Comparison between ultrasound-guided percutaneous radiofrequency and microwave ablation in benign thyroid nodules

ABSTRACT

Objective: The purpose of this study was to compare the efficacy and safety of radiofrequency ablation (RFA) and microwave ablation (MWA) for the treatment of benign thyroid nodules (BTNs).

Methods: Patients with BTNs were treated in our hospital, including 72 patients treated with RFA and 100 patients treated with MWA from June 2016 to March 2019. The volume reduction rates (VRRs), thyroid function, clinical status, and complications were compared at each postoperative duration to evaluate the efficacy and safety of the two modalities.

Results: The mean VRRs of the RFA group vs. the MWA group at 1, 3, 6, and 12 months were 22.7±13.4% vs. 24.0±16.1% (P = 0.681), 56.1±19.5% vs. 54.8±22.8% (P = 0.788), 77.9±21.0% vs. 68.7±19.1% (P = 0.038), and 85.4±18.9% vs. 75.8±19.4% (P = 0.029), respectively. There was no significant difference in the VRRs between the two treatments at 1 and 3 months and the RFA group achieved higher VRRs than MWA group at 6 and 12 months. Moreover, the symptom and cosmetic scores decreased significantly in both groups and all patients succeeded in preserving thyroid function. Of the total patients, 2.8% in the RFA group and 4% in the MWA group experienced voice changes after undergoing thyroid ablation, and one patient in the RFA group had intraoperative hemorrhage of about 10 mL.

Conclusions: RFA and MWA are both effective and safe techniques for treating BTNs. Higher VRRs were observed at the 6- and 12-month follow-ups in the RFA group.

KEY WORDS: Microwave ablation, radiofrequency ablation, volume reduction rate

INTRODUCTION

The incidence of thyroid nodules (TNs) has increased dramatically in the general population, reaching 27.76%–40.1% in China’s first-tier cities.[1,2] Majority of TNs are benign, and recent guidelines suggest that asymptomatic benign TNs (BTNs) with average growth only need regular follow-up.[3] However, active treatment modalities should be performed for compression symptoms, cosmetic reasons, or the possibility of a malignant transformation caused by BTNs.[4] In general, partial or total thyroidectomy is the preferred treatment. Some patients do not want to undergo surgery even if it may establish the pathological diagnosis and alleviate the symptoms. Moreover, several limitations of thyroidectomy cannot be ignored including laryngeal nerve injury, neck scar formation, permanent hypoparathyroidism, and intraoperative hemorrhage.[5,6] Hence, minimally invasive percutaneous ablation modalities, such as radiofrequency ablation (RFA), microwave ablation (MWA), ethanol ablation (EA), and laser ablation (LA), have been widely applied for BTNs in recent years.[7,8]

According to the current studies, EA is the first-line treatment modality for cystic TNs,[9] but its clinical significance is limited due to the complications of ethanol seepage.[10] LA reduces the volume of solid cold nodules in up to 50% in most patients.[11] Furthermore, RFA and MWA have been proven to be convenient and effective and to cause less pain and fewer complications.[12,13] Two retrospective studies had formulated different conclusions in comparing RFA and MWA. One study demonstrated that RFA had formulated different conclusions in comparing RFA and MWA. One study demonstrated that RFA

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was similar to MWA in terms of efficacy and safety,[14] while another study concluded that better results could be achieved when performing RFA than MWA at 6-month follow-up.[15] Whether one of them is superior over the other is a matter of debate, when these two modalities have been rapidly developed in China. This article aimed to compare the efficacy and safety of RFA and MWA in the treatment of BTNs.

MATERIALS AND METHODS

This retrospective study comparing RFA and MWA and the utilization of these techniques was approved by the Ethics Committee of Zhongshan Hospital. Patients were required to read and sign an informed consent prior to the procedure.

Patients

All patients undergoing percutaneous thermal ablation (RFA or MWA) for BTNs from June 2016 to March 2019 were retrospectively considered for this study at Zhongshan Hospital of Fudan University, Shanghai, China. A total of 72 patients were treated with RFA, while a total of 100 patients were treated with MWA. Inclusion criteria were as follows: (a) ultrasound (US) findings suggesting a benign nodule and benign cytologic confirmation by US-guided fine-needle aspiration cytology (FNAC), (b) presence of either compressive or cosmetic problems, (c) anxiety about a malignancy, (d) refusal to undergo surgery or contraindications for surgery, and (e) serum levels of thyrotropin and thyroid hormone within the normal range. Exclusion criteria were as follows: (a) retrosternal growth, (b) cytologic results indicating malignancy, (c) the abnormal function of the vocal cord on the contralateral side of the lesion, and (d) serum levels of thyrotropin and thyroid hormone not within the normal range.

Equipment

S2000 US equipment (Siemens, Germany) was used for MWA treatment. SonoVue (Sine Pharma, Italy) was used as the US contrast agent. Medsphere RF Generator S-500 (Medsphere, Shanghai, China) was used for RFA treatment. MTC-3C microwave system (Viking, Shanghai, China) was used for MWA treatment. The microwave antenna was 16 G, and the RFA electrode was 19 G.

Preablation assessment

Before ablation, US [Figure 1a] and contrast-enhanced US (CEUS) were performed by the same radiologist with 10-year experience in thyroid imaging. Thyroid tumors were carefully evaluated for their structure, morphology, components (mainly solid, >50% solid; mainly cystic, >50% liquid), volume, and vascularity. The volume of each nodule was directly calculated using our CEUS machine. Subsequently, US-guided FNAC, laryngoscopy, laboratory tests, and clinical states were performed. To confirm the benign nature of the nodules, performing US-guided FNAC at least once was highly recommended. Laryngoscopy was performed to evaluate the vocal fold structure and function. Laboratory tests included thyroid function (i.e., serum thyroid-stimulating hormone [TSH], free triiodothyronine [FT3], free thyroxine [FT4], antithyroglobulin antibodies [TG-Ab], and thyroid peroxidase-Ab [TPO-Ab]), complete blood count, and blood coagulation tests. Moreover, every patient was assessed for symptom scores (Score 1, absent; Score 2, mild intermittent; Score 3, mild continuous; and Score 4, moderate) and cosmetic scores (Score 1, no palpable mass; Score 2, no cosmetic problem but a palpable mass; Score 3, cosmetic problem on swallowing only; and Score 4, a readily observable cosmetic problem).

Procedure

The treatment procedures were performed by LX.L who had a 10-year experience in RFA and MWA in our hospital. Before ablation, the patients were placed in the supine position with mild hyperextended neck, and local anesthesia was administered subcutaneously. A mixture of 2% lidocaine and 0.9% normal saline was infused into the surrounding thyroid capsule under US guidance to achieve a “liquid isolating region”[16] and to protect the vital structures of the neck (carotid artery, trachea, esophagus, and nerve) from thermal damage. If the nodule was mainly cystic, fluid aspiration was performed first.[17,18] The output powers for RFA and MWA were set between 10–20 W and 25–35 W, respectively. The “moving-shot technique”[19] was applied during the procedure, and each nodule was treated by moving the antenna or electrode in a unit-by-unit manner called the conceptual ablation units.[20] The whole treatment was monitored using real-time US, and the ablation was stopped when the hyperecho covered the whole nodule [Figure 1b]. After the procedure, all patients were given an ice bag and received intravenous dexamethasone 10 mg to reduce the side effects of ablation.

Figure 1: A 46-year-old male had a nodule in his thyroid gland. (a) An ultrasound showed a mainly solid nodule before ablation. (b) An ultrasound showed an inhomogeneous internal echo in the ablated area. (c) Contrast-enhanced ultrasound showed that there was no contrast agent filling in the ablated nodule, indicating that the blood perfusion in the nodule disappeared and the ablation was completed. (d) Three months after the ablation, the volume of the nodule evidently decreased.
Postablation evaluation and data analysis
CEUS was performed in every patient 1 day after ablation to evaluate the effectiveness of the treatment [Figure 1c]. In addition, ablation was performed when the CEUS showed contrast enhancement in the ablated areas. To measure the volume and volume reduction rate (VRR), CEUS was performed in the same manner as before at 1, 3, 6, and 12 months after treatment [Figure 1d]. VRRs (%) were calculated according to the following formula: VRR% = ([baseline volume - final volume] × 100/baseline volume). Moreover, thyroid function test (i.e., TSH, FT3, FT4, TG-Ab, and TPO-Ab), symptom score, cosmetic score, and immediate and late complications were observed at each follow-up visit.

For the statistical analyses, Statistical Package for the Social Sciences 23.0 (IBM Corp., Armonk, NY, US) software was used. GraphPad Prism software version 6 (GraphPad Software, Inc., 7825 Fay Avenue, Suite 230, La Jolla, CA 92037 USA) was used to draw the graphs. Quantitative data were expressed as the mean ± standard deviation, and categorical variables were expressed as the frequencies. Preablation, postablation, and follow-up variables were compared using a paired t-test. Between the two groups, an independent-sample t-test was performed to compare the age, nodular volume, VRR, and symptom and cosmetic scores. The sex distribution, the location of the nodule, the component of the nodule, and the complications were analyzed using Chi-square test. P < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics of the radiofrequency ablation and microwave ablation groups
Patients with TNs were treated with percutaneous thermal ablation in our hospital. Among them, patients were classified into the RFA group (n = 72) and the MWA (n = 100) group according to the initial treatment strategy. The baseline characteristics of the patients enrolled in the two groups are shown in Table 1. The RFA group consisted of 47 females and 25 males (mean age: 46.3 ± 16.3). The MWA group consisted of 66 females and 34 males (mean age: 52.0 ± 15.9). The volume of the nodules treated with RFA did not show a more statistically significant difference compared to nodules treated with MWA (10.7 ± 5.9 ml vs. 13.0 ± 7.9 ml, P = 0.131). Before treatment, there were also no significant differences between the RFA and MWA ablation groups according to other US characteristics and clinical characteristics.

Contrast-enhanced ultrasound characteristics of the nodules
Among the 172 patients, CEUS demonstrated a significant reduction of the vascular signals and lack of enhancement in the ablated area because of necrosis induced by RFA or MWA. However, the margin of one nodule was not absolutely ablated in the MWA group, and a triangular contrast medium perfusion inside the ablation lesions was found by CEUS. No additional ablation was performed for the proximity of the nerve close.

At 1, 3, 6, and 12 months, the mean volumes of the ablated nodule in the two groups were significantly less than the mean volumes before ablation. The VRRs between the RFA group and MWA group at 1, 3, 6, and 12 months were 22.7% ± 13.4% versus 24.0% ± 16.1% (P = 0.681), 56.1% ± 19.5% versus 54.8% ± 22.8% (P = 0.788), 77.9% ± 21.0% versus 68.7% ± 19.1% (P = 0.038), and 85.4% ± 18.9% versus 75.8% ± 19.4% (P = 0.029), respectively. The mean nodular VRRs at 1 and 3 months showed no significant difference between the two groups, and the RFA group achieved higher VRRs than that of the MWA group at 6 and 12 months by the same radiologist.

Symptom score, cosmetic score, and complications
There was no significant difference in the symptom score between the RFA group and the MWA group at 1, 3, 6, and 12 months, with 1.75 ± 0.97 versus 1.81 ± 0.99 (P = 0.693), 1.28 ± 0.54 versus 1.32 ± 0.58 (P = 0.647), 1.14 ± 0.28 versus 1.17 ± 0.29 (P = 0.498), and 1.04 ± 0.11 versus 1.05 ± 0.13 (P = 0.597), respectively [Figure 2a]. The cosmetic score between the RFA group and the MWA group showed no statistically significant differences at 1-, 3-, 6-, and 12-month follow-up visits, with 1.75 ± 1.01 versus 1.80 ± 1.10 (P = 0.761), 1.43 ± 0.78 versus 1.49 ± 0.85 (P = 0.637), 1.15 ± 0.43 versus 1.19 ± 0.48 (P = 0.574), and 1.05 ± 0.29 versus 1.08 ± 0.32 (P = 0.529), respectively [Figure 2b]. A significant improvement of symptom and cosmetic score was found after thermal ablation at last follow-up (P < 0.05).

Complications were observed in 7 of the 172 patients after ablation. Voice change occurred in two patients in the RFA group and in four patients in the MWA group. Laryngoscopy revealed that vocal cord immobility was observed, and it was treated with mecobalamin, and patients recovered after 2 weeks. In addition, a single patient in the RFA group had intraoperative tracheal and esophageal injury after ablation were not observed.

Table 1: Baseline characteristics of patients with benign thyroid nodules treated with radiofrequency ablation and microwave ablation

| Characteristics                        | RFA group (n=72) | MWA group (n=100) | P     |
|----------------------------------------|-----------------|-------------------|-------|
| Age (years)                            | 46.3±16.3       | 52.0±15.9         | 0.105 |
| Sex (male/female)                      | 25/47           | 34/66             | 0.922 |
| Location (isthmus/left/right)          | 2/38/32         | 3/56/41           | 0.913 |
| Component (mainly solid/mainly cystic) | 56/16           | 66/34             | 0.093 |
| Nodular volume (ml)                    | 10.7±5.9        | 13.0±7.9          | 0.131 |
| Symptom score                          | 2.24±1.21       | 2.27±1.27         | 0.876 |
| Cosmetic score                         | 1.91±1.11       | 1.98±1.17         | 0.693 |

Values are presented as the mean±SD. SD=Standard deviation, RFA=Radiofrequency ablation, MWA=Microwave ablation.
DISCUSSION

Our study revealed that RFA and MWA were both effective and safe techniques for BTNs, and a better efficacy was achieved in the RFA group at 6- and 12-month follow-up than in the MWA group by the same radiologist.

In our practice, surgical resection should be considered for nodules ≥3 cm. However, the disadvantages of surgery, such as hypothyroidism, recurrent laryngeal nerve palsy, and bleeding or scar formation, have posed major concerns. Thyroid hormone supplement due to hypothyroidism was required in 28% of the hemithyroidectomy patients, 100% of the near-total patients, and 87% of the subtotal patients. Hence, all these complications reduce the quality of life for the patients.

RFA and MWA are widely used to treat benign and malignant tumors of the liver, lung, and kidney and are recently developed for BTNs. Research studies demonstrated a significant decrease in volume, and the mean VRR was 70.2%–84.79% after performing RFA at 6 months. Lim et al. reported that the efficacy of RFA and MWA not only significantly remained at 3 years but also was well maintained throughout the follow-up period with a mean VRR of 93.4% at 4-year follow-up. Yue et al. treated BTNs with MWA and reported that the mean VRR was 65% at 6-month follow-up with 30.7% index nodules disappearing in a recent study. In addition, the symptom and cosmetic score also had decreased significantly. All these studies have reported that both techniques were feasible and effective in treating BTNs. To the best of our knowledge, there are few articles that compared the efficacy of these two modalities performed by the same radiologist. Our data showed that no statistically significant difference was observed in VRRs between the two groups at 1 and 3 months. On the contrary, increased VRRs were achieved in the RFA group at 6 and 12 months; moreover, VRRs of some patients decreased by less than a quarter in the MWA group in our study. Cheng et al. reported that MWA usually results in a high central temperature, which may lead to the carbonization in the ablated area, with the carbonized lesion difficult to be absorbed. Therefore, RFA is better than MWA in the long term, and further investigation is necessary to prove this conclusion.

The incidences of complication were low, and ablated patients were able to preserve the thyroid function. A total of 2.8% of patients in the RFA group and 4% of patients in the MWA group had voice changes after ablation, and they all recovered after administering a medication. Voice changes might be caused by the injury of the recurrent laryngeal or vagal nerve. The vagal nerve is usually located between the common carotid artery and internal jugular in the carotid sheath, and it may be next to the thyroid gland. During the ablation, thermal injury resulted in the dysfunction of the recurrent laryngeal nerve and changes in the vagal nerve. Therefore, performing the moving shot and hydrodissection technique during ablation might minimize the injury of the nerves. Moreover, CEUS was showed the vascularity of the nodule, and US was beneficial in distinguishing the nodule and the anatomic structures of the neck. One patient had an intraoperative blood loss of approximately 10 ml during RFA. He received long-term clopidogrel treatment and stopped receiving the medication 5 days before ablation. Patients with long-term use of antiplatelet or anticoagulant medications might be required to stop >5 days before treatment. Other adverse events (i.e., skin burns, infection, hyperthyroidism, and tracheal and esophageal injury) were not observed during the follow-up.

Figure 2: (a) A graph showed the nodular symptom score between the radiofrequency ablation and microwave ablation groups before ablation and at 1-, 3-, 6-, and 12-month follow-up. (b) A graph showed the nodular cosmetic score between the radiofrequency ablation and microwave ablation groups before ablation and at 1-, 3-, 6-, and 12-month follow-up. Significant decreases in symptom and cosmetic score after ablation in the radiofrequency ablation group and in the microwave ablation group (all <0.05) (radiofrequency ablation group, patients treated with radiofrequency ablation; microwave ablation group, patients treated with microwave ablation; month)
period. Hence, it was clear that RFA and MWA are effective in treating BTNs because they are highly safe modalities with fewer complications.

It was notable that CEUS played a vital role during the whole study. CEUS had high specificity and decreased the misdiagnosis rate of malignant nodules.[35–37] Conventional Doppler US was not able to show the microvessels due to the thinner tube and lower speed. However, CEUS was able to show the microvascular perfusion with microbubble flowing in the microcirculation.[38] As most nodules included in our study were ≥3 cm, they were characterized by rich blood vessels, large volume, and close proximity to the nerves. The vascularization, morphology, and location of the nodules were carefully examined using CEUS, which was able to determine the appropriate scope for ablation, before ablation. In addition, these had contributed to the highly complete ablation rate. One day after the ablation, CEUS was performed to immediately assess the result of the ablation and to determine if additional treatment was needed when CEUS showed zones of residual enhancement. At the later follow-up, the actual volume was observed to evaluate the efficacy of thermal ablation. In general, combined with CEUS, RFA, and MWA were considered to be effective and safe techniques in treating BTNs.

There were some limitations in our study. First, the sample size in each group was small, and the follow-up period was short (mean: 11.4 months). A larger sample size and longer follow-up duration would be needed to enhance our conclusion. Moreover, further study is necessary to analyze the solid and cystic nodules separately.

CONCLUSION

Regarding the significant decrease in volume, a significant improvement of clinical status, and fewer complications of RFA and MWA are both effective and safe techniques in treating BTNs. Increased VRRs were observed at 6- and 12-month follow-up in the RFA group by the same radiologist.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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