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ORIGINAL ARTICLE

Safety and efficiency of ultrasound-guided low power microwave ablation in the treatment of cervical metastatic lymph node from papillary thyroid carcinoma: a mean of 32 months follow-up study

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Abstract

Purpose To evaluate the safety and efficiency of microwave ablation (MWA) with low power of 20 w, respectively, in the treatment of cervical metastatic lymph node (CMLN) from papillary thyroid carcinoma (PTC) with a mean of 32-month follow-up.

Methods Eleven patients in total with 24 cervical lymph nodes (LNs) diagnosed with CMLN from PTC underwent MWA at a power of 20 w. We recorded images of the LNs under ultrasound first before MWA and 1, 3, 6, 12, months after MWA, and then every 6 months, respectively. The volumes of the LNs were compared before MWA and at each follow-up point after MWA. The thyroglobulin (Tg) test was performed before MWA and 3 months after MWA.

Results All patients were successfully treated, and they showed no major complications. Before MWA, the mean volume of the LNs was $364.15 \pm 306.89\ mm^3$, which decreased to $234.10 \pm 230.34\ mm^3$, $107.51 \pm 129.47\ mm^3$, $20.88 \pm 39.27\ mm^3$, $3.38 \pm 12.74\ mm^3$, and completely disappeared at the follow-up point of 1, 3, 6, 12, and 18 months after MWA, respectively. The mean Tg was 11.81 ± 7.50 ng/ml, a data significantly decreased to 0.43 ± 0.11 ng/ml 3 months after MWA ($P = 0.000$). In the follow-up period, no recurrent lesions were found.

Conclusions For the treatment of CMLN from PTC, low power MWA showed good safety and efficacy. MWA is likely to be a candidate for patients with high risks or who refuse reoperation.

Keywords Thermal ablation · Microwave · Ultrasound · Papillary thyroid carcinoma Metastatic lymph node

Introduction

The incidence of thyroid cancer has significantly increased in the past few decades, yet in recent years it has progressively been stabilized [1, 2]. Papillary thyroid carcinoma (PTC) is the commonest thyroid carcinoma type. Most patients with PTC can be cured by surgery and radioiodine therapy; whereas after surgery, there are still 15%–30% of patients afflicted with cervical metastatic lymph nodes (CMLN) [3–5]. These patients normally need to undergo repeated surgery. Yet reoperations can lead to complications because of adhesions and anatomical structural alterations. Another problem of reoperation is related to the patients' fear of it. To solve this problem, a less invasive technique is required, as an alternative choice of therapy.

Microwave ablation (MWA), as a less invasive technique, has been suggested as an excellent treatment of liver carcinoma, renal tumor as well as lung cancer [6–9]. There are a large number of published researches about MWA applied for thyroid-related disease therapy, which have reported good results as well [10–12]. To our knowledge, there is only one research fixating on MWA treatment in recurrent PTC with a short term follow-up, which applied a high power of 40 w [13]. Nevertheless, the longer time

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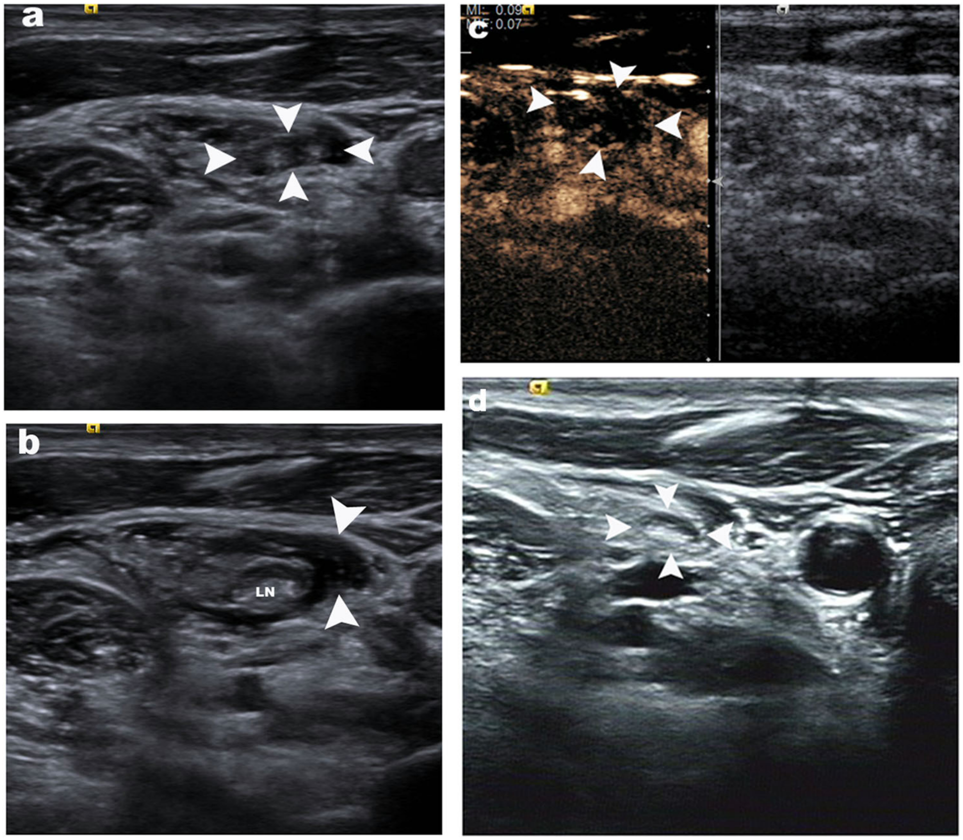

Fig. 1 A 33-year-old female patient (no. 8) with cervical metastatic lymph node (CMLN) from papillary thyroid carcinoma (PTC) underwent microwave ablation (MWA). The ultrasound images before and after ablation are shown here. **a** A lymph node (LN) (white arrowhead) was detected in the level III of right neck. The size and volume of the LN were $14.3 \times 3.7 \times 7.0$ mm, and 192.59 mm^3, respectively. **b** Before the MWA, a hydrodisscetion was conducted to prevent vital organs near the LN from burning. A normal saline area with echoless area (white arrowhead) around the LN was identified under ultrasound. **c** After MWA, a contrast-enhanced ultrasound was conducted to ensure that the LN was ablated completely. A non-perfusion area (white arrow) was detected under ultrasound. **d** Three months after MWA, the size and volume of the LN (white arrow) were $4.8 \times 2.3 \times 4.5$ mm and 25.83 mm^3, respectively. Six months after MWA, the LN disappeared

effect of MWA with lower power in CMLN from PTC remains unknown.

The aim of this study is to retrospectively evaluate the safety and efficiency of MWA using low power (20 w) for the treatment of CMLN cases (from PTC), with a mean follow-up period of 32 months.

Methods and materials

This retrospective study was approved by the ethics committee. We had the informed consent of all patients.

Patients

Inclusion criteria: (1) the patients diagnosed with PTC and having undergone thyroidectomy; (2) the patients detected with enlarged cervical lymph nodes (LNs) and diagnosed with metastasis from PTC by CNB, or the washout thyroglobulin concentration; (3) radioactive iodine therapy performed after thyroidectomy; (4) patients with high risks of surgical complication or those refusing reoperation. Exclusion criteria: (1) patients with other metastasis besides cervical lymph nodes; (2) patients with serious bleeding tendencies; (3) pregnant women.

From May 2014 to June 2015, 12 patients with 26 cervical lymph nodes from PTC underwent MWA in our hospital. One patient with two positive lymph nodes did not return for the follow-up inspections. This retrospective study recruited 11 patients, with a total of 24 lymph nodes.

Equipment

Siemens Acuson S2000 (Siemens Mountainview, USA) or Mylab Twice ultrasound system (Esaote, Italy) was used for image collection before and after MWA as well as for guidance during MWA. A microwave ablation system (ECO-100A1; YIGAO Microwave System Engineering Co.

Table1 Clinical characters and outcomes of the lymph nodes (LN) by microwave ablation (MWA)

Patients no.	LN no.	Sex	Age	Side	Location	Largest diameter	Volume (mm^3)	MWA energy (J)	Follow-up (month)	Complete absorbed (month)
1	1	Female	33	Right	III	6.5	72.40	640	42	6
	2			Right	II	10.8	281.08	1660	42	12
	3			Right	II	4.3	31.30	360	42	3
	4			Left	V	7	132.79	1020	42	6
	5			Left	V	12.5	428.09	2460	42	18
2	6	Female	54	Right	III	15.2	1011.08	3160	42	12
	7			Right	IV	12.4	473.73	2740	42	12
3	8	Female	41	Right	III	13.5	680.66	2420	36	6
	9			Right	III	10.4	348.82	1680	36	6
	10			Right	IV	6.4	70.95	620	36	3
4	11	Male	32	Right	III	9.3	261.24	1140	36	6
	12			Right	III	8.9	154.02	860	36	6
5	13	Female	47	Left	IV	11.9	387.12	980	36	6
6	14	Female	31	Right	VI	6.5	98.43	600	30	6
	15			Right	II	18.3	788.31	2280	30	6
7	16	Female	32	Right	V	12.7	393.07	2540	30	12
8	17	Female	33	Right	III	14.3	192.59	1020	24	6
9	18	Male	51	Left	IV	8.9	222.61	1100	24	6
	19			Left	IV	10.4	288.25	1220	24	12
10	20	Female	31	Right	IV	12.1	378.78	1180	18	12
	21			Left	IV	16.5	1149.03	3480	18	18
	22			Left	III	6.9	142.37	980	18	12
	23			Left	III	3.1	14.99	240	18	1
11	24	Male	59	Left	V	14.6	737.79	1920	18	12

Ltd, Nanjing, Jiangsu Province, China) and 16 G (1.6 mm in diameter) cooled needle antennas designed for superficial organs were applied for microwave ablation.

Pre-MWA assessment

Before MWA, all patients underwent a meticulous US examination. We recorded the location, size, blood flow, and surroundings of the cervical LNs. Volumes of the lymph nodes were calculated by the equation of $V = \pi abc/6$, where: V denotes volume; a is the largest diameter; b and c are the remaining two perpendicular diameters. Contrast-enhanced ultrasound (CEUS) was conducted to observe perfusion of the lymph nodes. Thyroglobulin (Tg) test was also performed before MWA.

Procedure of MWA

The procedure was carried out by a doctor with 5-year experience in MWA. The procedure was guided by ultrasound. Patients were placed in the supine position. Their necks were exposed fully. After patients underwent local infiltration anesthesia with 1% lidocaine, normal saline (NS) was injected around the lymph nodes, which prevented nerves, blood vessel and other important organs of patients from burning (Fig. 1b). A 16 G sharp needle 4 cm in length was applied to puncture the skin. Next, the antenna was pushed into the target lymph node via the tunnel, which appeared after the sharp needle was pulled out. This method was applied in our previous research, which we named "Teng's needle puncture method" [12]. It was difficult to insert the antenna into the lesion in some cases with small lymph nodes. The "ablating puncture" technique was used to place the antenna as follows: the ablated mode was turned on after the antenna needle reached the surface of the lesion, and then the needle was placed into the lesion. We suggest using "ablating puncture" method if the antenna fails to be inserted into the lesion by the conventional method since the thermal damage risk of this puncture method may be higher than that of the conventional method. For small lesions, fixed ablation was enough, and for some big lesions, the "moving-shot" technique was applied [14, 15]. The output power was 20 w for all treatments. A hyperecho area was observed on the ultrasound during the procedure of ablation. Ablation was stopped after the hyperecho area covered the LN completely. Then, a CEUS was performed to check the effect of the ablation. The perfusion area should be re-ablated if the contrast agent remained within the LN. The MWA procedure would be considered completed if there was no contrast agent in the LN (Fig. 1c). After MWA, all patients were observed for 2 h, and paid attention to possible emerging complications such as bleeding, hoarseness or skin burns.

Follow-up

Cervical US was introduced at 1, 3, 6, and 12 months after MWA, and then every 6 months thereafter. We recorded the size of lesions and calculated the volume and volume reduction rate (VRR) of the ablated LNs. The equation of VRR was shown here: VVR (%) = ([initial volume − final volume] × 100%)/initial volume. Three months after MWA, all of the patients underwent the thyroglobulin test again. Computed tomography (CT) or ultrasound (US) examination was performed every 6 months after MWA to exclude distant metastasis.

Statistics and analysis

SPSS 22.0 was employed for statistical analysis. Continuous data was shown as the mean ± standard deviation (the range). Paired *t*-test was performed to compare the changes of size, volume of LNs as well as Tg level before and after MWA. We considered $P < 0.05$ of statistical significance.

Results

The present study included 11 patients (8 females and 3 males) with 24 metastatic cervical LNs. The mean age was 40.36 ± 10.52 years (ranging from 31–59 years). All 24 cervical LNs were diagnosed with metastatic from PTC by CNB, or from the washout thyroglobulin concentration. Patient no. 1 and no. 10 had five lesions and four lesions, respectively. Their lesions were located at different sides of their body. Patient no. 3 had three lesions. Patient no. 2, no. 4, no.6, and no. 9 all had two lesions. Every remaining patient had one lesion. The detailed information of the LNs is listed in Table 1.

The MWA procedures of all the LNs were successfully carried out. All the LNs were ablated with a power of 20 w. The mean ablated time and energy was 75.63 ± 45.44 s (range 12–174 s) and 1512.50 ± 908.77 J (range 240–3480 J), respectively. Twenty-four LNs all disappeared in 18 months after MWA (Fig. 1). Before MWA, the largest diameter was 10.56 ± 3.90 mm (range 3.1–18.3 mm), a data decreased to 8.64 ± 3.45 mm (range 0–14.9 mm), 6.08 ± 3.46 mm (range 0–12.4 mm), 2.32 ± 3.24 mm (range 0–10.9 mm), 0.56 ± 1.78 mm (range 0–7.1 mm) and completely disappeared 1, 3, 6, 12, and 18 months after MWA, respectively. Before MWA, the volumes of the LNs were 364.15 ± 306.89 mm^3 (range 14.99–1149.03 mm^3), which decreased to 234.10 ± 230.34 mm^3 (range 0–924.65 mm^3), 107.51 ± 129.47 mm^3 (range 0–432.98 mm^3), 20.88 ± 39.27 mm^3 (range 0–171.97 mm^3), 3.38 ± 12.74 mm^3 (range 0–59.52 mm^3) and completely disappeared 1, 3, 6, 12, and 18 months after MWA, respectively. The variations of volume before and after MWA are shown in Fig. 2. The mean VRR of the LNs was 38.43 ± 20.29% (range 0.29–100%), 75.20 ± 17.20% (range 35.18–100%), 95.45 ± 8.60% (range 59.83–100%), 99.34 ± 2.85% (range 86.10–100%) and 100% in 1, 3, 6, 12, and 18 months after MWA, respectively. The reduction of the largest diameter and volume of LNs were of statistical significance ($P = 0.000$). The mean Tg was 11.81 ± 7.50 ng/ml (range 4.29–25.64 ng/ml), a data significantly decreased to 0.43 ± 0.11 ng/ml (range 0.31–0.65 ng/ml) 3 months after MWA ($P = 0.000$) (Table 2).

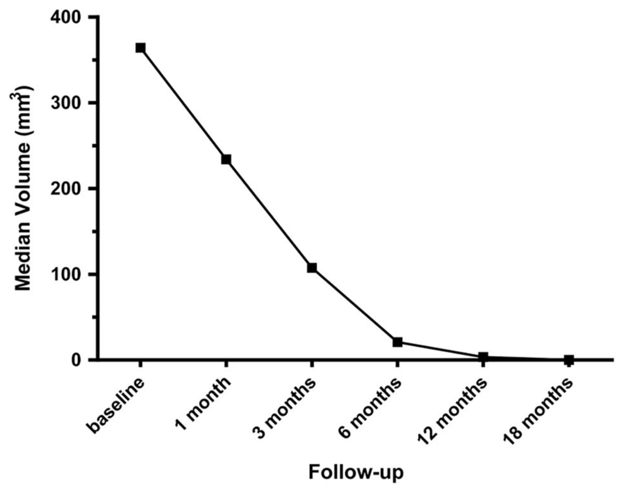

Fig. 2 The changes of median volume before and after MWA at each follow-up point

All patients received the MWA procedure smoothly. After MWA, no patient required painkillers, and they showed no serious complications, such as bleeding, infection, skin burns, or nerve injuries. In our follow-up period (mean of 32 months; range 18–42 months), no new recurrent lesions or distant metastases were detected.

Discussion

As our retrospective research suggested, low power MWA in treatment of CMLN from PTC was safe and efficient. All the treated LNs were absorbed within 18 months after MWA. No new recurrent lesion were found in a mean follow-up period of 32 months (range 18–42 months).

Previous researches have suggested that PEI has excellent performance and no major associated complications in the treatment of CMLN from PTC [16–20]. Yet a large number of patients treated by PEI often require more than one round of treatment. Other researches suggested that under this type of condition, RFA and laser ablation also have a good impact [21–31]. In accordance with the 2015 American Thyroid Association guideline, all of the noted minor intensive treatments except MWA were considered as

Table 2 Changes of largest diameter, volume, and thyroglobulin (Tg) after microwave ablation (MWA)

	Before MWA	Last follow-up	*P*-value
Mean of largest diameter (mm)	10.56 ± 3.90	0	= 0.000
Mean of volume (mm^3)	364.15 ± 306.89	0	= 0.000
Mean of Tg (ng/ml)	11.81 ± 7.50	0.43 ± 0.11	= 0.000

alternative modalities of treatment for patients who were poor surgical candidates or refused reoperation [32]. Although MWA has almost the same performance as RFA has in malignant diseases of the liver [33, 34], rare research about MWA has been discussing the treatment of CMLN from PTC except for Yue's study [13], in which they treated the recurrent lesions from PTC with a short time follow-up using a high power of 40 w. Some researchers applied a low power of 20 w to treat benign thyroid disease [35, 36]. Yet the efficiency of low power MWA in the treatment of CMLN from PTC with a long-term follow-up period remains unknown. To our knowledge, CMLN (more than three LNs) located on different sides of a patient's body and treated with MWA has not yet been mentioned.

The present study suggests that low power MWA is capable of treating LNs well. We treated CMLN from PTC using a low power of 20 w and yielded positive results. The thyroglobulin level significantly decreased after MWA. All LNs completely disappeared in the follow-up period, the fastest absorption was after 1 month, and the slowest (two LNs) absorption was after 18 months. The results seem better than those yielded from Yue's research, showing that 30.4% nodules completely disappeared, and 52.2% nodules were small scar-like lesions [13]. The possible reasons are as follows: first, a low power of 20 w could make the course of coagulative necrosis milder, and a less "over burned" area would appear. Accordingly, the ablated area could be absorbed faster. Second, some LNs in the present study were small and easy to absorb. Finally, instead of small scar-like lesions, as seen in Yue's study, a longer follow-up period in our study provided enough time for the complete absorption of ablated areas.

Our findings suggested that MWA is efficient even for cervical LN metastases that were more than three and located on both sides of a patient's body. Our study included two patients with more than three lesions, located on different sides of the neck. Some previous researches formulated an inclusion criterion involving fewer than three lesions for thermal ablation [13, 23]. In some researches, an inclusion criterion of no more than four metastases was designed [26]; yet in our study, two patients with more than three lesions were well treated by MWA. One of the patients (no. 1) had five metastases and the other patient (no. 10) had four metastases. The lesions were located at different sides of the participants' necks, respectively. Finally, all of the noted lesions disappeared, and no new metastases occurred. Yet there are some details we must highlight in MWA treatment regarding multiple lesions: First and foremost, a number list should be organized before we perform MWA in line with the sequence of ablation and the locations of the LNs. This could be proven conducive to avoiding omissions; moreover, smaller and deeper LNs should be ablated first since hyperechoic regions after MWA, on ultrasound imaging, can make the small and deep LNs difficult to monitor. Finally, the procedure of hydrodissection for small LNs should be accurate to inject the fluid around the LNs. If the fluid is injected into LNs, the hypoechoic nature of the fluid may be confused with the hypoechoic of the LNs, and further the LNs will be difficult to find out.

In the present research, MWA was proven safe for CMLN treatment. All the 11 patients with 24 LNs were treated successfully, and they showed no major complications. We injected plenty of fluid around LNs before MWA to protect local vessels, nerves, and other important structures. This was the most important consideration to avoid major complications. Yet hydrodissection alone cannot effectively prevent any damage. In accordance with our experience in thyroid nodules treatment [12], thermal damage risk is much higher under the condition that the lesion has adhesions with surrounding tissues even by using the hydrodissection. Besides, if the adhesion is serious, implementation of hydrodissection could be even impossible. Fortunately, none of CLNs in our study showed the serious adhesion as mentioned, which might be another important reason for no appearance of serious complications. Furthermore, rather than injecting a mixture of 0.9% lidocaine and normal saline, as performed in Yue's study [13], we used pure normal saline to inject around the LNs, since we were cautious of lidocaine producing palsy of the surrounding nerves, which would make it difficult for us to know if the real cause of any nerve damage was actually attributed to our procedure.

There were a number of other strength in this study: On the one hand, different form some other studies that made a small incision about 1–2 mm [13, 37], the present study used a short sharp needle to make a hole in the skin, which was termed as "Teng's needle puncture method" to introduce the antenna into the target LNs. The method caused less skin injury and was proven effective in our previous study [12]. On the other hand, since the microwave antenna was not sufficiently sharp, it was difficult to puncture the antenna into the small LN; the "ablating puncture" technique was employed to place the antenna. When the antenna needle reached the surface of the lesion, the ablated mode was turned on, and then the needle was placed into the lesion. Given that the needle's radiating segment to emit energy is nearly 3 mm away from the shaft tip, the risk of thermal damage caused using "ablating puncture" method may be higher than that using the conventional method. Thus, we will use "ablating puncture" method if the conventional method fails to puncture into the lesion. When we use the "ablating puncture" method, the needle tip should be very close to the lesion to reduce the damage of surrounding tissues. Using this technique, the antenna was placed successfully into a lesion; the largest diameter of the lesion was only 3.1 mm. The course of the treatment is presented in Video 1.

Yet the present study has several limitations as follows: First, the sample size was small; second, MWA was not compared with surgery or other less invasive techniques; besides, some LNs small in size in our study could be followed by active observation; finally, the mean follow-up period of 32 months might not be sufficient for this slowly progressing disease. Accordingly, a randomized controlled trial with a longer follow-up and a large sample is needed in the future.

Conclusion

Our research suggested that MWA for the treatment of CMLN from PTC is a safe and effective therapeutic strategy. It may be an alternative choice for patients with high surgical risks or refusing reoperation.

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Compliance with ethical standards

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

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

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