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Safety of ultrasound-guided high-intensity focused ultrasound ablation for diffuse adenomyosis: A retrospective cohort study

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ABSTRACT

Objectives: To evaluate the safety of ultrasound-guided high-intensity focused ultrasound (HIFU) ablation for patients with diffuse adenomyosis.
Methods: This was a retrospective cohort study. The data was collected from 417 symptomatic adenomyosis patients who underwent ultrasound-guided HIFU between January 2012 and December 2015 at 1st Affiliated Hospital of Chongqing Medical University, Chongqing, China. Among them were 260 patients with diffuse adenomyosis (Group D) and 157 patients with focal adenomyosis (Group F). All patients underwent contrast-enhanced magnetic resonance imaging (MRI) one week before and the day after HIFU treatment. Successful treatment with HIFU was measured by the non-perfused volume ratio (NPVR). Intraprocedural and postprocedural adverse effects and complications were recorded to assess the safety of the procedure. Patients were followed-up for three months post-treatment. Complications were given a grade A through F according to the SIR Standards.
Results: All patients successfully completed the procedure, non-perfused regions appeared in 415 (99.5%) patients. The non-perfused volume ratio (NPVR) of Group D was significantly lower than that of Group F ($P < 0.05$). During the procedure, the odds ratio of skin-burning pain was 1.7 (OR = 1.617, 95% CI: 1.103–2.532), when comparing Group D with Group F, while the odds ratio of inguinal pain was equal to 2.0 (OR = 2.038, 95% CI: 1.161–3.580), when Group F was compared to Group D. 97 patients (23.3%) received nominal therapy due to complications ([Society of interventional radiology, SIR]-B grade), among them, there were 62 cases (23.8%) in Group D and 35 cases (22.3%) in Group F. No significant difference was found between the two groups ($P > 0.05$) and neither of the reported complications of SIR-C-SIR-F occurred within the two groups.
Conclusions: Based on our results, ultrasound-guided HIFU is safe for the treatment of diffuse adenomyosis, and controlling the ablation zone is crucial to ensure patients' safety.

1. Introduction

Adenomyosis is a common benign gynecologic disease that is characterized by the presence of ectopic endometrial glands and stroma within the myometrium. Its symptoms include menorrhagia, secondary dysmenorrhea, and sometimes accompanied by subfertility [1]. The distinguishing factors of magnetic resonance imaging (MRI) in adenomyosis include a focal or uneven width of the junction zone, low signal of the junction zone, high signal spots on T2-weighted image scattered within the junction zone when hemorrhage, and unclear zone margins [2]. Based on histopathology, adenomyosis is divided into two types: the diffused-type, defined as the heterotopic endometrial tissue scattering throughout the uterine musculature, and the focal-type, defined as circumscribed nodular aggregate of smooth muscle, endometrial glands, and stroma within the myometrium [3].

Both surgical procedures and medical therapies are viable treatment options for adenomyosis [4]. Among them, hysterectomy is considered as a radical therapy, however, this surgery does not allow the patient to retain her uterus. Conservative uterine-sparing surgeries such as cytoreductive surgery, laparoscopic resection, and adenomyomectomy are also problematic due to

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ill-defined endometrial-myometrial boundaries [5]. Medical therapies include the use of gonadotrophin-releasing hormone agonist (GnRHa), Danazol, oral contraceptive and progestational hormone, etc. However, symptoms may recur shortly after discontinuation of the medical treatment. Other treatments include intrauterine device, uterine artery embolization, levonorgestrel-releasing intrauterine system, and high-intensity focused ultrasound (HIFU), these treatment options play an important role in uterine-sparing treatment for adenomyosis.

HIFU is a noninvasive thermoablative technique which has been successfully utilized in the treatment of malignant solid tumors of the liver, breast, pancreas, and bone [6–8]. HIFU has also been used for patients with uterine fibroids and has achieved satisfying results [9,10]. Recently, HIFU ablation has been applied to the treatment of adenomyosis [11,12]. Several studies have examined the safety profile of ultrasound guided HIFU in treating patients with adenomyosis [11,12], however, they have not separated the two types of adenomyosis which can be distinguished by histopathological and MRI features for HIFU treatment. Although HIFU is considered to be a very low-risk procedure, safety is of concern for HIFU ablation of diffuse adenomyosis, as the uterus is in close proximity to structures such as the bowel, urinary bladder, and lumbosacral plexus [13]. However, demonstration of the safety of HIFU therapy for the treatment of diffuse adenomyosis is lacking. The aim of this study is to assess the safety of HIFU ablation for diffuse adenomyosis as compared to safety outcomes of focal adenomyosis.

2. Material and methods

2.1. Study design and patients

This was a retrospective cohort study, the data was collected from 417 symptomatic adenomyosis patients who underwent ultrasound-guided HIFU between January 2012 and December 2015 at 1st Affiliated Hospital of Chongqing Medical University, Chongqing, China. This study was approved by the Ethics Committees of Chongqing Medical University. Every patient signed an informed consent form prior to HIFU treatment. The diagnose of adenomyosis was confirmed by preprocedural MR imaging. According to the MR imaging, patients were divided into two groups: diffuse adenomyosis group (Group D) and focal adenomyosis group (Group F).

Inclusion criteria for this study were as follows: premenopausal adult women (age greater than 18 years), presenting with clinical symptoms of dysmenorrhea and/or menorrhagia, patients agreed to undergo MRI, and MRI evidence of the endometrial-myometrial junctional zone thickness of more than 30 mm for diffuse adenomyosis or a lesion diameter larger than 30 mm for focal adenomyosis. Exclusion criteria included abdominal surgical scar in the proposed path of the ultrasound beam (specifically scar that had either caused obvious attenuation of B-model ultrasound in detecting tissues behind or scar over 15 mm), clinical examination or ultrasonography showed endometrial disease, pelvic endometriosis or other uncontrolled systemic disease, patients with standard MRI contraindications, an inability to communicate with the nurse or physician during the treatment, uncontrolled diabetes, abnormal liver and renal function, and women during menstruation, pregnancy or lactation.

2.2. Preprocedural preparation

Every patient ingested liquid food for three days prior to and followed by a single dosage of liquid bowel preparation solution (2000 mL of complex polyethylene glycol electrolyte solution) on the afternoon of the day before the procedure. An enema was performed in the morning of the treatment day. Every patient was asked to remove hair in the region from the umbilicus to the superior margin of the pubic symphysis, degreasing and degassing the skin of the lower abdominal region to avoid air bubbles in the acoustic pathway. During the procedure, patients were positioned prone on the HIFU table, with the anterior abdominal wall contacted with the degassed water. A urinary catheter was inserted to control the bladder volume with saline injection. A water balloon compressor was used to push away the bowel in the acoustic pathway and to avoid intestinal damage.

2.3. Ultrasound-guided HIFU ablation

Ultrasound-guided HIFU ablation was performed with the model JC focused ultrasound tumor therapeutic system (Chongqing Haifu medical Technology Co., Ltd., Chongqing, China) equipped with an ultrasound imaging device (MyLab 70; Esaote, Genova, Italy) for real-time guidance during the procedure. This device included an ultrasonic transducer which operated at the frequency of 0.8 MHz and acoustic power ranged from 300 W to 400 W with a focal region of 1.5 mm × 1.5 mm × 10 mm. The treatment was completed with the thickness of 5 mm per section and performed in the uterine wall which thickness more than 30 mm. The sonication began with the deep section and moved toward the shallow sections of the adenomyosis lesion. The concentrated area was required to be at least 10 mm away from both the boundary of the uterus and the endometrium. Real-time ultrasonographic imaging was used to guide treatment focus only on the target region and circumvent adjacent organs or tissues. In order to reduce discomfort and remain conscious, HIFU ablation was performed under intravenous conscious sedation with fentanyl and midazolam hydrochloride. The depth of sedation was monitored by a nurse. The ultrasonic energy was adjusted based on the tolerance of patient and the impact was monitored via gray-scale ultrasound during the procedure. Once the gray-scale covered the planned ablation zone, the sonication was terminated. All patients were observed for 2 h before being discharged or returned to the wards.

2.4. Outcome measures

All patients underwent MRI one week prior to and one day after the HIFU procedure. Preprocedural MRI helped to define the type and volume of the adenomyotic lesion and location of the uterus and a postprocedural MRI was used to evaluate the non-perfused volume (NPV). The volume of adenomyotic lesions and NPV were measured by the following equation [14] for the prolate ellipsoid: volume = $0.5233 \times a \times b \times c$. (a, b, c were the longitudinal dimension, anterior-posterior dimension and transverse dimension, respectively). The measurement of the volume of adenomyotic lesions for Group F, patients with focal adenomyosis, was defined as the volume of the part of the uterus where the focal adenomyotic lesions were located (see Fig. 1A and B). Unlike Group F, the Group D, patients with diffuse adenomyosis, lesions were scattered throughout the whole uterus, therefore, the volume of uterus is equivalent to the total volume of lesions (see Fig. 2A and B). The NPVR was defined as the NPV divided by the lesion volume. Successful treatment [15] with HIFU was determined as an occurrence of the NPV of no less than 1 cm^3 in the planned ablation zone.

All adverse effects and complications for patients were recorded by a nurse both during and after the procedure to assess the safety of HIFU. According to the Society of Interventional Radiology (SIR), clinical practice guidelines [16] which were formulated by the