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Clinical significance of bladder training in preoperative localization of high-intensity focused ultrasound ablation of uterine fibroids

Short title: Bladder training for HIFU ablation

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ABSTRACT

Objectives: High-intensity focused ultrasound (HIFU) is widely used to treat uterine fibroids. HIFU preoperative localization of uterine fibroids can be used to determine whether the patient is a suitable candidate for HIFU treatment. This study investigated the clinical significance of bladder training in improving the success rate of HIFU preoperative localization uterine fibroids.

Material and methods: Our sample consists of patients who planned to undergo HIFU treatment in our hospital but who were failed in previous HIFU preoperative localization. They were recruited between July 2021 and April 2022, and randomly divided into experimental and control groups. A total of 150 patients were enrolled. Each group consisted

of 75 patients. The patients in the experimental group adopted the procedure of drinking water multiple times and retaining urine. The training program lasted three days. The patients in the control group were required to keep regular drinking and urination habits without any special instructions or requirements.

Results: There were no statistically significant differences between the two groups in maximum bladder capacity, residual urine volume of bladder, bladder filling levels, and bladder shape change. After bladder training, the maximum bladder capacity and the degree bladder shape change of the patients in the experimental group were improved significantly. The success rate of HIFU preoperative localization in the patients in the experimental group was significantly higher than that of the control group.

Conclusions: Bladder training can effectively improve the success rate of HIFU preoperative localization of uterine fibroids.

Key words: leiomyoma; uterus; high-intensity focused ultrasound ablation; urinary bladder

INTRODUCTION

Uterine fibroids are benign neoplasms commonly occurring among reproductive-aged women, with prevalence varying between 30–50% [1]. The overall prevalence of uterine fibroids in China is about 10–15% [2]. Most uterine fibroids are asymptomatic, while 25% of the present symptoms such as abnormal menstrual bleeding, bulk-related symptoms, reproductive dysfunction, anemia, pelvic pressure, and frequent urination. Hysterectomy is the most common method used to treat uterine fibroids; however, this is unsuitable for women with reproductive desires. The use of myomectomy is restricted according to the location and size of the fibroid, and is associated with the risk of postoperative complications, recovery from which lasts several weeks [3]. Thus, non-surgical treatment is strongly required for women with uterine fibroids.

High-intensity focused ultrasound (HIFU), a noninvasive ablative technique, is widely used to treat uterine fibroids due to its minimal invasiveness, simple operation, high efficiency, safety, and the low risk of post-operative pain and complications associated with

the technique. Other benefits of the treatment include short hospital stay, fast recovery, uterine preservation, and fertility retention [4]. HIFU preoperative localization of uterine fibroids can be used to determine whether the patient is a suitable candidate for HIFU treatment [3, 5].

During HIFU preoperative localization, a Foley catheter is inserted into the patient's bladder to expand the bladder with distilled water, after which the patient is placed in the prone position on the treatment table. A balloon filled with purified water is placed between the HIFU transducer and the patient's abdomen to compress and push the bowel loops away from the HIFU track, thereby eliminating the formation of air bubbles and reducing the thickness of the subcutaneous fat layer. In this study, we aim to improve bladder function by substituting the Foley catheter.

MATERIAL AND METHODS

Study setting

Our sample consists of patients who planned to undergo HIFU treatment in our hospital but who failed in HIFU preoperative localization. They were recruited between July 2021 and April 2022, and randomly divided into experimental and control groups. The inclusion criteria were as follow: (1) The patient had uterine fibroids and were failed in HIFU preoperative localization; (2) The patient agreed to undergo HIFU preoperative localization three days after completing bladder training under medical guidance; (3) The patient voluntarily participated in this study after signing the consent letter. The exclusion criteria were as follows: (1) The patient already had a history of bladder surgery; (2) The patient suffered from existing urinary tract diseases; (3) The patient suffered from serious systemic diseases; (4) An ultrasonic channel could not be created via bladder filling due to improper positional relationship between uterus and bladder; (5) The patient withdrew from the study; (6) The patient did not perform bladder training as required; (7) The patient decided not to undergo HIFU preoperative localization after commencement of the study.

This was a double-blind study. The patients in the experimental group adopted the procedure of drinking water multiple times and retaining urine; specifically, they each drank

500–1000 mL of water, and refrained from urinating when feeling the need to urinate for as long as reasonably possible. As soon as each patient experienced significant discomfort from the urine retention, she was permitted to evacuate all the urine. Then the patient drank water again and repeated the aforesaid training procedure. Each cycle was performed three times per day, and the training program lasted three days. The patients in the control group were required to keep regular drinking and urination habits without any special instructions or requirements.

Bladder filling levels

- Adequate filling: images of uterus, muscular wall of the uterus, and the endometrium are clear.
- Overfilled: uterus width is reduced, cervix becomes elongated and thinner, and the uterus becomes retroverted.
- Inadequate filling: pelvic cavity cannot be detected using ultrasound due to gas-filled intestine.

Bladder shape change

- Excellent change: the bladder stretches, and diameter of the shape-changed bladder is equivalent or larger than the cross-sectional diameter of the entire uterus.
- Good change: the bladder stretches, and diameter of the shape-changed bladder is shorter than the cross-sectional diameter of the entire uterus.
- Poor change: bladder shape is almost unchanged, or improper positional relationship exists between the shape-changed bladder and the uterus, thus the bladder cannot affect the movement of the uterus.

Statistical analysis

SPSS22.0 was used for statistical analysis. Normally distributed measurement data were described with mean and standard deviation ($\acute{x} \pm s$). The group t-test method was used for comparing the two groups. Non-normally distributed measurement data were described with M (P25, P75), and the Mann-Whitney U test was used for comparing the two

groups. Enumeration data were expressed in percentage (%), and the Chi-square (χ^2) test or Fisher's exact test was used for comparing the two groups. All statistical tests in this study were two-tailed tests, whereby $p < 0.05$ represents a statistically significant difference.

Data collection

A total of 150 patients were enrolled. Each group consisted of 75 patients.

RESULTS

The clinical characteristics of the patients are presented in Table 1. There were no statistically significant differences between the two groups.

As mentioned, none of the participants were successful in their previous HIFU preoperative localization of the fibroids. The participants in the experimental group received bladder training during the 3-day period. Thereafter, all participants received preoperative localization treatment again. Compared with the control group, the rates of successful preoperative localization of fibroids in the experimental group were found to be significantly higher (Tab. 2).

DISCUSSION

Uterine fibroids are benign tumors that can be completely cured by surgery, albeit at the risk of the patient experiencing trauma and complications. As a technique for treating uterine fibroids, HIFU focuses low-intensity ultrasonic waves *in vitro* on specific areas of the target fibroids, instantly generating high temperatures of 60–100℃ in the specific area, thus causing coagulation necrosis of fibroids [6, 7]. HIFU has enjoyed growing popularity in recent years by virtue of its high safety and effectiveness, in that it inflicts minimal damage to tissues outside the target area. Precise ablation leads to the absorption and shrinkage of fibroids following coagulation necrosis, generating minimal trauma whilst maintaining the integrity of the uterus [8]. Previous studies have shown that with HIFU the risks of bleeding, pelvic adhesion and uterine rupture during late pregnancy are low. Bohlmann et al. [9]

reported that patients' recovery and pregnancy preparation times after HIFU treatment are significantly shortened, compared with other treatments. HIFU is performed under real-time ultrasound monitoring. The ultrasound waves accurately focus on the fibroid and make the fibroid coagulate and become necrotic instantly. There is a 5–7 cell layer-thick transitional zone of a width of 50 μm between the necrosis area and the surrounding normal tissues, and thus HIFU almost produces no damage to the normal tissues surrounding the lesions and the uterus-nearby tissues and organs (such as fallopian tubes, ovaries, and the structure and function of the pelvic floor) [10].

Preoperative localization is an essential step for HIFU ablation. The patient is prone on the treatment table. The entire uterus could be clearly visible under airborne ultrasound. The ultrasonic channel is the zone within which therapeutic ultrasound safely reaches the target area and covers the planned treatment area to the maximum extent. The ultrasonic channel is displayed as a triangle on the monitor screen and the ultrasound focal point is the triangle's top vertex [11]. Whether gas-filled intestine, bone, scar, foreign body, calcified tissue and gas occur within the ventral ultrasonic zone should be observed [12]. Preoperative localization is helpful in determining whether the patient is a suitable candidate for HIFU ablation. The depth of the fibroids must fall within the focal length of the treatment head, and no tissues that are vulnerable to damage such as gas-filled organs and nerves should be found in the ultrasonic zone. Since tissue more strongly reflects ultrasonic waves, the proportion of tissue (such as bones, calcified tissues, and scars) occurring within the ultrasound zone should be minimized as far as possible in order to enable more ultrasonic energy to reach the target area [11]. The ultrasonic channel for HIFU preoperative localization is optimized by applying auxiliary measures to minimize the factors compromising safety and effectiveness [13]. A water balloon is placed between the treatment head and the abdominal skin during localization. The water balloon is pushed towards the abdominal cavity via movement of the treatment head so that the intestine within the ultrasonic zone can be pushed out of the ultrasonic zone, thus ensuring an obstructed ultrasonic zone. It is also advisable to adjust the angle of incidence of the ultrasound in order to avoid the intestine. Other methods can also be used to move the intestine away from the ultrasonic zone, *e.g.*, injecting normal saline into the

bladder to induce the bladder into pushing away the intestine, thereby obtaining the optimized ultrasonic zone.

However, water balloons have some advantages. The water in the balloons can produce artifacts in the ultrasonic image, reducing image clarity, and affecting the surgeon's manipulation. The larger the water balloon, the greater the interference. If a too large water balloon is used to push the intestine, the uterus and the fibroids may be pushed towards the sacrum, increasing the patient's reaction during treatment and thus raising the risk of nerve injury. A particularly large water balloon constitutes a large contact area between the balloon and abdominal skin, inevitably increasing the pressure on abdominal skin, reducing blood circulation and abdominal skin heat dissipation, and increasing the incidence of skin scalding during treatment [14]. For these reasons, water balloons are not conductive to HIFU preoperative localization or treatment.

The bladder is a cystic cavity organ, adjacent to the intestinal tract. It is located between the uterus and the pubis symphysis when empty and can expand into the pelvic cavity or even the abdominal cavity when filling. Generally, the bladder volumes at first desire to void and normal desire to void are 150–250 mL and 350–500 mL, respectively. The maximum bladder capacity is 400–600 mL. The bladder capacity at a strong desire to void is called urgent desire to void capacity [15–17]. The size and shape of the bladder vary with filling levels and the condition of adjacent organs. The bladder can reach the abdominal cavity at its maximum filling. The bladder filling process can not only facilitate ultrasonic wave transmission, but also enables surgeons to identify other organs. A filled bladder by virtue of its altered shape can change the positions of the uterus and fibroids. When the bladder is full, the bladder neck rises, and the intestine is pushed into the abdominal cavity. During localization, the bladder shape can be fully changed by squeezing from the treatment head, and the intestine in the ultrasonic zone can be pushed out by the enlarged bladder [17]. Figuratively, the bladder can be regarded as a natural water balloon which via the process of expansion can assist HIFU preoperative localization, thereby realizing better ultrasonic permeability and clearer imagery [18]. It is recommended that bladder filling levels be adjusted by varying the amount of normal saline injected into the bladder according to the

HIFU preoperative localization or treatment requirements, thus creating a safe ultrasonic channel. Due to its elasticity, viscoelasticity and extensibility, the bladder with its better shape after filling is more conducive to HIFU preoperative localization.

This study has focused on the significance of bladder training in HIFU preoperative localization in patients with uterine fibroids. It is the decision of the surgeon as to whether a full or semi-full bladder is needed (depending on the positions and size of the patient's uterus and fibroids), whether a water balloon is required, and the appropriate size of the water balloon and the degree of bladder shape change [19]. Since the bladder wall muscles are elastic and viscoelastic, they can be extended to a great extent when the bladder is overfilled, and still contract when the bladder is empty. Repeated retention of urine can raise the maximum bladder capacity, and repeated muscle contraction can change bladder compliance, which is conducive to improving bladder shape change.

CONCLUSIONS

In this study, participants in both groups were patients who failed in the previous localization. No statistically significant difference among grouping baselines was found, indicating reasonable grouping. All participants underwent localization after 3 days of bladder training. The success rate of localization of the experimental group after bladder training was significantly higher than that of the control group, indicating that bladder training can effectively improve the success rate of HIFU preoperative localization. Bladder training can be performed on the patients who failed in the previous HIFU preoperative localization to improve the success rate of the later preoperative localization. This study provides preliminary evidence indicating the benefits of bladder training on HIFU preoperative localization in patients with uterine fibroids. In future research, we aim to focus on intervention methods of bladder training to further investigate the clinical significance of bladder training in HIFU preoperative localization.

Author contributions

SL designed the study. XH and SL carried out the data collection and analysis. XH drafted the

manuscript. SL revised the manuscript. All the authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki as well as relevant guidelines and regulations. This study was approved by the Medical Ethics Committee of West China Second University Hospital, Sichuan University [YXKY2021LSP135]. Written informed consent to participate in this study was obtained from all participants. The clinical registration number of this study is ChiCTR2100048225upon the approval from Chinese Clinical Trial Registry.

Conflicts of interest

All authors declare that they have no conflicts of interest.

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Table 1 Clinical characteristics of participants

Item	Value
Age [years] (mean ± SD)	37.7 ± 7.62
Body mass index (mean ± SD)	22.2 ± 3.39
Past surgery history (mean ± SD)	
Yes	46 (61.3%)
No	29 (38.7%)
Abdominal wall thickness (mean ± SD)	28.7 ± 7.52
Abdominal scar	
Yes	32
No	43
Urinary irritation symptoms	
Yes	5 (6.67%)
No	70 (93.3%)
Stress urinary incontinence	
Yes	4 (5.33%)
No	71 (94.7%)
Uterine volume (length × width × height)	73.4 (15.8)
Volume of the largest fibroid (length × width × height)	44.2 (14.8)

Table 2 Details of bladder function and HIFU preoperative localization

Item	Control group	Experimental group	p-value
Maximum bladder capacity [mL] during the previous localization	387 ± 161	445 ± 180	0.089
Residual urine volume [mL] of bladder during the previous localization	31.0 ± 12.2	27.5 ± 15.5	0.303
Bladder filling levels in this study			
Adequate	21 (28.0%)	29 (38.7%)	0.355
Excessive	53 (70.7%)	45 (60.0%)	
Inadequate	1 (1.33%)	1 (1.33%)	
Bladder shape change in this study			< 0.01
Excellent	9 (12.0%)	29 (38.7%)	
Good	21 (28.0%)	25 (33.3%)	
Poor	45 (60.0%)	21 (28.0%)	
Maximum bladder capacity [mL] for localization after bladder training	503 ± 205	620 ± 170	< 0.01
Residual urine volume [mL] of bladder for localization after bladder training	40.0 ± 18.3	37.0 ± 17.2	0.383
Was a water balloon required for localization?/What was the volume of the water balloon?			
> 800 mL	10 (13.3%)	5 (6.7%)	< 0.01
400–800 mL	37 (49.3%)	11 (14.7%)	
< 400 mL	23 (30.7%)	18 (24%)	
None	5 (6.7%)	41 (54.7%)	

Was HIFU preoperative localization successful?			
Yes	0 (0%)	35 (46.6%)	< 0.001
No	75 (100%)	40 (53.4%)	

HIFU — high-intensity focused ultrasound