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A retrospective comparison of microwave ablation and high intensity focused ultrasound for treating symptomatic uterine fibroids

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ABSTRACT

Objectives: To retrospectively compare the effectiveness and safety of percutaneous microwave ablation (PMWA) and ultrasound-guided high-intensity focused ultrasound (USgHIFU) for treating symptomatic uterine fibroids.

Methods: Seventy-three women with symptomatic uterine fibroids who met the inclusion criteria were enrolled in our study from September 2012 to December 2013. Thirty-one patients with forty uterine fibroids underwent PMWA, and forty-two patients with fifty-one uterine fibroids underwent USgHIFU. A contrast-enhanced MRI was performed before and after treatment, and all patients were followed up for 6 months. Assessment endpoints included symptom severity scores (SSS), treatment time, ablation rate, fibroid regression rate and adverse events.

Results: The mean age of the patients in our study was 35.4 ± 6.2 years (range, 21–49 years), and the median volume of uterine fibroids was 95.7 cm^3 (60.3–131.5 cm^3). The ablation rate of uterine fibroids was 79.8 ± 18.2% and 77.1 ± 14.9% in the PMWA group and the USgHIFU group, respectively, and showed no significant difference between the groups. Changes in SSS after PMWA were similar in the PMWA group (47.7 pre-treatment vs. 29.9 post-treatment) and USgHIFU group (42.1 pre-treatment vs. 24.6 post-treatment). The regression rate of uterine fibroids also showed no marked difference between the two groups (PMWA, 50.3%; USgHIFU, 52.4%). The median treatment time of the PMWA group was 46.2 min, which was demonstrably superior to USgHIFU. Finally, the occurrence rate of adverse events was the same in the two groups.

Conclusions: The safety and effectiveness of PMWA and USgHIFU in the treatment of uterine fibroids were similar; however, the median treatment time of PMWA was shorter than that of USgHIFU.

1. Introduction

Uterine fibroids, which are frequently encountered benign tumors in women of reproductive age, have typically been treated by hysterectomy in past years. However, in recent years, there is an increasing appreciation that diseases that cause harm require therapies that are harmless. Many women with uterine fibroids are choosing minimally invasive treatments, such as high-intensity focused ultrasound (HIFU) and percutaneous microwave ablation (PMWA). HIFU, a non-invasive thermal ablation technique that uses a focused ultrasound beam to ablate fibroid tissue, which has been widely used in the treatment of uterine fibroids and has proved to be extremely safe and effective [1–4]. PMWA is a minimally invasive thermal ablation technique for treating uterine fibroids by inducing coagulation necrosis of the target fibroids. Previous studies have demonstrated that PMWA has a higher potential for the conservative treatment of uterine fibroids [5–7].

Both HIFU and PMWA are thermal ablation techniques, and they are both safe and reliable alternative treatment methods for uterine fibroids. However, until now, there have been no clinical trials to compare the therapeutic effects of HIFU and PMWA, so whether there are obvious differences in symptom improvement, treatment time, ablation rate, regression rate and adverse events between these two approaches remains unknown. In this research, we retrospectively compare the results of these two treatment methods.

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2. Materials and methods

2.1. Patients and enrollment

This retrospective study was approved by the Ethics Committees at Chinese PLA General Hospital, and all enrolled patients signed informed consent for the treatment and for the future use of the data collected.

Seventy-three women with symptomatic fibroids were enrolled in the study between September 2012 and December 2013. Uterine fibroids were confirmed by contrast enhanced magnetic-resonance imaging (CE-MRI) before treatment. Before choosing treatment, the patient was informed of the possible efficacy and side effects of both treatments to allow her to come to a rational decision. Thirty-one women with forty uterine fibroids underwent PMWA, and forty-two women with fifty-one uterine fibroids underwent USgHIFU.

The selection criteria for this study were as follows: presence of a clinical syndrome, such as menorrhagia, dysmenorrhea, lower abdominal pain, urinary frequency; age older than 18 years but premenopausal; diameter of uterine fibroids $\geq$4 cm and $\leq$10 cm; and no previous surgical treatment or other minimally invasive treatment (such as UAE, cryoablation, radiofrequency). Patients with active menstruation, pregnancy, pelvic infection, severe heart disease, severe cerebrovascular disease, mental disorder, or malignant tumors were excluded from the study.

2.2. PMWA and USgHIFU procedure

2.2.1. PMWA procedure

We used a KV2100 Microwave tumor treatment device (Nanjing Kangyou Microwave Energy Sources Institute; frequency, 2450 MHz; needle type, internal water-cooling; electrode diameter, 15 G; electrode length, 180 mm; power, 0–100 W; distance from the aperture of the MW emission to the needle tip, 11 mm). The principle of microwave treatment is to cause tumor necrosis by heating tissue via the thermal energy produced by the agitation of water molecules. For the PMWA procedure, the patient laid on her back on the operating table. After intravenous anesthesia (flurbiprofen ester 2 mg/kg, propofol 4 mg/kg/h; intravenous anesthesia for this surgical treatment method is easy, simple, and has a rapid effect) was established, PMWA procedures were performed by the same experienced doctor. First, the percutaneous microwave electrode was placed into the fibroids under the guidance of ultrasound. Based on the dose–effect relation of microwave ablation, the output power was set at 50 W. A single microwave electrode was used for uterine fibroids with diameters of 4–5 cm, and a double microwave electrode with a distance of approximately 1.5 cm between electrodes was used for uterine fibroids larger than 5 cm. The distance between the electrode tip and the pseudocapsules was greater than 5 mm. During MW emission, the ablation area was monitored by ultrasound in real time. MW emission was stopped when the entire lesion was covered with hyperechoic microbubbles. Finally, contrast-enhanced ultrasound (SonoVue, Bracco Sine Pharm) was performed immediately after the procedure for preliminary evaluation of ablation efficacy, and if blood stream perfusion was detected in the fibroid, a supplementary treatment was performed.

2.2.2. USgHIFU procedure

The USgHIFU ablation procedure was performed by using a JC USgHIFU tumor therapeutic system (Chongqing Haifu Technology, Chongqing, China; transducer diameter, 20 cm; focal length, 15 cm; frequency, 0.8 MHz; power, 0–400 W). All patients were given preoperative intestinal preparation, mandatory enema and skin preparation, and patients were placed in the prone position. During the operation, an intravenous sedative (midazolam, 1–4 mg) and analgesic (fentanyl, 50–400 μg) were given to maintain conscious sedation. A water balloon compressor was used to push away the bowel in the acoustic pathway and to avoid intestinal damage. Patients were requested to report any discomfort, and their vital signs were monitored. Treatment began by placing the focus into the uterine fibroid at least 1 cm away from the pseudomembrane of the fibroid and 1.5 cm from the endometrium to prevent injury to the normal myometrium and endometrium. Targeted lesions were fractionally ablated, slice by slice, from the deep to the shallow regions of the tumor.

2.3. Study endpoints

The study's primary endpoints were symptom severity scores (SSS, containing 8 questions regarding the severity of symptoms, scale of scores was 5–40), treatment time (time from sonication emission to the completion of ultrasonic emission), ablation rate (the percentage of non-perfused fibroid volume after treatment compared to before treatment measured by enhanced images), regression rate of uterine fibroids (fibroid volume changes using volumes determined before treatment and after 6 months by T2-weighted MRI; fibroid volumes by MRI were calculated according to the formula $4/3\pi \times (d/2)^3$, where d = (length + width + height)/3 and adverse events (according to updated the standards established by the Society of Interventional Radiology [8]).

2.4. Statistical analysis

Normal distribution tests were conducted for the variables, and non-normal distribution data were analyzed after normal transformation. The NPV ratio, treatment time, ablation rate, SSS, regression rate, and rate of adverse effects were statistically analyzed using one-way ANOVA and the Mann–Whitney U test and chi-square test. Statistical significance was set at a P-value less than 0.05, and statistical analysis was performed by using SPSS19.0 software (SPSS, IBM Company, Chicago, USA).

3. Results

3.1. Baseline information

A total of 73 women with symptomatic fibroids in the period from September 2012 to December 2013 underwent either PMWA (31 women) or USgHIFU (42 women) therapy in a single session at our institution. The average age of the patient was 35.4 ± 6.2 years (range, 24–50 years), the mean fibroid diameter was 66.2 ± 11.2 mm (range, 40.3–100.0 mm), and the mean fibroid-related SSS was 31.2 ± 7.2 (19–38) before treatment. The baseline demographic data of the two groups are given in Table 1, which shows no significant differences in the baseline data between the PMWA group and the USgHIFU group.

3.2. Post-procedure evaluation of PMWA

The PMWA procedure was successfully performed for all 31 patients in this group. The median treatment time was 46.2 min (range, 35.4–60.7 min) for patients, the immediate mean ablation rate after treatment was 79.8 ± 14.9% (range, 70.9–99.1%), the average regression rate was 52.4% (range, 43.1–68.7%) at 6 months after the procedure, and the mean SSS decreased from 32.6 to 21.3, falling by an average of approximately 10.2 points (range, 5.4–16.7) (Fig. 1, Table 2). The common adverse events after treatment were lower abdomen pain, vaginal discharge and low-grade fever; these symptoms were generally mild, were classified as grade A or B according to the unified standardized Society of Interventional Radiology (SIR) grading system, did not require medical attention, and lasted

Table 1
Baseline data of patients in PMWA and USgHIFU.

Variable	PMWA	USgHIFU
Patient number	31	42
Age (year)	38.3 ± 6.0 (25–49)	37.6 ± 8.4 (24–50)
BMI[a] (kg/m^2)	21.8 ± 2.8 (17.1–28.2)	21.9 ± 3.3 (16.1–29.1)
Fibroid location: AW/PW/LW[b] (*n*)	10/13/17	15/19/17
Fibroid diameter (cm)	68.6 ± 12.7 (40.3–100.0)	65.0 ± 10.8 (40.6–91.1)
Symptom severity score (SSS)	31.2 ± 7.2 (21–38)	30.6 ± 6.4 (19–37)

[a] BMI: body mass index.
[b] AW: anterior wall; PW: posterior wall; LW: lateral wall.

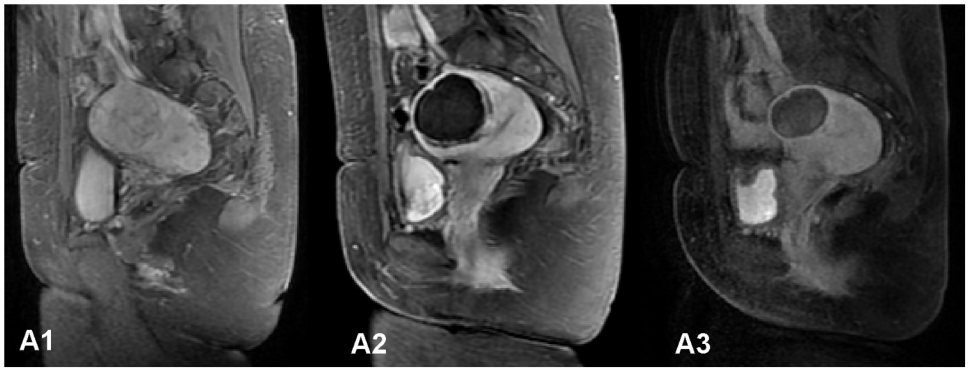

Fig. 1. contrast-enhancement sagittal MRI before and after PMWA treatment: (A1) fibroid shows enhanced slightly before treatment; (A2) fibroid shows almost complete necrosis on contrast-enhanced MRI immediately after treatment; (A3) the fibroid size shrink obviously and the area of necrosis still is visible on contrast-enhanced MRI at 6 months after treatment.

for 1–2 days. After PMWA treatment, no patient suffered serious adverse events belonging to grade C that required hospital treatment (Table 2).

3.3. Comparison of the results of USgHIFU versus PMWA

USgHIFU was successfully performed for all 42 patients in this group. The median treatment time was 92.5 min (range, 54.3–121.6 min), and this was significantly longer compared to the treatment time in the PMWA group. The fibroid ablation rate, average regression rate and drop in SSS at 6 months after treatment were 77.1 ± 18.2% (range, 60.2–97.4%), 50.3% (range, 39.2–65.5%) and 9.4 (range, 4.8–14.9), respectively, which were similar to the PMWA group (Fig. 2, Table 2). The most frequently reported adverse events were lower abdomen pain, sacrococcyx pain, hip pain and radiating pain in the lower limbs. These commonly occurred 1–3 days after treatment, were classified as grade A or B according to the SIR grading system and resolved spontaneously without any other treatment. After USgHIFU treatment, no patient suffered from serious complications (grade C). There was no significant difference in the incidence rate of severe adverse events between the two groups (Table 2).

4. Discussion

In recent years, minimally invasive surgical technology had become the focus of treatment for uterine fibroids. The minimally invasive thermal ablation techniques of USgHIFU and PMWA are being used with increasing frequency to manage uterine fibroids. The decision to compare the success in ablating fibroids between these two techniques was based on the fact that there were no available data showing which technique has a greater advantage [9].

Since Kanaoka et al. reported for the first time in 2005 that microwave endometrial ablation improves menorrhagia caused by large submucous fibroids [10], other scholars have researched this technique. Zhang et al. reported that PMWA for fibroids was feasible and safe, with a fibroid regression rate of 78.7% and 93.1% at 6 and 12 months after ablation, respectively, and there were no serious adverse events in any patient after the treatment [5]. There have been many reports on the use of HIFU for ablating uterine fibroids, and research has shown that the fibroid regression rate was 26.8% and 40.9% at 6 and 12 months, respectively, after this treatment [11]. The data showed that PMWA appeared to have advantages over HIFU, but actually, the regression rate of the fibroid was limited by the ablation rate. The greater the extent of ablation, the more obvious the shrinkage in fibroid after treatment [12]. Because the limitations of the clinical project artificially restricted the ablation rate to 50% during HIFU treatment in the above research results [13], which was significantly less than that of PMWA, the regression rate of the fibroid after HIFU treatment was less than that of PMWA. In this research, according to our clinical research plan, we increased the volume of ablation during USgHIFU treatment to the extent that safety permitted, and there

Table 2
The comparison results between PMWA and USgHIFU in treating uterine fibroids.

Variable	PMWA	USgHIFU
Ablation rate (%)	79.8 ± 14.9% (70.9–99.1%)	77.1 ± 18.2% (60.2–97.4%)
Treatment time (min)	46.2* (35.4–60.7)	92.5* (54.3–121.6)
Regression rate at 6 months after treatment (%)	52.4% (43.1–68.7%)	50.3% (39.2–65.5%)
Changes in SSS at 6 months after treatment (score)	10.2 (5.4–16.7)	9.4 (4.8–14.9)
Incidences of adverse event (SIRC)	0	0

* $P = 0.006$.

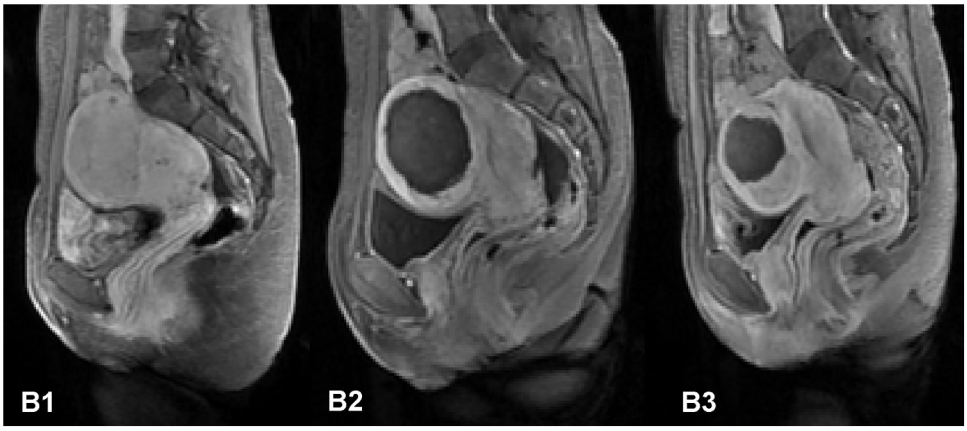

Fig. 2. contrast-enhancement sagittal MRI before and after USgHIFU treatment: (B1) fibroid shows enhanced slightly before treatment; (B2) the NPV is visible inside uterine fibroid on contrast-enhanced MRI immediately after treatment; (B3) the fibroid size shrink obviously although the NPV ratio decrease than 6 months before on contrast-enhanced MRI.

was no significant difference in the ablation rate between PMWA and USgHIFU; therefore, there was also no significant difference in the regression rate between the two groups. As the volume of the fibroid diminished, the physical symptoms (such as menorrhagia, prolonged menstruation, pain, discomfort in the pelvic area, and urinary frequency) associated with it gradually eased [14], and the SSS of the two groups at 6 months after treatment significantly decreased, with no significant difference between the two groups. Most adverse events were mild to moderate in severity, no patient suffered from serious complications higher than grade C according to the SIR grading system, and the incidence of adverse events was similar in each group.

In this study, the treatment time was shorter in the PMWA group compared to the USgHIFU group. The primary reason for this difference in results is likely related to the principle mechanism of action of the two therapy methods. In PWMA, the microwave ablation electrode is accurately inserted into the fibroid using ultrasound guidance, and the microwave generator located in the front of the ablation electrode emits an electromagnetic wave with a frequency of 900–2450 MHz. The resulting agitation of water molecules in the adjacent tissue produces friction and causes a rise in tissue temperature, which can reach more than 100 °C, and this is enough to induce coagulation necrosis of the tissue [15,16]. HIFU creates a coagulation necrosis region with temperatures of 60–100 °C produced by a tightly and precisely focused high-intensity ultrasound beam that agitates tissue ions and produces ion friction [17]. Because PMWA is not limited by charring and can produce an instantaneous high temperature, it has a much broader power field, up to 2 cm in diameter [18], and the cooling effect of blood flow during treatment is reduced. Therefore, it can produce a larger zone of ablation in a shorter amount of time. In contrast, the focal regions of HIFU are 3 mm × 8 mm and must follow the treatment principle from point to plane to volume, and there is energy attenuation during transmission of the ultrasonic wave and a cooling effect due to blood flow during treatment [19,20]. This leads to a tissue temperature produced by HIFU that is significantly lower than that of MWA, and the ablation efficiency is decreased.

An increasing number of women with symptomatic fibroids are demanding minimally invasive therapies that retain the organs and their functions, and PMWA and HIFU are both effective and safe strategies for these patients. PMWA had a higher treatment efficacy and was suitable for most patients, but it required hospitalization and general anesthesia. HIFU, a noninvasive therapy, did not require hospitalization and general anesthesia and had a high cost [21]. Therefore, with current technology, PMWA was relatively suitable for large and hypervascular uterine fibroids, and HIFU was more specifically suited to small uterine fibroids and hypovascular uterine fibroids.

Possible limitations inherent to this retrospective study were its nonrandom population, small sample size, and single-center nature. Therefore, further high-quality, multiple-center, and large-sample randomized controlled trials are required before these methods can be widely used in clinical medicine.

5. Conclusion

Based on our results, both PMWA and USgHIFU are safe and effective modalities in the treatment of uterine fibroids; however, PMWA is ultimately more efficient than USgHIFU.

Conflicts of interest

All authors have no conflicts of interest.

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