Received:
31 January 2018

Revised:
16 March 2018

Accepted:
06 April 2018

<https://doi.org/10.1259/bjr.20180132>

Cite this article as:

Aoki M, Tokue H, Miyazaki M, Shibuya K, Hirasawa S, Oshima K. Primary postpartum hemorrhage: outcome of uterine artery embolization. *Br J Radiol* 2018; **91**: 20180132.

FULL PAPER

Primary postpartum hemorrhage: outcome of uterine artery embolization

^{1,2}MAKOTO AOKI, MD, ²HIROYUKI TOKUE, MD, PhD, ²MASAYA MIYAZAKI, MD, PhD, ²KEI SHIBUYA, MD, PhD, ²SATOSHI HIRASAWA, MD, PhD and ¹KIYOHITO OSHIMA, MD, PhD

¹Department of Emergency Medicine, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan

²Department of Diagnostic and Interventional Radiology, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan

Address correspondence to: Dr Makoto Aoki
E-mail: aokimakoto@gunma-u.ac.jp

Objective: To assess the efficacy of uterine artery embolization (UAE) for the management of primary postpartum hemorrhage (PPH) and to determine the factors associated with clinical outcomes especially in relation to the ovarian artery.

Methods: A retrospective analysis of 33 patients who underwent UAE for primary PPH was performed. Clinical data were used regarding maternal characteristics, cause of bleeding, mode of delivery, bleeding onset after delivery, risk factors for PPH, presence of coagulopathy, details regarding the UAE procedure, and types of ovarian artery flow. We defined two types of ovarian artery flow by initial aortography before UAE (Type A: ovarian artery flow arose directly from the aorta to the uterine artery; Type B: ovarian artery flow that did not obviously arise from the aorta). Clinical success was defined as cessation of bleeding after UAE without the need for hysterectomy. Univariate analysis was performed to determine factors related to clinical outcomes.

Results: The major indication of UAE was uterine atony (82%; 27/33). Extravasation of contrast medium was observed in 15 (45%) patients. The clinical success rate was 85% (28/33). In five patients, embolization failed, and these patients were managed by hysterectomy. Univariate analysis showed that retained placental tissue ($p < 0.001$), type of ovarian artery ($p < 0.001$) and the existence of extravasation of contrast medium ($p = 0.049$) were related to the clinical success rate.

Conclusion: The clinical success rate was 85% (28/33), and some PPH patients were thought to need ovarian artery embolization in addition to UAE.

Advances in knowledge: Initial aortography before UAE may be useful to predict the failure of UAE and the need of ovarian artery embolization. Obvious ovarian arterial blood flow to the uterus by aortography could be a warning sign.

INTRODUCTION

Severe post-partum hemorrhage (PPH) accounts for approximately 25% of maternal deaths worldwide.¹ Uterine artery embolization (UAE) has been the standard treatment option for PPH because of its low invasiveness and high success rate.^{2,3} Despite the high success rate of UAE for PPH, patients with intractable PPH sometimes need surgery for uncontrolled bleeding.⁴ From previous articles, the existence of disseminated intravascular coagulation and massive transfusion requirements were reported as indicators of the failure of UAE.^{4,5} On the other hand, the relationship between the embolized arteries and the clinical failure of UAE remains unclear. Of the natural collateral circulation to the uterus, ovarian arteries were reported to be related to clinical failures after UAE for symptomatic uterine fibroids.^{6–9} Ovarian artery embolization (OAE) was noted to be a technically challenging procedure and OAE

with UAE could significantly increase the risk of ovarian dysfunction; thus, OAE was considered to be controversial.⁸ In this study, we evaluated the relationship between the embolized arteries, especially ovarian arteries, and clinical failure of UAE in PPH patients.

METHODS AND MATERIALS

Patient selection

The protocol of this retrospective study was approved by the research ethics board of Gunma University hospital without the need for informed consent. Between January 2008 and December 2016, all females who underwent UAE for PPH in Gunma University were included in this study.

Analyzed items and definitions

A review of obstetric charts was performed to collect data on females who underwent UAE for PPH regarding

Figure 1. Initial aortography before conventional uterine artery embolization. (a) The initial aortography showed an obvious ovarian artery from the aorta to the uterus (arrow head) and the bilateral uterine arteries (arrow). (b) Initial aortography showed the bilateral uterine arteries leading to the uterus (arrow).

maternal characteristics, cause of bleeding, mode of delivery, bleeding onset after delivery, risk factors for PPH, amount of blood transfusion during the day of the UAE procedure, presence of coagulopathy, details regarding the UAE procedure, complications related to UAE, and clinical outcome.

The cause of bleeding was determined by obstetricians and was divided into six categories: uterine atony, trauma (including cervical or vaginal laceration and deep episiotomy wound), retained products of conception (including placental accrete and percreta), placenta previa, uterine rupture, and coagulopathy. Coagulopathy was defined in this study according to the following criteria: serum fibrinogen concentration $<150 \text{ mg dl}^{-1}$; prothrombin time $>3 \text{ s}$ or activated partial thromboplastin time $>5 \text{ s}$; or thrombocytopenia defined as a platelet count $<50,000$ per cubic millimeters.⁴

Details regarding the UAE procedure included the existence of contrast extravasation, embolized arteries, and type of embolic materials. In addition, we focused on the ovarian artery and defined two types of ovarian artery flow (Figure 1). With Type A, the initial aortography before UAE revealed ovarian artery flow arising directly from the aorta to the uterus and with Type B the initial aortography before UAE revealed that ovarian artery flow did not obviously arise from the aorta.

Obstetric maneuvers used to control hemorrhage were documented and included uterine massage, uterine packing, administration of uterotonic agents, and surgical interventions. The latter included the repair of lacerations in the lower genital tract, exploration of the uterine cavity, laparotomy to determine the bleeding focus or to remove a hematoma, uterine suturing, uterine wall repair, uterine or internal iliac artery ligation, and hysterectomy.

Angiography and embolization technique

Emergency digital subtraction angiography and UAE were performed with local anesthesia by one of four interventional radiologists (HT, MM, SK and HS, with 13,14, 16 and 19 years of experience, respectively) in our conventional angiographic suite. A 5-Fr sheath was inserted into the right common femoral

artery. Firstly, the initial aortography was performed at the level of renal arteries with a 4-Fr pigtail catheter (Terumo Clinical Supply Co. Ltd., Gifu, Japan) to identify the uterine artery and/or other potential bleeding sites. A 5-Fr cobra catheter (Medikit Co. Ltd., Tokyo, Japan) was introduced over a 0.035 inch guide-wire (Terumo Clinical Supply Co., Ltd., Gifu, Japan) to assess the internal iliac arteries and its branches such as uterine arteries. Basically, bilateral uterine arteries were selected with a 5-Fr cobra catheter or a microcatheter (Estream 2.0; Toray Medical Co. Ltd., Tokyo, Japan) and embolized with gelatin sponge particles (Serescue; Nippon Kayaku Co. Ltd., Tokyo, Japan). We basically used absorbable and nonpermanent embolic materials. After completing the embolization of uterine arteries, we again performed aortography to search for other bleeding arteries such as ovarian arteries, inferior epigastric arteries, internal pudendal arteries, and vaginal arteries. In principle, OAE was not done because OAE is a challenging procedure and could take much time to finish the embolization. Exceptionally, we did OAE if the interventional radiologist thought OAE could arrest the hemorrhage and the patient was in a stable condition sufficient to undergo OAE and consented to have the procedure. After the embolization of uterine arteries and actively bleeding arteries, whether the vaginal bleeding was arrested or not was confirmed by obstetricians. In the case of continuous active vaginal bleeding, an additional UAE or hysterectomy was considered.

Definitions

Clinical success was defined as cessation of bleeding after UAE (including repeated UAE) without hysterectomy. Technical success was defined as cessation of bleeding on the post-embolization angiogram and cessation of vaginal bleeding at speculum inspection performed immediately after UAE.

Statistical analysis

Outcome was compared between the patient group that required hysterectomy after UAE [Hys(+)] and the patient group that did not need hysterectomy after UAE [Hys(-)]. In recording the characteristics of the study patients, firstly, we identified the normality of each variable using the Kolmogorov–Smirnov test. Then, continuous variables were shown as medians and interquartile ranges. Comparisons of each continuous variable between Hys(+) and Hys(-) were performed with the Mann–Whitney *U* test. The variable of age was shown as mean $\pm$ standard deviation, and comparisons were performed with *t*-tests. Categorical variables were shown as counts and percentages, and the comparisons of each categorical variable were performed with Pearson's χ^2 tests or (when appropriate) Fisher exact tests. Univariate analysis was performed to determine factors associated with clinical success. Statistical analysis was performed with SPSS Statistics v. 23.0 (Armonk, NY). $p < 0.05$ was considered to be statistically significant.

RESULTS

33 patients were studied (mean age, 34 ± 5.2 years; mean pregnancy duration, 37 ± 3.6 weeks) (Table 1). The technical success rate of UAE was 100%; however, the clinical success rate was 85%. Of the 28 Hys(-) patients, 15 had extravasation on angiography, while none of the 5 Hys(+) patients had extravasation.

Table 1. Characteristics of study patients

	Hys(+) <i>n</i> = 5	Hys(−) <i>n</i> = 28	<i>p</i> -value
Maternal characteristics			
Nulliparous	0	11 (35%)	0.143
Previous cesarean delivery	2 (40%)	7 (23%)	0.052
Twin pregnancy	0	4 (13%)	1.000
Type of delivery			0.672
Vaginal delivery	3 (60%)	15 (45%)	
Cesarean delivery	2 (40%)	18 (55%)	
Primary post-partum hemorrhage details			
Uterine atony	3 (60%)	24 (86%)	0.216
Trauma	0	9 (32%)	0.290
Retained placental tissue	5 (100%)	2 (7.1%)	<0.001
Placenta previa	0	1 (3.6%)	1.000
Uterine rupture	0	1 (3.6%)	1.000
Coagulopathy	4 (80%)	19 (68%)	1.000
Transfusion, U, median (IQR)	20 (21)	14 (14)	0.173
Periembolization details			
Type of ovarian artery (Type A)	5	2	<0.001
Extravasation of contrast medium	0	15	0.049
Nature of embolic materials			1.000
Gelatin sponge only	5	24	
Gelatin sponge and permanent embolic material use	0	4	

IQR, interquartile range.

Table 2. Arteries embolized

Arteries embolized	Hys(+), no. of patients	Hys(−), no. of patients
UA		
Bilateral UA	3	18
Single UA	0	1
UA + anterior branch of IIA		
Bilateral UA + anterior branches of bilateral IIA	2	2
Bilateral UA + anterior branch of single IIA	0	3
Single UA + anterior branch of single IIA	0	1
Anterior branches of bilateral IIA	0	1
Other arteries embolized		
Ovarian artery	0	2
Inferior epigastric artery	1	3
Vaginal artery	0	2
Pudendal artery	0	3

IIA, internal iliac artery; UA, uterine artery.

All five Hys(+) patients were multipara. As to details of the PPH, 27 patients (81%) had uterine atony. All Hys(+) patients had retained placental tissue. Approximately 70% of studied patients had coagulopathy.

Embolization of 99 arteries was performed in 33 patients (Table 2). In 15 patients with extravasation on angiography, selective embolization was performed for arteries showing active bleeding, and embolization of the uterine artery was done. In 18

patients without extravasation by angiography, firstly, embolization of the uterine artery was also done. In addition to the uterine artery, we embolized arteries suspected of supplying blood to the uterus on angiography such as the internal iliac artery, inferior epigastric artery, and ovarian artery. Among the 33 patients studied, the ovarian artery was embolized in 2, and in these 2 patients hysterectomy was obviated.

As to embolic materials, all Hys(+) patients were embolized with gelatin sponge only and four of the Hys(-) patients were embolized with gelatin sponge and permanent embolic material.

Seven patients had Type A ovarian artery flow (Table 3). Among these seven patients, the ovarian artery was embolized in one patient, which obviated hysterectomy. Of the other six patients in whom the ovarian artery was not embolized, five needed hysterectomy.

Among the Type A patients, five wanted to preserve fertility and not to undergo OAE. Of the remaining two patients, OAE was successfully done in one patient and was not successfully cannulated in the other patient. Among Type B patients, one patient was thought to need OAE and underwent that procedure. Putting results for both Type A and Type B patients together, the total technical success rate of OAE was 67% (2/3)

26 of the 33 patients were followed up by other hospitals after discharge. Of the other seven patients who were available for follow up, two became pregnant. There were no morbidities or mortalities. Univariate analysis showed that the clinical success of UAE was related to retained placental tissue ($p < 0.001$), the type of ovarian arteries ($p < 0.001$) and the existence of extravasation in UAE ($p = 0.049$), but was not related to maternal characteristics, type of delivery, or the other PPH details.

DISCUSSION

This study demonstrated that the ovarian artery flow defined by initial aortography as having two types might be predictive of failure of UAE and the need for OAE for primary PPH. OAE is thought to be rarely necessary for controlling severe PPH.⁴ Among previous articles, there were only two reports of cases that demonstrated the need for OAE accompanied by UAE for controlling severe PPH.^{10,11} Our study suggested that the necessity of OAE for patients who were supposed to have the blood from ovarian artery to uterus and this was one finding of this study.

In addition, another finding was that initial aortography could distinguish PPH patients who needed OAE from those who did not. The usefulness of initial aortography for depicting the origin of the ovarian artery was firstly reported by Rathod et al¹² and there has been only one short report of cases.¹⁰ The study of Wang et al revealed that the necessity for OAE was confirmed with selective ovarian artery angiography and that in all the studied patients, hysterectomy was obviated owing to OAE.¹⁰ In comparison with Wang et al's study, our results revealed that an initial aortography could substitute for selective ovarian artery angiography to evaluate the arterial blood supply from the ovarian artery to the uterus and that the blood supply could indicate the need for OAE. This was a novel finding because angiography of the ovarian artery is a challenging procedure and in some patients with severe PPH there was not sufficient time to perform selective ovarian artery angiography.

To gain precise information such as the quantity of ovarian artery flow to the uterus, we recommend the use of initial aortography before conventional UAE. This is because after conventional UAE, the amount of the blood supply from the ovarian artery to the uterus was thought to be increased and the initial aortography provided more useful information.

Table 3. Characteristics of seven Patients with Type A ovarian arteries

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age	30	33	27	44	31	41	41
Type of delivery	Vaginal	Cesarean section	Vaginal	Cesarean section	Cesarean section	Vaginal	Vaginal
Cause	Atony	Atony	Retained placental tissue	Retained placental tissue, atony	Retained placental tissue	Retained placental tissue, atony	Retained placental tissue, atony
Coagulopathy	Positive	Positive	Positive	Negative	Positive	Positive	Positive
Transfusion ^a	46	26	26	15	44	20	14
Angiographic findings	Extravasation	Pseudo aneurysm	No active bleeding	No active bleeding	No active bleeding	No active bleeding	No active bleeding
Embolized arteries ^b	Both UA + left IIA + right OA	Left UA + right IIA	Both UA + both IIA	Both UA	Both UA + both IIA + left IEA	Both UA	Both UA
Additional management	TAE	Conservative management	Hysterectomy	Hysterectomy	Hysterectomy	Hysterectomy	Hysterectomy

IEA, inferior epigastric artery; IIA, internal iliac artery; OA, ovarian artery; TAE, transcatheter arterial embolization; UA, uterine artery.

^aPacked red blood cells.

^bAll arteries were embolized with gelatin sponge.

The use of initial aortography for symptomatic uterine fibroids has been well studied; however, clinical efficacy was very limited.⁶⁻⁸ The possible explanation of the usefulness of initial aortography in PPH patients could be that the ovarian artery was greatly dilated to accommodate the increased blood flow during pregnancy and the ovarian artery was more clearly depicted and more easily evaluated in patients with PPH than in patients with uterine fibroids.¹⁰

Whether the UAE for PPH could obviate hysterectomy was certainly affected by multiple confounders and we had to explain the other confounders. Firstly, this study did not determine that the presence of a coagulopathy or massive transfusion needs might be related to the failure of UAE. A statistically significant difference in the presence of a coagulopathy and massive transfusion needs between Hys(+) and Hys(-) was not observed. This could be explained by the high rates of coagulopathies (70%) and massive transfusion needs (73%) among these study patients. Secondly, this study demonstrated a significant difference in the rates of retained placental tissue between Hys(+) and Hys(-). All of the Hys(+) patients had retained placental tissue. Retained placental tissue is known to be the most common cause of secondary PPH¹³ and was reported to be associated with the failure of UAE.¹⁴ A retained placenta itself also could result in atony and contribute to severe hemorrhage.¹⁵

As to embolic materials, we usually used gelatin sponge only. Among Hys(-) patients, two pudendal arteries, one uterine artery, and one inferior epigastric artery were embolized with microcoils. In coagulopathic conditions, the use of permanent embolic material was reported to be effective in arresting bleeding.¹⁶ Among Hys(+) patients, 80% of the Hys(+) patients had coagulopathy; however, none underwent UAE with permanent embolic material. After the UAE procedure, we confirmed the completeness of embolization of the target arteries by angiography and permanent embolic materials were not required.

Limitations

Potential limitations of this study should be acknowledged. Firstly, this was a small retrospective cohort study and the sample size was small especially regarding the number of

Hys(+) patients and/or the number of patients who underwent OAE. Because of the small sample size, we could not calculate the independent risk of the initial aortography for the failure of UAE.

Secondly, about the measurements of ovarian artery blood flow, vasoconstriction and vasospasm could affect the ovarian artery blood flow. Aortography for severe hemorrhagic PPH patients may underestimate ovarian arterial flow to the uterus.¹⁰

Thirdly, only 7 of the 33 patients were followed up after the UAE procedure. Most of the patients who underwent UAE were followed up by a primary maternity hospital; therefore, we could not obtain information on fertility after the procedure and could not evaluate exactly the safety of UAE in this study.

Fourthly, clinical decision-making was based on input from interventional radiologists, obstetricians and patients. All Hys(+) patients had obvious ovarian artery flow directly from the aorta; however, we did not embolize the ovarian artery. This was because in four patients, UAE was technically successful and these patients hoped to maintain fertility. In one patient, the ovarian artery was not successfully cannulated. Consequently, all Hys(+) patients did not choose to undergo a second UAE procedure and provided informed consent for a hysterectomy. If those who underwent hysterectomy had a second UAE, they could have avoided hysterectomy.

Finally, this study's clinical success rate was almost the same compared with previous large studies in spite of the low frequencies of OAE and repeat UAE.^{4,17} Cheong et al revealed that half of the patients (4/8) who underwent UAE with OAE needed a repeat UAE or hemostatic hysterectomy¹⁷ and the clinical success of UAE with OAE was definitively affected by multiple confounders. Prospective, multicenter studies with larger sample sizes are needed to confirm our findings.

CONCLUSION

Initial aortography before UAE may be useful to predict the failure of UAE and the need for OAE. Obvious ovarian arterial blood flow to the uterus by aortography could be a warning sign.

REFERENCES

1. Al-Zirqi I, Vangen S, Forsen L, Stray-Pedersen B. Prevalence and risk factors of severe obstetric haemorrhage. *BJOG* 2008; **115**: 1265-72. doi: <https://doi.org/10.1111/j.1471-0528.2008.01859.x>
2. Deux JF, Bazot M, Le Blanche AF, Tassart M, Khalil A, Berkane N, et al. Is selective embolization of uterine arteries a safe alternative to hysterectomy in patients with postpartum hemorrhage? *AJR Am J Roentgenol* 2001; **177**: 145-9. doi: <https://doi.org/10.2214/ajr.177.1.1770145>
3. Ganguli S, Stecker MS, Pyne D, Baum RA, Fan CM. Uterine artery embolization in the treatment of postpartum uterine hemorrhage. *J Vasc Interv Radiol* 2011; **22**: 169-76. doi: <https://doi.org/10.1016/j.jvir.2010.09.031>
4. Lee HY, Shin JH, Kim J, Yoon HK, Ko GY, Won HS, et al. Primary postpartum hemorrhage: outcome of pelvic arterial embolization in 251 patients at a single institution. *Radiology* 2012; **264**: 903-9. doi: <https://doi.org/10.1148/radiol.12111383>
5. Touboul C, Badiou W, Saada J, Pelage JP, Payen D, Vicaute E, et al. Efficacy of selective arterial embolisation for the treatment of life-threatening post-partum haemorrhage in a large population. *PLoS One* 2008; **3**: e3819. doi: <https://doi.org/10.1371/journal.pone.0003819>
6. Barth MM, Spies JB. Ovarian artery embolization supplementing uterine embolization for leiomyomata. *J Vasc Interv Radiol* 2003; **14**(9 Pt 1): 1177-82. doi: <https://doi.org/10.1097/01.RVI.0000085772.71254.CF>

7. Pelage JP, Walker WJ, Le Dref O, Rymer R. Ovarian artery: angiographic appearance, embolization and relevance to uterine fibroid embolization. *Cardiovasc Intervent Radiol* 2003; **26**: 227–33. doi: <https://doi.org/10.1007/s00270-002-1875-3>
8. Binkert CA, Andrews RT, Kaufman JA. Utility of nonselective abdominal aortography in demonstrating ovarian artery collaterals in patients undergoing uterine artery embolization for fibroids. *J Vasc Interv Radiol* 2001; **12**: 841–5. doi: [https://doi.org/10.1016/S1051-0443\(07\)61509-7](https://doi.org/10.1016/S1051-0443(07)61509-7)
9. White AM, Banovac F, Yousefi S, Slack RS, Spies JB. Uterine fibroid embolization: the utility of aortography in detecting ovarian artery collateral supply. *Radiology* 2007; **244**: 291–8. doi: <https://doi.org/10.1148/radiol.2441060796>
10. Wang MQ, Liu FY, Duan F, Wang ZJ, Song P, Song L. Ovarian artery embolization supplementing hypogastric-uterine artery embolization for control of severe postpartum hemorrhage: report of eight cases. *J Vasc Interv Radiol* 2009; **20**: 971–6. doi: <https://doi.org/10.1016/j.jvir.2009.04.049>
11. Kim JE, So YH, Kim BJ, Kim SM, Choi YH, Sung CK. Postpartum hemorrhage from non-uterine arteries: clinical importance of their detection and the results of selective embolization. *Acta Radiol* 2017; **1**: 284185117738547. doi: <https://doi.org/10.1177/0284185117738547>
12. Rathod KR, Deshmukh HL, Asrani A, Salvi VS, Prabhu S. Successful embolization of an ovarian artery pseudoaneurysm complicating obstetric hysterectomy. *Cardiovasc Intervent Radiol* 2005; **28**: 113–6. doi: <https://doi.org/10.1007/s00270-004-0259-2>
13. Park HS, Shin JH, Yoon HK, Kim JH, Gwon DI, Ko GY, et al. Transcatheter arterial embolization for secondary postpartum hemorrhage: outcome in 52 patients at a single tertiary referral center. *J Vasc Interv Radiol* 2014; **25**: 1751–7. doi: <https://doi.org/10.1016/j.jvir.2014.05.009>
14. Yamasaki Y, Morita H, Miyahara Y, Ebina Y, Okada T, Yamaguchi M, et al. The factors associated with the failure of transcatheter pelvic arterial embolization for intractable postpartum hemorrhage. *J Perinat Med* 2014; **42**: 359–62. doi: <https://doi.org/10.1515/jpm-2013-0242>
15. Bateman BT, Berman MF, Riley LE, Leffert LR. The epidemiology of postpartum hemorrhage in a large, nationwide sample of deliveries. *Anesth Analg* 2010; **110**: 1368–73. doi: <https://doi.org/10.1213/ANE.0b013e3181d74898>
16. Kanematsu M, Watanabe H, Kondo H, Goshima S, Kato H, Furui T, et al. Postpartum hemorrhage in coagulopathic patients: preliminary experience with uterine arterial embolization with N-butyl cyanoacrylate. *J Vasc Interv Radiol* 2011; **22**: 1773–6. doi: <https://doi.org/10.1016/j.jvir.2011.08.016>
17. Cheong JY, Kong TW, Son JH, Won JH, Yang JI, Kim HS. Outcome of pelvic arterial embolization for postpartum hemorrhage: a retrospective review of 117 cases. *Obstet Gynecol Sci* 2014; **57**: 17–27. doi: <https://doi.org/10.5468/ogs.2014.57.1.17>