

Occlusion of Uterine Arteries Using Transcatheter Embolization

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Section:

OB/GYN & Reproduction

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I. Description

Transcatheter uterine artery embolization (UAE) is a minimally invasive technique that involves the injection of small particles, gelfoam, coils, or glue into the uterine arteries to block the blood supply to the uterus and uterine fibroids. It potentially serves as an alternative to hysterectomy. UAE has also been used to treat postpartum hemorrhage, cervical ectopic pregnancy, uterine arteriovenous malformations, and adenomyosis.

For individuals who have uterine fibroids who receive transcatheter UAE, the evidence includes randomized controlled trials and systematic reviews. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The majority of studies have compared UAE with hysterectomy and myomectomy and found similar levels of symptoms and quality of life across all treatment groups. Benefits for women undergoing UAE included avoiding surgery and maintaining their uteruses, lower complication rates, and lower blood transfusion rates. However, patients undergoing UAE had higher reintervention rates compared with patients who had surgery. Smaller trials have compared UAE with laparoscopic occlusion and magnetic resonance image guided focused ultrasound surgery. Additional trials with larger sample sizes comparing UAE with these and other uterus-preserving procedures are needed. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have persistent uterine fibroids despite prior uterine artery embolization who receive repeat transcatheter UAE, the evidence includes case series. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. Case series have shown that a high degree of symptom relief is possible after a repeat UAE for uterine fibroids. Moreover, evidence from randomized controlled trials on the safety and efficacy of UAE for initial treatment of uterine fibroids may indicate a benefit for patients in need of repeat procedures for the same indication. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have postpartum uterine hemorrhage who receive transcatheter UAE, the evidence includes case series and a systematic review. Relevant outcomes are overall survival, symptoms, and treatment-related morbidity. The systematic review of case series assessing over

1400 women reported success rates of stopping bleeding that ranged from 58% to 98%. Postpartum uterine hemorrhage is an emergency situation with serious potential consequences (ie, maternal mortality). Conducting randomized controlled trials is particularly difficult in this setting and may be unnecessary when there are sufficient uncontrolled data. Though from case series, there is evidence reporting on over 1400 women. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have cervical ectopic pregnancy who receive transcatheter UAE, the evidence includes case series. Relevant outcomes are treatment-related morbidity. Only a few case series with a small number of patients have been published. Additional studies, especially controlled studies comparing UAE with medication or surgery, are needed to assess the safety and efficacy of UAE in patients with cervical ectopic pregnancy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have uterine arteriovenous malformations who receive transcatheter UAE, the evidence includes case reports, case series, and a systematic review. Relevant outcomes are symptoms, and treatment-related morbidity. Only case reports and case series with a small number of patients have been published. A systematic review identified 54 women in 40 studies with uterine arteriovenous malformations treated with UAE. Additional controlled studies comparing UAE with hysterectomy are needed to assess the safety and efficacy of UAE in patients with uterine arteriovenous malformations. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have adenomyosis who receive transcatheter UAE, the evidence includes case series and a systematic review. Relevant outcomes are symptoms, and treatment-related morbidity. A systematic review of case series data found short-term improvement in 83% of patients and long-term improvement in 65% of patients, suggesting possible recurrence of symptoms over time. All studies were case series, which might have been subject to selection and/or observational biases. Additional case series published after the review have reported that patients with greater necrosis of adenomyosis and patients with higher vascularity of lesions may experience higher response rates to UAE. Controlled studies comparing UAE with medication or surgery and studies reporting long-term symptom recurrence rates are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

II. Criteria/Guidelines

- A. Transcatheter embolization of uterine arteries as a treatment of uterine fibroids or as a treatment of postpartum uterine hemorrhage is covered (subject to Limitations and Administrative Guidelines) when recommended by a gynecologist when the following criteria are met:
 1. Asymptomatic fibroids of such size that they are palpable abdominally and are a concern to the patient; OR
 2. Excessive uterine bleeding as evidenced by either profuse bleeding lasting more than 8 days, or anemia due to acute or chronic blood loss; OR
 3. Pelvic discomfort caused by myomata, either acute severe pain, chronic lower abdominal pain, or low back pressure or bladder pressure with urinary frequency not due to urinary tract infection.

- B. One repeat transcatheter embolization of uterine arteries to treat persistent symptoms of uterine fibroids after an initial uterine artery embolization is covered.
 - 1. One repeat uterine artery embolization may be performed when there is documentation of continued symptoms such as bleeding or pain. Repeat procedures may be most appropriate when there are persistent symptoms in combination with findings on imaging of an incomplete initial procedure, as evidenced by continued blood flow to the treated regions. Limited data from case series have suggested a high rate of success following repeat procedures for this purpose, with most patients reporting relief of symptoms.
- C. The patient understands and is informed of the risks associated with future fertility/pregnancy.

III. Limitations

Transcatheter embolization for the management of all other indications, including cervical ectopic pregnancy, uterine arteriovenous malformation, and adenomyosis is not covered.

IV. Administrative Guidelines

- A. Precertification is not required. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria. The following information should be kept in the patient's medical record and be made available upon request:
 - 1. Supporting documentation that the procedure is medically necessary for the condition.
 - 2. Pelvic ultrasound or MRI report performed within the past three months.
 - 3. A current negative endometrial biopsy report for patients with a history of abnormal uterine bleeding or when endometrial cancer is suspected
- B. The following evaluations (if applicable) must be performed prior to the procedure and documented in the patient's medical records:
 - 1. A current negative pregnancy test result for child-bearing age patients suspected of being pregnant.
 - 2. A current negative test for any sexually transmitted diseases (e.g., gonorrhea and chlamydia) for patients with a history of pelvic inflammatory disease or for patients at risk of or suspected of having a sexually transmitted disease.

CPT Codes	Description
37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction
36245-36247	Selective catheter placement, arterial system; each first, second, or third order branch, respectively

V. Background

UTERINE FIBROIDS

Uterine leiomyomata (i.e., fibroids) are extremely common benign tumors that can be submucosal (located primarily within the uterine cavity below the endometrium), intramural (with the uterine wall or myometrium), or subserosal in location. Patient symptomatology, physical examination findings, and imaging results are related to the location of the fibroids. Individuals may have fibroids in any or all of these locations within the uterus.

Treatment

Treatment for uterine fibroids is usually sought when they are associated with menorrhagia, pelvic pain, urinary symptoms (ie, frequency), or are suspected to cause infertility. Treatment options include medical therapy with gonadotropin agonists or progestins or various types of surgical therapy. Hysterectomy is considered the definitive surgical treatment for those who no longer want to maintain fertility. Various types of myomectomy, which describes the removal of fibroids with retention of the uterus, have also been described. Hysteroscopic myomectomy involves removal of submucosal fibroids using a resectoscope or a laser. Subserosal fibroids can be removed via an open abdominal or laparoscopic approach. Laparoscopic laser coagulation of uterine fibroids is a unique approach in that the fibroid is not physically removed, but instead multiple (up to 75) laparoscopic laser punctures of the uterine fibroid are performed to devascularize the fibroid and induce atrophy.

There is interest in techniques that directly devascularize the uterine fibroid by interrupting the uterine arteries. One technique, uterine artery embolization, involves selective catheterization of the uterine arteries with an injection of embolization material. Uterine artery embolization has also been used to control bleeding in situations such as severe postpartum hemorrhage, cervical ectopic pregnancy, bleeding uterine arteriovenous malformation (AVM), and adenomyosis.

Ectopic pregnancies account for up to 2% of pregnancies and are the leading cause of first-trimester maternal mortality. Patients present with pelvic pain and vaginal bleeding. First-line treatment for patients with minimal symptoms is systemic methotrexate. In patients with high β -human chorionic gonadotrophin response to methotrexate may not be adequate, and the patient is susceptible to complications such as hemorrhaging, resulting in the need for a hysterectomy.

Uterine AVMs are rare but may cause severe genital hemorrhaging. There are two types: low-flow AVM is characterized by an abnormal vascular network without visible early venous drainage and high-flow AVM, which has early venous drainage. Uterine AVMs may be congenital or acquired. Risk factors for acquired AVMs are prior uterine surgery such as dilatation and curettage, myomectomy, and cesarean section. Treatment options include hysterectomy, uterine artery ligation, and uterine artery embolization.

Adenomyosis is characterized by the diffuse or focal growth of endometrial glandular and stromal tissue in the muscular layer of the uterus. The etiology of adenomyosis is unknown. Symptoms include dysmenorrhea, menorrhagia, infertility, and an enlarged uterus may be found on physical examination. Treatment options include surgery and hormone therapy.

UAE FOR TREATMENT OF UTERINE FIBROIDS

Initial UAE Procedure for Uterine Fibroids

A number of randomized controlled trials (RCTs) evaluating UAE for the treatment of uterine fibroids and several systematic reviews of these RCTs have been published. RCTs have compared UAE with hysterectomies, myomectomies, laparoscopic occlusion of uterine arteries, and focused ultrasound.

Systematic Reviews

A 2014 Cochrane review included 7 RCTs comparing UAE with other surgical interventions in women with symptomatic uterine fibroids. Four of the RCTs excluded women who desired pregnancy in the future. The comparator intervention was hysterectomy in 3 trials, hysterectomy or myomectomy in 2 trials, and myomectomy in 2 trials. Reviewers' primary outcomes were patient satisfaction and live birth rates (the latter analysis limited to studies where the comparison intervention was a uterine-sparing procedure). Pooled analyses did not find statistically significant differences in patient satisfaction with UAE or other interventions after 2 years (6 trials; odds ratio [OR], 0.94; 95% confidence interval [CI], 0.59 to 1.48) or 5 years (2 trials; OR=0.90; 95% CI, 0.45 to 1.80). A single study reported live birth rates, so a meta-analysis was not possible. UAE was associated with a higher rate of minor complications at 1 year (6 trials; OR=1.99; 95% CI, 1.41 to 2.81), and there was no statistically significant difference between groups in the rate of major complications. Moreover, the UAE group was significantly less likely to require a blood transfusion than the surgery group (2 trials; OR=0.07; 95% CI, 0.01 to 0.52). The rate of further surgical interventions within 2 years was significantly increased in the UAE group (6 trials; OR=3.72; 95% CI, 2.28 to 6.04).

In a 2014 systematic review and meta-analysis, Das et al identified 10 studies comparing the efficacy of 1 embolic agent used in UAE with another intervention or comparing 2 embolic agents. Five studies were RCTs, and five were controlled trials that were not randomized. Embosphere microspheres were used in all of the RCTs. In a pooled analysis of data from 2 studies comparing microspheres with spherical polyvinyl alcohol for the treatment of uterine fibroids, there were no statistically significant between-group differences in outcomes (uterine volume reduction, dominant fibroid volume reduction). Data from other studies were not pooled, but a qualitative analysis of study findings did not suggest that any agent was superior or inferior to any other agent.

A 2013 systematic review and meta-analysis by Martin et al focused on comparing complications and reintervention rates following UAE and surgery for symptomatic uterine fibroids.⁴ Surgery was not defined in this meta-analysis, so it is unclear whether myomectomies were also included with hysterectomies. Outcomes for UAE and surgery were stratified by study design (RCTs, nonrandomized studies, case series). Eight RCTs comparing UAE with a surgical intervention were included, for a total of 350 patients undergoing UAE and 346 patients undergoing surgery. Among the UAE cases in the RCTs, the most common complications were discharge and fever (4%), postembolization syndrome (2.9%), pain (2.9%), and groin complications (2.9%). The most common complications among patients undergoing surgery were urinary stress incontinence (3.8%), pressure symptoms (2.9%), and menorrhagia (2.6%). Three trials presented reintervention data and, in a meta-analysis of these studies, there was a significantly higher risk of reintervention

after UAE than after surgery, but a wide confidence interval indicates imprecision in the risk estimate (OR=6.04; 95% CI, 2.0 to 18.1).

In 2011, van der Kooij et al published a systematic review and meta-analysis of RCTs comparing UAE with surgery (hysterectomy/myomectomy) for treating symptomatic uterine fibroids and presenting up to 5 years of follow-up data.⁵ Reviewers identified 11 articles reporting on 5 RCTs. The overall intraprocedural and early postprocedural complication rates were similar with both procedures. However, hospital length of stay, need for blood transfusion, and febrile morbidity was significantly lower in the UAE group than in the surgery group. At 12 months, a pooled analysis of 2 studies found a significantly higher reintervention rate in the UAE group than in the surgery group (OR=5.78; 95% CI, 2.14 to 15.58). Pooled analyses of quality of life (QOL) variables at 12 months found no significant differences between groups. Results were similar after 5 years. The reintervention rate was significantly higher in the UAE group at 5 years, based on pooled analysis of 2 trials (OR=5.41; 95% CI, 2.48 to 11.81).

Randomized Controlled Trials

UAE vs Hysterectomy or Myomectomy

The multicenter Randomized Trial of Embolization vs Surgical Treatment for Fibroids (REST) assigned patients 2:1 to undergo UAE (n=106) or surgery (n=43 hysterectomies, n=8 myomectomies). The UAE group had lower postoperative pain (3.0 vs 4.6, respectively) and faster recovery (eg, median length of hospitalization, 1-day vs 5-day, respectively). Of seven identified pregnancies in the UAE group, two resulted in successful live births. Five-year follow-up data from the REST trial were published in 2011. A total of 144 (92%) of 157 randomized patients were included in the 5-year analysis. QOL and symptom scores were similar in both groups at 5 years: mean symptom score was 4.5 in the UAE group and 4.8 in the surgery group (scores ranged from 15 [markedly worse] to 5 [markedly better]). At 5-year follow-up, 27 (25%) of 106 in the UAE group and 2 (4%) of 51 in the surgery group had received an additional intervention for continued or recurrent symptoms. The total rate of further intervention for symptoms or adverse events over the 5-year period was 32% in the UAE group and 4% after surgery. In the UAE group, there were 3 procedural failures, 8 repeat UAEs, and 18 hysterectomies. Note that a woman had both a repeat UAE and a hysterectomy, and 2 women were not embolized after randomization and subsequently underwent surgery.

The EMbolization versus hysterectoMY (EMMY) trial from the Netherlands included 177 women with uterine fibroids and heavy menstrual bleeding who were scheduled to undergo hysterectomy. They were randomized to UAE (n=88) or hysterectomy (n=89). By the 2-year follow-up, 19 (23%) of the 81 women who received UAE had undergone a hysterectomy. An analysis of health-related QOL outcomes at 2 years found similar improvement in both groups. The Defecation Distress Inventory score improved significantly in only the UAE group starting at 6 months. A report of 5-year outcomes data from the EMMY trial was published in 2010. At 5 years, 70 (79%) of 89 patients originally randomized to the hysterectomy group and 75 (85%) of 88 patients in the UAE group completed questionnaires. In an intention-to-treat analysis, 23 (28.4%) of 81 patients who had received UAE underwent hysterectomy during the 5 years. Including patients who had subsequent hysterectomies, 58 (71.6%) of 81 patients in the UAE group no longer had menorrhagia. There were no significant differences between groups in health-related

QOL at 5 years, as assessed by the Physical and Mental Component scores of the 36-Item Short-Form Health Survey. Ten-year outcomes were reported by de Bruijn et al in 2016.¹¹ Completed questionnaires were available for 131 (75%) of 177 randomized patients at 10 years. An additional 5 hysterectomies were performed between the 5- and 10-year follow-ups, for a total of 28 (35%) hysterectomies in the UAE group. At 10 years, there were no statistically significant differences between groups in health-related QOL or in urinary and defecation function.

In 2012, findings of the Fibroids of the Uterus: Myomectomy versus Embolization (FUME) trial from the U.K. were published.¹² The investigators randomized women with symptomatic fibroids to UAE (n=82) or myomectomy (n=81). Mean hospital stay was significantly shorter after UAE (2 days) than after surgery (4 days; $p<0.001$). There were no significant differences in minor or major complications. A total of 120 (74%) of 163 women were available for the analysis of the primary outcome measure (QOL). There were no significant differences between groups in change in QOL scores from baseline to 1 year. Nine (11%) patients in the UAE group required additional intervention (6 hysterectomies, 2 myomectomies, 1 repeat embolization) and 3 (4%) patients in the myomectomy group later underwent hysterectomy.

UAE vs Laparoscopic Occlusion of Uterine Arteries

An RCT by Hald et al (2007) in Norway evaluated clinical outcomes in 66 premenopausal women (mean age, 43 years) with symptomatic uterine fibroids who were assigned to laparoscopic occlusion of uterine arteries or UAE. Women who wanted to bear children in the future, had a large uterus, had undergone multiple open abdominal surgeries, and who had bleeding disorders were excluded. The primary outcome was a reduction in blood loss at 6 months postintervention, as measured by a pictorial blood loss assessment chart. Fifty-eight women underwent treatment, 29 in each group. The proportion of women who had a reduction in blood loss after 6 months did not differ between the treatment groups (52% after UAE vs 53% after laparoscopy; $p=0.96$). Follow-up data were reported in 2009 at a median of 48 months posttreatment (range, 8-73 months).¹⁴ The cumulative clinical failure and recurrence rate was significantly lower in the UAE group (17% [n=5]) than in the laparoscopy group (48% [n=17]; $p=0.02$). Moreover, fewer patients in the UAE group (7% [n=2]) had a hysterectomy than in the laparoscopy group (28% [n=8]; $p=0.41$). The authors concluded that UAE is superior to laparoscopic occlusion of uterine arteries for treatment of uterine fibroids.

UAE vs Focused Ultrasound

In 2017, Barnard et al published an RCT and a cohort study comparing the use of UAE with magnetic resonance imaging guided focused ultrasound surgery (MRgFUS) for the treatment of uterine fibroids. Premenopausal women with symptomatic uterine fibroids were randomized to MRgFUS (n=27) or UAE (n=22). Women who declined randomization were enrolled in a nonrandomized cohort study; 43 underwent MRgFUS, and 40 underwent UAE. The outcome of interest was recovery during the first 6 weeks postprocedure, captured in symptom diaries that included information on return to work, return to normal activities, medication use, symptoms, and adverse events. Separate multivariate analyses of the RCT and the cohort populations found similar conclusions: opioid use was significantly higher in the UAE group, and length of time to first

day fully back to work and first day back to normal activities were also significantly longer for patients treated with UAE. Treatment time was significantly longer in the MRgFUS group.

Section Summary: Initial UAE Procedures for Uterine Fibroids

Most of the current evidence, including a number of RCTs and systematic reviews, has compared UAE with surgery (hysterectomy or myomectomy) for treating uterine fibroids. A Cochrane review found similar levels of patient satisfaction after UAE and surgery. A potential benefit of UAE over hysterectomy is that, depending on the location of the fibroids, the uterus and fertility may be preserved. Other benefits of UAE over hysterectomy and/or myomectomy include lower blood transfusion rates and lower complication rates. However, studies with long-term follow-up have shown that patients undergoing UAE have higher reintervention rates. Single RCTs have compared UAE with laparoscopic occlusion and MRgFUS. UAE had higher clinical success rates and lower reintervention rates than laparoscopic occlusion. Recovery was longer and opioid use higher among patients undergoing UAE compared with MRgFUS. Additional research comparing other uterus-sparing procedures with UAE are needed. The available evidence from RCTs does not suggest that any one embolization agent is superior to another.

Repeat UAE Procedures for Recurrent or Persistent Uterine Fibroid Symptoms

No RCTs focusing on repeat UAE were identified; there are published case series. In 2009, McLucas and Reed published a study in which the charts of 1058 women who had undergone initial bilateral UAE at several U.S. centers were reviewed. Forty-two (4%) patients had documented persistent symptoms, and they were offered a second bilateral UAE. Thirty-nine patients had repeat procedures, and 34 (87%) of them completed a follow-up questionnaire at least 6 months postembolization. Before the second UAE procedure, 27 (79%) of the 34 women reported severe bleeding, with only 2 (6%) women reported severe bleeding postprocedure. Similarly, the number of women with severe pain decreased from 20 (59%) to 2 (6%), and with severe pressure decreased from 18 (53%) to 2 (6%). Four women experienced severe levels of one or more symptoms after the second UAE.

In 2006, Yousefi et al reported on 24 patients who underwent repeat embolization for recurrent or persistent symptoms 6 to 66 months after the initial UAE. The most common symptoms were pressure and/or bulk symptoms (n=15), recurrent heavy bleeding (n=12), and pelvic pain or cramping (n=7). Follow-up data were available on 21 (87.5%) of 24 after the second UAE; 19 (90%) reported symptom control.

Section Summary: Repeat UAE Procedures for Recurrent or Persistent Uterine Fibroid Symptoms

There is a lack of RCTs on repeat UAE for the treatment of symptoms associated with recurrent uterine fibroids. However, there are data from case series showing high rates of success after a second UAE for recurrent or persistent symptoms.

UAE FOR POSTPARTUM UTERINE HEMORRHAGE

No RCTs or other comparative studies evaluating UAE for treating postpartum hemorrhage were identified. Several systematic reviews of the literature on treatments for postpartum hemorrhage have been published.

Systematic Reviews

In 2016, Sathe et al reported that rates of successful bleeding control with UAE in uncontrolled studies ranged from 58% to 98%, with a total of 1251 (87%) of 1435 patients in 15 studies achieving successful control of bleeding. Previously, in 2012, Rath et al published a systematic review of the literature on second-line treatment of postpartum hemorrhage.¹⁹ Success rates of UAE for postpartum hemorrhage reported in uncontrolled studies ranged from 70% to 100% and from 60% to 83% when the hemorrhage was associated with placenta accreta.

Case Series

Among the representative, larger case series is the 2013 retrospective evaluation by Kim et al of data on 121 women with postpartum hemorrhage, 60 women of whom underwent UAE and 61 of whom underwent a cesarean hysterectomy at a single center in Korea. The clinical success rate for UAE (which was not explicitly defined) was reported as 96%. Eleven patients treated with UAE experienced transient fever after the procedure, and there was a case of ovarian failure. Two patients were subsequently treated with cesarean hysterectomy. Among the 61 patients at the same center who underwent cesarean hysterectomy, the success rate was 93%. Four patients in this group underwent UAE immediately following cesarean hysterectomy due to arterial hemorrhage at extrauterine sites (2 cases) and bleeding from uterine collateral vessels (2 cases).

In 2011, Ganguli et al published data on 66 women who underwent UAE for the treatment of postpartum hemorrhage. The clinical success rate (defined as obviation of hysterectomy) was 95%. Three (5%) of 66 women had a subsequent hysterectomy. In addition to the 3 clinical failures, there were 3 (5%) major complications after UAE: one case each of lower-extremity deep vein thrombosis, postprocedural pancreatitis, and presumed endometritis. Nine pregnancies after UAE were identified; there were two spontaneous abortions and seven viable gestations.

In 2009, Kirby et al retrospectively analyzed data from 43 women who underwent UAE for primary postpartum hemorrhage. Clinical success was defined as cessation of bleeding without the need for repeat embolization, laparotomy, or hysterectomy and without mortality. Eight (19%) of 43 women had a hysterectomy before UAE in an attempt to stop bleeding. Of the remaining 35 women, clinical success was achieved in 29 (83%) women. Considering the sample as a whole, the clinical success rate was 29 (67%) of 43. Complications among women who had UAE without a previous hysterectomy included one case each of groin hematoma, inadvertent perforation of the left obturator artery during UAE, bleeding necrotic fibroid tumor, and symptoms consistent with endometritis.

Section Summary: UAE for Postpartum Uterine Hemorrhage

There is a lack of RCTs or other controlled studies on UAE for the treatment of postpartum hemorrhage. Case series involving totaling over 1400 patients have shown a high rate of successfully stopping the bleeding. Without treatment, there is a high likelihood of significant ongoing hemorrhage and maternal mortality. Given that this is an emergent, often clinically complex situation that can result in maternal mortality, it may not be practical to conduct RCTs and positive case series data may suffice. There is a lack of RCTs or other controlled studies on UAE for the treatment of postpartum hemorrhage. Case series involving totaling over 1400 patients have shown a high rate of successfully stopping the bleeding. Without treatment, there is a high likelihood of significant ongoing hemorrhage and maternal mortality. Given that this is an

emergent, often clinically complex situation that can result in maternal mortality, it may not be practical to conduct RCTs and positive case series data may suffice.

FERTILITY AND PREGNANCY OUTCOMES AFTER UAE FOR UTERINE FIBROIDS OR POSTPARTUM HEMORRHAGE

Several systematic reviews and an RCT on fertility and pregnancy outcomes after UAE have been published.

In 2014, Doumouchtsis et al identified 17 studies (total N=675 participants) reporting on fertility outcomes after UAE for postpartum hemorrhage. To be selected, studies had to report on 5 or more cases. None identified was an RCT. A total of 168 (25%) of the 675 patients wanted a pregnancy following UAE and 126 (75%) of the 168 women who desired pregnancy conceived. There were 136 term live births and 30 cases of pregnancy loss (ectopic pregnancy, miscarriage, elective abortion). In 2013, Mohan et al identified 21 studies reporting pregnancy outcomes and/or pregnancy complications after UAE for the treatment of uterine fibroids or postpartum hemorrhage. Reviewers reported that the cumulative pregnancy and miscarriage rates among women trying to conceive following UAE for uterine fibroids were 59% and 28%, respectively, and the cumulative live birth rate was 65%. The term delivery rate was 61%. In the studies on UAE for postpartum hemorrhage, the cumulative pregnancy rate, based on a small number of pregnancies, was 87.2%. Rates of miscarriage and live births were not reported following UAE for postpartum hemorrhage. Most studies included in the systematic review were observational and had no or inadequate controls. The single RCT identified is described below.

In 2008, Mara et al conducted an RCT, randomizing 121 women with uterine fibroids who desired future pregnancies to UAE or myomectomy. Participants were followed for a mean of 25 months; they were advised to wait for at least 6 months postprocedure before attempting to conceive. At final follow-up, 13 (50%) of 26 women in the UAE group who tried to conceive became pregnant compared with 31 (76%) of 40 in the myomectomy group; the difference between groups was not statistically significant. Among women in the UAE group who became pregnant, the spontaneous abortion rate was 64%, and the live birth rate was 19%. In the myomectomy group, the spontaneous abortion rate was 23%, and the live birth rate was 48%.

Section Summary: Fertility and Pregnancy Outcomes After UAE for Uterine Fibroids or Postpartum Hemorrhage

Reviews of fertility and pregnancy outcomes after UAE have suggested that successful pregnancy is possible after UAE for the treatment of uterine fibroids or postpartum hemorrhage. One review found higher rates of miscarriage and postpartum hemorrhage with UAE than with myomectomy, though the numbers in each group trying to conceive were small. There are limited data on pregnancy outcomes in women who became pregnant following UAE for the treatment of postpartum hemorrhage.

UAE FOR CERVICAL ECTOPIC PREGNANCY

No RCTs or other comparative studies evaluating UAE for treating cervical ectopic pregnancy were identified. The published literature consisted of small case series. Sample sizes ranged from 2 to 20 patients, and most studies had fewer than 10 patients.

In 2017, Kwon et al retrospectively reviewed the charts of 13 women who had ectopic pregnancies that were refractory to systemic methotrexate who were then treated with UAE.²⁶ Locations of the ectopic implantation were: cesarean scar (n=6), cervix (n=5), fallopian tube (n=1), and uterine cornua (n=1). Outcomes were technical success, clinical success, and complications. Results were reported for all patients, regardless of the ectopic implantation site. Mean gestational age at the time of diagnosis was 8.5 weeks (range, 3-14 weeks). Median follow-up was 25 weeks (range, 4-85 weeks). Technical success was 100%. Clinical success was achieved in 10 (77%) patients. Three patients experienced recurrent vaginal bleeding (2 instances of which occurred in patients who had cervical ectopic pregnancies) and underwent repeat embolizations. The uteri of all 13 patients were preserved.

Hu et al (2016) retrospectively reviewed the charts of 19 women who had cervical pregnancies and were treated with UAE followed by curettage. The median gestational age of the fetuses at the time of UAE was 7.4 weeks (standard deviation, 1.6). One procedure was deemed an emergency due to profuse bleeding; the remaining 18 were nonemergency procedures. There were no reports of further vaginal bleeding following UAE. None of the patients underwent a hysterectomy due to the cervical pregnancy.

Nine patients were followed for up to 39 months. Eight of the nine resumed normal menstruation. Only one attempted to conceive, and she had an uncomplicated pregnancy and a vaginal delivery.

The largest prospective series was conducted in China by Xiaolin et al (2010). Patients received methotrexate injections before, during, and after the UAE procedure. Median follow-up was 12 months (range, 1-50 months). Two (10%) of 20 patients had recurrent vaginal bleeding; the other 18 had no significant bleeding after UAE. Five (25%) patients had an additional curettage procedure due to bleeding and/or high levels of β -human chorionic gonadotropin. The uterus was preserved in all patients, and normal menses resumed after 2 to 4 months. Eight (50%) of 16 women who attempted to conceive achieved a normal pregnancy within 1 year. There were 2 miscarriages and 6 live births at term.

Section Summary: UAE for Cervical Ectopic Pregnancy

Cervical ectopic pregnancy is an emergent, rare, and clinically complex situation that may preclude gathering controlled data for evidence. However, because there are only a few case series available, the largest of which included 20 patients, additional case series are needed to inform a determination of efficacy. The limited noncomparative evidence is insufficient to determine the effect of UAE on health outcomes.

UAE FOR UTERINE ARTERIOVENOUS MALFORMATION

No RCTs or other comparative studies evaluating UAE for treating uterine arteriovenous malformations (AVMs) were identified. The published literature consists of case reports, small case series, and a systematic review.

Systematic Reviews

A 2016 systematic review by Yoon et al of literature on acquired uterine AVMs identified 54 women treated with UAE in 40 studies published between 2003 and 2013, primarily case reports. There were 22 unilateral and 32 bilateral procedures. Thirty-three (61%) of 54 patients had symptoms controlled with the initial embolization procedure. Nine of 13 patients who underwent

repeat UAE experienced resolution of symptoms. No major complications were reported after UAE.

Case Series

The following case series were published since the Yoon systematic review. In 2017, Barral et al described using ethylene vinyl alcohol copolymer (Onyx) as the embolic agent for UAE in the treatment of uterine AVMs. Records from 12 women, mean age 33 years, were reviewed. After a mean follow-up of 29 months, 11 of the 12 women achieved clinical success, defined as the absence of bleeding at 1 month following embolization.

The largest series, published in 2014 by Kim et al in Korea, retrospectively reviewed data from a single center on 19 patients who underwent UAE as first-line treatment of bleeding uterine AVMs. All patients presented with intermittent or progressive vaginal bleeding after gynecologic procedures or obstetric events. The UAE procedures were bilateral, and a variety of embolization agents were used. Seventeen (89.5%) of 19 patients had immediate clinical success following the UAE, defined as cessation of bleeding without symptom recurrence and resolution of the uterine AVMs on postoperative imaging studies.

Section Summary: UAE for Uterine Arteriovenous Malformation

The limited noncomparative evidence is insufficient to determine the effect of UAE on health outcomes in patients with bleeding associated with uterine AVMs. Additional data, ideally controlled trials comparing UAE with alternative uterine-sparing treatments, are needed to determine the safety and efficacy of UAE for treating uterine AVMs.

UAE FOR ADENOMYOSIS

No RCTs or other comparative studies evaluating UAE for treating adenomyosis were identified.

Systematic Reviews

In a 2011 systematic review of publications from 1999 through 2010, Popovic et al evaluated the literature on UAE for patients with adenomyosis, alone or in conjunction with uterine fibroids. Reviewers identified 8 case series reporting short-term follow-up in patients with adenomyosis alone. After a median follow-up of 9.4 months (range, 3-12 months), 85 (83%) of 102 patients had marked or complete improvement in clinical symptoms. Six case series reported long-term follow-up (median, 40.6 months; range, 17-60 months). Marked or complete improvement occurred in 135 (65%) of 208 patients, suggesting recurrence of symptoms over time in some patients. No deaths or serious adverse events were reported.

Case Series

Additional case series have been published since the Popovic systematic review. In 2017, de Bruijn et al provided 7-year QOL data on 28 women with adenomyosis treated with UAE. Outcomes were Uterine Fibroid Symptom Quality of Life (UFS-QOL) questionnaire and Symptom Severity Score (SSS). A higher UFS-QOL score indicates a better QOL and a lower SSS indicates an improvement in symptoms. Patients were considered asymptomatic if their SSS was less than 20 and their UFS-QOL score was greater than 80. At 7 years posttreatment, 3 women had undergone a second UAE, and 5 women had undergone a secondary hysterectomy. Median SSS at baseline was 72 (range, 23-100) and improved to 17 (range, 0-44). Median UFS-QOL score at baseline was 31 (range, 20-88) and improved to 98 (range, 9-100).

In 2016, Zhou et al evaluated short- (12-month) and long-term (5-year) outcomes for 252 women following UAE treatment for adenomyosis. Outcomes of interest were dysmenorrhea and menorrhagia. Subgroup analyses were conducted by lesion vascularity: (1) blood supply equality of the uterus (“equal” if left and right uterine arteries supplied blood equally, otherwise “unequal”) and (2) vascularity degree (“hypervascular” if vessels abundant at margin and center of lesions, “isovascular” if vessels abundant at margin but not core, and “hypovascular” if vessels lacking at margin and core). Following UAE, both short- and long-term rates of dysmenorrhea improvement and menorrhagia improvement were statistically similar among the equal and unequal blood supply groups, with improvement rates reported between 68% and 77%. However, improvement rates in dysmenorrhea and menorrhagia differed statistically among the vascularity groups, with patients in the hypervascular group experiencing higher rates of improvement than the other groups.

In 2016, Wang et al prospectively reported on 117 premenopausal patients with adenomyosis who underwent UAE. A total of 115 (98%) of 117 patients who successfully underwent bilateral UAE were included in the analysis. At 12 months, patients were queried about change in dysmenorrhea symptoms. Thirteen (11.3%) patients reported slight symptom improvement, 64 (55.7%) reported moderate improvement, and 31 (27.0%) reported marked improvement. Seven (6%) patients reported no change.

In 2015, Bae et al retrospectively reviewed outcomes for 50 women who underwent UAE for symptomatic adenomyosis and were followed for at least 18 months. At baseline, 41 (82%) of 50 women had both heavy menstrual bleeding and dysmenorrhea; the remainder reported only 1 of these 2 symptoms. The extent of postprocedure necrosis of adenomyosis imaged with magnetic resonance imaging was significantly associated with the likelihood of experiencing symptoms at follow-up. In receiver operating characteristic curve analysis, a cutoff of 34.3% necrosis was the most predictive of symptom recurrence (area under the curve, 0.721; 95% CI, 0.577 to 0.839; $p=0.004$). Among 12 patients with less than 34.3% necrosis, 58% were symptom-free at 18 months; among 40 patients with greater than 34.3% necrosis, 94% were symptom-free at 18 months.

Section Summary: UAE for Adenomyosis

There is a lack of RCTs or other controlled comparative studies on UAE for the treatment of adenomyosis. Several case series and a systematic review are available. The systematic review found short-term symptom improvement in 83% of patients and long-term improvement in 65% of patients. Preliminary evidence from case series published after the systematic review showed that patients with greater necrosis of adenomyosis and patients with higher vascularity of lesions had higher response rates to UAE. A case series with 7 years of follow-up reported that 5 (18%) of 28 patients underwent a subsequent hysterectomy. Additional data from controlled trials are needed, especially on long-term efficacy and recurrence rates.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
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Ongoing			
NCT01834703	Randomized Controlled Trial of Uterine Artery Embolization (UAE) Versus High-Intensity-Focused-Ultrasound (HIFU) for Treatment of Patients With Uterine Fibroids	200	May 2017 (ongoing)
NCT00995878	The FIRSTT Study: Comparing Focused Ultrasound and Uterine Artery Embolization for Uterine Fibroids	180	Dec 2017
NCT02884960a	Safety and Efficacy of Embosphere® Microspheres for Uterine Fibroid Embolization Compared to Embosphere® Microspheres for Symptomatic Relief from Uterine Fibroids	118	Oct 2018
NCT02942537	Single Blinded Randomized Study of Volume Reduction of Uterine Fibroids after Uterine Artery Embolization versus Computer Tomography or Ultrasound Guided Percutaneous Microwave Ablation Evaluated by Magnetic Resonance Imaging	36	Jul 2019
NCT02260752	Comparing Options in Management : Patient-Centered Results for Uterine Fibroids	10,000	Sep 2019
NCT01563783a	The TRUST (Treatment Results of Uterine Sparing Technologies) Study	260	Dec 2020
NCT02163525a	The TRUST (Treatment Results of Uterine Sparing Technologies) U.S.A. Study	300	Dec 2022
Unpublished			
NCT02819609a	Comparing Patient-Centered Outcomes after Treatment for Uterine Fibroids	12,234	Jan 2015 (completed)

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

Summary of Evidence

For individuals who have uterine fibroids who receive transcatheter UAE, the evidence includes randomized controlled trials and systematic reviews. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The majority of studies have compared UAE with hysterectomy and myomectomy and found similar levels of symptoms and quality of life across all treatment groups. Benefits for women undergoing UAE included avoiding surgery and maintaining their uteruses, lower complication rates, and lower blood transfusion rates. However, patients undergoing UAE had higher reintervention rates compared with patients who had surgery. Smaller trials have compared UAE with laparoscopic occlusion and magnetic resonance image guided focused ultrasound surgery. Additional trials with larger sample sizes comparing UAE with these and other uterus-preserving procedures are needed. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have persistent uterine fibroids despite prior uterine artery embolization who receive repeat transcatheter UAE, the evidence includes case series. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. Case series have shown that a high degree of symptom relief is possible after a repeat UAE for uterine fibroids. Moreover, evidence from randomized controlled trials on the safety and efficacy of UAE for initial treatment of uterine fibroids may indicate a benefit for patients in need of repeat procedures for the same indication.

The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have postpartum uterine hemorrhage who receive transcatheter UAE, the evidence includes case series and a systematic review. Relevant outcomes are overall survival, symptoms, and treatment-related morbidity. The systematic review of case series assessing over 1400 women reported success rates of stopping bleeding that ranged from 58% to 98%. Postpartum uterine hemorrhage is an emergency situation with serious potential consequences (ie, maternal mortality). Conducting randomized controlled trials is particularly difficult in this setting and may be unnecessary when there are sufficient uncontrolled data. Though from case series, there is evidence reporting on over 1400 women. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have cervical ectopic pregnancy who receive transcatheter UAE, the evidence includes case series. Relevant outcomes are treatment-related morbidity. Only a few case series with a small number of patients have been published. Additional studies, especially controlled studies comparing UAE with medication or surgery, are needed to assess the safety and efficacy of UAE in patients with cervical ectopic pregnancy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have uterine arteriovenous malformations who receive transcatheter UAE, the evidence includes case reports, case series, and a systematic review. Relevant outcomes are symptoms, and treatment-related morbidity. Only case reports and case series with a small number of patients have been published. A systematic review identified 54 women in 40 studies with uterine arteriovenous malformations treated with UAE. Additional controlled studies comparing UAE with hysterectomy are needed to assess the safety and efficacy of UAE in patients with uterine arteriovenous malformations. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have adenomyosis who receive transcatheter UAE, the evidence includes case series and a systematic review. Relevant outcomes are symptoms, and treatment-related morbidity. A systematic review of case series data found short-term improvement in 83% of patients and long-term improvement in 65% of patients, suggesting possible recurrence of symptoms over time. All studies were case series, which might have been subject to selection and/or observational biases. Additional case series published after the review have reported that patients with greater necrosis of adenomyosis and patients with higher vascularity of lesions may experience higher response rates to UAE. Controlled studies comparing UAE with medication or surgery and studies reporting long-term symptom recurrence rates are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

CLINICAL INPUT FROM PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 3 physician specialty societies and 2 academic medical centers while this policy was under review in 2012. There was a consensus among reviewers that uterine artery embolization (UAE) is medically necessary for treating uterine fibroids and near-consensus agreement that UAE is medically necessary for treating postpartum hemorrhage, particularly for the indications stated in the American College of Obstetricians and Gynecologists Practice Bulletin No. 76 (detailed in the next section). Clinical input was mixed on repeat UAE and UAE for managing the cervical ectopic pregnancy. One reviewer who disagreed that repeat UAE is investigational provided detailed input on clinical situations in which a repeat procedure might be appropriate.

Practice Guidelines and Position Statements

American College of Obstetricians and Gynecologists

In 2014, American College of Obstetricians and Gynecologists (ACOG) reaffirmed its 2008 Practice Bulletin on alternatives to hysterectomy in the management of leiomyomas. This Bulletin (No. 96) contained the following statement on uterine artery embolization (UAE): “Based on long- and short-term outcomes, uterine artery embolization is a safe and effective option for appropriately selected women who wish to retain their uteri.”

In 2013, ACOG issued a committee opinion on the management of acute abnormal uterine bleeding in nonpregnant reproductive aged women.³⁸ This opinion was reaffirmed in 2017. The committee listed UAE among the surgical options for acute abnormal uterine bleeding and stated that the need for surgical treatment, including UAE, is based on the clinical stability of the patient, the severity of bleeding, contraindications to medical management, the patient’s lack of response to medical management, and the underlying medical condition of the patient.

In 2015, ACOG reaffirmed Practice Bulletin (No. 76) on the management of postpartum hemorrhage. The bulletin stated that UAE might be indicated under the following circumstances:

“A patient with stable vital signs and persistent bleeding, especially if the rate of loss is not excessive, may be a candidate for arterial embolization. Radiographic identification of bleeding vessels allows embolization with Gelfoam, coils, or glue. Balloon occlusion is also a technique used in such circumstances. Embolization can be used for bleeding that continues after hysterectomy or can be used as an alternative to hysterectomy to preserve fertility.”

Society of Obstetricians and Gynecologists of Canada

In 2015, the Society of Obstetricians and Gynecologists of Canada published clinical guidelines on management of uterine leiomyomas. The guidelines stated: “Of the conservative interventional treatments currently available, uterine artery embolization has the longest track record and has been shown to be effective in properly selected patients.”

Society of Interventional Radiology

The 2010 (reviewed and unchanged in 2014) quality improvement guidelines from the Society of Interventional Radiology stated that UAE is indicated in women with uterine leiomyomas that are causing significant symptoms. Absolute contraindications to UAE included a viable pregnancy, active infection, and suspected uterine, cervical, or adnexal malignancy (unless the procedure is being performed for palliation or in conjunction with surgery). A desire to maintain fertility was deemed a relative contraindication.

U.S. Preventive Services Task Force Recommendations:

Not applicable

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

VI. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii's Patients' Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA's determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

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