Ultrasound guided percutaneous microwave ablation of benign thyroid nodules: Safety and imaging follow-up in 222 patients

Wenwen Yue, Shurong Wang, Bin Wang, Qingling Xu, Shoujun Yu, Yonglin Zhang, Xiju Wang

A B S T R A C T

Objective: Microwave ablation is a minimally invasive technique that has been used to treat benign and malignant tumors of liver, lung and kidney. Towards thyroid nodules, only a few cases are reported so far. The aim of the study was to investigate the effectiveness and safety of ultrasound-guided percutaneous microwave ablation in the treatment of benign thyroid nodules with a large sample.

Materials and methods: A total of 477 benign thyroid nodules in 222 patients underwent microwave ablation in our department from July 2009 to March 2012. Microwave ablation was carried out using microwave antenna (16G) under local anesthesia. Nodule volume, thyroid function and clinical symptoms were evaluated before treatment and at 1, 3, and more than 6 months. The study was ethics committee approved and written informed consents were obtained from all patients.

Results: All thyroid nodules significantly decreased in size after microwave ablation. A 6-month follow-up was achieved in 254 of 477 nodules, and the mean decrease in the volume of thyroid nodules was from 2.13 ± 4.42 ml to 0.45 ± 0.90 ml, with a mean percent decrease of 0.65 ± 0.65. A volume-reduction ratio greater than 50% was observed in 82.3% (209/254) of index nodules, and 30.7% (78/254) of index nodules disappeared 6-month after the ablation. The treatment was well tolerated and no major complications were observed except pain and transient voice changes.

Conclusions: Microwave ablation seems to be a safe and effective technique for the treatment of benign thyroid nodules. Further prospective randomized studies are needed to define the role of the procedure in the treatment of thyroid nodules.

1. Introduction

Thyroid nodules are common and occur in up to 50% of the adult population [1]. Although most thyroid nodules are benign, some nodules require treatment for cosmetic reasons, subjective symptoms or anxiety about a malignant change [2]. Furthermore, if large compressive thyroid nodules are untreated, they may result in life-threatening conditions because of the potential acute onset of respiratory crisis [3].

The conventional treatments for thyroid nodules are levothyroxine medication, ethanol injection, laser ablation, radiofrequency ablation and thyroid surgery. However, both surgery and medication have drawbacks. Although surgery is curative, it can cause some problems such as upper airway obstruction, non-esthetic scars, injuries to the laryngeal nerves, iatrogenic hypothyroidism and so on. Moreover, the efficacy of thyroid hormone suppressive therapy is still controversial [4]. Therefore, non-surgical minimally invasive modalities, such as ethanol injection, laser ablation and radiofrequency ablation, have been attempted, yielding good results [5–7].

Microwave ablation is a minimally invasive technique that has been used to treat benign and malignant tumors [8–10]. In the thyroid gland, Bing Feng (Bing Feng, unpublished data) reported positive results for 11 cases of microwave ablation in benign thyroid nodules as an initial trial. Our study was to define the safety and effectiveness of microwave ablation using a larger series of 477 cases.

2. Materials and methods

2.1. Patients

A total of 477 thyroid nodules in 222 patients (58 male and 164 female, median age 50.7 ± 10.5, range 15–80 years) were treated with ultrasound-guided microwave ablation in our department from July 2009 to March 2012. 320 of the nodules were mainly solid, 136 mixed and 21 mainly cystic. In addition, 4 nodules developed in 2 patients were background of hyperthyroidism, with 5 nodules...
in Hashimoto’s thyroiditis as follows. This study is a retrospective study design, and a written informed consent was obtained from every patient before the procedure.

For the whole group of 222 patients we selected with the following inclusion criteria: (a) the presence of subjective symptoms (compressive symptom, neck discomfort, foreign body sensation); (b) ultrasound findings that remitted as a benign nodule; (c) unsuited or unwilling to undergo surgery; (d) anxiety about a malignancy. The exclusion criteria were: (a) ultrasound findings that remitted as a malignancy nodule (length diameter than transverse diameter, ill-defined margins, microcalcifications, marked hypoechoic) and (b) biopsy pathological results indicated malignancy.

2.2. Equipment

2.2.1. Microwave ablation instrument

The microwave unit (KY-2000, Kangyou Medical, Nanjing, China) consists of a microwave generator, a flexible low-loss coaxial cable and a cooled shaft antenna. The generator is capable of producing 1–100 W of power at 2450 MHz, in the form of pulse or continuous. The microwave antenna is 16G, needle type (1.9 mm in diameter and 3 or 5 mm in length) coated with polytetrafluoroethylene to prevent adhesion. To prevent shaft overheating, distilled water is circulated through dual channels inside the antenna shaft, continuously cooling the shaft.

2.2.2. Ultrasound system

Sonograms for thyroid nodules were performed with Toshiba 790A and GE LogiqE9 in terms of 2D, color doppler ultrasound and ultrasonic contrast, before ablation and at each follow-up.

2.3. Pre-ablation assessment

Before treatment all patients underwent the ultrasound examination, contrast-enhanced ultrasound and laboratory data, and an appropriate puncture route was chosen on ultrasound. Three largest perpendicular diameters of the nodules were measured by ultrasound immediately before microwave ablation and during each follow-up. The nodular volume was obtained by multiplying the three diameters of the nodules by 0.525 (ellipsoid volume). The composition of the nodules was assessed by ultrasound examiner subjectively, and was classified as mainly solid, mixed and mainly cystic type. The mainly solid nodules have a solid portion greater than 80%, while the mainly cystic nodules have a cystic portion greater than 80% (Fig. 1). The others were defined as a mixed type (Fig. 2).

Laboratory tests included thyroid tests (triiodothyronine [T3], free thyroxine [fT4], thyroid stimulating hormone [TSH]), complete blood counts and blood coagulation tests (prothrombin time, activated partial thromboplastin time). Patients on antiplatelet or anticoagulant treatment withdrew therapy 72 and 48 h before microwave ablation procedure, respectively.

2.4. Procedure

All the microwave ablations were carried out by the same operator (Shurong Wang) under ultrasound control with the same scanner. The patient was placed in the supine position with hyper-extended neck, and a venous catheter was inserted in a forearm vein. A multiparametric monitor was connected to the patient monitoring continuous electrocardiogram, PO2, breath rate and blood pressure. After localization of the best puncture site, local anesthesia with 2% lidocaine was performed subcutaneously. A mixture of 0.9% lidocaine and physiological saline was infused into the surrounding thyroid capsule to achieve a “liquid isolating region”, protecting the vital structures of the neck (carotid artery, trachea, esophagus, nerve) from the thermal injury (Fig. 1). Before microwave ablation, ultrasound guided biopsy was performed on all nodules. Then the internally cooled microwave antenna (16G) was positioned in the thyroid nodule along its short axis. During the microwave ablation, a power output of 30–50 W was usually used and the variations in the echo from the nodule were monitored by real-time ultrasound. The therapy was not stopped until the hyperecho covered the whole nodule. Then all patients underwent the second biopsy to assess treatment efficacy. For mixed/mainly cystic nodules, we performed microwave ablations only after aspiration of internal fluid.

After ablation, enhanced-contrast ultrasound was performed on every patient to investigate the boundaries of the included necrosis, thus evaluating whether the treatment was absolute or not. During the whole procedure, we intermittently asked the patients how they felt intended to assess the status of phonation.

2.5. Post treatment care

Microwave ablation was performed on an inpatient basis. At the end of the treatment, we evaluated the complications and kept the patients under observation for 30 min with compression of the neck lasting 15–20 min.

2.6. Follow-up evaluation

Ultrasound examination, laboratory tests and clinical symptoms were examined immediately after ablation. Ultrasound examinations (size, echogenicity, intranodular vascularity) were also performed at the 1, 3, and more than 6-month follow-up. However, our central concern for this study was the volume reduction ratio which was calculated by the following equation: volume reduction ratio (%) = [(initial volume – final volume) × 100]/initial volume.

A 6-month follow-up was achieved in 254 of 477 nodules, and the longest follow-up was as far as 24-month.

2.7. Analysis and statistics

Statistical analysis were performed using SPSS, version 16.0. Post-microwave ablation nodule volume recorded was compared with pretreatment volume by means of the Paired-samples t-test. Multiple linear regression was performed to assess the correlation between volume reduction ratio and the baseline volume. One-way ANONA (analysis of variance) was used to examine the relationship between the volume reduction ratio and the compositions of the nodule. Data were reported as mean ± S.D. and the significance was set at 0.05.

3. Results

The changes in the volume of the nodules before microwave ablation and at each follow-up period are summarized in Table 1. Before ablation the volume of index nodules was 2.13 ± 4.42 ml, and the volume of the nodules was 1.25 ± 2.34 ml, 0.74 ± 1.40 ml, 0.45 ± 0.90 ml at the 1-month, 3-month and 6-month follow-up (p < 0.01), respectively. All differences were statistically significant (Table 1 and Fig. 2).

Mixed nodules showed a significantly better treatment than the mainly solid nodules, similar tendencies were observed comparing the mainly cystic nodules against the mixed nodules (p = 0.000) (Fig. 3). Moreover, a significant inverse correlation was found between baseline volume and the volume reduction ratio after microwave ablation (r = −0.242, p = 0.026) (Fig. 4).
3.1. Ultrasound imaging

At baseline there were 320 nodules appeared mainly solid, 136 mixed and 21 mainly cystic. During the whole procedure, the microwave antenna was always clearly visualized with real-time ultrasound as a hyperechoic line. After ablation, color power doppler ultrasound showed a significant reduction of the vascular signals, as a result of necrosis induced by microwave ablation. Also non-enhancement was showed on enhanced-contrast ultrasound (Fig. 5).

Though the echogenicity of the nodule was increased obviously at the end of the procedure, it was lower than that observed before ablation on the follow-up ultrasound examination.

3.2. The related clinical changes

Treatment was well tolerated. A mild sensation of heat in the neck was experienced by most patients, whereas, no one claimed the procedure to stop. 8 patients (3.6%) complained of voice changes, all recovering within 3 months spontaneously. Choking and coughing at the end of treatment was present in 12 individuals, but this disappeared without any treatment, 8 patients within 24 h, 4 a week respectively. No tranquilize medicines were given before or after ablation. No cases of local infection, skin burning or damage to the vital structures of the neck were observed, and the needle tracks were all recovered within one week. Prior to microwave ablation treatment, 2 patients had hyper-thyroidism, the T3, T4 decreased significantly at the subsequent one month follow-up, and the clinical symptoms alleviated as well.

Ultrasound guided biopsy performed immediately after the ablation showed somewhat carbonization with naked eyes (Fig. 5), and the light microscopy shows a reduction of thyroid follicle in the coagulative necrosis, with the follicular epithelium contracted the epithelium cell nucleus shrunked and solidified obviously (Fig. 5).
The number, size, and symptoms relating to thyroid nodules all tend to increase as years go by, spoiling quality of life [3]. The conventional treatments for thyroid nodules include levothyroxine medication, ethanol injection, laser ablation, radiofrequency ablation and thyroid surgery. Levothyroxine therapy inducing thyroid suppression is a common option for thyroid nodules. However, only a few patients achieve a significant reduction of nodule size, what’s worse, the medication may cause seriously side effects such as trial fibrillation or reduced bone density [11]. Though thyroid surgery can remove the nodule itself and the fear of malignancy, it usually causes some adverse effects, for instance, scar formation, wound infection, iatrogenic hypothyroidism and recurrent laryngeal nerve palsy [12].

Since the first trial of ethanol injection to thyroid cystic in 1990 [13], it has been used as an alternative treatment in various benign thyroid diseases. They reported that the mean volume reduction ratio was 43–65% at a 4.4-to-24 month follow-up [6,14]. However the ethanol treatment has some drawbacks. Multiple sessions of treatment are needed to obtain a total cure. With the increasing of sessions, the risk of complications increases as follows [15]. Furthermore, alcohol leakage can cause extra glandular fibrosis and local pain.

By contrast, the thermal ablation such as laser and radiofrequency ablation is generally controllable. Besides, the thermal
Ablation usually needs only one session of treatment to achieve cure totally, making it more cost-and time-effective.

Another way to induce thyroid tissue necrosis by heat is microwave ablation, as demonstrated by Wright et al. [16] in a feasibility study in experimental animals. So far, only Bing Feng et al. have reported a preliminary experience with this technique to handle thyroid nodules.

The thermal ablations use some degree of heating to destroy tissue, obtaining variable nodule volume reduction. On the basis of the reports, the mean volume reduction ratio of laser, radiofrequency and microwave ablation was 44.0–62% [7,17,18], 50.9–84.1% [5,19,20] and 45.99% (Bing Feng, unpublished data) respectively. In our study, the mean nodule volume reduction ratio was 65 ± 65% at the 6-month follow-up with 30.7% (n = 78) index nodules disappearing. Regarding microwave ablation, Bing Feng et al. reported that mixed/mainly cystic nodules showed a better treatment response than the mainly solid tumors. This might be due to the homogeneous conduction of heat, the absence of a heat sink effect and removal of the cystic component. In our study, the mixed nodules decrease in volume more than the mainly solid ones, and the mainly cystic nodules got a better treatment than the mixed ones. The results seems to be similar to the findings above. Besides, we also discovered that better volume reduction rate was obtained in smaller nodules than in bigger ones. However, the reason was still remain unknown and further trials were needed to answer the question.

Thermal injury to the recurrent laryngeal nerve injury is a serious complication. Reports by thyroid surgeons show that recurrent laryngeal nerve injury occurs temporarily in up to 2.3–9.8% of cases and permanently in 1.1–2% [12]. Similarly, in ethanol, laser ablation and radiofrequency ablation the incidence of transient was
0–3.3% [6,13,14], 0–8% [7,17,18] and 0–3.3% [5,19,20], respectively. No permanent nerve injury cases happened.

In our study, there were 8 patients (3.6%) complained of voice changes, thus the incidence was not very different from that reported from other modalities. But it was much lower than the results of Bing Feng et al. According to our analysis, the lower rate might due to the formation of the “liquid isolating region” which can protect the nerve from thermal injury.

5. Conclusions

Microwave ablation can achieve shrinkage of nodule size and relief of clinical symptoms. Side effects and failures were few although not negligible. Microwave ablation seems to be a safe and effective technique for the treatment of benign thyroid nodules. Further prospective randomized studies are needed to define the role of the procedure in the treatment of thyroid nodules and explorations about the immunological reaction of microwave ablation are all necessary.

Role of the funding source

This work was supported by the Shandong Province Science and Technology Development projects (item numbers: 2011YD18028 and the Yantai Science and Technique Plan (item numbers: 2010156).

Competing interest statement

No competing interests.

References