Uterine Artery Embolization in the Treatment of Postpartum Uterine Hemorrhage

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ABSTRACT

Purpose: To evaluate the clinical effectiveness and safety of uterine artery embolization (UAE) in the treatment of primary postpartum hemorrhage (PPH), secondary PPH, and PPH associated with cesarean section.

Materials and Methods: All women who underwent UAE for obstetric-related hemorrhage during a 52-month period culminating in April 2009 were included. Clinical success was defined as obviation of hysterectomy. Blood product requirements before and after UAE were calculated. Statistically significant associations between subject characteristics and clinical success were evaluated. The two subgroups of women with uterine artery pseudoaneurysms and women who underwent cesarean section were examined separately as well.

Results: Sixty-six women (mean age, 33 years; range, 17–47 y) underwent UAE, with an overall clinical success rate of 95% (98% for primary PPH, 88% for secondary PPH, and 94% for PPH associated with cesarean section) and an overall complication rate of 4.5%. Mean pre- and postembolization transfusion requirements were 3.1 U and 0.4 U of packed red blood cells, respectively. The only significant characteristic identified for the cases that necessitated hysterectomy was an increased transfusion requirement after UAE (increase of 1.0 U; P = .02). Uterine artery pseudoaneurysms were associated with secondary PPH (P = .01) and cesarean section (P = .03).

Conclusions: The threshold for UAE in women with PPH should be low, as it is associated with a high clinical effectiveness rate and a low complication rate. Uterine artery pseudoaneurysms should be suspected in women presenting with secondary PPH after cesarean section.

ABBREVIATIONS

PPH = postpartum hemorrhage, PRBCs = packed red blood cells, UAE = uterine artery embolization

Despite advances in medical, surgical, and endovascular therapy, which have decreased the maternal mortality rate by 99% during the past century in the United States (1), obstetric hemorrhage continues to be a leading cause of maternal morbidity and mortality. The incidence of obstetric hemorrhage varies depending on the definition used. Postpartum hemorrhage (PPH), defined as blood loss exceeding 500 mL, is a common entity that complicates as many as 18% of all deliveries (2,3). More severe obstetric hemorrhage, defined as blood loss in excess of 1,000 mL, may occur in 1%–5% of all deliveries (4). Obstetric hemorrhage continues to be the single most important cause of maternal mortality worldwide, accounting for 25%–30% of all maternal deaths, and it represents the most common maternal morbidity in the developed world (2,5,6).

Since its introduction as a treatment for PPH in 1979 (7,8), UAE has been shown to be associated with high technical success rates and good clinical outcomes for the treatment of primary and secondary PPH (9–12). However, optimal patient selection and the appropriate position of UAE in the treatment decision tree for PPH remain to be elucidated. Current studies in the literature lack standardization in patient selection as well as embolization techniques, and there is a lack of randomized controlled trials comparing pharmacologic, surgical, and endovascular interventions (9,13). Moreover, it appears that, despite encouraging results in the literature and its potential role in
uterine salvage and preservation of future childbearing potential, UAE continues to be underutilized as a treatment for PPH. Referring clinicians’ awareness of the procedure is still limited (14). As the number and percentage of cesarean sections deliveries increases in the United States (15), more data are required in regard to the effectiveness of UAE for PPH in the population of women who have had a cesarean section delivery.

The purpose of this retrospective study was to analyze and report the clinical outcomes including clinical effectiveness and safety of uterine artery embolization (UAE) for the treatment of obstetrical uterine hemorrhage at a single tertiary-care obstetric hospital in terms of primary and secondary PPH and in the population who had previously undergone a cesarean section.

MATERIALS AND METHODS

Patient Selection
The study was conducted with the approval of our institutional review board with waiver of informed consent, and was compliant with Health Insurance Portability and Accountability Act regulations. All women who underwent UAE for obstetric reasons (those with leiomyoma- or tumor-related uterine hemorrhage were excluded) at a single institution during a 52-month period culminating in April 2009 were included in the study.

UAE Technique
All subjects were referred to the vascular and interventional radiology service for UAE by the obstetric service at the hospital. UAE for the treatment of PPH was performed only after all usual obstetric maneuvers for the treatment of PPH were used. This usually included intravenous uterotonic agents, aggressive uterine massage, manual extraction of the placenta, examination and repair of genital lacerations, and often balloon tamponade (ie, Bakri balloon placement).

The protocol and technique for UAE for PPH is relatively standardized in our division and each procedure was performed by a fellowship-trained interventional radiologist, of which a total of nine were involved. All procedures were performed with fluoroscopy (Axiom Artis; Siemens, Munich, Germany; or Advantix; General Electric, Milwaukee, Wisconsin). UAE was routinely performed through a 4- or 5-F vascular sheath (Avanti; Cordis, Bridgewater, New Jersey) placed via the right common femoral artery. Flush pelvic aortograms were not routinely obtained. Internal iliac arteriography was commonly performed to localize the “take-off” the uterine arteries, and also to assess for other sites of bleeding, such as from the internal pudendal artery. A 4-F Glide Cobra catheter (Terumo, Tokyo, Japan), a 5-F Cobra C2 catheter (Cook, Bloomington, Indiana), or a 5-F Roberts uterine catheter (Cook) were used to selectively catheterize the anterior division of the internal iliac artery. Selective catheterization of the uterine arteries was performed with the primary catheter or through a coaxial microcatheter (Renegade Hi Flo; Boston Scientific, Natick, Massachusetts; or Progreat, Terumo) if necessary.

Selection of the contralateral uterine artery (up and over the iliac bifurcation) was routinely performed first. After superselective angiography confirmed catheter position in the distal uterine artery, often in the horizontal portion of the artery, embolization was performed. As long as a pseudoaneurysm was not visualized with selective uterine angiography, embolization was performed with the use of absorbable gelatin sponge (Gelfoam; Pharmacia and Upjohn, New York, New York), administered in a slurry with saline solution and contrast medium. Embolization was performed until stasis of flow in the uterine artery was achieved (Fig 1). With the same femoral arterial access, the ipsilateral uterine artery was then selected and embolized in a similar manner in all cases. If a pseudoaneurysm was identified, it was embolized with metallic embolization microcoils (Tornado; Cook) through a microcatheter.

Clinical Endpoints
Primary PPH was defined as hemorrhage that occurred within the first 24 hours after delivery. Secondary PPH was defined as hemorrhage occurring more than 24 hours after delivery.

For each study subject, the hospital electronic medical record and radiologic images and reports were reviewed. Data collected included the indication for the procedure, patient age, parity and obstetric history, mode of delivery (vaginal or caesarian section), timing of PPH in relation to time of the delivery, transfusion requirement before UAE and after UAE, length of hospital stay after UAE, subsequent hysterectomy, and subsequent pregnancy. UAE procedural data collected included embolization technique and embolic material used, angiographic findings, and UAE procedural complications.

Data Analysis and Statistics
Technical success was defined as successful catheterization of both uterine arteries with embolization to stasis, embolization of a nonuterine pelvic vessel giving rise to active contrast agent extravasation, or successful coil embolization of a specific vascular lesion (ie, pseudoaneurysm). Clinical success of UAE was defined as obviation of subsequent hysterectomy. The range and mean requirements for administered blood products before and after UAE were calculated.

With two-sample t tests, Wilcoxon–Mann–Whitney tests, or Fisher exact tests when appropriate, statistically significant associations between subject characteristics (age, gravidity, parity, primary vs secondary PPH, packed red blood cells [PRBCs] administered before and after UAE, and length of hospital stay after UAE) and clinical success were evaluated. Statistical differences between women who required hysterectomy and those who did not were evaluated with these methods. Statistical differences comparing those with identified uterine artery pseudoaneu-
rysms and those without were also examined. These analyses were also performed with the sample limited to those women who had cesarean section deliveries. Statistical analysis was performed with Stata statistical software (Stata, College Station, Texas). A P value lower than .05 was considered to indicate statistical significance.

RESULTS

Study Group Characteristics

A total of 76 women (mean age, 33 years; range 17–47 y) underwent UAE at our institution for obstetric-related hemorrhage during the study period. The technical success rate was 100%. The mean gravidity of the women was 2.6 (range, 1–10) and the mean parity of the women was 1.8 (range, 0–9). Of these 76 women, six women underwent UAE for hemorrhage related to an intrauterine ectopic pregnancy (16,17) and three women underwent UAE performed in conjunction with prophylactic placement of internal iliac occlusion balloons for hemorrhage control during elective cesarean section delivery associated with known placenta accreta/percreta (18,19). Only one woman underwent hysterectomy before UAE, in whom embolization was performed for persistent vaginal hemorrhage, and this woman did not require further intervention after UAE. These 10 subjects were excluded from the analysis. Of the remaining 66 women, only three went on to subsequent hysterectomy, indicating a clinical success rate of UAE of 95% (Table 1), and a hysterectomy rate of 5% (three of 66). No women in the study had a repeat UAE procedure.

The reasons for subsequent hysterectomy in the three women included persistent PPH in two women and endometritis in one woman (2 weeks after UAE). The woman who underwent hysterectomy for endometritis and one of the two women who underwent a hysterectomy for persistent PPH were found to have retained placenta accreta on pathologic examination. The third woman who underwent a hysterectomy underwent a cesarean section delivery, presented with a secondary PPH 28 days after delivery, and had persistent PPH 3 days after a conventional UAE necessitating a hysterectomy.

In addition to these three clinical failures, there were three complications potentially related to the UAE procedure, including one woman who developed a left lower-extremity deep vein thrombosis, one woman who developed postprocedural pancreatitis, and one woman who was readmitted for intravenous antibiotic treatment for presumed endometritis who underwent UAE as well as dilation and curettage. Each of these complications is graded as a major complication according to the Society of Interventional Radiology guidelines (20). There were no minor
complications. One other woman experienced a peripartum seizure that did not appear related to the UAE procedure. There was no mortality related to UAE procedures and the overall complication rate was 4.5% (three of 66).

Of the 66 women included in the study, 50 (76%) underwent UAE for primary PPH and 16 (24%) for secondary PPH. Forty-eight women (73%) underwent UAE for primary PPH and 16 (24%) for secondary PPH. Of the 66 women included in the study, 50 (76%) underwent UAE for primary PPH and 16 (24%) for secondary PPH. Forty-eight women (73%) underwent UAE for primary PPH and 16 (24%) for secondary PPH.

Three women underwent selective unilateral internal pudendal embolization for active contrast agent extravasation: two were treated with Gelfoam slurry and one underwent coil embolization of the vessel, with resolution of active contrast agent extravasation in each. Three women underwent coil embolization of a uterine artery pseudoaneurysm as the etiology. Of these three women, two had a mean transfusion after UAE of 1.3 U (range, 0–12 U) of PRBCs and the mean postembolization transfusion requirement was 0.4 U (range, 0–4 U) of PRBCs. The mean hospital stay after UAE was 3.5 days (range, 1–12 d).

The only significant difference in subject characteristic means when comparing those who went on to undergo hysterectomy and those who did not was the number of transfusions required after treatment (difference of 1.0 U ± 0.5; *P* = .02, *t* test). The women undergoing hysterectomy had a mean transfusion after UAE of 1.3 U ± 1.3 whereas the others had a mean transfusion after UAE of 0.3 U ± 0.1. The presence of a uterine artery pseudoaneurysm was significantly related to delayed bleeding, ie, secondary PPH (*P* = .03).

Nine pregnancies were identified after UAE in nine women. Of these nine pregnancies, there were two spontaneous abortions and seven viable gestations, six of which had standard vaginal deliveries and one of which was delivered via cesarean section. Therefore, seven of 66 women had a subsequent viable pregnancy (10.6%). Of note, one of these women had a retained placenta with her subsequent pregnancy necessitating a dilation and curettage and another woman had a repeat primary PPH with the subsequent pregnancy. She was not referred for UAE, but instead was treated by hysterectomy at that time.

### Table 1. Clinical Effectiveness and Complication Rates of UAE Overall and by Subgroups of Primary and Secondary PPH

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Subjects</th>
<th>Clinical Effectiveness</th>
<th>Type of Complications</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>66</td>
<td>63/66 (95)</td>
<td>Lower-extremity DVT, pancreatitis, endometritis</td>
<td>3/66 (4.5)</td>
</tr>
<tr>
<td>Primary PPH</td>
<td>50</td>
<td>49/50 (98)</td>
<td>Lower-extremity DVT, pancreatitis</td>
<td>2/50 (4.0)</td>
</tr>
<tr>
<td>Secondary PPH</td>
<td>16</td>
<td>14/16 (88)</td>
<td>Endometritis</td>
<td>1/16 (6.3)</td>
</tr>
</tbody>
</table>

Note.—Values in parentheses are percentages. DVT = deep vein thrombosis.

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**Primary PPH**

There were 50 women (mean age, 32.7 years; range, 17–44 y) who underwent UAE for primary PPH. Twelve of these 50 women (24%) had delivered via cesarean section. The mean gravidity of these women was 2.7 (range, 1–10) and the mean parity was 1.9 (range, 1–9). The mean preembolization transfusion requirement for this group of women was 3.3 U (range, 0–10 U) of PRBCs and the mean postembolization transfusion requirement was 0.4 U (range, 0–4 U) of PRBCs. One of these 50 women underwent subsequent hysterectomy for persistent PPH (clinical success rate of 98%). The mean post-UAE hospital stay was 3.9 days (range, 1–12 d).

**Secondary PPH**

There were 16 women (mean age, 32.4 years; range, 21–42 y) who underwent UAE for secondary PPH. Two of these women underwent subsequent hysterectomy, yielding a clinical success rate for this group of 88%. The mean gravidity of these women was 2.1 (range, 1–4) and the mean parity of these women was 1.8 (range, 1–4). The mean presentation was 25 days (range, 4–72 d) after delivery. The mean preembolization transfusion requirement for this group of women was 2.0 U (range, 0–6 U) of PRBCs and the mean postembolization transfusion requirement was 0.2 U (range, 0–4 U) of PRBCs. The mean hospital stay after UAE for this group was 2.0 days (range, 1–5 d).

The cause for secondary PPH was related to retained products of conception in 13 women and a uterine artery pseudoaneurysm in three women. Each of the three women with a uterine artery pseudoaneurysm had undergone cesarean section delivery, and each had successful coil embolization with no further intervention required. Six women in this secondary PPH group (38%) had delivered via cesarean section. Therefore, half of women (three of six, 50%) who had undergone a recent cesarean section and presented with secondary PPH were found to have a uterine artery pseudoaneurysm as the etiology.

**PPH Associated with Cesarean Section**

There were 18 women (mean age, 34.7 years; range, 26–44 y) who underwent UAE for PPH after cesarean section, six of whom had secondary PPH (Table 2). As described earlier, of the six women with secondary PPH after cesarean section, three (50%) were related to a pseudoaneurysm of the...
technique for controlling acute bleeding in a wide variety of obstetric and gynecologic disorders, including use as a uterus-sparing technique for PPH treatment. This study represents one of the largest case series of UAE for PPH described in the literature, with only Touboul et al (10) reporting a larger group of women undergoing UAE for PPH (N = 102) to our knowledge. Kirby et al (9) recently reported their results for UAE for primary PPH at three institutions, and reviewed the literature, which consisted of 15 other case series describing approximately 430 women. These studies describe high clinical success rates with relatively low complication rates, which coincide with the clinical success rate of 95% and complication rate of 4.5% found in the present study. The effectiveness of UAE for PPH is evidenced by the high technical success rate (100%) and dramatic reduction in blood product requirements after UAE (3.1 U PRBCs before and 0.4 U after) in the present study. Further benefits of UAE for PPH include the avoidance of surgical risks associated with hysterectomy, potential for fertility preservation, and generally shorter hospitalizations. For comparison, in a large multicenter study of cesarean hysterectomies (22), the median maternal length of hospital stay was 5 days, the mean numbers of units of PRBCs given were 4.6 intraoperatively and 3.7 postoperatively, and the morbidity and mortality rates were 34.9% and 1.6%, respectively.

However, despite a growing body of data attesting to the effectiveness of the procedure, it continues to be an underutilized procedure. A 2002 survey of maternity units in the United Kingdom (14) showed that 86% had never used UAE for severe PPH. Twelve percent had performed one to four cases in the previous 5 years, and just 2% had performed more than five cases. However, hysterectomy was the most common intervention performed for PPH in the survey, with 89% of the maternity units having performed at least one hysterectomy for major hemorrhage during the same 5 years. The reasons for low utilization of UAE for PPH cited in the study (14) included limited number of modern angiography units with a trained, skilled 24-hour-per-day on-call team and the perceived risk of transferring a patient in unstable condition to the angiography suite. These utilization findings were consistent with other survey studies (14,23).

Some centers have begun to develop multidisciplinary algorithms and rapid-response teams to optimize outcomes of PPH, as hemorrhage-related morbidity and mortality are

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<tbody>
<tr>
<td>Overall PPH</td>
<td>18</td>
<td>17/18 (94)</td>
<td>Type</td>
</tr>
<tr>
<td>Primary PPH</td>
<td>12</td>
<td>12/12 (100)</td>
<td>Incidence</td>
</tr>
<tr>
<td>Secondary PPH</td>
<td>6</td>
<td>5/6 (83)</td>
<td>Lower-extremity DVT, pancreatitis 2/18 (11.1)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Lower-extremity DVT, pancreatitis 2/12 (16.7)</td>
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<tr>
<td></td>
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<td></td>
<td>None</td>
</tr>
</tbody>
</table>

Note.— Values in parentheses are percentages. DVT = deep vein thrombosis.
often caused by avoidable delays in diagnosis and treatment (24–26). The American College of Obstetricians and Gynecologists has also suggested that use of protocols and hemorrhage drills may reduce morbidity and mortality associated with PPH (27). These protocols extend beyond the obstetric teams alone, and are dependent on the successful collaboration of providers from numerous disciplines, including interventional radiology. At our institution, we have a strong and responsive relationship with our obstetric and gynecology colleagues that encourages early consultation with interventional radiology, and endovascular management when appropriate, for women with PPH.

We experienced a complication rate of 4.5%, which is not negligible. However, it should be kept in mind that these women often experienced large-volume blood loss with associated coagulopathies and transfusion requirements, and these women also often underwent dilation and curettage procedures after delivery and before UAE. Therefore, although they occurred in temporal relationship with the UAE procedure, some of these cited complications may have resulted from the metabolic stresses of the PPH event and were not causally related to the UAE procedure, making the actual complication rate from the procedure likely lower. In the present series, the only complication that could be identified as directly procedure-related was in the patient who underwent a hysterectomy for endometritis 2 weeks after UAE, which would yield a complication rate of UAE for PPH of 1.5% (ie, one of 66). Given the effectiveness of the procedure with the relatively low incidence of complications after UAE, we propose that the threshold for embolization of the uterus with signs of PPH should be low.

Two of the three women who underwent a hysterectomy after UAE were found to have placenta accreta on pathologic examination. This suggests that UAE is very good for PPH secondary to uterine atony, but may be less effective for cases of retained products of conception. However, UAE does still appear to be effective in cases in which retained products of conception are the etiology and does not preclude a later hysterectomy, although this should be kept in mind in discussions with women and referring clinicians.

The data in the literature regarding UAE for PPH after caesarean section are limited. However, we identified similar high clinical and technical effectiveness rates for UAE in this subset of women. The most interesting characteristic in the analysis of this subset of women was the finding that, of the six women with secondary PPH after caesarean section, 50% (n = 3) were attributable to a pseudoaneurysm of the uterine artery or a branch thereof. Each of these women underwent coil embolization alone with successful PPH resolution. Iatrogenic pseudoaneurysm after caesarean section is an increasingly recognizable cause for secondary PPH (28,29), and should be prospectively considered in these women.

One woman who presented with a secondary PPH after caesarean section had undergone a conventional UAE at an outside hospital (and was therefore not included in our data) 24 days before presenting to our hospital with recurrent PPH (Fig 2). A uterine artery pseudoaneurysm was identified on the repeat arteriogram obtained at our hospital, which was successfully embolized. This reinforces the idea that nonselective Gelfoam embolization of the uterine ar-
terry is not a completely effective treatment for a pseudoaneurysm. Aside from the two women who had placenta accreta, it is possible the third woman in whom UAE failed had an unrecognized cesarean section–related pseudoaneurysm as the cause for PPH. However, we do not have imaging or pathologic proof that this was the case.

An area of interest to clinicians and women regarding UAE is its effect on subsequent fertility, and the data in the literature regarding this topic are limited (30,31). The transient subischemic conditions induced by UAE on the uterus raise the important question of long-term effect on future fertility. A recent review of the literature regarding fertility after UAE for PPH was performed by Delotte et al (32), which included 13 articles describing the fertility follow-up of a total of 168 women. In this population, 45 pregnancies were described, which resulted in 32 live births. There were eight miscarriages in this group (18%), which was not much higher than the 10%–15% rate of miscarriage generally described for first-trimester pregnancies. They concluded that UAE offers a safe and conservative alternative to surgical interventions for PPH in women who desire to preserve future fertility.

In the present series, nine pregnancies were identified after UAE in nine women. Of these nine pregnancies, there were two spontaneous abortions and seven viable gestations, for a miscarriage rate of 22%. Our findings appear to coincide with those found in other series, but the numbers are relatively low. There are not enough data to make definitive recommendations in this area, but the data suggest that the endometrium is not impaired by UAE. A careful discussion with women considering UAE who desire future fertility is warranted. However, the fact that UAE preserves the uterus and can preclude hysterectomy is vital in this regard.

As with other published series, the value of our findings is limited by the small number of women included and the retrospective, case-series nature of the study. All women included in the study group were initially referred from our obstetric colleagues. We do not know the number of women who underwent initial hysterectomy without referral to UAE during this time period. Also, the volume of blood loss that initiated referral to interventional radiology was not specifically assessed and we cannot be sure that all postpartum women with 500 mL or more of blood loss were referred for UAE. However, quantification of blood loss during PPH is inherently difficult and studies have revealed that uncomplicated deliveries often result in blood loss of more than 500 mL without any maternal compromise (13). Moreover, some advocate a broader definition for PPH to include any bleeding that results in signs and symptoms of hemodynamic instability, bleeding that could result in hemodynamic instability if untreated, or bleeding that fits the clinical definition of “need for blood transfusion” (33–35). Each woman in the present study did receive blood products before or during UAE, fulfilling this broader definition of PPH.

In conclusion, UAE for obstetric-related hemorrhage has a high clinical effectiveness for primary PPH (98%), secondary PPH (88%), and PPH related to cesarean section delivery (94%). This was associated with an overall complication rate of 4.5%, although some complications may have been related to hemorrhage-related comorbidities and other contemporaneous procedures. Blood product requirements after UAE were low, and the surgical risks and absolute loss of fertility associated with hysterectomy were avoided. Interventional radiology and UAE should be included in multidisciplinary algorithms and rapid-response team plans to optimize outcomes of women with PPH, and given the relatively low incidence of complications, we propose that embolization of the uterus should be considered early in the algorithm of PPH management.

REFERENCES


