Dokkyo Journal of Medical Sciences
47(1) : 15 ～ 25, 2020

Original

Efficacy and Complications of Emergent Transcatheter Arterial Embolization for the Management of Intractable Uterine Bleeding

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SUMMARY

Objective : Transcatheter arterial embolization (TAE), including uterine artery embolization (UAE), is effective for the management of obstetric and gynecologic hemorrhage. Some adverse effects have been reported with TAE, such as amenorrhea, endometrial trauma, and subsequent infertility. Herein we report the efficacy and complications of emergent TAE for the management of severe intractable uterine bleeding at our institute.

Methods : From 2010 to 2019, thirty-eight patients underwent emergent TAE for intractable uterine bleeding. We evaluated the efficacy and complications of TAE, including a change in menstruation, fertility, and pregnancy outcomes in perinatal patients (group A ; n＝23), and in patients with gynecologic hemorrhage (group B ; n＝15).

Results : In group A, 7 cases of retained placenta, 4 cases of postpartum hemorrhage, 2 cases of placenta accrete, 2 cases of uterine artery pseudoaneurysm, 2 cases of cervical pregnancy, 1 case of cesarean scar pregnancy, and 5 cases of unexplained hemorrhage were included. The median age of the group A was 37. In group B, 4 cases of uterine artery pseudoaneurysm, 2 cases of uterine arteriovenous malformation, 3 cases of uterine fibroids, 1case of adenomyosis, and 5 cases of unexplained hemorrhage were included. The median age of the group B was 39. The first attempt at TAE successfully controlled hemorrhage in 33 of 38 patients (86.8%) without major complications, and the remaining 5 patients required an additional attempt at TAE to control hemorrhage. One patient (2.6%) had transient buttock pain and foot ischemia. Among the 33 patients who had adequate follow-up care, all patients resumed regular menstruation. The median time to resume regular menstruation after TAE was 3 months (range, 1-13 months) in group A (n＝20) and 1 month (range, 1-6 months) in group B (n＝13). Four of patients had 6 pregnancies in total : 3 full-term live births, 2 missed abortions, and 1 artificial abortion. Among the 13 patients who desired pregnancy, 3 (23%) conceived spontaneously.

Conclusions : This retrospective study showed that emergent TAE may be effective and safe in treating intractable uterine bleeding with a high success rate. Ovarian and endometrial function were preserved based on the relatively early return of menstruation. Further prospective investigations with large number of patients are needed to confirm the preservation of ovarian function, fertility, and pregnancy outcome in reproductive-aged women.

Received December 6, 2019 ; accepted January 29, 2020
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Key Words : Transcatheter arterial embolization, uterine artery embolization, intractable uterine bleeding

INTRODUCTION

Transcatheter arterial embolization (TAE), including uterine artery embolization (UAE), is effective for the management of obstetric and gynecologic hemorrhage. TAE is minimally invasive and fertility-preserving, so it is becoming an alternative to surgical procedures. Indeed, the efficacy and safety of TAE for the treatment of postpartum hemorrhage (PPH) and symptomatic uterine fibroids have been well-established[1,2].

Some adverse effects have been reported with TAE in each clinical setting, including amenorrhea, trauma to the endometrium, loss of ovarian reserve, and subsequent infertility, although it is still a matter of debate[3,4].

Herein we report the efficacy and complications of emergent TAE for the management of severe intractable uterine bleeding at our institute.

MATERIALS AND METHODS

Patient characteristics

From January 2010 to April 2019, thirty-eight patients underwent emergent TAE, including UAE, for intractable uterine bleeding at Dokkyo Medical University Hospital. The patient population consisted of two groups : Group A (n=23, Table 1), patients with obstetric hemorrhage, and Group B (n=15, Table 2), patients with gynecologic hemorrhage except for malignancy. The median age for group A was 37 years (range, 25-44 years) and the median age for group B was 39 years (range, 25-51 years). The etiology of hemorrhage in group A was as follows : retained placenta, 7 ; postpartum hemorrhage with disseminated intravascular coagulopathy, 4 ; placenta accreta, 2 ; uterine artery pseudoaneurysm, 2 ; cervical pregnancy, 2 ; cesarean scar pregnancy, 1 ; and unexplained hemorrhage after normal vaginal delivery and cesarean section, 1 and 4, respectively (Table 1). The etiology of hemorrhage in group B was as follows : uterine artery pseudoaneurysm, 4 ; uterine arteriovenous malformation, 2 ; uterine fibroids, 3 ; adenomyosis, 1 ; and unexplained hemorrhage, 5 (Table 2). These patients were diagnosed by ultrasonography with color Doppler, MRI, and/or CT, and initially treated using standard obstetric and gynecologic procedures with emergent medical care. The obstetric maneuvers used to control hemorrhage included uterine massage, uterine packing, administration of uterine contraction agents, and appropriate treatment for disseminated intravascular coagulation (DIC) in patients with postpartum hemorrhage (PPH) for each clinical indication ; however, all of the patients enrolled in this study were refractory to these conservative treatments. In patients with gynecologic hemorrhage, special gynecologic procedures except for emergency care were not performed before TAE because all of the patients enrolled in the study desired less invasive surgery than a hysterectomy and the subsequent loss of fertility. TAE, including UAE, was performed after consultation with interventional radiologists when obstetrician-gynecologists determined that hemostasis was difficult to achieve using standard obstetric and gynecologic management (other than invasive surgical intervention), after disclosing the safety, efficacy, and complication rate of TAE, and obtaining informed consent from each patient.

This retrospective study was approved by the institutional review board.

Embolization methods

Digital subtraction angiography (DSA) and subsequent TAE were performed with local anesthesia by interventional radiologists. First, a 4.0-Fr introducer sheath (Radifocus Introducer IIH ; Terumo Co., Tokyo, Japan) was inserted into the right common femoral artery and a 4.2-Fr pig-tailed catheter (Hanako Excellent EN Catheter [Hi-MAX] ; Hanako Medical Co., Saitama, Japan) was used to assess the internal iliac arteries and its branches and/or other potential bleeding sites, such as ovarian, inferior epigastric, internal pudendal, and vaginal arteries. For selective catheterization of the uterine artery, a 2.0-Fr microcatheter (Michibiki PLUS ; Hanaco Medical Co.) was passed through the parent catheter with a 0.016-inch micro-guidewire (Sakigake ; Hanaco Medical Co.). To embolize the internal iliac artery, glue was infused through a 4.0-Fr catheter (Hi-MAX), the tip of which was placed in the anterior trunk and gradually pulled back in the main trunk with continuous infusion.

Table 1 Group A：Obstetrical hemorrhage

	age	diagnosis	Embolic vessels	Embolic material	Complications	Treatment after TAE	Time to resumption of menstruation (months)	Desire for pregnancy	Time to pregnancy (months) and outcome
1	40	retention of placenta	BIIA	GS			9 (during breastfeeding)	unknown	
2	35	retention of placenta	BUtA UIIA	NBCA, GS GS			2	—	
3	38	retention of placenta	BUtA	NBCA			13 (during breastfeeding)	+	
4	35	retention of placenta	BUtA	GS			1.5	+	7 SA (6Ws) 9 SA (9Ws) 19 NVD (39Ws)
5	31	retention of placenta	UUtA	GS			3	unknown	
6	39	retention of placenta	BUtA	GS			1	+	
7	41	retention of placenta	BUtA	NBCA			2	—	
8	25	PPH＋DIC (placental abruption)	BIIA	NBCA			3	unknown	
9	43	PPH＋DIC (placental abruption)	BIIA	NBCA	buttock pain, foot ischemia, hypomenorrhea		2	—	
10	35	PPH＋DIC (retroperitoneal hematoma)	UIIA	NBCA			unknown	unknown	
11	44	PPH＋DIC (uterine cervical fibroid)	UUtA UIIA	NBCA			3	—	
12	29	placenta accreta	URLA UIIA	NBCA GS		hys	—		
13	39	placenta accreta	BUtA	NBCA			5	+	
14	38	uterine artery pseudoaneurysm	UIIA	NBCA			4	+	
15	31	uterine artery pseudoaneurysm	BUtA	NBCA			1	unknown	
16	41	cervical pregnancy	UUtA UIIA	MTX＋GS			3	unknown	
17	31	cervical pregnancy	1st UUtA	MTX＋GS					
			2nd UUtA＋UOvA	NBCA			2	+	
18	38	cesarean scar pregnancy	BUtA	GS			unknown	unknown	
19	43	unexplained hemorrhage after CS	UUtA	NBCA			9 (during breastfeeding)	—	
20	37	unexplained hemorrhage after CS	BUtA	GS			12 (after breastfeeding)	+	
21	33	unexplained hemorrhage after CS	1st BUtA	GS					
			2nd UUtA	NBCA			2	+	
22	35	unexplained hemorrhage after CS	BUtA	GS			7 (during breastfeeding)	+	
23	37	unexplained hemorrhage after NVD	BUtA UOvA	GS			3	+	

Table 2 Group B : Gynecological hemorrhage

	age	diagnosis	Embolic vessels	Embolic material	Complications	Treatment after TAE	Time to resumption of menstruation (months)	Desire for pregnancy	Time to pregnancy (months) and outcome
1	40	uterine artery pseudoaneurysm	BUtA	NBCA			1	—	
2	25	uterine artery pseudoaneurysm	BUtA	GS			1	unknown	
3	34	uterine artery pseudoaneurysm	1st UUtA	GS					
			2nd BUtA	NBCA			1	—	15 NVD (38Ws)
4	27	uterine artery pseudoaneurysm	1st BUtA UOvA	GS					
			2nd BUtA UOvA	GS		GnRHa 2cycles	3	unknown	
5	39	AVM	UUtA	NBCA			1	+	6 NVD (40Ws), PPH 1,300 mL
6	41	AVM	UUtA	NBCA, TAGM			1	unknown	6 IA (9Ws)
7	49	uterine fibroids	BUtA	TAGM		hys	—		
8	50	uterine fibroids	BUtA	GS			1	—	
9	45	uterine fibroids	BUtA	GS			1	—	
10	51	adenomyosis	UUtA	GS		hys	—		
11	26	unexplained hemorrhage	BUtA	GS		GnRHa 4cycles	6	unknown	
12	18	unexplained hemorrhage (suspicious of uterine vessel abnormalities)	1st UUtA	GS					
			2nd BUtA	GS			5	+	
13	35	unexplained hemorrhage	BUtA	GS			1	unknown	
14	44	unexplained hemorrhage	BUtA	GS			1	—	
15	28	unexplained hemorrhage	BUtA	GS			1	—	

PPH : postpartum hemorrhage, DIC : disseminated intravascular coagulation, BIIA : bilateral internal iliac artery, UIIA : unilateral internal iliac artery, BUtA : bilateral uterine artery, UUtA : unilateral uterine artery, UOvA : unilateral ovarian artery, URLA : unilateral artery of the round ligament from external iliac artery, GS : gelatin sponge particles, NBCA : n-butyl-2-cyanoacrylate, TAGM : Tris-acryl gelatin microspheres, MTX : methotrexate, hys : hysterectomy, AVM : uterine arteriovenous malformation, SA : Spontaneous abortion, IA : induced abortion, CS : cesarean section, NVD : normal vaginal delivery, GnRHa : Gonadotropin releasing hormone agonist, Ws : weeks

Gelatin sponge particles ([GS] Gelpart or Serescue ; Nippon Kayaku Co., Tokyo, Japan) were commonly selected for absorbable and non-permanent embolic materials for TAE ; for some patients, trisacryl gelatin microspheres ([TAGM] EmbosphereV R ; Nippon Kayaku, Co.) were also used. Moreover, non-absorbable and permanent embolic materials (N-butyl-2-cyanoacrylate [NBCA] Histoacryl ; B. Braun, Melsungen, Germany) mixed with iodized oil (Lioiodol ; Guerbet, Tokyo, Japan) at a 1 : 4 ratio (20 % glue) was used to achieve complete hemostasis with or without GS. A 2.5-mL syringe containing 2.5 mL of 20% glue was connected to the microcatheter and the single-column injection technique was used.

The embolic arteries and materials were selected by interventional radiologists according to the findings of DSA and hemorrhage points in each case.

After embolization of the uterine arteries was completed, aortography was performed to search for other bleeding arteries. The effect of TAE was evaluated with respect to complete hemostasis, which was defined as hemostasis achieved by TAE alone and requiring no additional hemostatic interventions.

Follow-up

The patients were generally followed up at 2 weeks, 1 month, 3 months, 6 months, and thereafter at an internal of 3-6 month. Ultrasonography with color Doppler was routinely used if it was thought to be useful for each case, and pelvic MRI was scheduled 3-6 months after embolization as needed.

Changes in symptoms, complications associated with TAE, time to resumption of menstruation, time to pregnancy after TAE, and pregnancy outcomes were obtained from the medical records, and were compared between Group A and B to evaluate the efficacy and complications of TAE.

RESULTS

In group A, the following arteries were embolized : uterine arteries, 17 ; internal iliac arteries, 9 ; ovarian artery, 2 ; and artery of the round ligament from the external iliac artery (there was some overlap), 1. In group B, the following arteries were embolized : uterine arteries, 15 ; and ovarian artery, 1. These findings showed that embolization of multiple arteries, including the uterine arteries, was needed to control obstetric hemorrhage compared to gynecologic hemorrhage.

In group A, the following embolic materials were used : GS, 13 patients ; and NBCA, 14 patients (there was some overlap). In group B, the following embolic materials were used : GS, 13 patients ; NBCA, 4 patients ; and TAGM, 2 patients. These findings showed that NBCA was more frequently used as an embolic material for controlling obstetric hemorrhage compared to gynecologic hemorrhage. In group A, methotrexate was used combined with GS for 2 patients with cervical pregnancy.

The first emergent TAE attempt successfully controlled intractable hemorrhage in 33 of 38 patients (86.8%) without major complications. The remaining 5 patients needed an additional TAE attempt to control hemorrhage, as follows : cervical pregnancy, 1 ; unexplained hemorrhage after cesarean section, 1 ; uterine artery pseudoaneurysm, 2 ; and unexplained hemorrhage (suspicious of uterine vessels abnormality), 1 (Tables 1 & 2). Hemostasis was confirmed in all 5 patients who underwent a 2nd TAE attempt, therefore the success rate of controlling intractable uterine bleeding by TAE alone was 100% (38/38 patients).

Hysterectomy after the first TAE attempt was subsequently required as radical treatment in 3 patients for the following indications : adenomyosis ; uterine cervical fibroid ; and placenta accreta (one each).

One patient (2.6%) had transient buttock pain and foot ischemia, which promptly resolved without treatment.

The median follow-up period after TAE was 26.5 months (range, 4-114 months). Among the 33 patients in whom follow-up was adequate, all 33 resumed normal menstruation. The median time to resume regular menstruation after TAE was 3 months (range, 1-13 months) in group A (n=20) and 1 month (range, 1-6 months) in group B (n=13). The patient in group A who had transient buttock pain and foot ischemia, also had hypomenorrhea, which gradually resolved. There was no apparent relationship between the length of time for normal menstruation to resume and the vessels embolized or the embolic materials used.

Four patients had 6 pregnancies in total : 3 full-

term live births, 2 missed abortions, and 1 artificial abortion. Among 13 patients who desired pregnancy, 3 (23%) conceived spontaneously. Among the 3 full-term live births, there were no major obstetric complications except for a 1300 mL PPH (unknown etiology) in 1 patient.

DISCUSSION

The efficacy and safety of TAE, including UAE, for the management of intractable uterine bleeding have been reported for obstetric hemorrhage due to PPH, abnormal placentation, and cervical ectopic pregnancy, and for gynecologic hemorrhage due to uterine fibroids, adenomyosis, or uterine vessels abnormalities[1,2]. Obstetric hemorrhage remains a major cause of maternal morbidity and mortality and TAE has been recommended as the first choice of treatment for PPH when uterine balloon tamponade fails to control hemorrhage. Intractable gynecologic hemorrhage can lead to surgical interventions, including hysterectomy, and subsequent loss of fertility in reproductive-aged women.

Therefore, the role of TAE has recently become the subject of debate for these conditions. Although there are no fundamental objections regarding the effectiveness of TAE for the management of intractable uterine hemorrhage, there are several unresolved issues involving the effects of TAE on ovarian function, fertility, and pregnancy outcome.

Efficacy

The success rate of TAE for obstetric hemorrhage due to intractable PPH has been reported to be 87% ～100%[1], and 90.7% (95% confidence interval [CI] ; 85.7% －94.0%) in a systematic review for this condition[5]. This success rate for TAE is equivalent or superior to other surgical approaches [84.0% for balloon tamponade, 91.7% for uterine compression sutures, and 84.6% for iliac artery ligation of uterine devascularization][5]. The overall treatment failure rate for PPH resulting from abnormal placentation, such as placenta increta or percreta, which appears to be resistant to TAE and the main cause of hysterectomy after failed TAE, has been reported to be as high as 23%[6]. Moreover, the success rate for TAE is lower in patients with DIC, 37.5% of whom develop complications[7].

For gynecologic hemorrhage, especially symptomatic uterine fibroids, symptoms (menorrhagia, metrorrhagia, pelvic pain, and bulk symptoms) were significantly decreased after TAE[8]. The duration of menstruation was shortened, the fibroid volume was significantly reduced[8], and the hospital stay was shorter and recovery was faster compared with the surgery group[3]. Notably, repeat TAE or hysterectomy post-TAE was required for some patients due to inadequate symptom control.

Based on a randomized controlled trial (RCT) that compared TAE and hysterectomy in the treatment of severe symptomatic uterine fibroids, after 10 years of follow-up, 69% of all women underwent technically successful TAE and a hysterectomy was avoided. Moreover, the health-related quality of life and patient satisfaction rates did not differ between both groups[9]. In view of the short- and long-term clinical and quality-of-life evidence that is available, it was concluded that all women who are candidates for hysterectomy due to symptomatic uterine fibroids should be offered TAE as a treatment option[9].

In the current study, TAE was also extremely effective in controlling intractable hemorrhage. The first emergent TAE attempt successfully controlled hemorrhage in 33 of 38 patients (86.8%), and in the remaining 5 patients, complete hemostasis was achieved with an additional TAE attempt, thus achieving a success rate with TAE of 100% (38/38 patients). Among the 4 patients with PPH and DIC, the initial emergent TAE was effective without any complications.

Ovarian artery embolization (OAE) with UAE has been reported to control severe PPH[10]. In the current study, OAE was required to achieve complete hemostasis for 3 patients due to a cervical pregnancy, unexplained hemorrhage after a normal vaginal delivery, and a uterine artery pseudoaneurysm (Tables 1 & 2). It is well-known that OAE through uterine-to-ovarian artery anastomosis is an aggressive embolization technique[11]. TAE of the utero-ovarian collateral circulation is the most likely mechanism underlying a decline in ovarian reserve and premature menopause[11] ; however, in the current study 3 patients who underwent OAE reported prompt resumption of

normal menstruation between 1 and 3 months.

Embolic materials

Several embolic materials have been used in TAE. In the current study, GS and NBCA were used in 13 and 14 patients in group A, respectively, while GS, NBCA, and TAGM were used in 13, 4, and 2 patients in group B, respectively. This finding showed that NBCA was more frequently used as an embolic material for controlling obstetric hemorrhage compared to gynecologic hemorrhage.

NBCA is indicated for various conditions, including vascular diseases (aneurysms and malformations), hemorrhage (trauma and inflammation), tumors, and venous disease (varices), regardless of the location of the target lesion. TAE with a NBCA-Lipiodol mixture has been reported to be highly effective in achieving hemostasis in patients with PPH accompanied by DIC and might be the first-line therapeutic strategy, especially for patients with desired fertility[12].

More recently, TAGM has been used for embolization instead of GS. The outcomes of TAE with TAGM are comparable to TAE with GS, suggesting that both embolic agents are acceptable for the treatment of uterine fibroids[13].

The success rate of achieving immediate complete hemostasis may be dependent, in part, on the choice of embolic materials and embolic vessels. Our study showed that embolization of multiple arteries (primarily the uterine arteries) is needed to control obstetric hemorrhage compared to gynecologic hemorrhage, and NBCA is more frequently used for controlling obstetric hemorrhage compared to gynecologic hemorrhage.

Safety

TAE is thought to negatively impact endometrial blood flow, ovarian blood flow, endocrine function, and follicular development. The complication rate of TAE is 6%～9% and includes amenorrhea, permanent ovarian failure, fertility, transient fevers, groin hematomas, contrast reactions, pseudoaneurysms, and iliac artery perforation[1,14,15]. Ischemic complications, such as transient buttock or foot ischemia, small bowel necrosis, and uterine, vaginal, cervical, and bladder necrosis, are rarely reported[1]. Neurologic complications are also rare, such as neuropathies involving the sciatic nerve, perineal nerve, and lower limbs[1].

There were no significant complications related to TAE in the current study with the exception of one patient who had transient buttock pain and foot ischemia.

It has been reported that skillful catheterization, proper and gentle injection of embolic materials, and choosing the appropriate vessels obviate complications[16]. Therefore, the incidence of complications following TAE may be extremely low when TAE is performed by a well-prepared team together with interventional radiology specialists.

Changes in menstruation

It has been reported that all patients treated for PPH resumed normal menstruation[1]. There is a report that the most common untoward effect in patients with PPH undergoing TAE with GS for symptomatic uterine fibroids is transient amenorrhea ; menorrhagia improved in 90% of patients 12 months after treatment, although permanent amenorrhea was reported in 2 of 33 patients [6%][2].

In the current study, among the patients who had adequate follow-up evaluations, normal menstruation was restored in all 33 patients. Relatively early resumption of menstruation after TAE was observed in patients with obstetric (median, 3 months) and gynecologic hemorrhage (median, 1 month) ; only 1 patient had transient hypomenorrhea. Based on these results, it can be concluded that menstruation is not adversely affected by TAE.

Ovarian function

McLucas et al.[17] reported that serum hormone levels, such as follicle-stimulating hormone (FSH), anti-Müllerian hormone (AMH), and estradiol (E2), are not changed by TAE, suggesting that ovarian function is not adversely affected, and therefore women of reproductive age with uterine fibroids may consider TAE as a treatment option. Based on a study with a large sample size, it was confirmed that TAE did not affect ovarian reserve in women<40 years of age, as evidenced by no significant change in AMH levels after embolization[18].

There is a report, however, that the AMH level

recovered in patients treated for uterine fibroids who were<40 years of age, but not in patients ≧40 years of age[19]. The subtle difference in ovarian failure rates between TAE for PPH and TAE for fibroids may be explained by the younger age of patients undergoing the former procedure[20].

Therefore, additional prospective studies with a large number of patients are warranted to better elucidate the relationship between patient age and changes in ovarian function after TAE for obstetric or gynecologic hemorrhage.

Fertility

The 2013 Royal College of Obstetricians and Gynecologists guidelines conclude that there is poor evidence regarding TAE and fertility, and therefore recommends that women of childbearing age who wish to become pregnant in the near future should be offered TAE only after an informed discussion[21].

Preservation of fertility has been reported in patients with uterine fibroids[22] or intractable PPH[22]. In a systematic review, Mohan et al.[22] reported that pregnancy rates following TAE are comparable to age-adjusted rates in the general population. McLucus et al.[24] also reported in a review that pregnancy rates following TAE and myomectomy (48% and 46% for abdominal and laparoscopic myomectomy, respectively) were comparable and concluded that TAE is a valid alternative to myomectomy for women who wish to conceive. Moreover, Cheng et al.[23] reported that of 23 patients who attempted pregnancy, 19 (82.6 %) conceived, giving birth to 12 full-term live infants.

A possible adverse effect of TAE on fertility potential in patients with uterine fibroids has been reported[8], especially in the patients>40 years of age[25]. Specifically, Torre et al.[8] reported that TAE might have had a negative impact on fertility, which may not be related to ovarian function. Therefore, TAE should not be performed routinely in young women of reproductive age and extensive fibroids. TAE should only be considered after appropriate counselling with the women who still wish to conceive.

In the current study, among 13 patients who had desired fertility, 3 (23%) had natural conceptions. The pregnancy rate was relatively low compared with previous reports[23,24], possibly because the information regarding fertility in each patient was insufficient. Indeed, the follow-up period for some patients was relatively short and the information was only obtained from the medical records.

Based on the aforementioned studies, the adverse effects of TAE on fertility remain controversial and warrant further study.

Pregnancy outcomes

The pregnancy complication rates have been reported to be similar in patients with untreated uterine fibroids[22] ; however, higher pregnancy loss rates following TAE have been reported in patients with uterine fibroids compared with patients who have undergone a myomectomy[22,26,27]. In a systematic review Karlsen et al.[26] reported a pregnancy rate of 50% (13/26) after TAE and 78% (31/40) after myomectomy (no statistical difference) and a pregnancy loss rate of 60% (9/15) after TAE and 20% (6/15) after myomectomy [$p<0.05$]. Karlsen et al.[26] concluded that the pregnancy rate was lower and the pregnancy loss rate was higher after TAE than myomectomy. Karlsen et al.[26] also found very low-quality evidence regarding the assessed outcomes and the reported proportions are uncertain. Homer et al.[27] reported that the risk for pregnancy loss appeared to be increased after TAE compared with pregnancies complicated by fibroids matched for age and fibroid location (odds ratio [OR] 2.8, $p<0.0001$), and there was an increased risk for cesarean section (OR 2.1, $p<0.0001$) and PPH (OR 6.4, $p<0.0001$). In contrast, the risks for critical adverse obstetric complications, fetal growth restriction (FGR), preterm delivery, and malpresentation were no more likely after TAE when compared with women with untreated fibroids.

The increase in miscarriage rate suggests that the endometrial cavity incurs irreversible damage as a consequence of embolization. TAE-induced endometrial ischemia imparts a marked deleterious effect on potential implantation sites. A reduction in fibroid volume after TAE could result in distortion of the endometrial cavity, which is almost certain to escalate the risk for pregnancy loss in combination with relative endometrial ischemia[27].

While subsequent pregnancies are clearly possible after TAE for PPH, there are reports of recurrent

severe PPH at subsequent deliveries [31.6% -100 %][20,28]. It has been reported that TAE after the first delivery with PPH increased the rate of TAE after the second delivery [OR, 25.56 ; 95% CI, 9.86-66.23][29]. The increased risk for PPH is likely due to myometrial compromise as a consequence of embolization-induced ischemia, which might contribute to a reduced capacity for efficient contractility after delivery and consequently to uterine atony.

In the current study, 4 patients had 6 pregnancies in total, including 3 full-term live births and 2 missed abortions. Of the 3 full-term live births, one had a PPH, although the reason was not specifically identified. The pregnancy loss rate in the current study was 33% (2/6), which is consistent with previous reports[26,27]. The incidence of PPH in subsequent deliveries after TAE was also the same as in a previous report[29].

There are reports that pregnancy outcome is not affected by TAE in PPH patients[23,30].

The adverse effects on pregnancy outcome are also controversial. Therefore, to formally address the impact of embolization on pregnancy risk profiles, a prospective study that incorporates TAE and non-treatment arms is needed.

There were some limitations in this study. First, this was a retrospective study and the sample size was relatively small. Second, many causes of obstetric or gynecologic hemorrhage were included in this study, and the efficacy and complications of TAE were analyzed in all patients. Therefore, it is somewhat difficult to precisely assess the effect of TAE on menstruation, fertility, ovarian function, and pregnancy outcome because of the diverse patient backgrounds.

Nevertheless, the current study demonstrated the high success rate of TAE for emergency treatment of various causes of intractable hemorrhage without any deaths or major complications. One of the reasons for these excellent results may be that TAE was performed skillfully together with an interventional radiologists and a well-trained special team using a specific protocol.

There are many reports, such as meta-analyses, RCTs, and case series, regarding the efficacy and complications of TAE ; however, there were differences in TAE treatment protocols, patient backgrounds, embolic materials used or embolic vessels targeted, duration of follow-up, and skills of the interventional radiologists in each study. Therefore, it is difficult to compare the results of each report regarding efficacy, safety, and short- and long-term complications. Indeed, based on a review of fertility after TAE, Karlsen et al.[26] reported very low-quality evidence regarding the assessed outcomes. There is a need for well-designed prospective randomized studies to improve the evidence base.

There is no doubt that ovarian function, fertility, and pregnancy outcomes are for the most part unaffected by TAE based on recent studies. In patients with symptomatic uterine fibroids and desired fertility, TAE is becoming a valid alternative to myomectomy, although not a perfect alternative, but TAE should be included as a treatment option for all patients.

CONCLUSION

In conclusion, based on our retrospective study, emergent TAE may be effective and safe in treating intractable uterine bleeding with a high success rate and without major complications. Ovarian or endometrial function may be sufficiently preserved based on the relatively early recovery of normal menstruation after TAE. Nevertheless, there are inconsistent results regarding the effects of TAE on ovarian function, fertility, and pregnancy outcomes based on previous studies. Further prospective studies with a large number of patients are needed to confirm the preservation of ovarian function, fertility, and pregnancy outcomes in reproductive-aged women.

Acknowledgement. We are immensely grateful to our esteemed colleagues and well-prepared team of department of Radiology who cooperated with IVR.

Conflict of interest

We declare that we have no conflict of interest.

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