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REVIEW

Non-surgical Treatment of Adenomyosis

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Abstract

Purpose of Review Uterine-sparing excisional surgical techniques for adenomyosis are complex, carry significant risks, and after all have substantial recurrence rates. Consequently, there has been a trend towards adopting non-surgical treatments. This narrative review outlines the latest in non-surgical treatments for adenomyosis, highlighting their significance in managing this condition and stresses the importance of further research, especially concerning long-term outcomes and fertility implications.

Recent Findings Emerging evidence suggests that non-surgical techniques for the treatment of adenomyosis offer promising alternatives to traditional uterus-conserving surgery.

Summary LNG-IUS is recommended as the primary management strategy for adenomyosis. In our clinical evaluation, a pretreatment with GnRH-analogs, HIFU, or UAE prior to LNG-IUS insertion in enlarged uteri may mitigate treatment failure risks, notably device expulsion. Concurrently, post-intervention LNG-IUS application post non-surgical modalities can diminish recurrence probability. In large uteri with presence of multiple uterine fibroids, UAE may be preferable compared to thermal ablation procedures especially if there is no wish for pregnancy or comorbidities not allowing for a hysterectomy. For focal adenomyosis, especially when prioritizing fertility preservation, RFA may be considered due to its precise targeting, available data on pregnancy outcomes, and ease of incorporation into gynecological practice. In cases of localized disease of the anterior wall of the uterus without prior surgeries and no suspicion of concurrent endometriosis, HIFU can be favored.

Keywords Adenomyosis · Non-surgical treatment · Uterine artery embolization · Levonorgestrel-releasing intrauterine system · Radiofrequency ablation · High-intensity focused ultrasound

Introduction

Adenomyosis is a chronic, benign disease caused by ectopic endometrial glands and stroma leading to the formation of ill-defined lesions within the myometrium. These lesions can be either focal or diffuse (i.e., dispersed within the uterus) and are accompanied by hypertrophy and proliferation of neighboring myometrial cells.

The main symptoms of adenomyosis are pain (e.g., dysmenorrhea and pelvic pain) and abnormal uterine bleeding (AUB). Adenomyosis can also be associated with infertility and pregnancy complications, such as preterm delivery, intrauterine growth restriction, and pregnancy-induced hypertension [1, 2].

For decades, the key method for diagnosing adenomyosis was histological examination post-hysterectomy, which relied on the detection of endometrial glands and stroma within the myometrium. This reliance on post-surgical diagnosis contributed to an underestimation of the significance and prevalence of adenomyosis. Recently, however, the landscape of adenomyosis diagnosis has transformed considerably, thanks to advancements in imaging technologies such as transvaginal ultrasound and magnetic resonance imaging (MRI) [3]. Consequently, there has been a noticeable shift in the demographic profile of patients diagnosed with adenomyosis, which now includes younger women of reproductive age presenting with a diverse array of symptoms. This shift highlights the prevalence of adenomyosis as more common in younger patients than previously recognized. It is estimated to affect up to 15–20% of women of reproductive age and commonly overlaps with endometriosis and uterine fibroids [4]. These overlapping conditions should be taken into account when choosing the proper treatment.

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Despite its clinical significance, adenomyosis remains significantly understudied compared to endometriosis, as evidenced by the disparity in scientific literature. A search on PubMed reveals this gap, with only 3871 entries for "adenomyosis," markedly fewer than the 34,523 entries for "endometriosis." These numbers highlight the need for increased research and understanding in the field of adenomyosis.

The limited understanding of adenomyosis's nature, coupled with the absence of a standardized classification system, has resulted in a disorganized approach to treating this disease. Unlike endometriosis, there is currently no drug specifically labeled for the treatment of adenomyosis and only recently, have guidelines been developed for its management, such as those from the Asian Society of Endometriosis and Adenomyosis and the Society of Obstetricians and Gynecologists of Canada (SOGC) [5, 6].

Generally, the symptoms of adenomyosis can be controlled through hormonal treatment. For patients with treatment-refractory or severe symptomatology, hysterectomy is considered standard-surgical treatment. In cases where organ preservation is warranted, uterine-sparing surgical techniques have been proposed [13]. Surgical interventions range from laparoscopic myomectomy for removal of an adenomyoma to more complex procedures such as the Osada procedure for diffuse adenomyosis, involving laparotomy and flap reconstruction of the uterus [7]. The reported outcomes of surgical treatments include a pregnancy rate of 40%, a miscarriage rate of 21%, and a live-birth rate of 70% [8]. Surgical resection of adenomyosis is generally associated with significant perioperative risks and requires a highly advanced surgical skill set. Of particular concern is the risk of uterine rupture during pregnancy after surgery. When choosing such a procedure, one should bear in mind the significant recurrence rate, which ranges from 9 to 19% depending on the surgical technique used [9].

Given these complexities and risks, the past decades have seen a shift towards the development and adoption of less invasive treatment modalities for adenomyosis. Techniques such as Uterine Artery Embolization (UAE), High-Intensity Focused Ultrasound (HIFU), Percutaneous Microwave Ablation (PMWA), and Radiofrequency Ablation (RFA) have emerged as promising alternatives as reports increase on their efficiency and safety for the treatment of adenomyosis. In addition, pregnancies have been observed in small case series. In the meta-analysis "Pregnancy Outcomes after Uterus-sparing Operative Treatment," the comparison between non-surgical treatments (HIFU, RFA, and UAE) and surgical excision for adenomyosis showed no significant difference in pregnancy outcomes. Approximately 40% of women successfully conceived using non-excisional methods, with a 21% miscarriage rate, and the live birth rate was 70%—mirroring the outcomes of surgical excision treatments [8].

These advancements reflect a significant evolution in the therapeutic approach to adenomyosis, moving away from highly invasive surgeries toward minimally invasive interventions.

This narrative review concentrates on the existing evidence for non-surgical treatments and their significance in the management of adenomyosis.

Types of Adenomyosis

Different classification models for adenomyosis exist. Most of these models agree on a focal and disseminated disease, as well as adenomyosis of the inner and outer myometria. Among the various classification systems, the most comprehensive and commonly used model is that proposed by Kishi et al. [10] as follows.

Intrinsic adenomyosis (Subtype I) affects the uterine inner layer—known as the junctional zone; extrinsic adenomyosis (Subtype II) infiltrates the outer shell of the uterus; intramural adenomyosis (Subtype III) is encapsulated within intact muscular structures of the uterus; and indeterminate adenomyosis (Subtype IV) is a diffuse type that does not fit into the other three subtypes, making it difficult to categorize.

Data are emerging that the different subtypes—especially intrinsic versus extrinsic and diffuse versus focal—seem to have different etiologies and clinical profiles, making it important to distinguish between them. For example, intrinsic adenomyosis is more commonly associated with AUB and prior uterine surgery. In terms of age, patients with intrinsic adenomyosis are generally older compared to those with extrinsic adenomyosis. On the other hand, extrinsic adenomyosis is more frequently found in younger, nulligravid women and is notably associated with deep infiltrating endometriosis. It is found to cause more primary infertility compared to diffuse adenomyosis [11, 12].

Medical Treatment

Medical treatment is primarily indicated for patients with adenomyosis who wish to preserve their fertility or for those nearing menopause. It is also recommended for patients who are unsuitable for surgical intervention because of other medical comorbidities. The range of hormonal treatments available for adenomyosis includes combined oral contraceptive (COC) pills, progestins, the levonorgestrel-releasing intrauterine system (LNG-IUS), and gonadotropin-releasing hormone (GnRH) agonists and antagonists and danazol.

Available guidelines recommend using hormonal treatment as the first-line medical option for managing pain and AUB.

COCs function by inhibiting follicle-stimulating and luteinizing hormones, suppressing follicular growth and endometrial proliferation, thereby relieving AUB and chronic pelvic pain. However, their impact on adenomyotic lesions and uterine volume reduction is not well defined [13].

Dienogest, a synthetic oral progestin, stands out for its effectiveness in managing endometriosis-associated pain and adenomyosis symptoms. It is comparable or even superior to COCs and GnRH analogs in alleviating dysmenorrhea but shows less efficacy in reducing uterine volume and inducing amenorrhea [13]. The use of dienogest, especially in cases of intrinsic adenomyosis, may lead to spotting and unpredictable bleeding [14]. Furthermore, concerns about progesterone resistance, potentially due to KRAS mutations [15] in adenomyotic lesions, pose challenges to its effectiveness.

GnRH analogs, including agonists and antagonists, work by downregulating gonadotropin release, leading to reduced estrogen levels and consequent shrinkage of the uterus, thus alleviating adenomyosis-related pain. While effective, their long-term use is limited by hypoestrogenic side effects such as bone loss. GnRH antagonists, avoiding the initial flare-up effect seen with agonists, reduce uterine size and symptoms but face challenges in terms of cost and variable patient responses [13].

Although hormonal treatment provides only symptomatic relief, with symptoms likely to relapse immediately after cessation of treatment, it remains of great importance in suppressing the progression of adenomyosis.

Levonorgestrel-Releasing Intrauterine System (LNG-IUS)

LNG-IUS improves the symptoms associated with adenomyosis by inducing decasualization and atrophy of the endometrium and downregulating estrogen receptors through increased progesterone release. It is highly effective in reducing pain and AUB and is regarded to be more efficacious than COCs [16].

Recommended by the National Institute for Health and Care Excellence (NICE) in the United Kingdom, the Asian Society of Endometriosis and Adenomyosis guidelines (Level of evidence: Ib Grade B), and the Society of Obstetricians and Gynaecologists of Canada (SOGC), LNG-IUS is widely used as the first-line medical treatment for adenomyosis.

In a randomized controlled trial (RCT) 75 patients with AUB and/or dysmenorrhea and imaging-confirmed adenomyosis, those treated with LNG-IUS demonstrated higher scores on quality of life (QoL) measures compared to patients who underwent hysterectomy [17].

In patients with a lower disease burden of adenomyosis, LNG-IUS treatment notably improves health-related quality of life (HR-QOL), particularly in managing symptoms such as dysmenorrhea and AUB even reflecting on improved blood hemoglobin levels. Conversely, for patients with diffuse (Subtype IV) and extensive disease, the effectiveness of LNG-IUS in enhancing HR-QOL is significantly diminished. While it still provides some relief in dysmenorrhea and HMB, it does not improve blood hemoglobin level [18]. Another limitation in the use of LNG-IUS may be a higher expulsion rate in uteri larger than 150 ml [19].

No specific studies are available on the rate of hysterectomy for the treatment-failure of LNG-IUS in adenomyosis, but in cohorts for HMB, it is reported to be 3.7–6% after five years and longer [20].

Non-Surgical Interventions

All non-surgical interventions share a common origin in the field of radiology and have progressively integrated into the management of gynecological conditions over the past two decades. Given the advantages of rapid recovery and minimal invasive nature of non-surgical interventions, more gynecologists are considering them as a secondary treatment to traditional pharmacotherapy.

Non-surgical interventions for adenomyosis can be categorized into UAE and image-guided thermal ablation techniques. UAE, an angiographic technique, utilizes embolic agents delivered into uterine arteries to create ischemic necrosis within adenomyotic lesions. Owing to the disease's association with increased angiogenesis [21] and hypervascularity [22], UAE may offer targeted treatment selectivity.

Image-guided thermal ablations, encompassing HIFU, PMWA, and RFA, are minimally invasive methods that precisely target adenomyotic tissue under imaging guidance.

These ablation techniques utilize heat to differentially affect tissue based on temperature thresholds. Cell death occurs at temperatures exceeding 60 °C. Between 60 °C and 99 °C, tissue undergoes desiccation and protein coagulation. However, surpassing 100 °C can lead to vaporization and charring causing the destruction of the cytomolecular architecture of the tissue [23–25].

The principal distinction among HIFU, PMWA, and RFA lies in the type of energy source utilized the mechanism of its application to the adenomyotic lesion and a distinct heat-profile.

High-Intensity Focused Ultrasound HIFU

HIFU employs focused ultrasonic energy externally to thermally ablate adenomyotic lesions beneath the skin without surface disruption. This procedure can be

monitored using ultrasound or MRI to ensure accuracy. However, the effectiveness of HIFU is contingent upon an unobstructed path for the ultrasound beam; obstacles such as significant cutaneous scarring, abdominal wall thickness exceeding 5 cm, the presence of foreign materials, or bowel segments interposed due to adhesions can impede treatment efficacy [26]. An MRI-based study highlighted that 38.9% of patients suitable for UAE were ineligible for MRI-guided HIFU, predominantly due to bowel interposition [27].

The limited penetration of ultrasonic waves can also result in suboptimal ablation for deeply situated adenomyosis, such as lesions on the posterior uterine wall that often present with more severe pathology. Contrasting lesion locations, HIFU has shown superior efficacy in treating adenomyotic tissue located on the anterior uterine wall as compared to the posterior [28].

HIFU is recommended by the Asian Society of Endometriosis and Adenomyosis guidelines (Level of evidence 2a; Grade of recommendation B) [5] and mentioned by the SOGC Clinical Practice Guideline [6] (low level of evidence, conditional recommendation).

HIFU presents the largest patient cohort among all the above-mentioned image-guided thermal ablation procedures. A 2021 meta-analysis by Liu et al., encompassing 15,123 patients treated with HIFU, revealed a notable dysmenorrhea symptom relief rate of 84.2%. This finding aligns with the significant treatment effect observed, as indicated by a standardized mean difference (SMD) of 2.59 [29], corroborating earlier results reported by Marques et al. [26].

However, the available data on QoL did not demonstrate improvements in QoL scores post-HIFU treatment. Notably, there was a substantial reduction in menorrhagia severity scores from baseline to follow-up [29].

Adverse reactions primarily included lower abdominal pain (reported in 21.6% of patients, $n = 392$) and pain or discomfort in the treated area (12.8%, $n = 233$). Additionally, moderate adverse events such as superficial first to second-degree skin burns were resolved within 14 days using local dressing.

Reintervention rate was reported by Liu et al. at 11% after 24 months and longer for the combined group of HIFU and RFA (four studies).

Regarding fertility outcomes, a systematic review by Chen et al. assessed 557 patients who sought to conceive post-HIFU treatment. The study reported a pooled pregnancy rate of 53.4% and a live birth rate of 35.2% [30]. However, significant heterogeneity among the included studies suggests the need for a cautious interpretation of these findings, highlighting the necessity for further research to solidify the evidence regarding HIFU's effectiveness in fertility outcomes.

Percutaneous Microwave Ablation (PMWA)

PMWA employs electromagnetic energy to rapidly heat tissue, achieved by agitating water molecules within the tissue. This heating effect is facilitated by the insertion of a probe (antenna) through the skin under anesthesia. Similar to HIFU, PMWA is typically performed through a transabdominal approach, which limits its applicability for treating adenomyosis located on the posterior wall of retroverted or retroflexed uteri.

In comparison to HIFU and RFA, PMWA can generate higher temperatures, often exceeding 100 °C, due to its ability to propagate electromagnetic energy through dehydrated, charred, or desiccated tissue. Technological advancements, such as cooling systems, antenna arrays, and optimized delivery methods, have improved the clinical application of PMWA, enabling more uniform heat distribution across the target area. PMWA is mainly applied via transabdominal, laparoscopic, or less commonly, transvaginal approaches.

In the guidelines of the Asian Society of Endometriosis and Adenomyosis, PMWA is mentioned with a low grade of recommendation (Grade C) [5], and the SOGC advises that it should not be used outside a research context (low level of evidence, conditional recommendation).

A meta-analysis consisting of 513 patients across six studies observed symptom relief in 89.7% of cases, a substantial effect mirrored in a significant SMD of 4.27 [29]. The study by Li et al. on 107 patients revealed notable reductions in uterine volume post-treatment, along with improvements in uterine fibroid symptom and HR QoL scores, dysmenorrhea severity, menstrual volume, and hemoglobin levels. However, a substantial dropout rate was observed at the 12-month follow-up [31].

Adverse events reported post-PMWA included vaginal discharge, pain in the treatment area, fever, nausea, and vomiting, occurring in 51.3–72% of cases, but no significant complications such as uterine perforation or injuries to surrounding organs were noted [29, 31]. Information on pregnancy outcomes following PMWA treatment is currently unavailable.

Radiofrequency Ablation (RFA)

RFA involves inserting electrodes, directly into the target lesion under ultrasound guidance. This can be done during either laparoscopic surgery or transcervically under either transvaginal or integrated intrauterine ultrasound guidance. RFA utilizes high-frequency alternating electrical currents to generate heat, effectively controlling the temperature to prevent charring and keep it below 100 °C. This results in thermal fixation and coagulative necrosis while preserving the cellular structure of the tissue [23, 24].

RFA is mentioned in the Asian Society of Endometriosis and Adenomyosis guidelines (3b Grade of recommendation C) [5] and SOGC states similarly to PMWA that it should not be used outside a research context (low level of evidence, conditional recommendation).

A systematic review involving 396 patients across seven studies reported a 94.7% rate of symptom relief with RFA, along with a significant reduction in dysmenorrhea pain scores by 63.4% at 12 months [32]. However, specific data on QoL parameters are not available. One study showed normalization in bleeding patterns in 68.7% of cases with AUB.

The overall hysterectomy rate for treatment-failure at 12 months was $10.8 \pm 1.5\%$ in the same study [32]. Liu et al. reported an overall reintervention of 11% after 24 months and longer in the combined group of HIFU and RFA (four studies) [33].

In terms of fertility, the clinical pregnancy rate among those trying to conceive naturally was 42.7%, with an overall rate of 35.8%. The data, derived from a study of 31 patients, reported 41 pregnancies post-RFA, with a 66.7% delivery rate and a notable 62.5% rate of cesarean deliveries. There were no reported cases of uterine rupture following RFA treatment [34].

Uterine Artery Embolization (UAE)

UAE is an angiographic procedure that uses embolic agents injected into uterine arteries to cause ischemic necrosis in adenomyotic lesions. The procedure typically involves vascular access through the femoral artery in the groin area and is performed under sedation and local anesthesia. Given the disease's association with increased angiogenesis [21] and hypervascularity [22], UAE may offer targeted treatment selectivity. The occlusion of blood supply to the lesion results in hypoxia, ischemia, and tissue necrosis, with minimal impact on surrounding tissue [22].

This approach has been explored in recent decades as a treatment option for symptomatic adenomyosis, following its success in managing uterine fibroids.

UAE is recommended by the SOGC Clinical Practice Guideline [6] (strong recommendation, moderate evidence), NICE UK Interventional procedures guidance (IPG473) and the Asian Society of Endometriosis and Adenomyosis guidelines (Level of evidence 2a; Grade of recommendation B) for managing symptomatic adenomyosis [5]. It is offered to patients who have completed child-bearing and would like to preserve their uterus.

The current state of UAE on adenomyosis is depicted in a systematic review and meta-analysis by A.M. de Bruin et al. (2017). In a comprehensive study involving 1049 patients across 30 studies, UAE achieved significant symptom improvement in 83.1% of patients. QoL, particularly in cases of adenomyosis with uterine fibroids, also improved.

Complications were reported in 615 out of 1049 patients, with abdominal pain up to two weeks being the most common (87.4–361 out of 413 reported cases).

The study noted a short-term hysterectomy rate of 4%, which rose to 14.2% at 12 months. While the efficacy of UAE in the short-term is established, concerns arise regarding its long-term because of high symptom recurrence rates. Liu et al. observed a reintervention rate of 16.8% at 24 months or longer [33].

Notably, patients undergoing UAE often have larger uteri and more severe adenomyosis, indicating a possible selection bias. The size of the embolization agent and the blood supply of the lesion [22] are crucial factors influencing recurrence risk, as smaller embolization agents and well-vascularized lesions tend to have better outcomes [22]. Increased vascularization is not just seen in adenomyosis lesions but also in the eutopic endometrium. This should raise concerns in sterility treatment—beyond affecting ovarian vascularization, which was a relevant issue in the early phase of UAE treatments.

The review of de Bruin reported amenorrhea in 6.3% of the participants, all of whom were over 40 years of age. This complication could be due to the infarction of the basal endometrium with or without Asherman syndrome, as reported rates of proven ovarian failure are lower.

Data on pregnancy following UAE are limited. In their cohort study, Serres-Cousine et al. [35] reported pregnancy rate of 53% among 61 patients with adenomyosis. The disease represented only 16% of the overall analyzed cohort which consisted mainly of leiomyoma ($n = 398$). Of note is a lower pregnancy rate of 29% in isolated adenomyosis, whereas in the group of adenomyosis in the presence of fibroids, the pregnancy rate was 75%. Adverse pregnancy and neonatal outcomes were not observed.

It is important to note that data from the UAE treatment of uterine fibroids, such as those from the FEMME Trial [36], should not be directly applied to adenomyosis treatment due to differences in vascularization patterns between the two conditions. The anticipated outcomes from the "Quality of Life after Embolization vs. Hysterectomy in Adenomyosis" (QUESTA) Trial may provide more specific RCT data relevant to adenomyosis.

Comparative Analysis

A closer look at the available literature reveals distinct profiles for LNG-IUS, UAE, HIFU, PMWA, and RFA, each with their own set of benefits and constraints. Reading through the available literature on the different non-surgical interventions in detail, only a narrative comparison can be attempted (Table 1). Owing to the high heterogeneity and low quality, the data do not allow for a direct comparison in

Table 1 Summary highlighting the advantages and disadvantages of the different types of non-surgical treatment of adenomyosis

Non-surgical procedure	Functional Principle	Advantages	Disadvantages
Levonorgestrel-releasing intrauterine system (LNG IUS)	Intrauterine device, transvaginally inserted in office setting. LNG induces endometrial decidualization and atrophy, with anti-proliferative and anti-inflammatory effects	Recommended as first-line treatment Office procedure Combination as "adjuvant treatment" after non-surgical and surgical treatment	Less effective in diffuse adenomyosis, larger uteri; higher expulsion rate in large uteri
Uterine artery embolization (UAE)	Angiographic procedure under fluoroscopic guidance. Synthetic agents are injected through catheters into the uterine arteries, resulting in ischemia of the target tissue. It can be done as an outpatient procedure in most cases under sedation or local anesthesia	Suitable for large, diffuse adenomyosis, especially in the presence of uterine fibroids	Increased long-term reintervention rate Fertility concerns
High-intensity focused ultrasound (HIFU)	Concentration of high-intensity sonographic waves to heat and destroy tissue through coagulative necrosis. Requires magnetic resonance imaging or sonography to track the beam's path and monitor thermal response of tissue. Performed under conscious sedation on an outpatient basis	Effective for focal adenomyosis on the anterior wall Non-invasive (does not breach the skin)	Technical limitations Less effective for posterior wall lesions Prolonged ablation time
Radiofrequency ablation (RFA)	Ultrasound-guided placement of one or more RF needle electrodes, which deliver high-frequency alternating electrical currents that create ionic agitation in target tissue, resulting in heat generation and coagulative necrosis. It can be done as an outpatient procedure in most cases under sedation or local anesthesia	Precise targeting for smaller lesions Compared to HIFU and PMWA, it is impedance controlled and provides better monitoring of tissue during the procedure Easy incorporation into gynecological practice	Less successful for large uteri, diffuse disease No information on quality of life available
Percutaneous microwave ablation (PMWA)	A needle antenna with an exposed tip is advanced percutaneously into the lesion under sonographic guidance. Electromagnetic energy rapidly rotates water molecules in target tissue to cause tissue necrosis due to heat	Compared with HIFU and RFA, PMWA can reach higher temperatures ablate larger volumes, shorter ablation times	No Information on pregnancies available No information on reintervention rate

the mentioned meta-analysis and systematic reviews of the different intervention. Currently, there is not a single RCTs or comparative studies. Robust long-term data are needed to adequately counsel patients regarding the potential necessity for repeat interventions.

From a clinical perspective, LNG-IUS is recommended as the initial treatment option for adenomyosis. For patients with enlarged uteri, employing a "pretreatment" strategy with GnRH-analogs, HIFU, or UAE before inserting LNG-IUS may reduce the risk of treatment failure, such as device expulsion. Furthermore, implementing the LNG-IUS post non-surgical interventions has been associated with reduced rates of recurrence. This approach is recommended to optimize patient outcomes and minimize the probability of symptomatic relapse and reintervention.

In large uteri with presence of multiple uterine fibroids, UAE may be preferable compared to thermal ablation procedures especially if there is no wish for pregnancy or comorbidities not allowing for a hysterectomy.

For focal adenomyosis, especially when prioritizing fertility preservation, RFA emerges as a strategic option due to its integration into gynecological procedures like hysteroscopy or laparoscopy. Its unique advantage lies in the availability of integrated systems for both trans-cervical and laparoscopic applications, allowing gynecologists to employ RFA directly during surgeries. This adaptability is a significant benefit not shared by other non-surgical treatments such as HIFU or UAE. In cases of localized disease of the anterior wall of the uterus without prior surgeries and no suspicion of concurrent endometriosis, HIFU could be favored. PMWA cannot be recommended in cases where childbearing is not concluded, as there are no data on pregnancies available.

Conclusion

In the realm of uterine-sparing thermal ablation procedures for adenomyosis, technologies such as HIFU, RFA, and PMWA show early promise. Across all mentioned interventions in patients with adenomyosis, dysmenorrhea relief rates are well above 80% [29, 37]. Their effectiveness in managing adenomyosis-related pain and AUB bleeding is increasingly recognized. Additionally, the reintervention rates for these non-surgical methods, ranging from 11 to 17% [33], are comparable to those of surgical, uterus-sparing procedures, which vary between 9 and 19% [9].

Currently, concerns remain about the utility of non-surgical techniques in women with a pregnancy wish, despite encouraging results from one meta-analysis [8]. The limited number of patients treated with these methods, coupled with the high risk of bias and heterogeneity in studies, hinders definitive conclusions. Particularly in the case of UAE, there is a potential concern regarding impaired myometrial and endometrial function, which is crucial for pregnancy. Nevertheless, substantial uncertainties also persist for thermal ablation procedures: The current energy settings for these modalities are extrapolated from their application in fibroid treatment. Given the distinct histological characteristics of adenomyosis, including increased cellularity and less defined borders, there is a need to develop adenomyosis-specific parameters to optimize efficacy while minimizing thermal injury.

Furthermore, understanding the healing process post-treatment is vital for pregnancies itself as complications such as uterine ruptures have been reported for HIFU [38], RFA [39], and UAE [40].

In conclusion, while advancements in non-surgical treatments for adenomyosis offer promising alternatives to traditional surgery, their varying efficacies and potential risks underscore the need for further research and development of more refined techniques. The choice of treatment must be tailored to each patient's specific condition, balancing the benefits against potential complications, especially in the context of future fertility.

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Compliance with Ethical Standards

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References

1. Nirgianakis K, et al. Fertility, pregnancy and neonatal outcomes of patients with adenomyosis: a systematic review and meta-analysis. Reprod Biomed Online. 2021;42(1):185–206.
2. Horton J, et al. Reproductive, obstetric, and perinatal outcomes of women with adenomyosis and endometriosis: a systematic review and meta-analysis. Hum Reprod Update. 2019;25(5):592–632.
3. Tellum T, Nygaard S, Lieng M. Noninvasive diagnosis of adenomyosis: a structured review and meta-analysis of diagnostic accuracy in imaging. J Minim Invasive Gynecol. 2020;27(2):408–18.
4. Upson K, Missmer SA. Epidemiology of adenomyosis. Semin Reprod Med. 2020;38(2–03):89–107.
5. Harada T, et al. The Asian Society of Endometriosis and Adenomyosis guidelines for managing adenomyosis. Reprod Med Biol. 2023;22(1):e12535.
6. Dason ES, et al. Guideline No. 437: diagnosis and management of adenomyosis. J Obstet Gynaecol Can. 2023;45(6):417–29 e1.
7. Osada H. Uterine adenomyosis and adenomyoma: the surgical approach. Fertil Steril. 2018;109(3):406–17.
8. Jiang L, et al. Pregnancy outcomes after uterus-sparing operative treatment for adenomyosis: a systematic review and meta-analysis. J Minim Invasive Gynecol. 2023;30(7):543–54.
9. Younes G, Tulandi T. Conservative surgery for adenomyosis and results: a systematic review. J Minim Invasive Gynecol. 2018;25(2):265–76.
10. Kishi Y, et al. Four subtypes of adenomyosis assessed by magnetic resonance imaging and their specification. Am J Obstet Gynecol. 2012;207(2):114 e1–7.
11. Bourdon M, et al. Focal adenomyosis is associated with primary infertility. Fertil Steril. 2020;114(6):1271–7.
12. Bourdon M, et al. Adenomyosis of the inner and outer myometrium are associated with different clinical profiles. Hum Reprod. 2021;36(2):349–57.
13. Vannuccini S, et al. Role of medical therapy in the management of uterine adenomyosis. Fertil Steril. 2018;109(3):398–405.
14. Matsubara S, et al. Subtype I (intrinsic) adenomyosis is an independent risk factor for dienogest-related serious unpredictable bleeding in patients with symptomatic adenomyosis. Sci Rep. 2019;9(1):17654.
15. Inoue S, et al. Uterine adenomyosis is an oligoclonal disorder associated with KRAS mutations. Nat Commun. 2019;10(1):5785.
16. Shaaban OM, et al. Levonorgestrel-releasing intrauterine system versus a low-dose combined oral contraceptive for treatment of adenomyotic uteri: a randomized clinical trial. Contraception. 2015;92(4):301–7.
17. Ozdegirmenci O, et al. Comparison of levonorgestrel intrauterine system versus hysterectomy on efficacy and quality of life in patients with adenomyosis. Fertil Steril. 2011;95(2):497–502.
18. Ishizawa C, et al. Levonorgestrel-releasing intrauterine system improves menorrhagia-related quality of life in patients with symptomatic adenomyosis. Reprod Sci. 2023;30(3):966–73.
19. Lee KH, et al. Relationship between uterine volume and discontinuation of treatment with levonorgestrel-releasing intrauterine devices in patients with adenomyosis. Arch Gynecol Obstet. 2016;294(3):561–6.
20. Agarwal M, et al. Comparison of bleeding pattern and quality of life before and after the insertion of a levonorgestrel intrauterine system for heavy menstrual bleeding: a seven-year review. Cureus. 2023;15(3):e36142.
21. Harmsen MJ, et al. Increased angiogenesis and lymphangiogenesis in adenomyosis visualized by multiplex immunohistochemistry. Int J Mol Sci 2022;23(15).
22. Zhou J, et al. Outcomes in adenomyosis treated with uterine artery embolization are associated with lesion vascularity: a long-term follow-up study of 252 Cases. PLoS ONE. 2016;11(11):e0165610.
23. Wall MS, et al. Thermal modification of collagen. J Shoulder Elbow Surg. 1999;8(4):339–44.
24. Hong K, Georgiades C. Radiofrequency ablation: mechanism of action and devices. J Vasc Interv Radiol. 2010;21(8 Suppl):S179–86.
25. Organ LW. Electrophysiologic principles of radiofrequency lesion making. Appl Neurophysiol. 1976;39(2):69–76.
26. Marques ALS, et al. Is high-intensity focused ultrasound effective for the treatment of adenomyosis? A systematic review and meta-analysis. J Minim Invasive Gynecol. 2020;27(2):332–43.
27. Froling V, et al. Technical eligibility for treatment of magnetic resonance-guided focused ultrasound surgery. Cardiovasc Intervent Radiol. 2014;37(2):445–50.
28. Gong C, et al. Factors influencing the ablative efficiency of high intensity focused ultrasound (HIFU) treatment for adenomyosis: a retrospective study. Int J Hyperthermia. 2016;32(5):496–503.
29. Liu L, Wang T, Lei B. Image-guided thermal ablation in the management of symptomatic adenomyosis: a systematic review and meta-analysis. Int J Hyperthermia. 2021;38(1):948–62.
30. Chen Y, et al. Systematic review and meta-analysis of reproductive outcomes after high-intensity focused ultrasound (HIFU) treatment of adenomyosis. Best Pract Res Clin Obstet Gynaecol. 2023;92:102433.
31. Li S, et al. Efficacy of transabdominal ultrasound-guided percutaneous microwave ablation in the treatment of symptomatic adenomyosis: a retrospective cohort study. J Minim Invasive Gynecol. 2023;30(2):137–46.
32. Dedes I, et al. Radiofrequency ablation for adenomyosis. J Clin Med. 2023;12(9).
33. Liu L, et al. Risk of recurrence and reintervention after uterine-sparing interventions for symptomatic adenomyosis: a systematic review and meta-analysis. Obstet Gynecol. 2023;141(4):711–23.
34. Nam JH. Pregnancy and symptomatic relief following ultrasound-guided transvaginal radiofrequency ablation in patients with adenomyosis. J Obstet Gynaecol Res. 2020;46(1):124–32.
35. Serres-Cousine O, et al. Clinical investigation of fertility after uterine artery embolization. Am J Obstet Gynecol. 2021;225(4):403 e1–403 e22.
36. Sirkeci F, et al. Effects on heavy menstrual bleeding and pregnancy of uterine artery embolization (UAE) or myomectomy for women with uterine fibroids wishing to avoid hysterectomy: The FEMME randomized controlled trial. Int J Gynaecol Obstet. 2023;160(2):492–501.
37. de Bruijn AM, et al. Uterine artery embolization for the treatment of adenomyosis: a systematic review and meta-analysis. J Vasc Interv Radiol. 2017;28(12):1629–42 e1.
38. Liu Y, et al. Uterine rupture after high-intensity focused ultrasound ablation of adenomyosis: a case report and literature review. Int J Hyperthermia. 2023;40(1):2212885.
39. Xu M, Zhu XL. Complete uterine rupture with fetus external to uterus. Arch Gynecol Obstet. 2021;303(4):1117–8.
40. Yeaton-Massey A, et al. Uterine rupture after uterine artery embolization for symptomatic leiomyomas. Obstet Gynecol. 2014;123(2 Pt 2 Suppl 2):418–20.