



The role of interventional radiology in the management of abnormally invasive placenta: a systematic review of current evidences

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Abstract: Abnormally invasive placenta (AIP) is a potentially severe condition. To date, arterial embolization in women with postpartum hemorrhage due to AIP is the treatment option for which highest degrees of evidence are available. However, other techniques have been tested, including prophylactic catheter placement, balloon occlusion of the iliac arteries and abdominal aorta balloon occlusion. In this systematic review, we provide an overview of the currently reported interventional radiology procedures that are used for the treatment of postpartum hemorrhage due to AIP and suggest recommendations based on current evidences. Owing to a high rate of adverse events, prophylactic occlusion of internal iliac arteries should be used with caution and applied when the endpoint is hysterectomy. On the opposite, when a conservative management is considered to preserve future fertility, uterine artery embolization should be the preferred option as it is associated with a hysterectomy rate of 15.5% compared to 76.5% with prophylactic balloon occlusion of the internal iliac arteries and does not result in fetal irradiation. Limited data are available regarding the application of systematic prophylactic embolization and no comparative studies with arterial embolization are available.

Keywords: Postpartum hemorrhage; embolization; therapeutic; placenta; balloon occlusion; interventional radiology

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Introduction

Abnormally invasive placenta (AIP) is defined by an abnormal invasion of the placental chorionic villi beyond the decidua basalis (1). AIP is classically classified as accreta, increta and percreta, depending on the depth of penetration of the chorionic villi into the myometrium, with placenta percreta being the least common but most severe form of

AIP (1). The incidence of AIP parallels that of cesarean deliveries, Between the 1960s and 2002, the incidence of AIP increased from 1 in 30,000 pregnancies to 1 in 533; thus corresponding to a nearly 60-fold increase in 5 decades (2). AIP is a potentially severe condition that can lead to significant maternal morbidity and mortality (2). The diagnosis of AIP can be made or suspected on the

basis of imaging findings before delivery using ultrasound and magnetic resonance imaging which enables early identification of women with high risk of hemorrhage and plan the delivery (1,3-5).

The management of women presenting with AIP depends on local preferences. AIP can be managed using cesarean hysterectomy (the placenta is removed along with the uterus at the penalty of no future fertility), a full conservative management (the placenta is left *in situ*, thus preserving future fertility) or an extirpative approach (the placenta is removed along with invaded myometrium) (6-8).

Uterine artery embolization consists in occluding the uterine arteries and other arteries that participate to the uteroplacental complex vascularization using a percutaneous approach with specific occluding agents (9). However, in the setting of uterine artery embolization, postpartum hemorrhage due to AIP is challenging because of specific variables. First, it is often performed in emergency with potentially hemodynamically unstable women (9). Second, angiographic findings are often unusual, resulting in more complex and longer procedure time (10). Finally, AIP is a main cause of failed arterial embolization, with the need for repeat embolization in a non-negligible proportion of women (7,11,12).

Currently, arterial embolization in women with postpartum hemorrhage due to AIP is the therapeutic option that conveys highest degrees of evidence (10-15). However, other approaches have been tested, including prophylactic catheter placement, balloon occlusion of the iliac arteries and abdominal aorta balloon occlusion (16-20).

The purpose of this systematic review was to provide an overview of the currently reported interventional radiology procedures that are used for the treatment of postpartum hemorrhage due to AIP and suggest recommendations based on current evidences.

Search strategy, selection and data analysis

A computer-assisted literature search was performed by one radiologist to identify articles related to role of interventional radiology in the management of AIP. A literature search strategy was conducted first (Table 1). The MEDLINE, EMBASE, and Cochrane databases, from January 2008 to September 2019 inclusively were checked for relevant articles with the following MeSH terms and free keywords: “Abnormally invasive placenta”, “Placental abnormalities”, “Placenta accreta”, “Placenta

accreta spectrum”, “Placenta increta”, “Placenta percreta”, “Placenta previa”, “Postpartum hemorrhage”, “Aorta, Abdominal”, “Balloon Occlusion”, “Common iliac artery”, “Embolization, Therapeutic”, “Endovascular procedures”, “Iliac Artery”, “Internal iliac artery”, “Therapeutic Occlusion”, “Radiology, Interventional”, “Uterine artery” and “Uterine Artery Embolization”. An expanded search was used using Boolean operators. Review articles, letters, editorials, comments, case reports, unpublished articles, and articles without inclusion of raw data were not selected. When articles were considered eligible on the basis of their titles, their abstracts were analyzed to determine suitability for inclusion. The search was limited to studies published in English and involving humans. The list of articles was supplemented by cross-checking of the reference lists of all potentially relevant articles and by a hand search of references of all available reviews. An update was made to search for additional studies published after September 2019 before article submission. Table 2 shows details of the computer-assisted literature search.

Two radiologists with an experience of 30 and 5 years in endovascular procedures independently checked each identified article for fulfillment of inclusion criteria. The full text of relevant articles was analyzed and disagreement resolved by consensus. Inclusion criteria were as follows: (I) articles were written in English; (II) an interventional radiology technique (i.e., uterine artery embolization, balloon occlusion or intra-arterial catheter placement) was used; (III) the study population had at least 10 women with confirmed AIP; and (IV) when data were presented in more than one article, the most recent one was selected. Studies reporting women with placenta previa only and those in which AIP could not be individualized from a more general group of women with “placenta previa”, “abnormal placentation” or “pernicious placenta previa” were excluded.

The same radiologists independently extracted relevant data about study characteristics. They include: (I) name of first author; (II) year of publication; (III) number of women with AIP; (IV) respective numbers of placentas accreta, increta and percreta; (V) type of intervention; (VI) Rate of hysterectomy; (VII) estimated blood loss (EBL); (VIII) rate of complications due to the intervention; and (IX) radiation dose.

After exclusion of duplicate articles and those that did not fulfill the inclusion criteria a total of 54 articles were selected and ultimately analyzed (Table 3). Figure 1 shows the PRISMA flow diagram for the inclusion/exclusion of

Table 1 Search strategy table

Patients	Boolean operator	Intervention
Abnormally invasive placenta [key word]	AND	Aorta, Abdominal [MeSH]
Placental abnormalities [key word]		Balloon Occlusion [MeSH]
Placenta Accreta [MeSH]		Common iliac artery [key word]
Placenta accreta spectrum [key word]		Embolization, Therapeutic [MeSH]
Placenta increta [key word]		Endovascular Procedures [MeSH]
Placenta percreta [key word]		Iliac Artery [MeSH]
Placenta Praevia [MeSH]		Internal iliac artery [key word]
Postpartum Hemorrhage [MeSH]		Intervention [key word]
		Therapeutic Occlusion [MeSH]
		Radiology, Interventional [MeSH]
		Uterine Artery [MeSH]
		Uterine Artery Embolization [MeSH]

MeSH indicates Medical Subject Heading. Limits: human and publication date from January 2007 and September 2019 inclusively.

the studies.

Arterial embolization

Arterial embolization has been used for years in the treatment of postpartum hemorrhage, with high success rates (14,72-78). By comparison with the more common uterine atony, AIP is a complex situation. The angiographic findings in women with AIP are greatly variable. Some women have undergone prior surgery such as arterial ligations resulting in recruitment of extra-uterine arteries (79,80). In addition, it is often hard to anticipate the actual degree of aggressiveness of AIP (accreta or percreta) that contributes to the technical difficulty. For these reasons, full pelvic angiogram is needed because it is crucial to understand the vascularization of the placenta that is left in place and because the vascularization is often complex. It is important to consider that AIP is often more technically demanding compared to uterine atony (81,82). This is because multiple vessels may contribute to the placental vascularization and some of them supply blood to organs that are sensitive to ischemia such as the bladder or the gastrointestinal tract. Due to its aggressive nature, the arterial network of the AIP is complex with multiple feeding vessels. Uterine arteries are always involved in the placenta vascularization, however other arteries such as ovarian, pudendal, obturator, sacral, and inferior epigastric arteries can also participate to the uteroplacental vasculature (9,10).

Arterial embolization in women with postpartum

hemorrhage due to AIP has several goals. The primary objectives are to stop the distal bleeding and avoid surgical morbidity. The secondary objectives are to induce thrombosis of intervillous space, reduce the risk of further bleeding and improve the speed of placental resorption when conservative management is performed (9). The third objective is to preserve fertility and potential further pregnancies by avoiding uterine necrosis (83).

Choice of embolic agent

Several embolic agents can be used for the treatment of postpartum haemorrhage in women with AIP. Gelatin sponge, in the form of homemade torpedoes, is a temporary occlusive agent that was primarily or exclusively used by many authors (9,10,14,25,31,32,46,70). However, permanent or long lasting embolic agents such as monomeric n-butyl-2-cyanoacrylate (Histoacryl[®], Glubran2[®]) (84-86), metallic coils (85), polyvinyl alcohol particles, and calibrated particles >700 µm were used in combination with gelatin sponge in some studies (9,14,25,31). Other embolic agents such as ethylene vinyl alcohol copolymer (Onyx[®]) (87) are available but their use in AIP has not been evaluated yet (88). In the study of Sentilhes *et al.*, no associations were found between the rate of failure and the nature of the embolic material (12). However, each embolic agent may have specific advantages over another depending of the anticipated endpoint based on initial angiogram. Monomeric n-butyl-2-cyanoacrylate

Table 2 Characteristics and results of the computer-assisted literature search strategy

Search terms	Numbers of hits		
	PubMed*	Embase [†]	Cochrane [‡]
#1. "Abnormally invasive placenta" [key word]	105	87	7
#2. "Placental abnormalities" [key word]	206	208	14
#3. "Placenta Accreta" [MeSH]	1,247	2,308	61
#4. "Placenta accreta spectrum" [key word]	88	168	1
#5. "Placenta increta" [key word]	170	528	18
#6. "Placenta percreta" [key word]	307	763	18
#7. "Placenta Previa" [MeSH]	854	3,133	8
#8. "Postpartum Hemorrhage" [MeSH]	3,732	8,346	61
#9. "Aorta, Abdominal" [MeSH]	1,949	6,075	20
#10. "Balloon Occlusion" [MeSH]	1,141	5,025	10
#11. "Common iliac artery" [key word]	440	2,033	5
#12. "Embolization, Therapeutic" [MeSH]	13,924	2,210	7
#13. "Endovascular Procedures" [MeSH]	41,177	6,681	27
#14. "Iliac Artery" [MeSH]	1,762	6,268	8
#15. "Internal iliac artery" [key word]	468	1,921	1
#16. "Therapeutic Occlusion" [MeSH]	14,014	2,679	6
#17. "Radiology, Interventional" [MeSH]	544	10,920	60
#18. "Uterine Artery" [MeSH]	1,252	3,445	18
#19. "Uterine Artery Embolization" [MeSH]	943	1,223	3
#1 and #13	0	2	0
#3 and #13	11	12	0
#3 and #16	233	5	0
#6 and #13	2	3	0
#8 and #10	259	35	4
#8 and # 11	1	27	0
#8 and #19	170	221	1

MeSH indicates Medical Subject Heading. *, limits: human, female and publication date from January 2007 and September 2019 inclusively. [†], limits: human, women, article, publication date from January 2007 and September 2019 inclusively, and article. [‡], limits: publication date from January 2007 and September 2019 inclusively.

and calibrated particles are used for distal embolization while gelatin sponge torpedoes or metallic coils are used for proximal embolization (89).

Efficacy

Hwang *et al.* reported 40 women with AIP who underwent

arterial embolization (14). Technical success was achieved in all women (100%), with a further initial clinical success rate of 82.5% (33/40). Three women with AIP underwent hysterectomy after arterial embolization failed to stop the bleeding within 24 hours (14). The other three women underwent successful repeat embolization, yielding overall 92.5% clinical success rate. Four women experienced

Table 3 Main characteristics of studies included for analysis

First author, year, Ref	Number of AIP patients	AIP type A/I/P	Type of intervention	Rate of hysterectomy (%)	Estimated blood loss (mL)	Complication rate (%)	Radiation dose	Major points
Shrivastava et al. 2007 (21)	19	13/4/2	PBO IIA (19/19)	100 (19/19)	2,700 (up to 8,000)	16 (3/19)	NR	No differences in EBL and hysterectomy compared to no PBO
Tan et al. 2007 (22)	11	3/1/7	PBO IIA	64 (7/11)	2,011 (up to 5,000)	0 (0/11)	N.R	Lower EBL with PBO (P=0.042)
Mok et al. 2008 (23)	12	4/0/0	PBO IIA (6/12)	33 (4/12)	6,415 (up to 14,000)	0 (0/12)	NR	-
Yu et al. 2009 (24)	11	4/3/4	PUAE	27 (3/11)	3,190 (up to 13,000)	0 (0/11)	N.R	-
Diop et al. 2010 (25)	17	Accreta*	UAE	6 (1/17)	1,929	0 (0/17)	NR	-
Sivan et al. 2010 (26)	25	25/0/0	PCIIA (25/25) + UAE (23/25)	8 (2/25)	2,000 (up to 9,000)	0 (0/25)	NR	-
Carnevale et al. 2011 (27)	21	18/0/3	PBO IIA	100 (21/21)	1,671 (up to 4,000)	10 (2/21)	NR	Thromboembolism in two women
Amsellem et al. 2011 (28)	10	Accreta*	PBO IIA	40 (4/10)	900±754	0 (0/10)	NR	The endpoint was a conservative approach
Jung et al. 2011 (29)	17	Accreta*	UAE	18 (3/17)	1,823 (up to 4,500)	0 (0/17)	NR	-
Soyer et al. 2011 (9)	12	4/2/6	UAE	18 (2/11)	> 1,000	8 (1/12)	Skin dose 175.89 cGy (range, 90.21–351.78)	Clinical success of UAE in 82% of women
Ballas et al. 2012 (30)	59	24/0/35	PBO IIA	NR	2,165	3.4 (2/59)	NR	Case control study; EBL was greater in women with inflated balloons
Bouvier et al. 2012 (31)	14	10/0/4	UAE	43 (6/14)	2,242 (up to 3,500)	0 (0/14)	NR	-
Li et al. 2012 (32)	10	6/4/0	UAE	0 (0/10)	>500	10 (1/10)	NR	Secondary PPH conservative treatment
Panici et al. 2012 (33)	15	13/2/0	PBO AA	13 (2/15)	950	0 (0/15)	0.1 mGy	Case control study; greater EBL without PBOAA (3,375 mL)
Claussen et al. 2013 (34)	15	15/0/0	PBO IIA	53 (8/15)	4,150 (up to 16,000)	0 (0/15)	NR	EBL > 6,000 mL in 5 women

Table 3 (continued)

Table 3 (continued)

First author, year, Ref	Number of AIP patients	AIP type A/I/P	Type of intervention	Rate of hysterectomy (%)	Estimated blood loss (mL)	Complication rate (%)	Radiation dose	Major points
Hwang <i>et al.</i> 2013 (14)	40	Accreta*	UAE	7.5 (3/40)	NR	0 (0/40)	NR	Clinical success of UAE in 92.5% of women; one death due to DIC
Teixidor Viñas <i>et al.</i> 2014 (35)	27	8/2/17	PBO IIA [27]; PBO IIA + UAE [8]	11 (3/27)	1,920 (up to 12,000)	4 (1/27)	FRD 4.4 mGy (range, 0.4–15.1)	Balloon rupture in one woman; resolutive IIA thrombosis in one woman
Call <i>et al.</i> 2014 (36)	30	12/0/18	PBO IIA	100 (30/30)	846 (up to 1,700)	0 (0/30)	NR	Lower EBL in women with placenta percreta by comparison with historical control group
Darwish <i>et al.</i> 2014 (37)	32	Accreta*	PBO IIA	12.5 (4/32)	1,900	NR	NR	Lower EBL with PBO by comparison with retrospective group
Chou <i>et al.</i> 2015 (38)	12	1/6/5	PBO IIA	75 (9/12)	1,902 (up to 8,000)	17 (2/12)	NR	Popliteal thrombosis and EIA thrombosis (one woman each)
D'Souza <i>et al.</i> 2015 (39)	10	0/4/6	PBO IIA + UAE	33 (3/10)	1,200 (up to 4,000)	0 (0/10)	NR	
Duan <i>et al.</i> 2015 (40)	42	37/0/5	PBO AA + UAE	2.4 (1/42)	586	0 (0/42)	FRD 4.2 mGy,	
Izbizki <i>et al.</i> 2015 (41)	79	25/18/36	PCUA + UAE	94 (74/79)	NR	0 (0/79)	NR	Resolving decreased temperature of right lower limb in one woman
Salim <i>et al.</i> 2015 (42)	27	Accreta*	PBO IA1 [13]; Control [14]	46 (6/13); 50 (7/14)	4,950; 4,709	15 (2/13)	NR	Randomized trial; PBO IIA vs. control; no benefit with PBO IIA for EBL (P=0.72)
Omar <i>et al.</i> 2016 (43)	14	5/4/5	PBO IIA [11]; PBP CIA [3]	NR	43,000±70,000	7 (1/14)	NR	No differences in EBL with control group
Wei <i>et al.</i> 2016 (18)	45	22/20/3	PBO AA	9 (4/45)	835 (up to 6,000)	4 (2/45)	NR	Arterial thrombosis and ischemic injury of femoral nerve (one woman each)

Table 3 (continued)

Table 3 (continued)

First author, year, Ref	Number of AIP patients	AIP type A//P	Type of intervention	Rate of hysterectomy (%)	Estimated blood loss (mL)	Complication rate (%)	Radiation dose	Major points
Niola et al. 2016 (44)	27	A [21] P [6]	PUAE	37 (10/27)	NR	0 (0/27)	Skin dose 70.37 mGy (range, 18.53–234.27)	UAE was performed before delivery with the fetus in the uterus
Wu et al. 2016 (45)	230	30/112/88	PBO AA [203] + UAE [2]	0 (0/230)	921	0 (0/230)	FRD 5.1±3.0 mGy	–
Wang et al. 2016 (46)	18	10/5/3	UAE	6 (1/18)	1,372	0 (0/18)	NR	–
Angileri et al. 2017 (47)	37	14/3/20	PBO IIA	0 (0/37)	2,052	11 (4/37)	NR	Arterial thrombosis in 4 women
Cui et al. 2017 (48)	38; 31	13/12/13; 11/14/6	PBO AA [38] + UAE [12]; control group [31]	5 (2/38); 10 (3/31)	1,560±1,279; 2,145±1,160	8 (3/38)	FRD 3.3±1.1 mGy	No differences in EBL and hysterectomy rate. Arterial thrombosis (two women). UAE was needed in 12 women with PBO AA
Feng et al. 2017 (49)	30	9/17/4	PBO IIA (inflated in 27/30)	43 (13/27)	1,000 (up to 15,000)	0 (0/30)	NR	No benefit of PBO IIA compared to historical control group
Pan et al. 2017 (50)	26 19	18/7/1; 11/7/1	PUA [26]; control group [19]	23 (6/26); 37 (7/19)	2,060; 2,800	4 (1/26)	FRD 30.6 mGy (range: 5.5–104)	No differences in EBL and hysterectomy rate; uterine necrosis with PUA in one woman
Wang et al. 2017 (51)	57; 48	Accreta*; Accreta*	PBO AA [57] + UAE [16]; PBO IIA [48] + UAE [14]	NR	450; 619	NR	NR	Prospective study comparing PBOIAI vs. PBOAAA; EBL and FRD were lower with PBOAAA
Wang et al. 2017 (52)	10; 33	Increta*; Increta*	PBO AA; control	70 (7/10); 64 (21/33)	1,000 2,000	NR	NR	Lower EBL with PBO AA
Xie et al. 2017 (53)	30; 41	25/5	PBO AA [30]; Control group [41]	17 (5/30); 24 (10/41)	961±784; 1,560±1,353	3.3 (1/30)	NR	Lower EBL with PBO AA. No differences in hysterectomy rates
Al-Hadethi et al. 2017 (54)	25; 27		PBO IIA; control group	59 (16/25); 85 (23/27)	2,455±1,444; 1,992±1,498	8 (2/25)	NR	Dissection of CFA and bilateral CIA dissection (one woman each)

Table 3 (continued)

Table 3 (continued)

First author, year, Ref	Number of AIP patients	AIP type A/I/P	Type of intervention	Rate of hysterectomy (%)	Estimated blood loss (mL)	Complication rate (%)	Radiation dose	Major points
Luo et al. 2017 (55)	29	25/0/4	PBO AA [29] + UAE [2]	17 (5/29)	750 (up to 3,000)	0 (0/29)	NR	Hysterectomy in 5 women with percreta
Dai et al. 2018 (56)	20; 22	Accreta*; Accreta*	PBO IIA [20] + UAE [2]; control group [20] + UAE [14]	5 (1/22); 32 (7/22)	2,900±2,352; 4,550±2,367	5 (1/20)	-	Thrombosis of EIA in one woman. Lower EBL with PBO
Mei et al. 2018 (57)	20; 20	16/4/0; 16/4/0	PBO IIA [20]; control group [20]	0(0/20); 5 (1/20)	800±359 (up to 1,800); 1,875±1,904 (up to 7,600)	0 (0/20)	NR	Lower EBL with PBO IIA ± UAE; UAE was used when needed but no numbers were reported; no accreta in the study
Picel et al. 2018 (58)	90; 61	20/20/50; 32/14/15	PBO IIA; control group	100 (90/90); 100 (61/61)	2,360 (up to 2,500); 3,290 (up to 4,000)	9 (8/80)	DAP 32.8 µGym ²	Lower EBL with PBO IIA Dissection of oCIA; two pseudoaneurysms; acute limb ischemia
Ono et al. 2018 (59)	29	17/7/5	PBO CIA [29]	100 (29/29)	2,027±1,638	7 (2/29)	Skin dose 29.4±25.0 mGy	Balloon rupture in two women
Blumenthal et al. 2018 (60)	16; 19	4/3/9; 11/3/5	PBO AA; control group	94 (15/16); 89 (17/19)	2,007 (up to 20,000); 2,112 (up to 8,664)	6 (1/16)	NR	No differences in EBL
Li et al. 2018 (61)	199	39/60/13/29/52/6	PBO [112] (IIA 37; CIA 42; AA 33); control group [87]	11.6 (13/112); 32.8 (28/87)	1,550; 3,500	1.8 (2/112)	19.01 ± 13.33 mGy	Lower EBL with PBO IIA thrombosis in 2 women. Lower EBL with PBO in CIA and IAA
Huang et al. 2018 (62)	11; 6	10/1/0; 3/1/2	PUAE [11]; control group [6]	9 (1/11); 33 (2/6)	991.9±702; 3,448±1,767	-	NR	-
Rosner-Tenerowicz et al. 2018 (63)	13; 8	Perceta*; Percreta*	PBO IIA [13]; Control group [8]	100 (13/13); 100 (8/8)	1,492±1,239; 2,963 ± 1,534	8 (1/13)	NR	Lower EBL with PBO IIA
Sun et al. 2018 (64)	19	Increta*	PBO AA	31 (6/19)	1,200 (up to 9,000)	5 (1/19)	Skin dose 4.20±1.49 mGy	Thrombosis of IIA in one woman
Chodraui-Filho et al. 2019 (65)	35	9/11/15	PBO IIA + UAE	100 (35/35)	1,193 (up to 2,967)	11 (4/35)	NR	Arterial thrombosis in two women. Gluteal muscle necrosis in one woman

Table 3 (continued)

Table 3 (continued)

First author, year, Ref	Number of AIP patients	AIP type A//P	Type of intervention	Rate of hysterectomy (%)	Estimated blood loss (mL)	Complication rate (%)	Radiation dose	Major points
Liu et al. 2019 (66)	31	8/14/9	PBO AA [31] + UAE [3] + OAE [3]	3 (1/31)	1,906±1,118	6 (2/31)	FRD 4.33±0.79 mGy	Thrombosis of right femoral artery in two women favorably treated with thrombolysis
Mei et al. 2019 (67)	74; 100	Accreta*; Accreta*	PBO AA [74] + UAE [23]; PBO IIA [100] + UAE [47]	0 (0/74); 0 (0/100)	600 (up to 2,500); 600 (up to 2,500)	0 (0/74); 0 (0/100)	FRD 1.85 mGy (range, 2.9); FRD 25 mGy (range, 8–31)	No differences in EBL between the two procedures
Tokue et al. 2019 (68)	42	33/6/3	PBO IIA	36 (15/42)	3,706±3,852	0 (0/42)	FRD 25.5±8.2 mGy	Visualization of round ligament artery is associated with failed PBO IIA
Chen et al. 2019 (69)	83; 31	30/0/53; 28/0/3	PBO IIA [83]; control group [31]	100 (83/83); 100 (31/31)	3,000; 3,700	NR	NR	PBO IIA has not impact of maternal outcome using a propensity score
Yuan et al. 2020 (70)	28; 26	16/10/2; 18/7/1	UAE [28]; control group [26]	29 (8/28); 42 (11/26)	1,325±871; 4,483±2,295	0 (0/28)	NR	Lower EBL in UAE group
Lee et al. 2020 (71)	28	7/10/11	PBOAA [12] or PBO IIA [16]	100 (28/28)	1,826	0 (0/28)	NR	Lower EBL with PBO

*; 0 subgroup information was given. Table shows studies with more than 10 women with AIP. Studies were analyzed for the actual numbers of AIP and those that included women with AIP and placenta praevia were included when the actual number of AIP was ≥ 10 . DR, fetal radiation dose; NR, not reported; DAP, dose area product; AA, abdominal aorta; AIP, abnormally invasive placenta; CIA, common iliac artery; DAP, dose area product; DIC, disseminated intravascular coagulopathy; FRD, fetal radiation dose; IIA, internal iliac artery; OAE, ovarian artery embolization; PBOAA, prophylactic balloon occlusion of abdominal aorta; PBOCIA, prophylactic balloon occlusion of common iliac artery; PBOIIA, prophylactic balloon occlusion of internal iliac arteries; PPH, postpartum hemorrhage; PUAE, prophylactic uterine artery embolization; PCUA, prophylactic catheterization of uterine arteries; PCIIA, prophylactic catheterization of IIA; UAE, uterine artery embolization.

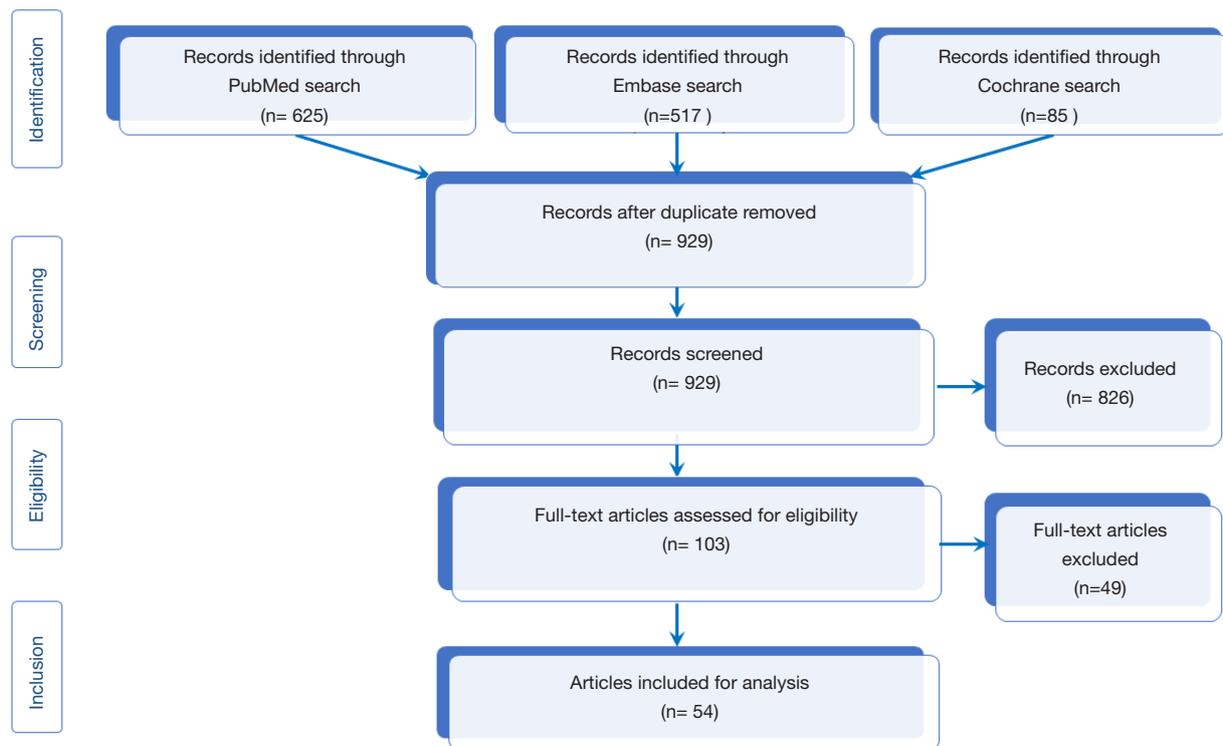


Figure 1 PRISMA flow diagram.

pelvic pain, nausea and urticaria. There were no major complications (14). Soyer *et al.* reported 12 women with AIP (accreta, n=6; percreta, n=6) with primary (n=10) or secondary (n=2) postpartum hemorrhage (9). Arterial embolization was successful in 10/12 women after one (n=7) or two (n=3) embolization sessions and hysterectomy was needed in only 2 women. These two women had placenta percreta and bladder involvement (9). Sentilhes *et al.* reported 24% (4/17) of failed embolization in women with AIP and postpartum hemorrhage (12). Li *et al.* reported 10 women with AIP (6 accreta, 4 increta) managed conservatively who experienced secondary postpartum hemorrhage (32). Using gelatin sponge particles or pledgets, technical success rate of embolization was 100% (32). Bleeding was controlled in all women during follow-up [11 ± 6.9 (SD) months; range 3–24 months], and no further bleeding occurred (32). One woman developed lower-extremity deep venous thrombosis on the side of artery access after uterine artery embolization with a favorable outcome after oral anticoagulation therapy, and no other major complications were reported (32).

Jung *et al.* reported 17 women with AIP for whom uterine artery embolization successfully controlled

postpartum hemorrhage in 14 of them (82.4%) (29). Three women underwent hysterectomy after uterine artery embolization failed to stop the bleeding. No complications except fever lasting for 1–2 days were observed (29). Wang *et al.* have reported a hysterectomy rate of 6% and no complications (46).

A systematic review including 177 women with AIP reported an 89.8% success rates for arterial embolization, with 11.3% of women requiring further hysterectomy (90). The complication rate was 11%, including uterine necrosis, endometritis, and synechiae (91,92). One favorable effect of uterine artery embolization in AIP treated with a conservative approach is to reduce the resorption delay of the placenta (93). Soyer *et al.* reported a median resorption delay of 17 weeks after embolization compared to 32 weeks in the absence of embolization ($P=0.036$) (93). As reported by Hequet *et al.*, retained placental tissues after arterial embolization can be removed using hysteroscopic resection (91).

Another option is to perform arterial embolization after cesarean delivery prior to hysterectomy in women with AIP (19). In a retrospective study, Wang *et al.* found lower EBL in seven women with AIP who received arterial

embolization after cesarean delivery but before hysterectomy (1,500 mL; range, 500–2,000 mL) by comparison with those who underwent cesarean hysterectomy alone (2,000 mL; range, 1,000–4,500 mL) ($P=0.04$) but no differences in transfusion requirements ($P=0.10$) and length of intensive care unit stay ($P=0.07$) (19). However, this approach resulted in significant decrease in median EBL ($P=0.004$), transfusion requirements ($P=0.009$), and length of intensive care unit stay ($P=0.04$) only in the specific subgroup of women with placenta increta (18). A compelling benefit of this approach is the absence of fetal radiation as the entire procedure is performed after cesarean delivery (19).

In woman with AIP who are undergoing a gravid hysterectomy because of a nonviable fetus, the concern for blood loss and morbidity is high. In this setting, pre-hysterectomy uterine artery/pelvic embolization can aid in devascularization of the uteroplacental vasculature, rendering a dry surgical bed (94). This can help obviate injury to surrounding vessels and reduce periprocedural blood loss. However, the actual benefit of this approach should be assessed with further studies (94).

Prophylactic procedures

Prophylactic uterine artery catheterization and/or prophylactic embolization

Prophylactic bilateral uterine artery catheterization consists in selective catheterization prior to cesarean delivery in order to expedite treatment, should embolization be needed (41). This approach has been first described by Sumigama *et al.* (95). These researchers observed a marked decreased blood loss using a “stepwise treatment” in four women with AIP (95). Prophylactic uterine artery embolization has been originally proposed by Yu *et al.* with the purpose of minimizing the risk of massive blood loss during delivery in women with AIP (24). This technique consists in placing catheters in the uterine arteries to perform arterial embolization before delivery (24).

To date, limited data are available regarding the application of prophylactic catheter placement and embolization. One evidence is that the prophylactic approach yields conflicting results in terms of blood loss and hysterectomy rate. Izbizky *et al.* performed prophylactic bilateral uterine artery catheterization and further embolization when needed in the management of 95 women with suspected AIP; of them 79 women (79/95, 83%) had actually AIP, 92 (92/95; 97%) had catheterization and 83

(83/92; 87%) had further embolization (41). Complications, including bleeding requiring blood transfusion (49%) and bladder surgery (37%) were reported but there were no major complications attributable to the endovascular procedures (41). One minor complication in the form of transient paresthesia and decreased temperature of lower limb was reported, presumably related to embolization with uneventful follow-up. Clinical success rate was 86%, with no maternal deaths, but 14% of patients received large-volume blood transfusion (41). Giurazza *et al.* reported systematic uterine artery embolization in 69 women with placental abnormalities before cesarean hysterectomy (96). Although 36 women (52.2%) did not require blood transfusion, 30 women (43.5%) required hysterectomy (96). Pan *et al.* evaluated the potential of prophylactic intraoperative arterial embolization during cesarean delivery in women with AIP (50). They found no differences in EBL between the 26 women with AIP who received prophylactic intraoperative arterial embolization (2,080 mL) and the 19 women with AIP who did not (2,800 mL) ($P=0.005$). Prophylactic intraoperative arterial embolization resulted in a lower EBL only for the subgroup of woman who did not undergo hysterectomy (50). In addition, prophylactic intraoperative arterial embolization did not alter the need for hysterectomy and massive blood transfusion (50). Of note, in this study, the total mean fetal absorbed radiation dose was 30.6 mGy (range, 5.9–104.0 mGy) and adverse events due to prophylactic intraoperative arterial embolization were reported in 11/26 women (42%), including transient buttock pain (4 women) and uterine necrosis (one woman) (50). Yuan *et al.* reported that prophylactic uterine artery embolization during cesarean delivery in women with placenta accrete resulted in significantly lower EBL by comparison with a control group (70).

Chou *et al.* reported the use of prophylactic embolization using metallic coils and gelatin pledgets or gelatin pledgets alone in 6 women with AIP (1 accreta and 5 percreta) before hysterectomy, with a mean EBL of 1,767 mL (range, 300–3,000 mL) (97). Yu *et al.* reported 11 women with AIP (7 accreta-increta, 4 percreta) who underwent systematic uterine artery embolization with gelatin sponge (no details were given to the form) (24). The mean estimated mean blood loss was 2,279 mL (range, 1,650–3,090 mL) and 3 women had hysterectomy. Peritonitis and endometritis were observed in one woman after embolization (24).

D’Souza *et al.* used a technique which combined prophylactic arterial balloon occlusion and immediate post cesarean uterine artery embolization with absorbable

gelatin sponge in 10 women with AIP (39). Mean EBL was 1,200 mL and 2 women only needed blood transfusion. However, 3 women had hysterectomy (39). Huang *et al.* reported that the 11 women with AIP who received prophylactic uterine embolization after delivery had less intraoperative blood loss [990.9 ± 701.7 (SD) mL] than the six who did not undergo embolization [$3,448.3 \pm 1,767.4$ (SD) mL] ($P=0.018$) but found no differences in hysterectomy rate between the two groups (62). One study has reported encouraging results using prophylactic catheterization and embolization with only two women (2/25; 8%) requiring hysterectomy. However, median EBL was 2,000 mL and reached up to 9,000 mL in one woman (26).

Meller *et al.* proposed the use of a hybrid operating room for catheter placement, prophylactic embolization and cesarean hysterectomy in the same session and in the same room, thus avoiding a two-step procedure in different rooms and patient transfer from one room to another (98). This approach resulted in less occurrences of catheter dislodgement by comparison with the two step procedures in two different rooms (0/30, 0% *vs.* 10/80, 12.5%; $P=0.04$) (98).

Of interest, in one study, two women with prophylactic placement of catheters in the uterine arteries had severe postpartum hemorrhage requiring immediate hysterectomy and embolization was not performed (33). This outcome questions the actual role of prophylactic placement of catheters in the uterine arteries (31). Six women (6/14; 43%) underwent hysterectomy (31). Moreover, postpartum hemorrhage was reported in only 7/14 women (50%), suggesting that embolization may be actually needed in only half of women with AIP (31).

However, one concern regarding this approach is the radiation dose delivered to the fetus when performed before delivery. Niola *et al.* reported mean uterine radiation dose up to 15.61 mGy with a range between 8.15 and 38.18 mGy when performing prophylactic embolization with the fetus inside the uterus (44). These researchers reported adequate development in all children with a limited follow-up of 6 months 11 days to 28 months 21 days (the mean follow-up time was not given), but the long term effect of this approach is not known. In addition, it should be noted that 10/27 women with AIP required hysterectomy and that this approach was used not only for invasive placenta but also for women with noninvasive placenta previa (44).

Prophylactic balloon catheter placement in iliac arteries

Prophylactic placement of balloon catheters in the iliac

arteries consists in placing one inflatable balloon catheter in each iliac artery under fluoroscopic guidance before cesarean section in women with AIP. Then, the balloons are inflated after the fetus has been delivered to control hemorrhage (99). This approach in women with AIP remains debated because of higher risks of complications than with embolization and the lack of comparative studies (22).

Some researchers have claimed a potential for prophylactic balloon catheters in the internal iliac arteries (22,27,36,37,40,42,49,55,57,58,63,100-110). Cali *et al.* reported the results based on a historical comparison of two groups of women with AIP (36). They found less blood loss in the group with balloon catheter placement (933 mL) than in that without catheter placement (1,507 mL) ($P<0.001$) only for women with placenta percreta (36). In this study, no complications related to the use of balloon catheter were reported (36). Tan *et al.* performed an historical comparison between 11 women with AIP who underwent cesarean section with prophylactic balloon occlusion and 14 who had cesarean section alone (22). They found reduced blood loss in the former group (2,011 mL) than in the latter one (3,316 mL) ($P=0.042$). Similarly, the amount of blood transfusion was decreased in the former group (1,058 mL) than in the latter (2,211 mL) ($P=0.005$) (22). Angstmann *et al.* used prophylactic balloon catheter placement in 12/22 women (55%) with AIP, of whom 8/22 (36%) had further embolization and ultimately hysterectomy (110). In these 8 women, however, blood loss was significantly lower [553 ± 119 (SD) mL] than in those who did not have balloon catheter and embolization [$4,517 \pm 711$ (SD) mL] ($P=0.0001$) (110). Angileri *et al.* used prophylactic balloon catheters in the internal iliac arteries in 37 women with AIP (20 percreta, 20; increta, 3; accreta, 14) (47). Post-partum hemorrhage occurred in only 5 women (14%) and arterial thrombosis in 4 (11%) but no women had hysterectomy (47). Recently, data from the University of California Morbidly Adherent Placenta Registry allowed comparing the outcomes of women with AIP who underwent cesarean hysterectomy with aortic/internal iliac artery balloon occlusion catheters compared to those of women who underwent surgical ligation of the internal iliac arteries compared and those who had no adjunctive procedures (71). Lee *et al.* found that aortic and iliac artery balloon occlusion were associated with lower EBL, transfusion requirements, intensive care unit admission rates, and adverse event rates compared with women who underwent internal iliac artery ligation prior to cesarean hysterectomy or women who had no adjunctive interventions prior to cesarean hysterectomy

for morbidly adherent placenta (71).

Several studies reported no benefit with the use of prophylactic balloon catheters in the internal iliac arteries with amounts of EBL, up to 16,000 mL using prophylactic balloon occlusion of the internal iliac arteries (21,23,34,43) or no benefit by comparison with historical control group (49). Bodner *et al.* found unfavorable results with the use of balloon-assisted occlusion of the internal iliac artery in 28 women with AIP using an historical comparison, with a rate of hysterectomy of 83% (5/6) in woman who underwent prophylactic occlusion compared to 100% (22/22) in women without occlusion (103). Only one randomized controlled trial has compared the potential of prophylactic balloon catheter placement in iliac arteries in women with prenatal diagnosis of AIP (42). In this trial, women were randomized to either preoperative prophylactic balloon catheters (n=13) or to a control group without balloon catheters (n=14). No differences were observed for the number of women with blood loss greater than 2,500 mL, number of plasma products transfused, duration of surgery, peripartum complications, and hospitalization length between the two groups (42). Although the absence of differences may be due to a small sample size, it must be noted that reversible adverse effects related to prophylactic balloon catheter insertion were observed in 2 of 13 (15.4%) women, consisting in leg pain and weakness without swelling in one woman and buttock claudication and abdominal pain in the other (42). Several complications due to the use of balloon catheters in the internal iliac arteries have been reported by several authors (17,38,41,47,54,58,59,64,65,100-105,111-113). Gagnon *et al.* reported left iliac artery rupture in a woman with suspected AIP in whom one balloon (Berenstein occlusion balloon catheter™ 8.5/11.5 mm) could only be placed into the distal portion of the left internal iliac artery because of tortuosity of the anterior division branches (21,111). Shrivastava *et al.* described 19 women with AIP who had iliac artery balloon catheter placement, resulting in 16% of balloon-related complications, including an internal iliac artery dissection that resulted in vascular occlusion and required iliofemoral bypass surgery (21). Sewell *et al.* reported popliteal artery thrombus after using internal iliac artery balloon catheter in one woman with AIP (accreta) without any sequelae (100). Matsueda *et al.* reported external iliac artery thrombosis using balloon catheter that was treated with heparin drip in one woman with AIP (accreta) with a favorable outcome (101); of interest a blood loss of 5,020 mL was reported in this woman, highlighting the

questionable role the procedure and its potential risk (101). Bishop *et al.* reported leg ischemia and arterial dissection in a woman with placenta percreta and bladder invasion who had prophylactic bilateral internal iliac artery balloon inflation and further bilateral pseudoaneurysm of internal iliac arteries, right pseudoaneurysm rupture and permanent claudication of the right leg (102).

A literature review including 15 case reports and five studies for a total of 20 articles reported a wide variability in outcomes (17). Of most importance, several vascular complications were described, including acute limb ischemia, common and external iliac artery thrombosis, bilateral pseudoaneurysms, unilateral arterial rupture, requiring thromboembolectomy, stent placement or arterial bypass (17,100,102). Later, Peng *et al.* reported rupture of multiple pseudoaneurysms after common iliac artery balloon occlusion in a woman with placenta accreta (112).

In the study by Ballas *et al.* among 59 women with AIP who prophylactic placement of balloon catheters in the internal iliac arteries, 30 (30/59, 51%) had actually balloon inflation during delivery when excessive bleeding occurred (30). This suggests that prophylactic placement of balloon catheters in the internal iliac arteries is unnecessary in a substantial number of women with AIP. Another study, using a propensity score found that prophylactic occlusion of internal iliac arteries has no impact on maternal outcome (69).

Despite using low radiation dose techniques, fetal radiation exposure is a significant concern when considering internal iliac artery balloon occlusion (114). Although variable, Teixidor Viñas *et al.* reported a mean fetal radiation exposure of 4.4±3.5 (SD) mGy (range, 0.4–15.1 mGy) during prophylactic balloon catheter placement in both internal iliac arteries before cesarean section in 27 women with AIP (35). But Kai *et al.* reported fetal radiation doses ranging between 12.88 and 31.6 mGy using the same procedure (115). The use of low fluoroscopy rate is recommended. In this regard, Semeraro *et al.* showed that the use of fluoroscopy rate of 7.5 pulses per second resulted in a median fetal absorbed radiation dose of 1,713.25 μGym^2 (Q1, 1,164.5; Q3, 2,274.5) compared to 660.70 μGym^2 (Q1, 440.9; Q3, 1,020.9) using a fluoroscopy rate of 2 pulses per second (P=0.027) (116).

Prophylactic balloon occlusion of the abdominal aorta

Prophylactic balloon occlusion of the abdominal aorta occlusion consists in placing inflatable balloons in the abdominal aorta via a femoral access under fluoroscopic

guidance (22). The balloon is positioned by an interventional radiologist prior to cesarean section and inflated after delivery of the fetus (22,99). The concept behind this approach is that internal iliac artery balloon occlusion often results in recruitment of pelvic arteries and exacerbation of the bleeding. This approach provides a more proximal occlusion, results in modest or even no recruitment of collateral vessels and a drier operative field (99).

In general, the use of prophylactic balloon occlusion in the abdominal aorta in the management of women with AIP is associated with encouraging results (18,40,48,117). A single-institution observational series of 45 women with AIP (accreta, n=22; increta, n=20; percreta, n=3) reported the use of prophylactic lower abdominal aorta balloon occlusion and suggested a reduced blood loss (mean EBL, 835 mL; range, 200–6,000 mL) resulting in the need for blood transfusion in 11/45 patients only (18). Duan *et al.* reported the most promising results using a combined technique that included temporary aortic balloon occlusion followed by uterine artery embolization for the treatment of 42 women with AIP, including 5 with placenta percreta (40). All women had cesarean section combined with temporary aortic balloon occlusion followed by uterine artery embolization. Forty-one women underwent successful cesarean section with conservation of the uterus. Hysterectomy was required in one (3.1%) women. There were no access-site complications after the endovascular procedure and no complications related to the intervention during follow-up (40). Similarly, Panici *et al.* and Luo *et al.* reported low EBL with no complications due to the use of prophylactic balloon occlusion in the abdominal aorta (33,55). A large study by Wu *et al.* reported a low EBL with no complications (45). Of interest, Liu *et al.* reported that prophylactic balloon occlusion of the abdominal aorta at the level of the renal artery resulted in lower EBL than when performed below the renal artery origin, particularly in women with placenta increta (117).

Only study reported no benefits in terms of EBL and hysterectomy rate with the use of prophylactic balloon occlusion of the abdominal aorta (48). In addition, in this study, uterine arterial embolization was needed in 12/38 women (32%) to stop the bleeding, highlighting that prophylactic balloon occlusion is a temporary means that needs further embolization or hysterectomy in women with severe bleeding (48).

The use of abdominal aorta balloon occlusion results in less adverse events than balloon catheter in iliac arteries. However, in the study of Wei *et al.* one patient

had lower extremity arterial thrombosis and another had ischemic injury to the femoral nerve (18). A study reported thrombotic complications in 12/121 women (10%) with AIP who underwent aortic balloon occlusion during cesarean delivery (118). Of them, 115 had the balloon inflated during surgery. One patient had venous thrombosis and 11 had arterial thrombosis involving the limb on the catheterization side. Eight women received arterial thromboembolism and four had conservative anticoagulation treatment (118).

Fetal radiation dose with temporary aortic balloon occlusion varies among studies. Duan *et al.* reported a fetal radiation dose of 4.2 ± 2.9 (SD) mGy (40) but Nieto-Calvache reported entrance skin dose and radiation absorbed dose by the fetus of 1.31 ± 0.96 (SD) mGy and 0.27 ± 0.28 (SD) mGy, respectively in 10 women with AIP using C-arm (119).

Recommendations

AIP is a potentially severe condition. However, a retrospective analysis by the Maternal Health Study Group of Canadian Perinatal Surveillance System (Public Health Agency of Canada) has reported that the incidence of AIP is 14.4 (95% CI: 13.4–15.4) per 10,000 deliveries (819 women with AIP among 570,637 deliveries) whereas the incidence of AIP with postpartum hemorrhage is 7.2 (95% CI: 6.5–8.0) per 10,000 deliveries (120), indicating that only 50% of women with AIP experience postpartum hemorrhage. The same ratio was observed in other studies (30). In other words, in 50% of women with AIP no interventional radiology procedures are needed (92), thus seriously questioning a systematic approach that results in non-negligible radiation dose delivered to the fetus and conveys a non-negligible risk of serious complications.

The application of interventional procedures depends on the obstetrical approach that has been anticipated on the basis of ultrasound and MR imaging findings (121). To date, large data are available regarding the application of prophylactic catheter placement, prophylactic balloon occlusion and embolization but no well-designed comparative studies between the three approaches are available. The use of balloon occlusion catheters remains debated but evidences suggest that their use conveys high degrees of morbidity (17,122). Studies, mostly retrospective, have evaluated the role of prophylactic placement of balloon occlusion catheters to control the bleeding at the time of delivery in women with AIP, with varied results. One non-controlled study involving 230 patients reported low EBL

using prophylactic balloon occlusion of the abdominal aorta (45) but another study based on randomization but with limited number of patients in the two groups did not report any advantages with the use of balloon catheter with respect to blood loss and the need for hysterectomy (42). In addition, the use of occlusive balloon may exacerbate bleeding from collateral vessels (68) so that additional intervention, such as uterine artery embolization is needed in a subset of women (57,67,123). Currently, the available evidence allows concluding that most of them result in less blood loss by comparison with women who have no prophylactic balloon occlusion (52,53,124,125).

In this systematic review, the pooled hysterectomy rate obtained from 8 studies reporting the use of uterine artery embolization was 15.5% (24/155) (9,14,25,29,31,32,46,70). This rate obtained from 22 studies that use prophylactic balloon occlusion of the internal iliac arteries was 76.5% (318/697) (21,22,27,28,34-39,47,49,54,56-58,63,65,67-69,71) and 12.1% (54/445) from 10 studies using prophylactic occlusion of the abdominal aorta (17,33,45,48,52,55,60,64,66,71).

The most effective balloon technique and also the one that results in less complications is prophylactic balloon occlusion of the abdominal aorta (51,124). Prophylactic balloon occlusion of internal iliac artery is less effective at reducing blood loss and the high incidence of adverse events it conveys should not lead to consider it as a first option (124). Another limitation to the use of prophylactic catheter placement is that they are placed before delivery raising major concerns regarding fetal radiation dose.

Conclusions

Historically arterial embolization has been performed for postpartum hemorrhage for decades (15,20,126). Large experience has been accumulated since the first description. Arterial embolization, should it be required, is performed by well-trained interventional radiologists under fluoroscopic guidance after delivery, only in woman with postpartum hemorrhage. This scenario requires dedicated centers for women with AIP where embolization is available 24 hours a day and 7 days a week (127). Pending such type of organization, arterial embolization on a case-by-case basis should be the preferred option. Well-designed randomized controlled trials are needed to truly demonstrate the safety and efficacy of occlusion balloons and prophylactic procedures and to best identify the women who should benefit of this approach. It appears that the

use of prophylactic occlusion should be restricted when the endpoint is hysterectomy. On the opposite, when a conservative management is wanted to preserve future fertility, arterial embolization should be the preferred option.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/qims-20-548>). RL serves as an unpaid Deputy Editor of *Quantitative Imaging in Medicine and Surgery*. OP reports relevant financial activities outside the submitted work (Consulting for Merit Medical, Terumo and Boston Scientific; Experimental study for Merit Medical). MPK reports relevant financial activities outside the submitted work (Consulting for Medtronic, Boston Scientific and Penumbra). The other authors have no conflicts of interest to declare.

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