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Clinical Experience of Ultrasound-guided High-intensity Focused Ultrasound Treatment for Gynecologic Disorders in Single Center

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Abstract

At 3, 6 and 12 month after treatment, symptom severity scores and health-related quality of life scores and reductions in volumes of uterine adenomyosis and fibroids revealed good effects. The complication was an acceptable and with supportive therapy all complications resolved without permanent side effects. Pregnancy is relatively safe after HIFU treatment, but it should be approached carefully.

USgHIFU is an effective non-invasive treatment for a variety of benign solid tumors in gynecology, such as uterine fibroids, adenomyosis, and retained placenta accreta, which are benign diseases of the uterus. USgHIFU also has less impact on the function of the uterus and ovaries, and has manageable and acceptable side effects.

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Introduction

Adenomyosis and uterine fibroids, common among women of childbearing age, are conditions that cause secondary menstrual cramps, excessive menstruation, vaginal bleeding, and various infertility.

Treatment modality for these diseases range from hysterectomy or myomectomy to conservative treatment, including radiofrequency (RF), uterine artery embolization (UAE), and high-intensity focused ultrasound (HIFU). HIFU treatment is non-invasive treatment modality that uses an external ultrasound energy source to induce thermal ablation for target tissue. Focusing ultrasound at a specific location causes protein denaturation and irreversible cell necrosis through heating and cavitation, resulting in direct damage to tumor vessels in the focal region (Figure 1) [1]. Several studies have shown that ultrasound-guided high intensity focused ultrasound (USgHIFU) ablation and magnetic resonance-guided high intensity focused ultrasound (MRgHIFU) ablation are safe and feasible alternatives for treating uterine fibroids [2-5] and adenomyosis [6-8]. Non-invasive nature which is associated with low morbidity and rapid recovery, with patients often able to return to normal activity in one day is the biggest advantage of HIFU treatment. Paragraph: use this for the first paragraph in a section, or to continue after an extract.

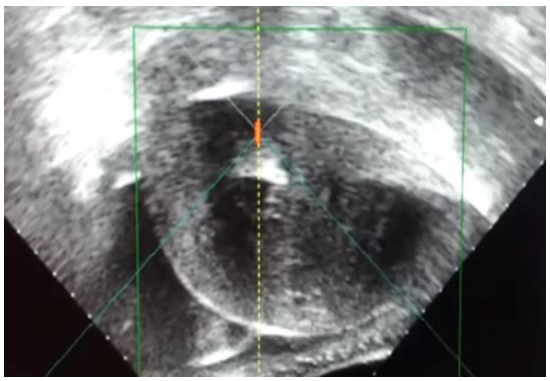

Figure 1: A hyper-echoic change was observed in the focus area in ultrasound image.

Safety and Efficacy of HIFU Treatment

Methods

We evaluated the efficacy and safety of USgHIFU treatment by assessing volume reduction, uterine fibroid symptoms, quality of life UFS-QOL score changes and adverse events [9]. UFS-QOL is composed of 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 gynecological field as a useful tool to objectively evaluate the severity of symptoms and health-related quality of life in patients with uterine fibroids. The UFS-QOL includes eight-item Symptom Severity Scale (SSS) and six dimensions of health-related quality of life (HRQOL).

Our study was a retrospective analysis of 1,807 women with fibroids or adenomyosis who underwent USgHIFU resection from February 2010 to October 2017 [10]. We diagnosed uterine fibroids and adenomyosis through each patient's history, physical examination, and diagnostic ultrasound (US) and magnetic resonance imaging (MRI) scans. Patients with 2 cm-12 cm diameter symptomatic uterine fibroids and patients with symptomatic focal and diffuse adenomyosis were included. Patients with pedicle fibroids, asymptomatic fibroids less than 5 cm in diameter, asymptomatic focal adenomyosis, evidence of known or suspected extensive pelvic adhesions, severe pelvic endometriosis, and history of acute pelvic inflammatory disease were excluded. We also excluded pregnant and lactating women, patients with abdominal wall thickness greater than 5 cm, patients receiving

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anticoagulant therapy, a history of cerebrovascular disease, unstable heart condition, hemolytic anemia and suspected malignancy.

The Purpose of the Study

Symptoms of each patient were surveyed objectively according to Symptom Severity Score (SSS) and Health Related Quality of Life (HRQOL) scores of UFS-QOL questionnaires. After scoring, questions one to eight of the UFS-QOL were summed. SSS was calculated using the following formula: transformed score = ((actual raw score – lowest possible raw score)/possible raw score range) x100. After the scores of questions nine to 37 of the UFS-QOL were summed, HRQOL was calculated using the following formula: transformed score = ((highest possible score – actual raw score)/possible raw score range) x100. Patients completed the UFS-QOL questionnaires prior to treatment and at three, six and 12 months after treatment. A higher SSS score means higher patient discomfort, and a lower HRQOL means lower patient satisfaction with daily life. The effectiveness of ablation by volume reduction rate was assessed by US and enhanced MRI. Uterine and target lesions in longitudinal (D1), anteroposterior (D2) and axial (D3) dimensions were measured. Uterine fibroid volume and uterine adenomyosis volume was calculated according to the following equation: $V = 0.5233 \times D1 \times D2 \times D3$ [11].

Single-session HIFU treatment was performed on all 1807 patients under conscious sedation. Gadolinium-enhanced MRI was examined before treatment, the day after treatment, and at 6 and 12 months after treatment to evaluate treatment response and relapse and new lesions. A three-month assessment was conducted by US scan alone.

Repeated measures of variance analysis of variance was used to determine statistical significance for changes in patients' symptom severity, quality of life score, and uterine volume at 3, 6, and 12 months after HIFU procedure. In this study, age was used as a confounding variable, and the statistical significance threshold was set at $p < 0.05$. All statistical analyzes were performed using R version 3.5.1 [12].

The age of the 918 patients diagnosed with uterine fibroids was 41.26 ± 6.35 years (mean ± SD). Of these patients, 368 were nulliparous and 550 were multiparous. A total of 195 patients had a cesarean section. Fifty patients underwent myomectomy and three underwent RF myolysis. HIFU treatment time (from 1st sonication shot to the last shot) was 86.13 ± 36.37 min (mean ± SD). HIFU ablation time (the sum of the shot times) was 1156.35 ± 568.98 sec (mean ± SD). HIFU treatment energy for each patient was 455 kJ ± 493 kJ (mean ± SD).

The age of the 889 patients diagnosed with adenomyosis was 41.06 ± 5.45 years (mean ± SD). Of these, 319 were nulliparous and 570 were multiparous. A total of 217 patients had a cesarean section. Fifty nine patients underwent myomectomy. Ten patients underwent RF myolysis and three patients underwent UAE. HIFU treatment time and HIFU ablation time were 79.36 ± 30.58 min (mean ± SD) and 1001.69 ± 453.59 sec (mean ± SD), respectively. HIFU treatment energy was 361 ± 181 kJ (mean ± SD).

Ethical approval

This study was approved by the Institutional Review Board of Incheon Christian Hospital (Approval number: 2012-01) and all procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional review board and with the 1964 Helsinki declaration and its later amendments or comp Ethical approval.

Results of HIFU treatment for uterine fibroids and adenomyosis

Pre-treatment uterine fibroid volume was 176.46 ± 149.87 cm^3 (mean ± SD). Pre-treatment SSS was 48.55 ± 21.17(mean ± SD) and UFS-QOL scores was 59.10 ± 23.15 (mean ± SD). Uterine fibroid volumes (reduction rate, %) were 79.87 ± 74.81 cm^3 (54.7%), 66.20 ± 81.49 cm^3 (62.5%) and 46.23 ± 54.7 cm^3 (73.8%) at three, six and 12 months after treatment, respectively ($p < 0.001$). SSSs were 24.74 ± 16.28, 23.72 ± 15.05 and 24.94 ± 15.15 (mean ± SD) at three, six and 12 months after treatment, respectively ($p < 0.001$). UFS-QOL scores were 79.42 ± 17.99, 81.69 ± 18.55 and 81.20 ± 15.96 at three, six and 12 months, respectively ($p < 0.001$). (Table 1, Figure 2).

In cases of adenomyosis, the pre-treatment uterine volume was 247.80 ± 145.84 cm^3 (mean ± SD). Pre-treatment SSS was 48.59 ± 20.97 and and UFS-QOL scores was 59.28 ± 23.11 (mean ± SD). Uterine adenomyosis volumes (reduction rate, %) were 137.49 ± 76.94 cm^3 (44.5%), 122.03 ± 73.56 cm^3 (50.7%) and 98.91 ± 60.92 cm^3 (60.1%) at three, six and 12 months after treatment, respectively ($p < 0.001$). SSSs were 24.87 ± 16.38, 23.58 ± 15.04, and 24.98 ± 15.11 (mean ± SD) at three, six and 12 months, respectively ($p < 0.001$). UFS-QOL scores were 79.64 ± 17.91, 81.59 ± 18.44 and 81.35 ± 15.88 (mean ± SD) at three, six and 12 months, respectively ($p < 0.001$) (Table 2, Figure 3).

Additional treatment and complications after HIFU treatment

Of 918 uterine fibroid patients, 42 showed recurrence of symptoms and 23 had new lesions. Nine patients diagnosed with uterine fibroids were treated with a repeat HIFU. Thirteen patients received hysterectomy and eight patients underwent myomectomy. Of 889 adenomyosis patients, 39 showed recurrence of symptoms and 17 had new lesions. Seventeen patients were treated with a second HIFU and 20 patients received hysterectomy. As complications, the neurological symptoms were foot drop and spondylolisthesis in 1 case each, transient unilateral leg weakness in 7 cases and unilateral sciatica nerve pain in 13 cases. There was one case of sleep apnea caused by intraoperative sedatives and one case of oncolytic syndrome with transient acute renal failure confirmed during recovery after the procedure. Mild first- and second-degree skin burns were observed in 7 and 12 cases, respectively, and transient hematuria in 29 cases.

	Before HIFU		After HIFU		*p* value
	Baseline	3 months	6 months	12 months	
Uterine fibroid volume (cm^3, Mean ± SD)	176.46 ± 149.87	79.87 ± 74.81	66.20 ± 81.49	46.23 ± 54.7	<0.001
Symptom severity scale (Mean ± SD)	48.55 ± 21.17	24.74 ± 16.28	23.72 ± 15.05	24.94 ± 15.15	<0.001
UFS-QoL† score (Mean ± SD)	59.10 ± 23.15	79.42 ± 17.99	81.69 ± 18.55	81.20 ± 15.96	<0.001

Table 1: Results of uterine fibroids to HIFU*
*HIFU: High-Intensity Focused Ultrasound; †UFS-QoL: Uterine Fibroid Symptom-Quality of Life

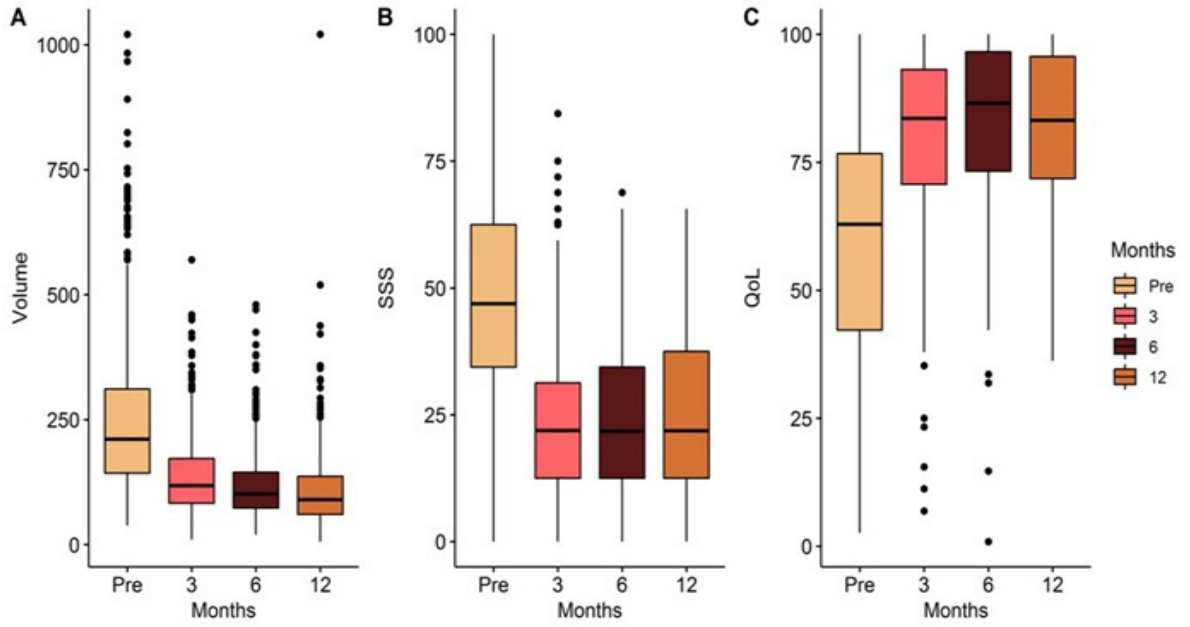

Figure 2: Improved fibroid volumes (cm^3), symptom severity score, and UFS-QoL during follow-up for patients with uterine fibroids

	Baseline	3 months	6 months	12 months	*p* value
Uterine volume (cm^3, Mean ± SD)	247.80 ± 145.84	137.49 ± 76.94	122.03 ± 73.56	98.91 ± 60.92	<0.001
Symptom severity scale (Mean ± SD)	48.59 ± 20.97	24.87 ± 16.38	23.58 ± 15.04	24.98 ± 15.11	<0.001
UFS-QoL† score (Mean ± SD)	59.28 ± 23.11	79.64 ± 17.91	81.59 ± 18.44	81.35 ± 15.88	<0.001

Table 2: Treatment response of adenomyosis to HIFU*

*HIFU: High-Intensity Focused Ultrasound; †UFS-Qo: Uterine Fibroid Symptom-Quality of Life

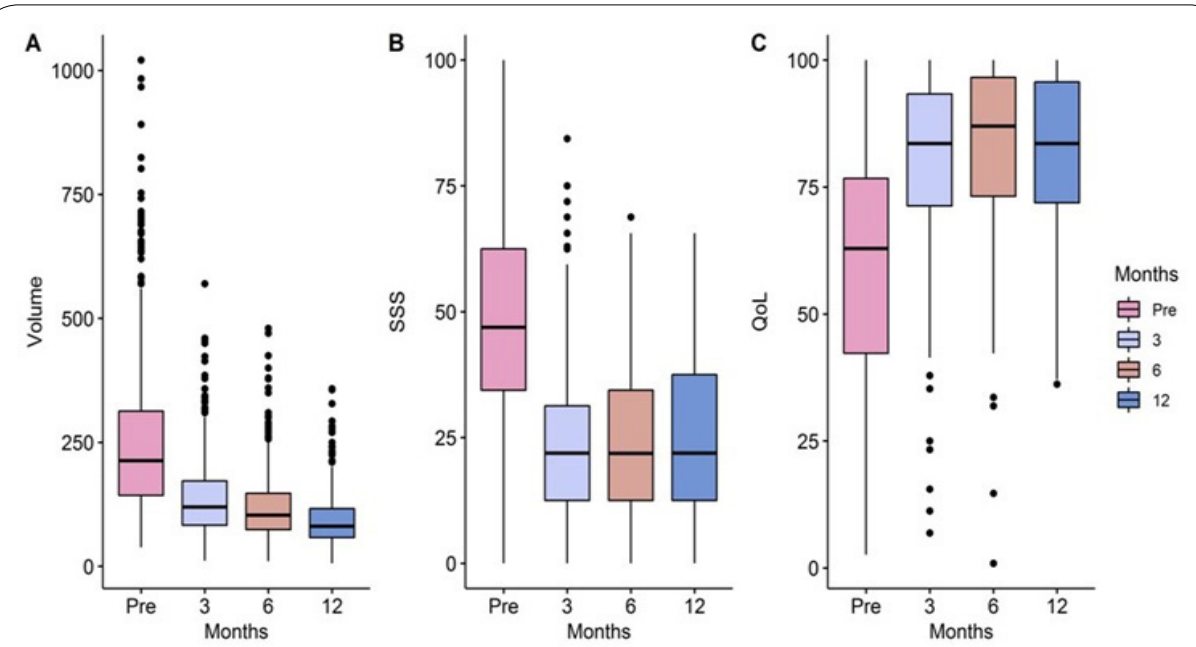

Figure 3: Improved uterine volumes (cm^3), symptom severity score, and UFS-QoL during follow-up for patients with adenomyosis

Two cases of simple laparoscopic closure were performed because small intestine perforation was observed on days 2 and 5, respectively, after HIFU treatment. With the exception of two cases of laparoscopic surgery, most of the complications recovered without permanent side effects with supportive care.

Discussion

In the 918 patients with fibroids we treated, the fibroid volume reduction outcomes were 54.7%, 62.5%, and 73.8%, respectively, at 3, 6, and 12 months after treatment ($p < 0.001$). These outcomes were comparable with outcomes reported in other studies. Ren et al. [13] have reported reduction rates of 27.2%, 47.9%, and 50.3% at 3, 6 and 12 months, respectively. Wang et al.2 have shown reductions of 46.7%, 68.2%, 78.9%, and 90.1% at 3, 6, 12 and 24 months, respectively. Our results of treatment energy and ablation time were similar to those reported in other papers using the same equipment. We saw improved SSSs and UFS-QOL scores out to 12 months after treatment. Improved UFS-QOL scores at 24 months after treatment have also been reported.2 Among 918 patients with uterine fibroids, 42 patients (4.6%) showed symptom recurrence, including 23 patients who were diagnosed with new lesion on follow-up MRI. In the treatment of these recurrent patients, a second HIFU treatment was applied only to patients who preferred HIFU treatment and met the criteria. For other recurrences, surgical myomectomy and hysterectomy were applied, and volume reduction, SSS, or UFS-QOL scores were not included in the statistical data.

In the 889 patients with adenomyosis we treated, the rates of reduction in uterine volume were 44.5%, 50.7%, and 60.1% at 3, 6, and 12 months, respectively, and improvements in SSS and UFS-QOL were statistically significant ($p < 0.001$). SSS and UFS-QOL improvements in other studies were 84.7%, 84.7%, and 82.3%, respectively, with remission rates at 3 months, 1 year, and 2 years after treatment [8]. In our study, adenomyosis volume reductions were less than those reported in other papers. This might be because we measured the volume of the entire uterus including the normal uterus site and irregular adenomyosis lesions. Of the 889 patients treated for adenomyosis, 39 (4.4%) relapsed, including 17 patients diagnosed with new lesions on MRI. In the treatment of these recurrent patients, a second HIFU treatment was applied only to patients who preferred HIFU treatment and met the criteria. For other recurrences, hysterectomy was applied.

The complication rate in our study was 4.6% (84/1807), including two cases of small bowel perforation at two and five days after ablation. These occurred when we tried to completely cure subserosal uterine fibroids around the intestine in two patients. However, a mistake was made in the reading of ultrasound images. Fortunately, the size of the intestinal lesions were only 1 cm. Thus, laparoscopic surgery was simply employed to correct the injuries without long-term sequelae. From then on, the risk of subsequent intestinal damage was effectively reduced by ensuring a safe range of 1 cm or more from the edge of the tumor. Following these steps might be helpful for the prevention of intestinal injury [14]. have reported that a total of 1,062 patients out of 9,988 (10.6%) had 1,305 adverse reactions. In that report, twobowel perforations occurred in two patients, both of which were confirmed and repaired surgically. Other complications were neurological symptoms including foot drop, temporary unilateral leg weakness, unilateral sciatica, and exacerbation of known spondylolisthesis. In addition, there were sleep apnea associated with sedatives during treatment, mild first to second-degree burns of the skin immediately after the procedure, and transient hematuria. Tumor lysis syndrome was observed during the recovery period. All recovered without any permanent side effects with supportive care. One case of foot drop took six months to recover. Cases of unilateral leg weakness and sciatic nerve pain took two months to recover. Other symptoms took less than two weeks to recover [13].

Ovarian reserve after HITU treatment

AMH is an effective indicator for evaluating ovarian reserve in that the value is not affected by menstrual cycle. It reaches its highest level after puberty and gradually decreases over time in normo-ovulatory women [15-19]. Seventy-nine women with symptomatic uterine fibroids and adenomyosis were recruited in our study from January 2014 to December 2014 [20]. All patients underwent HIFU treatment. Blood samples (10 ml) were taken prior to, and at six months after HIFU ablation and allowed to clot. Samples were centrifuged and serum was stored frozen at -20°C until assay. AMH levels were determined using an enzyme-immunometric assay (DSL, Webster, TX. USA). Inter- and intra-assay coefficients of variation were below 5% at the level of 3 μg/l and below 11% at the level of 13 μg/l. The detection limit of the assay was 0.026 μg/l.

Statistical analyses were performed using R version 3.0.2 [12]. Continuous variables with normal distribution were compared using paired t-test and grouped variables were compared using analysis of variance (ANOVA). If AMH level at each time point was not normally distributed, paired Wilcoxon's rank-sum test was used. Statistical significance was defined at $P < 0.05$.

The mean age of these patients was 40.5 years (range, 24 – 45 years). Of the 79 patients, 38 were nulliparous and 41 were multiparous. A total of 12 patients underwent cesarean section. 45 patients were diagnosed with uterine fibroid and 34 patients with adenomyosis. HIFU treatment time (mean ± standard deviation), HIFU ablation time and treatment energy were 73.5 ± 25.6 min, 994.7 ± 386.8 sec and 365 ± 157 kJ, respectively.

Pre-treatment uterine fibroid volume, SSS, and UFS–QOL scores were 174.02 ± 136.47 cm^3, 50.01 ± 7.81 and 61.27 ± 21.58, respectively. At six months after HIFU ablation, uterine fibroid volume, SSS and UFS-QOL score were 69.06 ± 56.93 cm^3, 22.06 ± 14.38 and 83.21 ± 20.53 respectively ($P < 0.01$). Pre-treatment uterine adenomyosis volume, SSS and UFS–QOL score were 222.56 ± 112.64 cm^3, 61.57 ± 22.36 and 42.69 ± 23.19, respectively. At six months after HIFU, uterine adenomyosis volume, SSS and UFS–QOL score were 111.54 ± 75.49 cm^3, 27.64 ± 18.02 and 78.49 ± 20.98, respectively ($P < 0.01$). All patients had regular cycles (28 – 35 days) before the treatment and at six months after HIFU. AMH levels before and at six months were 2.11 ± 2.66 μg/l and 1.84 ± 2.57 μg/l, respectively. There was no significant difference in AMH levels between the two time points ($P > 0.05$) (Table 3, Figure 4). In one report which examined the effect of UAE and hysterectomy on ovaries, AMH levels were significantly decreased during the entire follow-up period in both treatment groups (UAE and hysterectomy) compared to expected AMH levels due to aging; indicating that both UAE and hysterectomy could affect ovarian reserve [19]. Although our study had a relatively small number of study patients and follow-up period, no significant difference in AMH levels were found as a result of HIFU ablation. This may be explained by the fact that the ovary and its vessels are not involved in the treatment area. Therefore, HIFU ablation did not damage ovarian blood flow. Our preliminary data suggest that HIFU ablation is effective for uterine fibroids and adenomyosis without affecting ovarian reserve.

Unintended pregnancies after HIFU treatment

Our retrospective analysis was conducted in 1204 women with uterine fibroid or adenomyosis who underwent HIFU ablation from

	Mean (±SD†)
Treatment time (minutes)	73.5 (±25.6)
Ablation time (seconds)	994.7(±386.8)
Treatment energy (Joule)	364713.8(±156350.7)
AMH level before HIFU (μg/L)	2.11(±2.66)
AMH level 6 months after HIFU (μg/L)	1.84(±2.57)

Table 3: Therapeutic data of the 79 patients participated in this study.
†SD: Standard deviation

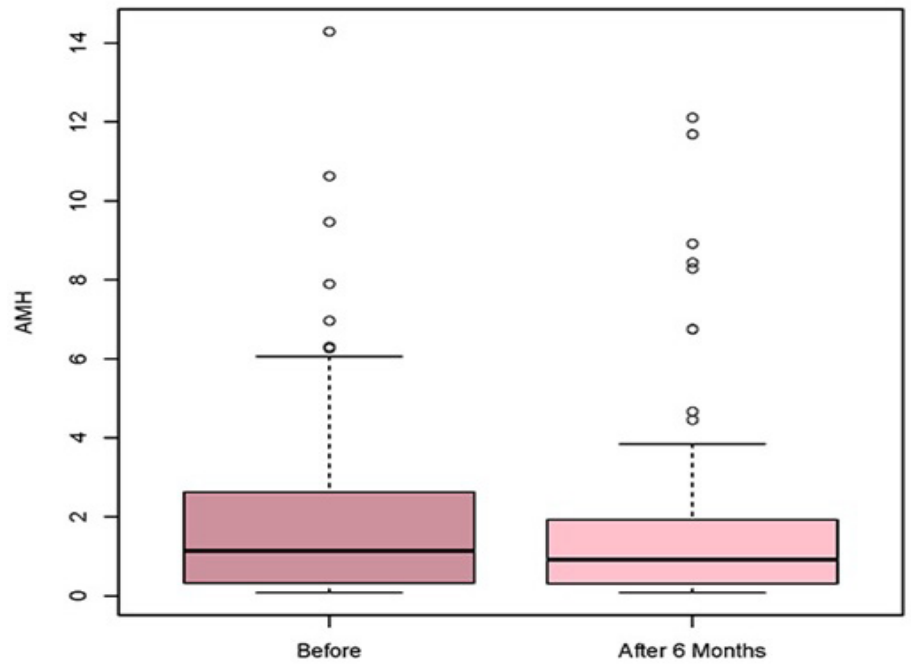

Figure 4: AMH levels after HIFU ablation for uterine fibroids and adenomyosis. AMH levels (μg/L) before and at 6 months after HIFU were not significantly different by Wilcoxon's rank sum test (P value= 0.4709)

February 2010 to January 2015 [21]. Among these women, there were 23 unintended pregnancies. The median age of the 11 patients with uterine fibroids was 32.9 years (range 26~41).

Two patients were multiparous. The mean values of HIFU treatment time and HIFU ablation time were 79.55 minutes and 604.8 seconds for fibroids, respectively. The median HIFU treatment energy was 458.3 kJ. The volume reduction rate and SSS six months after treatment were 69.4% and 20.5%, respectively.

The median age of the 12 patients with adenomyosis was 34.1 years (range 30~42). Six patients were multiparous. The median HIFU treatment time and median HIFU ablation time were 51.88 min and 652.8 sec for adenomyosis, respectively. The median HIFU treatment energy was 189.9 kJ. The volume reduction rate and SSS six months after treatment were 39.2% and 40%, respectively.

The possibility of future unintended pregnancy after HIFU cannot be excluded despite our explanation to each patient that its effects on pregnancy are unclear. Among the 23 unintended pregnancies, 12 developed no complication during pregnancy and continued until full term delivery. Eight vaginal and four cesarean section deliveries were also uneventful. Three patients experienced a spontaneous abortion. One patient with adenomyosis experienced preterm delivery at 25 weeks of gestation and five patients remained pregnant at that point. Two patients could not be contacted (Table 4).

Pregnancy outcomes	Uterine fibroid (n=11)	Adenomyosis (n=12)
Normal spontaneous delivery	5	3
Cesarean section	3	1
On-going pregnancy	2	3
Spontaneous abortion	1	2
Premature delivery	0	1
Follow-up loss	0	2
Mean treatment time (minutes)	79.55	51.88
Mean ablation time (minutes)	10.08	10.88
Mean energy (Joules)	458,334.3	189,896.7
Volume reduction rate (% by 6 months)	69.4	39.2
SSS reduction rate (% by 6 months)	20.5	40

Table 4: Outcomes of unintended pregnancies after USgHIFU treatment.
USgHIFU: Ultrasound-guided high intensity focused ultrasound; n: number; SSS: Symptom severity score.

In a report of 54 pregnancies in 51 women undergoing MRgHIFU treatment for uterine fibroids, the live birth rate was 41% of all pregnancies, with a spontaneous abortion rate of 28%, and an elective pregnancy termination rate of 11%. There were also 11 on-going pregnancies beyond 20 gestational weeks. There were two cases of

placenta previa without serious complications [22]. In our series, the full term delivery rate was 57.1 % (12/21), and spontaneous abortion rate was 14.3% (3/21).

In another study reporting the consequences of unintended pregnancies after USgHIFU resection of uterine fibroids, pregnancies progressed to full term in seven women and all births were via cesarean delivery without complications. Fifteen women underwent induced abortion and two women experienced a spontaneous abortion [23]. In a case series of deliveries after RF myolysis, there were three cases of uterine rupture during pregnancy [24] and four cases of term deliveries without any complications [25]. Even though the data were insufficient to compare the size and number of fibroids, all ruptured cases were conceived within three months of RF myolysis and three successful cases were conceived after 12 months. In our study, there was no uterine rupture during pregnancy or labor. However, three spontaneous abortions were observed when conceived within one year of HIFU.

Although the preliminary study for pregnancy after HIFU ablation is inspiring, this procedure should be approached with caution due to the high risk of maternal or fetal morbidity at delivery. Intensive surveillance of the mother and fetus is required and if there are earliest signs and symptoms of uterine rupture, a cesarean section must be performed as soon as possible.

Clinical application of HIFU treatment for retained placenta accreta

Retained placenta, one of the leading causes of postpartum bleeding, is a condition in which the placenta or membrane remains in the uterus during or after the third stage of labor. In many cases of retained placenta, placental villi are abnormally attached to the uterine myometrium. As the number of cesarean sections increases, the incidence of placental attachment increases, and although ultrasound has traditionally been a good method for diagnosing the placenta, magnetic resonance imaging (MRI) has been more used for diagnostic accuracy [26]. In additionally, the incidence of conservative treatments such as UAE or methotrexate has gradually increased. Although patients generally prefer conservative options rather than hysterectomy, the risk of infection or bleeding and a secondary hysterectomy [27].

We experienced a case of retained placental accreta in which the uterus was preserved by hysteroscopy following high-intensity focused ultrasound (HIFU) ablation [28].

A 33-year-old woman developed irregular vaginal bleeding, menorrhagia, and dysmenorrhea after cesarean section at 38 gestational weeks in October 2010. The patient was diagnosed as submucosal fibroid by ultrasonography and was admitted to the hospital for HIFU treatment on July 28, 2011.

The obstetrics history of the patient included one cesarean section and one artificial abortion. She also received a myomectomy seven years prior. Her vital signs were stable and there were nothing remarkable for general health. Physical examination revealed scars from a previous cesarean section, and pelvic examination revealed fist-sized uterine and vaginal spotting. There was a 3.2 × 2.0 × 1.5 cm hyperechoic lesion near the endometrial cavity, a thickened posterior uterine wall and intact both adnexae by transabdominal and transvaginal ultrasonography. Serum beta-human chorionic gonadotropin was normal and hemoglobin was 10.9 mg/dL on Initial laboratory findings. We thought an endometrial problem with a submucosal fibroid was suspected on the history and sonographic findings.

Under intravenous propofol sedation, we attempted to remove the uterine mass with hysteroscopic resection (RIWO Resectoscopes, Richard Wolf GmbH, Knittlingen, Germany). However the mass could not be completely removed because the hysteroscopy was difficult with blurred vision due to bleeding. Pathological examination of some removed tissue diagnosed necrotic chorionic villi with calcification.

Although the patient's vital signs were stable, vaginal bleeding continued and required other treatment. The patient was suggested to be treated with methotrexate as a drug, but was rejected, so we considered a combination therapy with HIFU and curettage. To obtain more information prior to HIFU treatment, MRI images were obtained and HIFU was performed using an ultrasound-guided HIFU tumor treatment system. (Model JC, Chongqing Haifu (HIFU) Tech Co., Ltd., Chongqing, China). The ultrasound machine (MyLab, Esaote, Genoa, Italy) was used for real-time monitoring of the HIFU procedure. Bladder volume was adjusted with sterile normal saline and uterine position was adjusted. The patient was treated in a prone position on the treatment equipment in a state of conscious sedation. The total energy of HIFU treatment was 24.55 kJ with a power of 250 W, and the total treatment time was 10 minutes. After HIFU treatment, vaginal bleeding symptoms improved and there were no other complications. Seven days later, we performed hysteroscopy to remove the lesion after HIFU treatment and to prevent endometrial adhesions for subsequent pregnancies. There was no bleeding in the lesion during hysteroscopy, which was due to coagulant necrosis of the lesion after HIFU treatment. After the procedure, the patient was stable without any abnormal vaginal bleeding accreta was shown as low signal intensity on (A) and low enhanced image on (C). (B) T2W1 and (D) contrast enhanced image was MRI finding 3 months later after HIFU combined with hysteroscopic resection (Figure 5). The lesions are not observed.

Retained placenta accreta is a challenging obstetrical problem; although rare, it remains a serious condition if not properly managed. Although hysterectomy is generally the recommended treatment for placental accreta, conservative treatment is needed as an alternative for patients wishing to become pregnant in the future. Traditionally conservative treatments include methotrexate and UAE, but both methods may require hysterectomy due to the risk of infection or bleeding because placental tissue remains. Some studies have suggested that hysteroscopic resection alone or in combination with UAE as a conservative treatment option, as well as being safe and effective, lowering the incidence of adhesions and improving fertility prognosis [29,30] However, treatment with hysteroscopic resection alone leaves the potential for repeat hysteroscopy (50.0%) or delayed hysterectomy (8.3%) [31].

Paek et al. [32] showed in a pilot study on fetal tissue in a sheep model that HIFU ablation could be successfully applied to placental tissue. Huang et al. [33] and a Xiao et al. [34] also showed that HIFU is an effective treatment method for cesarean pregnancy scarring.

Based on these studies, we envisioned HIFU treatment as a suitable alternative treatment option for patients with placental disease who may wish to preserve their fertility options in the future. Because the patient refused conventional treatments and the hysteroscopic resection had failed, we decided to apply HIFU treatment to the placenta accreta. We suggest HIFU with hysteroscopy to treat placental accreta while improving pregnancy options.

It will be important to consider the pros and cons of treatment methods for placenta accreta, and to select a treatment method suitable for the patient's situation and needs. Additional studies should be performed to assess the application of HIFU treatment followed by hysteroscopic resection for treating retained placenta accreta.

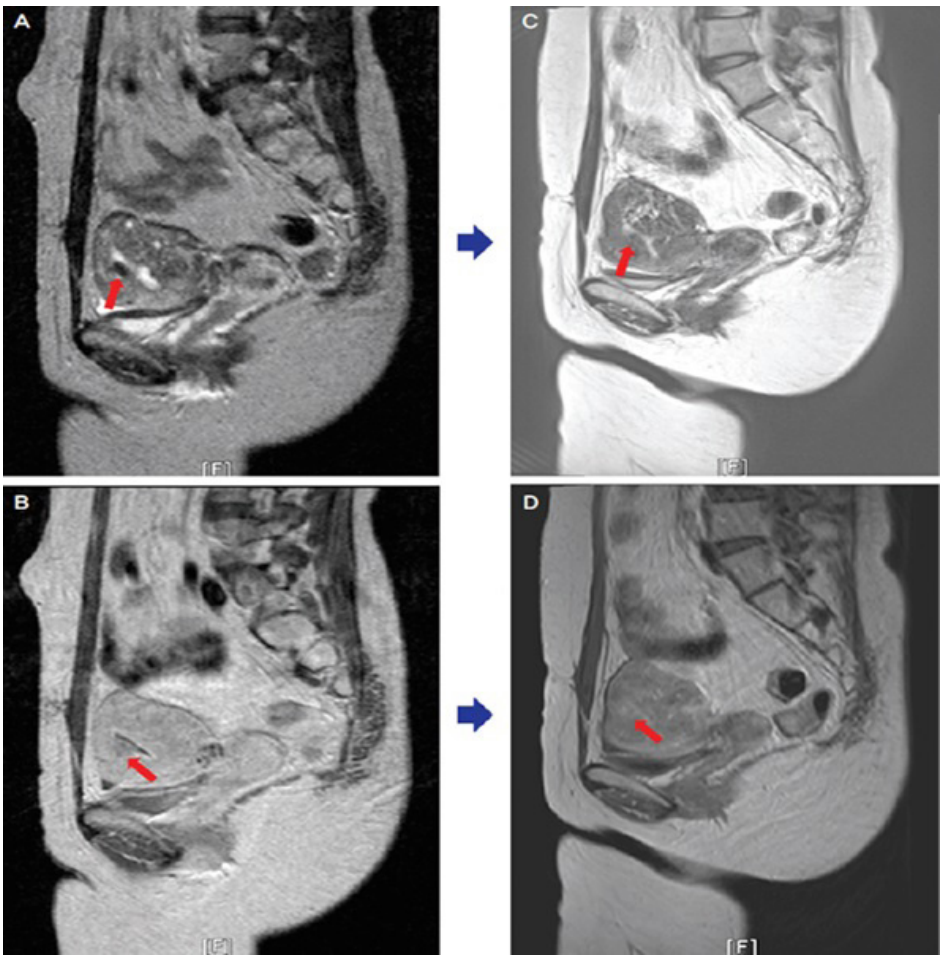

Figure 5: (A) T2W1 and (C) contrast enhanced image was MRI finding before HIFU ablation. The retained placenta accreta was shown as low signal intensity on (A) and low enhanced image on (C). (B) T2W1 and (D) contrast.

Competing Interests

The authors declare that they have no competing interests.

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