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ORIGINAL ARTICLE

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Comparison of stress response following microwave ablation and surgical resection of benign thyroid nodules

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Abstract

Purpose To compare the effects and safety of using microwave ablation (MWA) and surgical resection for the treatment of benign thyroid nodules (BTNs) under ultrasonic guidance and investigate the effects of this treatment on stress response.

Methods Patients with BTNs were divided into the MWA and operation groups (72 cases each). Interleukin (IL)-6, IL-8, serum tumor necrosis factor (TNF-α), and hydrostatic visual analog scale (VAS) prior to the operation, at 6 h, 24 h, and 72 h post-operation were compared between the two groups. Operation times, hospitalization times, hospitalization expenses, and postoperative complications in the two groups were also compared. All patients underwent routine ultrasound and thyroid function testing at 3 and 6 months post-operation for assessment of nodule changes and thyroid hormone levels.

Results Compared to the MWA group, the operation group had longer average operation times, longer hospital stays, a higher rate of neck pain after surgery, and a higher rate of fever ($P < 0.05$). Body temperature, as well as VAS, IL-6, IL-8, and TNF-α levels in the operation group were higher than those in the MWA group at 6 h, 24 h, and 72 h post-operation ($P < 0.05$). The levels of free thyroxine and free triiodothyronine in the operation group were lower than those in the MWA group ($P < 0.05$).

Conclusion MWA is a safe and effective treatment for patients with BTNs. The effects of MWA are more tolerable than those of surgical resection and the physiological function of the thyroid is preserved, which has high clinical value.

Keywords Microwave ablation · Benign nodules · Stress response · Clinical effect · Thyroid

Introduction

The incidence of thyroid nodules has increased annually, with rates of clinical diagnosis in adults ranging from 3–7% and the detection rate using ultrasound as high as 20–76% [1]. With the promotion and application of thyroid fine needle aspiration, core needle biopsy, and genetic testing, the benign and malignant properties of thyroid nodules can be essentially clarified before thyroid surgery. While the removal of malignant nodules is still mainly conducted via surgical resection, the treatment of benign thyroid nodules (BTN) via other means has become the focus of significant research.

Ultrasound-guided microwave ablation (MWA) is a minimally invasive ablation technique for the treatment of BTN, which has been shown to be effective in reducing the volume and symptoms of BTN [2]. Its use in thyroid nodules has been reported by Feng et al. and Yue et al. [3, 4]. A recent meta-analysis concluded that thyroid nodules constitute one of the most common diseases in clinical practice and has been detected in the general adult population using ultrasonography [5]. The present study explored the clinical value of MWA versus surgical resection for the treatment of BTN and any subsequent impact on the body's response.

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Materials and methods

Patients

We screened patients with biopsy-proven BTNs, seen between February 2016 and August 2017 at our hospital. Study inclusion criteria included a history or current status of local compressive symptom, neck discomfort or pain, foreign body sensations, cosmetic concerns, or ineligibility or refusal to undergo surgery [6]. Exclusion criteria included acute infections, substernal goiter, Graves' disease, nodular goiter with hyperthyroidism, hypothyroidism, Hashimoto's disease with subclinical hypothyroidism, severe cardiopulmonary disease, coagulopathy, surgical resection, and patients who could not be treated with surgery. A total of 144 eligible patients were divided into the MWA group ($n = 72$) and the operation group ($n = 72$). The study was approved by the local ethics committee (No. 2016018), and written informed consent was obtained from all patients prior to their enrolment.

Equipment and instruments

A microwave unit (KY-2000, Kangyou Medical, Nanjing, China) consisting of a microwave generator, a flexible low-loss coaxial cable, and a cooled shaft antenna was used. The generator was capable of producing 1–100 W of power at 2450 MHz either continuously or in a pulse. The length of the radiation tip was 3 mm. A model 2450-A disposable MWA needle was used. A Philips IU22 color Doppler ultrasound system equipped with a puncture guide was used. Nodule volume was calculated using the following equation: $\pi \times W \times D \times L/6$, where W was the width, D was the depth, and L was the length (all in centimeters) of the thyroid nodule [7].

Treatment

In the operation group, the thyroid nodule was removed under general anesthesia in the operating room. The patient was placed supine and a curved incision of 3.5–7 cm along the skin and 2 cm above the sternal notch was made in the skin and subcutaneous fat. The platysma, free platysma, and the sublingual muscles were then cut open to expose the thyroid tissue. For patients with bilateral nodules, a total thyroidectomy was performed. For patients with unilateral nodules, a unilateral thyroid lobectomy was performed.

Ultrasound-guided MWA was performed in the MWA group. The patient was placed in a supine position and the thyroid and surrounding cervical lymph nodes were ultrasonically examined to determine the location and size of the nodules. After routine anesthesia to the periphery of the nodules, the thyroid and carotid space, tracheal space, esophageal space, and posterior thyroid space were separated with a mixture (2% lidocaine+saline) to avoid thermal damage during the operation. A small incision was made at the puncture site, and the microwave knife was placed into the nodule under ultrasound guidance using 30 W of power for multi-point, multi-layer ablation until the nodule was covered by a strong echo generated by the thermal energy. For fluid-containing cystic nodules, the cystic fluid was first withdrawn and then the remaining nodule was subjected to MWA. After this, ultrasound was used to check whether the nodule ablation was complete and to confirm no active bleeding. If it was not complete, further ablation was applied. The patient was instructed to continue pressing the incision for 15 min to 30 min to prevent bleeding and exudation.

Effect and safety analysis

Operation time, hospitalization time, hospitalization cost, and any postoperative complications were assessed 3 and 6 months after the operation. Changes to the thyroid nodules were observed and the nodule reduction rate was calculated according to the following formula, which has been used previously: [(pre-treatment volume − volume at follow-up) / pre-treatment volume] × 100% [8]. Nodule recurrence and thyroid function were compared between the two groups, including changes in free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) levels.

Body stress response observation indicators

IL-6, IL-8, and TNF-α levels, as well as and visual analog scale (VAS) levels were compared between the day prior to surgery and 6, 24, and 48 h after surgery. The VAS method uses a 10-cm-long scale drawn on a table with numbers 0 and 10 at each end. The number, 0, indicates no pain and 10 indicates the most severe pain. The position on the scale was considered to represent the degree of pain experienced by the patient. The scale is often applied for estimation of pain but, can also be used for expression of patients' concern about compression; a higher concern is reflected in a higher score.

Statistical analyses

The analyses were performed using SPSS 20.0 statistical software (IBM, Armonk, NY, USA). Normally distributed data are expressed as mean ± standard deviation ($\overline{X} \pm s$). Comparisons between measurement data groups were performed via one-way ANOVAs. All count data is expressed in % of cases and was analyzed using χ^2 tests. $P < 0.05$ was considered to indicate statistically significant differences.

Table 1 Comparison of patient groups before surgery

	MWA group ($n = 72$)	Operation group ($n = 72$)	t/χ^2	P-value
Age (years)	44.4 ± 9.6	43.2 ± 9.4	0.758	0.450
Male (n%)	26 (36.1)	24 (33.3)	0.123	0.726
Systolic blood pressure (mmHg)	118.6 ± 16.1	115.4 ± 15.8	1.204	0.231
BMI (kg/m$^{2)}$	25.3 ± 3.2	25.5 ± 3.7	−0.347	0.729
Smoking (n%)	16 (20.6)	18 (17.6)	0.235	0.627
Body temperature (°C)	36.4 ± 0.4	36.5 ± 0.4	−1.500	0.136
Nodule condition				
Single nodule (n%)	55 (76.4)	56 (77.8)	0.039	0.843
Multiple nodules (n%)	17 (23.6)	16 (22.2)		
Nodule diameter (cm)	3.2 ± 0.6	3.4 ± 0.7	−1.841	0.068
Nodule volume (cm^3)	3.6 ± 0.7	3.8 ± 0.8	−1.596	0.113
Laboratory tests				
IL-6 (pg/mL)	11.8 ± 0.7	12.0 ± 0.9	−1.488	0.139
IL-8 (pg/mL)	16.9 ± 4.6	17.3 ± 4.9	−0.505	0.614
TNF-α (ng/L)	21.9 ± 5.3	20.8 ± 4.5	1.342	0.182
FT3 (pmol/L)	5.8 ± 0.9	5.7 ± 1.3	0.537	0.592
FT4 (pmol/L)	18.4 ± 5.6	18.8 ± 5.9	−0.417	0.677
TSH (μIU/mL)	2.4 ± 0.9	2.5 ± 0.8	−0.705	0.482

MWA microwave ablation, *BMI* body mass index, *IL* interleukin, *TNF* tumor necrosis factor, *FT3* free triiodothyronine, *FT4* free thyroxine, *TSH* thyroid-stimulating hormone

Results

Preoperative patient data

There were no significant differences in age, gender composition ratio, systolic blood pressure, BMI, smoking rate, nodule status, body temperature at admission, or laboratory test results between the two groups ($P > 0.05$) (Table 1).

Comparison of the two groups of patients during hospitalization

When compared with the MWA group, the operation group had a longer average operation time, longer hospital stays, and a higher rate of neck pain after surgery, and fever ($P < 0.05$). However, hospitalization costs were higher in the MWA group than in the surgery group ($P < 0.05$). There was no significant difference in the ratio of recurrent laryngeal nerve injury, surgical site infection, and postoperative neck congestion between the two groups ($P > 0.05$) (Table 2).

Body stress response comparison

There were no significant differences in IL-6, IL-8, TNF-α, or VAS levels between the two groups prior to the operation ($P > 0.05$). Levels of IL-6, IL-8, TNF-α, and VAS in the operation group were higher than those in the MWA group at 6, 24, and 72 h following the operation ($P < 0.05$). In the MWA group, levels of IL-6, IL-8, TNF-α, and VAS were highest 6 h post-operation and then decreased ($P < 0.05$). There were, however, no differences between these indexes 48 h after the operation and levels before the operation ($P > 0.05$). In the operation group, levels of IL-6, IL-8, TNF-α, and VAS were highest 6 h after the operation and then decreased ($P < 0.05$). However, these indexes 48 h after the operation remained higher than before the operation ($P < 0.05$) (Table 3).

Changes in thyroid nodule volume after treatment in the MWA group

Thyroid nodule volume was smaller 6 months (0.6 ± 0.3) than it was 3 months (1.2 ± 0.2) after treatment in the MWA group. Additionally, thyroid nodule volume was significantly smaller after MWA ($P < 0.05$).

Comparison of postoperative follow-up between the two groups

There were no nodule recurrences 3 months and 6 months after the operation. Six months after the operation, there was no hypothyroidism in the MWA group while there were four cases (5.6%) in the operation group, a statistically significant increase ($\chi^2 = 4.002$, $P < 0.05$). Thyroid function changes in the two groups were also compared. FT4 and FT3 levels in the operation group were lower than those in the MWA group ($P < 0.05$), while TSH levels were higher than those in the MWA group ($P < 0.05$). There were no significant differences in changes to the three thyroid function indexes in the MWA group ($P > 0.05$); FT4 and FT3 levels in the operation group were lower than those before surgery ($P < 0.05$), while TSH levels were higher than those before surgery ($P < 0.05$; Table 4).

Discussion

While the complete nodule in BTN cases can be removed, this is associated with an increased risk for a longer hospitalization, upper airway obstruction, non-esthetic scars, recurrent laryngeal nerve palsy, iatrogenic hypothyroidism, and increased difficulty with subsequent operations [9]. In recent years, minimally invasive ablation technologies for BTN have been developed and improved, gradually filtering

Table 2 Comparison of patient groups during hospitalization

	MWA group ($n = 72$)	Operation group ($n = 72$)	t/χ^2	P-value
Surgical time (min)	30.5 ± 9.4	60.0 ± 11.2	−15.663	0.000
Hospital stay (days)	3.5 ± 0.5	11.4 ± 2.7	−24.412	0.000
Hospital costs (yuan)	13787.3 ± 877.3	7790.8 ± 782.8	43.276	0.000
Complications (n%)				
Bleeding	0 (0.0)	2 (2.9)	2.028	0.154
Recurrent laryngeal nerve injury	0 (0.0)	2 (2.9)	2.028	0.154
Surgical infection	0 (0.0)	1 (1.4)	1.007	0.316
Neck pain	4 (5.6)	24 (33.3)	17.737	0.000
Neck congestion	0 (0.0)	3 (4.2)	2.980	0.084
Fever	0 (0.0)	4 (5.6)	4.002	0.045

MWA microwave ablation

Table 3 Stress response comparison between patient groups

	Time	VAS score	IL-6 (pg/mL)	IL-8 (pg/mL)	TNF-α (ng/L)
MWA group ($n = 72$)	1 day Preoperative	0.0	11.8 ± 0.7	16.9 ± 4.6	21.9 ± 5.3
	6 h Postoperative	0.7 ± 0.6[a]	17.4 ± 2.7[a]	36.8 ± 4.3[a]	35.1 ± 5.8[a]
	24 h Postoperative	0.0[b]	14.5 ± 1.1[a,b]	24.6 ± 4.4[a,b]	30.6 ± 4.2[a,b]
	48 h Postoperative	0.0[b]	11.2 ± 0.6[b,c]	16.4 ± 4.3[b,c]	22.4 ± 5.2[b,c]
Operation group ($n = 72$)	1 day Preoperative	0.0	12.0 ± 0.9	17.3 ± 4.9	20.8 ± 4.5
	6 h Postoperative	2.5 ± 0.7[a,d]	38.5 ± 4.2[a,d]	55.9 ± 6.8[a,d]	54.7 ± 7.1[a,d]
	24 h Postoperative	1.8 ± 0.4[a,b,d]	28.3 ± 4.9[a,b,d]	36.1 ± 4.0[a,b,d]	40.8 ± 7.9[a,b,d]
	48 h Postoperative	1.3 ± 0.4[a,b,c,d]	15.7 ± 2.8[a,b,c,d]	21.4 ± 3.2[a,b,c,d]	29.4 ± 6.2[a,b,c,d]

MWA microwave ablation, *IL* interleukin, *VAS* visual analog scale, *TNF* tumor necrosis factor

[a]$P < 0.05$; compared to 1 day preoperative

[b]$P < 0.05$; compared to 6 h postoperative

[c]$P < 0.05$; compared with 24 h postoperative

[d]$P < 0.05$; compared with the MWA group

Table 4 Changes in thyroid function in both patient groups

	Time	FT3 (pmol/L)	FT4 (pmol/L)	TSH (μIU/mL)
MWA group ($n = 72$)	1 day Preoperative	5.8 ± 0.9	18.4 ± 5.6	2.4 ± 0.9
	3 months Postoperative	5.5 ± 0.7	18.6 ± 4.4	2.3 ± 0.7
	6 months Postoperative	5.6 ± 0.8	18.4 ± 5.4	2.4 ± 0.8
Operation group ($n = 72$)	1 day Preoperative	5.9 ± 1.3	18.8 ± 5.9	2.5 ± 0.8
	3 months Postoperative	4.3 ± 0.9[a,c]	14.1 ± 4.2[a,c]	3.1 ± 1.9[a,c]
	6 months Postoperative	4.5 ± 0.8[a,c]	14.4 ± 3.7[a,c]	3.1 ± 1.7[a,c]

MWA microwave ablation, *FT3* free triiodothyronine, *FT4* free thyroxine, *TSH* thyroid-stimulating hormone

[a]$P < 0.05$; compared to 1 day preoperative

[b]$P < 0.05$; compared to 3 months postoperative

[c]$P < 0.05$; compared with the MWA group

into clinical practice. Among these, MWA is the most widely used.

MWA offers the advantages of a small degree of surgical trauma, rapid recovery time, fewer complications, a simple operation procedure, and no impact on patient appearance [4]. Here, we found that the time required for MWA surgery is often short and it is associated with decreased hospital stay length and reduced postoperative complications of pain and fever. Patients who underwent MWA treatment encountered no postoperative bleeding, recurrent laryngeal nerve injury, surgical site infections, or postoperative neck congestion, and fever. Only four cases in

the present study reported neck pain after surgery, mainly characterized by transient pain and a burning sensation. This discomfort in patients was aggravated during swallowing, although it was tolerable, and subsided 1 day after surgery.

Both treatments assessed here create a certain amount of bodily stress. TNF-α levels can reflect the degree of surgical injury or the early stress response of the impacted tissue [10–12]. IL-6 and IL-8 are involved in early postoperative inflammatory responses, and the body's stress response can be evaluated by acutely measuring the levels of both following surgery [13–16]. Therefore, the present study used IL-6, IL-8, and TNF-α levels as outcomes reflective of somatic stress. Our results reveal that there were no significant differences in IL-6, IL-8, or TNF-α levels between the MWA group and the operation group before the operation. However, levels of IL-6, IL-8, TNF-α, and VAS in the operation group were higher than those in the MWA group at 6, 24, and 72 h after the operation. This indicates that ultrasound-guided MWA of BTNs results in significantly lesser bodily stress than does surgical resection.

On outpatient follow-up 6 months after surgery, we found that nodule volume had gradually decreased after MWA treatment, with an average volume reduction rate of more than 50%. Additionally, no cases of recurrence were noted, indicating good therapeutic efficacy. It was critical to assess for thyroid damage, as the thermal damage caused by MWA could have damaged the thyroid area and led to changes in thyroid function. We found that thyroid function fluctuated between 3 and 6 months post-operation, although these fluctuations remained in the normal range and were not statistically significant. Previous studies have reported similar results [17–19]. In the operation group, four patients (5.9%) had hypothyroidism, a higher number than in the MWA group (0.0%). Additionally, levels of FT4 and FT3 in the operation group were lower than those in the MWA group at 3 and 6 months post-operation, while levels of TSH were higher than those in the MWA group.

The limitations of this study include its small sample size and the fact that all participants were residents of the Henan Province, China. Moreover, the patient assignment to treatment groups was not random. We informed the patients about two different treatments; the patients who underwent MWA were included in the MWA group, and those who selected operation were included in the operation group. In addition, most of these patients had predominantly single nodules. Furthermore, the observation time was short. Further large sample studies are needed to include multiple nodules. The long-term efficacy also needs further verification through large sample sizes and multi-center studies.

In summary, ultrasound-guided MWA for thyroid nodule surgery is an efficient procedure that inflicts less trauma on the body, can reduce hospitalization times, is safe and reliable, offers significant effects, is associated with minimal postoperative complications, maintains patient aesthetics, protects the physiological functions of the thyroid gland, and is easily adopted by patients. Overall, WMA is effective and less stressful. As surgical procedures are further standardized and optimized, MWA may be an effective method of treatment for BTNs, especially for patients with open surgical contraindications and concerns about open surgical scars affecting the aesthetics of the neck.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the local ethics committee (No. 2016018).

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

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