Microwave Ablation for Papillary Thyroid Cancer With Cervical Lymph Node Metastasis

Zhen-Long Zhao
China-Japan Friendship Hospital

Ying Wei
China-Japan Friendship Hospital

Xiao-Jing Cao
China-Japan Friendship Hospital

Li-Li Peng
China-Japan Friendship Hospital

Yan Li
China-Japan Friendship Hospital

Shu-Rong Wang
China-Japan Friendship Hospital

Jian-Qin Guo
China-Japan Friendship Hospital

Ming-an Yu (yma301@163.com)
Department of Interventional Ultrasound Medicine, China-Japan Friendship Hospital, Beijing, China
https://orcid.org/0000-0003-0797-4564

Research

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Abstract

Background: To evaluate the feasibility and safety of microwave ablation (MWA) for PTC with metastatic cervical lymph nodes who are ineligible for or refuse surgery.

Materials and Methods: Twenty patients of unifocal PTC with metastatic cervical lymph nodes from three hospitals were enrolled in this study, and MWAs were performed. Contrast-enhanced ultrasound was used to evaluate the extent of ablation. The volume of the ablated area and thyroid hormones were measured.

Results: PTC nodules in 9 patients completely disappeared at the end of follow-up. Compared with the volume before ablation, the mean volume reduction ratio of ablated lesions was 0.414 ± 0.700 (range: -1.92-0.95) at postoperative 6 months. The patients' thyroid function tests were normal at the end of follow-up. New lymph node metastasis was found in one patient during follow-up visits and she underwent a second MWA procedure. For the other patients, no new PTC nodule, local recurrence or cervical lymph node metastasis were suspected on ultrasound by the end of follow-up. No distant metastasis was encountered during the follow up. None of the patients developed hypocalcemia, permanent hoarseness or skin burns.

Conclusions: MWA is a minimal invasive and safe method in treating PTC with cervical lymph node metastasis.

Background

In recent years, thyroid cancer incidence has been increasing rapidly [1]. Although papillary thyroid cancer (PTC) is indolent, cervical lymph node metastasis (CLNM) is often encountered in PTC patients, with an incidence of approximately 35% macroscopically before surgery, and 80% microscopically in the specimens of cervical lymph nodes dissection (McHenry and Stulberg 2014) Although some studies reported that CLNM has no effect on prognosis [3], several recent studies reported that it is associated with local recurrence and distant metastasis and requires prompt treatment [4, 5]. Surgical management of PTC with cervical lymph node metastasis includes thyroidectomy with central compartment neck dissection (CCND), modified radical lymph node dissection and berry picking [6]. Generally, CCND needs extended surgical field with an increased surgical trauma and some elderly patients or patients with scar diathesis could not tolerate or are unwilling to undergo surgery. Besides, a few patients still suffered locoregional recurrence with an incidence of 37.2% after lymph node dissection[7]. Although modified radical lymph node dissection and berry picking has relatively smaller influence on the cervical lymphatic system and less complications [6], the surgical trauma is still large in case of multiple region metastasis. Therefore, for patients with multiple underlying diseases or cosmetic needs, a less invasive method of treating PTC with lymph node metastasis is needed.

Several investigators have reported that thermal ablation is safe and effective in treating low-risk papillary thyroid microcarcinomas [8–10] and metastatic lymph nodes[11–14]. Until recently, the beneficial role of MWA on PTC with CLNM hasn't been investigated. In present study, MWA was employed
to treat PTC with CLNM for patients who were ineligible or refused surgery. The aim of the present study was to evaluate the feasibility and safety of MWA for PTC with CLNM.

**Methods**

Our retrospective study was approved by the institutional review boards of the hospitals participating in the study. Written informed consent was obtained from each patient before the ablation procedure. The patients consented to publish their examination results and radiological images anonymously.

**Patients**

The clinical data of PTC patients with CLNM who underwent microwave ablation between January, 2013 and September, 2019 from 3 hospitals were retrospectively reviewed. In our practice, surgery was initially recommended to treat PTC with CLNM. The inclusion criteria were (i) patients with single PTC diagnosed by ultrasound (US)-guided fine-needle aspiration biopsy (FNAB); (ii) CLNM was suspected by conventional US or contrast-enhanced ultrasound (CEUS) and diagnosed with FNAB. (iii) patients were ineligible for surgery due to a high risk of general anesthesia (atrial fibrillation) and/or refused to undergo surgery (scar diathesis). (iv) The patient was followed up for at least 12 months. (v) Patients with long-term use of anticoagulant drugs were required to discontinue the medication at least 7 days before treatment. The exclusion criteria were (vi) distant metastasis was revealed by US and/or CT examinations; (vii) patients had severe blood coagulation disorder or serious cardiopulmonary disease. (viii) patients refused to sign informed consent.

**Preablation assessment**

Complete blood count, coagulation and thyroid function (TT3, TT4, fT3, fT4, and thyroid stimulating hormone [TSH]) tests were performed before treatment. Before MWA, three orthogonal diameters (the largest diameter and two perpendicular diameters) of each PTC nodule and largest diameter of metastatic lymph nodes were measured. The location, echogenicity, internal architecture, contour, shape (ratio of height/width) of the PTC nodule and lymph nodes were carefully evaluated using US. Tumor volumes were calculated using the following equations: \( V = \frac{\pi abc}{6} \) (\( V \) as volume, \( a \) as the largest diameter, and \( b \) and \( c \) as other two perpendicular diameters) and volume reduction ratio (VRR) = (initial volume - final volume)/initial volume. The change of lymph nodes was calculated with maximum length reduction ratio (LRR) = (initial maximum diameter - final maximum diameter)/initial maximum diameter.

**MWA Procedure**

MWA was performed by radiologists with more than 5 years of experience in MWA for thyroid nodules and malignant lymph nodes. Before MWA, intravenous access was obtained via an antecubital vein. Electrocardiography monitoring and pulse oximetry were routinely applied. Patients were placed in a supine position with the neck extended. After the neck was sterilized and locally anesthetized, an 18G core needle connected with an extension tube was inserted into the tissue spaces between the thyroid and adjacent structure like recurrent laryngeal nerve (RLN) and trachea along the thyroid capsule.
precisely guided by US. Then normal saline (NS) isolating fluid was injected to increase the distance between thyroid lobe and critical structures to at least 5 mm. After isolation, 0.5% lidocaine was injected along the thyroid capsule for analgesia. A cooled MWA antenna (17 G) with a 0.4 cm tip (Intelligent Basic Type Microwave Tumor Ablation System, Nanjing ECO Microwave System, Nanjing, China and Microwave Ablation System KY2000-915, Nanjing Kangyou Biological Energy Co. Ltd) was inserted freehand into the PTC nodule under US guidance. The power of ablation was 30W. The strategy of multiple point ablation was adopted. The sequence of ablation was first the rear edge, then the lateral edge, and followed by center as well as front edge of the ablation target, which could avoid the influence of hyperechoic thermal field on needle adjusting. For complete ablation of PTC nodule, the ablation zone must cover the whole tumor and extend at least 2 mm over the edge of tumor. The ablation was suspended if the patient coughed due to heat stimulation. After the thyroid nodule was ablated, the core needle was then inserted freehand into the tissue beside the metastatic lymph nodes guided by US and the needle tip was placed just outside the capsule of lymph nodes. The isolating fluid was injected to separate the lymph node from the surrounding critical structures like cervical vessels and nerves. The thickness of ring-like isolation band is at least 5 mm around the target lymph node. After adequate isolation, The MWA antenna was inserted freehand into the center of metastatic lymph nodes. The power was 30W. The strategy of multiple point ablation was adopted. To avoid heat injury to critical structures, at one ablation point, the radiation time of microwave is less than 15 s each time with a 5 second interval. During the ablation, the isolating fluid was continuously injected to maintain the thickness of isolation band and prevent heat injury. For lymph nodes, the ablation was terminated after the ablation zone covered the whole lymph node. The area of ablation zone was first evaluated with conventional US. The ablation zone is a mixed or hyperechoic area which covered the PTC nodule and lymph nodes on conventional US. Two minutes after ablation, CEUS was performed to further evaluate ablation effect. A complete ablation was defined as the non-enhancement ablation zone completely covered the PTC nodule and extended at least 1–2 mm from the tumor margin, and completely covered the metastatic lymph nodes on CEUS. An additional ablation was performed immediately if there was nodular enhancement inside ablation zone or the extended distance was less than 1–2 mm for the PTC nodule. The process of the procedure is shown in Fig. 1 and Fig. 2. At the end of the procedure, the puncture point was compressed for 30 minutes, and the patient remained under observation for an additional 2 hours in case of possible complications.

Follow-up

At clinical follow-up, US and thyroid function test were performed, as well as clinical evaluations at 6, 12 months and every 6 months thereafter. The patients underwent chest CT every year to screen metastasis.

Conventional US was performed to detect the developments of new PTC nodule, local recurrence and possible metastatic lymph nodes. The sizes of the ablation zone of PTC nodule and metastatic lymph nodes were measured by US. Local recurrence was suspected if nodular hypoechoic lesion was revealed by US at the edge of ablation zone. CEUS and US-guided FNAB were performed to evaluate the abnormal lesion suspected of local recurrence, new PTC nodule or metastatic lymph nodes.
Statistical methods

Statistical analyses were performed using SPSS version 24.0 (IBM, Armonk, NY, USA). Data were presented as mean ± standard deviation (SD), and the median and 25–75% interquartile range (IQR) was used if data did not fit a normal distribution. The results of thyroid function tests before and 1 day after thermal ablation were compared by paired t-test. Differences were considered significant when P < 0.05.

Results

As a result, 20 patients from three hospitals were enrolled in this study, including 7 men and 13 women aged 29–68 years (average: 43 ± 9 years). Three patients refused surgery because of scar diathesis. Seventeen are ineligible for surgery because of high risk of general anesthesia due to cardiovascular diseases. A total of 10 PTC nodules were detected on the left lobe and 10 on the right lobe; the maximum tumor diameter was 0.4–2.5 cm (average: 0.95 ± 0.47 cm). The metastatic lymph nodes distributed in the thyroid area. The maximum lymph node diameter was 0.4–2.5 cm (average: 0.94 ± 0.43 cm). The clinical characteristics of these 20 patients with PTC are summarized in Table 1.
Table 1
The clinical characteristics of the 20 patients of papillary thyroid cancer with CLNM

| Characteristics          | Description      | Nodules, n(%) |
|--------------------------|------------------|--------------|
| Maximum diameter (cm)    | ≤1               | 14(70%)      |
|                          | 1–2              | 5(25%)       |
|                          | >2               | 1(5%)        |
| Location                 | Left lobe        | 10(50%)      |
|                          | Right lobe       | 10(50%)      |
| Echogenicity             | Hypoechoic       | 19(95%)      |
|                          | Mixed echoic     | 1(5%)        |
| Malignant signs          | Lobulated shape  | 5(25%)       |
|                          | Microcalcifications | 18(90%) |
|                          | Extending the capsule | 2(10%) |
| Concurrent thyroid disease | Nodular goiter | 19(95%)     |
|                          | Hashimoto's thyroiditis | 2(10%) |
| Adjacent structures      | Adjacent to nerve | 4           |
|                          | Adjacent to trachea | 1           |
|                          | Adjacent to esophagus | 1          |
| Number of CLNM           | ≤3               | 15           |
|                          | 3–6              | 3            |
|                          | >6               | 2            |
| Region of CLNM           | Ipsilateral      | 19           |
|                          | Bilateral        | 1            |

Note: CLNM = cervical lymph node metastasis

Based on the CEUS result after ablation, complete ablation of PTC nodule and all metastatic lymph nodes was achieved in all 20 patients in one procedure. The technical success rate was 100%. The median ablation time was 232.2 seconds (78–570 seconds). Four patients have been followed for more than 48 months, two for more than 36 months, two for more than 24 months and twelve for more than 12 months. The median follow-up time was 21.5 months.
At the end of follow-up, PTC nodules in 9 patients (45%) completely disappeared, in which 2 nodules at the 12th month and 7 at 18th to 26th month. The median volume of target PTC lesions before ablation was 0.18 cm$^3$ (range: 0.03–3.93 cm$^3$), and the median volume was 0.06 cm$^3$ (range: 0.01–3.04 cm$^3$) at postoperative 6 months. The mean VRR was 0.414 ± 0.700 (range: -1.92-0.95) at postoperative 6 months. There was no statistical difference between thyroid function before ablation and thyroid function one day after ablation (P > 0.05). New metastatic lymph nodes were encountered in one 36-year-old female patient during the follow-up. Her PTC nodule was 2.5cm × 2.0cm × 1.5 cm in the right lobe with 3 metastatic lymph nodes in the right and region. She had 7 suspicious metastatic lymph nodes in the , , , and region at the 6th month follow-up. One of the suspicious lymph nodes was punctured and confirmed of metastasis by FNAB. She refused surgery again and underwent a second MWA procedure and all 7 lymph nodes were ablated successfully. No other metastatic lymph node was suspected at the last and 24th month follow-up. For the other patients, no new PTC nodule, local recurrence or cervical lymph node metastasis were suspected on US by the end of follow-up. No distant metastasis was encountered during the follow up.

As for complications, eight patients had neck edema and recovered within 7 days. Five patients had transient hoarseness and recovered within 3 days. Three patients had neck slight hematoma and recovered within 3 days after ablation. None of the patients developed hypocalcemia, permanent hoarseness or skin burns. None of the patients had bilateral vocal cord paralysis during the follow up.

Discussion

Thyroidectomy with CCND has been used for decades of years for PTC with CLNM, and the therapeutic effect of it has been demonstrated in several studies [15]. However, considering the surgical trauma of CCND and the negative effect on life quality in case of complications, it’s difficult to perform CCND on patients with multiple underlying diseases who are at high risk of death due to complications. It is reported in many studies that CLNM was common in PTC patients with clinically node-negative neck [16–18], and there was no difference in recurrence rates between patients undergoing thyroidectomy and thyroidectomy with prophylactic CCND [15, 18, 19]. Therefore, it is reasonable that the removal of imaging visible PTC metastatic lymph nodes alone may also be feasible for the prevention of recurrence.

Several studies on the thermal ablation of PTC have shown promising result regarding the safety and effectivity [8, 10]. A few other studies have a preliminary proof on the effectivity of thermal ablation of metastatic lymph nodes after surgery [13, 20]. These above results have demonstrated that thermal ablation could treat PTC and CLNM effectively.

In the present study, 20 PTC patients with CLNM was enrolled and treated with MWA, with technical success rates of 100%. The primary finding of this study was that MWA could treat PTC with CLNM invasion without serious complications. At the end of follow-up, all the volume of ablated area decreased and was essentially absorbed in 9 cases. No PTC local recurrence was found at the end of follow-up. One patient with a large PTC nodule developed metastatic lymph nodes 6 months after initial MWA and
underwent a second MWA procedure. No other metastatic lymph node was suspected at the 24th month follow-up after the second MWA. No major complications were encountered in all the cases. There were no delayed complications during the follow-up, either. During the follow-up period, metastatic lymph nodes recurred only in one case. Moreover, the successful second MWA of recurrence CLNM demonstrated that there had been no postoperative adhesion due to first ablation which could influence further MWA procedure or affect the patient's life quality.

According to our experience, the following factors are important for the successful ablation. First, high-frequency US has high diagnostic efficiency in diagnosing PTC and CLNM\(^{21–23}\). The relationship among PTC nodule, metastatic lymph nodes and important neck structures such as trachea, carotid vessels and nerves could be clearly revealed by US. The clear display of PTC and metastatic lymph nodes could ensure the accurate ablation of metastatic lymph nodes rather than normal lymph nodes. In contrast, it is difficult to identify all the metastatic lymph nodes precisely during neck exploration and CCND is the most effective way to clear all the suspected lymph nodes despite the surgical trauma. Second, the spatial resolution and time resolution of high-frequency US have advantages in the guidance during the procedure of MWA, including the precisely insertion of core needle and microwave antenna, evaluation and adjustment of the isolating fluid thickness during ablation, and evaluation of the thermal field as well as observation of the possible hematoma around the ablation zone. Third, for MWA of PTC with CLNM, safety and effectivity of the procedure is the most important. During the ablation, the thermal field could be revealed by US to ensure complete ablation and avoid carotid vessel injury at the same time. Heat injury could be prevented through different strategies. On one hand, low power and short radiation time were used to limit the heat conduction. On the other hand, isolating fluid around the ablation zone could protect the surrounding structures from heat injury effectively. After ablation, CEUS could evaluate the necrosis band and ensure the complete ablation of cancer and lymph nodes.

Our study has several limitations. First, the number of patients involved in this study is still small, and a further study enrolling more cases will lead to a more definite result. Second, although most tumor recurrence/persistence occur at the second year after operation according to the previous study\(^{24}\), the follow-up time is still short. Third, a comparison study between MWA and surgery for PTC with CLNM should be carried out.

**Conclusions**

In conclusion, we provide evidence that MWA can effectively treat PTC with CLNM without serious complications. The low power of 30W and short radiation time could limit the heat conduction and the isolating fluid around the ablation zone could protect the surrounding structure from heat injury effectively. Therefore, for some patients who are ineligible or refuse surgery, MWA is minimal invasive and safe for PTC with CLNM.

**Abbreviations**
Declarations

Ethics approval and consent to participate: Our retrospective study was approved by the institutional review board of our hospital. Written informed consent was obtained from each patient before the ablation procedure.

Consent for publication: The patients consented to publish their examination results and radiological images anonymously. Written informed consent was waived.

Availability of data and material (data transparency): The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors’ contributions: ZZL, YMA, WY have reviewed the ultrasound images and did the main measurement. PLL, WY, CXJ and LY have made substantial contributions to study design and revised the manuscript critically; ZZL drafted the article critically and contributed substantially to data collection and data analysis. All authors have provided final approval of the version to be published and have participated sufficiently in the work to take public responsibility for appropriate portions of the content.
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**Figures**
Figure 1

A 33-year-old woman had papillary thyroid carcinoma with metastatic lymph nodes underwent microwave ablation (A) PTC nodule (white arrow) was revealed on ultrasound. (B) Isolating fluid (black arrow) was injected into surrounding tissue to separate the PTC nodule (white arrow) from carotid artery (white arrowhead). (C) Isolating fluid (black arrowhead) was injected into surrounding tissue to separate the metastatic lymph node (white arrowhead) from trachea (black arrow). (D) Metastatic lymph node nodule was ablated safely after isolation. The hyperechoic band (white arrowhead) represents the thermal field of ablation. PTC = papillary thyroid carcinoma
Figure 2

A 33-year-old woman who had papillary thyroid carcinoma with metastatic lymph nodes underwent MWA (A&B) After MWA, nonenhancement area covered PTC nodule (white arrowhead) on CEUS. (C&D) After MWA, nonenhancement area covered metastatic lymph node (black arrowhead) on CEUS. MWA = microwave ablation, PTC = papillary thyroid carcinoma, CEUS = contrast-enhanced ultrasound.