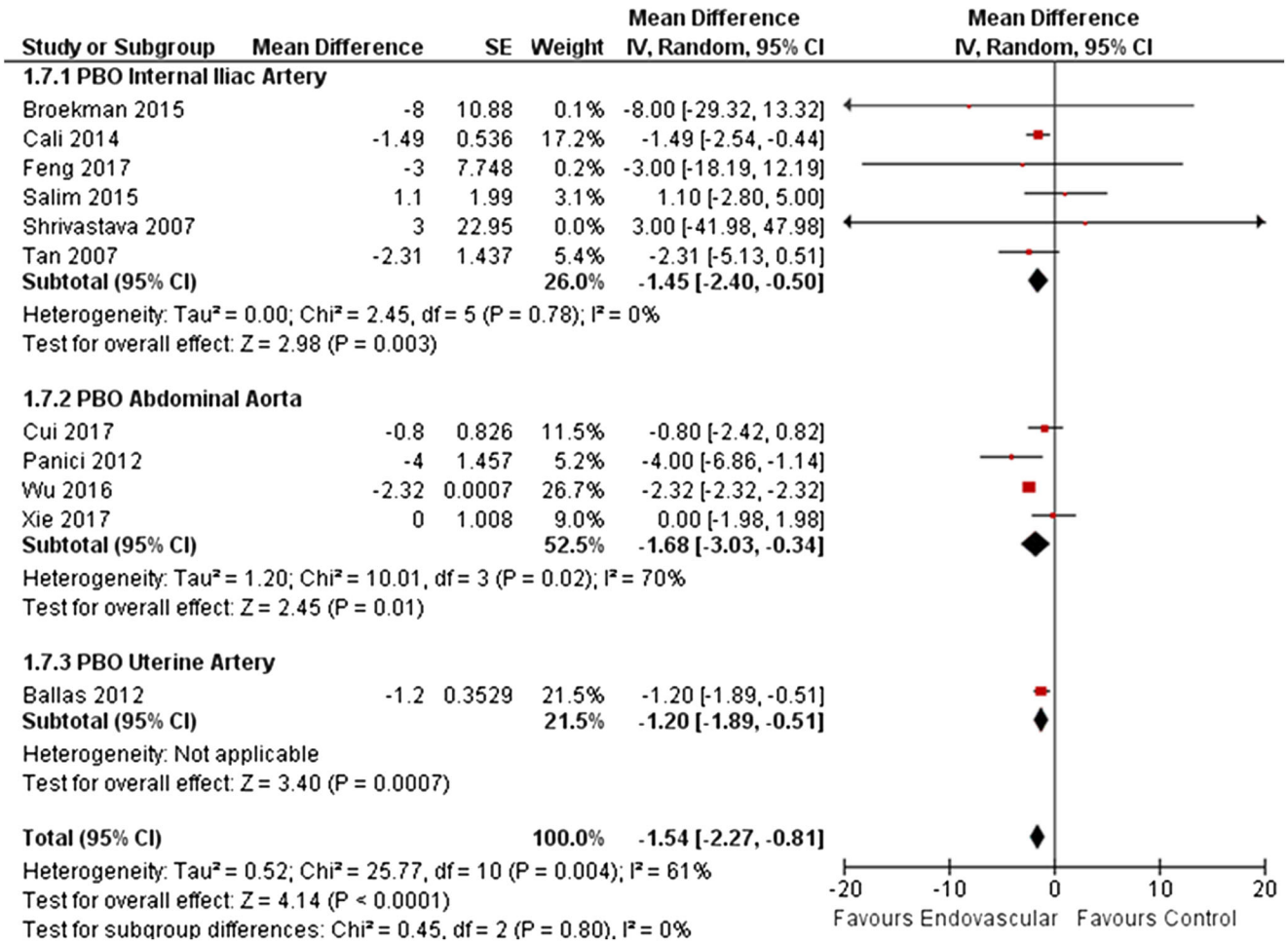

Fig. 4 Forest plot comparing the number of units of packed red blood cells transfused blood between the endovascular and control groups. Small squares represent mean differences for each of the included studies. *SE* standard error. For further details see Fig. 2 legend

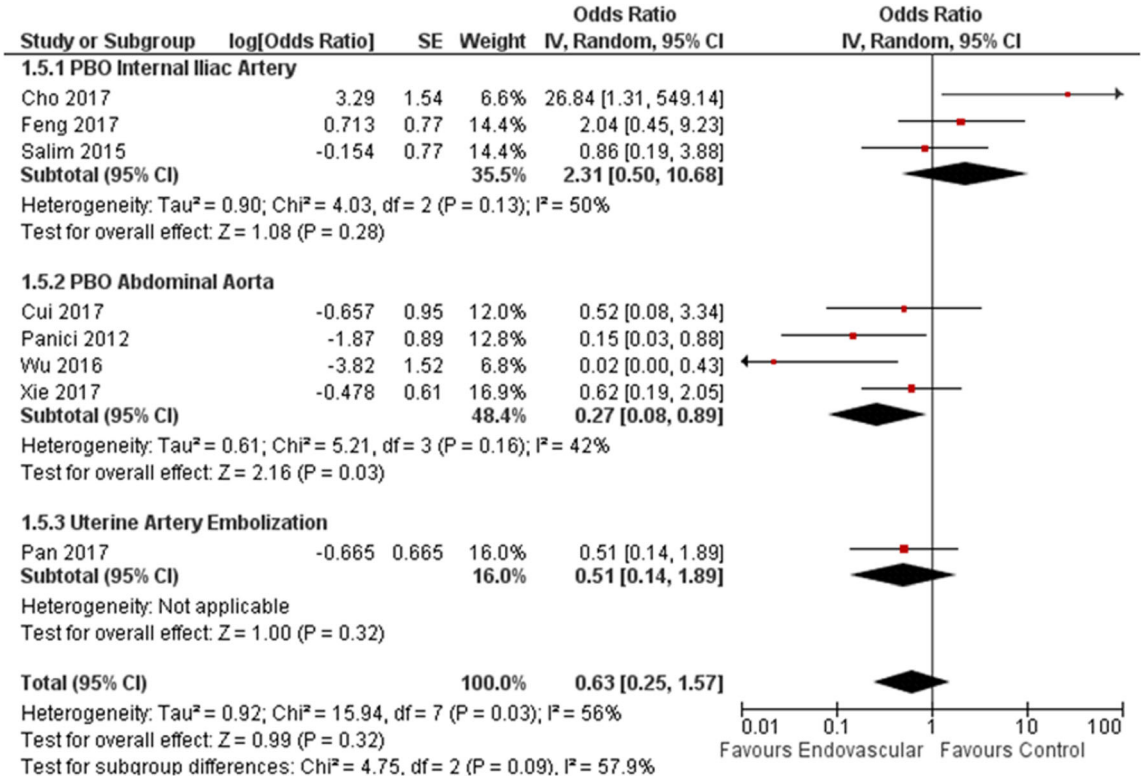

Fig. 5 Forest plot comparing hysterectomy rates between the endovascular and control groups. *SE* standard error. For further details see Fig. 2 legend

Discussion

This is the first systematic review and meta-analysis to assess the safety and effectiveness of different endovascular interventional modalities for haemorrhage control in deliveries complicated by abnormal placental implantation in a large cohort of patients. The main finding of this study is that, compared with control or no endovascular intervention, prophylactic endovascular intervention is effective for haemorrhage control during or after deliveries complicated by abnormal placentation. The hysterectomy rates were comparable between the endovascular and control groups. Interestingly,

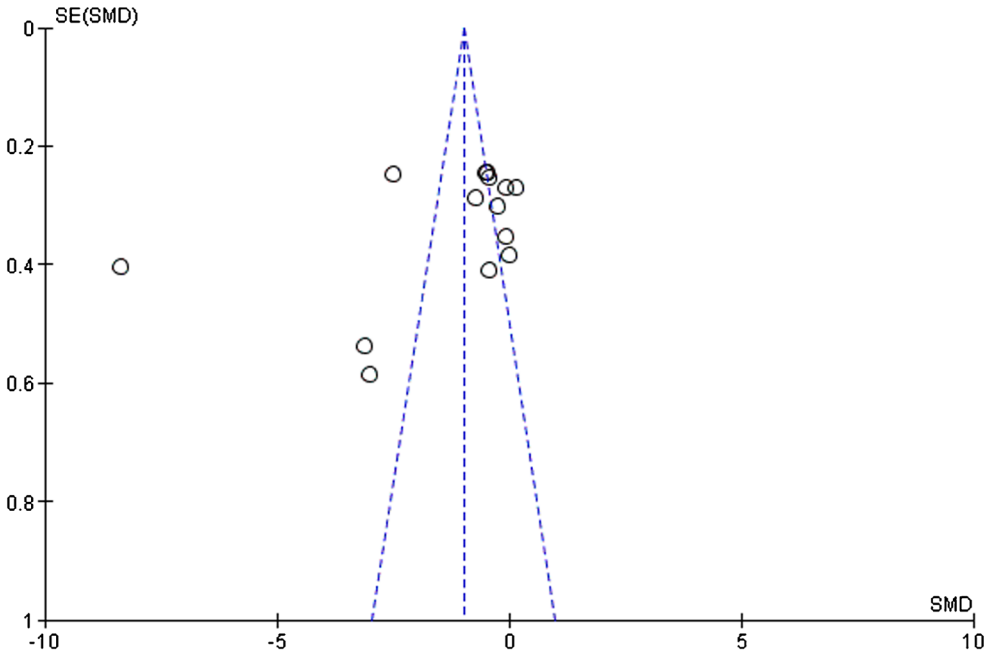

Fig. 6 Funnel plot of the standardized mean differences (*SMD*) in blood loss volume versus standard errors of all of the 14 studies that assessed blood loss volumes in endovascular interventions in comparison with those in control procedures. The x-axis is in millilitres. The dotted line represents the SMD in blood loss volume across all studies. Small circles represent all studies that compared blood loss volume between endovascular and non-endovascular interventions for haemorrhage control in deliveries complicated by placental abnormalities

patients who underwent PBOAA were less likely to have hysterectomy and had the lowest blood loss during delivery compared with those undergoing other endovascular interventions, with no significant endovascular complications. PBOAA offers a drier and cleaner surgical field than other endovascular interventions, improving visibility. However, PBOAA requires a larger introducer resulting in the need for a vascular closure device or surgical removal. It also requires a longer introducer to support the balloon against the aortic wall and to prevent balloon migration. Length of hospital stay and operative time were shorter in the endovascular group, although this did not reach statistical significance.

Mei et al. [91] performed a systematic review focusing on uterus-preserving treatment modalities for abnormal invasive placenta with no quantitative synthesis of outcomes and no reporting of the outcomes of treatment modalities for hysterectomy. Moreover, the review of Mei et al. included studies investigating surgical procedures and few studies reporting endovascular procedures, and was less comprehensive than our systematic review. Dilauro et al. [92] reviewed the literature regarding prophylactic IIA balloon occlusion in women with placenta accreta. However, their review was inconclusive as the evidence was mainly based on case reports and small retrospective studies.

Management of deliveries complicated by abnormal placentation might involve caesarean hysterectomy or caesarean section with uterus preservation. Endovascular intervention for haemorrhage control is used in both procedures with a significant difference between the two groups. In a subgroup analysis, PBOIIA was more effective in patients who underwent caesarean hysterectomy [18, 44] than in patients who underwent caesarean section with uterus preservation [19, 47, 55, 65, 67]. The reason for these conflicting results is that the position of the occlusion catheter balloon is important in controlling blood loss and varied between studies, with better results with PBOAA, as previously reported. Certainly, the current trend described in recent literature is that endovascular intervention is primarily used to control haemorrhage with the aim of uterus preservation to reduce morbidity. Tan et al. [19] suggested that PBOIIA for uterus preservation in deliveries complicated by placenta accreta can reduce haemorrhage and the hysterectomy rate, but this was not found in other studies [55, 65].

Notably, based on the results of this meta-analysis, the most effective endovascular modality for haemorrhage control in abnormal placental implantation is PBOAA as it was associated with the lowest blood loss and number of maternal and fetal complications, which is in agreement with the results of a previous study [69] that compared outcomes between PBOAA and PBOIIA in 105 patients. Furthermore, it was associated with the lowest maternal and fetal radiation doses and a lower hysterectomy rate. PBOIIA and PBOCIA were associated with lower limb-related complications and were less effective in haemorrhage control. This was also the case with PBOUA. The higher incidence of arterial thrombosis in this group of patients can be explained by the greater blood loss and need for transfusion combined with the hypercoagulable state during pregnancy. There is little evidence to assess the effectiveness of UA embolization, and based on a few case series and small retrospective studies which assessed UA embolization, this procedure is mainly used for the management of postpartum haemorrhage in patients who underwent caesarean section with uterus preservation. However, some cases of uterine atrophy and necrosis resulting in hysterectomy have been reported, in addition to recurrent bleeding requiring re-embolization. A recent systematic review assessing the short-term and long-term outcomes following arterial embolization for postpartum haemorrhage showed that embolization does not affect the menstrual cycle, fertility or subsequent pregnancies, but may be associated with abnormal placentation in subsequent pregnancies [93].

The limitations of this systematic review need to be acknowledged. Heterogeneity across some of the studies for some of the outcomes was significant. This can be explained by the inclusion of case reports, case series, retrospective cohort studies, small single-centre studies and different endovascular interventions.

To conclude, evidence regarding endovascular management of haemorrhage resulting from deliveries complicated by placental abnormalities is conflicting and there is a lack of properly powered prospective studies. Based on this study and available evidence, endovascular interventional modalities for deliveries complicated by placental abnormalities are effective for haemorrhage control. PBOAA was associated with fewer complications, less blood loss and lower radiation doses than other modalities. Further large, multicentre, randomized controlled trials with longer follow-up are needed to further assess these modalities and to provide guidance regarding the best endovascular intervention required in relation to the degree of placental invasion. However, such studies might be ethically questionable, as endovascular control of haemorrhage in deliveries complicated by abnormal placentation is essential in this potentially life-threatening condition.

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Compliance with ethical standards

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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.

Ethical approval Institutional Review Board approval was not required because this study was a meta-analysis of published literature.

Informed consent Written informed consent was not required for this study because it was a systematic review and meta-analysis of published literature.

Methodology
• Systematic review and meta-analysis

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