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Original Article

Effect of high-intensity focused ultrasound ablation on endometriosis of the abdominal wall

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Abstract: In this study, we aimed to explore the effect of high-intensity focused ultrasound (HIFU) ablation on endometriosis of the abdominal wall. A total of 25 patients with abdominal wall endometriosis were selected after HIFU treatment, and their demographic characteristics were retrospectively analyzed. The blood perfusion of focus before operation and the focus ablation during or after operation were evaluated using ultrasound contrast, and follow-up for 24 months. Thirty lesions were ablated in 25 patients. Intermittent pain disappeared 1 month after the operation, and patients' pain score significantly decreased, while the shrink ratio of lesions significantly increased with prolonged follow-up time. No severe complications were noted. HIFU ablation of abdominal wall endometriosis is an effective and safe method, with obvious long-term effects, and showed a significant guiding effect on the treatment of abdominal wall adenomyosis in the clinical setting.

Keywords: High-intensity focused ultrasound, endometriosis, abdominal wall, effect

Introduction

High-intensity focused ultrasound (HIFU) is a non-invasive treatment method that induces coagulation necrosis of the target tissues in vivo via ultrasound waves without injuring the adjacent normal tissues [1-4]. HIFU beams are precisely focused on a small region of diseased tissue to locally deposit high levels of energy; tissue temperature will rise to between 65°C and 100°C at the focus, destroying the diseased tissue via coagulative necrosis. Higher temperatures are usually avoided to prevent the boiling of liquids inside the tissue. Each sonication (individual ultrasound energy deposition) treats a precisely defined portion of the targeted tissue. The entire therapeutic target is treated by using multiple sonications to create a volume of treated tissue, according to a protocol developed by the physician. Anesthesia is not required, but sedation is generally recommended [5-7]. Recently, HIFU has been widely used in the treatment of uterine fibroids [8-10] and endometriosis [11-13].

Endometriosis is a common benign gynecological disorder affecting premenopausal women, which is characterized by the growth of ectopic endometrial glands and stroma deep within the myometrium [14-17]. Approximately 70% of patients present with varying extents of clinical symptoms, such as increased amount of menstrual blood loss, prolonged menstruation, and gradually aggravated dysmenorrhea, which may lead to sterility or recurrent pregnancy loss [11, 13, 18]. Abdominal wall endometriosis is one of the most common types of endometriosis, especially with the increasing trend of cesarean section in recent years [19-21]. When this ectopic growth arises, periodic bleeding would occur along with the change of menstrual cycle hormones. The growths would then fibrose to form aching masses, with surgery as the most effective treatment approach [21, 22]. However, due to the high rate of relapse and defects in the abdominal wall, a more secure and non-invasive approach is required in the clinical setting, such as HIFU. In this study, 25 patients with abdominal wall endometriosis after HIFU treatment were selected. Their demographic characteristics were retrospectively analyzed, with the aim to provide a significant reference on the study of abdominal

Table 1. Demographic characteristics of patients with abdominal wall endometriosis after high-intensity focused ultrasound treatment

Variables	Mean ± SD
No. of patients, n	25
No. of lesions, n	30
Age (years)	31.15 ± 3.61
BMI (kg/m^2)	22.28 ± 3.17
Time of cesarean delivery (years)	4.38 ± 2.73
Interval time from the last cesarean delivery (month)	18.92 ± 2.73
VAS	5.16 ± 2.00
Type of cesarean	
Vertical, n, %	8 (2/25)
Transverse, n, %	92 (23/25)
Subjective symptoms	
The texture of lesion, n	
Hardness	100 (30/30)
The degree of activity, n	
Good	17 (5/30)
Bad	83 (25/30)
Adhesion of the surrounding tissue, n	
Rectus	63 (19/30)
Subcutaneous fat layer	27 (11/30)
Touch pain	
Yes	97 (29/30)
No	3 (1/30)
Score of pain	3.65 ± 1.23
Protrusion of skin, n	
Yes	57 (17/30)
No	43 (13/30)

Note: BMI, body mass index; VAS, visual analogue scale.

wall endometriosis, and to further elucidate its potential treatment approach in the clinical setting.

Materials and methods

Patients

A total of 25 patients with abdominal wall endometriosis were hospitalized in our hospital from March 2014 to June 2016 were selected, and their basic clinical data following HIFU were retrospective analyzed. All patients were signed the pre-operative inform and ultrasound contrast using inform of the Capital Medical University Affiliated Beijing Maternity Hospital.

The inclusion criteria for this study was as follows: 1) abdominal wall endometriosis diagnosed via ultrasound or magnetic resonance imaging (MRI), and HIFU physician onboard ultrasound location sound channel security (the distance of focus superficial to skin was 15 mm and the distance of focus deep to abdominal was 15 mm); 2) the patient could accurately communicate verbally to the physician and nurse; 3) no operation of abdominal wall over the past 3 months, especially liposuction; and 4) patients without severe co-morbidities, such as cardiopathy, hypertension, or diabetes, and could tolerate 2-3 h in a prone position.

Operation

One day before the operation, all patients were put on a semi-liquid diet, and clystered at the night. At the morning of the operation, a urinary catheter was inserted, and prepared skin as the therapy region of hypogastrium before 30 min of operation, and degassing. To adjust the focused ultrasound tumor therapy system (JC200, Chongqing, China) to 1.5 mm × 1.5 mm × 8 mm, and oval focus region with the long axis of 8 mm and the short axis of 3 mm. Patients were positioned in the prone position, and the treatment region was immersed in low warm water, with the bladder constantly filled throughout the treatment process. Fentanyl was used according to the body weight of the patients to inhibit a certain level of awareness, and further to keep patients to tolerance adverse reaction, appropriate cardio-pulmonary function, and response to language with an effective analgesia and calm state.

Ultrasound contrast

Prior to administration of the ultrasound contrast, 59 mg sulfur hexafluoride contrast agent was calculated, and added to 5 ml normal saline. A bolus intravenous injection of 2 ml sulfur hexafluoride contrast agent was administered, followed by 5 ml normal saline. HIFU was initiated after 10 min of injection. During ablation with HIFU, a bolus injection of 1.5 ml sulfur hexafluoride contrast agent was used to evalu-

Table 2. The results of patients with abdominal wall endometriosis after high-intensity focused ultrasound treatment

Variables	Mean ± SD
Lesions volume, cm^3	3.58 ± 2.85
Non-perfused volume, cm^3	4.55 ± 3.60
Rate of massive gray-scale changes, %	90
Total treatment time, min	51.08 ± 26.20
Total sonication time, s	305.00 ± 119.80
Total sonication volume, cm^3	4.00 ± 1.74
Sonication time for 1 cm^3, s/cm^3	0.15 ± 0.22
Total energy, J	56525.00 ± 39793.86
EFF, J/cm^3	16.56 ± 17.80

Note: EEF, energy efficiency factor.

ate the ablation consequence. After HIFU, the ultrasound contrast of the ablation region showed a dot perfusion region; based on this, point-to-point HIFU treatment was performed with the ablation power of 100-300 W and a real-time ultrasound monitoring and evaluation. The distance of focus to skin and abdominal wall was 15 mm, and the distance of layer was 3 mm, and then stop when appeared the rod-like gray change or the whole gray change, and no bloodstream in color Doppler ultrasound. After HIFU, patients were followed up for 24 months, and any adverse effects or complications were recorded.

Statistical analysis

All data were expressed as the mean ± standard deviation (SD). Statistical analysis was performed with one-way ANOVA using the SPSS software (version 21.0, http://spss.en.softonic.com/). The Student's t-tests were performed in a group of two samples. $P < 0.05$ and $P < 0.01$ indicated significant differences and highly significant differences, respectively.

Results

Demographic characteristics of patients with abdominal wall endometriosis after high-intensity focused ultrasound treatment

A total of 25 patients with 30 abdominal wall endometriosis lesions was selected with the following characteristics: average age of 31.15 ± 3.61 years; body mass index (BMI) of 22.28 ± 3.17 m^2/kg; cesarean delivery time of 4.38 ± 2.73 years; last cesarean delivery interval time of 18.92 ± 2.73 months; and the visual analogue scale (VAS) of 5.16 ± 2.00 (**Table 1**). Of these, 92% of patients (23/25) underwent transverse cesarean sections, compared to 8% (2/25) who underwent vertical cesarean sections. The texture of lesion was hard in 100% of patients (30/30), and the degree of activity included good with the percentage of 17% (5/30) and bad with the percentage of 83 (25/30). Sixty-three percent of patients (19/30) exhibited adhesion to the surrounding rectus tissue, while 27% (11/30) demonstrated adhesion to the subcutaneous fat layer. Pain to touch was experienced in 97% (29/30), and the other no pain with the pain score of 3.65 ± 1.23. Skin protrusion was seen in 57% of patients (17/30).

The results of patients with abdominal wall endometriosis after high-intensity focused ultrasound treatment

As shown in **Table 2**, after HIFU treatment, the lesion volume was 3.58 ± 2.85 cm^3, non-perfused volume 4.55 ± 3.60 cm^3, rate of massive gray-scale changes 90%, total treatment time 51.08 ± 26.20 min, total sonication time 305.00 ± 119.80 s, and total sonication volume 4.00 ± 1.74 cm^3. The sonication time for 1 cm^3 was 0.15 ± 0.22 s/cm^3, while the total energy was 56525.00 ± 39793.86 J, with an energy efficiency factor (EFF) of 16.56 ± 17.80 J/cm^3.

A total of 10 patients with skin thermalgia and 25 patients with pain in the treatment area after high-intensity focused ultrasound

The adverse effects or complications following HIFU treatment is shown in **Table 3**. A total of 10 patients experienced skin thermalgia of Sir Class A, and that of 25 patients with the pain in the treatment area of Sir Class B.

Follow-up of patients with abdominal wall endometriosis after high-intensity focused ultrasound treatment

At 24 months' follow-up, the pain experience by all patients disappeared, while the VAS significantly decreased from 1.39 ± 1.32 in 1 month, 0.63 ± 0.87 in 6 months, 0.27 ± 0.59 in 12 months, and 0.00 ± 0.00 in 24 months (**Table**

Table 3. Adverse effects or complications of patients with abdominal wall endometriosis after high-intensity focused ultrasound treatment (n = 25)

Sir Class	Description	No.	Complications	No.
A	No therapy, no consequences	0	Skin thermalgia	10
B	Nominal therapy, observation, no consequences	0	Pain in the treatment area	25
C	Required therapy, minor hospitalization (< 48 h)	0	Sacrum/buttock pain	0
D	Major therapy, unplanned increase in level of care, Prolonged hospitalization (> 48 h)	0	Skin blister	0
E	Permanent adverse sequelae	0	Increased blood pressure	0
F	Death	0	Nausea or vomiting	0.0

Table 4. Follow-up of patients with abdominal wall endometriosis after the treatment of high-intensity focused ultrasound

Variables	1 month	6 months	12 months	24 months
VAS	1.39 ± 1.32	0.63 ± 0.87**	0.27 ± 0.59**	0.00 ± 0.00**
Rate of volume shrink (%)	40.70 ± 24.00	92.40 ± 12.10**	97.88 ± 6.56**	100 ± 0.00**

Note: **: P < 0.01; VAS, visual analogue scale.

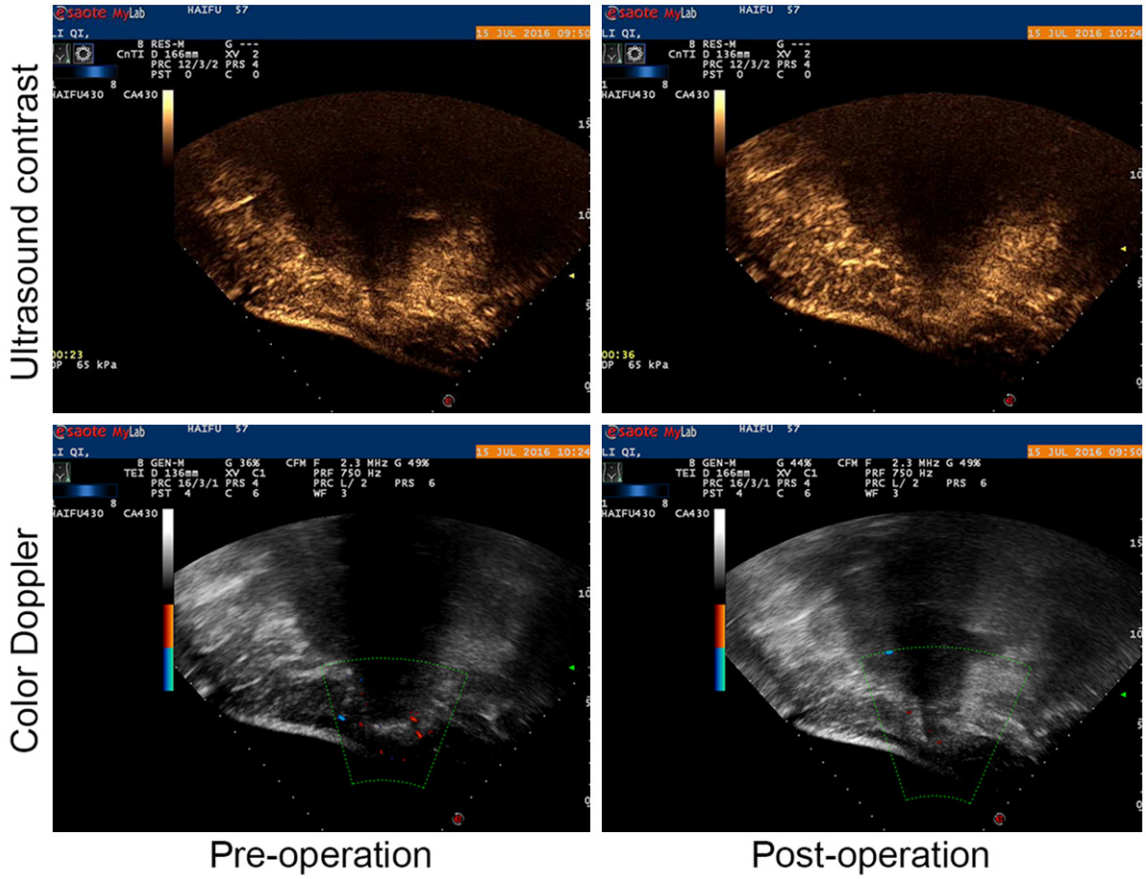

Figure 1. Pre-operation and post-operation ultrasound contrast and color Doppler images of patients with abdominal wall adenomyosis.

4). In addition, the rate of shrink volume significantly increased, from 40.70 ± 24.00 in 1 month, 92.40 ± 12.10 in 6 months, 97.88 ± 6.56 in 12 months, and 100 ± 0.00 in 24 months. The change of ultrasound contrast and color Doppler of pre-operation and post-opera-

tion was exhibited in **Figure 1**, and manifested as the blood perfusion of focus in pre-operation with the scape of 14 mm × 10 mm × 10 mm, and no any blood perfusion of focus with the scape of 19 mm × 12 mm × 15 mm, and had an obvious blood imaging of focus in pre-operation and disappeared in post-operation.

Discussion

Abdominal wall endometriosis is one of the most common extrapelvic endometriosis. It often occurs in the incision scar of a cesarean operation, and indicates that active endometrial tissue is present in the abdominal wall. The incidence is rapidly rising with the increasing of trend of cesarean section in recent years [20, 23, 24]. Ultrasound ablation is a non-invasive procedure that involves increasing temperature of a lesion to 65°C, and induces coagulative necrosis; it is currently widely used in the treatment of benign and malignant tumors of the uterus [25-27], breast [28, 29], pancreas [29-31], liver [8, 32], and others, and has become an indispensable therapeutic approach in the clinical setting.

As a non-invasive approach, ultrasound ablation does not cause the dissemination of the ectopic endometrium. Although it is limited by the size and location of the lesion, it can conformally ablate and does not damage the target tissue [2, 33, 34]. In this study, 25 patients with abdominal wall endometriosis after HIFU treatment were selected; 30 focuses were subjected to HIFU treatment, and the follow-up time was between 1 and 32 months, with the treatment time median of 46 min (12-113 min), ablation time median of 300 s (112-604 s), ablation volume median of 3.75 cm^3 (1.35-8.7 cm^3), and EFF median of 11.61 J/cm^3 (62.12-100 J/cm^3). The focus volume was 3.38 cm^3 (0.38-12.71 cm^3), and the deposition energy of unit volume ablation was low. With regard to the use of the ultrasound contrast agent, no adverse reaction was documented before, during, and after the operation. In fact, the contrast exhibited a guiding effect on the HIFU ablation scope. With the exception of skin causalgia and pain in the treatment region, patients were able to move freely, and assume their normal life and working schedules. After 1 month of operation, the periodic pain in all patients disappeared, and the touch pain median reduced from 4 to 1. Seven patients experienced complete resolution of pain, with obvious shrinking of their lesion volumes. Therefore, the use of ultrasound contrast to evaluate focus pre-operatively could determine the focus of blood perfusion. Similarly, its use intra-operatively could determine the focus ablation, and further help to confirm the therapeutic regimen.

After HIFU, 1 patient relapsed, and could touch a gelosis after 3 months of operation. Analysis of this case showed that the focus volume was 12.99 cm^3 before the operation, with no change of the focus gray with the average power of 117 W (100-200 W). The treatment time was 90 min, treatment ablation time 350 s, ablation volume 6.6 cm^3, and non-perfused volume 12.55 cm^3. the lower tolerance, and no coordinate. At 1 month follow-up, the hypogastrium was occasionally painful with a focus of 8.88 cm^3, and shrinkage of 32%. At 3 months' follow-up, the touch pain score was 1, with a focus volume of 1.31 cm^3 and shrinkage of 71%.

As recent studies have shown, HIFU ablation of abdominal wall endometriosis could improve the periodic pain and touch pain of patients, with superior efficacy and no side effects [6, 35, 36]. It could be conformal ablate focus furthest, and keep the integrity of skin and abdominal wall, and could repeated. In addition, it is also simple, fast, and easy receive. However, there were several limitations in this study, including the small sample size, and the retrospective nature of the study, as opposed to a multicenter, randomized control trial. Our future work will enact a standardized treatment regimen and provide an individual-based treatment according to specific patients.

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Disclosure of conflict of interest

None.

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