

Minimally invasive procedures in the management of uterine fibroids

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Abstract

Uterine fibroids are benign uterine tumors. In women during the reproductive period, uterine fibroids occur in about 25%, whereas after this time, they are observed in more than 40% of women. In the majority of women (about 20-50%), such tumors do not cause discomfort and do not require treatment. Asymptomatic uterine fibroids usually undergo only regular medical control, whereas symptomatic fibroids are an indication for treatment. Current treatment methods include surgical, pharmacological and minimally invasive treatment. Among the current commonly used methods, there are minimally invasive treatment options, which include Uterine Artery Embolization (UAE), Magnetic Resonance Guided Ultrasound Surgery (MRgFUS), MR-guided High Intensity Focused Ultrasound (MR-HIFU) and Laparoscopic Uterine Artery Occlusion (LUAO). The minimally invasive Ultrasound-guided High Intensity Focused Ultrasound method (US-HIFU) is new, but still experimental. The use of MRgFUS/MR-HIFU for the thermoablative treatment of fibroids was approved by the FDA (Food and Drug Administration) in 2004. As a minimally invasive method, it enables preservation of the uterus and eliminates the need for general anesthesia. LUAO is based on the use of the vascular clip, which is placed on the uterine artery at the level of the internal iliac artery. This procedure is performed bilaterally.

The use of UAE in obstetrics and gynecology was first described in 1987 as an effective method in the treatment of hemorrhage, which allows avoiding surgical intervention and enables the uterus to be preserved. An appropriate qualification of patients is crucial for high clinical efficacy and prevention of complications after UAE. The candidates should be women with symptomatic uterine fibroids, without other pathologies within the pelvis, who do not plan to get pregnant in the future.

The variety of uterine fibroids as for the location, size, and symptoms they can evoke, has enforced a very individual approach to each patient, to begin with observation and regular gynecological control, through a number of pharmacological and minimally invasive treatment methods, and ending with the removal of the uterus. It gives the doctors the tools, which, if used properly, can manage uterine fibroids and fulfil the expectations of the patient.

Key words: uterine fibroids, minimally invasive procedures, uterine artery embolization, Laparoscopic Uterine Artery Occlusion, MR-guided High Intensity Focused Ultrasound.

Introduction

Uterine fibroids are common benign monoclonal tumors of the uterine smooth muscle cells, consisting of a large amount of extracellular matrix, which contains collagen, fibronectin and proteoglycans. Fibroids are surrounded by a thin capsule made of fibrous connective tissue, whose fibers create a structure in the form of a network. In women during the reproductive period, uterine fibroids occur in about 25%, whereas after this time, they are observed in more than 40% of women. In the majority of women (about 20-50%), the fibroids do not cause discomfort and do not require treatment [1-4].

The main symptoms of uterine fibroids are heavy menstrual bleeding, abnormal uterine bleeding or compression symptoms. The latter may manifest as pelvic pain, impaired urination and constipation. The

influence of fibroids on female fertility is unclear. The factors impeding pregnancy include gamete transport disorders, uterine cavity distortions and endometrial disorders that hinder blastocyst implantation [5, 6].

Asymptomatic uterine fibroids, usually require only regular medical control, whereas symptomatic fibroids are an indication for treatment. Current treatment methods include surgical, pharmacological and minimally invasive treatment.

Minimally invasive methods in the treatment of uterine fibroids

Among the current commonly used methods, there are minimally invasive methods, which include Uterine Artery Embolization (UAE), Magnetic Resonance Guid-

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ed Focused Ultrasound Surgery (MRgFUS), MR-guided High Intensity Focused Ultrasound (MR-HIFU) and Laparoscopic Uterine Artery Occlusion (LUAO).

The minimally invasive Ultrasound-guided High Intensity Focused Ultrasound (US-HIFU) is new, but still experimental [7].

The use of MRgFUS/MR-HIFU for the thermoablative treatment of fibroids was approved by the FDA (Food and Drug Administration) in 2004. As a minimally invasive method, it enables uterine preservation and eliminates the need for general anesthesia. Magnetic resonance imaging (MRI) allows locating fibroids in real time and monitor the thermoablation of these benign uterine tumors with the use of ultrasound focused directly on the tumor. The evaluation of treatment takes place immediately after the procedure. Contraindications include patients who cannot have MRI scan (patients with a pacemaker or severe obesity), as well as those with extensive scars in the lower abdominal wall, due to the high risk of thermal damage to the skin [8]. In spite of the proper qualification of patients, cases of minor skin burns and a single case of burn of the entire thickness of the abdominal wall were described after MRgFUS/MR-HIFU [9, 10]. This is because during the procedure, high-intensity ultrasound is concentrated within the lesion. This leads to the raise of the target tissue temperature to over 55, and causes coagulative necrosis in the affected tissue area. The development of necrosis is immediate, which distinguishes this procedure from UAE, which causes ischemic necrosis [11].

Several studies of MRgFUS/MR-HIFU use in symptomatic uterine fibroids revealed consistent reduction of observed symptoms within 6 months after treatment. In one of them, 71% of women achieved a reduction of symptoms after a 6-month treatment, and in the majority of women the improvement of the quality of life and return to normal activities were reported [12]. In another study, a reduction in the volume of fibroids was observed by 30-40% in 6 months and by 20-40% in 12 months after the surgery [13].

Laparoscopic occlusion of uterine arteries involves the use of a vascular clip on the uterine artery at the level of the internal iliac artery. This procedure is performed bilaterally. Additionally, the lateral vessels of the ovaries and the uterus (in the proper ligament of the ovary) are coagulated with the use of bipolar forceps. The therapeutic effects obtained after laparoscopic uterine artery occlusion compared to the uterine artery embolization are similar. On the other hand, LUAO involves less pain and shorter hospitalization in comparison to UAE. Yet, more and more women who undergo LUAO are experiencing heavy menstrual bleeding within 6 months, in comparison to the patients treated with UAE [14].

The use of UAE in obstetrics and gynecology was first described in 1987 as an effective method in the

treatment of hemorrhage, which allows avoiding surgical intervention and enables the uterus to be preserved [15]. In the treatment of symptomatic uterine fibroids, this procedure was successfully used in 1994 in France and in the USA three years later [16, 17]. The growing interest in uterus preservation in many women with symptomatic fibroids placed the UAE in the forefront of the minimally invasive methods of fibroid treatment.

An appropriate qualification of patients is crucial for high clinical efficacy and the prevention of complications after UAE. The group of candidates should include women with symptomatic uterine fibroids, without other pathologies within the pelvis, who do not plan to get pregnant in the future. It is necessary to exclude adenomyosis occurring alone or coexisting with fibroids, because the effectiveness of UAE in such cases is limited [18]. The presence of pedunculated subserosal fibroids disqualifies from a surgery due to the risk of necrosis of abdominal changes.

There are many reports about successful pregnancy after UAE, but the existing evidence does not fully justify the use of this method as an alternative to pharmacological therapy or surgery (myomectomy) in women at an early age. This procedure should be used cautiously in women that declare the desire to get pregnant [2].

Patients qualified for UAE surgery are consulted by gynecologists and interventional radiologists. From the radiological side, the MRI examination determines the technical possibilities of the procedure. The gynecological qualification includes medical history, examination, ultrasound assessment of the reproductive organs and the type of fibroid. Furthermore, in order to exclude any ongoing neoplastic processes within the uterus, it is necessary to perform a cytological smear and endometrial biopsy. Microbiological examination of vaginal smear and the determination of the level of sex hormones allows assessing and avoiding potential post-medical complications (infections, iatrogenic damage to the ovaries) [2, 19].

Embolization of uterine arteries is performed by interventional radiologists under the control of digital angiography and involves the introduction of a vascular catheter from an injection in the area of the groin into the femoral artery, the aorta, the internal iliac artery and finally to the uterine artery. After placing the catheter deep in the uterine artery, the vessel is closed with polyvinyl alcohol (PVA, 500-710 μm) molecules. Embolization is continued until the blood flow in the vessel is completely blocked. The procedure lasts about 1 to 1.5 hours [2]. Most fibroids are vascularized by the uterine arteries. Additionally, 5 to 10% of fibroids are supplied by the ovarian arteries. Anastomoses between the uterine arteries occur in about 10% of cases, while between uterine and ovarian arteries in 10-30%.

The vascularization of fibroids is in the form of a dense plexus located circumferentially, whereas the

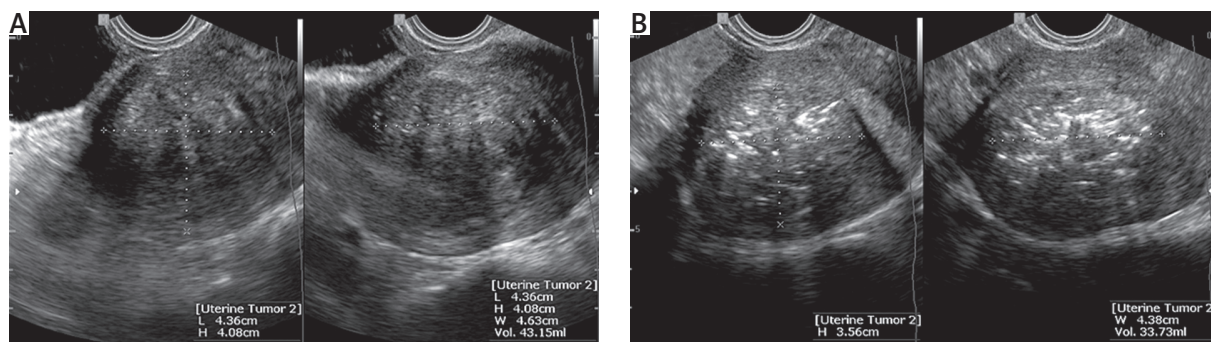


Fig. 1. Fibroid volume measured by ultrasound before (A) and 3 months after (B) uterine artery embolization. In this case fibroid volume decreased by 24%, from the initial 43 cm³ to 33 cm³ at 3 months follow-up. Additionally, due to ischemic necrosis, the fibroid tissue became hyperechogenic

lesion is most often avascular [20]. The lack of vascularization of these uterine tumors leads to ischemic necrosis within the embolized tissues, which consequently can lead to hyaline degeneration or coagulative necrosis. This process develops within a few months [21, 22].

The effectiveness of UAE is determined by the degree of improvement or resolution of symptoms. Clinical efficacy index for this procedure in the treatment of excessive menstrual bleeding, pelvic pain and pressure symptoms associated with tumor mass are located in the following ranges: 81-96%, 70-100% and 46-100%. A 25-60% reduction in uterine volume was observed within 3 to 6 months after the procedure [23, 24]. An example of fibroid volume measurements before and 3 months after UAE is shown on Fig. 1. The reduction of fibroids volume does not always reflect the improvement of clinical symptoms. In a long-term (up to 5 years) follow-up after UAE, in over 70% of patients there was a significant improvement in the quality of life, while 16-23% of the patients required another intervention [25, 26]. During the first week after UAE, approximately 10 to 15% of patients experienced the symptoms of a post-embolization syndrome, which is characterized by the occurrence of nausea, vomiting, malaise, subfebrile states, abdominal pain and elevated levels of leukocytes. Post-embolization pain, occurring in the first hours after surgery, is caused by the release of products of the ischemic fibroid tissue breakdown and requires intense analgesic treatment [17]. It is important to differentiate the symptoms of the post-embolization syndrome from more serious complications, i.e. sepsis. The treatment includes adequate pain control, hydration and possible antibiotic therapy.

Infection is potentially the most serious complication after UAE [27]. If the fever persists for 24 up to 48 hours after the procedure, sepsis may be suspected. In this case, the treatment requires the use of antibiotics, but also the need to remove the uterus. In the latter case, in less than 1% of cases, it might be life-threatening for the patient. Sepsis is more frequent when UAE is performed on large uteri (over 20 cm or

when the diameter of a single fibroid is greater than 9 cm, and in the case of coexistence of large submucosal fibroids) [2]. Another complication occurring after the embolization of submucosal fibroids is the expulsion of demarcated, necrotic pieces of fibroids through the cervical canal. This occurs in about 5% of cases [28]. In about 4% of women after UAE for a period of several weeks to many months, the abundant vaginal secretion can persist, resulting from the excretion of necrotic uterine fibroid tissue [24]. There are also complications connected with the angiography procedure itself, such as the occurrence of hematoma or infection in the place of catheter introduction, allergic reactions to contrast agents and damages to blood vessels. These complications occur in less than 1% of cases [27].

There are also reports on the nontarget embolization of other pelvic organs. This complication occurs as a result of the presence of anastomosis and variability of blood vessels. A special case of "nontarget embolization" is the post-embolization damage of the ovaries in patients undergoing this procedure, which is due to the presence of anastomoses between the vessels of the uterus and ovaries, but also the ingress of embolic material into the uterine branch of the uterine artery [18, 20, 28].

After UAE, a significant shortening and decrease of the amount of menstrual bleeding can be observed, which is considered a beneficial effect of this procedure. However, the total lack of menstruation, in many studies is given as the effect of post-embolization ovarian failure [29, 30].

The absence of menstruation after UAE is usually transient and limited to several cycles. The constant lack of menstruation occurs in about 15% of women over 45 years of age and in about 1% of women below this age, evoking the symptoms of premature menopause [31]. Currently, UAE is widely used in the United States of America and in Western Europe. This treatment is also recommended by NICE (UK's National Institute for Health and Clinical Excellence) as an alternative to hysterectomy [32].

Conclusions

The variety of uterine fibroids as for the location, size, and symptoms they can evoke has enforced a very individual approach to each patient, to begin with observation and regular gynecological control, through a number of methods of pharmacological and minimally invasive treatment, and ending with the removal of the uterus. It provides the doctors with tools, which if used properly, can solve the problem of uterine fibroids and fulfil the expectations of individual patients.

Disclosure

Authors report no conflict of interest.

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