



● Original Contribution

SAFETY AND EFFICACY OF ULTRASOUND-GUIDED HIGH-INTENSITY FOCUSED ULTRASOUND TREATMENT FOR UTERINE FIBROIDS AND ADENOMYOSIS

JAE-SEONG LEE,^{*} GI-YOUNG HONG,[†] KYE-HWA LEE,[‡] JUNG-HWA SONG,[§] and TAE-EUNG KIM[§]

^{*} Aegiroen Obstetrics Gynecology Clinic, Seoul, Republic of Korea; [†] Green Cross Medical Clinic Incheon, Republic of Korea;

[‡] Center for Precision Medicine Seoul National University Hospital, Seoul, Republic of Korea; and [§] Department of Obstetrics and Gynecology, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Incheon, Republic of Korea

(Received 18 February 2019; revised 22 August 2019; in final form 30 August 2019)

Abstract—The objective of this study was to assess the tolerability and efficacy of ultrasound-guided high-intensity focused ultrasound (USgHIFU) ablation using a Haifu JC Focused Ultrasound Tumor Therapeutic System (operating transducer frequency: 0.8 MHz, 300–400 W/cm²) under real-time ultrasound guidance (2.5- to 5.0-MHz imaging probe) for uterine fibroids and adenomyosis in 1807 patients (928 with fibroids and 889 with adenomyosis). Volume change and clinical symptom improvement after treatment were evaluated based on symptom severity scores and health-related quality of life scores using the Uterine Fibroid Symptom and Quality of Life questionnaires. At 3, 6 and 12 mo after treatment, symptom severity scores and health-related quality of life scores and reductions in volumes of uterine adenomyosis and fibroids all revealed good effects. The complication rate was 4.6% (84/1807). With supportive care, all complications resolved without any permanent adverse effects. Thus, USgHIFU is an effective, non-invasive modality for treating uterine fibroids and adenomyosis with manageable complications. (E-mail: tekim@catholic.ac.kr) © 2019 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: Uterine fibroid, Adenomyosis, High-intensity focused ultrasound ablation, Efficacy, Safety.

INTRODUCTION

Uterine fibroids and adenomyosis are common gynecologic disorders that affect women of reproductive age. They are frequently found to be underlying causes of dysmenorrhea, menorrhagia, urinary symptoms and subfertility. Uterine fibroids and adenomyosis have been treated mainly with surgical treatment in the past. However, these disorders are now increasingly treated with non-invasive methods. High-intensity focused ultrasound (HIFU) ablation is an effective non-invasive treatment modality using an external ultrasound (US) energy source to induce thermal ablation for a variety of solid tumors such as uterine fibroids and adenomyosis at depths through the intact skin. Based on its ability to concentrate US waves at the desired location, HIFU leads to protein denaturation and irreversible cell necrosis *via* heating effect and cavitation, causing direct

damage to tumor blood vessels at the focal spot (Fig. 1) (Jiang et al. 2013). Several studies have reported that ultrasound-guided high-intensity focused ultrasound (USgHIFU) ablation and magnetic resonance-guided focused US are tolerable and feasible alternatives for treating uterine fibroids (Funaki et al. 2009; Wang et al. 2012, 2013; Zhao et al. 2013) and adenomyosis (Wang et al. 2009; Zhou et al. 2011; Shui et al. 2015). The main advantage of HIFU is its non-invasive nature associated with low morbidity and rapid recovery (return to normal activity in 1 d). In this study, we evaluated the efficacy and tolerability of USgHIFU treatment by assessing volume reduction, uterine fibroid symptom, quality of life Uterine Fibroid Symptom and Quality of Life (UFS-QoL) score increase and adverse events (Spies 2002). UFS-QoL comprises 37 questions. Each question is assessed using a 5-point categorical scale (1 = not at all, 2 = a little bit, 3 = somewhat, 4 = a great deal, 5 = a very great deal). The UFS-QoL is widely used in the gynecologic field to objectively evaluate the severity of symptoms and health-related quality of life (HRQoL) in patients with uterine fibroids. The UFS-QoL consists of

Address correspondence to: Tae-Eung Kim, Department of Obstetrics and Gynecology, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 56, Dongsu-ro, Bupyeong-gu, Incheon, 21431, Republic of Korea. E-mail: tekim@catholic.ac.kr

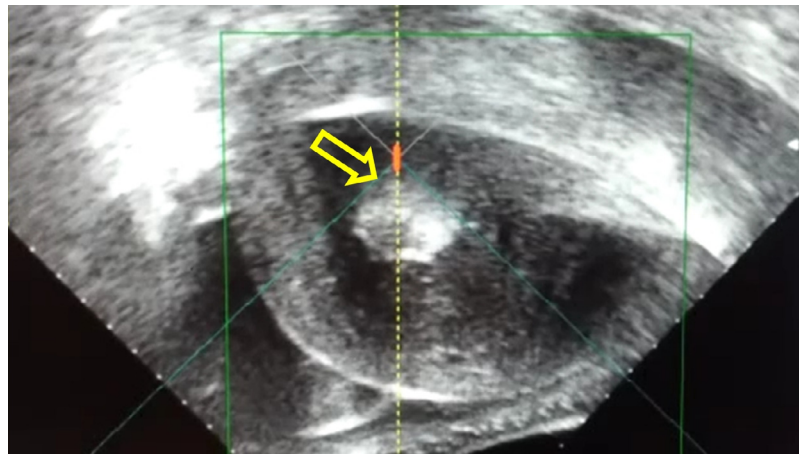


Fig. 1. Image of area treated with ultrasound-guided high-intensity focused ultrasound. A hyper-echoic change was observed in the focus area in ultrasound image.

an 8-item Symptom Severity Scale (SSS) and six dimensions of HRQoL.

METHODS

This retrospective analysis enrolled 1,807 women with uterine fibroids or adenomyosis who underwent USgHIFU ablation from February 2010 to October 2017. All patients were treated by Dr. Lee with 10 y of experience of treating HIFU. Diagnosis of uterine fibroids and adenomyosis was based on each patient's medical history, physical examination, diagnostic US and magnetic resonance imaging (MRI) scans. We included patients with 2- to 12-cm uterine myomas with moderate to severe symptoms and symptomatic focal and diffuse adenomyosis patients. Exclusion criteria were pedunculated uterine fibroids, asymptomatic uterine fibroids <5 cm in diameter, asymptomatic focal adenomyosis, any evidence of known or suspected extensive pelvic adhesions, a history of acute pelvic inflammatory disease, severe pelvic endometriosis, lower abdominal surgery, abdominal wall thickness >5 cm, pregnancy and lactation, dialysis, anticoagulation therapy, hemolytic anemia, history of cerebrovascular disease, unstable cardiac status and suspected malignancy.

Treatment was administered using a Haifu JC Focused Ultrasound Tumor Therapeutic System (Chongqing Haifu Technology, Chongqing, China) under real-time US guidance. The focused US transducer used in this study had a focal length of 135 mm, a diameter of 150 mm and an operating frequency of 0.8 MHz. An AU3 US imaging device (Esaote, Genoa, Italy) was used as the real-time imaging unit of the system. This 3.5- to 5.0-MHz imaging probe was located in the center of the HIFU transducer. During HIFU treatment, the lesion was treated with an acoustic power in a single-exposure dot mode at an intensity of 300–400 W/cm² and exposure

duration of 3-s intervals between exposures with at least 24 exposures per point. It was stopped when hyper-echoic white gray-scale change at the focus area appeared on the US image. After termination of treatment, total treatment time from the first sonication shot to the last shot, total time of sonication and total treatment energy were obtained. This study was approved by the ethics committee at Incheon Christian Hospital (No. 2012-1). Written informed consent was obtained before every procedure from each patient, who was informed of possible effects of HIFU on pregnancy rate and treatment outcome. All patients underwent careful bowel and skin preparation before HIFU treatment. Bowels were prepared to avoid adverse effects to adjacent bowel loops in the treatment field using 250 mL of MAGCOROL SOLN (magnesium citrate; Taejoon Pharm Inc, Seoul, South Korea) for 1 d. The skin of the lower abdominal wall was shaved and degreased with 70% alcohol. The epidermal skin was degassed with a vacuum suction device. A urinary catheter filled with sterile saline was inserted into the bladder to control bladder volume during the procedure. Intravenous conscious sedation with fentanyl, midazolam and propofol was administered during the procedure. Real-time guided ultrasonography was used to determine the location of uterine fibroids and adenomyosis during the procedure. We monitored the patient's pain, motion and vital signs, including blood pressure, pulse and oxygen saturation rate, during treatment and at least 12 h after the procedure. Our aim was to treat at least >80% of the lesions in the uterus. To prevent infection and inflammation of lesions, oral antibiotics and anti-inflammatory drugs were administered for 7 d after the treatment.

Symptoms of each patient were surveyed objectively using the SSS and HRQoL scores of the UFS-QoL questionnaires (Spies 2002). After the scores on questions 1 to

8 of the UFS-QoL were summed, the SSS score was calculated using the following formula: transformed score = ((actual raw score – lowest possible raw score)/possible raw score range) * 100. After the scores on questions 9 to 37 of the UFS-QoL were summed, the HRQoL score was calculated using the following formula: transformed score = ((highest possible score – actual raw score)/possible raw score range) * 100. Patients completed the UFS-QoL questionnaire before treatment and at 3, 6 and 12 mo after treatment. The higher the SSS score, the higher was the patient's discomfort. The lower the HRQoL, the lower was the patient's satisfaction with daily life. We evaluated the effect of ablation with the volume reduction rate determined with US and enhanced MRI. We measured the uterus and targeted lesions in the longitudinal (D1), anteroposterior (D2) and axial (D3) dimensions. We also calculated uterine fibroid volume and uterine adenomyosis volume as [Kroencke et al. 2006](#) $V = 0.5233 \times D1 \times D2 \times D3$.

All 1807 patients were treated with a single session of HIFU treatment under intravenous sedation. Each patient was examined before treatment, the next day and 6 and 12 mo after treatment using T2-weighted MRI imaging and T1-weighted MRI imaging with gadolinium injection. This process was performed to assess treatment response and recurrence as well as any new lesions. A 3-mo assessment was conducted with US scanning alone.

We used repeated-measures analysis of variance to determine the statistical significance of changes in patients' symptom severity, quality of life scores and uterine volumes at 3, 6 and 12 mo after the HIFU procedure. In this model, we used age as a confounding variable. We set the threshold of statistical significance at $p < 0.05$. All statistical analyses were performed using R Version 3.5.1 ([R Core Team 2018](#)).

RESULTS

Demographic data for 918 patients diagnosed with uterine fibroids and 889 patients diagnosed with adenomyosis by HIFU are summarized in [Table 1](#). The age of the 918 patients diagnosed with uterine fibroids was 41.26 ± 6.35 y (mean $\pm$ standard deviation [SD]). Of these patients, 368 were nulliparous and 550 were multiparous. A total of 195 patients had had a cesarean section. Fifty patients had undergone myomectomy, and 3 patients, radiofrequency myolysis. HIFU treatment time from the first shot to the last shot was 86.13 ± 36.37 min (mean $\pm$ SD). HIFU ablation time (the sum of shot times) was 1156.35 ± 568.98 s (mean $\pm$ SD). HIFU treatment energy for each patient was 455 ± 493 kJ (mean $\pm$ SD).

The age of the 819 patients diagnosed with adenomyosis was 41.06 ± 5.45 y (mean $\pm$ SD). Of these patients, 319 were nulliparous and 570 were multiparous.

Table 1. Demographic data of 1807 patients

	Uterine fibroids	Adenomyosis
No. of patients	918	889
Age*	41.26 ± 6.35	41.06 ± 5.45
No. of nulliparas	368	319
No. of multiparas	550	570
No. of previous cesarean sections	195	217
No. of previous myomectomies	50	59
Previous radiofrequency myolysis	3	10 (3 UAE)
Treatment time (min)*	86.13 ± 36.37	79.36 ± 30.58
Ablation time (s)*	1156.35 ± 568.98	1001.69 ± 453.59
Energy (kJ)*	455 ± 493	361 ± 181

UAE = uterine artery embolization.

* Mean $\pm$ standard deviation.

A total of 217 patients had had a cesarean section. Fifty-nine patients had undergone myomectomy. Ten patients had undergone radiofrequency myolysis, and 3 patients, uterine artery embolization. HIFU treatment time and HIFU ablation time were 79.36 ± 30.58 min and 1001.69 ± 453.59 s (mean $\pm$ SD), respectively. HIFU treatment energy was 361 ± 181 kJ (mean $\pm$ SD).

HIFU treatment for uterine fibroids

Pre-treatment uterine fibroid volume was 176.46 ± 149.87 cm³ (mean $\pm$ SD). Pre-treatment SSS and UFS-QoL scores were 48.55 ± 21.17 and 59.10 ± 23.15 (mean $\pm$ SD), respectively ([Table 2](#)). Uterine fibroid volumes (reduction rate, %) were 79.87 ± 74.81 cm³ (54.7%), 66.20 ± 81.49 cm³ (62.5%) and 46.23 ± 54.7 cm³ (73.8%) at 3, 6 and 12 mo after treatment, respectively ($p < 0.001$). SSSs were 24.74 ± 16.28 , 23.72 ± 15.05 and 24.94 ± 15.15 (mean $\pm$ SD) at 3, 6 and 12 mo after treatment, respectively ($p < 0.001$). UFS-QoL scores were 79.42 ± 17.99 , 81.69 ± 18.55 and 81.20 ± 15.96 at 3, 6 and 12 mo, respectively ($p < 0.001$) ([Fig. 2](#)). A representative case of a multiparous female diagnosed with multiple uterine fibroids is illustrated in [Figure 3](#). These fibroids were touching the endometrium, causing severe vaginal bleeding and menorrhagia. Twelve months after treatment, a few necrotic uterine fibroids were expelled. The volume reduction rate of another necrotic uterine fibroid was 78.7%.

HIFU treatment for adenomyosis

Pre-treatment uterine volume for adenomyosis was 247.80 ± 145.84 cm³ (mean $\pm$ SD). Pre-treatment SSS and UFS-QoL scores were 48.59 ± 20.97 and 59.28 ± 23.11 (mean $\pm$ SD), respectively ([Table 3](#)). Uterine adenomyosis volumes (reduction rate %) were 137.49 ± 76.94 cm³ (44.5%), 122.03 ± 73.56 cm³ (50.7%) and 98.91 ± 60.92 cm³ (60.1%) at 3, 6 and 12 mo after treatment, respectively ($p < 0.001$). SSSs were 24.87 ± 16.38 , 23.58 ± 15.04 and 24.98 ± 15.11 (mean $\pm$ SD) at

Table 2. Response of uterine fibroids to HIFU

	Before HIFU		After HIFU		<i>p</i> Value
	Baseline	3 mo	6 mo	12 mo	
Uterine fibroid volume (cm ³)	176.46 ± 149.87*	79.87 ± 74.81	66.20 ± 81.49	46.23 ± 54.7	<0.001
SSS score [†]	48.55 ± 21.17	24.74 ± 16.28	23.72 ± 15.05	24.94 ± 15.15	<0.001
HRQoL score [‡] (six dimensions [§])	59.10 ± 23.15	79.42 ± 17.99	81.69 ± 18.55	81.20 ± 15.96	<0.001

HRQoL = Health Related Quality of Life; SSS = Symptom Severity Scale.

* Values are means ± standard deviation.

† SSS transformed score = ((actual raw score – lowest possible raw score)/possible raw score range) * 100.

‡ HRQoL transformed score = ((highest possible score – actual raw score)/possible raw score range) * 100.

§ Concern, Activities, Energy/Mood, Control, Self-conscious, Sexual Function.

3, 6 and 12 mo, respectively ($p < 0.001$). UFS-QoL scores were 79.64 ± 17.91 , 81.59 ± 18.44 and 81.35 ± 15.88 (mean ± SD) at 3, 6 and 12 mo, respectively ($p < 0.001$) (Fig. 4). A representative case of a nulliparous patient diagnosed with posterior focal adenomyosis is illustrated in Figure 5. Eleven months after treatment, her uterine volume reduction rate was 63.7%.

Additional treatments after HIFU for uterine fibroids and adenomyosis are outlined in Table 4. Of 918 patients with uterine fibroids, 42 experienced a recurrence of symptoms and 23 had a new lesion. Nine patients diagnosed with uterine fibroids underwent a repeat HIFU. Thirteen patients underwent hysterectomy, and 8 patients underwent myomectomy. Of 889 patients with adenomyosis, 39 experienced a recurrence of symptoms and 17 had a new lesion. Seventeen patients

underwent a second HIFU treatment, and 20 patients, hysterectomy.

Complications are summarized in Table 5. Complications included one case of foot drop, one case of aggravated spondylolisthesis, 7 cases of transient unilateral leg weakness, 13 cases of unilateral sciatic nerve pain, 1 case of tumor lysis syndrome with transient acute pre-renal failure, 1 case of sleep apnea caused by sedative agents, 17 cases of first-degree skin burn, 12 cases of second-degree skin burn and 29 cases of transient hematuria. Two cases of small bowel perforation were noted 2 and 5 d after ablation, respectively. In both cases, attempts were made to treat subserosal uterine fibroids near the intestine. Simple laparoscopic closure was performed in small bowels. With supportive care, all cases recovered without any permanent adverse effect.

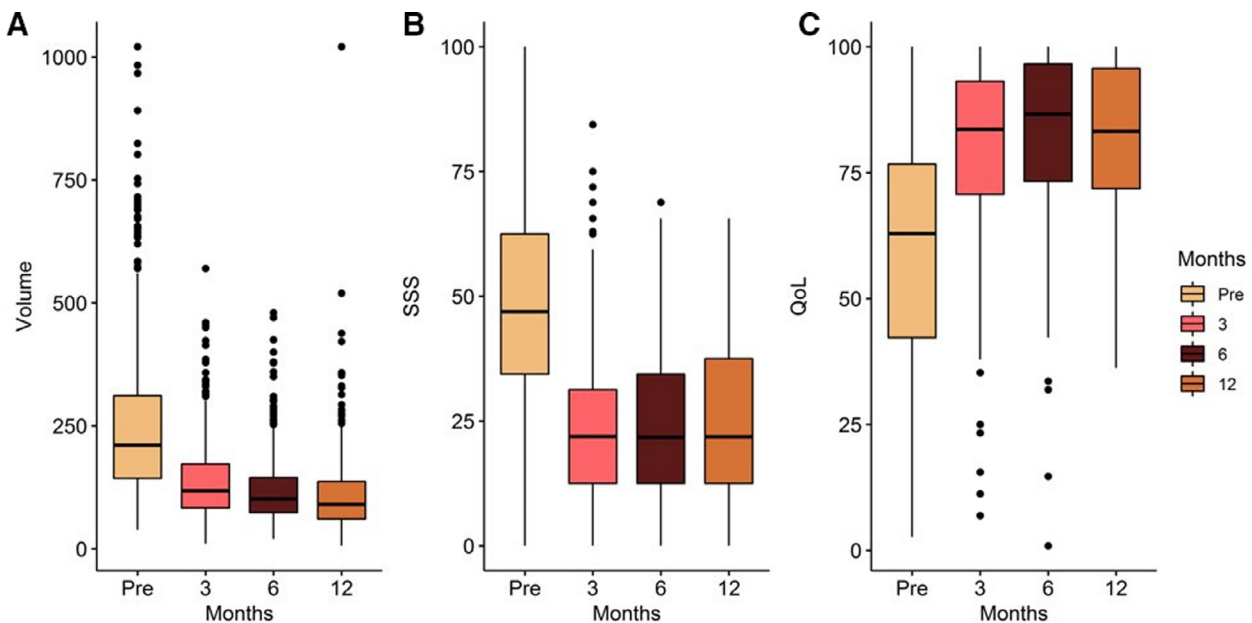


Fig. 2. Comparison of uterine fibroid volume (cm³), SSS score and QoL score among four time points before and after treatment for patients with uterine fibroids. Boxes represent lower quartile, median and upper quartile. The ends of the vertical lines indicate the largest and smallest observations as outliers representing extreme values. QoL = quality of life; SSS = Symptom Severity Scale.

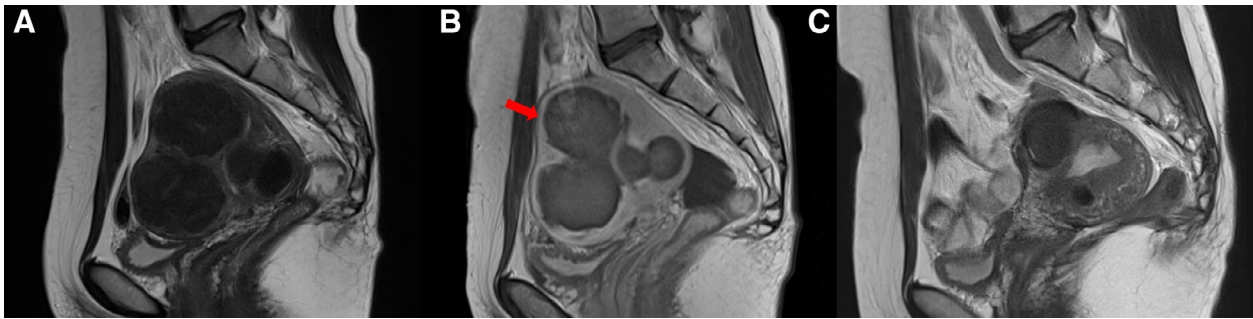


Fig. 3. HIFU treatment of a multiparous female diagnosed with multiple uterine fibroids. In the MRI scan are 4.5×4.4 -cm (44.6 cm^3), 4.3×3.9 -cm (34.2 cm^3), 2.1×1.7 -cm (3.9 cm^3) and 2.9×2.3 -cm (6.3 cm^3) fibroids touching the endometrium in the T2-weighted MRI sagittal image (A) located at the anterior uterine wall and the gadolinium-enhanced T1-weighted MRI image after HIFU treatment (B). The arrow indicates a non-perfused uterine fibroid after HIFU. Twelve months later, a few necrotic uterine fibroids were expelled, followed by a decrease in the volume of another necrotic uterine fibroid to 3.1×2.1 cm (9.5 cm^3). The volume reduction rate was 78.7% (C). HIFU = high-intensity focused ultrasound; MRI = magnetic resonance imaging.

In our study, we experienced 31 unintended pregnancies after HIFU. Among these pregnant patients, 25 developed no complication during pregnancy and continued the pregnancy to a full-term delivery. Fourteen vaginal and 11 cesarean section deliveries were also uneventful. Three patients experienced a spontaneous abortion. One patient with adenomyosis experienced pre-term delivery at 25 wk of gestation, and 2 patients could not be contacted (Table 6). Pregnancy data were obtained only if pregnant patients contacted us to inform us of the pregnancy.

DISCUSSION

Among 918 patients diagnosed with uterine fibroids, three follow-ups were conducted after HIFU treatment. Uterine fibroid volume reductions were 54.7%, 62.5 and 73.8% at 3, 6 and 12 mo after treatment, respectively ($p < 0.001$). These outcomes were comparable to outcomes reported in other studies. Ren *et al.* (2009) have reported reduction rates of 27.2%, 47.9%, and 50.3% at three, six, and 12 mo, respectively. R Core Team (2018). Wang *et al.* (2012) reported reductions of 46.7%, 68.2%, 78.9% and 90.1% at 3, 6, 12 and 24 mo, respectively. In the present study, treatment energy and

ablation time were similar to those reported in other papers using the same model. We saw improved SSS and UFS-QoL scores until 12 mo after treatment. Improved UFS-QoL scores at 24 mo after treatment have also been reported (Wang *et al.* 2012). Among 918 patients with uterine fibroids, 42 (4.6%) experienced symptom recurrence, including 23 who were diagnosed with a new lesion on follow-up MRI. Additional interventions in these patients included a second HIFU treatment, myomectomy and hysterectomy. Treatment was based on the principle of surgery. The second HIFU treatment was applied to patients who wanted HIFU treatment and met the criteria. Volume reduction, SSS score or UFS-QoL score was not included in the statistical data when patients underwent surgery, including myomectomy and hysterectomy.

Among 889 patients in the adenomyosis group, uterine volume reduction rates were 44.5%, 50.7% and 60.1% at 3, 6 and 12 mo, respectively. Improved SSS and UFS-QoL scores during follow-up for patients with adenomyosis were statistically significant ($p < 0.001$). In other studies, relief rates were 84.7%, 84.7% and 82.3% at 3 mo, 1 y and 2 y after treatment, respectively (Shui *et al.* 2015). In our study, adenomyosis volume reductions were less than those reported in other papers.

Table 3. Response of adenomyosis to HIFU treatment

	Baseline	3 mo	6 mo	12 mo	<i>p</i> Value
Uterine volume (cm^3)	$247.80 \pm 145.84^*$	137.49 ± 76.94	122.03 ± 73.56	98.91 ± 60.92	<0.001
SSS score [†]	48.59 ± 20.97	24.87 ± 16.38	23.58 ± 15.04	24.98 ± 15.11	<0.001
HRQoL score [‡] (six dimensions [§])	59.28 ± 23.11	79.64 ± 17.91	81.59 ± 18.44	81.35 ± 15.88	<0.001

HRQoL = Health Related Quality of Life; SSS = Symptom Severity Scale.

* Values are means $\pm$ standard deviation.

[†] SSS transformed score = ((actual raw score – lowest possible raw score)/possible raw score range) * 100.

[‡] HRQoL transformed score = ((highest possible score – actual raw score)/possible raw score range) * 100.

[§] Concern, Activities, Energy/Mood, Control, Self-conscious, Sexual Function.

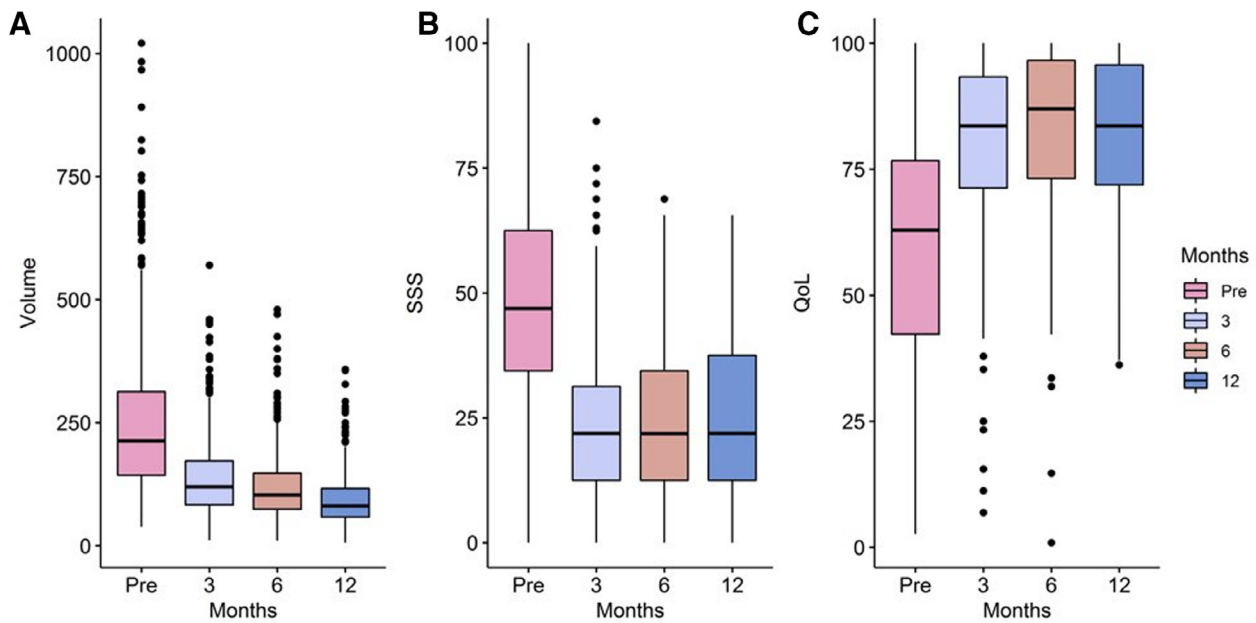


Fig. 4. Comparison of uterine volume (cm^3), SSS score and QoL score among four time points before and after treatment for patients with adenomyosis. *Boxes* indicate the lower quartile, median and upper quartile. The ends of vertical lines indicate the largest and smallest observations as outliers representing extreme values. QoL = quality of life; SSS = Symptom Severity Scale.

This might have occurred because we measured the volume of the entire uterus, including the normal uterus site and irregular adenomyosis lesions. Among 889 uterine adenomyosis patients, 39 (4.4%) experienced symptom recurrence, including 17 patients who were diagnosed with a new lesion on follow-up MRI. A second HIFU treatment and hysterectomy were performed. Treatment was also based on the principle of hysterectomy. The second HIFU treatment was administered to patients who wanted HIFU treatment and met the criteria.

The complication rate in this study was 4.6% (84/1807), including 2 cases of small bowel perforation 2 and 5 d after ablation. We tried to completely cure subserosal uterine fibroids around the intestine. However,

there was a mistake in the reading of US images. Fortunately, the lesion of the intestinal injury was only 1 cm. Thus, laparoscopic surgery was simply terminated without long-term sequelae. After two cases of complications, the risk of intestinal injury was effectively reduced by strict pre-operative bowel preparation, careful intra-operative intestinal protection, a well-controlled range of ablation and maintenance of a distance of at least 1 cm from the tumor margin. Adhering to these steps might help prevent intestinal injury. [Chen et al. \(2015\)](#) have reported that a total of 1062 of 9988 patients (10.6%) had 1305 adverse reactions. In that report, two bowel perforations occurred in two patients, both of which were confirmed and repaired surgically. Other



Fig. 5. HIFU treatment of nulliparous adenomyosis. MRI reveals $7.5 \times 6.4\text{-cm}$ (148.2 cm^3) adenomyotic uterus on MRI sagittal image (A) and gadolinium-enhanced T1-weighted MRI image (B) after HIFU treatment. *Arrow* indicates non-perfused area after HIFU. After 11 mo, the uterine volume decreased to 5.2×4.5 (53.8 cm^3), as illustrated in the T2-weighted MRI image. The rate of uterine volume reduction was 63.7% (C). HIFU = high-intensity focused ultrasound; MRI = magnetic resonance imaging.

Table 4. Recurrence and additional treatments after HIFU

	Uterine fibroids	Adenomyosis
No. of treatments	918	889
No. of symptom recurrences	42	39
No. of new lesions	23	17
Second HIFU	9	17
Hysterectomy	13	20
Myomectomy	8	-

HIFU = high-intensity focused ultrasound.

Table 5. Complication profiles after HIFU treatment

Complication	No. of patients
Foot drop	1
Aggravation of known spondylolisthesis	1
Transient leg weakness	7
Transient sciatic nerve pain	13
Tumor lysis syndrome	1
Small bowel perforation	2
Sleep apnea	1
First-degree burn	17
Second-degree burn	12
Transient hematuria	29
Total	84

HIFU = high-intensity focused ultrasound.

Table 6. Outcomes of unintended pregnancies after HIFU treatment

Pregnancy outcome	Uterine fibroids (N = 13)	Adenomyosis (N = 18)
Normal spontaneous delivery	9	5
Cesarean section	3	8
Spontaneous abortion	1	2
Premature delivery	0	1
Follow-up loss	0	2

complications were foot drop, aggravation of known spondylolisthesis, transient unilateral leg weakness, unilateral sciatic nerve pain, tumor lysis syndrome with transient acute pre-renal failure, sleep apnea associated with sedative agents, first- and second-degree skin burns and transient hematuria. With supportive care, all complicated cases recovered without any permanent adverse effects. One woman with foot drop took 6 mo to recover. Those with unilateral leg weakness and sciatic nerve pain took 2 mo to recover. Women with other symptoms took less than 2 wk to recover.

In the beginning of our HIFU experience, we had sufficiently sedated patients who complained of discomfort during treatment with propofol. In these cases, there were many symptoms associated with nerve damage because we could not determine the nerve pain. However, these symptoms and risks decreased greatly after we changed intravenous conscious sedation to midazolam and lower propofol doses (0.3–0.6 mg/kg/h by

continuous infusion) during treatment. Other injuries could be avoided with increased treatment experience. Other researchers have reported complications after USgHIFU such as vaginal bleeding, lower abdominal pain and low-grade fever (Ren *et al.* 2009). Some authors have reported effects of USgHIFU on sexual function after treatment of uterine fibroids compared with conventional myomectomy and had partial improvement in sexual function after both procedures (Wang *et al.* 2013). There were a few cases of decreased vaginal secretion after treatment in our experience as well. However, no patient experienced sexual dysfunction.

HIFU treatment for uterine fibroids and adenomyosis must be approached with caution because significant complications that cause maternal or fetal morbidity can occur. Qin *et al.* (2012) reported that pregnancy can occur within 1 y after USgHIFU ablation of uterine fibroids. Intensive surveillance of the mother and fetus is needed, and cesarean section should be performed at the earliest signs and symptoms of uterine rupture. Although we only obtained data on pregnancies if the pregnant patients contacted us, we believe that USgHIFU treatment can effectively treat uterine fibroids and adenomyosis and allow safe parturition after treatment.

Our experience with HIFU is encouraging. With its very good therapeutic effects and acceptable side effects for treatment of uterine fibroids and adenomyosis, HIFU is the best non-invasive treatment so far. We hope that soon a well-designed prospective trial and clinical study, including MRI-based classification and location, blood circulation in the uterine leiomyoma and localization or segmentation of diffuse adenomyosis, will be published.

Conflict of interest disclosure—No potential conflict of interest was reported by authors of this study.

REFERENCES

- Chen J, Chen W, Zhang L, Li K, Peng S, He M, Hu L. Safety of ultrasound-guided ultrasound ablation for uterine fibroids and adenomyosis: A review of 9988 cases. *Ultrason Sonochem* 2015;27: 671–676.
- Funaki K, Fukunishi H, Sawada K. Clinical outcomes of magnetic resonance-guided focused ultrasound surgery for uterine myomas: 24-month follow-up. *Ultrasound Obstet Gynecol* 2009;34: 584–589.
- Jiang L, Hu B, Guo Q, Chen L. Sonographic and histological development of high intensity focused ultrasound in rabbit muscle. *Exp Ther Med* 2013;5:33–38.
- Kroencke TJ, Scheurig C, Kluner C, Taupitz M, Schnorr J, Hamm B. Uterine fibroids: Contrast-enhanced MR angiography to predict ovarian artery supply—Initial experience. *Radiology* 2006;241:181–189.
- Qin J, Chen JY, Zhao WP, Hu L, Chen WZ, Wang ZB. Outcome of unintended pregnancy after ultrasound-guided high-intensity focused ultrasound ablation of uterine fibroids. *Int J Gynaecol Obstet* 2012;117:273–277.
- R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, 2018. Available at: <https://www.R-project.org>.

- Ren XL, Zhou XD, Yan RL, Liu D, Zhang J, He GB, Han ZH, Zheng MJ, Yu M. Sonographically guided extracorporeal ablation of uterine fibroids with high-intensity focused ultrasound: Midterm results. *J Ultrasound Med* 2009;28:100–103.
- Shui L, Mao S, Wu Q, Huang G, Wang J, Zhang R, Li K, He J, Zhang L. High-intensity focused ultrasound (HIFU) for adenomyosis: Two-year follow-up results. *Ultrason Sonochem* 2015;27:677–681.
- Spies J. The UFS-QOL, a new disease-specific symptom and health-related quality of life questionnaire for leiomyomata. *Obstet Gynecol* 2002;99:290–300.
- Wang W, Wang Y, Tang J. Safety and efficacy of high intensity focused ultrasound ablation therapy for adenomyosis. *Acad Radiol* 2009;16:1416–1423.
- Wang W, Wang Y, Wang T, Wang J, Wang L, Tang J. Safety and efficacy of US-guided high-intensity focused ultrasound for treatment of submucosal fibroids. *Eur Radiol* 2012;22:2553–2558.
- Wang X, Qin J, Wang L, Chen J, Chen W, Tang L. Effect of high-intensity focused ultrasound on sexual function in the treatment of uterine fibroids: Comparison to conventional myomectomy. *Arch Gynecol Obstet* 2013;288:851–858.
- Zhao WP, Chen JY, Zhang L, Li Q, Qin J, Peng S, Li KQ, Wang ZB, Chen WZ. Feasibility of ultrasound-guided high intensity focused ultrasound ablation of uterine fibroids with hyperintense on T2-weighted MR imaging. *Eur J Radiol* 2013;82:e43–e49.
- Zhou M, Chen JY, Tang LD, Chen WZ, Wang ZB. Ultrasound-guided high-intensity focused ultrasound ablation for adenomyosis: The clinical experience of a single center. *Fertil Steril* 2011;95:900–905.