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Review Article

Possibilities for Treating Adenomyosis with Minimally Invasive Procedures

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Abstract

The benign condition known as adenomyosis is brought on by the invasion of the myometrium by endometrial glands and stroma. It is a prevalent gynaecological condition that affects women who are fertile. 15 - 25% of women who are of reproductive age are thought to be affected. It is a crippling condition that affects young women who are nulliparous and multiparous, resulting in a range of symptoms like infertility, dysmenorrhea, and menorrhagia.

The conservative treatment of adenomyosis is becoming more popular these days. It has been treated up to this point with either a hysterectomy or local adenomyoma excision that preserves the uterus. These days, three thermal ablation methods-HIFU (high-intensity focused ultrasound), RFA (radio frequency ablation), and PMWA (percutaneous microwave ablation)-are suggested for the treatment of adenomyosis. Pregnancy outcomes were not significantly different between non-surgical (HIFU, RFA, PMWA) and surgical excision, according to a small number of studies.

Keywords: *Adenomyosis; HIFU (High-Intensity Focused Ultrasound); RFA (Radio Frequency Ablation); PMWA (Percutaneous Microwave Ablation)*

Introduction

The therapeutic approach to adenomyosis has advanced significantly, shifting from extremely invasive operations to less invasive interventions, as seen by these developments. According to Bird., *et al*. [1], adenomyosis is characterised by the benign invasion of endometrium into myometrium, which results in a diffusely enlarged uterus with ectopic, non-neoplastic endometrial glands surrounded by hypertrophic hyperplasia musculature under a microscope.

Infertility, uterine enlargement, menorrhagia, and dysmenorrhea are the primary clinical manifestations of adenomyosis [2]. Anaemia from menorrhagia lowers women's quality of life. Preterm delivery, IUGR, and pregnancy-induced hypertension are among the pregnancy difficulties and infertility it may cause.

It is now known that nulliparous younger women are also impacted, in addition to older multiparous women [3]. Although the specific cause of adenomyosis is unknown, several theories have been put forth to explain it. Among these are frequent deliveries, intense curettage, and high oestrogen levels that result in endometrial hyperplasia. Another theory is that the endometrial tissue invaginated into the myometrium as a result of repetitive micro-trauma to the endometrial basal lamination caused by strong uterine contractions

during menstruation. This process, which is brought on by inflammation, local estrogen production, epigenetic modifications, and somatic mutations, is referred to as endomyometrial interface disruption.

Additional theories include the expansion of peritoneal pelvic endometriosis into the myometrium, differentiation of embryonic stem or progenitor cells, and metaplasia of the embryonic remnant. Increased internal OS stiffness has also been suggested as a possible reason, as it may restrict menstrual flow, which raises myometrial contractility and ultimately leads to endometrial invasion of the myometrium [4,5].

Focal and diffuse adenomyosis are the two primary forms of the condition. It is referred to as focal when the lesions are localised and diffuse when the endometrial glands and stroma are scattered throughout the myometrium. Kishi., *et al*. [6] have now provided the most thorough and widely used model for classifying adenomyosis. It separates adenomyosis into [subtype 1] as intrinsic adenomyosis. It impacts the junctional zone, which is the innermost layer of the uterus. Subtype ii of extrinsic adenomyosis penetrates the uterus' outer layer, Intramural adenomyosis [subtype iii] is contained inside the uterus's intact muscular framework. The diffuse form of indeterminate adenomyosis [subtype iv] is hard to classify because it does not fall into any of the other three categories.

Increased uterine and uterine cavity size, coupled endometrial hyperplasia, and insufficient uterine contraction are the causes of profuse bleeding in adenomyosis.

Adenomyosis-related dysmenorrhea progresses over time, and colicky pain results from irregular myometrial contractions. Adenomyosis is diagnosed by MRI, transvaginal ultrasound, pelvic examination, and clinical signs and symptoms.

With the advent of transvaginal ultrasound and magnetic resonance imaging (MRI), adenomyosis can now be accurately diagnosed, which is essential for determining the best course of treatment. Due to its ease of use, dependability, and accessibility, transvaginal ultrasonography is used as the first-line diagnostic method for adenomyosis. Adenomyosis is diagnosed using MRI as a second-line modality.

Although adenomyosis has been classified into a number of subgroups based on imaging and histological findings, there is still disagreement about which should be applied consistently. In order to describe and report the sonographic aspects of adenomyosis, a panel of experts known as MUSA (Morphological Uterus Sonographic Assessment) came to an agreement in 2015 about terminology, definitions, and measurements. 2019 saw further refinement of these criteria, which separated the signs of adenomyosis into INDIRECT signs, such as globular uterus, asymmetric myometrial thickening, fan-shaped shadowing, translational vascularity, irregular junctional zones, and interrupted junctional zones, and DIRECT SIGNS, such as myometrial cysts, hyper echogenic islands, and echogenic subendometrial lines and buds [7].

Currently, surgery is the primary therapeutic option for adenomyosis. Although hysterectomy is seen as a curative treatment, it is intrusive and unreliable for women who wish to keep their ability to procreate. Adenomyomectomy, or local conservative surgical removal of the affected uterine portion, is the conservative surgical approach. Gonadotropin-releasing hormone analogues (GnRHa), levonorgestrel-releasing intrauterine systems (LNG-IUS), and contraceptive pills are examples of medical management [8]. Minimally invasive and noninvasive treatments with a focus on uterine conservation have gained popularity in recent years. Uterine artery embolization (UAE), high-intensity focused ultrasound (HIFU), and microwave ablation (MWA) are examples of minimally invasive procedures.

Image-guided thermal ablation and less invasive surgical methods are now showing promise in addressing symptomatic adenomyosis, surpassing the options of hysterectomy and fertility-preserving surgical treatments. By using concentrated ultrasonic energy externally:

HIFU, or high-intensity focused ultrasound:

- HIFU, or high-intensity focused ultrasound, thermally ablates adenomyosis lesions beneath the skin without causing surface damage. This method of thermal ablation is noninvasive.

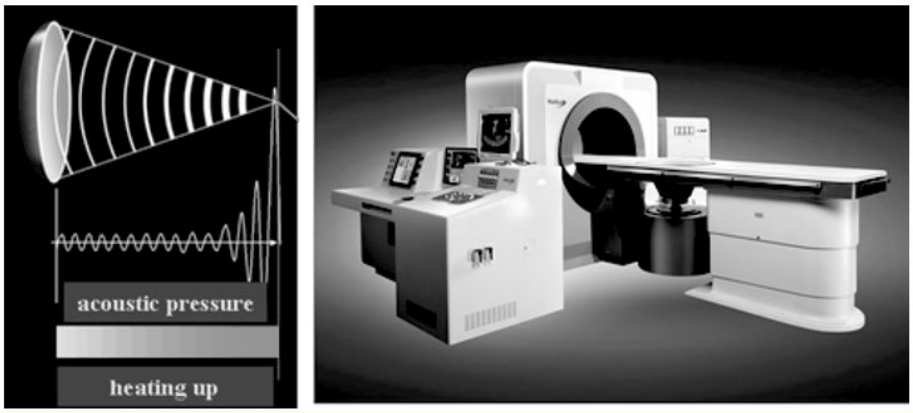

Figure 1

- The ultrasonic beam in this is produced by a concave extracorporeal transducer. This beam, which is directed by MRI or ultrasound, has a thermal, mechanical, and tissue-cavitation effect on the target area.
- When using HIFU, ultrasonic beams are steered to specific body parts after entering the tissues acoustically. An inexpensive and readily accessible alternative for real-time anatomic imaging, ultrasound is also useful for tracking how well a treatment is working. Similar applications are also served by MRI-guided high-frequency ultrasound, which offers high-resolution anatomical features and the benefit of real-time temperature mapping.
- Any obstruction to the ultrasound beam, such as severe abdominal scarring from prior surgeries, an abdominal wall thickness greater than 5 cm, the presence of foreign material, or an interposed bowel segment because of adhesions, may hinder the effectiveness of HIFU treatment [9].
- Suboptimal ablation results from restricted ultrasonic wave penetration if the lesions are on the posterior uterine wall.
- The SOGC clinical practice guidelines mention HIFU and the Asian Society of Endometriosis and Adenomyosis guidelines support it (poor level of evidence, conditional recommendation) [10].
- With HIFU, no significant treatment side effects are observed; nevertheless, a 2 - 8% frequency of minor side effects is reported. The most frequent post-HIFU symptoms include vaginal discharge, lower abdomen pain, superficial skin burns, and pain and discomfort at the treatment site. Leg discomfort, intestinal perforation, and deeper skin burns are less common side effects.
- Due to denervated tissues and resulting skin sensory loss, patients with abdominal surgical scars have been found to experience a higher frequency of skin burns. By providing enough intestinal preparation, bowel damage can be prevented.
- In terms of fertility, HIFU does not impact ovarian reserve and yields better results in terms of post-treatment conception and subsequent risk of uterine rupture. In this case, it can be concluded that HIFU is a safe and efficient therapy option for lowering adenomyosis symptoms, such as menorrhagia and dysmenorrhea, and that it is a better therapeutic alternative than local excision of adenomyoma in infertile patients, leading to greater rates of conception and live births.

- After HIFU treatment, there is a considerable decrease in the volume of the uterus and the adenomyoma lesion. For patients with severe preoperative dysmenorrhea, it offers significant relief. Patients with increased wall thickness lesions on the posterior uterine wall and lesions with an abundant blood supply have experienced issues when utilizing HIFU [11].
- Compared to anterior wall lesions, posterior wall lesions are less ablated because thermal energy may find it more difficult to reach the lesion because of its greater distance.
- The uterine position, the volume and vascularization of the adenomyotic lesion, the lesion's distance, and the thickness of the abdominal wall-ideally less than 1 cm-all affect the viability and effectiveness of HIFU.

Radiofrequency ablation, or RFA: The process of radiofrequency ablation, or RFA:

- It entails placing electrodes straight into the lesion while being guided by ultrasound. Either laparoscopic or USG guidance is used for this implantation. Under transvaginal or integrated intrauterine USG supervision, it can also be implanted transcervically.

Figure 2

- RFA produces tissue necrosis by using high-frequency alternating electrical current, which produces heat through ionic friction.
- This generator successfully lowers the temperature below 100 degrees Celsius to avoid charring tissues; this preserves the tissue's cellular structure while causing thermal fixation and coagulative necrosis [12,13].
- RFA is effectively used to treat menorrhagia, dysmenorrhea, and issues associated with adenomyosis, including persistent anemia.
- By avoiding abdominal incision, uterine scars and bleeding, and needless tissue removal, RFA offers a less invasive option for preserving the uterus and has an advantage over surgery in terms of fertility. This can reduce complications, such as uterine rupture during a subsequent pregnancy.
- RFA's sole disadvantage is its incapacity to truly monitor the temperature settings after the probe has been implanted; this could result in intrauterine adhesions and endometrial thermal damage, which is detrimental for individuals who want to preserve their fertility.
- Abdominal pain, vaginal discharge, and temporary fever are the most commonly reported side effects of RFA, which is generally thought to be a safe thermal ablation method.

- The Asian Society of Endometriosis and Adenomyosis guidelines make reference to RFA. A retrospective research evaluating the midterm outcomes of transvaginal RFA for the treatment of symptomatic uterine adenomyosis was conducted by Hai., *et al*. At one, six, and twelve months of follow-up, they discovered noteworthy uterine volume reduction rates of 35%, 40%, and 41%, respectively; dysmenorrhea and other symptoms have been significantly decreased.

PMWA (Percutaneous microwave ablation): The most modern thermal ablation technique, known as PMWA (Percutaneous microwave ablation):

- It uses electromagnetic microwaves to cause heat and coagulative necrosis in tissue, which causes the organ to shrink and relieves associated symptoms [14].

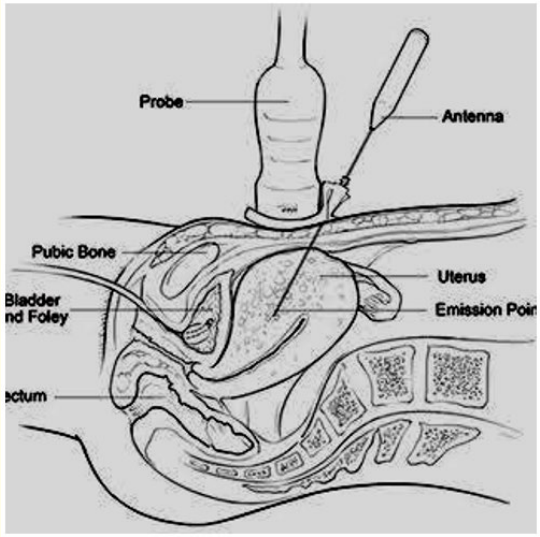

Figure 3

- In PMWA, heat is produced by quickly rotating adjacent water molecules using electromagnetic radiation. The percutaneous insertion of an electrode into the lesion under ultrasound guidance is essential to its operation.
- Procedure: The ablutions are carried out in a supine position while under general anaesthesia. There is a thermosphere-equipped ablation generator with thirteen gauze antennae. This generator has an output power range of 5 to 100 watts and runs at a frequency of 2.45 GHz ± 50 MHz. Imaging and needle guidance require a high-quality ultrasound machine. The effect of PMWA on adenomyosis can be assessed by contrast-enhanced ultrasonography and dynamic contrast-enhanced MRI; contrast-enhanced ultrasonography allows for the dynamic, real-time observation of PMWA's influence on localised adenomyosis. Before and right after MWA, 2-4 cc of SonoVue injection is used to increase contrast for sonography. A skin incision the size of the microwave antenna's tip must be made on the skin if the percutaneous approach is being employed. Since the needle is entered through the vagina's anterior or posterior fornix, there is no need to make an incision on the vagina if the vaginal route is utilised. The shortest path must be selected for microwave ablation. Additionally, MWA can be performed under laparoscopic guidance. Because microwave ablation can transfer electromagnetic energy through burned, desiccated, or dehydrated tissues, it can produce temperatures that are higher than those produced by HIFU and RFA—often surpassing 100 degrees Celsius.

- The therapeutic implications of PMWA have increased because to technology improvements such cooling systems, antenna arrays, and enhanced delivery methods, which allow for more uniform heat distribution across the target area.
- Numerous clinical studies attest to MWA's substantial impact on fetal uterine adenomyosis, which shrinks the uterus and alleviates menorrhagia and dysmenorrhea symptoms. However, it was also noted that microwave ablation had a poor effect on diffuse adenomyosis and that the incidence of complications was high in this condition. This is because diffuse thickening of the uterus makes it difficult to focus on obvious lesions, and ablation is unable to effectively treat hidden lesions, such as those near the uterine intimal or serial layer, which results in incomplete ablation of the lesion. Therefore, it is advisable to carefully consider the application of MWA based on the particulars of each instance before proceeding, and to choose a customised ablation technique.
- A number of variables, including the patient's age and the ablation rate, affect how well microwave ablation works to treat adenomyosis. Less energy is needed for a lesion of the same size in older patients because their oestrogen levels are lower than those of younger patients.
- Skin burns or scalds, local pain, nerve damage, vaginal discharge, and infection are among the frequent side effects of microwave ablation. significant issues. include bladder damage, intestinal perforation, intestinal blockage, and occasionally intestinal haemorrhage. Few studies demonstrate that when laparoscopy and ablation technologies are used together, critical organs including the intestine and pelvic vasculature can be avoided during antenna insertion.

Uterine artery embolization (UAE): Uterine artery embolization (UAE) is an angiographic technique in which ischemia necrosis in the adenomyotic lesion is caused by injecting embolic substances into the uterine arteries.

- This is done under sedation and local aesthetic and requires access through the groin area. By specifically blocking the blood supply tissue, UAE provides focused treatment that causes tissue necrosis, ischemia, and hypoxia with little impact on neighbouring tissues [15].

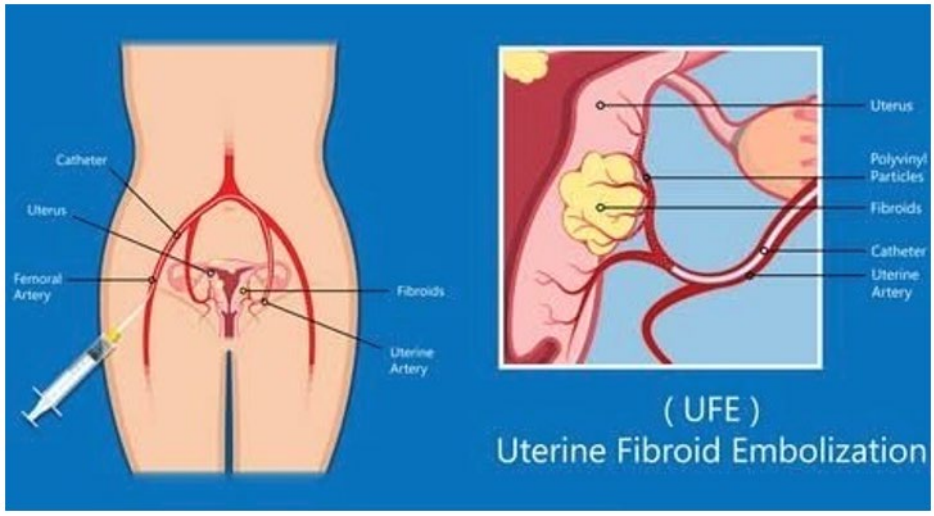

Figure 4

- Following its success in treating uterine fibroids, this therapy approach has been investigated recently in the past ten years for the treatment of adenomyosis.
- For the treatment of symptomatic adenomyosis, it is advised by the NICE UK interventional procedure recommendations (level of evidence 2a, grade of recommendation B) and the SOGC clinical guidelines (strong recommendation, intermediate evidence). It is available to patients who wish to keep their uterus intact after they have finished having children.

Multiple microwave endometrial ablation (mMEA)

- This type of microwave ablation, which targets menorrhagia brought on by adenomyosis, can be performed twice or even three times in the same area. Compared to a single MEA, it has a longer operating time [16].
- Research indicates that compared to a single MEA, there is a higher satisfaction rate. Its drawback is that a second ablation raises the possibility of problems, particularly thermal injury to the intestinal region.

Conclusion

The aforementioned ablation techniques are safe, effective, and have a low risk of problems. They also have favourable effects, including a reduction in uterine volume, the shrinkage of adenomyotic lesions, and symptom relief. Regarding safety, these methods have no discernible impact on ovarian function and do not adversely affect fertility. However, the lesion characteristics, patient characteristics, desire to preserve the uterus, fertility, and infrastructure should all be taken into consideration when choosing the best thermal ablative approach. In conclusion, given the unique histological features of adenomyosis, such as increased cellularity and less defined borders, it is necessary to develop adenomyotic-specific parameters to maximise the efficacy while minimising the complications. Currently, their effectiveness in managing adenomyosis-related pain and AUB bleeding is well recognised.

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