



Research article

Efficacy and safety of thermal ablation modalities for the treatment of papillary thyroid microcarcinoma: Systematic Review and network meta-analysis

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ABSTRACT

Background: Thermal ablation (TA) modalities such as radiofrequency ablation (RFA), microwave ablation (MWA), and laser ablation (LA) have been widely used in the treatment of papillary thyroid microcarcinoma (PTMC) patients. Based on previous small-sample meta-analyses, this network meta was designed to further compare the efficacy and safety of these thermal ablation methods in PTMC patients.

Methods: China National Knowledge Infrastructure (CNKI), Wanfang, PubMed, Embase, and the Cochrane Library databases were searched to retrieve relevant studies published before May 2022. The efficacy outcomes was recurrence and lymph node metastasis (LNM), the safety outcome included operation time, intra-operative blood loss, hospital stays and complications. The Newcastle-Ottawa Scale (NOS) was selected for the risk of bias assessment. Stata 14.0 was used for statistical analysis.

Results: Twenty-nine articles were included. Based on as least 6 months follow up, our analysis discovered no significant statistical differences in all efficacy and safety outcomes between MWA, RFA, and LA groups. Moreover, three TA treatments all produced significant least operation time, hospital stays, and complications than surgery group. Additionally, our study found that RFA showed relatively less complications, LNM, operation time and intra-operative blood loss, compared with other TA treatments. MWA indicated the lowest probability of recurrence, LA showed the longest hospital stays.

Conclusions: MWA, RFA, and LA are all effective treatment strategies for patients with PTMC, but could not completely replace conventional surgical treatment.

1. Introduction

Thyroid cancer (TC) is the 9th most frequently diagnosed cancer, with an estimated 586 000 new cases worldwide in 2020 [1]. Papillary thyroid carcinoma (PTC) is the most common subtype of TC, accounting for about 85 % [2]. The incidence of PTC is recently increasing markedly due to the incidental detection of small PTCs or widespread ultrasound (US) screening [3,4]. The World Health Organization defined PTC measuring 10 mm or less as papillary thyroid microcarcinoma (PTMC) [5]. Generally, MPTC has a very

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favorable prognosis, with a disease-specific mortality rate of less than 1 % [6].

Nowadays, thyroid surgery is recommended as the standard treatment for PTMC by most professional society guidelines [7]. Although surgery has the advantage of a low recurrence rate, it is considered overtreated due to its disadvantages, a high risk of complications, and the need for long-term medication. Besides, surgery comes with higher medical costs [8,9]. The American Thyroid Association (ATA) emphasized active surveillance for PTMC [7]. Although active surveillance has presented favorable results, a previous study of 5-year follow-up results reported that 8.7–32 % of patients delayed surgeries owing to significant anxiety [10]. That may cause more extensive surgery and subsequent profound complications than immediate surgery. Therefore, minimally invasive treatment techniques without serious complications should be proposed for PTMC patients.

As a new strategy, thermal ablation (TA) has been considered an alternative treatment for malignant tumors [11–13]. TA mainly includes microwave ablation (MWA), radiofrequency ablation (RFA), and laser ablation (LA). RFA is a method that employs high-frequency electrical energy to induce thermal effects and eradicate malignant cells. This technique involves the insertion of a needle electrode into the tumor, guided by ultrasound, while ensuring the safeguarding of adjacent tissues through cooling mechanisms. LA employs a laser to generate thermal effects, leading to the destruction of tumor cells. Similar to RFA, this procedure involves the insertion of a needle into the tumor under ultrasound guidance. MWA employs microwave energy to generate thermal effects, resulting in the eradication of tumor cells. Comparable to RFA and LA, this procedure entails the insertion of a needle into the tumor under ultrasound guidance.

TA is used primarily on patients with recurrence PTC and benign nodules [14]. Emerging studies have also reported that TA was used for treating primary PTMC [8,15,16]. Furthermore, some meta-analysis has shown that all thermal ablation techniques were effective and safe for treating PTMC [17–19]. Although several meta-analyses have discussed the efficacy and safety between TA and surgery, few studies compare the efficacy and safety of MWA, RFA, and LA for treating PTMC patients by network meta-analysis. Therefore, with a network meta-analysis, we aimed to compare the relative effectiveness and safety of MWA, RFA, and LA for PTMC patients.

2. Materials and methods

2.1. Literature search strategy

We performed a current meta-analysis using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement and the PRISMA network meta-analysis extension statement [56,57]. China National Knowledge Infrastructure (CNKI), Wanfang, PubMed, Embase, and Cochrane Library databases were searched to identify relevant studies that compared the relative efficacy and safety of MWA, RFA, and LA in patients diagnosed with PTMC and were published from the database establishment to May 22, 2022. The following search terms were used: (papillary thyroid cancer OR papillary thyroid carcinoma OR papillary thyroid microcarcinoma) AND (microwave ablation OR radiofrequency ablation OR laser ablation). We also manually searched the references of relevant reviews to include eligible studies. Search strategies were summarized in [Supplementary Table 1](#). The literature retrieval and selection process was performed independently by two investigators. Any discrepancy was solved by discussion.

2.2. Eligibility criteria

According to the Population, Intervention, Comparator, Outcomes, and Study designs (PICOS) structure, the included studies should meet the following criteria:

- (1) Studies targeted on patients clinically diagnosed with PTMC;
- (2) Intervention or control groups received MWA, RFA, LA, or surgery (total thyroidectomy or thyroid lobectomy) treatment;
- (3) Study endpoints included comparison of the efficacy (recurrence and LNM) and safety outcomes (operation time, intra-operative blood loss, hospital stays and complications) of MWA, RFA, LA, or surgery treatment.
- (4) Studies with any comparative designs (i.e., randomized controlled trials [RCTs], prospective cohort studies [PC], or retrospective cohort studies [RPC]);

The exclusion criteria were.

- (1) Animal/cell researches were excluded;
- (2) Letters, case reports, comments, reviews, and conference abstracts were excluded;
- (3) Studies not published in an international peer-reviewed journal;

2.3. Data extraction

Two authors independently selected eligible studies by screening titles, abstracts and full texts. Then, one author (Lifei Li) extracted data, and another (Zhijian Kou) examined the data. The following items were abstracted according to the standard protocols: the first author's surname, publication year, location, study design, sample size, mean age, gender, the diameter of the nodule, type of TA, operation time, intra-operative blood loss, hospital stays, recurrence, lymph node metastasis, and complications. Any discrepancy was solved by discussion.

2.4. Quality assessment

Our study adopted the Newcastle-Ottawa Scale (NOS) [58] to assess the methodological quality of eligible studies. NOS ranges from 0 to 9-star systems with, NOS scores ≥ 7 as high and < 7 as low.

2.5. Statistical analysis

Standardized mean difference (SMD) with 95 % confidence intervals (CI) for continuous variable or odds ratio (OR) with 95 % CI for a dichotomous variable were determined to compare the efficacy and safety of three types of TA for PTMC. I^2 testing was utilized to calculate statistical heterogeneity. $I^2 > 50\%$ was considered the presence of heterogeneity among studies. The analysis was performed using the random-effects model as appropriate. Otherwise, the fixed-effects model was adopted. Additionally, when combining the results of direct and indirect comparisons, our study assessed inconsistency by node splitting analysis. If $P > 0.05$, the direct comparison result is consistent with the indirect comparison result; otherwise, it is inconsistent. A simple numerical summary of cumulative ranking is to estimate the surface under the cumulative ranking (SUCRA) for each type of TA. Also, a funnel plot was used to test publication bias in our network meta-analysis.

Stata 14.0 software (Stata Corp.) was used in the present Network Meta-Analysis (NMA).

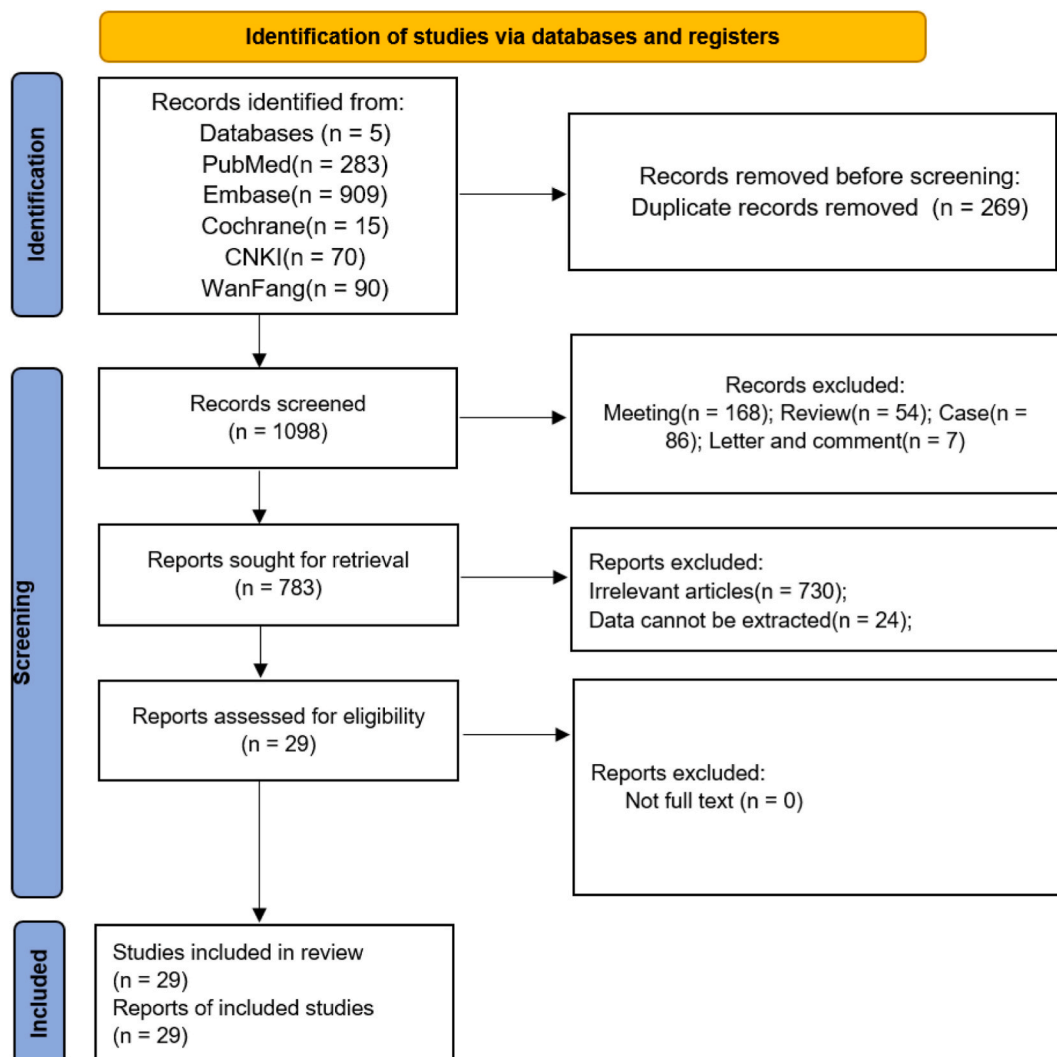


Fig. 1. Flow diagram of literature screening and search results.

3. Results

3.1. Selection of studies for inclusion

Initially, 1367 articles were retrieved, of which 269 duplicated articles and another 1045 articles (86 case reports, 168 conference abstracts, 54 reviews, 730 irrelevant articles, and seven letters and comments) were excluded after reviewing their titles and abstracts. In addition, since the original data was presented in the form of charts, accurate data was difficult to extract, 24 articles were excluded after reviewing the full text. Finally, 29 articles [8,9,15,16,20–44] were included in the present study (Fig. 1).

3.2. Characteristics of the included studies

Among the 29 included articles, all studies were conducted in China and were retrospective. All included studies involved 4789 PTMC patients, and the mean age ranged from 37 years to 50 years. Far more women than men were included. The average nodule diameter is greater than 4 mm. The included PTMC patients were solitary, single lesions, with no evidence of extrathyroidal invasion, lymph node metastasis, or distant metastasis. Most research follow-up time is more than 6 months. Out of 29 studies, 18/29 evaluated MWA, 7/29 evaluated RFA, 3/29 compared MWA vs. LA and RFA, and 1/29 evaluated LA. And 23, 22, 17, 9, 7, and 28 reported the operation time, intra-operative blood loss, hospital stays, recurrence, LNM, and complications, respectively (Table 1). The NOS quality was moderate-high overall. Fig. 2 presents the network diagram of evidence for each type of TA's treatment efficacy and safety.

3.3. Quality assessment of eligible studies

Supplementary Table 2 shows the results of quality assessment. Overall, all included studies received moderate to high quality evaluation scores (6–8 points), and because all included studies were retrospective designs, full marks were obtained in terms of patient selection and comparability. The only concern is that different degrees of data missing due to retrospective data collection methods were found in the four included studies, which is the main reason for the 6-point evaluation.

3.4. Analysis of inconsistency

In the evidence network diagram, there were three closed loops in the operation time (MWA-LA-surgery, Fig. 2A), hospital stays (MWA-LA-surgery, Fig. 2C), and complications (MWA-RFA-LA-surgery, Fig. 2F). Node splitting analysis indicated no inconsistency in

Table 1
Study characteristics of the included studies.

Study	Location	Study design	N (TA/RS)	Mean age (TA/RS)	Type of TA	Assessment criteria
Zu et al., 2021 [8]	Beijing, China	Retrospective	320/324	44.99 ± 10.62/43.91 ± 11.47	MWA	1,2,3,4,5,6
Li et al., 2019 [34]	Beijing, China	Retrospective	168/143	47.36 ± 10.75/49.18 ± 11.41	MWA	4,5,6
Wang et al., 2021 [44]	Qingdao, China	Retrospective	63/83	43.56 ± 14.17/43.32 ± 10.89	MWA	1,3,4,6
Xu et al., 2018 [45]	Shanghai, China	Retrospective	41/46	45.8 ± 10.2/46.2 ± 1.5	MWA	1,2,3,6
Li et al., 2018 [9]	Beijing, China	Retrospective	46/46	43.63 ± 9.27/49.59 ± 9.0	MWA	1,2,3,6
Shen et al., 2019 [46]	Shanghai, China	Retrospective	20/38	48.80 ± 10.71/47.55 ± 12.41	MWA	3,5,6
Yao et al., 2020 [47]	Shanghai, China	Retrospective	120/120	45.86 ± 8.30/46.02 ± 8.11	MWA	1,2,3,6
Sun 2021 [48]	Shenyang, China	Retrospective	40/40	40.31 ± 13.4/40.32 ± 11.3	MWA	1,2,3,6
Wang et al., 2020 [49]	Jinmen, China	Retrospective	36/36	45.6 ± 8.5/46.1 ± 8.9	MWA	1,2,3,6
Zhou et al., 2020 [25]	Shanghai, China	Retrospective	51/50	44.72 ± 9.94/42.16 ± 10.28	MWA	1,2,3,6
Ma et al., 2017 [26]	Hangzhou, China	Retrospective	30/35	46.10 ± 8.20/49.97 ± 10.30	MWA	6
Wang et al., 2019 [27]	Diabingshan, Chian	Retrospective	35/35	46.18 ± 8.35/45.16 ± 7.58	MWA	1,2,3,6
Zhang et al., 2022a [28]	Heze, Chian	Retrospective	41/41	46.82 ± 6.33/46.65 ± 6.25	MWA	1,2,3,6
Chen et al., 2018 [29]	Hangzhou, China	Retrospective	49/40	44.88 ± 11.04/45.78 ± 13.74	MWA	1,3,6
Li et al., 2021a [30]	Huizhou, China	Retrospective	62/62	47.23 ± 15.30/46.95 ± 15.14	MWA	1,2,6
Li et al., 2021 [31]	Anshan, China	Retrospective	40/40	50.22 ± 1.52/50.85 ± 1.52	MWA	6
Zhang et al., 2022 [32]	Huanggang, Chian	Retrospective	54/54	48.6 ± 7.8/47.1 ± 8.3	MWA	1,2,3,6
Chen et al., 2021 [33]	Chendu, China	Retrospective	75/82	18–75	MWA	1,2,4,5,
Zhang et al., 2020 [17]	Beijing, China	Retrospective	94/80	45.4 ± 10.8/44.1 ± 9.6	RFA	1,2,3,4,5,6
Zhang et al., 2021 [35]	Beijing, China	Retrospective	133/133	45.77 ± 9.88/45.68 ± 10.79	RFA	1,3,6
Song et al., 2021 [36]	Beijing, China	Retrospective	115/103	44.9 ± 10.4/45.4 ± 9.9	RFA	1,2,3,4,5,6
Yan et al., 2021 [37]	Beijing, China	Retrospective	332/332	44.1 ± 9.5/43.8 ± 9.5	RFA	1,2,3,4,5,6
Du et al., 2021 [38]	Zheng, China	Retrospective	37/37	45.42 ± 6.12/44.62 ± 5.97	RFA	1,2,3,4,6
Feng et al., 2021 [39]	Hangzhou, China	Retrospective	102/115	47.4 ± 11.2/43.9 ± 10.7	RFA	1,3,6
Wang et al., 2020a [40]	Neimenggu, China	Retrospective	84/87	45.8 ± 10.2/46.2 ± 11.5	RFA	1.2.3.6
Zhou et al., 2019 [16]	Shanghai, China	Retrospective	36/45	41.5 ± 11.3/41.6 ± 9.6	LA	1,3,4,6
Zhou et al., 2020a [41]	Shanghai, China	Retrospective	33/34	37.9 ± 10.1/41.8 ± 13.4	MWA vs LA	1,3,6
Shen et al., 2019a [42]	Huzhou, China	Retrospective	45/52	43.7 ± 6.6/40.5 ± 7.8	RFA vs MWA	6
Gong et al., 2019 [43]	Nanjing, China	Retrospective	75/79	49.67 ± 7.39/48.86 ± 7.42	RFA vs MWA	6

MWA, Microwave Ablation; RFA, Radiofrequency Ablation; LA, Laser Ablation.

1, operation time; 2, intra-operative blood loss; 3, hospital stays; 4, recurrence; 5, lymph node metastasis; 6, total complications.

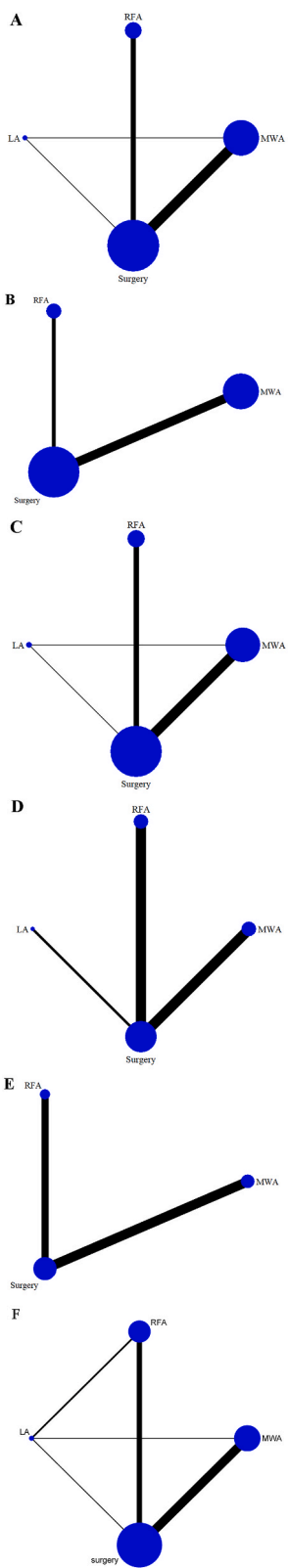


Fig. 2. The network diagrams for operation time(A), intra-operative blood loss(B), hospital stays(C), recurrence(D), LNM(E), and complications(F). The network diagrams were drawn to show the relationships of various treatments in each outcome measure, where each node reflects a treatment; the line between two nodes indicates there is a direct comparison.

MWA			
0.70 (-0.87, 2.26)	RFA	A	
-0.37 (-2.80, 2.07)	-1.60 (-3.81, 1.69)	LA	
-4.79 (-5.69, -3.90)	-5.49 (-6.77, -4.21)	-4.43 (-6.86, -1.99)	Surgery

MWA		
6.55 (-0.88, 13.99)	RFA	B
-3.81 (-7.84, 0.22)	-10.36 (-16.67, -4.06)	Surgery

MWA			
-0.06 (-1.11, 1.00)	RFA	C	
1.44 (-0.26, 3.14)	1.50 (-0.41, 3.40)	LA	
-3.36 (-3.98, -2.74)	-3.30 (-4.15, -2.45)	-4.80 (-6.51, -3.09)	Surgery

MWA			
0.51 (0.13, 2.09)	RFA	D	
1.02 (0.13, 8.35)	2.00 (0.25, 16.23)	LA	
0.84 (0.31, 2.29)	1.65 (0.61, 4.42)	0.82 (0.13, 5.21)	Surgery

MWA		
1.23 (0.23, 6.52)	RFA	E
0.73 (0.35, 1.55)	0.60 (0.13, 2.66)	Surgery

MWA			
1.88 (0.68, 5.23)	RFA	F	
1.07 (0.23, 4.94)	0.57 (0.13, 2.55)	LA	
0.22 (0.13, 0.37)	0.12 (0.05, 0.29)	0.21 (0.05, 0.92)	Surgery

(caption on next page)

Fig. 3. The relative treatment effects of MWA, RFA, LA, and surgery for operation time(A), intra-operative blood loss(B), hospital stays(C), recurrence(D), LNM(E), and complications(F). The results are presented as the SMD and 95 % CI or the OR and 95 % CI for each outcome (the column treatment comparing with the row treatment). For (A), (B), and (C), the SMD < 0 favor the column treatment. For (D), (E), and (F), the OR < 1 favor the column treatment.

the operation time and complications ($P > 0.05$), while there was the presence of heterogeneity in the hospital stays ($P < 0.05$).

3.5. Detection of publication bias

The publication bias was assessed by using the funnel plot. Our results indicated that the funnel plot was asymmetry in the operation time, intra-operative blood loss, hospital stays, and complications, demonstrating publication bias (Supplementary Figure 1-3, 6). However, the funnel plot was symmetry in recurrence and LNM, which suggested no publication bias (Supplementary Figs. 4-5).

4. Outcomes

4.1. Comparison of operation time

Twenty-three studies with 4024 patients compared the operation time between MWA, RFA, LA, and surgery groups. The present results suggested no statistically significant differences in operation time between MWA, RFA, and LA group. In addition, the current results indicated that MWA (SMD = -4.79; 95 %CI = -5.69 to -3.90), RFA (SMD = -5.49; 95 %CI = -6.77 to -4.21), and LA (SMD = -4.43; 95 %CI = -6.86 to -1.99) group produced significantly shorter than that of surgery group (Fig. 3A). In terms of the operation time, the maximum SUCRA value of the RFA group was 86.3 % (Table 2), followed by the MWA group (60.7 %) and LA group (52.9 %), indicating the operation time of the RFA group was shortest.

4.2. Comparison of intra-operative blood loss

Seventeen studies with 3158 patients compared the intra-operative blood loss between MWA, RFA, and surgery groups. There were no statistically significant differences in intraoperative blood loss between MWA and RFA groups. Additionally, the RFA group (SMD = -10.36; 95 %CI = -16.67 to -4.06) had less intra-operative blood loss than the surgery group (Fig. 3B). Regarding intra-operative blood loss, the maximum SUCRA value of the RFA group was 97.8 % (Table 2), followed by the MWA group (50.6 %), which indicates that intraoperative blood loss of the RFA group was the least.

4.3. Comparison of hospital stay (day)

Twenty-two studies with 3801 patients compared the hospital stay between MWA, RFA, LA, and surgery groups. The present results suggested no statistically significant differences in hospital stay between MWA, RFA, and LA groups. Besides, the current results indicated that MWA (SMD = -3.36; 95 %CI = -3.98 to -2.74), RFA (SMD = -3.30; 95 %CI = -4.15 to -2.45), and LA (SMD = -4.80; 95 %CI = -6.51 to -3.09) group produced significantly shorter than that of surgery group (Fig. 3C). In terms of hospital stay, the maximum SUCRA value of the LA group was 96.3 % (Table 2), followed by the MWA group (52.9 %) and the RFA group (50.8 %), which indicates that the hospital stay of the LA group was shortest.

4.4. Comparison of recurrence

Nine studies with 2469 patients compared the recurrence between MWA, RFA, LA, and surgery groups. The present results suggested no statistically significant differences in recurrence between MWA, RFA, and LA group (Fig. 3D). In terms of recurrence, the maximum SUCRA value of the MWA group was 64.4 % (Table 2), followed by the LA group (60.9 %) and the RFA group (19.9 %), which indicates that the MWA group was less likely to recurrence among PTMC patients.

Table 2

Rank probability of efficacy and safety for ablation technique and surgery (%).

Treatments	Operation time	Intra-operative blood loss	Hospital stays	Recurrence	LNM	Complications
MWA	60.7	50.6	52.9	64.4	60.0	52.7
RFA	86.3	97.8	50.8	19.9	67.8	88.8
LA	52.9	-	96.3	60.9	-	57.9
Surgery	0.0	1.6	0.0	54.8	22.1	0.6

MWA, Microwave Ablation; RFA, Radiofrequency Ablation; LA, Laser Ablation; LNM, lymph node metastasis; Surgery, total thyroidectomy or thyroid lobectomy.

4.5. Comparison of LNM

Seven studies with 2226 patients compared the LNM between MWA, RFA, and surgery groups. There were no statistically significant differences in LNM between MWA and RFA groups (Fig. 3E). Regarding LNM, the maximum SUCRA value of the RFA group was 67.8 % (Table 2), followed by the MWA group (60.0 %), which indicates the RFA group was less likely to have LNM.

4.6. Comparison of total complication numbers

Twenty-eight studies with 4632 patients compared the complications between MWA, RFA, LA, and surgery groups. The results suggested no statistically significant differences in total complication between MWA, RFA, and LA groups. Besides, the current results showed that MWA (RR = 0.22; 95 %CI = 0.13 to 0.37), RFA (RR = 0.12; 95 %CI = 0.05 to 0.29), and LA (RR = 0.21; 95 %CI = 0.05 to 0.92) group produced significantly fewer complications than that of surgery group (Fig. 3F). In terms of total complication, the maximum SUCRA value of the RFA group was 88.8 % (Table 2), followed by the LA group (57.9 %) and the MWA group (52.7 %), which indicates that the RFA group had the lowest risk of the total complication.

5. Discussion

PTMC is becoming more prevalent owing to the increased sensitivity of ultrasound and the development of fine-needle aspiration. PTMC is an indolent tumor with very low morbidity and mortality rates. Thyroid surgery is the primary treatment for PTMC. However, some studies think that PTMC is overtreated. Recently, TA (MWA, RFA, and LA) has been considered an alternative treatment for PTMC [8,16,45,46]. However, there are few studies to compare the efficacy and safety of MWA, RFA, and LA for treating PTMC patients. Therefore, the present study compared the relative effectiveness and safety of MWA, RFA, and LA for PTMC patients to provide a reference for clinical practice.

The efficacy and safety of each treatment were sequenced using the surface under the cumulative ranking curve (SUCRA) [47], and the optimal treatment regimen was determined. SUCRA would be 1 when a treatment is certain to be the best and 0 when a treatment is certain to be the worst". According to the results of the SUCRA value, our study found that RFA showed the lowest probability of having common complications and LNM, and the least operation time and intra-operative blood loss, compared with other TA treatments. Besides, MWA indicated the lowest probability of recurrence, and LA showed the lowest probability of the least hospital stays in the present study. Therefore, RFA may be an effective and safe treatment method for PTMC with the superior advantage of having a shorter operation time and hospital stay, fewer complications and LNM versus surgery.

Our pooled results reported that RFA was superior to surgery in operation time, intra-operative blood loss, hospital stays, and complications, while no statistically significant difference in recurrence between the MWA, RFA, and LA groups. Previous studies [15, 48] also found that compared to surgery, RFA had a shorter operation time, fewer complications, and very fewer cases of recurrence or metastasis. This may be because ultrasound-guided RFA achieves treatment by inducing coagulative necrosis of target tissues through radiofrequency thermal effect, which has the advantages of simple operation, minimally invasive, and quick recovery [22]. Moreover, RFA can be performed on an outpatient basis and has a short recovery time, with most patients able to return to normal activities within a few days. RFA has also been shown to preserve thyroid function and prevent the need for thyroid hormone replacement therapy.

The present study also found that both MWA and LA were superior to surgery in operation time, hospital stays, and complications, consistent with previous meta-analyses. For example, Li et al. indicated that MWA had the characteristics of minimal invasiveness, fast recovery, high aesthetics, and few surgical complications in the treatment of PTMC. Also, Our pooled results reported no statistically significant difference in recurrence between the MWA and LA groups. Zhou et al. reported that the complication rates did not differ between the MWA and the LA groups, and no local recurrence or distant metastasis occurred in either group.

The present results indicated that MWA, RFA, and LA groups produced significantly fewer complications than the surgery group, consistent with the previous meta-analysis's conclusions [17,18]. For example, Shen et al. [18] reported that patients undergoing TA had a low complication rate with a pooled statistically significant difference (3.39 % vs. 12.94 %, $p < 0.001$). Besides, a meta-analysis by Choi et al. [17] demonstrated that TA's complication rate was 3.2 %. The most common complication is voice change after TA due to thermal injury and bleeding, lidocaine injection, inflammation, fibrosis around the nerve, and other risk factors [49,50]. Because the thyroid gland is anatomically located close to the recurrent laryngeal nerve. Several studies also thought hypothyroidism and hypocalcemia were common complications during the treatment. They reported hypothyroidism is as high as 75 %, whereas permanent hypocalcemia ranges from 0 % to 3.1 % [51,52]. Besides, the operation time is a part of safety because the longer operation time sometimes means more tissue damage, anesthetics, and bleeding risk. Our study indicated no statistically significant differences in operation time between the MWA, RFA, and LA groups. In contrast, MWA, RFA, and LA groups were significantly shorter than the surgical group. Also, there were no statistically significant differences in intraoperative blood loss between MWA and RFA groups, while the RFA group had less intraoperative blood loss than the surgery group. TA could be performed in an outpatient clinic, and the procedures are completed rapidly without general anesthesia. All three modalities are less invasive than surgery and can be performed on an outpatient basis, which reduces the risk of infection and shortens recovery time.

5.1. Strength and limitations

The present study was the first to evaluate the efficacy and safety between MWA, RFA, and LA in PTMC patients using a network

meta-analysis that combined direct and indirect information on each treatment's relative effectiveness, even if there was a lack of head-to-head comparisons. Moreover, we calculated the SUCRA for each therapy to further rank the three types of TA, which is different from the previous studies. We can rank multiple treatments according to the size of SUCRA [47]. Especially when both treatments have the most considerable probability of being the best or the probabilities of different treatment rankings are close, the SUCRA can help us make a quick decision [53]. Therefore, the SUCRA is more meaningful for clinical decision-making [54]. Moreover, endpoints, including operation time, intra-operative blood loss, hospital stays, recurrence, lymph node metastasis, and complications, were appraised in this meta-analysis. Most of these indicators were not assessed in previous meta-analyses [17,19,55]. Notably, compared with other meta-analyses, the current meta-analysis showed that the RFA, MWA, and LA are acceptable treatments to manage PTMCs in terms of efficacy and safety and also provided valuable reference information for the selection of TA techniques during the treatment of PTMCs.

However, our study has some limitations. Firstly, all included articles in our study were retrospective design, and some articles had small sample sizes [22,31,42,43], which caused recall bias and low certainty. Although a systematic search of online databases was conducted, publication bias was detected in the pooled analyses of the operation time, intra-operative blood loss, hospital stays, and complications. The results should be interpreted with caution. Secondly, all studies were conducted in China. However, other regions, such as Europe, Australia, and the United States, may differ in medical technology and level. In further research, high-quality studies in other areas should be included. Thirdly, in the twenty-nine articles included in the meta-analysis, most (18/29) evaluated MWA, 7/29 evaluated RFA, and only a few evaluated LA. The number of patients enrolled by different techniques could be more consistent, which may lead to a certain bias in the results. Finally, although our study reported the recurrence of TA, TA is a novelty technology that has not been followed up long enough to evaluate its long-term safety and efficacy. Therefore, more comprehensive follow-up period studies are still needed to validate whether the results are durable or reproducible. Finally, in the process of data extraction and analysis of complications, since most of the original literature did not grade the severity of complications, we only compared the difference in the overall incidence of complications after different TA treatments, which may also lead to certain bias. The research on the type and frequency of serious complications of different TA treatments needs to be further refined.

6. Conclusion

In conclusion, the findings in this meta-analysis indicated that compared with other TA modalities, RFA demonstrated the lowest probability of having common complications and the least operation time and intra-operative blood loss in treating patients with PTMC. Besides, MWA revealed the lowest probability of recurrence, while LA showed the lowest probability of the least hospital stays. Therefore, MWA, RFA, and LA are all effective treatment strategies for patients with PTMC, but could not completely replace conventional surgical treatment. Clinically, the surgeon should choose a specific technique based on the patient's clinical features, relevant investigations and the patient's wishes.

CRedit authorship contribution statement

Binyi Li: Writing – original draft, Methodology, Conceptualization. **Ying Qian:** Investigation, Formal analysis. **Yong Huang:** Resources, Project administration. **Zheng Li:** Formal analysis, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2024.e25536>.

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