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(RESEARCH ARTICLE)

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Efficacy and safety of ultrasound-guided high-intensity focused ultrasound for uterine adenomyosis: Preliminary experience from a case series

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Abstract

Objective: This prospective cohort study was to evaluate the efficacy and safety of ultrasound-guided High-Intensity Focused Ultrasound (HIFU) in the treatment of uterine adenomyosis.

Methods: Ten premenopausal women with symptomatic adenomyosis underwent ultrasound-guided HIFU therapy. Their symptoms were compared using symptom severity scores before and at 3, 6 and 12 months after treatment. The sizes of their uteri and adenomyotic lesions at 6 months after treatment were compared with those of pre-treatment as determined by magnetic resonance imaging.

Results: The menstrual pain scores were reduced by 45.5% (-83.3–100%) at 3-month, 57.3% (-83.3–100%) at 6-month and 27.9% (-100–100%) at 12-month after treatment. The modified Uterine Fibroid Symptom and Quality of Life scores were reduced by 50.0% (9.1–69.7%) at 3-month, 40.9% (27.3–66.7%) at 6-month and 39.5% (0–70.0%) at 12-month after treatment. The uterus and adenomyosis volumes were reduced by 24.4% (1.2–42.0%) and 46.3% (2.1-78.4%) at 6-month after treatment, respectively. Two patients (20%) had significant treatment-related complications and three patients (30%) required subsequent surgical interventions.

Conclusions: Although ultrasound-guided HIFU appears to provide symptomatic relief to most patients with adenomyosis, its long-term effectiveness and safety require further evaluation in a larger cohort of patients, and may improve with clinical experience.

Keywords: Adenomyosis; Focused ultrasound; HIFU; Ultrasound-guided

1. Introduction

Uterine adenomyosis is a common disorder in women of childbearing age. It is commonly associated with uterine enlargement, due to the presence of ectopic endometrial glands and stroma within the myometrium. It can give rise to significant symptoms, most commonly menorrhagia and dysmenorrhea [1]. Hysterectomy is used to be the definitive and standard treatment. However, nowadays more and more women prefer uterine preservation, especially for women with future fertility wish. Medical treatment mainly allows the control of symptoms, whereas uterus-sparing surgeries or interventions, such as electrocoagulation of the involved myometrium, excision of adenomyotic foci or uterine artery embolization are associated with variable degree of success and risk of recurrence [1-3].

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Recently, high-intensity focused ultrasound (HIFU) therapy has been used as a safe and effective uterine-sparing alternative in the treatment of uterine adenomyosis [4-6]. HIFU can be performed under either magnetic resonance (MR) or ultrasound guidance for target localization and treatment monitoring, causing focal thermo-ablation of the adenomyotic lesions [6-10]. While ultrasound-guided HIFU (USg HIFU) has been increasingly popular in China for the treatment of adenomyosis [11,12], this treatment modality is not available in many other countries. At our center, with accumulating experience in using USg HIFU in the treatment of uterine fibroids [13], we have started a prospective cohort study on the use of this treatment for adenomyosis in a small series of women since 2016. This article reports the first local experience in Hong Kong, in evaluating the efficacy and safety of USg HIFU in treating adenomyosis.

2. Methods

The followings were the eligibility criteria for enrolment: (1) premenopausal women, over 35 years of age, with no future childbearing plans; (2) significant symptoms related to adenomyosis, intractable to standard medical therapy; (3) uterine size less than 22 weeks' gestation; (4) localized adenomyotic lesion or adenomyoma as judged by contrast MR imaging, involving only anterior or posterior uterine wall, and not both; (5) abdominal wall thickness of less than 5 cm from MR imaging measurement; and (6) no history suggestive of possible extensive pelvic adhesions such as history of major open pelvic surgery, pelvic inflammatory disease or pelvic endometriosis.

Research ethics approval was obtained from the Institutional Review Board of the University of Hong Kong / Hospital Authority Hong Kong West Cluster. Written informed consent was obtained before treatment from all women.

2.1. HIFU Treatment

Following a detailed medical history and a gynecological examination, women eligible for HIFU treatment would have a cervical smear and an endometrial sampling if needed, and a pelvic ultrasound assessment. All women had MR imaging to confirm the diagnosis, to establish the extent and location of adenomyosis, to assess the accessibility of the lesions to treatment, and to exclude other associated uterine or ovarian pathology.

The JC HIFU system (Chongqing Haifu Technology, Chongqing, China; Figure 1) consisted of a 0.8 MHz therapeutic ultrasound transducer of 15 cm in focal length and 12 cm in diameter, and a real-time 3.5 MHz diagnostic ultrasound scanner integrated in the centre of the therapeutic transducer (Figure 2). Both transducers were submerged in a degassed water reservoir system and were controlled by a master computer unit.

Figure 1 JC high-intensity focused ultrasound system

In order to familiarize the patients with the treatment process, they would need to go through a pre-treatment planning. Also, during the planning, the treatment target was carefully located. The depth and the proximity of the target to the adjacent structures were determined. At the same time, the likelihood of the presence of a bowel loop along the path of sonication was evaluated.

All patients had pre-treatment mechanical bowel preparation. The lower abdominal skin was degassed with suction, degreased with alcohol and shaved. The urinary bladder was catheterized to allow adjustment of the bladder volume. All patients were placed in prone position, with the lower abdominal skin put in contact with degassed water. The target adenomyotic lesion and the important anatomical points (bladder, uterine fundus, sacrum and sacral promontory) were located with the diagnostic ultrasound. This was to ensure that no normal structures such as bowel loops were in the acoustic pathway.

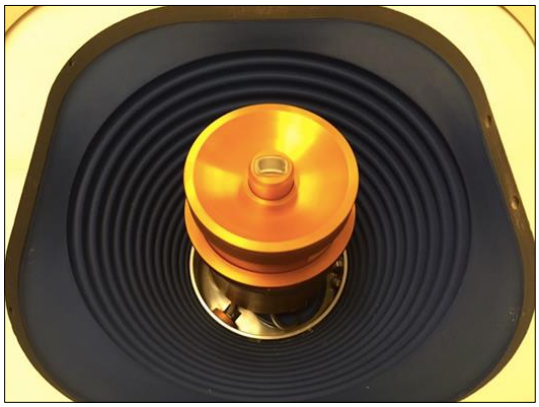


Figure 2 Real-time diagnostic ultrasound scanner integrated in the centre of the therapeutic ultrasound transducer

All treatments were performed by the principal author (VYTC). The details of the HIFU treatment have been described in previous articles [6,8,9,13]. The treatment of adenomyosis is similar to that of uterine fibroid. However, due to the lack of a pseudocapsule in adenomyosis, the ablation energy and ablation areas for adenomyosis are generally less than that of fibroid treatment in order to minimize the risk of extensive tissue damage.

During treatment, all patients were put under monitored anesthetic care, which was administered by our anesthesiologist (SWL). The desired volume of the target adenomyotic lesion was identified and was ablated in slices of 5 mm, from deep to shallow region under real-time ultrasound monitoring, using a therapeutic acoustic power output of 300–350 W. Treatment was limited to the inside of the adenomyotic lesion, with 10 to 15 mm margin at all borders. From real-time ultrasound monitoring, the adequacy of ablation was determined by the degree of grey scale changes [14]. Paracetamol and diclofenac were given for post-treatment pain relief if needed. Patients were discharged the next morning.

2.2. Follow-up

At 3, 6 and 12 months after treatment, all women had assessment of their symptoms by completion of the symptom severity scores. At 6 months, all women had MR imaging to evaluate the sizes of their uteri and adenomyotic lesions.

2.3. Effectiveness

Treatment effectiveness was evaluated using two symptom severity scores including the menstrual pain score and the modified Uterine Fibroid Symptoms Quality of Life questionnaire (UFS-QOL) [15]. The menstrual pain score assessed the degree of pain during menstruation using a 10-point Likert scale from 1 (not at all) to 10 (a very great deal). The eight-item UFS-QOL used a 5-point Likert scale to assess both menstrual bleeding and bulk-related symptoms [15]. Responses were scored from 1 (not at all) to 5 (a very great deal) with total scores ranging from 8 to 40.

As secondary outcome measures, the volumes (V) of the uteri and the adenomyotic lesions were measured in longitudinal (D1), anteroposterior (D2), and transverse (D3) dimensions and were calculated using the following formula: V = 0.5233 X D1 X D2 X D3.

2.4. Complications

Complications were reported according to the Society of Interventional Radiology (SIR) Standards of Practice Committee Classification of Complications by Outcome [16]. Major complications were defined as Class C, which required minor therapy or hospitalization of less than 48 hours; Class D, which required major therapy, unplanned increase in the level of care, or prolonged hospitalization of more than 48 hours; Class E, which having permanent adverse sequelae; and Class F, which resulted in death [16].

2.5. Statistical Analysis

Data were expressed as median and range or mean ± standard deviation (SD), when appropriate. The paired Student *t* test or the Wilcoxon rank sum test was used to compare differences between outcome measures, when appropriate. A *p* value of less than 0.05 was considered statistically significant.

3. Results

Ten patients underwent HIFU treatment between July 2016 and March 2020. The median age at the time of treatment was 45.5 years (range 37–50 years). All patients had heavy and painful menses. The median treatment time (time from the first to the last sonication) was 95 minutes (range 62–178 minutes). The median sonication time (time of ablation when energy was being delivered to the target) was 1,396 seconds (range 419–2,006 seconds). The median energy delivered was 516,503 joules (range 111,897–771,356 joules). All patients completed the follow-up at 12-month.

Table 1 Changes in Menstrual Pain Score (MPS) after HIFU treatment

	MPS	**Reduction in MPS (%)**	***p****
Pre-treatment	5.5 (3-7.5)	NA	NA
3-month	2.75 (0-5.5)	45.55 (-83.3-100)	0.0065
6-month	2.25 (0-5.5)	57.25 (-83.3-100)	0.0076
12-month	4.25 (0-6)	27.95 (-100-100)	0.0222
Data are given as median (range).			
*Compared to pre-treatment.			
NA: not applicable			

Table 2 Changes in modified Uterine Fibroid Symptoms Quality of Life Questionnaire (UFS-QOL) after HIFU treatment

	UFS-QOL	**Reduction in UFS-QOL (%)**	***p****
Pre-treatment	28 (21-33)	NA	NA
3-month	14 (10-20)	50 (9.1-69.7)	0.0003
6-month	13.5 (10-24)	40.9 (27.3-66.7)	<0.0001
12-month	16 (9-28)	39.5 (0-70)	0.0015
Data are given as median (range)			
*Compared to pre-treatment.			
NA: not applicable			

The menstrual pain scores before and after treatment are summarized in Table 1 and Figure 3; and the modified UFS-QOL scores in Table 2 and Figure 4. Two patients (20.0%) had adenomyosis in the anterior uterine wall and 8 (80.0%) in the posterior wall. The volumes of the uteri and the adenomyotic lesions measured from MR imaging before and 6-month after treatment, and the corresponding percentage volume reduction are summarized in Table 3. The MR images of one of the patients are illustrated in Figure 5.

Three patients (30%) required additional intervention after HIFU treatment. Two patients had hysterectomy 36 and 15 months after HIFU due to persistent heavy menses. One of these patients had the largest uterus volume (1488.6 cm^3) in this series but she strongly preferred uterus preservation. One patient had repeat HIFU 18 months after her first treatment. She had improvement of her symptoms during the first 6 months of the treatment but symptoms worsened after 12 months.

Table 3 Changes in uterus and adenomyosis volume after HIFU treatment

	Pre-treatment	**6-month**
Uterus volume (cm^3)	441.85 (240.0-1488.6)	321.7 (166.8-1170.9)
Uterus volume reduction (%)	NA	24.4 (1.2-42.0)
p	NA	0.0029
Adenomyosis volume (cm^3)	144.55 (43.7-1130.3)	64.45 (17.2-249.4)
Adenomyosis volume reduction (%)	NA	46.3 (2.1-78.4)
p	NA	0.0129
Data are given as median (range).		
NA: not applicable		

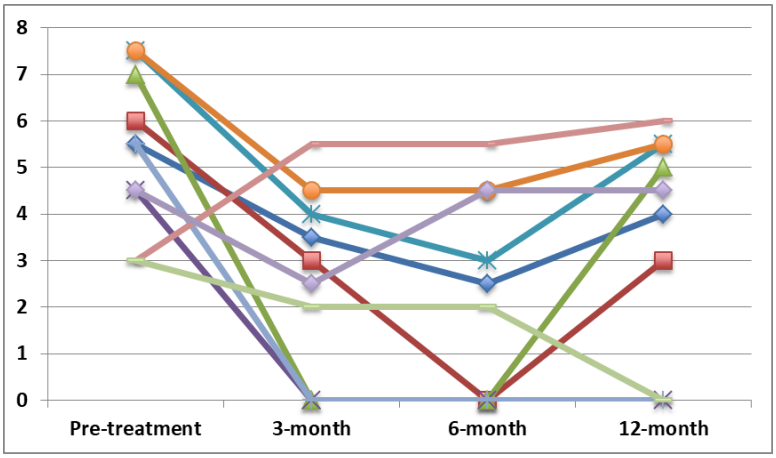


Figure 3 Menstrual pain scores (y-axis) of each patient before and after treatment

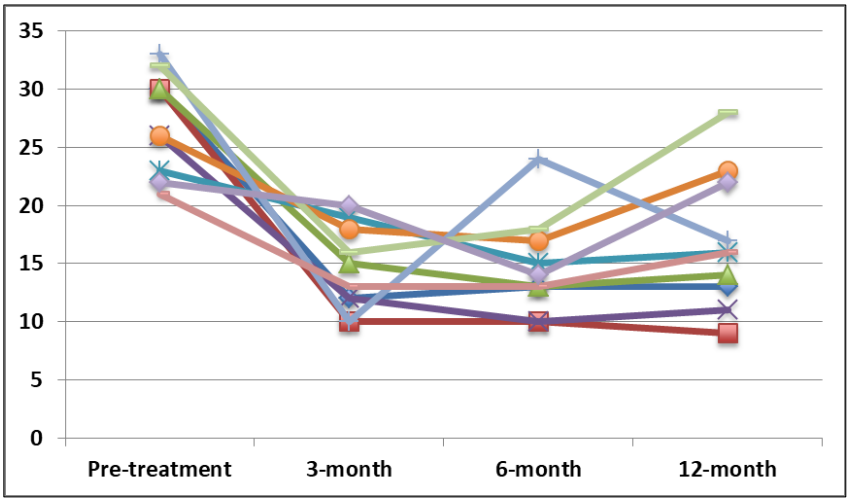


Figure 4 Modified Uterine Fibroid Symptoms Quality of Life Questionnaire (UFS-QOL, y-axis) of each patient before and after treatment

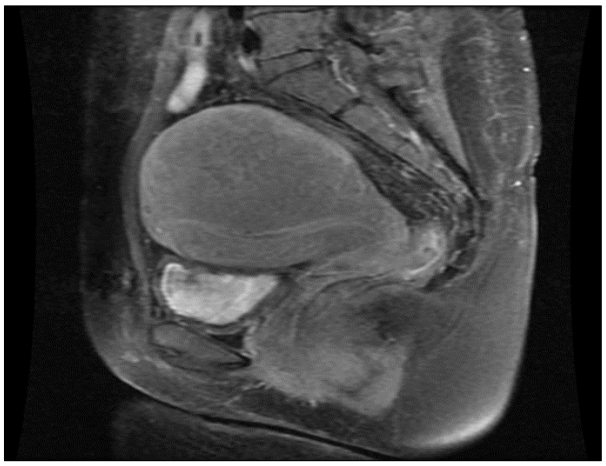
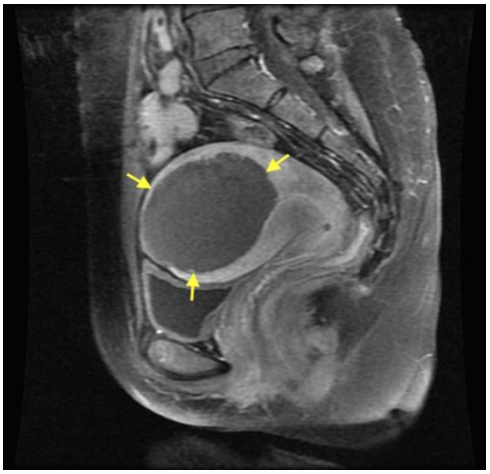
A.  B. 

Figure 5 Magnetic resonance (MR) images from a 43-year-old woman with adenomyosis. (A) Pre-treatment MR image shows adenomyosis at posterior wall. (B) MR image 6-month after HIFU shows a 5.5x6.2x6.9 cm ablated area (arrows)

Two patients had major complications. One patient had thermal bowel injury requiring small bowel resection, which had been reported previously [17], and was suspected to be due to overly extensive ablation of the adenomyotic lesion (SIR Class D). The other patient had prolonged nerve injury with buttock pain and bilateral lower limb weakness requiring physiotherapy and walking support, which completely recovered after 6 months (SIR Class C). None of the patients reported menopausal symptoms or became amenorrheic after treatment.

4. Discussion

Uterine adenomyosis can cause significant morbidity, and its management is still challenging, particularly in women with fertility wishes [1]. Although various uterine-sparing interventions have been described for the management of adenomyosis, including myometrial or adenomyoma reduction or excision, uterine artery embolization, or myometrial electrocoagulation, there are not enough studies in the literature to support the efficacy of one treatment modality over the other [1,2]. The findings from this study suggest that HIFU can be effective in relieving the symptoms of adenomyosis, including menorrhagia and dysmenorrhea.

Although it is increasingly popular to use HIFU in China for the treatment of adenomyosis [10-12], this treatment modality is still considered a novel technology in many other countries. We believe sharing our findings from this small case series is important to enhance experience, and to make this treatment more generalizable and universally acceptable. This study is the first local experience of USg HIFU for adenomyosis in Hong Kong, which can serve as background information for the potential expansion of this treatment in the management of adenomyosis, both locally and nationally.

The treatment outcomes from our series were similar to those reported previously [6,11,12], with over 80% of patients showed improvement of symptoms. Also mentioned in our previous study on uterine fibroids [13], due to limitation of MR imaging resources, the post-treatment non-perfused volume was not available as part of our outcome measures. However, we believed that the degree of symptomatic relief and the need for subsequent intervention were more important indicators of treatment success. Nevertheless, our findings suggested the potential of HIFU as an alternative minimally invasive treatment modality for adenomyosis.

In our series, the re-intervention and complication rates were 30% (3/10) and 20% (2/10) respectively, both of which seemed higher than our own experience in treating uterine fibroids [13], and other image-guided HIFU studies for adenomyosis [6,9,11,12]. While it was apparent that the number of cases in our series was too small for us to make a definitive conclusion, we also believed that treatment success would likely improve with growing experience on the technique and utilization of this technology.

It is expected that HIFU will continue to grow in popularity as a uterine-sparing option in treating adenomyosis because of its minimally invasive nature. The main limitations of this study clearly are the small number of cases, the relatively short follow-up duration and the lack of information on the post-treatment non-perfused volume. Nevertheless, despite

these shortcomings, HIFU is a potential advancement in treatment of adenomyosis. Although USg HIFU appears to provide symptomatic relief to most of our patients, its long-term effectiveness and safety in treating adenomyosis require further evaluation in a larger cohort of patients, and may improve with clinical experience, as suggested in studies from larger treatment centers [10-12].

5. Conclusion

USg HIFU appears to be an effective minimally invasive modality in treating adenomyosis. With more evidence available on its safety and long-term outcomes, this treatment can be a potential preferred uterine-sparing option for women with symptomatic adenomyosis.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

All authors declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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