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The Emergent Pelvic Artery Embolization in the Management of Postpartum Hemorrhage: A Systematic Review and Meta-analysis

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Importance: Postpartum hemorrhage (PPH) is an emergent obstetric complication and the leading cause of maternal mortality. Pelvic arterial embolization (PAE) is an effective treatment for intractable PPH. However, a unique protocol has not been accepted in obstetrical practice.

Objective: To evaluate its efficiency, safety, complications, and outcomes, we conducted a systematic review and meta-analysis of PAE for PPH in the literature.

Evidence Acquisition: The Medline, the database of abstract of reviews, the index to allied health literature, and the Chinese database Sino-Med were searched on March 31, 2020, for studies on PAE for PPH. The data for PAE indication, agents, arteries, success rate, complications, and outcomes were extracted and syncretized for meta-analysis.

Results: From 1075 identified articles, 113 abstracts or full articles were retrieved and 43 studies were finally identified as meeting the including criteria. The results demonstrated that the indications for PAE were as follows: uterine atony, placental abnormality, delivery tract injury, disseminated intravascular coagulation, arteriovenous malformation, and vaginal hematoma. The embolization agents mostly in order were gelatin sponge particles, polyvinyl alcohol particles, Gelfoam, *N*-butyl cyanoacrylate, microcoil, and glue; for arteries, they were mostly uterine artery and internal iliac artery. The clinical success rate was 90.5%, whereas the technical success rate was 99.3%. The most common complications of PAE were postembolization syndrome and menstrual abnormality.

Conclusions and Relevance: The emergent PAE is a safe and effective method with high success rate in life-threatening PPH management. Gelatin sponge granules measuring 500 to 1000 μm in diameter have safe results. Pelvic arterial embolization may affect the recovery of menses and increase PPH in the subsequent pregnancy, but there was no noted correlation with fetal growth restriction.

Target Audience: Obstetricians and gynecologist, family physicians

Learning Objectives: After participating in this activity, physicians should be better able to explain the causes of PPH; identify which arteries should be chosen for embolization; and describe the advantages of PAE for PPH management.

Postpartum hemorrhage (PPH) is the leading cause of maternal mortality worldwide.[1,2] It is commonly defined as an estimated blood loss of greater than 500 mL after a vaginal birth or a loss in excess of 1000 mL after a cesarean delivery.[3,4] In 2017, the American College of Obstetricians and Gynecologists defined PPH as the cumulative blood loss greater than or equal to 1000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the delivery of the baby.[5] Despite the lack of a universal definition, the most common definition of severe PPH is more than 1500 mL of blood loss.[6] The strategy for management of PPH is multidisciplinary and comprehensive with treatment based on the cause.[7] For PPH preventive purposes, most common cases are managed with uterine contractive agents after the birth of the baby. If the first-line therapy of uterine massage and drug therapy for PPH fails,[8,9] then a second-line therapy such as intrauterine tamponade is needed.[10,11] If the conservative procedures fail to control hemorrhage, uterus-sparing surgical options including pelvic arterial embolization (PAE), uterine or internal iliac artery ligation, B-lynch suture, and uterine compression suture could be considered.[12,13] As a last resort, hysterectomy may be used.[5]

In recent years, emergent PAE has become more common and plays an important role in the management of intractable PPH because of its multiple advantages, such as efficacy, safety, minimal invasiveness, few complications, and fertility preservation.[14–16] Although many studies on PAE for PPH have been reported, a unique protocol has still not been established in the obstetrical environment. The aim of this article was to conduct a systemic review and meta-analysis of the literature on managing patients with emergent PAE for PPH. The main goal was to assist in finding the best embolic agents, choosing the right arteries, reducing complications, and helping in reserve fertility.

SOURCES

Electronic databases including Medline, Cochrane Database of Systematic Reviews, ClinicalTrials.gov, Health Technology Assessment, the Chinese database Sino-Med, and Chinese National Knowledge Infrastructure Database were searched without applying any language restrictions from inception until March 31, 2020. The literature search strategy used the keyword "postpartum hemorrhage" and "pelvic artery embolization" without filters. Publications were cross-checked and duplicates were removed. The titles and abstracts of all articles were examined, and the full articles in English or Chinese were scrutinized, considering for potential relevance. The reference list of the articles was also screened to identify relevant publications. This step of the work and the following analysis stages were performed independently by X.Q.Z. and Y.T.Z.

STUDY SELECTION

Researchers read the 113 abstracts or full articles that were remaining from the 1075 related articles for further determination and resolved any disagreement about the inclusion. We also excluded those including case reports, reviews, or any indications for excluding, such as those not for original research article, prophylactic PAE before delivery, used for other disease other than PPH, studies on animals, or PAE used before the third trimester. At last, 43 articles of emergency PAE on PPH have detail description in embolization agents, embolization arteries, complications, or success rate. In these 43 articles, some articles may not cover every index for us to do analysis. The articles included for meta-analysis on each objective were presented in Figure 1.

We assessed the study quality by review to see if the author had quantitative data and detail description about the embolization material, embolized pelvic artery names, number of the complications, and digital success rate. Collected data were extracted and transferred into new preform by X.Q.Z. and Y.T.Z. independently. The authors' first name, year of publication, number of cases, indication for procedure, embolization material, arteries embolized, success rate or number, and complications in detail were extracted. The original authors were not contacted (Fig. 1).

Definitions

The indication of PAE is the reason why embolization was used for PPH or the reason for PPH, besides the only name of PPH.

Embolization agents are the materials used for the embolization, such as gelatin sponge particles (GSPs), microcoils, glue, Gelfoam, microsphere, pledgets, and chemicals. In the review, the material described in certain names would be included in the analysis. Those ones without a certain name were excluded from the analysis for embolization agents.

Arteries chosen for embolization are the names of the pelvic arteries chosen for embolization described in the procedure. Bilateral or unilateral, single artery should be clearly described.
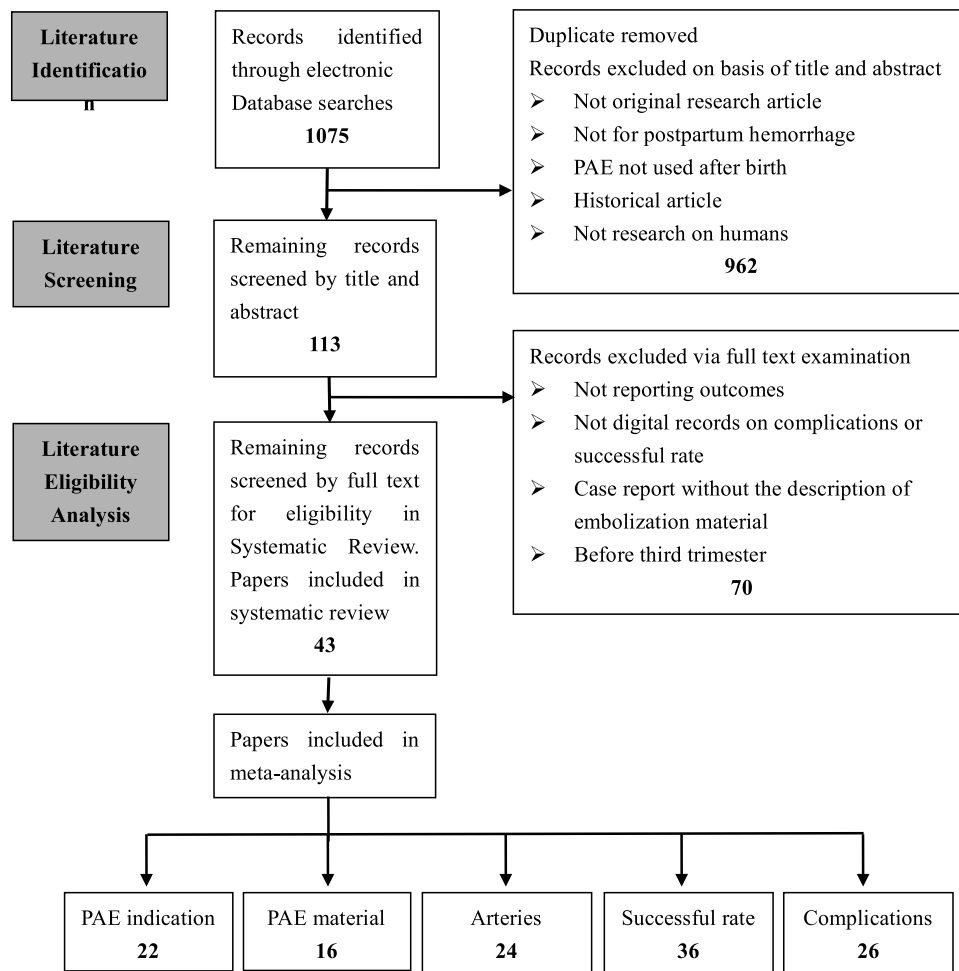
FIG. 1. Flow diagram of systematic review process.

Success rate is the technical or clinical successful percentage of the PAE procedure. Digital numbers should be described in the article, that is, a percentage or successful number with the number applied with embolization.

The complication of PAE were medical complication incidences from PAE, which were described in detail with digital numbers. The rough mention of the complication names without incidence number would be excluded from the analysis.

Data Collection Process

This study was registered in the National Institute for Health Research with PROSPERO number CRD4 2020154710. It followed the PRISMA guidelines for reporting systematic reviews and meta-analysis.[17] It was approved by the Institutional Review Board of Southern Medical University Shunde Hospital and funded by Foshan Medical Research Foundation (fund number FSHealth20190300).

X.Q.Z. and Y.T.Z. independently extracted the raw data for contents in the definitions from the 43 articles, ensuring consistency with our definitions in the list. These were recorded on a specifically developed extraction form. We endeavored to locate additional data for this systematic review, including seeking supplementary tables. At times, the extracted data differ from the objectives, for instance, for studies pertaining to PAE for cervical pregnancy hemorrhage, we ensured that the denominator included only emergency embolization for PPH. We resolved any discrepancies by carefully checking and examining the study's methods and results. Selected studies presented outcome data in different ways, most commonly as percentages. Figure 1 presents the detail from the selected studies to this review.

RESULTS

Studies Included

Initial searching identified 1075 records across the database from January 1, 1979, to March 31, 2020.

TABLE 1
Analysis of Indications of PAE for PPH

Indications	No. Cases, n	Rate, %
Uterine atony	165	37.84
Placental abnormality	100	20.94
Delivery tract injury	68	15.6
DIC/unstable hemodynamics	46	10.55
AV malformation/pseudoaneurysm	31	7.11
Vaginal hematoma	11	2.52
Failed with artery ligation	8	1.83
Others	7	1.61
Total	436	100

Note: Publication period: July 1, 1979, to March 31, 2020. Number of studies: 22.

Placental abnormality included placental previa, placental accrete, placental abnormality implantation, and placental retention. Delivery tract injury included cervical laceration and vaginal laceration. Others included multiple indications.

Figure 1 illustrates the process of screening and reviewing articles to meet the inclusion criteria. In the final stage, 43 articles including 1488 cases remained for systematic review and meta-analysis. In these 43 studies, 22 articles analyzed the indication for PAE, 16 articles gave detail description for the embolization material, 24 studies described the names of the certain arteries for PAE, 36 studies reported digital success rate, and 26 described the complications in digits and detailed outcomes after PAE. The statistical summary of the studies on indication, embolizing material, embolized arteries, success rate, and complications were demonstrated in Figure 1.

Indications of PAE

There were 22 studies that analyzed the reason for PAE, including 616 cases. Among them, 436 were subclassified as the reason for PPH.[18,19] The rest 180 cases were just classified as PPH without subclassification. Among the 436 subclassified cases, uterine atony was the most common reason for PAE (165, 37.84%). This also indicated indirectly that atony was the most common reason for PPH.[20] Placental abnormality followed atony as the second reason for PAE (100, 22.94%).[21] Placental abnormality includes placenta accreta (15), placenta previa (17), abnormal placental implantation (23), and placental retention (16); the remaining 29 were described as placental abnormality.[22,23] Delivery tract injury was the third reason for PAE (68, 15.60%). There were 48 cervical lacerations or vaginal lacerations in them. It is important to point out that there were 11 vaginal hematomas managed with PAE. For these cases, there were difficulties in finding the bleeding site because of the huge hematoma.[24] The rest of indications for PAE in these studies include disseminated intravascular coagulation (DIC) and

arteriovenous (AV) malformation. There are 46 cases (10.55%) with DIC or unstable hemodynamics that were managed with PAE. Among these cases, 8 patients underwent hysterectomy. There were 31 patients with pseudoaneurysm or AV malformation who need PAE.[25] Among them, 13 had newly formed AV malformation and the remaining 18 had pseudoaneurysm. The patients with pseudoaneurysm were found to have difficulty in stopping the bleeding with the conservative treatment; half of them were found to have rupture (9/18) through angiography. However, PAE was efficient for these patients with 100% (18/18) success rate (Table 1).

The Selection of Embolic Agents

A total of 16 studies including 511 cases reported their use of embolic agent in detail. Absorbable GSPs are widely used in 278 patients (54.4%) independently (180) or combined (98) with other embolic agents. Few complications other than fever were reported when GSPs were used for embolization. Polyvinyl alcohol particles (PVAs) were used in 103 patients (20.16%) as an embolic agent, in which 54 were combined with GSPs. Among the 3 reports that used PVAs as the embolic agent, 2 studies reported uterine massive necrosis or uterine infarction followed by late hysterectomy.[26,27] There were 86 cases (16.83%) embolized with Gelfoam, in which 44 of them were combined with GSPs. These cases had no complications other than a few of them with small intramyometrial hematic collection. There were 32 patients blocked with microcoil for PPH in 7 reports, in which 2 studies reported pelvic organ ischemia or long-standing fever followed by uterine necrosis and common perineal and tibial neuropathy.[27,28] N-butyl cyanoacrylate (NBCA) was used in 56 cases with a result of assurance for blocking hemorrhage, especially those by extravasation from a single nonuterine

TABLE 2
Analysis of Embolization Material Used in PAE for PPH

Material	No. Cases, n	Rate, %
GSPs	180	34.42
GSPs + PVAs	54	10.32
GSPs + Gelfoam	44	8.41
NBCA	56	10.71
PVAs	49	9.37
Gelfoam	42	8.03
Microcoil	31	5.93
Glue	12	2.29
Calibrated microsphere	7	1.34
Combination of ≥3 materials	44	8.41
Total	523	100

Note: Publication period: July 1, 1979, to March 31, 2020. Number of studies: 16.

artery.[29] Embolic agents used in the remaining cases were glue in 12 and calibrated microsphere in 7 cases. There were 44 cases described in combination of 3 or more as embolic agents (Table 2).

Arteries Selection for Embolization

Twenty-four studies described the arteries for embolization including a total 763 cases. Pelvic arterial embolization was applied to bilateral uterine arteries in 457 cases and unilateral uterine arteries in 21 cases (total 478, 62.65%).[30] Other arteries used for PAE were internal iliac artery (68, 8.91%), round ligament artery, and ovary artery (45, 5.9%). In addition, epigastric artery, vaginal artery, and internal pudendal artery were used in a few cases. Obturator artery, cervical artery, vesical artery, and rectal artery were rarely used for PAE. There were 64 cases that were embolized with multiple arteries (Table 3).

Complications

There were 26 studies that described complications in detail, including 661 cases, in which there were 86 cases with recent complication.[31,32] The PAE's recent complication rate is 13.01%. The most common reported complication for PAE is postembolization syndrome (50/385, 13.0%), including fever, nausea, and pelvic pain.[33,34] But surprisingly, menstrual abnormality happened after a high digit of 22.8%. In addition, there were 37 hysterectomies from a total of 661 PAE managements (5.6%). Furthermore, hysterectomy reached to 22.7% (5/22) in subsequent pregnancy with PPH managed with PAE. Other complications include neuropathy (9.4%, 6/64), organ ischemia/infarction (4.9%, 3/61), hematoma (2.9%, 5/172), and procedure accident (3.2%, 4/123) (Table 4).

TABLE 3
Analysis of Pelvic Arteries Chosen for Embolization in PPH

Arteries Chosen	No. Cases, n	Rate, %
Bilateral uterine artery	457	59.90
Unilateral uterine artery	21	2.75
Internal iliac artery	68	8.91
Round ligament artery	45	5.90
Ovary artery	35	4.59
Epigastric artery	30	3.94
Vaginal artery	25	3.28
Internal pudendal artery	11	1.44
Obturator artery	3	0.39
Cervical/rectal artery	4	0.52
Combination of arteries	64	8.39
Total	763	100

Note: Publication period: July 1, 1979, to March 31, 2020. Number of studies: 24.

TABLE 4
Complications of PAE for PPH

Complications	Cases/Observed Patients	Rate, %
Post embolization syndrome	50/380	13.2
Menstrual abnormality	65/285	22.8
Hysterectomy	37/661	5.6
Hysterectomy in repeat pregnancy	5/22	22.7
Massive necrosis	3/61	4.92
Neuropathy	6/64	9.38
Hematoma	5/172	2.91
Procedure complications	4/123	3.03

Note: Number of studies: 26. Cases included: 661.
Postembolization syndrome included patients with fever and lower abnormal pain. Procedure complications included vessel perforation during procedure and iatrogenic thrombosis.

We reviewed the cases of uterine necrosis after PAE for PPH in the literature and analyzed its occurrence and revelation to embolizing material. Among these cases, 6 reports described the material used for PAE. Four of them used PVAs, 1 used metallic microcoils, and 1 used PVAs + GSPs.[35]

Success Rate

There were a total of 37 articles that calculated the success rate for a summary number of 1274 cases. These studies defined clinical successful embolization when the bleeding stopped and recovered well after the procedure. Those had continuous hemorrhage or need further procedures to save life, such as hysterectomy, would not count as clinically successful. The overall clinical success rate is 90.5% (1153/1274). Four studies reported technical and clinical success rate after the embolization.[36] The overall technical and clinical success rates were 99.28% (276/278) and 88.13% (245/278), respectively (Table 5). Pelvic arterial embolization failure is usually resulted from complicated clinical condition of DIC, unstable hemodynamics, hemorrhage from the artery different from the blocked one, tract trauma, and uterine atony.[37,38] Technical skills may be a factor to influence the success rate. For these clinical unsuccessful patients, most of them need intensive treatment with hysterectomy or repeat PAE.

TABLE 5
Technical and Clinical Success Rate of PAE

Observation	Studies	Observed, n	Successful, n	Success Rate, %
Technically successful	4	278	276	99.3
Clinically successful	36	1274	1153	90.5

DISCUSSION

Why and When to Use PAE

According to the 2019 World Health Organization statistics, there were approximately 295,000 maternal deaths worldwide each year, or approximately 810 pregnant women die every day.[2] The number of maternal deaths caused by bleeding accounted for 27.1% of the total maternal deaths, of which two thirds were PPH.[1] In China, although oxytocin is routinely administered after the delivery of the baby to prevent uterine atony and PPH, PPH is still the leading cause, accounting for about a quarter of maternal deaths; nearly 1000 pregnant women die each year because of PPH.[39] If conservative treatment fails, emergency PAE or a hemostatic operation including uterine artery ligation and hysterectomy is needed to save lives. Delay of initiating these procedures often leads to hypovolemic shock, DIC, multiple organ failure, or even death. Therefore, the timing of emergent PAE is important.[5,40]

The American College of Obstetricians and Gynecologists' clinical management guidance of PPH in 2017 pointed out that the indication for uterine artery embolization was that the patient in normal hemodynamics but still have persistent slow bleeding after noninvasive therapy (uterotonic agents, uterine massage, uterine compression, and manual removal of any clots).[5] Gayat et al[41] summarized 5 risk factors that require PAE for placental increta: abnormal placenta increta, prothrombin time (PT) of less than 50% or international standardization ratio (INR) greater than 1.64, fibrinogen level less than 2 g/L, detectable troponin, and heart rate greater than 115 beats per minute. Each risk factor was defined as 0 or 1 to calculate the total SPPH (severe PPH) scores. The SPPH score of 0 means low risk, and when the SPPH score is greater than or equal to 2, approximately 70% of the patients need emergency intervention to control PPH.[41] However, there has been no clear consensus when to perform emergent PAE for PPH. The reasons may include the following 3 aspects. First, because of the subjectivity of estimating the amount of PPH and judging the failure of conservative treatment, initiation of interventional therapy is not uniform. Second, PAE is a minimally invasive treatment. In view of its uncertain long-term effects on uterine and ovarian function, it is not advisable to conduct embolization prematurely. Third, PAE for PPH is interdisciplinary; it requires the cooperation of the obstetrics service, interventional radiology, and intensive care unit. Hence the complexity of starting the procedures may affect the real time for arterial embolization. Therefore, obstetricians should take into account PPH guideline as well as the practical situation such as patient's condition and the cooperation experience with the interventional

radiology departments.[42] It is generally believed that interventional therapy should be considered in case the estimated blood loss reach 1000 mL or more and the hemorrhage management failed with the conservative treatment.[11] Importantly, DIC patients are not suitable for interventional therapy because of their extensive coagulation dysfunction.

Where to Apply Embolization

Pelvic arterial embolization is performed in the interventional room in most medical institutions, but some cases are carried out in the operating room.[20,43] The average length of the procedure is approximately 87 minutes, which varies widely depending on the operator's experience.[35,44]

Pelvic arterial embolization includes mainly the following 3 steps. First, the operator should confirm if the catheter is in the correct pelvic blood vessel and determine the site of the hemorrhage through pelvic angiography. Angiography can detect contrast medium extravasation with a threshold flow rate of 1 to 2 mL/min.[44] It may be difficult to detect extravasation when the bleeding is slow, intermittent, or diffuse with an atonic uterus. Embolization should be considered first at the site with extravasation. Second, the operator performs bilateral uterine arterial embolization. If bilateral uterine arterial embolization fails to stop bleeding, embolization of anterior branch of bilateral internal iliac artery is feasible. Finally, if the internal iliac artery embolization fails, the other bleeding sites should be carefully searched with angiography through the abdominal aorta or external iliac artery.[45] Generally, if the patient is stable, uterine arterial embolization is preferred to reduce the occurrence of complications. If the patient is in shock, the internal iliac artery embolization is a priority to ensure the rapid control of bleeding. In life-threatening PPH, resuscitative endovascular balloon occlusion of the aorta can be used in an emergency situation. The procedure involves obtaining arterial access through the common femoral artery, passing a vascular sheath, floating a balloon catheter to the appropriate section of the aorta, and inflating the balloon to occlude blood flow.[46,47] In addition, because prostanoid drugs can induce marked spasm of uterine artery, ideally uterine arterial embolization should be performed at least 30 minutes after prostaglandin analog administration in order to guarantee the therapeutic effect.[35] In some cases, nonuterine arteries may be the major sources of PPH; their detection and selective embolization are important for successful hemostasis.[45]

How to Choose Embolic Agent

The choice of embolic agent mainly depends on 2 principles. First, hemostasis is fast and effective. Second,

selective embolization is performed in the target blood vessels to reduce the occurrence of adverse reactions. There are temporary embolism agents and permanent embolism agents with different materials and sizes.[48] The former includes gelatin sponge or blood clot, and the latter includes metal coils, PVAs, NBCA, and microspheres. Hemostasis effects and complications differ in the embolization material and size. When the embolic agent is large, it can achieve extensive hemostasis by the proximal embolization of large blood vessels, whereas when embolization agent is too small, complications such as ischemia and necrosis could occur by distal embolization of small vessels.[49] Some authorities suggested that the threshold size of embolization material is 500 μm.[50]

Gelatin sponge granules are the main embolic agent for PPH. They achieve rapid hemostasis because of mechanical obstruction and thrombus formation in the vessel lumen. Gelatin sponge can be absorbed within 2 to 6 weeks. The clinical success rate of gelatin sponge for PPH is 79% to 93.9%.[51] Poujade et al[52] recommended using gelatin sponge with a diameter greater than 1 mm to avoid complications caused by distal vascular obstruction.[52] Soro et al reported that 1 or 2 mm of gelatin sponge occluded almost the same-sized artery. There were no significant differences for microscopic necrosis between 1 and 2 mm of gelatin sponge embolization. However, the qualitative inflammatory reaction around the embolized artery with 2 mm particles was significantly greater than 1 mm particles.[52] Therefore, GSPs should be neither too large to aggravate the inflammatory reaction nor too small to increase the possibility of distal vascular ischemia necrosis. The current literature suggests using a diameter of 500 to 1000 μm gelatin sponge granules for embolization in PPH.[16,53] Other embolic agents are used less often. Hemostasis of NBCA is based on the mechanism of rapid polymerization and hardening in an ionic fluid without abundant clotting factor. Compared with gelatin sponge, NBCA is more suitable for patients with severe and persistent bleeding such as a pseudoaneurysm, arterial rupture, or AV fistulas.[29,33] In some institutions, metallic coils or particles are used mainly to occlude ruptured pseudoaneurysms.[29] In addition, because even the largest microsphere may pass through the AV shunts and escape into the systemic circulation, the use of microsphere as PAE agents is controversial.[29] PAV particles are not recommended for clinical use because of their many adverse reactions.[52]

In summary, according to the majority of the reports, gelatin sponge granules with a diameter of 500 to 1000 μm were the safest and most effective as embolic agents for PPH, and the metal coils and NBCA should be restricted and only used for special cases, such as a pseudoaneurysm, arterial rupture, or AV fistulas.

What Influences Success

The success rate of PAE in the treatment of PPH generally refers to clinical success rate of hemostasis, which can be achieved without relying on a second embolization or surgical intervention. In an experimental study of uterine artery embolization reported by Tang et al,[16] the effective rate of pelvic arterial embolism was 100%.[16] Ruiz et al[54] summarized 21 studies (including 1739 patients) and reported that the global success rate of PAE for PPH was 89.4% on average, ranging from 79% to 100%.[54] The largest study by Kim et al[35] (including 257 patients) reported a success rate of 90.7%. After failure of embolization, the emergency hysterectomy rate was 7%, the re-embolization rate was 4.1%, and the mortality was 0.9%.[32] Possible factors responsible for clinical failure of PAE include a history of prior surgery, spasm of the arteries, unilateral embolization, proximal embolization, and DIC.[55] Cheong et al[32] indicated that DIC was an important independent prognostic factor for PPH patients treated with PAE.[32] Studies showed that cesarean delivery may increase the probability of PAE, but the success rate of PAE is not related to the mode of delivery.[35,56] In a retrospective controlled cohort study, PPH patients who underwent therapeutic PAE were compared with those without PAE. Data suggest that PAE is effective for the treatment of most severe PPH.[57] In view of the lack of complications and unwarranted effects, clinical use of PAE in severe PPH seems justified, particularly in view of the life-threatening condition and potential to preserve fertility in affected patients.[58,59]

In addition to the hemostatic status and uterine atony, attention should be focused on the bleeding site differing from the routine ones, which means we should pay attention to the arteries rather than uterine arteries for the cases with difficult management.[60] Furthermore, clinical failure is related to placenta accreta/percreta, hemoglobin level, PT, fibrinogen, and number of transfusion.[21,38,61] Another study concluded that the procedure failure is related to DIC, transfusion, and embolization of both uterine and ovary arteries.[62,63] In the report of Urushiyama et al,[64] failure is related to DIC score/PT ratio, platelet count, fibrinogen, fibrin degradation products, and all failure cases with a DIC score greater than 9.[64]

What Affects Complications

The complications of PAE were not uncommon. The mortality rate of severe PPH treated with PAE is 0.9%. In addition, the rate of other major complications was

varying. In general, the most common complication is postembolization syndrome including fever, nausea, and pelvic pain. The main short-term complications include 3 categories: (1) traumatic complications, such as vascular tear or rupture, puncture site aneurysm, and AV thrombosis[59]; (2) ischemic complications, such as ischemia or necrosis of the uterus, vagina, bladder, or distal limbs[58]; and (3) infectious complications, such as puncture site infection or sepsis. The occurrence of these complications may be closely related to the nature and size of embolic agent, vascular anastomosis system, and vascular embolization technology.[38]

Massive necrosis of the uterus is a rare but severe complication after PAE. Most reports about uterus necrosis after PAE for PPH were case report. Poujade et al[52] reviewed literature including altogether 19 cases of uterine necrosis and concluded that the size and nature of the embolizing agent, the presence of the anastomotic vascular system, and the embolization technique itself with the use of free flow embolization may be the factors involved in uterine necrosis.[52] Our analysis on the literature revealed that permanent embolization materials such as metallic microcoils/PVAs have more chances with complication of massive necrosis.

Influence on Future Reproduction

One of the purposes of PAE instead of hysterectomy to manage PPH is to preserve the uterus and reproductive function, so it is extremely important to evaluate its effect on fertility, including menstruation, ovarian reserve, and pregnancy.

It is hard to evaluate the fertility by pregnancy rate because the PPH and its management may influence the patient's desire to have pregnancy. Some complications certainly affect the reproductive ability such as uterine ischemia/infarction/necrosis and hysterectomy, but their incidences are very low.[65] For the menstrual change and the complications in subsequent pregnancy, it seems PAE may influence the reproduction in some aspects.[66,67]

Most of the literature reported that approximately 91% to100% patients who had undergone PAE have resume their menstrual periods,[36,59,68] but acute ovarian function failure and uterine apoplexy were reported after PAE in a few reports.[69] Inoue et al[70] reported that 113 patients were followed up after PAE and resumption of menses occurred in 106 women (93%).[70] Different from the high menstrual recovery rate, the subsequent pregnancy rate was generally low. Soro et al[59] reviewed 38 literatures (including 1072 patients) and concluded that the subsequent pregnancy rate is 23.2% after PAE.[59] Some research compared the subsequent pregnant rate after PAE with that of the general population. Results showed the former was lower than the latter, but the difference is not statistically significant.[59] Probably this result is because of the small data pool. The ischemic injury of endometrium caused by PAE may play a role in subsequent pregnancy loss, but some of the studies included too many patients who did not want to conceive or patients who had concerns about pregnant complications, so the subsequent pregnant rate may be underestimated. In addition, the PPH recurrence rate in subsequent pregnancy after pelvic arteries embolization was significantly higher than that of normal population ranged from 1% to 50% and the average rate was 14%.[70] Inoue et al[70] reported that the PPH recurrence rate was 23.3% after delivery and 16.7% underwent hysterectomy because of placenta accreta.[70] These data indicated that temporary blockage of blood flow to the uterus may lead to uterine and endometrial ischemia, thereby it may increase the incidence of PPH in subsequent pregnancy. However, the effect of PAE on placentation in the subsequent pregnancy is unclear.

Some authorities suggest that PAE may lead to chronic ischemia in the endometrium by reducing the supply of blood flow to the uterus, thereby affecting the blood exchange of the uterus and placenta and limiting fetal growth. However, Fiori et al[69] reported that 60% of patients after PAE were able to deliver healthy, normal weight newborns through vaginal delivery.[69] Soro et al[59] reported 61 newborns born after PAE; the average birth weight was 3250 g, and the average gestational age was 38 weeks. Only 3 of them were less than gestational age.[53] These numerical values indicated that PAE has no direct effect on the placental blood supply and fetal growth. The formation of collateral circulation develops very quickly after PAE. It plays an important role for the recovery of normal uterine circulation; the influence to fetal growth and development in subsequent pregnancy was limited.

The Radiation Exposure

During PAE, patients are inevitably affected by radiation because the observation relies on fluorescence. According to a Canadian cardiologist's recommendation, patients with skin doses exceeding 4 Gy are at risk of skin injury.[71] Generally speaking, PAE is relatively safe because the radiation dose absorbed by the skin within 10 to 35 minutes' fluorescent time of intervention therapy ranges from 450 to 1600 mGy.[55] Pertaining to ovary, a radiation dose of 2 to 3 Gy in the ovary causes ovarian damage to 1% to 5% cases; a dose of 6.25 to 12 Gy causes damage to 25% to 50% cases within 5 years. Ovarian castration requires a radiation

doses of 20 to 30 Gy. The literature indicates that, within fluorescent time of 10.9 to 27 minutes, the radiation dose absorbed by the ovarian ranges from 7 to 378 mGy.[72] According to Minano et al,[73] during fluorescent time of 26.9 minutes, the mean radiation dose absorbed by the ovary was 149 mGy, and the mean dose area product was 196 Gy·cm.[73] In summary, the ovarian dose in the treatment of PAE is low, and the risk of adverse effects is low. Nevertheless, it is still necessary for medical workers to minimize radiation exposure. The interventional operator can decrease the radiation dose by shortening the fluorescent time, using lower frequency pulse fluorescence and using the radiation beam precisely.

LIMITATIONS AND CONSTRAINTS

Most of the studies referred in this article are retrospective analysis. In addition, they lacked data on the course and duration of labor before PPH. Furthermore, the amount of blood loss could not be accurately calculated because the hemorrhage was usually rapid and urgent. Pertaining to PAE, it is practical if there is sufficient time to arrange the procedure and there is cooperation between obstetricians and interventional radiologists. How to form and organize the team efficiently in emergency will be a topic in study.

However, some studies will not demonstrate the complications if the complication did not happen. It is possible that some complication incidences in this article could be higher than it actually happened. For example, the overall incidence of neuropathy of the 4 studies was 9.4%, but most of the studies did not describe this complication because it did not happen, and these data are not included in the total number. Another example is infection, which has only 1 report in the 10 cases.

CONCLUSIONS

In conclusion, emergent PAE is a safe and effective method with high success rate in management of life-threatening PPH. Using the absorbable gelatin sponge granules with a diameter of 500 to 1000 μm as embolic agent is a better choice. Pelvic arterial embolization retains uterus mostly but may affect the recovery of menses after. In subsequent pregnancy, they could have higher complications, but usually it does not influence the fetal growth when conceived. Patient should be closely monitored and comprehensively managed in consecutive pregnancy to decrease recurrent PPH. Because there is currently no randomized controlled study to explore the effect of PAE on ovarian reserve function, the impact of PAE on fertility still needs further clarification.

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