Uterine Artery Embolization Treatment for Adenomyosis

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For symptomatic patients with adenomyosis, a variety of treatment options are available based on the patient's age, physical and psychological needs, and traditional treatment methods. These treatments include surgical removal, subtotal hysterectomy, or total hysterectomy. However, the surgical removal of adenomyosis is difficult and not satisfactory for diffuse adenomyosis; thus, it is not often performed. Adenomyosis also increasingly begins at a younger age of onset, and there is a need to retain the uterus. In addition to the above surgical treatment, oral contraceptives, Mirena (LNG-IUS), gonadotropin-releasing hormone agonist (GnRH-a), and other conservative treatments are also options for managing adenomyosis. The poor compliance of long-term oral contraceptives, the irregular vaginal bleeding after LNG-IUS, and menopausal symptoms of the expensive GnRH-a contribute to the short-term use of these methods. Therefore, for patients who require treatment for their symptoms, but unwilling to undergo surgical treatment because they are afraid of surgery or have other reasons not to undergo surgery (such as medical and surgical contraindications or religious beliefs), there is a choice of uterine artery embolization (UAE) method. This interventional embolization technology has a history of nearly 20 years and has achieved satisfactory clinical efficacy [1]. Its advantages are the preservation of the uterus, easy operation, quick recovery after surgery, and few postoperative complications. Therefore it has become one of the effective alternatives in the treatment of symptomatic adenomyosis.

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12.1 The Principle of UAE Treatment of Adenomyosis

Adenomyosis is the invasion of the glandular into the uterine myometrium from the basal layer of the endometrium, causing diffuse or focal hyperplasia of the surrounding smooth muscle and fibrous connective tissue. These lesions have a rich neovascular network and poor tolerance to ischemia and hypoxia. However, the surrounding normal uterine tissue has a rich vascular communication network and a strong tolerance to ischemia and hypoxia. Therefore after bilateral uterine arteries are embolized, the vascular network and the blood supply to the adenomyosis are blocked. Thus it can result in ischemic necrosis of the lesion, which will then be dissolved and absorbed. Finally, the adenomyosis reduces in sizes or even disappears. In term, it can effectively reduce the amount of menstrual bleeding, to achieve the purpose of relieving the heavy bleeding.

12.2 Indications and Contraindications of UAE

12.2.1 Indications of UAE

1. The patient is willing to receive UAE treatment and understand the possible complications.
2. Symptomatic adenomyosis without fertility requirements, including dysmenorrhea and excessive menstruation.
3. Patients with adenomyosis who have failed non-surgical treatment, refused surgery, or have multiple previous surgeries, which are difficult to achieve a good result in repeat surgical treatment.
4. Patients with pelvic endometriosis (including ovarian endometriosis cysts) should be informed that UAE is not effective for the above diseases. If the patient fully understands and requests, UAE can be used to treat uterine adenomyosis, combined with laparoscopic treatment of pelvic endometriosis (including ovarian endometrioma).
5. For patients with symptomatic adenomyosis with fertility requirements, the use of UAE should be with caution; if patients strongly require UAE treatment, they must be informed that UAE may cause ovarian or endometrial necrosis, resulting in secondary infertility. Even though it is rare, it may still happen.
6. In patients with recurrence of adenomyosis after UAE, 3-D digital CT angiography may indicate that the blocked uterine artery has been reopened. If the blood supply of the lesion does not come from the ovarian source, the patient may undergo a second UAE treatment.

12.2.2 The Contraindications for UAE [2]

1. Complicated urogenital system infection.
2. Coexistence of known or suspected gynecological malignancies.

3. General contraindications for interventional embolization, such as a recent history of stroke, contrast agent allergy, skin infection at the puncture point, renal insufficiency, or severe immune suppression of the body.
4. Digital 3-D reconstruction by CT angiography suggests that the blood supply of the adenomyosis lesions is mainly from bilateral ovarian arteries.

12.3 Preoperative Assessment and Examination

1. Medical history and evaluation: A patient for UAE surgery needs a comprehensive evaluation, including a detailed gynecological history, such as menstrual history, previous pregnancy, birth planning, gynecological diseases, and previous pelvic surgery, and medical history to identify various comorbidities, such as diabetes, high blood pressure, taking anticoagulants, etc. It is necessary to fully inform the patient and sign the informed consent of the operation for her to understand the advantages and disadvantages of the UAE treatment, the expected effect, and potential complications.
2. Evaluation of dysmenorrhea:The visual analog scale (VAS) of pain and chronic pain rating scale are used to evaluate the degree of dysmenorrhea in patients with adenomyosis. The VAS pain score is mainly a score for the patient's last dysmenorrhea. The chronic pain rating scale is mainly used to score the degree of dysmenorrhea in the past 6 months and its impact on life and daily activities [3].
3. Evaluation of menstrual flow: Heavy menstrual flow refers to menstrual volume > 80 ml per cycle (equivalent to more than 20 sanitary napkins). Scanty menstrual flow refers to menstrual volume < 5 ml per cycle (less than one sanitary napkin).
4. In addition to routine examinations, such as blood routine, coagulation function, liver and kidney function, and electrocardiogram, it is recommended that patients undergo sex hormone level testing on days two to four before menstruation to assess ovarian function. Blood levels of CA125 are recommended before and after treatment. Before surgery, for patients with the large uterus (such as more than 3 months of pregnancy) or medical complications, such as obesity, diabetes, and hypertension, if any of them is at risk of thrombosis, it is recommended to perform a Doppler venous ultrasound examination of both lower extremities to assess the presence or absence of thrombosis before surgery.
5. Imaging assessment: MRI examination is currently the most accurate assessment method. MRI examination can provide better spatial resolution and contrast resolution and is not affected by sound and shadow. It can accurately assess the size, location, and the number of lesions. It can be used as one of the effective differential diagnosis methods of adenomyosis and uterine fibroids [4, 5]. Ultrasound examination is an acceptable alternative method, which has the advantage of being cheap. Depending on the size of the uterus, transabdominal and transvaginal B-ultrasound examinations are sometimes required for evaluation. CT can clearly show the condition of pelvic blood vessels at all levels. Compared with

the invasiveness and lag of digital subtraction angiography (DSA), CT angiography combined with digital 3-D reconstruction technology can evaluate the source of the blood supply artery of adenomyosis before operation to plan the surgical approach and reduce the blindness of the operation, which can improve the success rate of the operation [6, 7]. It can also effectively classify the type of blood supply to the adenomyosis:

Based on the degree of bilateral uterine artery blood supply to the adenomyosis, it is divided into (a) bilateral balanced type of uterine artery blood supply, (b) unilateral main type of uterine artery blood supply, and (c) only one side uterine artery blood supply.

Based on the degree of vascularization of the lesion, the lesion is divided into (a) rich blood flow type, (b) general blood flow type, and (c) non-rich blood flow type or scanty blood flow type.

According to the above characteristics of blood supply, the selection, distribution, and quantification of the embolic agent specifications can be guided to fully embolize the vascular network of the adenomyosis lesion. Therefore, assessing whether the blood supply of adenomyosis lesion is abundant and the source of blood supply to the adenomyosis before surgery, one can predict the efficacy of UAE treatment of adenomyosis. It is recommended that qualified hospitals perform digital 3-D reconstruction of CT angiography before UAE to clarify the blood supply artery and blood supply type of adenomyosis lesions to assist in screening patients suitable for UAE and guide the operation [8].

12.4 Operation Procedure of UAE

After the successful arterial puncture procedure, arteriography is performed first to determine the structure and distribution of the abdominal pelvic blood vessels and to assess the vascular network and to see whether there is a variation in the blood supply to the lesion.

1. The choice of embolizing agent: UAE can choose from many embolizing agents. Generally, granular embolizing agents are selected. They can be divided into absorbable and non-absorbable. The absorbable embolizing agent is sodium alginate microsphere particles (KMG), and the non-absorbable embolic agent is represented by polyvinyl alcohol (PVA). The other embolic agents commonly used for other organs, such as steel rings, absolute ethanol, and ultra-liquid lipiodol, are not recommended for use in UAE. The choice of the particle size of the embolizing agent: the particle diameter of the embolizing agent is mainly 500–700 μm, and some can also be selected from 300–500 μm or 700–900 μm. In adenomyosis, the internal vascular network is relatively small, and the outer vascular network is not obvious. In order to achieve a better embolization effect, a smaller particle embolization agent can be appropriately selected. The effect of arterial embolization is inversely proportional to the particle size of the embolizing agent.

2. Degree of embolism: Embolism is divided into two types: complete embolism and incomplete embolism. Incomplete embolism is based on blocking as much of the vascular network of the lesion as possible, without embolizing the normal vascular network of the uterus. The CT DSA imaging will show a complete or partial disappearance of the vascular network of the adenomyosis. The complete embolization requires that as much as possible, the embolization agent is released into the uterine artery and its branches that supply blood to the adenomyosis and the vascular network of the adenomyosis to be all blocked. In DSA, the imaging showed that the vascularity of the adenomyosis is completely disappeared, and the main uterine artery only partially appears or not appear at all. In order to obtain better clinical efficacy, adenomyosis must be a complete embolism.
3. Intraoperative medication: Patients with adenomyosis may also have associated with hidden endometritis due to long-term menorrhagia. Therefore, antibiotics may be used to prevent infection in UAE surgery when it is necessary.

12.5 Postoperative Treatment of UAE

The arterial puncture point can be compressed to stop the bleeding, and the puncture point can be bandaged with elastic tape, and the lower extremity must be immobilized for 6–12 hours; if a blood vessel clip is used, the immobilization duration can be shortened, and the patient can get out of the bed earlier. Observe the color and skin temperature of both lower extremities after the operation, and mark the pulsating of the dorsal arteries of the foot. Observe regularly to prevent thrombosis. Postoperative antibiotics are not routinely used.

12.6 Complications of UAE

1. Intraoperative complications:
   (a) Local bleeding or hematoma: Hemorrhage or hematoma at the puncture site is a relatively common complication, mostly manifested as subcutaneous swelling at the puncture site, but severe cases can cause a large pelvic retroperitoneal hematoma. After the elimination of coagulation defects before surgery, it can be treated by compression and hemostasis.
   (b) Arterial spasm: During the operation, the guidewire repeatedly stimulates the blood vessel, especially in a long operation, which may cause arterial spasm, resulting in leg numbness and pain during the operation, and it will then affect the operation. Analgesic drugs can be used to relieve pain, and intra-arterial injection of 2% lidocaine 5 ml is used to reduce the pain stimulation at the wound.
   (c) Arterial puncture injury: Arterial puncture injury during operation is rare. However, because the pelvic artery is located in the retroperitoneal space, once the artery is punctured, it will be difficult to compress it for hemostasis, resulting in a large retroperitoneal hematoma. The bleeding will threaten the

life of the patient; an emergency laparotomy is needed to stop the bleeding. Therefore, the UAE procedure should be performed with care and gentleness, and the direction of the blood vessel path should be recognized, following the direction of no or minimal resistance when resistance is encountered.

2. Postoperative complications:
   (a) Pain: Almost all patients will experience pain after surgery. It is currently believed that pain is related to ischemia of the adenomyosis lesion and the uterus after UAE. The degree of pain varies from mild to severe colic. The analgesic method depends on the severity of the pain, and non-steroidal anti-inflammatory drugs, self-controlled analgesia, and opioids orally or parenterally can be selected. The duration of the pain varies, and it is gradually relieved 2–5 days after surgery. If the pain is more than 1 week and is more severe, alert should be raised to the possibility of serious complications, such as secondary infection and accidental thrombosis.
   (b) Post-embolism syndrome: Post-embolism syndrome manifests as pelvic pain, nausea, vomiting, fever, fatigue, myalgia, discomfort, and leukocytosis. Most occurred within 24 hours after surgery and gradually improved within 7 days. It is a common postoperative complication. Postoperative fever is generally not higher than 38 °C, as postoperative heat absorption usually does not require antibiotic treatment.
   (c) Thrombosis: it is divided into arterial and venous thrombosis. Arterial thrombosis is mainly caused by excessive compression of the puncture point or embolization by the embolization agent, etc., which causes ischemic necrosis of tissues, organs, and limbs. Prompt discovery is especially important, and pulsations of the dorsalis pedis artery should be monitored every 30 minutes after surgery. If there is thrombosis or embolism, it is necessary to balance the risk of thrombolysis and secondary bleeding. Relevant departments in the hospital should be consulted and prepare for thrombus removal. Venous thrombosis mostly forms in the lower limb, and it occurs after postoperative immobilization of the legs or bed rest. The presentation is manifested as lower limb swelling, skin color changes, and skin temperature changes; after thrombosis, if emboli fall off, which can lead to serious life-threatening complications, such as pulmonary embolism and cerebral embolism, resuscitation needs to be urgently available.
   (d) Arterial rupture or dissection: As a serious complication, surgical repair is required.
   (e) Mis-embolized other blood vessels: Because the anterior branch of the internal iliac artery not only branch out the uterine artery, it also has the vesical artery, vaginal artery, internal pudendal arteries, etc. When other pelvic arteries are mistakenly embolized, large and small labial necrosis, bladder necrosis, and other complications may occur.
   (f) Infection: The operation of UAE involves only a type I incision. Wound infection is relatively rare. Inflammation is mainly due to necrosis of the lesion after embolization, resulting in aseptic inflammation. However, the infection can be due to communication between the uterine cavity and the

outside world via the cervix and vagina. Poor hygienic care can cause uterine cavity infection, leading to endometritis, pyometra, salpingitis, tubal ovarian abscess, or secondary infection of the lesion. At this time, antibiotic treatment is often effective. If it is necessary, surgical drainage or uterine excision is required, and in severe cases, fatal sepsis can occur. The long-term sequel of infection may also result in intrauterine adhesions and infertility.

(g) Allergic reaction or rash: anti-allergic treatment may be given.

(h) Vaginal discharge: Some patients will have persistent vaginal bloody discharge after surgery, usually within 2 weeks, and very few may last for several months. Short-term vaginal discharge is common.

(i) Menorrhagia: Some patients have partial endometrial necrosis after embolization of the uterine artery vascular network, and there may be a significant decrease in menstrual flow, but no obvious hormonal abnormalities are seen. If there are no fertility requirements, follow up observation is not necessary.

(j) Amenorrhea: a long-term complication of UAE is treatment-induced amenorrhea. Ovarian amenorrhea is mainly due to the cessation of blood supply to the ovary, because sometimes the uterine artery gives rise to an ovarian branch in which blood flow is blocked by UAE, resulting in ischemic necrosis of the ovary, ovarian failure, and amenorrhea. Long-term hormone replacement therapy may be required to maintain the level of hormones in the body. Uterine amenorrhea is caused by extensive ischemic necrosis of the endometrium, and the growth of the endometrium is impaired. It does not affect hormone secretion and can be observed, but the patient may have a fertility problem.

(k) Others: Other serious complications are rare. The incidence of venous thromboembolic complications is about 0.4%. There are also fatal sepses associated with UAE operations, including femoral nerve injury, bilateral iliac artery embolism, ischemic uterine infarction, large and small labial necrosis, local bladder necrosis, bladder and uterine fistula, uterine wall injury, embolism agent spillage leading to both toes, or even rare complications, such as necrosis of the heel. About 2.4%–3.5% of patients need to be admitted to the hospital again, and 1.0%–2.5% of patients need unplanned surgery. However, overall, UAE mortality has not increased compared with hysterectomy [1].

12.7 Follow-Up Time and Efficacy Evaluation after UAE Treatment

1. Follow-up time: After UAE treatment, re-evaluation is required at 1, 3, and 6 months and once a year after that. The contents of the follow-up include changes in the size of the lesion, menstrual conditions, sex hormone levels, and changes in dysmenorrhea and CA125 levels.

2. Evaluation of clinical efficacy: A large number of clinical trial data showed that 98%–100% of patients could tolerate and complete the operation, 85%–94% of patients had improved abnormal vaginal bleeding, and 77%–79% of patients got improvement in dysmenorrhea, and the average uterine volume decreased by 35%–60%. For patients who were followed up for more than 5 years, more than 75% of patients had normal or improved menstrual flow after the operation. The cumulative recurrence rate at 5 years was 10%–15%, which was lower than the recurrence rate of surgical removal. About 20% of patients may require further surgery after UAE, such as hysterectomy, removal of residual adenomyosis, or UAE again, to control the symptoms of adenomyosis.

12.8 Other Issues

1. Effect on ovarian function: It is currently believed that whether the ovarian function is affected is positively related to age. The prevalence of early menopause after UAE for women aged 45 and younger is 2%–3%, while the incidence for women older than 45 can reach 8%. It is considered that the embolization agent enters the ovarian artery along with the blood flow to reduce the ovarian function [9].
2. Pregnancy after UAE: At present, there is no definite conclusion about the safety of pregnancy after the UAE. There are reports of cases of successful pregnancy after UAE and delivery. However, adverse outcomes of pregnancy after UAE, including spontaneous abortion, premature delivery, abnormal placenta, preeclampsia, postpartum hemorrhage, etc., have also been observed, and the rate of cesarean section has also increased. Among them, some of the increased risks are related to the high proportion of women in UAE who are elderly and infertile. In addition, hysteroscopy examination of patients 3–9 months after UAE found that only 40.2% of patients after the UAE had a normal endometrial appearance. Therefore UAE may cause endometrial abnormality that affects pregnancy and its outcomes. Therefore, for women considering future births, UAE should be used with caution in the treatment of adenomyosis [1].
3. Repeat UAE treatment can be performed, but the evidence for these operations is limited. Available data show that 1.8% of patients received UAE treatment again. If the choice is appropriate, 90% of patients can successfully control symptoms after the second UAE operation. Therefore, for patients with recurrent adenomyosis after UAE, it is recommended to perform CT angiography followed by digital 3-D reconstruction to assess the condition of the pelvic vascular network, especially whether the uterine artery is recanalized or whether there are other new blood vessels to supply blood to the lesion to assess whether UAE can be effectively repeated.

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