Original Article

The efficacy and safety of microwave ablation versus conventional open surgery for the treatment of papillary thyroid microcarcinoma: a systematic review and meta-analysis

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Background: Microwave ablation (MWA) technology has been applied to the treatment of papillary thyroid microcarcinoma (PTMC); however, its use as an alternative to conventional open surgery (OS) remains controversial, because it belongs to non-tumor radical treatment. Our article sought to compare the efficacy and safety of MWA and OS in the treatment of PTMC.

Methods: We searched seven databases for studies evaluating the treatment of patients with PTMC using MWA as intervention group and OS as control group, the main outcome contained intra-operative, post-operative and follow-up outcomes. Review Manager 5.4 was used to estimate the effects of the results of the included articles and Cochrane Risk of Bias 2.0 was used to assess the risk of bias. The data were pooled to calculate the mean differences (MD) with 95% confidence intervals (CIs) for the continuous data and the odds ratio (OR) with 95% CIs for the dichotomous data.

Results: A total of 13 studies, comprising 1,088 and 1,081 patients in the MWA and OS groups, respectively, were identified that compared the results of MWA to OS in the treatment of PTMC. All of the articles were at low risk of bias. There were no differences in terms of the recurrence rate (OR =0.80, 95% CI: 0.37 to 1.77; P=0.59) or lymph node metastasis (OR =0.71, 95% CI: 0.26 to 1.95; P=0.51) between the 2 groups. However, compared to the OS group, the MWA group had a shorter operation time (MD =–44.85, 95% CI: 5.73 to 20.68; P<0.00001), less intra-operative blood loss (MD =–23.37, 95% CI: –29.57 to –17.17; P<0.00001), a smaller surgical incision (MD =–47.04, 95% CI: –81.93 to –12.14; P=0.008), a shorter postoperative hospital stay (MD =–4.19, 95% CI: –5.46 to –2.92; P<0.00001), lower hospitalization expenses (MD =–85.65, 95% CI: –133.86 to –37.45; P<0.00001), and fewer complications (OR =0.23, 95% CI: 0.16 to 0.33; P<0.00001).

Conclusions: This meta-analysis suggests that MWA is better than OS at treating PTMC in terms of both intra-operative and post-operative outcomes. Due to the quality and number of the included studies, the long-term effects and suitability of MWA in the treatment of PTMC need to be further studied.

Keywords: Microwave ablation (MWA); open surgery (OS); papillary thyroid microcarcinoma (PTMC); meta-analysis

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Introduction

Thyroid nodules are common diseases in the endocrine system. Most thyroid nodules are benign, but 5–15% are malignant (1). The most common type of thyroid malignancy is papillary thyroid carcinoma (PTC), which accounts for 70% of thyroid malignancies. Papillary thyroid microcarcinoma (PTMC) refers to a PTC ≤1 cm in diameter (2). In recent years, the incidence and detection rate of thyroid cancer has been rising, and most thyroid cancers are low-risk PTMC (3). Studies have shown that the mortality rate of PTMC patients is about 0–2.2% (4,5). The stable attributable mortality rate of thyroid cancer indirectly reveals the low risk and low mortality of PTMC.

The current standard of care for PTMC is conventional open surgery (OS). However, the risk of OS is high. In OS, normal thyroid tissue may be innocently removed, parathyroid glands are involved, and cervical lymph nodes are dissected (6). Further, various types of complications can occur after OS, which can seriously affect the quality of life and the health of patients.

In recent years, minimally invasive technology has developed rapidly. Ultrasound-guided microwave ablation (MWA) technology has achieved good safety and therapeutic effects in the treatment of benign thyroid nodules, and compared to OS, MWA technology results in fewer postoperative complications, has no effect on thyroid function, causes less trauma, and enables the faster recovery, and improved appearance of some PTMC patients (7-9). However, Tong's study mentioned that MWA only inactivates cancer nodules and does not remove the surrounding lymph nodes, and has a high risk of residual cancer foci and lymph node metastasis, even after microwave ablation, there are still a few tumors with recurrence and lymph node metastasis, which can not be used as a routine treatment for primary operable primary thyroid cancer (10). Therefore, MWA is a non-radical treatment for tumors, and its use as a routine treatment remains controversial (11).

To date, no systematic review has been conducted on the efficacy and safety of MWA and OS in the treatment of PTMC patients. By summarizing the published literature on the efficacy and safety of MWA versus OS in the treatment of PTMC, we strictly select and evaluate relevant research, extract data and merge them with a meta-analysis, compare the efficacy and safety indexes during surgery, postoperatively, and in a follow-up period to systematically evaluate the advantages and disadvantages of these 2 treatment schemes, then draw comprehensive conclusions and provide an evidence base for clinical decision making. We present the following article in accordance with the MOOSE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-22-243/rc).

Methods

Literature search strategy

We systematically searched 7 electronic databases, PubMed, Excerpta Medica Database (EMBASE), Cochrane Library, Web of Science, WanFang database, China National Knowledge Infrastructure (CNKI), and Chinese BioMedical Database (CBM), from their establishment to March 2022, using the following keywords: (I) microwave ablation (MWA); (II) open surgery (OS); and (III) papillary thyroid microcarcinoma (PTMC). In the strategy, all these words were combined using the Boolean operators "AND" or "OR". There were no restrictions on the publication language in the literature search. The search strategy, including the literature search and reference list screening, was developed by 2 of the authors, but it should be noted that this search strategy may not have captured all the relevant studies.

Study selection

To be eligible for inclusion in our meta-analysis, the studies had to meet the following criteria: (I) include patients in the stable stage of PTMC; (II) include a MWA test group; (III) include an OS control group; (IV) examine the main outcome indicators of intra-operative outcomes (i.e., operation time, blood loss, and incision size), post-operative outcomes (i.e., length of hospital stay, and hospitalization expenses), and follow-up outcomes (i.e., complication rate, recurrence rate, and lymph node metastasis) and (V) the study design can be prospective or retrospective, and the publication language can be English or Chinese. Studies were excluded from our meta-analysis for the following reasons: (I) the research examined other diseases; (II) the research compared other interventions; (III) the study lacked available data; and (IV) the article was a review, abstract, or duplicate publication.

Data extraction and quality assessment

The data extraction was performed independently by 2 investigators (N Liu and Q Hu), and any disagreements were resolved by consensus or consultation with a third

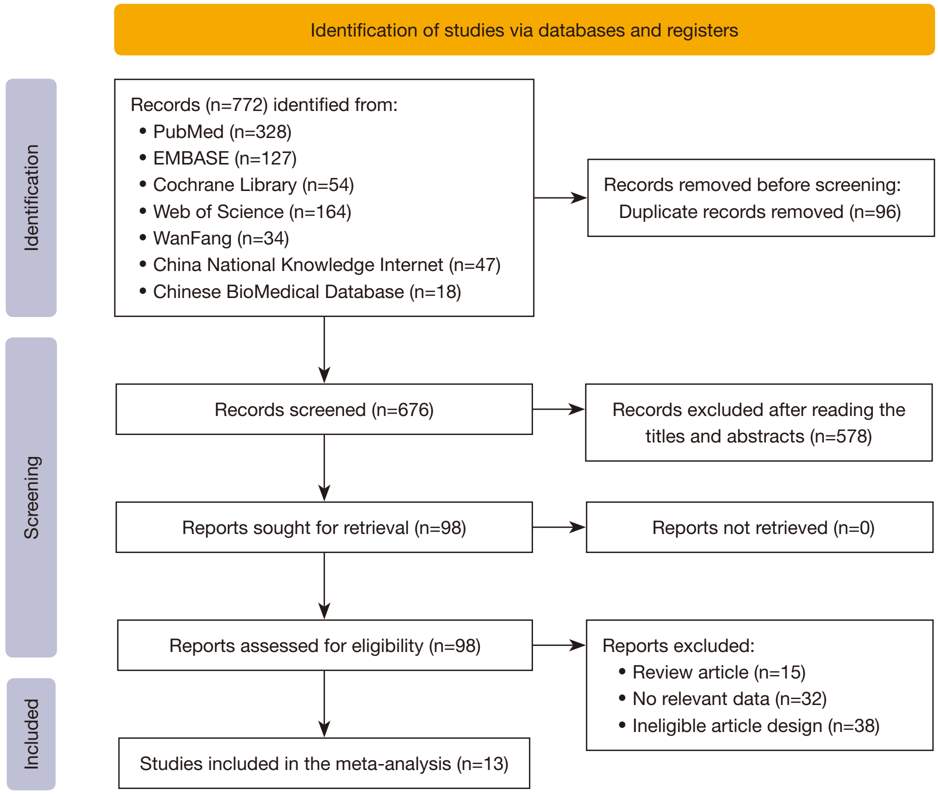

Figure 1 Flow chart for eligible studies.

reviewer. Prespecified data elements were extracted from each study using a structured data abstraction form. The data extracted included the study authors, study design, patient characteristics (i.e., age and gender), year of research duration, and follow-up period. As all the included studies were non-randomized clinical trials, the risk-of-bias assessment was performed using the Cochrane Risk of Bias 2.0.

Statistical analysis

In our study, the meta-analysis was performed with Review Manager 5.4 (The Cochrane Collaboration, 2020) to estimate the different effects between the MWA and OS groups of patients with PTMC. In brief, we used the odds ratio (OR) for the pooling effects of the binary variables and the mean difference (MD) for the continuous variables. The statistical heterogeneity between the studies was assessed using the chi-square test or Cochran's Q test, and the I^2 statistic, which measured inconsistencies across study results and describes the proportion of total variation in study estimates due to heterogeneity rather than sampling errors. If there was no statistical heterogeneity among the included studies, a fixed-effects model was used for the meta-analysis, but if there was heterogeneity among the included studies, a random-effects model was used. The Egger's test and a funnel plot were used to examine potential publication bias.

Results

Search process

The literature search retrieved 772 unique studies, and after the removal of duplicate files, 676 articles were screened to determine their eligibility. From these, 578 articles were further excluded based on the screening of the abstracts and titles. The full text of 98 articles were reviewed to determine the type of article, the outcome data of interest, and the study design. Ultimately, 13 articles were included in our meta-analysis and subjected to data extraction (12-24). The literature search process, the inclusion and exclusion criteria, and the final sample size are illustrated in *Figure 1*.

Table 1 Main characteristics of the studies included in the meta-analysis

Study	Study design	No. of patients		Gender (M/F)		Age (years)*		Mean diameter of nodule (mm)*		Follow-up	Duration
		MWA	OS	MWA	OS	MWA	OS	MWA	OS		
Ma 2017	Retrospective study	30	35	3/27	7/28	46.10±8.20	49.97±10.30	–	–	6 months	January 2014 to November 2015
Chen 2018	Retrospective study	49	40	9/40	5/35	44.88±11.04	45.78±13.74	–	–	24 months	January 2014 to February 2017
Li 2018	Retrospective study	46	46	16/32	13/33	43.63±9.27	49.59±9.0	4.49±1.55	4.29±1.37	42 months	February 2014 to August 2017
Xu 2018	Retrospective study	41	46	12/29	16/30	45.8±10.2	46.2±11.5	8.87±1.01	8.13±1.22	–	January 2012 to October 2017
Gong 2019	Retrospective study	79	73	26/53	20/53	49.32±7.48	48.86±7.42	6.31±1.71	6.28±1.69	1 month	May 2014 to February 2018
Huo 2019	Retrospective study	50	50	14/36	12/38	43.66±9.54	45.14±9.82	7.14±2.26	6.95±2.42	6 months	January 2016 to December 2017
Li 2019	Retrospective study	168	143	36/132	29/114	47.36±10.75	49.18±11.41	–	–	12 months	January 2013 to September 2018
Wang 2019	Retrospective study	35	35	19/16	20/15	46.18±8.35	45.16±7.58	–	–	–	December 2017 to December 2018
Wang 2020	Retrospective study	36	36	18/18	19/17	45.6±8.5	46.1±8.9	–	–	6 months	April 2018 to April 2019
Yao 2020	Retrospective study	120	120	19/101	22/98	45.86±8.30	46.02±8.11	5.89±1.12	5.96±1.05	12 months	January 2017 to December 2018
Zhou 2020	Retrospective study	51	50	11/40	14/36	44.72±9.94	42.16±10.28	4.46±1.39	4.30±1.25	18 months	May 2014 to January 2017
Wang 2021	Retrospective study	63	83	12/51	24/59	43.56±14.17	43.32±10.88	4.5±1.1	4.5±1.1	24 months	2016 to 2018
Zu 2021	Retrospective study	320	324	83/237	77/247	44.99±10.62	43.91±11.47	4.99±1.93	5.11±1.88	7 years	July 2013 to June 2020

*, the data were presented as mean ± standard deviation. MWA, microwave ablation; OS, open surgery.

Characteristics of included studies

Table 1 presents a comprehensive description of each trial included in the meta-analysis. All of the 13 included studies were non-randomized retrospective studies. A total of 2,169 patients (1,088 MWA patients and 1,081 OS patients) were included in the meta-analysis. The sample sizes of the studies ranged from 65 to 644. The mean diameter of the nodules was >4 mm. As MWA is a relatively new treatment for PTMC, all the research studies had been published after 2017.

Results of quality assessment

The quality of the included studies and the risk of bias were assessed in accordance with the Cochrane Risk of Bias 2.0. Of the 13 articles, all were non-randomized clinical trials, 2 articles did not include all the outcome variables of interest, and 3 articles had a short or no follow-up period.

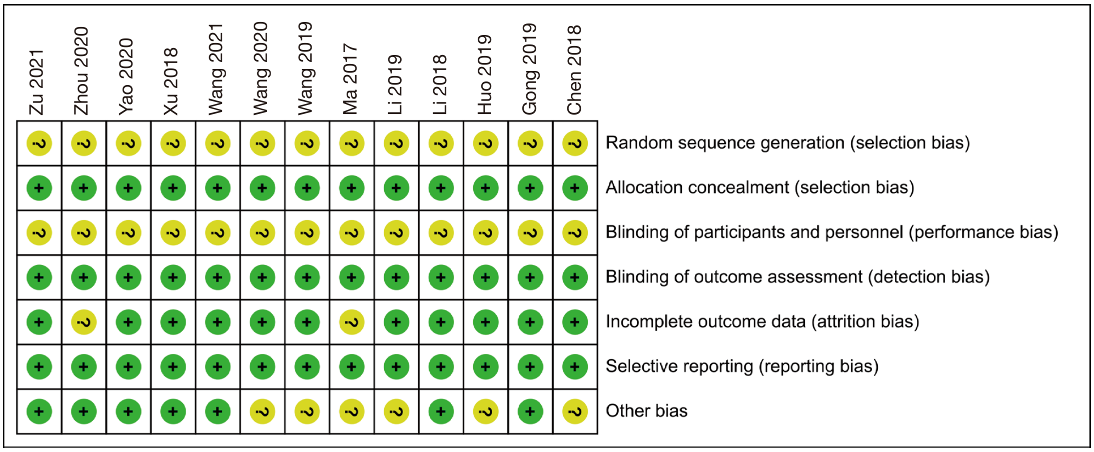

Figure 2 Summary of Cochrane risk of bias assessments of included studies: low risk (green), unclear risk (yellow), and high risk (red).

Table 2 Results of the meta-analysis of the outcomes of interest.

Outcome of interest	Studies (n)	Patients (n)	MD/OR	95% CI	P	I^2 (%)
Intra-operative outcomes						
Operation time	10	1,641	–44.85 (MD)	–58.08 to –31.62	<0.00001	100
Blood loss	9	1,552	–23.37 (MD)	–29.57 to –17.17	<0.00001	99
Incision size	5	1,083	–47.04 (MD)	–81.93 to –12.14	0.008	100
Post-operative outcomes						
Length of hospital stay	9	1,401	–4.19 (MD)	–5.46 to –2.92	<0.00001	99
Hospitalization expenses	5	1,166	–85.65 (MD)	–133.86 to –37.45	0.0005	100
Follow-up outcomes						
Complication rate	12	2,023	0.23 (OR)	0.16 to 0.33	<0.00001	0
Recurrence rate	8	1,670	0.8 (OR)	0.37 to 1.77	0.59	0
Lymph node metastasis	8	1,659	0.71 (OR)	0.26 to 1.95	0.51	0

MD, mean difference; OR, odds ratio; CI, confidence interval.

The summary bias assessment of each included article were shown in *Figure 2*.

Results of meta-analysis

The results of the meta-analysis are summarized in *Table 2*.

Intra-operative outcomes

Of the 13 studies, 10 (comprising 1,641 patients) examined operation time. The MWA group had a significantly shorter operation time than the OS group (MD =–44.85, 95% CI: –58.08 to –31.62; P<0.00001, random-effects model; see *Figure 3*). Of the 13 studies, 9 analyzed blood loss. The pooled results showed that the MWA group had significantly less blood loss than the OS group (MD =–23.37, 95% CI: –29.57 to –17.17; P<0.00001, random-effects model; see *Figure 4*). Of the 13 studies, 5 (comprising 1,083 patients) reported on incision size. Overall, the pooled estimate showed that the incision size of the MWA group was significantly less than that of the OS group (MD =–47.04, 95% CI: –81.93 to –12.14; P=0.008, random-effects model; see *Figure 5*).

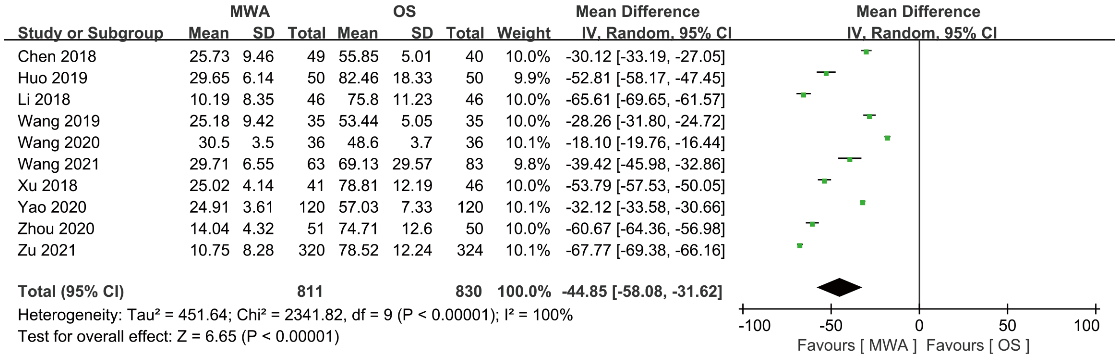

Figure 3 Forest plot evaluating the outcome of operation time. MWA, microwave ablation; OS, open surgery.

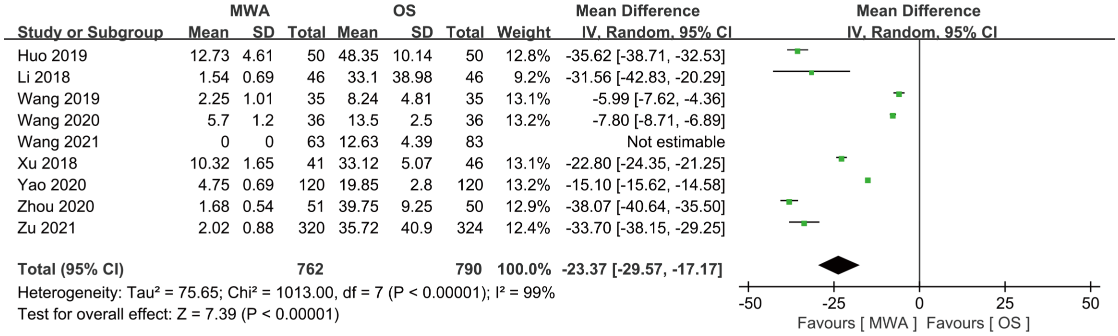

Figure 4 Forest plot evaluating the outcome of blood loss. MWA, microwave ablation; OS, open surgery.

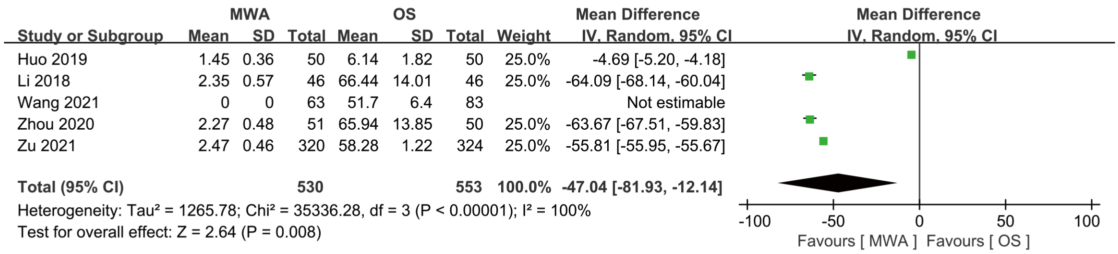

Figure 5 Forest plot evaluating the outcomes of incision size. MWA, microwave ablation; OS, open surgery.

Post-operative outcomes

Of the 13 studies, 9 (comprising 1,401 patients) evaluated the length of hospital stay. The pooled result showed MWA had a significant beneficial effect in decreasing patients' length of hospital stay (MD =–4.19, 95% CI: –5.46 to –2.92; P<0.00001, random-effects model; see *Figure 6*). Of the 13 studies, 5 assessed hospitalization expenses. The pooled data revealed that the hospitalization expenses of the MWA group were significantly less than those of the OS group (MD =–85.65, 95% CI: –133.86 to –37.45; P=0.0005, random-effects model; see *Figure 7*).

Follow-up outcomes

Of the 13 studies, 12 (comprising 2,023 patients) examined complications. The complication rate of the MWA group was significantly decreased compared to that of the OS group (OR =0.23, 95% CI: 0.16 to 0.33; P<0.00001, fixed-effects model; see *Figure 8*). Of the 13 studies, 8 (comprising 1670 patients), examined the recurrence rate, but no significant difference was found between the MWA group

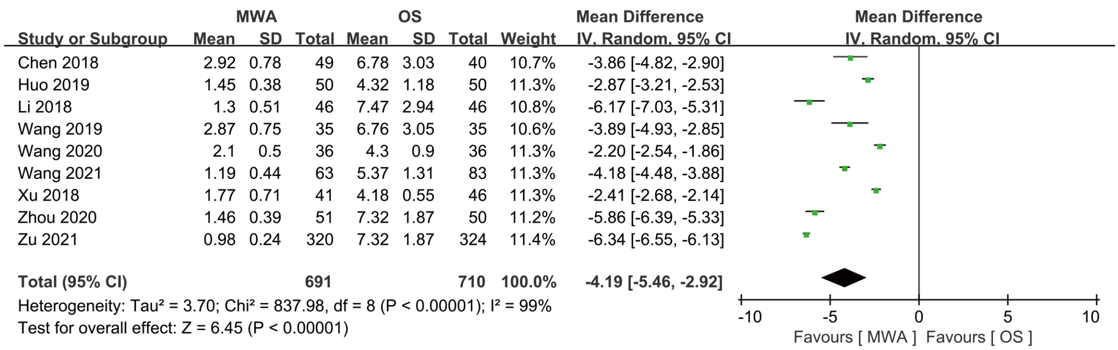

Figure 6 Forest plot evaluating the outcome of length of hospital stay. MWA, microwave ablation; OS, open surgery.

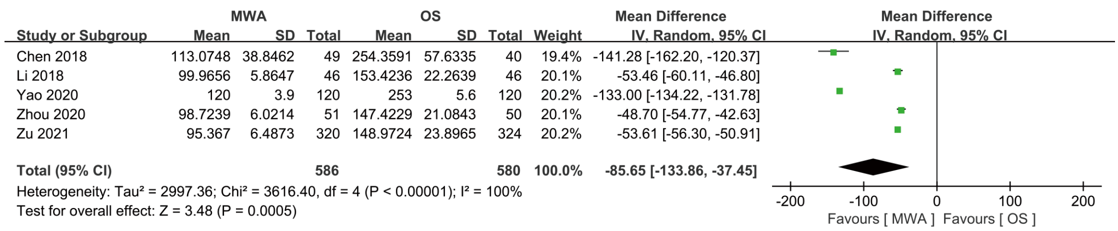

Figure 7 Forest plot evaluating the outcome of hospitalization expenses. MWA, microwave ablation; OS, open surgery.

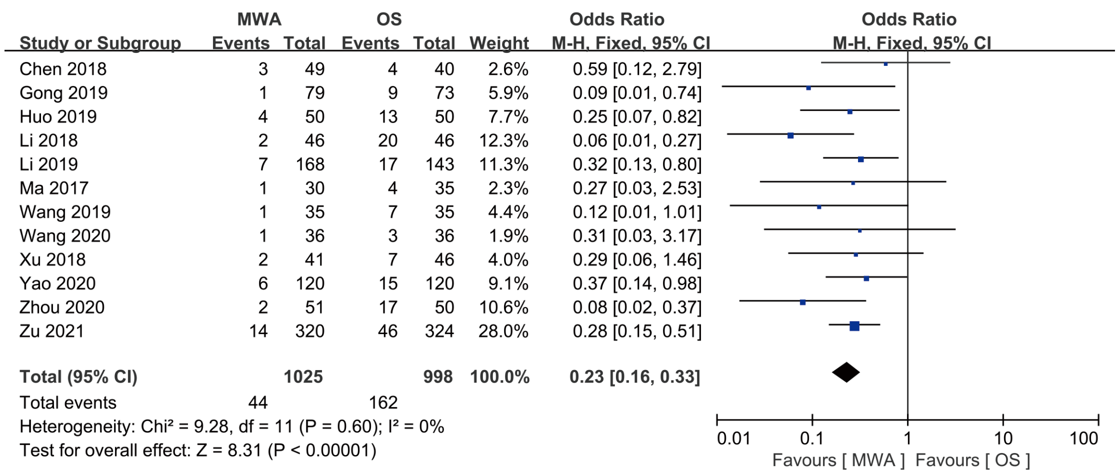

Figure 8 Forest plot evaluating the outcome of complication rate. MWA, microwave ablation; OS, open surgery.

and the OS group (OR =0.80, 95% CI: 0.37 to 1.77; P=0.59, fixed-effects model; see *Figure 9*). Similarly, a meta-analysis of the differences in lymph node metastasis between the 2 groups was conducted, but no significant difference was found (OR =0.71, 95% CI: 0.26 to 1.95; P=0.51, fixed-effects model; see *Figure 10*).

Results of publication bias

If >10 studies were included in the meta-analysis, the data were evaluated for publication bias. Thus, we examined the funnel plot for the complication rate. As *Figure 11* showed, the plot was approximately symmetrical, and Egger's test

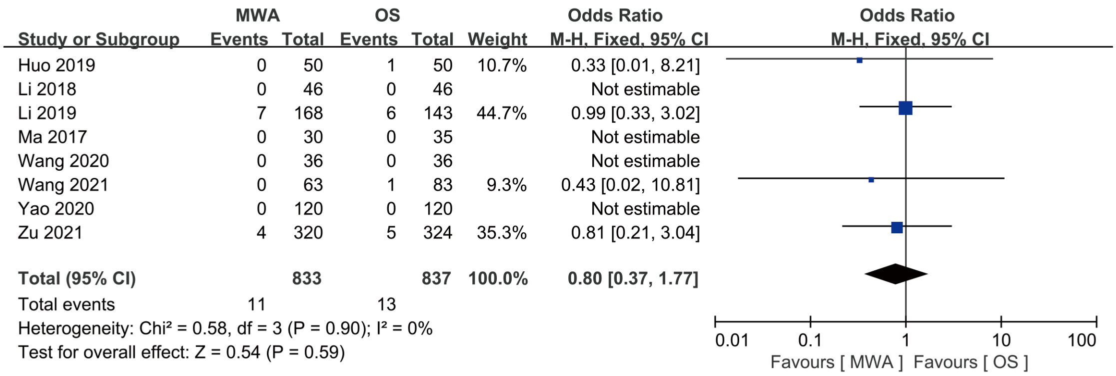

Figure 9 Forest plot evaluating the outcome of recurrence rate. MWA, microwave ablation; OS, open surgery.

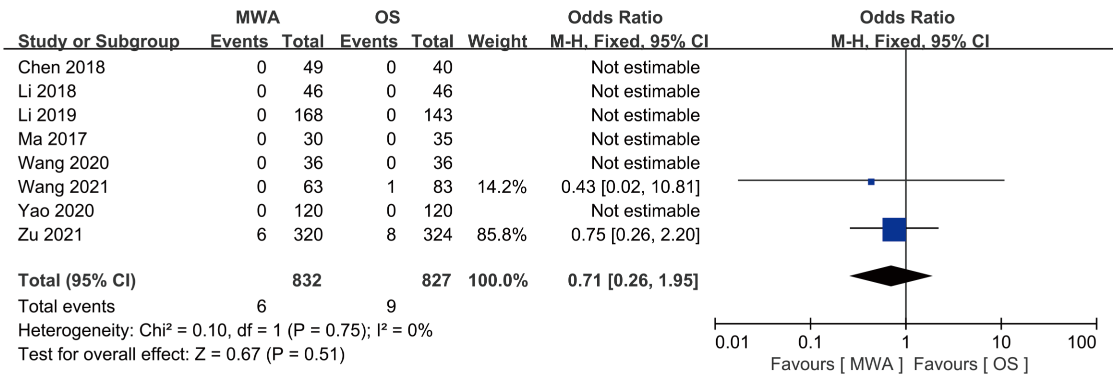

Figure 10 Forest plot evaluating the outcome of lymph node metastasis. MWA, microwave ablation; OS, open surgery.

also revealed no significant publication bias (P=0.718).

Discussion

Traditional thyroidectomy is a mature technique used in the treatment of PTMC, and the effect is accurate, but due to the need for an incision of 6–8 cm, the injury is relatively large and bleeding is relatively high (25,26). Additionally, hematomas can compress the trachea and esophagus, and even cause suffocation, the neck flap, muscles, nerves, and blood vessels can be greatly damaged during the operation, normal blood and lymphatic reflux can be destroyed, and parathyroid-gland damage can cause complications, such as hypocalcemia convulsions (27,28). With the improvement of modern minimally invasive technology, MWA technology has been applied in the clinical treatment of various benign and malignant tumors, such as those in the liver, lungs, and kidneys (29-31). This minimally invasive treatment, which has a number of advantages, including less adverse reactions, a shorter operation time, less intra-operative blood loss, and a shorter postoperative hospital stay, is increasingly being used in the treatment of thyroid surgery, and its clinical treatment has been widely recognized (32,33).

In this study, a meta-analysis was conducted of 13 studies to compare the efficacy of MWA and OS in the treatment of PTMC. Compared to the OS group, the MWA group had a shorter operation time (MD =–44.85, 95% CI: 5.73 to 20.68; P<0.00001), less intra-operative blood loss (MD =–23.37, 95% CI: –29.57 to –17.17; P<0.00001), a smaller surgical incision (MD =–47.04, 95% CI: –81.93 to –12.14; P=0.008), a shorter postoperative hospital stay (MD =–4.19, 95% CI: –5.46 to –2.92; P<0.00001), lower hospitalization expenses (MD =–85.65, 95% CI: –133.86 to –37.45; P=0.0005), and fewer complications (OR =0.23, 95% CI: 0.16 to 0.33; P<0.00001), and the differences were statistically significant. However, there was no significant difference in the incidence of recurrence (OR =0.80,

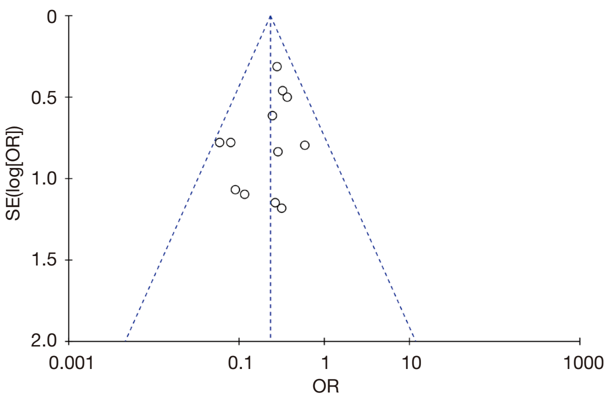

Figure 11 Forest plot: MWA versus OS for the complication rate. MWA, microwave ablation; OS, open surgery; OR, odds ratio.

95% CI: 0.37 to 1.77; P=0.59) or lymph node metastasis (OR =0.71, 95% CI: 0.26 to 1.95; P=0.51) between the 2 treatment methods during the follow-up period. The above results showed that MWA has a good effect on PTMC.

MWA uses electrodes to generate microwaves. The polar molecules in the tissue move at high speed in the microwave field and generate heat by friction. The temperature of the tissue increases under the action of thermal energy, and is followed by dehydration, protein denaturation, and irreversible necrosis (34,35). Finally, under the immune phagocytosis of the body, the necrotic tissue slowly shrinks and disappears, which achieves the purpose of eliminating local tumors. Ablation only causes damage to a part of the normal thyroid tissue and does not affect thyroid function. Thus, the long-term use of thyroid hormone replacement drugs can be avoided, and it has little effect on patients' quality of life (36). The ablation is generally performed under local anesthesia, and due to precise positioning by ultrasound, the location, size, texture, and blood supply of the tumor nodules can be comprehensively explored (37). Additionally, by reducing the risk of tissue damage around the thyroid gland, such as the esophagus, trachea, and parathyroid glands, and protecting the surrounding tissue by the intraoperative fluid barrier, the treatment effect is enhanced and the risk of complications is reduced. Compared to OS, MWA has obvious advantages, such as its use of general anesthesia and a larger incision, especially for patients at high surgical risk, with scar constitution, a short lifespan, or those who need surgery as soon as possible (38).

In the included studies, the most common complications in the MWA group were transient hoarseness or choking after drinking water, which mainly occurred because the target nodule ablation was close to the dorsal capsule, the "liquid barrier" was insufficient, or during the puncture process (39). If the gland and surrounding tissue are squeezed or the ablation time is too long, the "liquid isolation zone" shrinks, and thermal damage leads to nerve damage. Additionally, the lever prying method requires the operator to have extensive practical experience. If the timing is not good for lever prying, it is easy to damage the nerve or cause residual tumor (40). In the OS group, complications may have been reduced due to advances in surgical techniques, including the use of intraoperative neuromonitoring. Additionally, no patients in either group experienced life-threatening complications, such as postoperative bleeding, laryngeal edema, or dyspnea (41).

As awareness of thyroid cancer increases, it is hoped that in the future, the biological behavior of indolent PTC will be screened as ablation indications, and ablations will be able to be performed with certainty (42). It has been reported that central lymph node metastases does not affect the prognosis of PTMC patients. However, the use of MWA to treat patients with potential central lymph node metastases should be considered with caution, and patients suitability should be strictly controlled (43). To avoid the excessive pursuit of minimally invasive surgery, the preoperative screening of non-invasive PTMC is key; however, the questions of how to identify non-invasive PTMC patients and accurately evaluate preoperative lymph nodes require further study (44).

This study had a number of limitations. First, MWA treatment of thyroid cancer is currently uncommon, and various studies on MWA were only in the explorative stage. Second, the included studies were all studies that had been conducted in the past 5 years; thus, the long-term effects of MWA are not yet known, especially the long-term recurrence rate and postoperative cancer metastasis rate. Finally, the included studies were all non-randomized clinical trials, and the lack of randomized, double-blind, large-sample randomized controlled trial data may have reduced the quality of the present study.

Conclusions

In conclusion, compared to OS, the use of MWA in the treatment of PTMC has the advantages of producing less trauma, a faster recovery, and fewer complications. The efficacy of MWA is similar to that of OS, and its clinical application value is high. However, the current follow-up time of studies is short, and the MWA technique may still have uncertain hidden dangers, such as tumor recurrence and lymph node metastasis. Long-term follow-up studies with large samples need to be conducted to further confirm our results, and the suitability of MWA for patients needs to be further evaluated.

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Footnote

Reporting Checklist: The authors have completed the MOOSE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-22-243/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-22-243/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that any questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved.

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