European Radiology (2023) 33:233–243
https://doi.org/10.1007/s00330-022-08962-6

ONCOLOGY

Microwave ablation vs. surgery for papillary thyroid carcinoma with minimal sonographic extrathyroid extension: a multicentre prospective study

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Received: 28 November 2021 / Revised: 24 April 2022 / Accepted: 11 June 2022 / Published online: 30 June 2022

Abstract

Objectives Minimal extrathyroid extension (mETE) was removed from the TNM staging system. This study was designed prospectively to compare the safety and efficacy of microwave ablation (MWA) versus surgery for treating T1N0M0 papillary thyroid carcinomas (PTC) with sonographically detected mETE.

Methods From December 2019 to April 2021, 198 patients with T1N0M0 mETE-PTCs evaluated by preoperative ultrasound from 10 hospitals were included. Ninety-two patients elected MWA, and 106 patients elected surgery for treatment. MWA was performed using extensive ablation with hydrodissection. Surgery consisted of lobectomy with ipsilateral central lymph node dissection (CLD), lobe and isthmus excision with ipsilateral CLD and total thyroidectomy with ipsilateral CLD. The rates of technical success, cost, oncologic outcomes, complications and quality of life of the two groups were assessed.

Results The follow-up times for the MWA and surgery groups were 12.7 ± 4.1 and 12.6 ± 5.0 months, respectively. The technical success rate was 100% for both groups. Oncological outcomes of the two groups were similar during the follow-up (all $p > 0.05$). The MWA group had a shorter operation time, less blood loss and lower costs (all $p < 0.001$). Three complications (3.3%) were reported in the MWA group and 4 (3.8%) in the surgery group ($p = 0.846$). The surgery group had higher scores for scar problems and anxiety ($p < 0.001$ and $p = 0.003$, respectively).

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Conclusions Microwave ablation was comparable in the short term to surgery in terms of treatment safety and efficacy in selected patients with T1N0M0 mETE-PTC detected by ultrasound.

Key Points

- *Microwave ablation is comparable to surgery in the safety and short-term efficacy for PTCs with sonographically detected mETE.*
- *Thermal ablation is technically feasible for mETE-PTC treatment.*
- *Patients with mETE-PTC have similar quality of life in the two groups, except for worse scar problems and anxiety in the surgery group.*

Keywords Papillary thyroid carcinoma · Ultrasound · Surgery · Complications · Ablation

Abbreviations and acronyms

CLD	Central lymph node dissection
gETE	Gross extrathyroid extension
HADS	Hospital Anxiety and Depression Scale
LNMs	Lymph node metastasis
LTP	Local tumour progression
mETE	Minimal extrathyroid extension
MWA	Microwave ablation
PTC	Papillary thyroid carcinoma
TA	Thermal ablation
THYCA-QoL	Thyroid Cancer-specific Quality of Life
US	Ultrasound

Introduction

The incidence of papillary thyroid carcinoma (PTC) is increasing rapidly worldwide [1]. In general, PTCs show indolent characteristics, especially those in stage T1 [2], but some clinically aggressive features still result in controversy regarding clinical significance and disease management [3].

Extrathyroid extension (ETE) of the primary tumour was reported as a risk factor for poor prognosis and has been accepted as an important factor for determining surgical extent in patients with PTC [4, 5]. On histology, ETE has been divided into two grades based on the extent of invasion. One grade is 'minimal ETE (mETE)', which was defined as an invasion of the tumour to the capsule, sternothyroid muscle, or perithyroidal soft tissue, and the other is 'gross ETE (gETE)', including extension to subcutaneous soft tissues, the larynx, the trachea, oesophagus, or the recurrent laryngeal nerve, and extension to the prevertebral fascia, mediastinal vessels, or the carotid artery [6]. In the recently released 8th American Joint Committee on Cancer (AJCC) TNM staging system, mETE was removed from the T3 stage classification, which means that a PTC diameter no more than 2 cm with mETE (mETE-PTC) was reclassified as T1 [7].

Lobectomy is recommended by most professional society guidelines as the definitive treatment for those reclassified T1 stage PTCs [8, 9]. Although most patients who undergo surgery have excellent outcomes, surgery may lead to temporary or permanent recurrent laryngeal nerve paralysis, hypothyroidism, hypoparathyroidism [10, 11], and an unsightly scar [12]. In addition, many surgeons are also seeking a less aggressive method for tumours with such an indolent nature, such as partial thyroidectomy [13, 14].

Thermal ablation (TA) has been reported as an optional curative treatment method for T1N0M0 PTC treatment with the advantage of minimal invasiveness [15–19]. However, PTCs with ultrasound (US)–detected mETE are always excluded from TA due to the possibility of aggressive features and the high risk of thermal injury [20]. No research has yet been performed to prove its feasibility.

This study aimed to compare the safety and efficacy of microwave ablation (MWA) versus open surgery for treating T1N0M0 PTC with sonographically detected mETE.

Materials and methods

Patients

This prospective multicentre study was approved by the Institutional Ethics Committees of PLA General Hospital. Informed consent was obtained from all patients or their responsible caregivers before enrolment.

The inclusion criteria were as follows: (1) single solitary suspicious thyroid nodule diameter of 2 cm or less detected by US; (2) preoperative sonographically detected invasion of the capsule, sternothyroid muscle, or perithyroidal soft tissue; (3) no sonographic evidence of lymph node metastasis or distant metastasis; (4) fine needle aspiration (FNA) or core needle biopsy (CNB)–confirmed PTC before ablation or surgery; and (5) no prior therapy for thyroid issues. Patients with severe conditions, vocal cord palsy, clinically apparent multicentricity or coexisting thyroid malignancies such as medullary carcinoma were excluded.

We identified sonographically detected capsule invasion or mETE with features of capsular abutment by the nodule, subtle capsular distortion or bulging of the normal thyroid contour, but without replacement of the strap muscle or obtuse

margins between the tumour and trachea, oesophagus, mediastinal vessels, or carotid artery [21].

The eligibility of patients was evaluated by interventional radiologists and surgeons. Surgery and MWA were recommended for the eligible patients if they refused AS, with the notification of the advantages and disadvantages of both methods and that surgery was the current standard therapy while thermal ablation was just a new technique. Patients chose MWA or surgery according to their will.

From December 2019 to April 2021, 201 patients were admitted according to the inclusion criteria. After exclusion of 3 patients, 198 patients were enrolled in the present study, and 92 were treated with MWA 106 with surgery (Fig. 1). Patients were divided into an MWA group and a surgery group according to their operation method.

Pre-ablation evaluations

Laboratory tests, including complete blood count and thyroid function tests, and imaging studies, including chest radiography, US of the thyroid and cervical lymph nodes, and examinations of the bilateral vocal cords with fiberoptic laryngoscopy, were performed in all patients before treatment.

US examination played a key role in characterising the target tumour and distinguishing the relationship between the tumour and the thyroid capsule by experienced ultrasonography physicians with more than 12 years of experience. The instruments applied included Philips iU22 Ultrasound System (Philips Healthcare), Siemens Acuson Sequoia 512 Ultrasound System (Siemens) or a Mindray M9 Ultrasound System (Mindray). For each tumour, the maximal diameter (a) and two orthogonal diameters (b and c), echogenic features and the internal vascularity on US and the location of capsule extension were assessed. The volume of tumours observed by US was estimated by the ellipsoid formulation $V = \pi abc/6$. According to the US presentation of the internal nodule on colour Doppler flow imaging (CDFI), the nodular vascular scores were classified into four grades (18). The anterior capsule refers to the capsule close to the anterior cervical muscle, the medial capsule close to the trachea, the lateral capsule close to the carotid sheath, and the posterior capsule close to the retropharyngeal space.

Operation procedures

MWA

High-resolution linear probes (6–12 MHz) were employed in the guidance of biopsies, preablation evaluation, ablation procedures and follow-up. The MWA system applied in this study was the KY-2000 2450 MHz microwave system (KY2000, Canyon Medical Instruments) with a 16-gauge, Teflon-coated, internal-cooled microwave antenna.

All MWA procedures were performed by experienced ultrasonography physicians with more than 7 years of experience on interventional sonography. The operation procedure of MWA for mETE-PTC was the same as that described in earlier papers for lesions located centrally on the gland [17]. Hydrodissection was performed more carefully in mETE-PTC ablation to prevent unexpected thermal injury. A safe distance between the tumour and the critical structure was maintained throughout the operation to protect the critical structures from

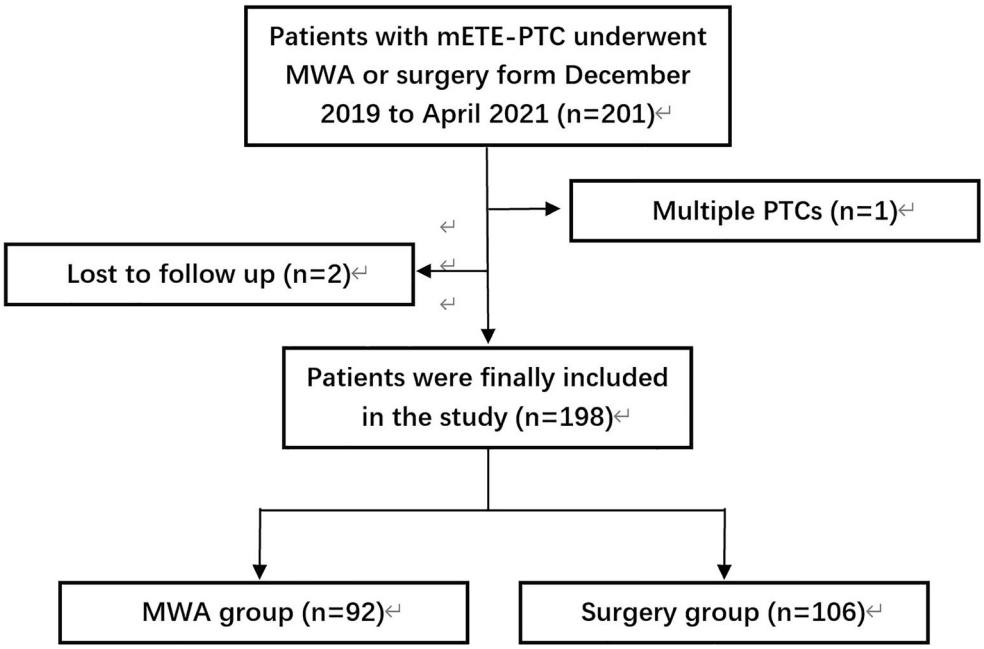

Fig. 1 Research flowchart. MWA, microwave ablation; mETE-PTC, papillary thyroid carcinoma with minimal extrathyroid extension

thermal injury [22]. Contrast-enhanced ultrasound (CEUS) (SonoVueR used as contrast agent) was performed to evaluate the completeness of the ablation 1 h later, which required the ablation area to be extended no less than 3 mm beyond the tumour edge (Fig. 2).

Surgery

Thyroidectomy was performed by surgeons with more than 6 years of experience in thyroid surgery. The range of thyroid excision was determined according to the ATA guidelines. Of all the patients, 6 (5.7%) underwent lobectomy with ipsilateral central lymph node dissection (CLD), 45 (42.5%) underwent lobe and isthmus excision with ipsilateral CLD, and 55 (51.9%) underwent total thyroidectomy with ipsilateral CLD because of the presence of sonographic benign nodules in the other lobe. The glands and lymph nodes excised were sent for pathologic examination to identify the pathological type.

For both groups, the operation time was defined as from the beginning of skin disinfection until the patient left the operating room. Immediate postoperative pain score scaled from 0 to 10 according to the patient feeling. The costs of MWA included the preoperative examination, operation (MWA needle and other consumable fees), local anaesthesia fees and hospital bed, nursing and postoperative medication fees if needed. The costs of surgery included the preoperative examination, operation (including the use of nerve monitoring, haemostatic materials and other consumables), general anaesthesia, hospital bed, nursing and postoperative medication fees. Complications were defined according to the reporting standards of thyroid ablation [15].

Follow-up

All patients in both groups had their TSH suppressed in a range of 0.5–1 mU/L to reduce tumour recurrence risk. The US presentations and thyroid functions of patients were evaluated and recorded at the 3rd, 6th, and 12th months in the first year after treatment and every 6–12 months thereafter. CEUS was performed 6 months and 12 months after MWA to verify the effectiveness of the treatment. The effectiveness of MWA was defined as the absence of enhancement of any areas of the mass. Ultrasonographically suspected local tumour progression (LTP), lymph node metastasis (LNMs) or new lesions of both groups were confirmed by biopsy.

The LTP was defined as the appearance of a new nodule with typical features of thyroid cancer in the edge of the ablation zone and confirmed by FNA or CNB. LNMs were the new detected abnormal lymph nodes with pathologic results of PTC metastasis. New lesion was defined as new recurrent malignant thyroid tumour in thyroid gland. Distant metastasis was PTC cells metastasised to other organs beyond cervical lymph nodes. Additional ablation or surgical resection might

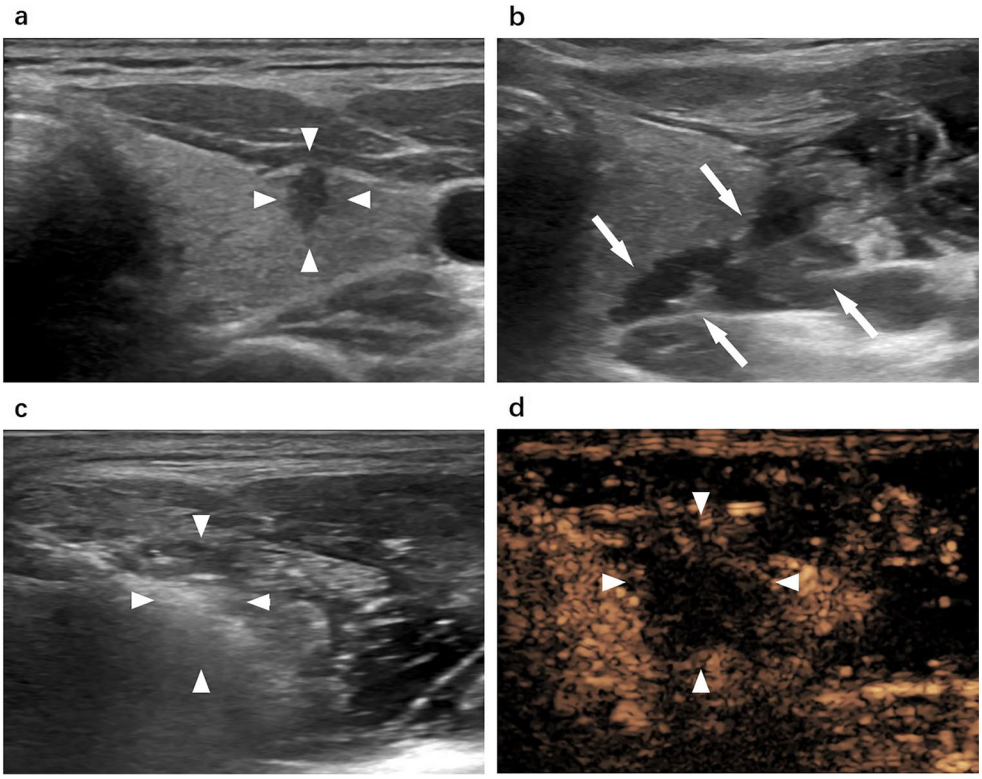

Fig. 2 Images in a 47-year-old man with papillary thyroid carcinoma with minimal capsule invasion in the right lobe of the thyroid treated with microwave ablation. **a** Pre-ablation US image of the tumour (arrowheads). **b** Hydrodissection technique (arrows) was used to protect the carotid artery and vagus nerve. **c** Hyperechoic pattern in tumour during the ablation procedure (arrowheads). **d** Postablation contrast-enhanced US image shows no enhancement in the tumour area (arrowheads)

be applied for unsuccessfully treated or recurrent tumours based on patients' intentions.

We used two Chinese version questionnaires to evaluate the quality of life of patients in both groups during the follow-up, including the Thyroid Cancer-specific Quality of Life (THYCA-QoL) and the Hospital Anxiety and Depression Scale (HADS). The THYCA-QoL is a specific scale for patients with thyroid cancer, consisting of seven symptom areas and six single items [23]. HADS is commonly used in diagnosing anxiety and major depressive disorders in patients with cancer [24].

Statistical analysis

Quantitative data measurements are described as the means ± standard deviations (SDs). We compared data for the two groups using Student's unpaired *t* test. Categorical data comparisons were performed using the chi-squared test or Fisher's exact test. Patients' progression-free survival curves were generated by Kaplan-Meier method, and between-group differences were assessed by log-rank test. All analyses were performed with SPSS26. Difference was considered significant when $p < 0.05$.

Results

The number of enrolled patients and operators' experience in the 10 participating institutions are listed in Supplementary Table 1. The mean follow-up times for the MWA and surgery groups were 12.7 ± 4.1 and 12.6 ± 5.0 months, respectively.

Patients and tumours

The general information of the two groups is shown in Table 1, and tumour characteristics are shown in Table 2.

The diameter and volume of tumours in the MWA group vs. surgery group were 0.81 ± 0.30 cm vs. 0.89 ± 0.33 cm and 0.23 ± 0.33 mL vs. 0.32 ± 0.37 mL, respectively ($p = 0.067$ and $p = 0.067$). No difference was found in US characteristics, including tumour echogenicity, vascularity, calcification and location (all $p > 0.05$). The numbers of tumours with T1a stage and T1b stage in the MWA group vs. surgery group were 77 (83.7%) vs. 82 (77.4%) and 15 (16.3%) vs. 24 (22.6%), respectively ($p = 0.263$). The numbers of tumours extending anterior, posterior, medial and lateral thyroid capsules in the MWA group vs. surgery group were 49 (53.3%) vs. 52 (49.1%), 17 (18.5%) vs. 30 (28.3%), 11 (12.0%) vs. 12 (11.3%) and 15 (16.3%) vs. 12 (11.3%), respectively ($p = 0.378$).

Pathology result of the surgery group

The pathological results of excised thyroid gland in the surgery group are shown in Supplementary Table 2. Presence of preoperative US-undetectable additional microcarcinomas was confirmed in 6 (5.7%) patients, and central LNMs in 26 (24.5%) patients, with ≤ 5 nodes in 20 patients, 6–10 in 4 patients and 11–20 in 2 patients. Pathology results also showed 12 (11.3%) tumours confined in the gland without capsule invasion, 93 (87.7%) with invasion into the capsule or through the capsule into fibrous or adipose tissue around glands (mETE), and 1 (0.9%) adjacent to a few skeletal muscles outside the capsule (gETE).

Treatment variables and safety

The treatment variables and complications of the two groups are presented in Tables 3 and 4. The MWA group had shorter operation time, less blood loss, lower postoperative pain score and lower treatment costs in general than the surgery group (all $p < 0.05$).

Complete absence of enhancement at CEUS was observed in all target tumours at the end of ablation. The technical success rate was 100%. In the MWA group, 3 (3.3%) complications were reported, which were all hoarseness, while in the surgery group, 4 (3.8%) complications, including 2 (1.9%) hoarseness (one ipsilateral and one contralateral to the primary tumour) and 2 (1.9%) infections, were reported ($p = 0.846$). In the subgroup analysis of stage, the incidences of complications of MWA vs. surgery were 2 (2.6%) vs. 4 (4.9%) in T1a and 1 (6.7%) vs. 0 (0%) in T1b (all $p > 0.05$). In subgroup analyses of anterior, posterior, medial and lateral thyroid capsule extension, the incidences of complications of MWA vs. surgery were 0 (0%) vs. 3 (5.8%), 3 (17.6%) vs. 0 (0%), 0 (0%) vs.0 (0%) and 0 (0%) vs. 1 (8.3%), respectively. The complication incidence rate of MWA for tumours with posterior capsule extension was significantly higher than surgery ($p = 0.019$). Of all the complications that occurred, 1 (0.9%) patient in the surgery group had permanent recurrent laryngeal nerve injury (ipsilateral to the primary tumour), which demonstrated persistent dysphonia and documented palsy by fiberoptic laryngoscopy more than 6 months after surgery. All voice hoarseness reported in the MWA group recovered within 3 months after ablation.

Treatment efficacy

The oncological outcomes of the two treatment methods are shown in Supplementary tables 3.1–3.2. Patients in the MWA group had no new lesions in the remaining parenchyma of the gland, while 1 (0.9%) patient in the surgery group had a new lesion in the contralateral lobe ($p = 0.352$). The MWA group included 2 (2.2%) cases with cervical LNMs, and the surgery

Table 1 General information of patients undergoing MWA and surgery

Parameter	MWA (n = 92)	Surgery (n = 106)	p value
Gender, n (%)			0.447
Male	16 (17.4%)	23 (21.7%)	
Female	76 (82.6%)	83 (78.3%)	
Age (y), mean ± SD			0.499
≤ 60	85 (92.4%)	95 (89.6%)	
> 60	7 (7.6%)	11 (10.4%)	
BMI, mean ± SD	22.7 ± 3.4	23.6 ± 2.9	0.059
CCI, n (%)			0.716
0	87 (94.6%)	98 (92.5%)	
1	3 (3.3%)	6 (5.7%)	
2	2 (2.2%)	2 (1.9%)	
Thyroid disease, n (%)			0.357
Hashimoto's thyroiditis	10 (10.9%)	14 (13.2%)	
Subacute thyroiditis	0	0	
Hypothyroidism	0	2 (1.9%)	
Hyperthyroidism	0	0	
Laboratory studies, mean ± SD			
fT3 (pmol/L)	4.6 ± 0.98	4.9 ± 1.3	0.155
fT4 (pmol/L)	15.9 ± 2.6	15.4 ± 3.0	0.227
TSH (mIU/L)	2.1 ± 1.2	2.4 ± 1.4	0.095
Leukocyte (10^9/L)	5.9 ± 1.3	5.8 ± 1.4	0.712
Platelet (10^9/L)	246.7 ± 55.4	245.3 ± 58.4	0.867

MWA, microwave ablation; *BMI*, body mass index = weight (kg) ÷ height $(m)^2$; *CCI*, Charlson Comorbidity Index

Normal reference ranges for laboratory studies: fT3 (pmol/L): 2.76~6.3; fT4 (pmol/L): 10.42~24.32; TSH (mIU/L): 0.35~5.5; leukocyte (109/L): 4~10; platelet (109/L): 100~300

group included 2 (1.9%) cases with cervical LNMs in the untreated central neck during follow-up (p = 0.866). No LTP or distant metastasis was identified in either group. No significant differences between the two groups were found in either stage or capsule extension location subgroup analysis (all $p \geq 0.05$).

Quality of life

The results of the THYCA-QoL and HADS questionnaire scores are shown in Supplementary Table 4. The THYCA-QoL showed similar results regarding the specific domains affected, including voice, sympathetic symptoms, throat/mouth problems, psychological problems, sensory problems cold sensitivity, and weight gain, and had similar scores for the two groups (all $p > 0.05$), but for problems with scarring, the score of the surgery group was significantly higher ($p < 0.001$). The HADS questionnaire showed a higher anxiety score in the surgery group (p = 0.010) and similar depression scores between the two groups (p = 0.985). These results indicate a similar quality of life in the two groups, except for worse results for scar problems and anxiety in the surgery group.

Discussion

Current guidelines advise a reduction of diagnostic and therapeutic burden for low-risk thyroid cancers [25]. The available management approaches for T1N0M0 PTCs include surgery, thermal ablation, and active surveillance.

Active surveillance may be a good option for tumours located in the centre of the thyroid gland, but for mETE-PTCs, there are higher risk of developing into gETE and then upstaging to T3 in long-term surveillance. The psychological pressure of some patients about the progression of the disease also makes treatment necessary. Surgical resection is so aggressive that may do more harm than benefits for tumour with such indolent nature. US-guided thermal ablation represents an intermediate approach between active surveillance and surgery for mETE-PTC treatment with a principle of as little therapy as possible. In so far, MWA might be a better choice than surgery. In this multicentre prospective study, we

Table 2 Tumours characteristics of MWA and surgery groups

Characteristics	MWA (n = 92)	Surgery (n = 106)	p value
Size, mean ± SD			
Maximal tumour diameter (cm)	0.81 ± 0.30	0.89 ± 0.33	0.067
Tumour volume (mL)	0.23 ± 0.33	0.32 ± 0.37	0.067
Echogenicity, n (%)			0.947
Hypoechoic	81 (88.0%)	93 (87.7%)	
Heteroechoic	11 (12.0%)	13 (12.3%)	
Vascularity, n (%)			0.942
Absent	51 (55.4%)	57 (53.8%)	
Grade I	28 (30.4%)	31 (29.2%)	
Grade II	10 (10.9%)	13 (12.3%)	
Grade III	3 (3.3%)	5 (4.7%)	
Calcification, n (%)			0.085
Absent	45 (48.9%)	39 (36.8%)	
Present	47 (51.1%)	67 (63.2%)	
Tumour Location, n (%)			0.99
Left	40 (43.5%)	47 (44.3%)	
Right	42 (45.7%)	48 (45.3%)	
Isthmus	10 (10.9%)	11 (10.4%)	
Location of capsule extension, n (%)			0.378
Anterior	49 (53.3%)	52 (49.1%)	
Posterior	17 (18.5%)	30 (28.3%)	
Medial	11 (12.0%)	12 (11.3%)	
Lateral	15 (16.3%)	12 (11.3%)	
Stage, n (%)			0.263
T1a	77 (83.7%)	82 (77.4%)	
T1b	15 (16.3%)	24 (22.6%)	
Biopsy, n (%)			0.334
FNA	86 (93.5%)	95 (89.6%)	
CNB	6 (6.5%)	11 (10.4%)	

T1a, tumour diameter ≤ 1 cm; *T1b*, 1 cm < tumour diameter ≤ 2 cm

Vascularity: grade I: colour signals in < 25% of the nodule; grade II: colour signals in 25–50% of the nodule; grade III colour signals in > 50% of the nodule

compared the efficacy and safety of MWA and surgery in patients with US-detected T1N0M0 mETE-PTC, and our results demonstrated that MWA was technically feasible and we observed no significant different with surgery in terms of oncologic efficacy in short-time follow-up.

The first challenge faced by MWA treatment for PTC with mETE was its safety. The overall complication rates of MWA vs. surgery in our study were 3.3% vs. 3.8%. Similar results of 3.0–3.3% after TA and 1.2–4.5% after surgery were reported in previous studies [26–29]. However, it should be noted that MWA of tumours with posterior capsular extension has a significantly higher risk of hoarseness than surgery, with rates of 17.6% vs. 0%. This may be attributable to the proximity of the recurrent laryngeal nerve of tumours located near the posterior capsule. Thermal ablation necessitates a larger ablation zone, thereby increasing the risk of thermal injury to surrounding structures. This may indicate that, for tumours near the posterior capsule, MWA has a higher risk of temporary recurrent laryngeal nerve injury. However, all 3 cases of hoarseness due to mild thermal injuries quickly recovered within 3 months after treatment and no abnormality was found in vocal cord by laryngoscopy. In addition, 1 (0.9%) case of hoarseness in the surgical group was permanent. This may indicate that the damage to nerves caused by heat tends to be temporary, but inadvertent transection is hard to recover, and further research is valuable. Therefore, TA is safe in selected patients with T1N0M0 mETE-PTC.

LNM, especially central LNM, was another challenge for MWA. Some studies have shown favourable outcomes of TA in PTC without extrathyroidal invasion in a long-term follow-up [15, 30, 31]. Yan et al reported that 2.42% developed recurrent lesions, and 0.97% developed LNMs at a mean

Table 3 Treatment variables and complications of MWA and surgery groups

Parameter	Total			Subgroup of stage					
	MWA (n = 92)	Surgery (n = 106)	p value	T1a			T1b		
				MWA (n = 77)	Surgery (n = 82)	p value	MWA (n = 15)	Surgery (n = 24)	p value
Total operation time (min), mean ± SD	32.7 ± 5.1	96.6 ± 29.9	< 0.001	32.6 ± 5.2	94.6 ± 26.7	< 0.001	33.3 ± 5.9	103.4 ± 38.8	< 0.001
Intraoperative blood loss (mL), mean ± SD	0.2 ± 0.8	27.0 ± 20.6	< 0.001	0.2 ± 0.9	28.8 ± 21.8	< 0.001	0.3 ± 0.7	21.0 ± 14.8	< 0.001
Immediate postoperative pain score, mean ± SD	1.4 ± 0.9	3.2 ± 2.0	< 0.001	1.4 ± 0.9	2.9 ± 1.8	< 0.001	1.5 ± 1.2	4.3 ± 2.3	< 0.001
Cost (yuan), mean ± SD	22,898.9 ± 11,981.5	26,327.5 ± 8778.7	0.025	22,821.0 ± 12,164	24,878.1 ± 8158.6	0.218	23,298.8 ± 11,387.7	31,098.4 ± 9223.4	0.024
Major complications, n (%)	3 (3.3%)	4 (3.8%)	0.846	2 (2.6%)	4 (4.9%)	0.451	1 (6.7%)	0	0.200
Hoarse	3 (3.3%)	2 (1.9%)		2 (2.6%)	2 (2.4%)		1 (6.7%)	0	
Choking cough	0	0		0	0		0	0	
Skin burn	0	——		0	——		0	——	
Infection	0	2 (1.9%)		0	2 (2.4%)		0	0	

Table 4 Treatment variables and complications in different location of capsule extension of MWA and surgery groups

Parameter	Subgroup of location of capsule extension											
	Anterior			Posterior			Medial			Lateral		
	MWA (n = 49)	Surgery (n = 52)	p value	MWA (n = 17)	Surgery (n = 30)	p value	MWA (n = 11)	Surgery (n = 12)	p value	MWA (n = 15)	Surgery (n = 12)	p value
Total operation time (min), mean ± SD	32.6 ± 5.5	95.9 ± 28.8	< 0.001	33.2 ± 5.1	92.1 ± 33.4	< 0.001	32.8 ± 5.0	107.3 ± 30.6	< 0.001	32.5 ± 5.1	99.8 ± 24.7	< 0.001
Intraoperative blood loss (mL), mean ± SD	0.2 ± 0.8	28.7 ± 23.0	< 0.001	0.4 ± 1.3	24.0 ± 15.7	< 0.001	0.2 ± 0.6	33.3 ± 26.1	< 0.001	0.1 ± 0.3	21.3 ± 12.5	< 0.001
Immediate postoperative pain score, mean ± SD	1.5 ± 0.9	2.7 ± 1.6	< 0.001	1.5 ± 1.1	3.8 ± 2.2	< 0.001	0.8 ± 0.8	2.4 ± 1.2	< 0.001	1.3 ± 0.7	4.7 ± 2.4	< 0.001
Cost (yuan), mean ± SD	26,186.9 ± 9223.4	25,015.0 ± 7729.4	0.604	21,086.7 ± 11394.5	28,253.8 ± 8949.8	0.022	18,609.6 ± 3416.7	22,252.9 ± 4560.2	0.047	17,357.1 ± 3513.3	30,985.5 ± 12,736.5	0.004
Major complications, n (%)	0	3 (5.8%)	0.089	3 (17.6%)	0	0.019	0	0	1	0	1 (8.3%)	0.719
Hoarse	0	1 (1.9%)		3 (17.6%)	0		0	0		0	1 (8.3%)	
Choking cough	0	0		0	0		0	0		0	0	
Skin burn	0	——		0	——		0	——		0	——	
Infection	0	2 (3.8%)		0	0		0	0		0	0	

follow-up time of about 4 years and Zhang et al reported new lesions development and LNMs of TA vs. surgery for PTMC over 5 years follow-up, with incidences of 1.1% vs. 1.3% and 0 vs. 1.3%, respectively. Consistent with these results, 0 vs. 0.9% of new lesions and 2.2% vs. 1.9% of lymph metastases were found after MWA and surgery in our study. This may be part of the fact that mETE has no significant influence on the prognosis in solitary PTC [32–34]. In addition, our results showed that regardless of the tumours in T1a or T1b stage and the locations of capsule extension, the prognosis of the MWA group was similar to that of the surgical group. However, it should be noted that these results may be part of the short follow-up time and indolent nature of the tumour regardless of treatment strategy. Pathological results after dissection in surgery group showed that 24.5% patients had ultrasound-undetectable LNM and 5.7% had additional microcarcinoma foci, which could be similar in the MWA group for the same inclusion criteria. MWA could not eliminate ultrasound-undetectable LNM and microcarcinomas foci. Therefore, there were occasions that, for patients in the MWA group, only the primary lesion can be treated, but metastatic lymph nodes and additional foci remain. This might affect the incidence rate of LNM and NTC during the follow-up. Therefore, longer follow-up time was required to verify the LNM and NTC rate in this study. MWA may be as effective in the short term as surgery in treating primary thyroid cancer lesions.

Quality of life is an important measure for tumours with such good prognosis. The THYCA-QoL and HADS questionnaire results in our study showed similar scores in both groups, except for worse results for scar problems and anxiety in the surgery group. The higher anxiety scores of the surgery group may be related to the long-term thyroid hormone replacement therapy or that patients seriously anxious about their disease tend more to adopt surgical resection. MWA damages thyroid function less and does not require life-long hormone replacement, which may improve the patient's survival experience. However, further preoperative psychological evaluation is needed.

The cost and convenience of treatment for patients cannot be ignored for tumours with such a high prevalence. In our centre, patients with TA can choose outpatient or inpatient treatment. Outpatients can be discharged after 1 h of postoperative observation without obvious discomfort. Hospitalised patients can be discharged the next day after 1 day of postoperative observation. But for patients who underwent surgery, they were generally discharged 2–3 days after the operation for postoperative observation in our country. At the same time, ablation treatment does not require general anaesthesia, which reduces the risk of anaesthesia accidents. However, this may be affected by national factors, and further multi-country studies are needed.

Evaluation of tumour relies on preoperative ultrasonographic images. Previous studies reported a sensitivity of 87.5% in the diagnosis of mETE with sonography [35, 36], and our surgery group result showed an accuracy of 87.7%. Of the remaining, 11.3% were capsule-invasion-free and 0.9% were gETE. In addition, consistent with previous study [29], 6 (5.7%) patients in the surgery group had US-undetectable microscopic cancer foci, and 26 (24.5%) patients had clinically negative LNMs. These suggest that this may be same in the MWA group. Studies reported no clear benefit of prophylactic CLD in patients with clinically node-negative PTC [29, 37, 38]. Long-term observational studies are needed to determine whether these US-undetectable subtle lesions, LNMs and gETE will affect the survival prognosis of patients after ablation.

This study has several limitations. First, the number of cases is small and the follow-up time is short. Papillary thyroid carcinoma is a tumour with indolent nature, positive events after operation may take a considerable time to be observed and the results may vary as subsequent studies are carried out. Second, the assessment of tumour depends largely on the experience of the sonographer and occult PTCs and LNMs may be missed due to the sensitivity limitation of US. It remains unclear whether these are clinically relevant. Third, the diagnosis of PTC is based mostly on cytological samples, some aggressive histological types may not be excluded [39] and the effect of different subtypes on prognosis cannot be analysed. However, the above two points are unavoidable problems that MWA needs to face in the real world. In this study, patients in both groups were enrolled with results of preoperative ultrasound assessment and FNA or CNB. The comparison results of the two treatment methods should be more persuasive in a long follow-up for the same inclusion criteria. Further comparison with active surveillance would be especially valuable to clarify the clinical significance of ablation therapy.

In conclusion, MWA was comparable in the short term to surgery in terms of treatment safety and efficacy in selected patients with T1N0M0 mETE-PTC detected by ultrasound. More patients with longer follow-up will be necessary to validate whether these findings are durable.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00330-022-08962-6.

Acknowledgements All authors contributed to the idea, gathered the information, interpreted the data, and wrote and approved the final version of the manuscript.

Funding The authors state that this work has not received any funding.

Declarations

Guarantor The scientific guarantor of this publication is Ping Liang.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethics approval Institutional Review Board approval was obtained.

Methodology
- prospective
- diagnostic or prognostic study
- multicentre study performed at one institution

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