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REVIEW

An Updated Review of Thermal Ablation Technology for Uterine Fibroids and Adenomyosis: Focusing on Protecting Fertility

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Abstract: There is a growing trend towards minimally invasive or noninvasive alternatives for gynecological disorders due to their rapid alleviation of symptom, expedited recovery, and minimal risks of postoperative complications. Thermal ablation technology has been commonly advocated as a minimally invasive therapeutic methods in recent years, including microwave ablation, radiofrequency ablation, and high-intensity focused ultrasound. The increasing application scenarios require updated and systematic research, and more evidence to promote their appropriate use. The objective of this review is to summarize the latest views of ablation from a prospective of fertility protection, endeavor to clarify the clinical value of thermal ablation technology in protecting fertility by assessing parameters such as ablation rates, alleviation of disease symptoms, re-intervention rates and post-treatment pregnancy rates. We review the clinical studies of ablation for uterine fibroids and adenomyosis treatment in the past 10 years, summarize the limitation and the prospects of its development in the treatment process, so as to provide clinicians with advice on the best practice. In the management of uterine fibroids and adenomyosis, thermal ablation technology offers improved fertility preservation and minimizes normal tissue injury compared to traditional surgical approaches for patients pursuing reproductive goals. In the future, thermal ablation technology will play a significantly enhanced role in preserving fertility for individuals requiring treatment for uterine fibroids and adenomyosis, guided by indications. But further research is still needed in the form of more extensive randomized prospective trials to provide stronger evidence supporting this perspective.

Keywords: fertility protection, radiofrequency ablation, microwave ablation, high-intensity focused ultrasound, uterine fibroids, adenomyosis

Introduction

Uterine fibroids and adenomyosis are prevalent gynecological disorders. The prevalence of uterine fibroids in women of reproductive age ranges from 5.4% to 77%. Epidemiological studies have shown that women experiencing infertility have a significantly higher incidence (2.18 times) of uterine fibroids compared to those without fertility problems.[1] Additionally, adenomyosis, which affects 20–35% of women in their fertile age range and is highly prevalent worldwide, is associated with female infertility.[2] Hysterectomy, which is widely recognized as the primary therapeutic approach, is highly effective in relieving symptoms. However, both traditional gynecological surgeries and laparoscopy surgeries inevitably are inevitably invasive procedure with a protracted recovery period, which can cause permanent damage or functional loss of reproductive function.[3,4] Therefore, non-surgical alternatives for preserving the uterus are becoming increasingly popularity among women seeking to avoid major surgical interventions. When planning treatment for patients with reproductive objectives, it is crucial to fully consider the preservation of fertility. For patients who do not

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desire definitive surgical management or fail to respond to pharmacological interventions, there is a high demand for alternative uterus-sparing procedures due to their minimally invasive and fertility-preserving nature.[5]

The advancement of minimally invasive surgical technology represents significant progress in terms of precautionary measures and mitigating the impact on reproductive capabilities for treating gynecological diseases. Thermal ablation technology is a commonly advocated minimally invasive therapeutic method in recent years. Compared to conventional surgical methods, it offers certain advantages such as no hospitalization, shorter operation time, and fewer complications. During the treatment, the lesions are treated with high temperature to eradicate them and achieve therapeutic effects. Ultrasound (US) is utilized as a guidance tool during the ablation procedure, providing continuous monitoring of the depth and position of the lesion.[6] This ensures the maintenance of a secure distance, effectively mitigating any potential harm to neighboring organs and tissues.[7] Currently, thermal ablation techniques, such as radiofrequency ablation (RFA), microwave ablation (MWA), and high-intensity focused ultrasound (HIFU), have been extensively applied and studied as minimally invasive clinical treatments.[8]

Thermal ablation technology has been widely utilized for the treatment of gynecological diseases, specifically to effectively manage and care for uterine fibroids and adenomyosis (Figure 1); compared with open operation or laparoscope, it offers reduced damage and maximum preservation of fertility.[9] Despite the advantages offered by thermal ablation technology, its widespread clinical application remains challenging due to the high level of expertise and steep learning curve for inexperienced practitioners.[10] In addition, the management of thermal ablation technology in relation to fertility preservation remains inadequate, and previous research has not extensively elucidated its overall application. Hence, we conducted a comprehensive literature search spanning nearly a decade to retrieve the latest studies on thermal ablation techniques for the treatment of uterine myoma and adenomyosis. Due to significant heterogeneity in study

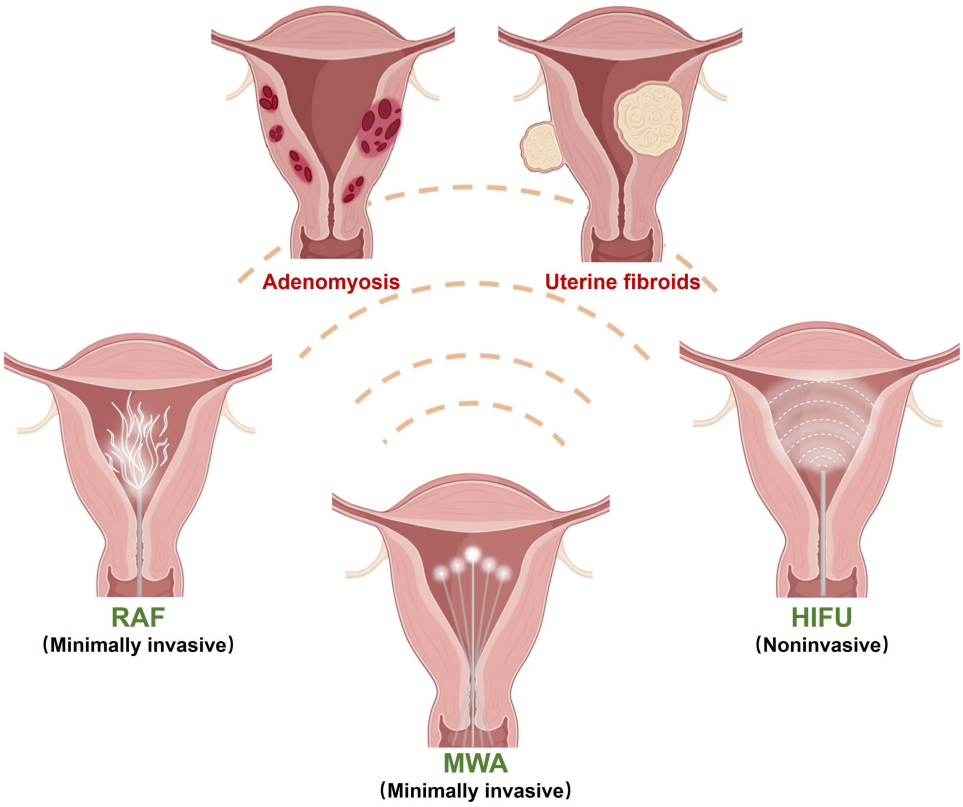

Figure 1 Thermal ablation therapies for uterine fibroids and adenomyosis.
Abbreviations: RFA, radiofrequency ablation; MWA, microwave ablation; HIFU, high-intensity focused ultrasound.

methods and populations, the field is summarized using both comparative and categorical approaches, while selecting typical or representative studies for focused analysis. Moreover, we will briefly examine the limitations and potential for advancement, with the objective of providing a valuable point of reference to improve patients' strategies for fertility preservation (Table 1).

Table 1 Comparison of Three Types of Thermal Ablation Technology

	REF	Symptom improvement	Advantages	Disadvantages	Complications
RAF	[11]	RFA can achieve sustainable results within 5 years, particularly in women over the age of 45 with a single fibroid (volume less than 180 cm^3).	For small-sized myomas; minimally invasive; less trauma and bleeding	Constrained by the location and size of focus; longer time required; may require multiple treatments; requires surgery under anesthesia	Abdominal pain; erythema and skin reaction; urinary tract infection
	[12]	The uterine volume reduction rate was 35.8% at 1 month, increasing to 40.8% at 6 months and reaching 41.2% at 12 months post-RFA. Dysmenorrhoea and symptom severity score showed significant decline, while the reintervention rate was 18.5%.			
	[13]	The pregnancy success rate reached 50% of 81 patients after RFA.			
MWA	[7]	The remission rate of dysmenorrhea symptoms in patients after ultrasound-guided percutaneous microwave ablation is over 80%, with significant relief within 3 months and sustained improvement up to 12 months post-treatment.	For larger ablation volume; shorter operation times; minimally invasive; lower costs	Hospitalization and general anesthesia	Lower abdominal pain; fever, vaginal discharge; and slight vaginal bleeding
	[14]	During an average 8.1-month follow-up, it was observed fibroid shrinkage (mean 70.3 cm^3) in all patients after MWA treatment. Over a 12-month clinical follow-up, significant symptom improvement and excellent quality of life were noted.			
HIFU	[15]	The women's dysmenorrhea score, measured by a numerical rating scale, significantly decreased at 3 months post-HIFU treatment and remained stable from 3 to 12 months. Hypermenorrhea was also reduced to some extent with a mean difference of −0.54.	Non-invasive; no anesthesia or hospitalization required; high precision	Constrained by the location and size of focus; may require multiple treatments	Skin disruption, swelling; lower abdominal discomfort; sciatic nerve pain; slight vaginal bleeding with discharge
	[16]	After HIFU treatment for uterine leiomyomas, 54 pregnancies occurred in 51 women with an average conception time of 8 months. The live birth rate was 41%, while the rates of spontaneous abortion and elective pregnancy termination were 28% and 11% respectively.			

Abbreviations: REF, references; RFA, radiofrequency ablation; MWA, microwave ablation; HIFU, high-intensity focused ultrasound.

Radiofrequency Ablation (RFA)

Before its implementation in gynecology, RFA has been widely adopted in various surgical subspecialties for the treatment of adrenal gland, breast, kidney, bone, lung, pancreas, and thyroid cancers.[17] RFA utilizes high-frequency alternating current to generate temperatures ranging from 85 to 100°C, which sequentially targets and reduces the size of each focal point. This process induces coagulative necrosis in the targeted tissue while minimizing damage to surrounding tissues, resulting in a significant alleviation of associated symptoms. Radiofrequency waves, due to their long wavelength, low frequency, and low energy on the electromagnetic spectrum (ranging from 3 kHz to 300 GHz), are an optimal choice for precise and predictable tissue ablation. Moreover, the addition of real-time paired US to the RFA allows for more precise localization of the focus.[18]

The performance of RFA can be achieved through different approaches, including laparoscopic, transcervical, and transvaginal methods. In 2002, laparoscopic US-guided RFA was first introduced as a uterine-conserving procedure for treating uterine fibroids. Laparoscopic RFA demonstrates efficacy in the treatment of small, non-irritating symptomatic leiomyomas. After treatment, the patient's symptoms will remain improved for an extended period and a low rate of re-intervention.[19] Additionally, it can be rapidly acquired with a majority of gynecologists reporting confidence and no escalation in adverse events compared to experienced RFA surgeons following their fifth supervised procedure.[20] Another technology focused on a transcervical approach to RFA began its development in 2005. Transcervical RFA, performed under local anesthesia only, with minimal operative duration and expedited postoperative recovery, is indicated for the treatment of small, solitary or superficial leiomyomas, particularly those that are not amenable to surgical hysteroscopy.[21,22] The study revealed that women underwent with transcervical RFA for symptomatic uterine fibroids experienced substantial and long-lasting alleviation of fibroid-related symptoms.[23] Additionally, transcervical RFA presents a reduced degree of surgical trauma and lower surgical risk compared to laparoscopic RFA; however, its treatment outcome may be comparatively inferior to that achieved through translaparoscopic RFA.[24] Sonata uses a transcervical approach without incisions to ablate fibroids, and this device received Food and Drug Administration (FDA) approval in 2018.[25] It has proven to be an efficacious treatment option for high-risk patients, such as those with obesity, cardiac disease, coagulopathy, or multiple previous surgeries, who presentwith diverse pre-existing conditions. Because the advantages of a bloodless and concise surgical procedure that is minimally invasive are paramount for such individuals.[26] Furthermore, substantial symptom improvement even in cases involving large myomas measuring ≥5 cm.[27] The published data on the treatment of fibroids using Sonata has demonstrated significant median reductions in total and perfused uterine fibroid volume, as well as improvements in menstrual bleeding, symptom severity, and improvements in health-related quality of life at 12 months post-ablation.[28] In addition, it demonstrates both safety and efficacy for up to 12 months in alleviating abnormal uterine bleeding associated with submucous, intramural, and transmural fibroids.[29] However, Sonata cannot ablate pedunculated fibroids, namely FIGO type 0 and type 7 myomata.[28] As for transvaginal RFA, it has been recently suggested as the optimal technique due to its ability to be performed on an outpatient basis, its emphasis on safety and quick recovery leading to a prompt return to regular menstruation, significant decrease in myoma size, and effective treatment of anemia.[30] Its enhanced dependability, decreased expenses, and shorter time frame make it the preferred choice among other minimally invasive techniques.[31] The transvaginal RFA procedure was conducted on 19 patients in a study, resulting in a remarkable enhancement of the quality of life score, and no major complications were observed during the process.[32] Furthermore, research findings that the patient's age, initial size of the myoma, degree of myoma vascularization, and duration of RFA may exert an influence on the treatment outcome.[33]

At present, many studies has consistently demonstrated that RFA effectively alleviates symptoms associated with uterine fibroids and adenomyosis (Figure 2). It is particularly beneficial for women aged 45 and above who have a single fibroid with a volume of no more than 180 cm^3.[11] The findings of a systematic review revealed that fifteen studies demonstrated a significant reduction in the severity of bleeding following RFA. Additionally, it was highlighted that RFA is effective in achieving short-term (≤12 months) reduction of bleeding symptoms.[34] RFA may be considered a minimally invasive alternative for women who wish to preserve their reproductive potential.[35] In addition to its minimally invasive nature, RFA offers the advantage of minimal or no hospitalization. Additionally, US-guided RFA is also suitable for patients with adenomyosis who desire to preserve fertility and alleviate symptoms because it effectively safeguards the

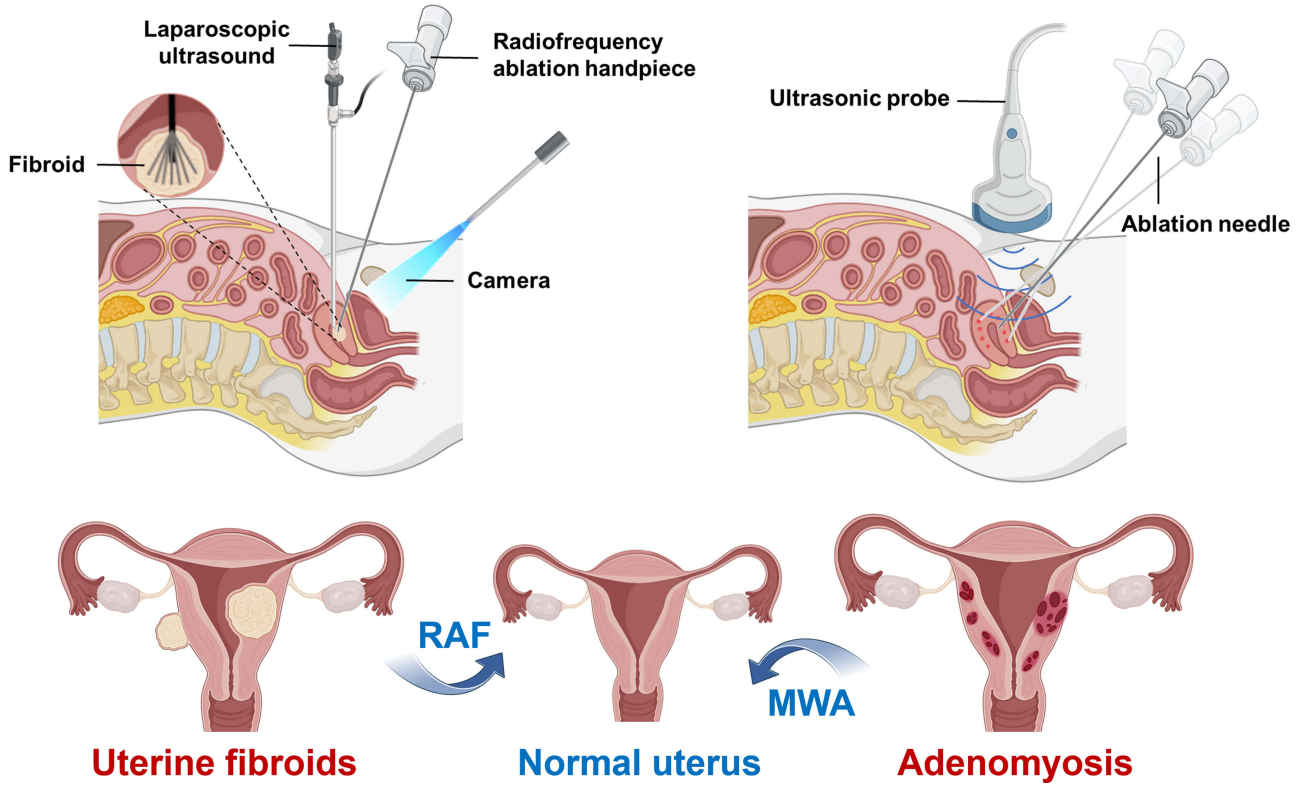

Figure 2 The uterus was normalized by thermal ablation of uterine fibroids and adenomyosis.
Abbreviations: RFA, radiofrequency ablation; MWA, microwave ablation.

structural integrity of the uterus, reduces uterine volume, alleviates clinical manifestations, and preserves normal endocrine and reproductive functions in patients.[12,13] The comparative study conducted by Melody Taheri et al on RAF, uterine artery embolization (UAE), and HIFU, reveals that RFA demonstrates the most significant reduction in fibroid volume.[36] And the objective of RFA is to decrease the size of fibroids, while UAE impacts the overall dimensions of the uterus. Despite HIFU being non-invasive, RFA offers several theoretical advantages including cost-effectiveness, shorter treatment times, and superior rates of complete ablation.[37] Additionally, the prevalence of intrauterine adhesion formation after myomectomy can be as high as 45%, whereas no synechiae have been observed following RFA during hysteroscopic evaluation.[38] To mitigate the recurrence rate following RFA, which has been reported to be nearly 20%, prior research has employed US-guided RFA in conjunction with a levonorgestrel-releasing intrauterine system as a straightforward, secure, and efficacious alternative for managing symptomatic adenomyosis.[39] In addition, limited research has been conducted on the adverse outcomes associated with RFA. The most commonly observed complications include abdominal pain, erythema and skin reaction at the insertion site, as well as symptoms indicative of urinary tract infection.[40] The majority of reported complications were classified as minor events such as pain, discharge, and adhesion that did not necessitate any intervention. However, even though RFA for uterine myoma is widely acknowledged as a safe and effective procedure, there remains a potential risk of pelvic organ penetration and burn injuries. The surgeon should take into account the possibility of causing thermal injury to adjacent organs in cases where there are suspected severe adhesions or co-existing endometriosis. It is of utmost importance to closely observe the focal point using ultrasonography and establish the duration according to the heightened echogenicity of the fibroid during a RFA procedure.[41]

Microwave Ablation (MWA)

MWA is a thermal treatment modality that utilizes a microwave antenna to generate electromagnetic waves. Real-time US imaging enables monitoring of the ablation range, microwaves are directed towards the targeted lesion under real-

time US imaging guidance, resulting in localized tissue coagulation and necrosis. Crucially, this method guarantees the safeguarding of adjacent tissues and organs, ultimately leading to alleviation or eradication of symptoms.[42,43] The first report by Zhang et al in 2011 demonstrated the applicability of US-guided percutaneous MWA (PMWA) for treating symptomatic adenomyosis, indicating its effectiveness in symptom relief with no major complications observed. Since then, US-guided MWA has gained increasing acceptance and recognition among clinicians and patients due to its inherent advantages, including minimal invasiveness, low complication rates, accelerated post-treatment recovery, ease of performance, as well as reduced time and economic costs compared to alternative treatments.[44]

The US-guided PMWA technique effectively treats symptomatic adenomyosis and uterine fibroids (Figure 2). [45,46] Presently, numerous research studies have been conducted to explore the post-ablation assessment, including technical efficacy, clinical efficacy, and safety. The ablation rate is a key parameter for evaluating the efficacy of MWA. In principle, the ablation rate for adenomyosis should exceed 70%, with most reported rates of MWA surpass 90%. In terms of evaluating clinical effectiveness, dysmenorrhea score, UFS-QOL scale, and PBAC score are commonly employed to assess symptomatic relief; while CA125 and hemoglobin levels are employed to assess clinical efficacy as well.[47] A study found that there was significant relief from dysmenorrhea and menorrhagia, a notable decrease in serum CA125 levels, a substantial enhancement in serum hemoglobin levels, as well as a considerable reduction in both the size of the uterine body and adenomyosis lesion within three months following treatment during a 12-month follow-up after MWA.[7] Studies have shown that the remission rate of dysmenorrhea symptoms in patients undergoing US-guided percutaneous MWA exceeds 80%, with significant relief within three months post-treatment and sustained improvements up to 12 months later.[48] The utilization of MWA also leads to the restoration of a regular menstrual cycle and a decrease in excessive bleeding, and it can greatly ameliorate anemia symptoms in patients suffering from adenomyosis.[49] Furthermore, the utilization of MWA demonstrates significant efficacy in reducing both uterine and lesion volumes, with particularly favorable long-term outcomes.[50] A previous study showed that the ablated lesion continued to shrink for one year after ablation, resulting in a gradual improvement in the symptom relief rate over time within one year after ablation.[14,51] The evaluation of efficacy, moreover, plays a pivotal role as an essential component. Contrast-enhanced sonography (CEUS) and enhanced MRI can be used interchangeably for observing the ablation range treated with MWA. CEUS can serve as a preferred non-invasive examination modality for initial assessment and follow-up purposes. The identification of non-enhancing areas on pretreatment CEUS indicates satisfactory treatment outcomes.[52] Meanwhile, enhanced MRI can provide comprehensive evaluation of the relationships among uterine myomas, the entire uterus, and surrounding tissues.[53]

The benefits of MWA are evidently apparent. The US-guided MWA showcases a highly favorable safety profile owing to its remarkably minimally invasive nature in comparison to other more intrusive treatment modalities.[47] In spite of the treatment outcomes and quality of life improvements are similar between UAE and MWA, MWA presents a lower risk of embolic complications, better tolerability, and reduced cost.[54] Furthermore, in comparison to other thermal ablation methods, MWA is a relatively simple and time-saving procedure, likely due to its ability to achieve higher tissue temperatures and larger ablation volumes based on the principal mechanisms of different ablation methods.[55,56] In a retrospective study comparing the median treatment times between MWA and HIFU for symptomatic uterine fibroids, the MWA group had a significantly shorter median treatment time of 46.2 minutes compared to the HIFU treatment group, which had a median treatment time of 92.5 minutes.[57] The efficacy of HIFU and RFA treatments is constrained by the location and size of the myomas. During HIFU ablation, there is a gradual attenuation of energy during transmission of the US wave. In situations where the myomas are located at a significant depth, there is a possibility that the US wave may not possess adequate penetrating capability to achieve desired outcomes, potentially leading to incomplete ablation of lesions.[37] Similar to HIFU, RFA is mostly effective for small-sized myomas due to limitations imposed by tissue impedance that hinder efficient energy delivery to tissues and limit temperature control during ablation. This study also revealed that women with myomas exceeding 75 cm^3 exhibited elevated reoperation rates and reported lower satisfaction levels following RFA.[58] Therefore, MWA is more suitable for the treatment of large and multivessel fibroids.[57] A meta-analysis, encompassing 38 studies involving 15,908 patients with symptomatic adenomyosis from the period of 2000–2020, revealed that PMWA exhibited superior efficacy compared to RFA and HIFU, particularly when assessing local treatment response based on parameters such as non-perfused volume ratio and volumetric reduction rate of the

uterus and lesion.[8] Additionally, the microwave therapy exhibited superior efficacy in alleviating pain compared to RFA for adenomyosis.[51] In summary, when compared to HIFU and RFA, MWA offers several advantages: consistently higher tissue temperatures, a larger ablation volume, shorter operation times, less sensitivity to tissue type resulting in more consistent outcomes, reduced procedural pain due to its non-reliance on electrical conduction into the lesion, and freedom from impedance limitations. However, MWA treatment necessitates hospitalization and general anesthesia.[57]

MWA is a secure therapy with minimal occurrence of significant complications. Common minor complications after ablation include lower abdominal pain, fever, vaginal discharge, and slight vaginal bleeding. Generally, no additional invasive treatment is required, and post-ablation discomfort usually disappears within a short time. At times, the presence of intense pain during the procedure may require ending the ablation treatment earlier than planned, leading to a restricted range of ablation and inability to accomplish the predetermined goal. However, there is still a lack of knowledge regarding the optimal anesthesia approach for ablation procedures, highlighting the need for further prospective studies.[47] With the support of US guidance, a comprehensive monitoring system is implemented to track the correlation between the needle trajectory and the nidus, along with its neighboring areas. Ensuring precise depth and positioning of the ablation needle within the nidus through continuous monitoring in real-time is crucial to maintain a safe distance, thus minimizing any potential risks to vital organs, endometrium, and serosal layer. To reduce the potential interference of gas caused by percutaneous puncture in the abdomen, US-guided MVA can be utilized for subserous adenomyomas located near the rectum or posterior wall.[7] This enables enhanced visualization of the tissue surrounding the ablation zone, thereby minimizing complications and ensuring complete ablation. To reduce the risk of pelvic organ injury during ablation procedures, artificial ascites can effectively establish a protective barrier between lesions and adjacent organs, thereby increasing the physical distance separating them.[59] Therefore, it is recommended that individuals who have a history of abdominal surgery with complications related to pelvic adhesions or those with lesions located in close proximity to the pelvic organs should consider utilizing the artificial ascites method. This approach aims to improve the effectiveness of ablation procedures and minimize the occurrence of severe complications. Moreover, appropriate patient selection and effective preoperative planning can further decrease the incidence of complications. In order to minimize the potential for harm to healthy tissue and achieve an effective ablation range, it is essential to establish clear guidelines for terminating the procedure in the treatment plan and adhere strictly to them throughout the operation. However, previous studies have lacked uniformity in their adoption of termination criteria, with individual research centers implementing their own standards.[7] There are still many clinical challenges that remain unresolved in this area, which highlights the need for more prospective multicenter studies of excellent quality to enhance therapeutic effectiveness and promote further standardization of the ablation procedure.

High-Intensity Focused Ultrasound (HIFU)

While other minimally invasive therapies, such as RFA or MWA, use an electrode or antenna to deliver electromagnetic waves, HIFU therapy utilizes US waves as carriers of energy.[60] The treatment principle of HIFU is to heat, cavitate, and damage blood vessels by concentrating energy on the target location causing blood supply disruption, eventually inducing thermal coagulative necrosis of biological tissues.[61,62] The technique offers several advantages, including the lack of radiation exposure and the ability to selectively treat target fibroids without causing damage to the endometrium, which makes it particularly suitable for women with disease-related problems of fertility.[63] More importantly, HIFU provides the only truly non-invasive approach.[64,65] Given its noninvasive nature, HIFU carries minimal chances of complications such as bleeding or infections. Additionally, this procedure can be conveniently conducted on an outpatient basis, contributing to its swift worldwide acceptance. The first global clinical application of HIFU for the treatment of uterine fibroids took place in China in 2002.[66] Since its initial clinical use, this technique has gained recognition for its safety, satisfactory therapeutic efficacy in symptom management, ability to preserve the uterus, radiation-free nature, and avoidance of hospitalization. Over the past two decades, HIFU has been extensively employed as a highly effective and safe treatment modality for uterine fibroids and adenomyosis.[66–68]

In order to precisely pinpoint the focal point of HIFU at the intended target and effectively evaluate therapeutic responses, both US-guided and MRI-guided devices are widely employed in this regard.[69] In US-guided HIFU (US-HIFU), echogenic changes resulting from tissue water boiling or acoustic cavitation are utilized to pinpoint the target

location, offering real-time capability and insensitivity to motion.[70] Additionally, the US possesses the capability to accurately predict HIFU propagation within the human body due to leveraging the same physical properties utilized in both therapy and imaging. However, the measurement of temperature change remains challenging in the US, and as the treatment progresses, there is a noticeable degradation in image quality.[70,71] Consequently, this may potentially result in increased damage to normal endometrial tissue. A study found that CEUS can effectively enhance US guidance during HIFU ablation of uterine fibroids while maintaining safety.[72] The clinical application of MR-guided HIFU (MR-HIFU) has been received approval from the US FDA in 2004 for treating symptomatic uterine fibroids.[73] In terms of real-time temperature measurements, MR imaging exhibits a significant advantage over US. The utilization of MR thermometric monitoring extends beyond the focal point of HIFU, encompassing the neighboring structures as well, enabling the operator to discern intended thermal responses at the target and identify any undesired heating occurring in its vicinity. The temporal precision of MR imaging, however, is comparatively lower than that of US and occasionally encounters disruptions caused by target movement or the presence of adjacent intestinal loops. Temperature feedback plays a vital role in hyperthermia applications, as the achievement of a high non-perfused volume (NPV) percentage necessary for effective treatment relies on maintaining consistently elevated temperatures over an extended duration.[74] Although previous studies have shown that only contrast-enhanced MR imaging can quantify NPV or NPV ratio, Zhou et al discovered that quantitative parameters from CEUS may be useful for evaluating the therapeutic effect of HIFU.[75,76] The correlation between the NPV ratio and enhancement intensity and rate was found to be negative, while it exhibited a positive correlation with arrival time, peak time, and enhancement time.

The assessment of post-therapeutic outcomes greatly relies on the significance of the NPV ratio, as it exhibits a strong correlation with the treatment's enduring efficacy. The NPV percentage after HIFU should be maximized, aiming for a minimum of 80%.[77] A study highlighted that the clinical effectiveness rate was approximately 80% when the NPV reached or exceeded 70%.[78] Several studies investigating the HIFU treatment for uterine fibroids or adenomyosis have reported a correlation between lesions located on the posterior wall and a lower NPV ratio, as well as a higher incidence of local and symptomatic recurrence one year post-treatment.[79,80] Liu et al demonstrated that achieving an NPV ratio higher than 70% resulted in an acceptable re-intervention rate during the follow-up period after HIFU.[81] The alleviation of dysmenorrhea following treatment serves as a crucial measure to evaluate the efficacy of adenomyosis management.[79] A study demonstrated that HIFU exhibited significant efficacy in alleviating dysmenorrhea associated with adenomyosis, particularly in those with severe symptoms.[15] However, previous studies have also demonstrated that HIFU is associated with a higher risk of reintervention.[82] Given the high recurrence rate observed in some patients shortly after HIFU ablation, it is imperative to explore alternative therapeutic schedules in order to achieve a lower recurrence rate. Gonadotropin-releasing hormone analogues (GnRH-a) are utilized in the medical treatment of uterine fibroids. Pretreatment using GnRH-a prior to HIFU ablation has the potential to minimize uterine fibroid size and vascularity, resulting in reduced treatment duration and improved tissue responsiveness towards HIFU. The studies have demonstrated that the combination of HIFU with GnRH-a treatment exhibits superior efficacy compared to HIFU monotherapy alone.[83–85] The same principle applies to managing adenomyosis. Generally, as the size of uterine fibroids increases, longer treatment duration is required.[61] Therefore, operators should be mindful of the maximum size of uterine fibroids that can be ablated in one session. And it is of utmost importance to precisely identify the position of bowel loops using imaging techniques due to the unpredictable nature of intestinal peristaltic motion during the procedure.[86] Regarding the typical adverse effects observed after undergoing HIFU treatment, they mainly include skin disruption, swelling beneath the skin, discomfort in the lower abdomen, sciatic nerve pain, and a slight amount of vaginal bleeding accompanied by discharge. No mortality cases have been reported thus far, and the majority of complications were not significantly adverse.[71] Therefore, the successful treatment with HIFU can be achieved through meticulous participant selection, thorough planning, and diligent technique monitoring during ablation.[87]

The Impact of Thermal Ablation Technology on Fertility

RFA may enable a minimally invasive, uterine preserving and protecting fertility option. It has shown promising results in improving quality of life and reducing symptom severity scores.[88] The results of a case report demonstrated a significant 68% reduction in fibroid volume and resolution of dysmenorrhea symptoms following RFA for uterine

fibroids.[89] Additionally, this infertile couple achieved successful full-term delivery, followed by assisted reproduction technology. Furthermore, from the data that is currently available, it can be inferred that most patients who underwent RFA treatment were able to successfully carry their pregnancies to full term without any adverse effects on their newborns.[90] In a study involving patients with adenomyosis, who underwent US-guided RFA, the successful delivery rate of live birth was found to be 84.6%.[13] Moreover, a recent study explicitly pointed out that the combination of RFA and GnRH-a resulted in higher natural conception rates and pregnancy rates, effectively relieving clinical symptoms, protecting postoperative ovarian function, and reducing recurrence rates.[91] Hence, considering fertility preservation, RAF treatment could be a more favorable alternative for patients. Nevertheless, it is imperative to conduct additional research with a considerably larger sample size in order to comprehensively evaluate pregnancy outcomes and establish the safety of RFA for women aiming to conceive in the future.[20] However, the utilization of this method is still limited; this may be attributed in part to the lack of FDA approval for fertility preservation.

MWA appears to be an optional, fast, and safe therapy for patients with symptomatic uterine fibroids and adenomyosis who wish to preserve their fertility. MWA localizes at focal lesions, ensuring the preservation of the organizational structure outside these lesions, particularly the pelvic vascular structure; therefore, it does not yield any statistically significant impact on ovarian function.[92] A study involving 169 women of reproductive age was conducted to observe unplanned pregnancies that occurred after the treatment of uterine fibroids with MWA. The research revealed that nine women experienced unplanned pregnancies, among whom three chose to continue with the pregnancy and successfully delivered healthy term infants without any significant obstetric complications.[93] These findings strongly suggest that patients who undergo MWA treatment for uterine fibroids may have a natural ability to conceive, and higher rates of ablation may potentially improve fertility in infertile patients. However, it is important to note that current research on this topic is limited, and further prospective studies with larger sample sizes are needed to investigate the impact of MWA on fertility and pregnancy outcomes.

The advantages of HIFU lie in its non-invasive nature, precision, safety, efficacy, and absence of scarring. Another potential benefit is that this treatment modality does not impact fertility. In contrast to the UAE procedure, HIFU does not expose the ovaries to ionizing radiation. The post-HIFU procedure assessment of anti-Mullerian hormone levels, conducted after 6 months, demonstrated no significant decrease and exhibited no discernible difference.[94] It confirmed that ovarian vessels had not been destroyed during the procedure. Moreover, preliminary pregnancy outcomes following MR-HIFU demonstrate promising results, characterized by a notable success rate in terms of both delivered pregnancies and ongoing gestations.[16] The most significant finding was that MR-HIFU treatment did not exhibit an elevated incidence of spontaneous abortions or pregnancy complications in the conducted studies.[95] HIFU presents a compelling minimally invasive alternative for women seeking to conceive and deliver after undergoing treatment for uterine fibroids or adenomyosis, and the current body of research increasingly supports this notion. Based on a comprehensive analysis of a recent case report, it was even preliminary demonstrated that MR-HIFU was successfully applied in patients with an early-stage pregnancy, without any therapy-related complications.[96] HIFU can be regarded as a viable option for individuals who satisfy the eligibility requirements and reject alternative approaches. However, the technique of US-HIFU/MR-HIFU is a recently incorporated method in the noninvasive approaches employed for preserving fertility during treatment of uterine fibroids and adenomyosis, there continues to be a scarcity of data that is of superior quality.[97] Additionally, there is a lack of comparative research or randomized clinical trials that assess the effectiveness of HIFU in comparison to other treatment options.[98] Therefore, it is of utmost importance to carry out randomized controlled trials for the purpose of comparing the reproductive outcomes between HIFU and standard care, with the aim of providing substantial evidence for women desiring conception.[99]

Conclusion

In the current era of rapid-paced living, there is a growing inclination towards treatment methods that are minimally invasive, providing shorter durations for treatment and accelerated recuperation after surgery. In addition, individuals who wish to maintain their fertility while keeping their uterus intact may find minimally invasive treatments to be a more advantageous choice. The thermal ablation therapies of MWA, RFA, and HIFU collectively belong to the realm of minimally invasive treatments. The success of thermal ablation therapies is characterized by their remarkable ability to

significantly reduce the volume of fibroids or adenomyosis, effectively alleviating the clinical symptoms of the disease and minimizing its recurrence. Furthermore, these therapies not only protect fertility by preventing spontaneous abortion and pregnancy complications but also improve prospects for better pregnancy outcomes and higher live birth rates. Undeniably advantageous, these procedures ensure effectiveness, safety and expedite postoperative recovery. Consequently, they present a viable alternative for patients who decline hysterectomy treatment. Clinicians should thoroughly evaluate the benefits of these approaches and take into account individual patient circumstances to determine the most appropriate treatment option. More significantly, these three treatments can be considered as potential options for infertile patients with gynecological diseases (such as uterine fibroids and adenomyosis) who desire to preserve their fertility. However, extensive randomized prospective trials are still required to more effectively demonstrate the advantages and disadvantages of these technologies.

Author Contributions

Qing Zhang, Xiaowen Liang and Zhiyi Chen conceived the study and worked on its design. Qing Zhang and Xiaowen Liang contributed to the data analysis and the manuscript writing. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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