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Retrospective Study

Usefulness of transcatheter arterial embolization for eighty-three patients with secondary postpartum hemorrhage: Focusing on the difference in angiographic findings

Bong-Man Kim, Gyeong-Sik Jeon, Min-Jeong Choi, Nam-Soo Hong

Abstract

BACKGROUND

Transcatheter arterial embolization (TAE) has been widely used as an effective and a safe treatment method and was often used as an alternative to the surgical management, but studies on the efficacy and the safety for patients undergoing secondary postpartum hemorrhage (PPH) are limited.

AIM

To evaluate the usefulness of TAE for secondary PPH focusing on the angiographic findings.

METHODS

We conducted a research from January 2008 to July 2022 on all 83 patients (mean: 32 years, range: 24-43 years) presented with secondary PPH and they were treated with TAE in two university hospitals. The medical records and angiography were retrospective reviewed in order to evaluate the patients' characteristics, delivery details, clinical status and peri-embolization management, angiography and embolization

details, technical/clinical success and complications. The group with active bleeding sign and the group without it were also compared and analyzed.

RESULTS

On angiography, 46 (55.4%) patients showed active bleeding signs such as contrast extravasation ($n = 37$) or pseudoaneurysm ($n = 8$) or both ($n = 1$), and 37 (44.6%) patients showed non-active bleeding signs such as only spastic uterine artery ($n = 2$) or hyperemia ($n = 35$). In the active bleeding sign group there were more multiparous patients, low platelet count, prothrombin time prolongation, and high transfusion requirements. The technical success rates were 97.8% (45/46) in active bleeding sign group and 91.9% (34/37) in non-active bleeding sign group, and the overall clinical success rates were 95.7% (44/46) and 97.3% (36/37). An uterine rupture with peritonitis and abscess formation occurred to one patient after the embolization, therefore hysterostomy and retained placenta removal were performed which was a major complication.

CONCLUSION

TAE is an effective and a safe treatment method for controlling secondary PPH regardless of angiographic findings.

INTRODUCTION

Postpartum hemorrhage (PPH) remains still as one of the major cause of maternal morbidity and mortality, which is responsible for about 25% of maternal deaths worldwide^[1,2]. Secondary PPH is defined as an abnormal or an excessive bleeding from the birth canal occurring from 24 h up to 12 wk postpartum. The overall reported secondary PPH incidence that happened in the developed countries is lower than that of primary PPH, accounting for about 0.47%-1.44% in all deliveries^[3-5].

The initial management of secondary PPH includes intravenous uterotonic agents administration, blood transfusion, fluid resuscitation, vaginal packing, uterine massage and a repair for the birth canal laceration. However, if these treatments are not successful, a surgical or an endovascular treatment can be considered as an option.

Since Brown *et al*^[6] first applied the transcatheter arterial embolization (TAE) to PPH, TAE has been widely used as an effective and a safe treatment method and was often used as an alternative to the surgical management^[7-9].

Primary and secondary PPH have similarities that they can be a life-threatening condition, but their differences can be found particularly from the time and the cause of bleeding. It is also known that an active bleeding foci such as pseudoaneurysm and contrast extravasation are more commonly found in the secondary PPH^[9].

Since studies on the efficacy and the safety for patients undergoing secondary PPH are limited^[10-12], ³ the purpose of this study is to evaluate the effectiveness and the safety of TAE for patients with secondary PPH as well as to identify the differences between the two groups according to the presence and the absence of their active bleeding signs on angiography.

MATERIALS AND METHODS

Patients

This retrospective study was approved by our institutional review board, and the informed consent was waived. All consecutive patients who underwent TAE for the uncontrolled secondary PPH from January 2008 to July 2022 in two university hospitals were included. In this report, the uncontrolled PPH is defined as a condition when bleeding persists despite the previously mentioned treatment. The two patients who underwent the TAE in March and June of 2011, had previously been included in the other study^[7]. A total of 83 women patients (mean age: 32.0 years; range: 24-40 years) were comprised for undergoing TAE in their secondary PPH. The patients either gave birth in our hospitals or were transferred from other institutions that did not have the

intensive care unit or the angiography unit. All TAE was determined by an obstetrician who examined the patient and was referred to the interventionist.

The patients were divided into two groups according to the presence or absence of active bleeding sign on angiography. If there were a contrast extravasation or pseudoaneurysm found on angiography the patient was grouped in an active bleeding group, and when there were only spastic uterine artery or hyperemia finding on angiography the patient was grouped in a non-active bleeding group.

Embolization Procedure

Angiography and TAE were performed by interventional radiologists from each institution. An unilateral femoral artery was accessed by using a 5-F vascular sheath. Pelvic angiography was performed initially to evaluate the pelvic vascular anatomy and to detect the bleeding focus. The anterior division of the internal iliac artery (IIA) or IIA were catheterized with a 5-F angiographic catheter (Yashiro; Terumo, Tokyo, Japan, or Cobra or Roberts; Cook, Bloomington, Indiana), and selective study was performed. Afterwards, a selective embolization of the target artery was performed by using a microcatheter (Renegade; Boston Scientific, Natick, Massachusetts, or Asahi Masters Parkway Soft; Asahi, Nagoya, Japan, or Progreat; Terumo). Essentially, target artery is an artery that shows active bleeding sign in the active bleeding group and the target arteries for the non-active bleeding group are both uterine arteries. Embolization was performed as selectively as possible, but when catheterization failed or hemostasis was insufficient after the embolization, the anterior division of IIA or the IIA itself was unavoidably embolized. Absorbable gelatin sponge particles (Cutanplast; Mascia Brunelli Spa, Milan, Italy or Caligel; Aicon Pharm SCI&TEC Co., Ltd., Hangzhou, China) were the first selection to use as the embolic material. Other materials such as polyvinyl alcohol (PVA) particles (Contour; Boston Scientific), metallic microcoils (Tornado; Cook or Vortex; Boston), and N-butyl cyanoacrylate (NBCA; Histoacryl; B. Braun, Melsungen, Germany) were used depending on the angiographic findings, the degree of catheterization and the operator's preference. After TAE, a vaginal

examination was performed by an obstetrician to confirm that the successful hemostasis of vaginal bleeding was achieved. If the bleeding persisted, additional angiography was performed to find another potential bleeding site such as ovarian artery followed by an additional embolization.

Data Analysis and definitions

Medical records and radiologic images were reviewed to collect the data about the patient's characteristics, mode of delivery, a suspected clinical cause of PPH, bleeding pattern (abrupt or intermittent), number of days to receive TAE after childbirth, peri-embolization management, laboratory findings (hemoglobin, coagulation battery), TAE characteristics, TAE outcomes, and complications.

The clinical cause of PPH was divided into five categories: Uterine atony/subinvolution, retained placenta, uterine artery injury, abnormal placentation and unknown. The uterine artery injury was defined as a case of pseudoaneurysm found in computed tomography (CT) or ultrasonography before the procedure. Hemoglobin level is indicated as the lowest level before and after the procedure; however, platelet count (lowest level), prothrombin time (PT) and activated partial thromboplastin time (most prolonged level) were recorded before the procedure, which may have been affected by the transfusion. Peri-embolization management was classified into five groups: only transfusion, intravenous uterotonic agents, vaginal packing including intrauterine balloon tamponade, surgical intervention and conservative treatment. Hypotension was defined as a systolic blood pressure < 90 mmHg before TAE. Angiographic findings were classified into two groups: active bleeding sign (pseudoaneurysm or contrast extravasation) and non-active bleeding sign (only spastic uterine artery or hyperemia). Embolization data was collected on the embolic material, number of embolized arteries and time spent on the embolization procedure. The complications were classified as a major or a minor complications according to the Society of Interventional Radiology guidelines^[13]. The technical success was defined as a successful embolization for the target vessels, and the clinical success

as the cessation of bleeding after TAE without the need of repeated TAE or surgery during the hospital stay.

Univariate analysis of categorical data was assessed using a χ^2 test, and univariate analysis of continuous data was assessed using a *t* test. Statistical analysis was performed with the SAS version 9.4 (SAS Inc., Cary, NC, USA). *P* < .05 was considered statistically significant.

RESULTS

The clinical characteristics of the 46 (55.4%) patients in the active bleeding sign group and the 37 (44.6%) patients in the non-active bleeding sign group are summarized on Table 1. Although there were no distinct differences between the two groups on their delivery mode, there were significantly more multiparous patients in the active bleeding group than in the non-active bleeding group. Secondary PPH was caused by retained placenta (26/83, 31.3%), atony (21/83, 25.3%) and uterine artery injury (2/83, 2.4%). However, the majority number of 33 (39.8%) patients showed no definite cause of bleeding before and after TAE.

Table 2 shows characteristics of the clinical status and peri-embolization management. There were no significant differences statistically between the two groups in their hemodynamic stability and hemoglobin levels during the administration and the initial management, but when compared with the non-active bleeding group, the active bleeding group's platelet count was low, PT was prolonged, and the requirement of blood transfusions were high.

During the initial treatment to control PPH, transfusion was performed most often in both groups, and the next frequently performed procedure was the administration of uterotonic agents. Six patients who had taken dilatation and evacuation for a retained placenta were considered to have undergone surgical intervention.

Table 3 summarizes the details of angiography and embolization according to the angiographic findings. The most common angiographic finding in the active bleeding group was extravasation (*n* = 37), followed by pseudoaneurysm (*n* = 8) and

pseudoaneurysm with extravasation ($n = 1$). Most patients from non-active bleeding group showed hyperemia ($n = 35$) whereas 2 patients showed only spastic UA. Embolization was performed on both uterine arteries ($n = 52$) in most cases. Hemostasis was successful in the active bleeding sign group even when the embolization was only performed on the unilateral uterine artery ($n = 12$) or unilateral internal pudendal artery ($n = 1$). On the other hand, the bleeding continued even after the embolization of bilateral uterine arteries for 4 patients, so additional embolization of the both anterior division or both internal iliac arteries were performed and the bleeding was controlled afterwards.

The embolic materials used for TAE are summarized in Table 4. Only particles such as gelatin sponge particles or PVA were used to treat 54 patients, and for other 20 patients both particles and permanent materials were used. The rest of 9 patients with active bleeding signs were treated with hemostasis which was successfully achieved by using only NBCA for one artery (eight uterine arteries and one internal pudendal artery).

The technical success rates were 97.8% (45/46) in active bleeding sign group and 91.9% (34/37) in non-active bleeding sign group, and the overall clinical success rates were 95.7% (44/46) and 97.3% (36/37) respectively. Technical failure occurred in four patients, and dissection happened during the superselection of the target artery (two uterine artery, one ovarian artery, one round ligament artery). There were 3 patients with clinical failure and among them two patients were from the active bleeding sign group and one patient was from the non-active bleeding sign group. Two of them received repeat TAE and the other one underwent subtotal hysterectomy, and hemostasis was successfully achieved.

There was one major complication related to the embolization in non-active bleeding group. A 28-year-old primiparous patient gave birth through vaginal delivery at 27 wk and 5 d of pregnancy, and was transferred after being treated at another hospital due to intermittent bleeding. Ultrasound scan performed 48 d after the delivery revealed a mixed echogenic lesion measuring 8.9 cm × 6.7 cm × 7.4 cm, presumably

retained placenta. On Day 52 after delivery, TAE was performed using gelatin sponge particles for both uterine arteries due to diffuse hyperemia. After TAE, the patient's symptoms improved and was discharged. At the time of outpatient visit on the 8th day after the procedure, CT scan was performed for fever, abdominal pain, and diffuse tenderness; and it was diagnosed as uterine rupture with peritonitis and abscess formation. The operation was performed on the same day, and the left fundus of the uterus was dehiscence (about 1.5 cm), and the retained placenta became necrotic and was adhered to the omentum and bowel, and ascites mixed with pus were observed in the pelvic cavity. Therefore, hysterotomy, removal of retained placenta, debridement, omentectomy, and primary repair were performed, and the pathology was confirmed as infarcted placental tissue with calcification. After that, the symptoms improved and the patient was discharged 13 d after the surgery.

As for minor complications, 65 (78.3%) patients had post-embolization syndrome such as transient fever or abdominal pain and all were recovered through a conservative treatment. There were no significant differences between these two groups according to the presence or absence of an active bleeding sign in technical success, clinical success, and complication.

All patients were available to follow-up after being discharged, the median and mean of the follow-up periods were 1 mo and 12.5 mo (range: 0 to 168 mo), respectively. For many patients there were no medical records on their regular menstrual cycle resumption; among them three women became pregnant and gave birth without any complications during their follow-up periods.

DISCUSSION

Limited studies^[10-12] have shown that TAE for secondary PPH is effective and safe. This study aimed to investigate on the usefulness of TAE and whether there were any differences according to angiographic findings in a relatively large number of patients with secondary PPH.

From the present study, the most common cause of secondary PPH was unknown (39.8%), followed by retained placenta (31.3%), atony/subinvolution (25.3%) and uterine artery injury (2.4%). Unlike the other studies, we were not able to find many cases caused by placenta anomaly. The limitation of this study was that the cause of the bleeding was unknown in many cases, and most procedures were performed without knowing the cause in reality because of urgency. It is considered important to control bleeding first.

There were no significant differences in vital signs, hemoglobin levels, and peri-procedure management between the active bleeding group and non-active bleeding group; but the active bleeding group showed lower platelet count, more PT prolongation, and higher transfusion requirements than the non-active bleeding group. These findings may suggest that more bleeding occurred in the active bleeding group than the non-active one.

Contrast extravasation and pseudoaneurysm on digital subtraction angiography are thought to suggest active arterial bleeding, and are generally known to be more frequent in secondary than in primary PPH^[9]. In the present study, the angiographic findings of this study are as follows; contrast extravasation ($n = 37$, 80.4%), pseudoaneurysm ($n = 8$, 17.4%), contrast extravasation with pseudoaneurysm ($n = 1$, 2.2%), and indirect bleeding was shown for spastic uterine artery ($n = 2$, 5.4%) and hyperemia ($n = 35$, 94.6%). The active arterial bleeding sign was 55.4%, which was higher in frequency than 32.4%-48% as from other studies happened to secondary PPH patients^[10-12] and it happened more frequently than a larger study in primary PPH patients^[8]. Active bleeding sign was significantly related to multiparity among maternal characteristics. Pseudoaneurysm is known to occur frequently in association with traumatic events such as cesarean section, dilatation and curettage, and pelvic surgery, but there have also been reports that it has also occurred in uncomplicated, spontaneous vaginal delivery^[14]. Therefore, since there is a risk that pseudoaneurysm may occur with delivery alone, it is predicted that repeated childbirth itself may be a risk factor for showing active bleeding signs such as pseudoaneurysm.

Also in this study, only particle embolic materials were used the most, followed by only gelatin sponge particles ($n = 40$), gelatin sponge particles and PVA ($n = 12$), and only PVA ($n = 2$). For 9 patients from the active bleeding sign group, embolization was performed for one artery (8 uterine arteries and 1 internal pudendal artery) using only NBCA, and hemostasis was successfully achieved. There is a study on gelatin sponge particles that all patients with pseudoaneurysm or pseudoaneurysm rupture-induced extravasation were successfully treated with gelatin sponge particles as the main embolic material^[15,16]. Since Pleage *et al*^[10] first reported the use of NBCA for treating pseudoaneurysm to a patient with secondary PPH, a number of studies^[17-19] have reported using NBCA in patients with intractable PPH. Indications of using NBCA for patients with PPH could be one of the followings: An active bleeding sign, or unstable hemodynamical condition, or failed embolization with gelatin sponge particles, or PPH with disseminated intravascular coagulation^[9]. Therefore, in that kind of situation NBCA can be used with caution by an experienced interventionist.

This study includes a relatively large number of patients and resulted with the clinical success rate of 96.4% (80/83). It clearly shows that TAE was effective for treating secondary PPH which consistently followed the results from other previous studies^[10-12]. As aforementioned from the results of this study, there was one major complication related to the embolization. An uterine rupture with peritonitis and abscess formation occurred to one patient after the embolization. A 28-year-old primigravida who had a normal vaginal delivery, had no other risk factors to occur the uterine rupture^[20]. The embolic material used for TAE was the gelatin sponge particles similar in size that was used by other patients, and the procedure was successfully completed without any special events. However, 8 d after TAE was performed, a fever and an abdominal pain occurred, and uterine rupture with peritonitis and abscess formation was diagnosed through CT. After the treatment that included hysterotomy and removal of retained placenta, the patient was cured and discharged. Fifty months later the patient was pregnant and gave birth without any further complications. There are few case reports on the uterine rupture after the uterine artery embolization^[21-23]. It was about a history

of UAE with bleeding or leiomyoma that happened several years ago, and uterine rupture occurred in the subsequent pregnancy. However, in the case of our patient, it is different that uterine rupture occurred during the puerperium period, and one could not find any reports relating to this case. Even after the uterine artery embolization, the bleeding control was not appropriate, so both IIA ($n = 3$) and the anterior division of both IIA ($n = 1$) were additionally embolized, but there were no complaints of ischemia or neurologic complication from the patient.

The median and mean of the follow-up periods for all patients after TAE were 1 mo and 12.5 mo (range: 0 to 168 mo), which overlapped with the amenorrhea period during breastfeeding, so there were limitations in evaluating the late complication related to either menstruation or fertility. However, there have been no records of complaints or counseling request from the patient regarding it. Two patients had additional pregnancies. In addition to the aforementioned patient with peritonitis, one became pregnant 17 mo after the delivery and had normal vaginal delivery. Although controversy remains, there are studies^[8,24,25] showing that the treatment do not appear to be adversely affecting the recovery of the normal menstrual cycle and the subsequent pregnancy.

This study has several limitations. First, the temporal sequence relationship between some factors and active bleeding may be unclear. Second, in the case of patients transferred from other hospitals, some initial data may be missing or inaccurate. Third, in this study, the most common cause of PPH was unknown because there was no clear description in the medical record. Fourth, since there were no consistent guidelines for treating PPH, an indication for requesting TAE may differ depending on hospitals' policies and clinicians' treatment methods. This not only applies to two hospitals that participated in this research, but it may also happen among obstetricians from each hospital. Fifth, since the embolic material is determined by the operator's judgment, a different embolic material may be selected even for similar patients' conditions and angiographic findings. Lastly, patients with a long-term follow-ups are rare, so their information on menstruation and fertility are also limited.

CONCLUSION

In conclusion, as this study involved a relatively large number of patients, TAE is an effective and a safe treatment for secondary PPH patients regardless of the presence or absence of active bleeding signs.

ARTICLE HIGHLIGHTS

Research background

TAE has been widely used as an effective and a safe treatment method and was often used as an alternative to the surgical management, but studies on the efficacy and the safety for patients undergoing secondary PPH are limited.

Research perspectives

A study with a large number of patients is needed.

Research conclusions

TAE is an effective and a safe treatment method for controlling secondary PPH regardless of angiographic findings.

Research results

TAE was performed in 83 patients, 46 (55.4%) patients with active bleeding signs while 37 (44.6%) patients did not. In the active bleeding sign group there were more multiparous patients, low platelet count, prothrombin time (PT) prolongation, and high transfusion requirements. The technical success rates were 97.8% (45/46) in active bleeding sign group and 91.9% (34/37) in non-active bleeding sign group, and the overall clinical success rates were 95.7% (44/46) and 97.3% (36/37).

Research methods

Patients were divided into two groups according to the presence or absence of active bleeding signs and analyzed

Research objectives

To evaluate the usefulness of transcatheter arterial embolization (TAE) for secondary postpartum hemorrhage (PPH) focusing on the angiographic findings.

Research motivation

To identify the usefulness of TAE and the differences according to the presence and the absence of their active bleeding signs on angiography.

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