Original Article
Clinical study of ultrasonic guided percutaneous microwave ablation in the treatment of benign thyroid nodules with a one-year follow-up

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Abstract: Objective: The aim of this study was to investigate the efficacy and safety of ultrasound guided microwave ablation (MWA) with “moving-unit ablation and continuous fluid isolation” in the treatment of benign thyroid nodules. Methods: A total of 65 patients with benign thyroid nodules (98 nodules) were treated from October 2015 to June 2017. They were treated by MWA with “continuous fluid isolation and moving-unit” under ultrasonic guidance. All patients were subjected to measuring of preoperative and postoperative 1, 3, 6, and 12-month values of nodule volume-reduction ratios (VRR), largest diameter, FT3, FT4, TSH, and complication rates. Results: A total of 98 nodules underwent ultrasound-guided MWA, smoothly. Thyroid nodules were significantly decreased in size after MWA. Preoperative maximum diameter of the nodules was 2.95 ± 0.54 cm and the volume was 5.32 ± 2.08 cm³, values were 1.47 ± 0.61 cm and 1.12 ± 0.67 cm³ twelve months after the operation (P < 0.01, respectively). At postoperative 1, 3, 6, and 12 months, VRRs were 11.85%, 29.07%, 60.23%, and 78.86% (P < 0.01). Thyroid function status was normal at postoperative 1, 3, and 6 months (P > 0.05). Conclusion: With ultrasound guidance, MWA with “continuous fluid isolation and moving-unit ablation” for treatment of benign thyroid nodules is safe and effective. It is minimally invasive with fewer complications.

Keywords: Thyroid nodules, ultrasonic guided, microwave ablation

Introduction
Thyroid nodules are a common occurrence in the general population. Thyroid goiter occurrence is growing. Thyroid nodule detection rates can be as high as 76%, according to ultrasound scans in the general population, especially in the context of multinodular goiters [1, 2]. Most thyroid nodules are benign, with cancer occurring in approximately 7-15% of cases [3, 4]. Asymptomatic benign nodules thyroid nodules (BTN) generally do not require any treatment but are monitored by clinical ultrasound examinations. However, treatment can be necessary for subjective symptoms, cosmetic concerns, or patient fears concerning malignant transformation [3]. Subtotal thyroidectomy has been the primary treatment for large goiters. Most patients undergoing surgery have a permanent scar in the neck with greater psychological iminations. In addition, these patients need to take levothyroxine after surgery to prevent hypothyroidism. They may develop adverse effects, such as atrial fibrillation and reduction of bone density [5].

Microwave ablation (MWA) is minimally invasive technique used for thermal tissue ablation. Compared with radiofrequency ablation (RFA) and percutaneous laser ablation (PLA), percutaneous microwave ablation (MWA) has the advantages of fast heating up, strong coagulation ability, large solidification range, and high stability [6]. With the development of intelligent
microwave ablation needles, mobile ablation has become safer. Multiple nodules can be ablated with the maximum normal thyroid tissue retained. This is not possible with endoscopic surgery [7-9].

Because of the diversity of thyroid benign nodes and the diversity of populations in China, there are no China expert guidelines on thermal ablation for thyroid benign nodes. Microcarcinoma and metastatic cervical lymph nodes can be found. Only Zhejiang Province expert consensus on thermal ablation for thyroid benign nodes, microcarcinoma, and metastatic cervical lymph nodes (2015 edition) exists in China. Objective data is urgently needed. Therefore, the present study aimed to analyze the clinical data of 98 cases of benign thyroid nodules, retrospectively, estimating the efficacy, safety, and complications of “moving-unit ablation, and continuous fluid isolation” under ultrasonic guided MWA in the treatment of benign thyroid nodules.

Materials and methods

Patients

A total of 65 patients with 98 benign thyroid nodules were selected from October 2015 to June 2017. There were 23 males and 42 females, aged 16–76 years, with an average age of 38.7 ± 13.1 years. All patients received MWA treatment under ultrasonic guidance [7, 10].

Inclusion criteria were based on expert consensus concerning thermal ablation for thyroid benign nodes, microcarcinoma, and metastatic cervical lymph nodes (2015 edition) [12]: 1) Subjective symptomatic or cosmetic problem; 2) Refusal of or ineligible for surgery; 3) Ultrasound anatomy structure less clear; and 4) Abnormal coagulation function.

A total of 87 cases of nodular goiters and 11 cases of thyroid adenoma were confirmed by pathological diagnosis though preoperative ultrasound guided 18 G bard biopsies.

Ultrasound assessment and laboratory evaluation

All patients underwent preoperative ultrasound assessments, including location of thyroid nodules, quantity, size, internal structure, and metastasis of suspicious lymph nodes.

Three orthogonal in diameter of each thyroid nodule (thyroid nodule maximum diameter and vertical diameter of other two) was measured. The proportion of the nodules maximum diameter (A) and a cross section of two vertical diameter nodules (B and C), preoperative nodule volume V, was calculated as follows.

\[ V = \frac{\pi \times a \times b \times c}{6} \]

Complete thyroid hormone status was observed, including thyroid stimulating hormone (TSH), free T3 (FT3), free T4 (FT4), thyroid peroxidase antibody (TMAb), thyroglobulin antibody (TGab), platelet count (PLT), prothrombin time (PT), and activated partial thromboplastin time (AT-PP).

All patients were examined with postoperative 1, 3, 6, and 12-month assessments, including thyroid ultrasound examinations and laboratory tests.

Microwave ablation equipment

Microwave ablation instrumentation (KY-2000 Kangyou Medical, Nanjing, China) included a...
microwave generator, flexible low-loss coaxial cable, and cooled shaft antenna. The microwave generator released 1 to 100 W of power at 2450 MHz. The internally cooled needle microwave antenna was KY-2450A-1 and 16-gauge. Microwave emission length was 3 mm and coated with polytetrafluoroethylene to prevent adhesion. To prevent overheating of the shaft and to avoid skin injuries, chilled distilled water was circulated by a peristaltic pump through dual channels inside the shaft and the bar temperature of the microwave antenna was kept stable at 28-32°C. BK-FF800 color Doppler ultrasonic diagnostic instrument (BK company, Denmark) was used for image guidance, with a probe frequency of 3–12 MHz.

Procedure

Each patient was positioned supine with the neck in a mild extension. A venous catheter was inserted into a forearm vein before ablation. Parameters, such as PO$_2$, continuous electrocardiograms, breath rates, and blood pressure, were monitored by a multi-parametric monitors.

According to thyroid nodule sizes, locations, and internal components, the best puncture routes and ablation methods were selected. Local anaesthesia with 2% lidocaine was performed subcutaneously at the location, needle path, and anterior and lateral surface of thyroid gland isolation zone between true and false envelope. Saline was injected into the posterior envelope clearance of the thyroid gland. With a connected tube, liquid isolation with a width greater than 3 mm was continued to prevent thermal damage [7]. According to nodule location, a needle was inserted at the midpoint of clidomastoid and beside the trachea. A power output of 20 to 40 W was used during MWA. Under guidance, MWA was performed along with moving-unit ablation (MUT), which has been proven effective in ablation of thyroid nodules [10].

Thyroid nodules were assumed to be multiple units. Ablation was taken from one unit to another (Figure 1, U1-U2-U3). Needle was inserted into the deep border of lower edge plane, then pulled out from deep to shallow while the ablation formed a “line”. A needle was inserted into the “line” to take ablation in the same plane. Planar ablation was completed by repeating the ablation process, then formed a “surface”. Ablation of the other “surfaces” of the nodules was completed from the bottom to up and formed a “body”. Finally, ablation of the entire nodule was completed. Aspiration to cystic or cystic mixed nodules was taken before ablation and multi-point and multi-faced ablation was taken until the nodules were completely covered by a strong echogenic mass of heat.

If the thyroid nodule was larger, the nodule bipolar was ablated first, then the body to avoid thermal interference [13]. After ablation, the region (nodule and surrounding 0.1–0.5 cm) turned into a short hyperechoic region. The ablation range was larger than the actual volume of the nodule. Ultrasonic contrast showed the nodule filling defect area larger than the original nodule enhancement area to ensure nodules were ablated completely. Nodular tis-
Ultrasonic guided percutaneous microwave ablation to treat benign thyroid nodule

Table 1. Changes in thyroid nodule volume before and after MWA (n = 98, X ± S)

<table>
<thead>
<tr>
<th>Time</th>
<th>Maximum diameter (cm)</th>
<th>Volume (cm³)</th>
<th>VVR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before MWA</td>
<td>2.28 ± 0.56</td>
<td>3.52 ± 0.31</td>
<td>-</td>
</tr>
<tr>
<td>1 month after MWA</td>
<td>2.11 ± 0.25</td>
<td>3.09 ± 0.27</td>
<td>17.11 ± 2.28</td>
</tr>
<tr>
<td>3 months after MWA</td>
<td>1.26 ± 0.32*</td>
<td>1.52 ± 0.45*</td>
<td>58.78 ± 3.61*</td>
</tr>
<tr>
<td>6 months after MWA</td>
<td>0.71 ± 0.18*</td>
<td>0.78 ± 0.24*</td>
<td>77.26 ± 3.78*</td>
</tr>
<tr>
<td>12 months after MWA</td>
<td>0.43 ± 0.51**</td>
<td>0.44 ± 0.11**</td>
<td>89.82 ± 2.84**</td>
</tr>
</tbody>
</table>

F P Compared with before MWA. *P < 0.05; **P < 0.01.

Table 2. Changes in thyroid function before and after MWA (n = 55, X ± S)

<table>
<thead>
<tr>
<th>Time</th>
<th>FT3 (µmol/L)</th>
<th>FT4 (µmol/L)</th>
<th>TSH (mIU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before MWA</td>
<td>6.43 ± 1.14</td>
<td>19.51 ± 2.27</td>
<td>2.25 ± 0.47</td>
</tr>
<tr>
<td>1 month after MWA</td>
<td>6.57 ± 1.39</td>
<td>20.14 ± 2.15</td>
<td>2.31 ± 0.52</td>
</tr>
<tr>
<td>3 months after MWA</td>
<td>6.28 ± 1.07</td>
<td>19.54 ± 1.36</td>
<td>2.37 ± 0.22</td>
</tr>
<tr>
<td>6 months after MWA</td>
<td>6.33 ± 1.56</td>
<td>21.16 ± 1.05</td>
<td>2.19 ± 0.72</td>
</tr>
</tbody>
</table>

FT3: free triiodothyronine; FT4: free thyroxine; TSH: thyroid-stimulating hormone. The normal range of thyroid function in our hospital: FT3 3.5-6.5 (µmol/L); FT4 11.5-23 (µmol/L); TSH 0.55-4.78 mIU/L.

Follow-up

Thyroid nodule volume, maximum diameter, and other indicators were evaluated at 1, 3, 6, and 12 months after MWA treatment. Calculation formula of volume reduction rate (VRR) of thyroid nodules was:

\[ VRR = \frac{\text{initial thyroid nodule volume - final thyroid nodule volume}}{\text{initial thyroid nodule volume}} \times 100\% \]

VRR > 50% was regarded as successful treatment at follow-up. Thyroid function was reexamined (TSH, FT3, FT4) 1 month after the operation.

Statistical analysis

SPSS19.0 statistical software (SPSS Inc., Chicago, IL) was used for data analysis. Measurement data are expressed as mean ± SD. ANOVA was used to compare data from different groups. Student’s t-test was used to compare data between thyroid nodule volume and thyroid function before and after ablation. P-values less than 0.05 are considered to be significant.

Results

In this study, a total of 98 benign thyroid nodules, in 65 patients, were successfully treated under ultrasound guided MWA. All nodules after ablation showed high gasification echo changes, and hypoechocic a few minutes later. Contrast-enhanced ultrasonography showed no contrast agent filling and the nodules were completely ablated. Sonographic findings before and after MWA are shown in Figures 2 and 3.

Changes in nodule volume after MWA

At 3 months, 6 months, and 12 months after the operation, the volume of thyroid nodules was significantly smaller than before MWA (P < 0.01 respectively). VRR was significantly lower than before MWA (P < 0.01 respectively). Three months after MWA, 15 nodules with sizes...
between 0.8~1.2 cm disappeared. Nodules size of 5.6 cm × 3 cm × 2.8 cm with VRR 33.2% showed no internal blood flow signals, but the peripheral blood flow signals were normal. Twelve months after MWA, 35 nodules sized 1.9~2.9 cm disappeared. Results are shown in Tables 1 and 2.

Complications

There were 3 cases of intra-operative bleeding, 1 case of bleeding after aspiration, and 2 cases of accidental bleeding. Guided hemostasis ablation was timely.

In 4 cases (6.15%), intra-operative blood pressure increased, up to 21.9~25.3 kPa or 13.0~14.4 kPa.

Nitroglycerin dropped to regulate blood pressure (regulating changes of blood pressure). Ablating was continued after returning to normal.

There were 11 cases of neck pain (16.92%), with immediate relief after the operation.

There were 25 cases of neck swelling (38.46%). No hematoma was detected by ultrasonic scanning.

There were 3 cases of mild dyspnea after 2 sides thyroid focuses ablation (4.61%). Oxygen supply was increased. This was relieved after intravenous injections of aminophylline and dexamethasone. Patient returned to ward and was discharged the next day.

There was 1 case of laryngeal never injury. The voice recovered within 10 postoperative days.

There were 9 cases spreading of pain towards to the root of ears, disappearing 1~2 days postoperatively.

No burns of skin, infections, or post-operation hemorrhages were reported.

No discomfort was reported at follow-up.

Discussion

Thyroid nodules are common. If treatment is needed, traditional surgery remains the most common treatment. Thyroid nodules are characterized by multiple nodules, with a size disparity and dispersed location. However, with open surgery, it is difficult to resect small nodules [14]. Open surgery has great trauma and postoperative recurrence. It is easy to damage normal thyroid function. Thyroxine replacement therapy after the operation often causes adverse consequences, such as osteoporosis in postmenopausal women, along with cardiac hypertrophy, fibrillation atrial, and reduction of bone density [5, 15].

With the transformation of the medical model and development of minimally invasive precision medical technology, patients not only have the desire to cure tumors but also hope to keep the beauty of the neck and thyroid function as much as possible. Therefore, treatment of thyroid nodules has gradually developed in a minimally invasive manner. MWA is a newly developed percutaneous thermal ablation technique. Compared with RFA and PLA, MWA produces more energy and has the advantages of large ablation range, short treatment time, and more complete tumor inactivation. It can be used in the treatment of larger volumes of thyroid nodules and multiple nodules [16, 17].

Feng et al. [10] used MWA to treat 11 cases of benign thyroid nodules, followed up for 1~9 months. Results showed that VRR was 45.99% and postoperative thyroid function of all patients remained normal. This indicated that MWA has a high reliability and security in benign thyroid nodule treatment. Liu and colleagues [18] researched ultrasonic guided MWA, treating 308 patients and 324 benign thyroid nodules. Follow-up showed that VRRs at 3 months, 6 months, and 12 months after treatment were (37.26 ± 78.84)% , (64.22 ± 43.37)% , and (82.19 ± 21.93)% , showing a remarkable curative rate. The present study researched ultrasonic guided MWA, treating 65 patients with total 98 benign thyroid nodules. Follow-up showed that VRRs at 1, 3, 6, and 12 months after treatment were 11.85%, 29.07%, 60.23%, and 78.86%. Nodules decreased obviously, in accord with previous research results [18]. No thyroid function changes were noted statistically at 1 month after MWA, compared with before MWA. No patients had severe complications during or after the operation.

Ultrasonic guided MWA thermal ablation did not disturb the normal thyroid tissue in the
maximum extent. Ablation treatment is located accuracy.

TSH, FT3, and FT4 are active parts of thyroid hormones, directly reflecting the functional status of the thyroid gland. Results showed no significant changes in thyroid hormones before and after the operation, indicating that microwave ablation had no effects on patient thyroid function.

The thyroid gland is rich in blood circulation and nerves are densely distributed. Thus, the safety of MWA for treatment of thyroid nodules is an important key factor for its popularization and application. Incidence of recurrent laryngeal nerve injuries caused by radiofrequency ablation and laser thermal ablation for thyroid nodules is 2-4% [19]. Avoiding heat damage to important structures around the thyroid gland is very important. The most common methods of protecting the neck structures are “incomplete ablation”, “lever pry”, and “liquid isolation” [20]. This study was guided by real-time ultrasound monitoring. The needle was inserted at ablation pathway of midpoint beside trachea, using “moving-unit ablation (MUT)” and “continuous fluid isolation technology”. Advantages are as follows: better mobile ablation flexibility, the size of the ablation unit can be adjusted by the movement of the tip of the needle, and thermal damage can be avoided to the vital structures around the thyroid gland to the maximum extent. MUT ablation of thyroid nodules, followed by “line-surface-body” model, could reduce or avoid an incomplete nodule ablation. Liquid isolation must be formed continuously during ablation, with continuous infusion of saline, forming a 3-5 mm “isolation zone” in the medial or lateral space of the thyroid gland nearby the tracheal esophageal groove. Liquid isolation is helpful for the prevention of injuries of the great vessels, recurrent laryngeal nerves, the trachea, and the esophagus. Bipolar MWA is also a safe and effective treatment for benign thyroid nodules [13]. Only 1 patient had transient hoarseness, occurring in the early stages of the ablation technique. The energy of microwave ablation is relatively high and absorption time of liquid isolation zone is short. Thus, heat transferred to recurrent laryngeal nerves and caused transient thermal injury. Neck swelling was most common after microwave ablation. There were 25 cases in the study. The reason was subcutaneous dropsy caused by injections in the neck of lidocaine and saline as “isolation fluid”. Discomfort was caused by temporary enlargement after thyroid nodules ablation. All nodules were close to the thyroid anterior capsule. High frequency ultrasound can detect and guide the hemostasis of the bleeding point in time with good effects. With intraoperative monitoring, adverse reactions can be detected in time (such as elevated blood pressure, voice changes, bleeding). Moreover, high frequency ultrasound can guide properly with better control.

In summary, ultrasound guided MWA with “continuous fluid isolation” and “moving-unit ablation (MUT)” treatment is safe and effective in the treatment of benign thyroid nodules. It has advantages of less trauma, fewer complications, quicker recovery, and little physiological interference to the patient. There are no scars after the operation and it is worth popularizing in clinical practice.

Disclosure of conflict of interest

None.

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