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Uterine Myomas: Extravascular Treatment

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Uterine fibroids are common benign tumors that affect the female reproductive tract. They are responsible for considerable morbidity and deterioration of life quality. The main advantages offered by mini invasive techniques are low grade of invasiveness and short times of hospitalization. The most diffuse technique is uterine artery embolization (UAE). Common concerns with UAE include postprocedural pain, postembolization syndrome, and risk of infection. Image-guided thermal ablation techniques like radiofrequency ablation, percutaneous microwave ablation, and imaging-guided high-intensity focused ultrasound were introduced to overcome the side effects related to UAE and surgery. The aim of this review is to briefly analyze the ablative procedures and their role in the management of symptomatic fibroids, and to describe the safety profile and outcomes of these modalities.
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Introduction

Myomas or leiomyomas, commonly defined as uterine fibroids (UFs), are monoclonal tumors originating from the smooth muscle of the myometrium with a large extracellular matrix component containing collagen, proteoglycan, and fibronectin.[1] They are the most frequent benign tumors of the female genitourinary tract affecting women of reproductive age. The peak of prevalence is in the fifth decade of life with involvement of over 50% of 40-year-old women.[2,3] The tendency of UFs to enlarge during pregnancy or with the use of oral contraceptive therapy, and to decrease after menopause, is explained by their estrogen-dependence.[4]

UFs have a broad impact on women's health and lifestyle, and represent a costly public health issue: although many women with myomas may have no symptoms and be unaware of the disease, significant clinical manifestations such as dysmenorrhea, menorrhagia, back pain, sensation of pelvic pressure, subfertility and reduced quality of life are generally present in a quarter of affected patients.[5-7] Due to relevant symptoms, almost a third of women with leiomyomas will require treatment.[5] Although surgery is still the main management strategy, the choice of treatment is guided by the patient's age and desire to preserve fertility, or avoid radical surgeries such as hysterectomy. The number, size and position of fibroids evaluated by high-quality ultrasound (US) examination in simple cases and by magnetic resonance imaging (MRI) (Fig. 1A, B) in other more complex pathologic conditions may influence their management.[8] In women who have completed pregnancy, symptomatic UFs are mostly treated via radical hysterectomy, while conservative strategies are preferred in women who wish to preserve fertility. Myomectomy, uterine artery embolization (UAE) and fibroids ablation represent alternative treatments to preserve the uterus. Although hysterectomy is still the most commonly performed procedure for symptomatic fibroids with the lowest rate of re-intervention, it obviously entails the drawbacks of any surgical procedure, namely higher complication rates with less favorable satisfaction of the patient and ability to return to normal activities.[8] UAE was the only valid conservative treatment for a long period[4]; in the last years, the need for alternatives to surgery has led to the development of other nonsurgical uterine-sparing approaches, notably thermal ablation techniques which include high-intensity focused ultrasound (HIFU), radiofrequency (RF), and percutaneous

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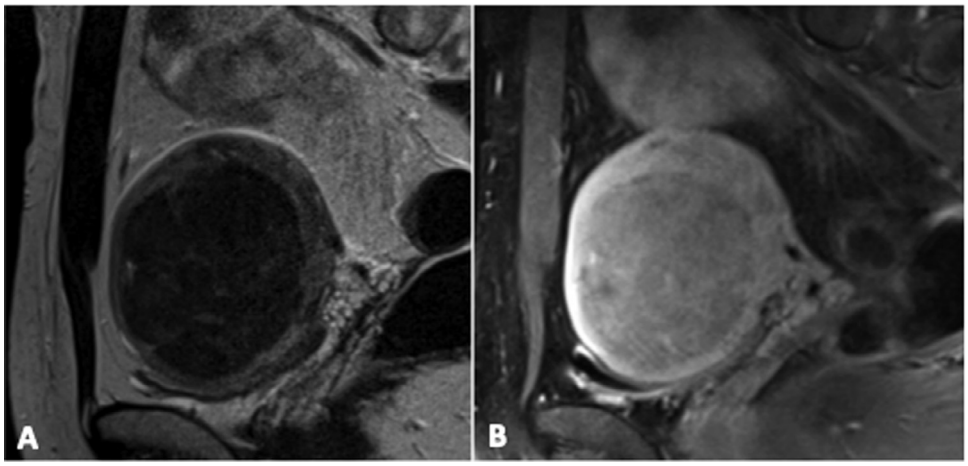

Figure 1 Pretreatment MRI images of an uterine fibroid suitable for percutaneous approach (A,B).

microwave (PMW) ablation. These new techniques are increasingly being exploited for the minimally invasive treatment of symptomatic leiomyomas.

The purpose of this review is to briefly analyze the ablative procedures and their role in the management of symptomatic fibroids, and to describe the safety profile and outcomes of these modalities.

Literature Research

An extended literature search was performed by two independent investigators using the PubMed databases for studies related to human medicine published from January 2010 to December 2019 in the English language. The Mesh terms "ablation techniques" and "leiomyoma" or "uterine fibroid" or "symptomatic uterine fibroid" were used, and combined with the Boolean operator "AND." Moreover literature search was completed with the following terms: "interventional radiology," "percutaneous thermal ablation," "percutaneous microwave ablation" or "MWA," "radiofrequency" or "RF," and "high-intensity focused ultrasound" and "HIFU."

Articles that described outcomes and complications of thermal ablation for UFs by using HIFU, RF, and MW were included. Reviews, case series, case reports, and articles reporting previously published data were excluded from the analysis.

At first, the reviewers checked the results at both the title and abstract level. Then, the full-texts of the selected articles were retrieved and reference lists were manually cross-checked to find any additional relevant study. In case of disagreement between the 2 reviewers, a further author was consulted to achieve a consensus.

Data from the selected studies were extrapolated and collected into a form specifically designed for each ablation modality.

The primary endpoint was to evaluate the feasibility and safety of the given technique. The secondary endpoint was to investigate the effectiveness in terms of improvement of symptoms and quality of life.

The feasibility was defined as technical success rate, in particular as the completion of the procedure according to the planned protocol.

Clinical success was determined thorough the symptoms severity score (SSS) of the Uterine Fibroids and the Quality of Life questionnaire (UFS-QoL).[9]

Complications were graded according to the SIR (Society of Interventional Radiology) classification system; major complications were therefore defined as adverse events which may lead, if left untreated, to substantial morbidity and disability, increase the level of care, result in hospital admission or considerably lengthen the hospital stay.[10] All the other complications were classified as minor.

Analysis of the Results

The initial search strategy yielded a total of 280 potentially relevant citations. After removal of case reports, case series, reviews, guidelines, and original articles not in the field of interest, and after accurate check of reference lists of the full-text articles retrieved, there were finally 93 studies which fulfilled the inclusion and exclusion criteria.

Here, we provide a per technique analysis of the results.

RFA

Various studies estimated the safety and efficacy of RFA in the treatment of symptomatic UFs using different devices and therapeutic routes. Twenty-eight studies were found eligible for inclusion in our systematic search (**Table 1**). In the articles analyzed,[11-38] the procedures were performed via percutaneous (15 articles) (**Fig. 2**), transvaginal (8 articles) and transcervical approach (5 articles). The study with the largest number of patients treated (1216) was published by Yin et al,[14] with a subgroup of 740 menopausal women presenting a lower postoperative recurrence rate than the premenopausal one.[14]

Table 1 The Table Summarizes All Reviewed Series of Uterine Fibroids Treated by RFA, According to Each Variable Included in Review Process

Study	Pts	Fibroids Treated per pt	Fibroid Dimension	Treatment Time	Ablation Rate	RFA Delivery	Technical Success	Clinical Success	Complications	Follow-Up (mo)	Rate of Reintervention
Berman J 2014	Baseline 135 104 with 36 mo data	n.a.	n.a.	n.a.	n.a.	PL; US guidance	n.a.	SSS from 60.2 to 27.6 HRQL from 39.2 to 77.8	No procedure- or device-related AE during the last 12 mo of the trial	36	11% (14 of 135 pts)
Bongers M 2014	50	2.4	3.2 cm 18.8 cc	38.8 min	Volume reduction at 3 mo 68.8%	TFA; US guidance	n.a.	Improvement at 6 mo SSS 59.7%, HRQoL 263%	2 serious AE (overnight admissions for abdominal pain and bradycardia)	6	0
Braun K 2016	40	4.2	6 cm	1.9 h	n.a.	PL; US guidance	n.a.	n.a.	1 minor non device-related (uterine serosal laceration) 1 device-related (bleeding probe insertion site) No postoperative complications	46.4 ± 21.0 d	0
Brölmann H 2016	50	1.8	3.2 cm	n.a.	Volume reduction 3 mo 54.7% 12 mo 66.6%	TFA; US guidance	n.a.	Improvement at 12 mo SSS decreased 55.1 ± 41.0% HRQOL 277 ± 483%	34 minor AE procedure- or device-related: dysmenorrhea, abnormal uterine bleeding, pelvic pain and/or cramping, urinary tract infections, fibroid expulsion, abdominal pain, bradycardia	12	4
Carrafiello G 2009	11	1	5.5 cm 101.5 cm^3	20 min	Mean volume reduction 46.9-91% (1-9 mo)	PL; US guidance	100%	SSS baseline: 50.30 SSS FU: 13.38 QOL score baseline 62 QOL score end FU 90.4	No intra- or postoperative complications	9	1 hysterectomy for persistent pain and menorrhagia
Cho H 2014	24	n.a.	112.37 cm^3	n.a.	Volume reduction 24 mo: 84.2%	TV; US guidance	n.a.	SSS from 75.9 to 11.6 HRQoL from 46.1 to 90.2	No serious or life-threatening complications Postoperative pain in 33.3% pts increased vaginal discharge in 27.7% pts	24	6 myomectomies 3-6 mo after RFA
Chudnoff S 2019	147	3.0	2.5 cm 71.1 cm^3	n.a.	Mean maximal volume reduction 62.4%	TFA; US guidance	n.a.	HRQoL: 43.7 point improvement SSS: 32.1 point improvement	2 procedure-related serious AE in 2 pts (1.4%) Non serious procedure-related AE in 74 pts (50.3%).	12	1 elective hysterectomy in a pt at 12-month
Chudnoff S 2013	135	5.0	0.7-9.7 cm 80.4 cm3	126 min	Volume reduction 3 mo:39.8% 12 mo:45.1%	PL; US guidance	n.a.	Improvement at 12 mo SSS:34.5 HRLQ:42.2	Device-related AE in 5 pts (3.7%) 1 serious AE event (pelvic abscess), 0.7%	12	1 surgical reintervention for persistent bleeding (0.7%)
Galen D 2014	Phase II 69 Phase III 135	Phase II: 3 Phase III: 4	n.a.	Phase II: 2.33 h Phase III: 1.88 h	Uterine volume decrease baseline and 12 mo Phase II: 28.7% Phase III: 25.7%	PL; US guidance	n.a.	Improvement at 12 mo Phase II SSS 83.7% HRQL 89.8% Phase III SSS 56.5% HRQL 110.4%	Phase II: one serious device-related AE (hematoma abdominal wall), 1.4% 6 procedure-related AE, 10%(4 abdominal pain,2 urinary tract infections)	12	n.a.

Table 1 (*Continued*)

Study	Pts	Fibroids Treated per pt	Fibroid Dimension	Treatment Time	Ablation Rate	RFA Delivery	Technical Success	Clinical Success	Complications	Follow-Up (mo)	Rate of Reintervention
									Phase III: 5 device-related AE (pelvic abscess, sigmoid colon laceration, uterine serosal burn, severe lower abdominal pain, vaginal bleeding) 3.7%		
Galen D 2013	124	n.a.	n.a.	n.a.	n.a.	PL; US guidance	n.a.	post treatment decrease in monthly bleeding -45.1% (submucous myomas) -31.8% (intramural myoma)	n.a.	12	n.a.
Garza-Leal J G 2019	17	2.1	2.5 cm	n.a.	n.a.	TFA; US guidance	n.a.	SSS from 64.9 to 27.6 HRQoL from 27.2 to 76.0	n.a.	64.4	11.8% at 5.4 y, with 2 hysterectomies
Garza-Leal J G 2011	31	2 total 76	0.5 to 10.0 cm	n.a.	Mean uterine volume reduction 12 mo: 81.2 cm3 in 14 of 29 (73.7%)	PL; US guidance	3 intraoperative protocol deviations		Improvement at 12 mo SSS: 38.1 (82%) HRQoL:37.6	AE in 7 pts: abdominal pain (4), urinary tract infections (2), an abdominal wall vascular injury (1)	12
no repeat treatments or procedures											
Guido R 2013	124	n.a.	n.a.	n.a.	n.a.	PL; US guidance	n.a.	Improvement at 24 mo SSS:35.7 HRLQ:40.9	one serious AE procedure related	24	4.8% for bleeding between 12 and 24 mo
Hudgens J 2019	125	3.1	2.5 cm 72.3 cc	procedural time 2.5 h	Mean maximal volume reduction 63.8%	TFA; US guidance	n.a.	SSS and HRQoL improvements at 12 mo: 33.8 points and 45.8 points	0.0% of device related AE; 0.8% procedure-related serious AE (deep venous thrombosis)	12	99.2% of pts free from surgical reintervention
Iversen H Dueholm M 2017	66	1	122.5 mL	n.a.	Volume reduction 103.4 mL	PL; US guidance TV; US guidance	n.a.	Improvement at 9 mo (n = 53) SSS 27.1 HRQOL 22.1	n.a.	58.9	35% (7 myomectomies and 15 hysterectomies)
Iversen H 2012	42	n.a.	197.3 cm3	for a 2-cm ablation (4.2 cm3): 2 min 3-cm (14.1 cm3) ablation:5 min 4-cm (33.5 cm3) ablation: 9 min	Volume reduction 69.7%	PL; US guidance	n.a.	Improvement at FU SSS 48.6% (from 60.7 to 31.2) HRQOL score 46.4% (from 55.6 to 81.4)	No complications	9 (n = 40)	Hysterectomy in 2 (4.7%) pts for other reasons

Table 1 (*Continued*)

Study	Pts	Fibroids Treated per pt	Fibroid Dimension	Treatment Time	Ablation Rate	RFA Delivery	Technical Success	Clinical Success	Complications	Follow-Up (mo)	Rate of Reintervention
Jiang X 2014	46	1	4.8 cm 67.4 cm^3	25 min	Volume reduction 72.1% at 6 mo 83.0% at 12 mo	TV; US guidance	n.a.	SSS baseline: 32.20 12 mo: 3.88 HRQL baseline: 71.85 12 mo: 96.54	No complications	12	8.7%
Kim CH 2011	69	n.a.	7.9 cm 304.6 cm3	17.8 min	12 mo volume reduction:74.0%	TV; US guidance	n.a.	Improvement at 12 mo SSS: from 57.0 to 12.1	No major complications Lower abdominal pain in 32 (46.4%) pts Vaginal discharge in 12 (17.4%)	12	n.a.
Krämer B 2015	RFA group n = 26 Myomectomy laparoscopic group n = 25	RFA group 2.9 $\pm$ 2.6 Myomectomy laparoscopic group 2.4 $\pm$ 1.6	n.a.	n.a.	n.a.	PL; US guidance	n.a.	RFA group SSS baseline: 38.9 SSS 24-month FU:16 Myomectomy laparoscopic group: SSS baseline: 41.8 SSS 24-month FU: 22.3 RFA group UFS-QOL baseline:77.1 UFS-QOL 24 mo: 89.4 Myomectomy: UFS-QOL baseline:70.2 UFS-QOL 24 mo FU: 85.6	RFA group: 1 serious complication (hypermenorrhea) Laparoscopic myomectomy group: 1 hematoma at the trocar site	24	n.a.
Lee Y 2010	66	1	4.9 cm	Complete ablation 3-cm myoma: 5 min 5-cm myoma:10 min	Volume reduction rate 3 mo 75.5% 6 mo 80.7%	TV; US guidance	n.a.	Improvement at 18 mo SSS: baseline 71.3 18 mo:10.3 HRQoL score baseline: 48.8 18 mo: 97.5	No major complications Postoperative pain within 1-7 days(3.4%) Vaginal spotting 4-8 weeks(5.1%) Increased vaginal discharge in 20.6% pts	18	3.4%
Marcos R G 2014	17	1	112.26 cm3	35.9 min	Volume reduction 57.38% US, 79.66% MRI at 6 mo	PL; US guidance	92.86% radiological success (fibroid necrosis $>$ 50% at 6 mo)	in 11/17 (64.7%)	No intraoperative complications Procedure related AE in 5 pts (29.4%)	6	18.7% Only 1 pt required hysterectomy
Meng X 2010	50	n.a.	4.68 cm 69.63 cm^3	n.a.	45 of 50 (90%) pts by RFA	PL; US guidance	n.a.	n.a.	No major complications	in hospital follow-up only	n.a.
Rattray D 2018	RFA, n = 23; Myomectomy, n = 22	3.4	n.a.	RFA: 70.0 min Myomectomy: 86.5 min	n.a.	PL; US guidance	n.a.	HRQL improvement RFA group: 62.2% Myomectomy group: 45.8%. SSS reduction at 3 mo ($-$44.8%) in both groups	No complications in RFA group 20 s asystole during a myomectomy procedure	3	1 laparoscopic hysterectomy in a subject of the RFA group with heavy menstrual bleeding

Table 1 (*Continued*)

Study	Pts	Fibroids Treated per pt	Fibroid Dimension	Treatment Time	Ablation Rate	RFA Delivery	Technical Success	Clinical Success	Complications	Follow-Up (mo)	Rate of Reintervention
Rey V 2018	205	n.a.	122.4 cm^3	17 min	Reduction 51.55% at 6 mo and 60% at 12 mo	TV; US guidance	n.a.	98.04% of pts satisfied	No intraoperative complication 2 (1.46%) pts with intracavitary free myoma (type III-b complications Clavien-Dindo classification)	12	n.a.
Robles R 2013	36	n.a.	n.a.	n.a.	Uterine volume decrease (12 mo) 48.2 cm3	PL; US guidance	n.a.	Improvement at 12 mo SSS: 53.7 HRLQ:50.4	no procedure-related complications	12	no hysterectomy
Turtulici G 2018	19	1.7	13.6 ml	28 min	Volume reduction 62.7%	TV; US guidance	100%	QOL score from 68 to 97 at 6 mo	No major immediate or late complications Minor complications in 2 pts(low fever, lower abdominal pain and fluid in pelvic pouches)	6	n.a.
Wu XJ 2016	51	1.2	3.63 cm 33.0 cm3	20-40 min	Volume reduction at 1-, 3-, 6-, and 12 mo of 28%, 57%, 63%, and 78%	TV; US guidance	n.a.	SSS Baseline: 45 ± 34 12-month: 0 QOL Baseline 65 ± 41 12-month: 100	No major complications lower abdomen pain after the procedure in six patients (12%) vaginal discharge in 11 patients (22%)	12	n.a.
Yin G 2015	Group A: 476 premenopause pts	1.7	4.5 cm	n.a.	Volume reduction at 24 mo Group A 88.3%	n.a.; US guidance	n.a.	after RFTA, HRQL higher than baseline in both the groups	Major complications in Group A-Group B Intraoperative bleeding (24.4%-28.5%), postoperative pain (23.1%-26.5%), postoperative bleeding (9.9%- 8.8%), recurrence (10.7%-2.4%), myoma neglection (6.1%-8.1%), and pelvic infection (3.6%-5.4%), intestinal perforation(0.21-0.27%)	36.5	n.a.
	Group B: 740 menopause pts	2.6	5.0 cm		Group B 90.3%						

PL, percutaneous laparoscopic; RFA, radiofrequency ablation; TFA, transcervical fibroid ablation; TV, transvaginal; US, ultrasound.

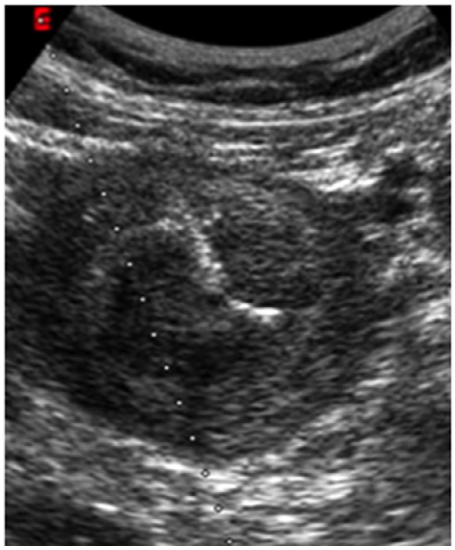

Figure 2 Intraprocedural image during treatment with RFA through percutaneous US-guided approach.

The most used ablation system in the series selected works with a low voltage, high frequency (45-500 kHz) alternating current, with a typical current level at 60 W and 60 Ω of 1 amp.[18]

RFA delivery approaches showed considerably different procedural times among the different techniques employed.

In a multicenter study, the use of a RF treatment device with incorporated US was described; the probe was inserted transcervically, with energy delivered at 150 W, ablating simultaneously different sections of the to-be-treated myoma for 4-7 minutes.[36]

Rey et al[33] by applying a lower RF power (100 W) despite the higher initial volume of the UFs (122.4 cm3 vs 18.3 cm3) reported a lower rate of reoperation (1.46% vs 8%).[33-36]

The mean maximal fibroid volume reduction after RFA at the end of the follow-up period was consistent across the range of treated fibroid volume.

Carrafiello et al[31] reported a significant reduction in volume in a patient with a 8-cm fibroid with shrinkage of 84% at 6 months, and 90% in 2 patients with fibroids greater than 6 cm, then stable at the next check-up 12 months later (**Fig. 3A, B**). Based on the analysis of a large cohort of patients, statistical analysis demonstrated that, with the exception of 1-month follow-up assessment, reductions in myoma diameter and volume were significant at 6, 12, and 24 months after RFA with an average volume reduction up to 90.3%.[14] In a study that exclusively analyzed the ablation of submucosal myomas, a high rate of volumetric reduction (84.2%) was reported at 24 months after the procedure.[17] The reduction in phases II and III of uterine volume over time using laparoscopic RFA (28.7% and 25.7%, respectively, at 12 months) were substantial, and probably contributed significantly to the decline of symptoms and improvement of quality of life, as indicated by the scores of the UFS-QoL questionnaire.[18]

Studies evaluating clinical success in terms of SSS and HRQoL all showed an improvement in both of these parameters. The VITALITY study proved that this significant clinical amelioration persisted through an average of 64.4 months after treatment with the Sonata System.[12] This system consists in a transcervical method able to ablate UFs with extreme precision, without resecting the adjacent endometrium and myometrium.[12]

The rate of surgical reoperation within 12 months was less than 10% in the studies analyzed. An early total laparoscopic hysterectomy was reported in a patient who underwent laparoscopic RFA, who complained of heavy menstrual bleeding at baseline and for 2 months postprocedure.[32]

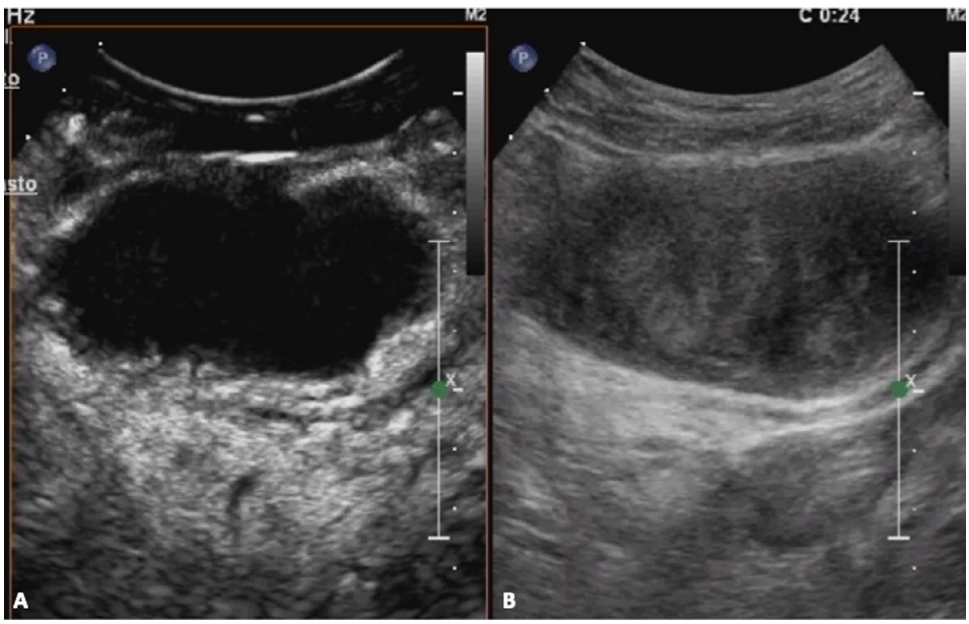

Figure 3 (A, B) Volume of ablation after percutaneous RFA.

In the series examined the procedures by RFA proved to be safe, and the periprocedural complications were sporadic. A type III-b complication according to the Clavien-Dindo classification was reported in 2 patients (1.46%) in a work.[33] In both instances, a hysteroscopy was necessary 30 and 45 days after the ablative session respectively, to remove an intracavitary free myoma.

Surgical reintervention rates after RFA for persistent symptoms are favorable, and do not significantly differ among different delivery approaches; moreover, the rate of reintervention favorably compares with those of other uterus-sparing techniques and myomectomy.[39]

RFA for uterine fibroids is broadly considered safe. Although serious procedural complications such as death or iatrogenic injury to the major abdominal organs have not been reported in any study, individual studies do not provide detailed definitions of the type and severity of complications, nor a complete list of complications encountered during follow-up, concerning the procedure or not. Only 1 study which reported the experience in the RFA treatment of a total of 1216 patients described 3 cases of bowel perforation related to the procedure.[14]

MWA

The characteristics of the selected articles are summarized in Table 2. In the largest cohort study dealing with PMW ablation of UFs the mean diameter of the fibroids ranged from 2.03 to 12.50 cm and the mean volume ranged from 4.40 to 1022.14 cm3.[40]

The power of generators used ranged from 50 W to 100W, with a frequency of 2450 Mhz. The gauge diameter of each antenna was between 13.5 and 16. The ablation time was variable and not always reported.

Commonly local anesthesia was applied combined with moderate sedation.

Where the myoma was too close to the intestine or the bladder, artificial ascites was provoked by injecting physiological saline to keep them away. Physiological saline was injected also into the uterine cavity to protect the endometrium before treating submucosal fibroids.[41]

A catheter could be inserted to fill the bladder for a better visualization of its wall and to improve fibroids position putting them closer to the abdominal wall.[42]

Zhao et al[43] reported the use of a water balloon to compress the abdomen aiming to push away the bowel from the acoustic pathway and ultimately to reduce the risk of damage during the procedure.

Under US guidance, the MW antenna was positioned into the fibroid (Fig. 4). When the diameter of the targeted lesion was less than 5 cm, 1 antenna was used, differently 2 antennas were positioned.[43]

The MW therapy was monitored by real-time US (Fig. 5) and was stopped when the hyperechogenic change, generated during the MW emission around the antenna, propagated to the whole nodule or when the temperature reached 60°C[42] (Fig. 6**A. B**).

The technical success rate of US-guided puncture of the fibroid was 100% in all the selected studies.

The volume reduction rate at 12 months was from 86.7% to 93.1%; Liu et al[40] who obtained an overall reduction rate in their series of 86.7% at 12 months reported that in some cases the ablation rate was less than 60% due to unsafe position of fibroids too close to the bowel or bladder.

In the studies reporting clinical success, a considerable improvement was demonstrated by the UFS-QoL both in terms of severity of symptom and quality of life, reaching levels similar to the healthy women after 12 months.[44,45]

No serious complications were observed. Among the minor complications, the most frequent were abdominal pain and vaginal discharge, however, considered normal phenomena probably due to endometrial inflammation caused by necrotizing liquefaction after ablation.

HIFU

The characteristics of the collected articles are detailed in Table 3.

The safety and efficacy of HIFU therapy have been thoroughly interrogated in the treatment of solitary or multiple uterine fibroids,[46-48] with diverse locations in the myometrium,[49,50] dimensions,[51] signal intensity on MR T2-weighted images,[52] in retroverted or anteverted uterus,[53] by using different approaches including daily scheduled programs,[54,55] volumetric ablation method,[56-58] thermometry feedback through real-time temperature display,[59] 3D quantification of response to therapy,[60] even in case of the bowel laying anterior to the uterus and accurately displaced after bowel-manipulation techniques.[61-63]

The procedures in the selected studies were all performed with patients in the prone decubitus, under MRI-guidance or real-time US monitoring. When comparing US with MR-guided HIFU in a prospective cohort of patients,[64] obviously the US-guided approach was superior in terms of treatment time compared to the time-consuming MR imaging procedures, and the treatment time was almost 1 hour shorter in the US-HIFU group than that in the MR-HIFU ($P = 0.021$).

The role of MR parameters in predicting the treatment outcomes of HIFU for uterine fibroids has been widely investigated, especially signal intensity on T2-weighted images,[65,66] dynamic contrast-enhanced MRI (DCE-MRI) metrics (Ktrans),[56] blood flow (BF), and blood volume (BV) as well[67,68] were demonstrated to be predictive of efficiency.

Moreover, T1-perfusion characteristics proved to be valuable in predicting the efficacy of the HIFU procedure.[69] The thickness of the subcutaneous fat in the anterior abdominal wall, peak enhancement, time to peak, and the ratio of area under curve (AUC) of the fibroid to the myometrium were statistically significant predictors for a negative predictive value (NPV) ratio of at least 90%.[70]

Fibroid enhancement pattern on T1w images, size, distance from the body surface, and signal intensity on T2w images were found to be predictive for the ablation dose.[64,71]

Table 2 The Table Summarizes All Reviewed Series of Uterine Fibroids Treated by MWA, According to Each Variable Included in Review Process

Study	Patients	Fibroid No	Fibroid Dimension	Treatment Time	Ablation Rate	Imaging Guidance	Technical Success	Clinical Success	Complications	Follow-Up	Second Treatment	Surgery
Fu Y 2019	32	38	5.6 cm oxytocin group; 5.6 cm control group	362 s oxytocin group; 485 s control group	95.4% oxytocin group 5.7% control group	US	100%	n.a.	No major complications Lower abdominal pain, vaginal secretions	MRI; 2 d	n.a.	n.a.
Ierardi AM 2019	14	n.a.	6.1 cm, 111.45 cm^3	3-5 min	Volume reduction 70.3 cm^3	US	100%	SSS 29 at 3 months, 13.2 at 6 months, and 0.6 at 12 months. QoL score 84.8 at 3 months, 98 at 6 months, and 100 at 12 months	No major complications Mild abdominal pain	MRI; at least one in a year	0	n.a.
Liu H 2016	311	405	5.1 cm; 95.01 cm^3	n.a.	Volume reduction rate: 63.5% 78.5% 86.7%	US	100%	Hb: from 88.84 $\pm$ 9.31 g/L to 107.14 $\pm$ 13.32 at 3 months and to 117.79 $\pm$ 6.51 at 12 months SSS and HRQL significantly improved post treatment	No major complications Lower abdominal pain (8.68%) Small amount of vaginal secretion (6.11%)	US; 3, 6, 12 mo	2 pts	n.a.
Nakamura K 2017	160	100	n.a.	50 s	n.a.	US	n.a.	n.a.	n.a.	10-96 mo	n.a.	13%
Xia M 2014	88	91	158.09 cm^3	300 s	QMAV: Hypointense: 46.58 cm^3 isointense: 44.46 cm^3 Hyperintense: 23.58 cm^3	US	100%	n.a.	n.a.	MRI; 5 d	0	n.a.
Xia M 2014	49	49	Intramural/subserous 5 cm; submucous 3 cm	n.a.	n.a.	US	100%	n.a.	n.a.	MRI; 7 d	0	n.a.
Yang Y 2014	22	22	4.9 cm	n.a.	Volume reduction rate 81.46% 90%	US	100%	Hb: from 88.64 g/L to 123.21 g/L at 3 months and to 125.92 at 12 months UFS-QOL: normal level at 1 year	No major complications Lower abdominal pain (31.82%) Small amount of vaginal secretion (100%) Bloody vaginal secretion (9%)	MRI; 3, 12 mo	0	n.a.
Yang Y 2019	69	69	$\geq$4 cm	520-3000 s	Volume reduction: from 221.74 cm^3 to 38.05 cm^3 at 12 mo	US	n.a.	SSS from 34.53 to 12.13; HRQoL from 45 to 86 at 12 mo	No major complications Lower abdominal pain	MRI; 3 d US; 3, 6, 12 mo	0	n.a.
Zhang B 2015	169	11 (in pregnant women)	5.30 cm	n.a.	NPV ratio: 88.03%	US	n.a.	All clinical symptoms were alleviated or disappeared gradually	No major complications Necrotic tissue discharge	CEUS: 1 d	n.a.	n.a.
Zhang Y 2017	60	78	3.2 cm	480-1440 s	Volume reduction: hypointense 62.42%,	US	n.a.		No major complications	MRI; 1, 6, 12,	0	n.a.

Table 2 (*Continued*)

Study	Patients	Fibroid No	Fibroid Dimension	Treatment Time	Ablation Rate	Imaging Guidance	Technical Success	Clinical Success	Complications	Follow-Up	Second Treatment	Surgery
					isointense 53.27%, hyperintense 47.43% on T1Wi; hypointense 67.32%, isointense 59.36%, hyperintense 42.63% on T2Wi			All clinical symptoms were alleviated or disappeared	Lower abdominal pain Sacrococcygeal pain	24 mo US; 1, 6, 12, 24 mo		
Zhang J 2011	40	40	n.a.	490 s	Shrinkage rate: 61.8% 78.7% 73.2% 93.1%	US	100%	n.a.	No major complications Lower abdominal pain (6 p2) small amount vaginal bloody secretions (7 pts, 6 of these recovered after 1 week)	MRI; 3, 6, 9, 12 0 mo		n.a.
Zhao WP 2015	311	40	68.6 mm	Procedural time 46.2 min	Ablation rate: 79.8% Volume reduction rate: 52.4%	US	100%	Change in SSS: 10.2	No major complications Lower abdomen pain Vaginal discharge Low grade fever	MRI; 6 mo	0	n.a.

Figure 4 The MW antenna positioned into the fibroid under US guidance.

Figure 5 MW therapy monitored by real-time US.

Technical success was high. In a few cases, the ablation was suspended due to severe pain experienced by the patient,[56,57,61] or was not achievable in accordance with the planned protocol for bowel interposition through the beam path, for thermal injury consequent to the presence of previous scars,[72] or insufficient temperature rise achieved.[63,73-75]

Mean procedural time in the collected articles ranged from 4.3 to 334.2 minutes; volumetric methods as well as the completion of a learning curve may improve the treatment speed.[58,76,77]

In most selected series, the patients experienced after treatment an improvement of their symptoms evaluated more frequently by the UFS-QoL questionnaire or by the SSS.

Some series with limited follow-up length described a few cases who underwent further HIFU treatment, UAE or surgery for enlarging residual tumor, unsatisfactory results, or persistent symptoms.[47,50,72,78] Some authors reported a high rate of re-interventions (47% at 15 months,[74] 58.64% at 5 years,[79] 66.7% at 60.7 months[80]). Gorny et al[81] described the cumulative incidence of additional treatments after MR-guided HIFU ablation of 19% and 23% at 36- and 48-month follow-up, respectively; older patients and hypointense fibroids were associated with fewer additional treatments needed.

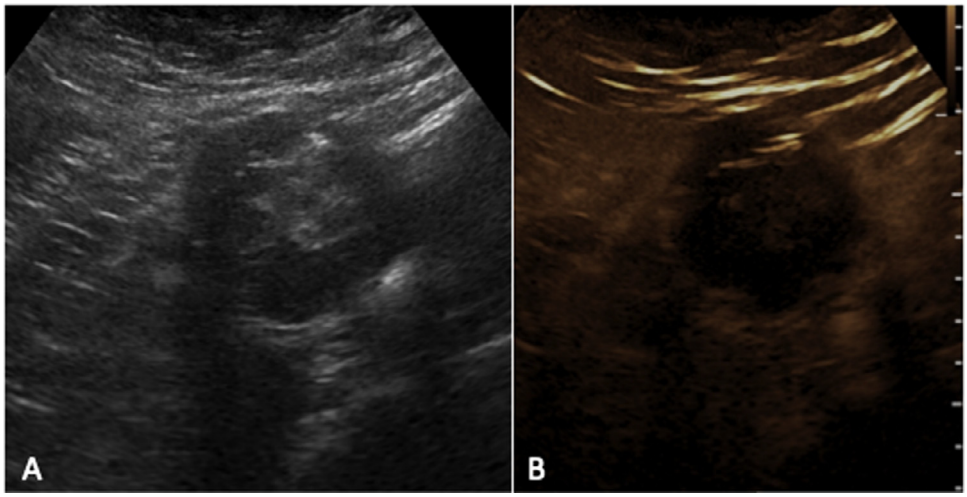

Figure 6 (A,B) CEUS performed immediately after the procedure reveals area of ablation.

The procedure is safe and well tolerated, and the complications more frequently reported were graded as minor.[82] The use of an additional cooling device might reduce the risk of thermal damage to the abdominal wall.[83]

Summary of the Analysis

Among the minimally invasive techniques, RF myolysis is currently considered a valid alternative for the treatment of UFs. It works delivering RF energy to myomas under US guidance in an attempt to destroy them directly through coagulative necrosis consequent to the oscillation and friction of water molecules. The ablation route can be laparoscopic, transvaginal, or transcervical, aiming to reduce the volume of the target fibroids with subsequent symptom relief.[84]

In this review, a real difficulty emerged in analyzing different outcomes between studies and this is largely attributable to differences in the basal volume of fibroids, quality of life and RFA delivery approaches. Despite this variability, there was a strong evidence of substantial reduction of fibroid volume, significant improvements in HR-QoL and SSS, and favorable rates of surgical reintervention after RFA.

Percutaneous MWA is capable of improving fibroid-related symptoms by reducing the volume of lesions, which offers numerous advantages when compared to other ablation techniques. Large volumes of necrosis (up to 6 cm in diameter) can be achieved introducing a single antenna via a single percutaneous access, thus reducing the risk of injury to the abdominal organs which may result from multiple insertions.[85]Although HIFU is a completely noninvasive, needle-free, ablation technique, safe, and effective in the treatment of UFs, it can take a long time: when compared to HIFU, MWA is less expensive and less time-consuming, producing a larger volume of ablation in a shorter amount of time.[4,43]

Several authors have evaluated the clinical utility of a microbubble US contrast agent (SonoVue) in the US-guided HIFU ablation.[86-89] In a randomized control trial, the investigators found that SonoVue could be safely used to enhance the ablative effects of HIFU in the treatment for uterine fibroids, increasing the rate of massive gray-scale changes ($P = 0.002$) and shortening the sonication time ($P = 0.001$).

This valuable effect was more remarkable when HIFU ablation started sooner after contrast media administration.[88]

US-guided intralesional ethanol injection combined with HIFU ablation required less treatment time and a lower dose than HIFU alone, reduced the periprocedural pain and adverse events commonly experienced by patients ($P < 0.05$).[90]

An increasing number of studies has demonstrated that HIFU ablation is a safe, "needle free," minimally invasive therapeutic strategy for uterine fibroids, and affords speedy recover.[91]

Despite these merits, HIFU ablation is less effective or even infeasible for certain conditions because of several limitations. Some of these factors can be surmounted, for instance, bowel loop interposition can be overcome by diverse manipulation techniques, whereas other limits related to tissue properties resistive to HIFU heating are more difficult to bypass.

Therefore, an accurate pretreatment selection is crucial to reduce the number of unsatisfactory on ineffective ablations.[75] MR features of the fibroid to be treated by HIFU are relevant to predict the ablation efficacy; notably, high signal intensity on T2-weighted images has been identified as the most relevant predictor of poor efficacy of HIFU.[56]

Similarly, DCE-MRI quantitative parameters, namely Ktrans, BV, and BF[56,67,77] were deemed to be prognostic determinant of HIFU efficacy, being negatively correlated with the immediate NPV ratio in symptomatic uterine fibroids. Indeed, in order to achieve substantial symptom relief, the NPV should be as large as safely achievable.[72] Partially ablated fibroids tend to regrow, and this may explain the relatively high re-intervention rate reported in studies using a restricted protocol.[80,92]

Table 3 The Table Summarizes All Reviewed Series of Uterine Fibroids Treated by HIFU, According to Each Variable Included in Review Process

Study	Patients	Fibroid No	Fibroid Dimension	Treatment Time	Ablation Rate	Imaging Guidance	Technical Success	Clinical Success	Complications	Follow-Up	Second Treatment	Surgery
Chen J 2017	1353	n.a.	n.a.	n.a.	NPVR 87.2%	US	n.a.	UFS score from 19.9 to 7.7; QoL score from 72.7 to 85.8	Major in 3 pts (skin burn); minor in 335	MRI; 12 mo	14	
Chen Y 2018	120	120	50.5 mm	Procedural time 34.5 to 77.3 min; sonication time 358.5 to 733.9 s	NPVR 72.8 to 94.2%	US	n.a.	n.a.	No major complications; minor complications reported	post-operative MRI; 7 d	n.a.	n.a.
Cheung VYT 2018	20	22	127.0 cm^3	Procedural time 137.5 min; sonication time 1518.5 s	volume reduction 75.9% at 12 mo	US	1 pt could not complete the procedure for pain	SSS reduction 44.9% at 12 mo	Minor complications reported	US; 12 mo MRI at 6 mo		3
Cho JY 2013	24	31	n.a.	Procedural time 334.2 min (5-6 d treatment schedule)	NPVR 50.6%	US	n.a.	SSS from 54.5 to 36.3	Minor in 19 pts	CDUS and MRI; 3 mo	n.a.	n.a.
Dobrotwir A 2011	100	n.a.	185 cm^3	n.a.	NPVR 67%; volume reduction at 12 mo 38%	MR	n.a.	SSS improvement of 51%	No complications	MRI; 12 mo	n.a.	n.a.
Dorenberg EJ 2013	7	7	8.2 cm; 271 cm^3	Procedural time 156 min; sonication time 104 min	NPVR 0.6-15.9%	MR	2/7 pts could not complete the procedure	n.a.	Minor in 1 pt	MRI; 30 d	2 UAE	3
Foreling V 2013	36	n.a.	53.2 cm^3	n.a.	NPVR 41.2%; volume reduction 35% at 6 mo	MR	n.a.	SSS from 42.2 to 26.6; UFS-QOL score from 66.4 to 87.9	No complications	Postoperative MRI	7 HIFU, 2 UAE	15
Froeling V 2013	50	n.a.	67.4 cm^3	n.a.	NPVR 23%	MR	n.a.	SSS from 43.8 to 25; UFS-QOL score from 67.7 to 82.8	No complications (except for pain)	Postoperative MRI; 13.3 mo	7 HIFU, 1 UAE	7
Gorny KR 2014	138	n.a.	343.3 cm^3	n.a.	NPVR 45.5%	MR	6 pts could not complete the procedure	n.a.	1 major complication (deep thrombosis); minor in 16 pts	Postoperative MRI; 2.8 y	23% at 48 mo	
He M 2018	81	346	36 cm^3	Procedural time 97.3 min; sonication time 549 s	NPVR 85.2%	US	n.a.	UFS score from 56.3 to 20.6; QoL score from 41.3 to 73.4	No major complications; minor complications reported	Postoperative MRI; 6 mo	n.a.	2
Hou R 2018	36	36	11.2 cm	Procedural time 104.0 min	NPVR 56%	US	n.a.	SSS and UFS-QOL reduced by 40.8 and 8.6	No major complications; minor complications reported	Postoperative MRI; 6 mo	n.a.	n.a.
Ikink ME 2014	51	n.a.	273 cm^3	n.a.	NPVR 20%	MR	n.a.	SSS from 53.1 to 43.4; HRQoL from 60.3 to 81.5	No complications	Postoperative MR; 15 mo	7; 5 UAE	12
Ikink ME 2014	8	9	7.7 cm	Procedural time 192 min	NPVR 71.9%	MR	1 pt could not achieve any NPV	n.a.	No major complications; minor complications reported	Postoperative MRI	n.a.	n.a.
Isern J 2015	319	330	87 (HIFU with SonoVue); 127 cm^3 (HIFU alone)	Sonication time 788 (group A) vs 1490 s (group B)	NPVR 72 vs 67%	US	50 pts could not achieve any NPV	n.a.	No major complications; minor complications reported	Postoperative MRI; 1 mo	n.a.	n.a.

Table 3 (*Continued*)

Study	Patients	Fibroid No	Fibroid Dimension	Treatment Time	Ablation Rate	Imaging Guidance	Technical Success	Clinical Success	Complications	Follow-Up	Second Treatment	Surgery
Jeong JH 2017	156 (40 using uterine elevator, 29 with downward traction)	n.a.	7.4 (uterine elevator) vs 6.9 cm (without elevator)	Procedural time 94.7 vs127.8 min	NPVR 67.9% vs 64.8%	MR	n.a.	SSS change ratio at 3 mo 40 vs 50%	Minor complications in 3% vs 11% of pts	Postprocedural MRI; 3 mo	2% vs 11%	
Jiang N 2014	80	80	4.7 (HIFU with SonoVue); 5.1 cm (HIFU alone)	Procedural time 73.4 vs 93.9 min; sonication time 810 vs 1017 s	NPVR 90.4% vs 82.8%	US	100%	n.a.	No major complications; minor complications	Postoperative MRI and CEUS	n.a.	n.a.
Keserci B 2017	74	204	6.5 cm; 158.5 ml	Procedural time 127.2 vs 128.4 min	NPVR 95.3% vs 63.8%	MR	n.a.	tSSS from 50.5 and 59.4 to 6.7 and 48.4	No major complications; minor complications reported	MRI; 6 mo	n.a.	n.a.
Keserci B 2018	120	339	7.3 (NPVR>90%) vs 6.8 cm (NPVR<90%)	Procedural time 148.4 vs 130.3 min	n.a.	MR	n.a.	tSSS from 56.1 and 60.4 to 8.0 and 46.9	No major complications; minor complications reported	MRI; 6 mo	n.a.	n.a.
Kim HS 2011	51	40	336.9 cm^3	n.a.	Volume reduction at 3 y 32.0%	MR	n.a.	SSS reduction at 3 y 47.8 points QOL improvement 39.8 points	No complications	MRI; 3 y	5 UAE	4
Kim YS 2011	10	10	8.9 cm	n.a.	NPVR 24.8%	MR	90%	n.a.	One case suspended for severe pain	Postoperative MRI	n.a.	n.a.
Kim YS 2012	27	27	11.3 cm	Procedural time 215.1 min	NPVR 64.2%	MR	100%	SSS from 37.4 to 24.0	Minor in 5 pts	MRI; 3 mo	n.a.	n.a.
Kim YS 2015	77	119	7.5 cm	Procedural time 212.4 min; sonication time 167.4 min	NPVR 72.7%	MR	95% (3 cases suspended for insufficient temperature elevation; 1 skin burn)	n.a.	Complications in 10 pts; 1 major complication (II grade skin burn)	Postoperative MR or interview	n.a.	n.a.
Kim YS 2016	266	n.a.	6.1 (HIFU) vs 7.7 cm (HIFU with maneuver)	n.a. (additional time of 13.8 min in the maneuver group)	NPVR 45.5% vs 75.0%	MR	94.2%	n.a.	No maneuver-related complications	Post-operative MRI	n.a.	n.a.
Kim YS 2016	152	240	6.9 cm	n.a.	NPV 116.1 ml	MR	95.4%	n.a.	Major in 1 pt (0.7%, skin burn); minor in 9 pts	Postoperative MRI	n.a.	n.a.
LeBlang SD 2010	80	147	175 cm^3	n.a.	NPVR 55%	MR	n.a.	n.a.	minor complications reported	MRI; 6.7 mo	n.a.	n.a.
Lee JY 2019	36	59	69.8 cm^3	Procedural time 44.6 min per fibroid	NPVR 74.8%	US	n.a.	UFS-QOL 63.2 SSS 22.4	No complications	MRI; 5 mo clinical fu 32.2 mo	n.a.	15.2%
Leung JHY 2014	20	22	216.6 cm^3	Procedural time 150 min (daily schedule)	NPVR 38%	US	n.a.	symptomatic improvement	Minor in 2 pts; 2 III grade skin burn in one pt	Postoperative US; MRI at 3 mo	n.a.	n.a.
Liu Y 2017	99 (67 in the surgery group)	n.a.	n.a.	88.43 min (vs 93.06)	n.a.	US	n.a.	total effective rate 99% (vs 97%)	No major complications; minor complications reported	1 y		1

Table 3 (*Continued*)

Study	Patients	Fibroid No	Fibroid Dimension	Treatment Time	Ablation Rate	Imaging Guidance	Technical Success	Clinical Success	Complications	Follow-Up	Second Treatment	Surgery
Liu Z 2017	422	n.a.	5.8 cm; 79.1 cm^3	Procedural time 80.0 min; sonication time 800 s	NPVR 83.1%	US	n.a.	n.a.	n.a.	Postoperative MRI	n.a.	n.a.
Lyon PC 2019	10	14	7.7 cm; 193.2 cm^3	Procedural time 113.3 min	NPVR 67.7% volume reduction rate at 3 mo 23.3%	US	n.a.	SSS from 56.5 to 40.6	no major complications; minor complications reported	Postoperative MRI; 24 mo	n.a.	2
Meng 2010	50	n.a.	4.8 cm; 71.0 cm^3	Procedural time 163.1 min	complete ablation in 58% of pts	US	n.a.	n.a.	Minor in 7 pts	CEUS; 7 d	n.a.	n.a.
Mindjuk I 2014	252	n.a.	5.3 cm; 91.8 cm^3	Procedural time 03:59 h	NPVR 88.7%	MR	n.a.	SSS from 45.1 to 14.5	No major complications; minor complications reported (hysteroscopic surgery for menstrual bleeding)	Postoperative and 6-mo MRI; 19.4 mo	11 HIFU, 11 UAE	6
Na Y 2018	892 (damaged group: 151; others: 741)	n.a.	128.0; 108.8 cm^3	Sonication time 1673.8 s;1102.1 s	NPVR: 76.8; 80.2	MR	n.a.	n.a.	Abdominal wall injury (assessed by MRI) in 16.9%; no clinical evidence of skin damage	n.a.	n.a.	n.a.
Orsi F 2015	33	37	419.24 vs 189.58 cm^3 (HIFU with SonoVue; HIFU alone)	Sonication time 1485 vs 2297 s	volume reduction 40.5 vs 47.2% at 6 months	US	100%	UFS-QOL score increased at least by 16 points	No complications	CEUS and MRI; 6 mo	4	n.a.
Park H 2017	17 (with GnRHa); 17 (no GnRHa)	20; 19	155.7 cm^3	Procedural time 125.1 min vs 123.4	NPVR 65.3% vs 59.1	MR	n.a.	n.a.	No complications	Postoperative MRI	n.a.	n.a.
Park MJ 2012	43	53	9.2 cm; 341.2 cm^3	Procedural time 216.0 min; sonication time 131.5 min	NPVR 57.4%	MR	97.7%	SSS from 43.2 to 25.8	Minor in 6 pts	MRI; 3 mo	n.a.	n.a.
Park MJ 2013	13	20	7.1 cm; 141.2 cm^3	n.a.	n.a.	MR	100%	n.a.	No complications	Postoperative MRI; 60.7 mo	n.a.	n.a.
Parsons JA 2017	73	82	7.3 cm	Procedural time 4.3 min	NPV 31.2 cm^3	US	93.2%	QOL score of 16.5-point increase; SSS of 63 point decrease	No major complications	Postoperative MRI (or pathology after surgery); MRI or clinical interview at 3-6 mo	n.a.	n.a.
Peng S 2012	291	291	5.6 (HIFU with SonoVue), 4.6 cm (HIFU alone)	n.a.	NPVR 86.0%; 83.0%	US	n.a.	n.a.	Minor in 45 (27.8%) and 31 pts (24.0%)	CEUS and MRI; 1 d	n.a.	n.a.
Peng S 2015	68	68	57.9 vs 58.5 mm (CEUS vs MRI)	Procedural time 96 min; sonication time 1148 s	NPVR 83.7 vs 84.2%	US	n.a.	n.a.	Minor complications	Postoperative MRI and CEUS	10 pts (14.7%) further consecutive HIFU session	n.a.

Table 3 (*Continued*)

Study	Patients	Fibroid No	Fibroid Dimension	Treatment Time	Ablation Rate	Imaging Guidance	Technical Success	Clinical Success	Complications	Follow-Up	Second Treatment	Surgery
Peng S 2015	403	n.a.	58.1 mm	Procedural time 92.0 min	NPVR 77.5%	US	n.a.	n.a.	n.a.	MRI; 1 mo	n.a.	n.a.
Quinn SD	280		396.3 cm^3	n.a.	NPVR 44.2%	MR	n.a.	n.a.	Minor in 11 pts (3.9%); major in 3 (1.1%: fibroid expulsion, major skin burn, persistent neuropathy)	5 y	58.64%	
Ruhnke H 2013	18	27	124.9 cm^3	Procedural time 244 min; sonication time 140 min	NPVR 36.4%	MR	4/18 pts could not complete the procedure (3 for pain, 1 for technical reasons)	SSS from 51 to 37	No major complications; severe pain in 4 pts	MR; 6 mo	n.a.	n.a.
Savic LJ 2015	24	n.a.	263.74 cm^3	n.a.	TLV and ELV reduction in 21 (87.5%) and 16 pts (66.6%) respectively	MR	100%	Symptomatic improvement in15/18 pts	No major complications; minor complications reported	MRI; 24 mo	n.a.	n.a.
Thiburce AC 2015	36	n.a.	255 cm^3	n.a.	NPVR 27%	MR	n.a.	SSS from 42.8 to 25.4	No major complications; minor complications reported	MRI; 6 mo clinical fu 21.4 mo	1 UAE	5
Trumm CG 2013	115	n.a.	5.4 cm; 89 cm^3	Procedural time 3.3 h	NPVR 88%	MR	93.5% (bowel interposition, system malfunction, movement)	SSS from 62.5 to 37.5	No major complications; minor complications reported in 2 pts	Postoperative MRI; 6 mo	n.a.	n.a.
Venkatesan MA 2012	11	12	246.7 cm^3	Procedural time 3.67 h; sonication time 54.6 m	n.a.	MR	n.a.	n.a.	11 minor complications	n.a.	n.a.	9/12 after 3 d (study protocol)
Voogt 2011	33	36	3-12 cm	n.a.	NPVR 21.7%	MR	n.a.	Discomfort score from 0.8 to 0.18	minor in 31 pts	MRI; 1 mo	1 UAE	1
Wang W 2012	76	78	5.7 cm	Procedural time 85 min	NPVR 80%	US	100%	UFSQOL score from 26 to 11 at 2 y fu	No complications	CEUS or MRI; 30 mo	4	0
Wang Y 2018	263	263	5.5 cm; 81.2 cm^3	n.a.	NPVR 81.2%	US	n.a.	n.a.	n.a.	post-operative MRI	n.a.	n.a.
Wang Y 2018	43 (MR) + 51 (US)	44 + 68	95.0 vs 126.9 cm^3	Procedural time 174.5 vs 114.4 min	Complete ablation in 23.3% vs 43.1% of pts; volume reduction 59.1 vs 52.7%	MR vs US	n.a.	tSSS from 26.6 to 14.6, vs from to 25.3 to 15.1	No major complications	MRI; 6 mo	n.a.	n.a.
Wei C 2017	65	78	5.2	n.a.	NPVR $>$70% group (n = 47); NPVR $<$ 70% group (n = 31)	MR	n.a.	n.a.	n.a.	DCE-MRI; 3 d	n.a.	n.a.
Xie B 2015	55 (type I: 27; type II: 28)	4.2 cm and 47.8 cm^3, vs 4.5 cm and 55.2 cm^3	Sonication time 858.4 vs 769.2 s	NPVR 83.0% vs 92.0%	US	n.a.	Symptomatic improvement	No major complications; minor complications reported	MRI; 12 mo	n.a.	n.a.	

Table 3 (*Continued*)

Study	Patients	Fibroid No	Fibroid Dimension	Treatment Time	Ablation Rate	Imaging Guidance	Technical Success	Clinical Success	Complications	Follow-Up	Second Treatment	Surgery
Yang S 2017	34	42	5.5 cm, 149.2 cm^3 (with GnRHa); vs 5.7 cm, 155.3 cm^3	Procedural time 102.0 vs 149 min; sonication time 25.4 vs 38.9 min	NPVR 69.2% vs 50.2%	US	n.a.	n.a.	No major complications; minor complications reported	Postoperative MRI	n.a.	n.a.
Yang Z 2014	40	52	156911 mm3	Procedural time 1714.25 s (HIFU + ethanol injection); 2478.20 s (HIFU alone)	ablation rate 99.13% vs 92.86%	US	n.a.	n.a.	Minor in 33 pts	Post-operative CDUS; CEUS at 1 mo	n.a.	n.a.
Yeo SY 2017	123	196	6.2 cm	n.a.	NPVR 54.0% (RIM sign present) vs. 83.7% (absent)	MR	96.7%	n.a.	No major complications; minor complications reported	post-operative MRI	n.a.	n.a.
Yu SC 2019	9 (HIFU with oxytocin); 24 (HIFU alone); 27 (UAE)	n.a.	5.9 cm, 108.5 $cm^{3;}$ vs 7.4 cm, 205.1 cm^3	n.a.	volume reduction at 15 mo 28.3%; 75.9%; 44.2%	US	n.a.	100% pts became symptom free t 6 mo; 29.2% (HIFU control); 63% of pts (UAE control)	No major complications; minor complications reported	n.a.; 15 mo	n.a.	n.a.
Zhang C 2017	26	53	52.7 cm^3	Procedural time 90.3 min; sonication time 774.0 s	NPVR 80.6%	US	n.a.	n.a.	No major complications; minor complications reported	Postoperative MRI	n.a.	n.a.
Zhang L 2010	21	23	6.0 cm; 97 cm^3	Procedural time 2.5 h; sonication time 20 min	NPVR 76.9%	MR	One procedure interrupted for pain	n.a.	Minor in 4 pts	MRI, 3 mo	n.a.	n.a.
Zhang W 2016	442	442	3.8 cm, 33.7 cm^3 (retroverted uterus); vs 3.7 cm, 31.6 cm^3 (anteverted)	Procedural time 57.7 vs 64.2 min; sonication time 520.1 vs 567.8 s	NPVR 85.2% vs 87.7%	US	n.a.	n.a.	No major complications; minor complications reported	Postoperative MRI	n.a.	n.a.
Zhao WP 2013	282	282	70.3 cm^3	Procedural time 106.1 min (126.4 min in T2-hyperintense)	NPVR 76.8% (T2-hypointense 86.3%; T2-isointense 77.1%; T2-hyperintense 67.6%)	US	n.a.	n.a.	No major complication; minor complications reported	MRI; n.a.	n.a.	n.a.
Zhao WP 2015	42	51	6.5 cm	Procedural time 92.5 min	NPVR 77.1%	US	100%	SSS from 42.1 to 24.6	Minor complications	MRI; 6 mo	n.a.	n.a.
Zhao WP 2017	172	172	60.4 cm^3	Procedural time 89 min	NPVR 76.2%	US	n.a.	SSS reduced by 10.8 points	No major complications; minor complications reported	Postoperative MRI; 1 y	18	4

Conclusion

Patients affected by uterine myomas may benefit from such uterus-preserving therapies, among which the choice depends on number, size, and location of the lesions to be treated, patient's age and preferences, and pregnancy wish, as well as the availability of therapy, and the experience of the therapist.

Image-guided ablative techniques unquestionably may offer many advantages over surgery with significant reduction in both perioperative complications and length of hospitalization. Some similar advantages may be observed also over UAE.

The future task of researchers, however, should be to take into consideration a randomized study to stabilize the exact role of each mini-invasive treatment, their indications, advantages, and disadvantages.

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