Systematic Review and Meta-Analysis

Medicine

OPEN

Efficacy and safety of single- and multiple-antenna microwave ablation for the treatment of hepatocellular carcinoma and liver metastases

A systematic review and network meta-analysis

Yi Han, PhD[a], Wangyang Zhao, PhD[b], Min Wu, MSc[b], Yingjun Qian, MD[c,*]

Abstract

Background: There is a myriad of microwave ablation (MWA) systems used in clinical settings worldwide for the management of liver cancer that offer a variety of features and capabilities. However, an analysis on which features and capabilities result in the most favorable efficacy and safety results has never been completed due to a lack of head-to-head comparisons. The aim of this study is to compare single-antenna and multiple-antenna MWA using radiofrequency ablation (RFA) as a common comparator in the treatment of very-early, early hepatocellular carcinoma (HCC) and ≤5 cm liver metastases.

Methods: This network meta-analysis was performed according to PRISMA guidelines. PubMed, Cochrane, and Web of Science databases were searched for comparative studies. Complete ablation (CA) rate, local tumor progression-free (LTPF) rate, overall survival (OS), and major complication rate were assessed. Subgroup analyses were further performed based on synchronous or asynchronous MWA generators and tumor size (<2 cm or ≥2 cm).

Results: Twenty-one studies (3424 patients), including 3 randomized controlled trials (RCTs) and 18 observational studies, met eligibility criteria. For CA, LTPF and major complications, as compared to single-antenna MWA, multiple-antenna MWA had relative risks (RRs) of 1.051 (95% CI: 0.987–1.138), 1.099 (95% CI: 0.991–1.246), and 0.605 (95% CI: 0.193–1.628), respectively. For 1-year and 3-year OS, as compared to single-antenna MWA, multiple-antenna MWA had odds ratios (ORs) of 0.9803 (95% CI: 0.6772–1.449) and 1.046 (95% CI: 0.615–1.851), respectively. Subgroup analysis found synchronized multi-antenna MWA was associated with significantly better LTPF by 22% (RR: 1.22, 95% CI 1.068, 1.421), and 21.4% (RR: 1.214, 95% CI 1.035, 1.449) compared with single-antenna MWA, and asynchronous multiple-antenna MWA, respectively, with more evident differences in larger tumors (≥2 cm).

Conclusion: Multi-antenna and single-antenna MWA showed similar effectiveness for local treatment of liver tumors, but synchronous multi-antenna MWA exhibited better LTPF compared to other MWA approaches, particularly for larger liver tumors (≥2 cm). Large-scale RCTs should be further conducted.

Abbreviations: CA = complete ablation, HCC = hepatocellular carcinoma, LMR = lymphocyte-to-monocyte ratio, LTPF = local tumor progression-free, MWA = microwave ablation, NMA = network meta-analysis, OR = odds ratios, OS = overall survival, RCT = randomized controlled trial, RFA = radiofrequency ablation, RR = relative risk, TACE = trans-arterial chemoembolization.

Keywords: hepatocellular carcinoma, liver cancer, microwaves, network meta-analysis

1. Introduction

Liver cancer is the fourth most common cause of cancer mortality worldwide.[1] Hepatocellular carcinoma (HCC) is the most frequent type of liver cancer, accounting for 85% to 90% of all primary liver malignancies.[2] The liver is also a common target for metastases, with 5% of patients diagnosed with liver metastases at the time of primary cancer diagnosis.[3] Previous clinical guidelines recommended surgical treatment (resection or liver transplantation) as the optimal approach to cure primary HCC and liver metastases.[4,5] However, only 10% to 20% of cancer patients are surgical candidates because of tumor inoperability,

This study has received funding from Johnson & Johnson Medical (Shanghai) Ltd.

The authors of this manuscript declare relationships with the following companies: YQ is an employee of Johnson & Johnson Medical (Shanghai) Ltd.; YH is a part-time employee, and WZ and MW are full-time employees of Shanghai VMLY&Rx Co., Ltd., which received financial support from Johnson & Johnson Medical (Shanghai) Ltd. for the conduct of this study.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Supplemental Digital Content is available for this article.

[a] Health Economics Research Institute, Sun Yat-Sen University, Guangdong, China, [b] Shanghai VMLY&Rx Co., Ltd., Shanghai, China, [c] Johnson & Johnson Medical (Shanghai) Ltd., Shanghai, China.

* Correspondence: Yingjun Qian, Johnson & Johnson Medical (Shanghai) Ltd., 65 Guiqing Road, Shanghai 200233, China (e-mail: yqian7@its.jnj.com).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc.
This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Han Y, Zhao W, Wu M, Qian Y. Efficacy and safety of single- and multiple-antenna microwave ablation for the treatment of hepatocellular carcinoma and liver metastases: A systematic review and network meta-analysis. Medicine 2022;101:51(e32304).

Received: 17 October 2022 / Received in final form: 21 November 2022 / Accepted: 28 November 2022

http://dx.doi.org/10.1097/MD.0000000000032304

patient unwillingness to undergo liver resection, or shortage of appropriate donors for liver transplantation,[6] leaving a large proportion of liver tumors requiring other therapies. Recent clinical guidelines recommend local ablation therapy for patients who develop HCC or metastatic liver lesions but are unsuitable for surgery as it is minimally invasive, safe, effective, and can be performed repeatedly.[5,7–9]

Radiofrequency ablation (RFA) and microwave ablation (MWA) are the most common thermal ablation technologies in current clinical settings.[9] While some studies have found similar results between the two technologies,[10–12] there are studies that have demonstrated that MWA reaches higher and faster temperatures compared to RFA. Furthermore, studies have shown that MWA results in larger ablation volumes and is less sensitive than RFA to heat sink effects.[10,13] Recent meta-analyses have demonstrated that MWA is more likely to reduce local tumor progression[14] and performs better in overall survival (OS) compared to RFA.[15,16] The reason for the different outcomes may pertain to the failure to consider feature and/or capability variations between the MWA systems.[17,18]

There is a myriad of MWA systems used in clinical settings worldwide that offer a variety of features, particularly in terms of antenna capabilities. The most conventional MWA system used for treating liver cancer (regardless of tumor size) uses a single antenna to deliver energy. For larger tumors, sequential ablations are needed when only using a single antenna. More recently, multiple antennas and simultaneous ablation capabilities have been used to create larger ablation zones when ablating larger tumors (usually ≥ 2 or ≥ 3 cm), achieved by using either a single high-power generator or multiple independent generators. Studies in animal liver models have found that MWA using multiple antennas simultaneously create larger ablation zones and more circular ablation zones than single-antenna MWA sequential ablations.[19–21] In addition, an in vivo animal study found that simultaneous three-antenna MWA ablation zones were three times larger than those created by single-antenna three sequential MWAs.[20] Furthermore, multi-antenna synchronized delivery of microwave energy enables in-phase waves generated from multiple antennas being activated simultaneously to create a more uniform heating zone than an asynchronized system.[22] Taken together, these findings highlight the potential benefits of multiple antennas, especially with synchronized microwave energy delivery to increase MWA efficacy.

To date, no meta-analysis has focused on the substantial between-study heterogeneity regarding different MWA system features in treatment efficacy and safety and no head-to-head trial has compared different MWA systems in the treatment of liver cancer in humans. In this study, we conducted a network meta-analysis (NMA) to compare the efficacy of single-antenna MWA versus multiple-antenna MWA (with multiple-antenna simultaneous ablation in partial or all tumors) using RFA as a common comparator. We also investigated whether a single MWA generator can effectively deliver microwave power to multiple antennas.

2. Materials and methods

The NMA was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Network Meta-Analyses (PRISMA-NMA) (see, Table S1, Supplemental Digital Content, http://links.lww.com/MD/I136, which illustrates the PRISMA Checklist).[23] The protocol was registered with PROSPERO (registration number: CRD42022328126).

2.1. Study search strategy

Two investigators independently searched PubMed, Cochrane Library, and Web of Science databases using search terms relevant to the following combinations: (hepatocellular carcinoma odds ratios (OR) liver metastases OR liver cancer) AND microwave ablation AND radiofrequency ablation. Table S2 (see Supplemental Digital Content (Table S2, http://links.lww.com/MD/I137), which lists the search strategy) shows the search strategies with the time spans of the searches in the above databases. The search was limited to studies published in English from January 1, 2001 to November 18, 2021. To identify other suitable articles, the bibliographies of the articles and conference proceedings of relevant meetings (including The Society of Interventional Radiology [SIR] Annual Meeting and Cardiovascular and Interventional Radiology Society of Europe [CIRSE] Annual Meeting from 2001 to 2021) were screened. Conflicts were resolved by discussion.

2.2. Eligibility criteria

Randomized controlled trials (RCTs) and observational studies comparing percutaneous MWA and RFA therapies were included in the analysis. Abstracts presented at conferences were also included if sufficient information on study design, characteristics of patients, interventions, and outcomes were available. Case reports, case series, reviews, meta-analyses, study protocols, letters, and commentaries were excluded from consideration.

The study population included very early or early HCC (single nodule < 5 cm in diameter or up to 3 nodules with a diameter < 3 cm each)[24,25] or liver metastases (tumors < 5 cm in diameter). Studies comparing single-antenna MWA versus RFA, multiple-antenna MWA versus RFA, or single-antenna MWA versus multiple-antenna MWA were included in the analysis. The "single-antenna MWA" group comprised studies that used single ablation or multiple sequential ablations that treated lesions with a unipolar needle and a single microwave generator. The "multiple-antenna MWA" group consisted of studies that either used mixed single/multiple-antennas MWA in which partial tumors were ablated using multiple antennas simultaneously or used pure multiple-antenna simultaneous ablations for all tumors included. The multiple-antenna MWA group was further divided into subgroups according to whether the antennas were connected to a single generator (synchronous multi-antenna MWA) or multiple independent generators (asynchronous multi-antenna MWA). In the synchronous multi-antenna MWA group, high output powers were distributed to activate and control several antennas from a single microwave source.[26] RFA with multiple electrodes was not included in the network analysis because of the lack of comparison studies using bipolar RFA in the treatment of liver cancer and the fact that simultaneous multi-antenna activation with RFA is not possible due to potential electrical interference.[27]

2.3. Outcome measures

Primary outcomes included complete ablation (CA) rate at 1 month and local tumor progression-free (LTPF) rate. CA is defined as no imaging tumor enhancement at the follow-up period. The definition of LTPF is the absence of local tumor progression documented as the absence of tumor foci at the edge of the ablation zone on contrast-enhanced imaging after one or more negative imaging visits.[27] If more than one LTPF rate was reported in a study, the longest time was used. Secondary outcomes included OS at one and three years and major complications. Major complications were defined as events that led to substantial morbidity and disability that increased the level of care, resulted in hospital admission, or substantially lengthened the hospital stay according to the SIR classification system for complications by outcome (SIR categories C–E).

2.4. Study selection and data extraction

Selected studies were examined by reading the full-text articles to assess whether they were eligible for inclusion in the study. Study screening was conducted by a single reviewer and validated by a second reviewer. Any disagreement was resolved by discussion. A single investigator extracted and summarized the following data from the selected studies: outcome data for each treatment arm (number of patients, number of patients with events for binary outcomes or percentages for targeted events, mean follow-up for time-to-event outcomes, definition of outcomes used in the study), characteristics of patients (demographic information, disease-related data such as tumor size and stage of disease at inclusion, details of the interventions including device brand, number of antennas, number of generators, number of insertions, ablation procedure, utilization of trans-arterial chemoembolization (TACE) or trans-arterial embolization, assessment of risk of bias), and other related data (authors and year of publication, title of the article, study design). Data were verified by a second reviewer. Disagreements were resolved by discussion or by a third independent reviewer.

2.5. Assessment of risk of bias

The Risk of Bias 2 tool (RoB 2)[28] was used to evaluate RCTs and the Newcastle-Ottawa Quality Assessment Scale (NOS)[29] was used to assess observational studies. The two independent reviewers assessed the quality of the studies, and any disagreement was adjudicated by a third reviewer.

2.6. Statistical analysis

Relative risks (RRs) with 95% confidence intervals (CIs) were calculated to compare CA rate, LTPF rate, and rate of major complications between groups. OS was compared by calculating OR with 95% CI. Absolute rates were calculated by applying the estimated treatment effect for each technology to the pooled reference treatment response estimated by the NMA. A random-effects model was used, and heterogeneity was assessed by estimating the I^2 statistic; an $I^2 > 50\%$ was considered as significant heterogeneity.[30] Since follow-up times varied across studies, a random-effects meta-regression was used to estimate the impact of follow-up times on LTPF and the occurrence of major complications. The transitivity assumption could not be statistically tested via assessment of consistency because no head-to-head comparison between single- and multiple-antenna MWA was found. We therefore compared the distributions of clinical and methodological variables that could act as effect modifiers across treatment comparisons.[31] The clinical or methodological features, which have been demonstrated to influence the efficacy of ablation include age, tumor size, and severity at baseline.[32–34] Similarly, the inconsistency test was omitted for the lack of direct comparison between single- and multiple-antenna MWA.[35] The ranking probabilities for each intervention were reported as the mean ranks. The publication bias was visualized by funnel plots for outcomes reported by 10 or more studies and performed by using a simple linear regression of the standardized estimate of treatment effect.[36] If asymmetry was detected in the funnel plot, there was probably heterogeneity in the NMA.[36] The R statistical software (Version 4.0.3) was used for statistical analysis, in which the "gemtc" package was used for statistical analysis. Funnel plots were generated using STATA (Version 15.1) and the "netfunnel" package.

2.7. Subgroup analyses

Subgroup analysis was conducted to investigate the impact of classification methods of MWA. The multiple-antenna MWA group was further classified according to the synchrony of generators: multiple-antenna MWA powered by a single generator (synchronous multiple-antenna MWA group) and multiple-antenna MWA powered by independent generators (asynchronous multiple-antenna MWA group). The study further compared the treatment effect between tumors with < 2 cm in mean diameter versus those ≥ 2 cm in mean diameter.

2.8. Ethical approval

Institutional Review Board approval and written informed consent were not required because this is a systematic review. Only data from published literature were used in this study.

3. Results

3.1. Description of studies and risk of bias

A total of 864 articles were identified from all databases searched. After title and abstract reading and duplication exclusion, 98 studies were screened by reading full-text documents. Twenty-one studies, including 3 RCTs and 18 observational studies, were included in the analysis (Fig. 1). Twelve studies compared single-antenna MWA versus RFA in patients with very-early or early HCC.[32–34,37–45] Seven studies compared multiple-antenna MWA versus RFA in patients with very-early and/or early HCC,[17,46–51] and two studies compared multiple-antenna MWA versus RFA in patients with liver metastases.[52,53] A detailed description of the summary of the included studies is presented in Table 1 and Tables S3–S4 (see Supplemental Digital Content [Table S3, http://links.lww.com/MD/I138 and Table S4, http://links.lww.com/MD/I139], which provide more details of the included studies).

Among the 3424 patients included, 1549 patients (45.0%) were treated with RFA and 1875 (55.0%) with MWA. The majority of patients in the MWA group were treated with single-antenna MWA (1363 patients, 72.7%); 512 patients (27.3%) were treated with multiple-antenna MWA (all studies used single/multiple-antenna mixed MWA – none used purely multiple-antenna MWA for all tumors included). Tumor size in any of the included studies was not significantly different between MWA and RFA, and it was similarly distributed in RFA arms across studies grouped by comparison, assuring transitivity in the network (see Table S4, Supplemental Digital Content, http://links.lww.com/MD/I139), which illustrates the tumor size in included studies). Transitivity assumption was also confirmed by the fact that age (63 years old vs 59 years old, $P = .205$) and the percentage of patient in Child-Pugh A/B at baseline (Child-Pugh A: 80% vs 76%, $P = .714$) were similar between RFA arms across treatment comparisons. The description of effectiveness (CA and LTPF) varied in the included studies, and all are listed (see Table S5, Supplemental Digital Content, http://links.lww.com/MD/I140), which shows the definition of primary outcomes used in included studies).

Risk of bias assessment reveals that randomization, outcome measurement, and reported results were conducted appropriately in all RCTs (see Figure S1, Supplemental Digital Content, http://links.lww.com/MD/I144), which illustrates the risk of bias item for each included RCT. However, because the devices used were difficult to mask to physicians, blinding in the RCTs could not be completely achieved resulting in bias due to deviations from intended interventions (see D2 column, Figure S1, Supplemental Digital Content, http://links.lww.com/MD/I144), which illustrates the risk of bias item for each included RCT. Quality assessment of observational studies is shown in Table S6 (see Supplemental Digital Content, http://links.lww.com/MD/I141), which shows the quality assessment of observational studies using the NOS scale.

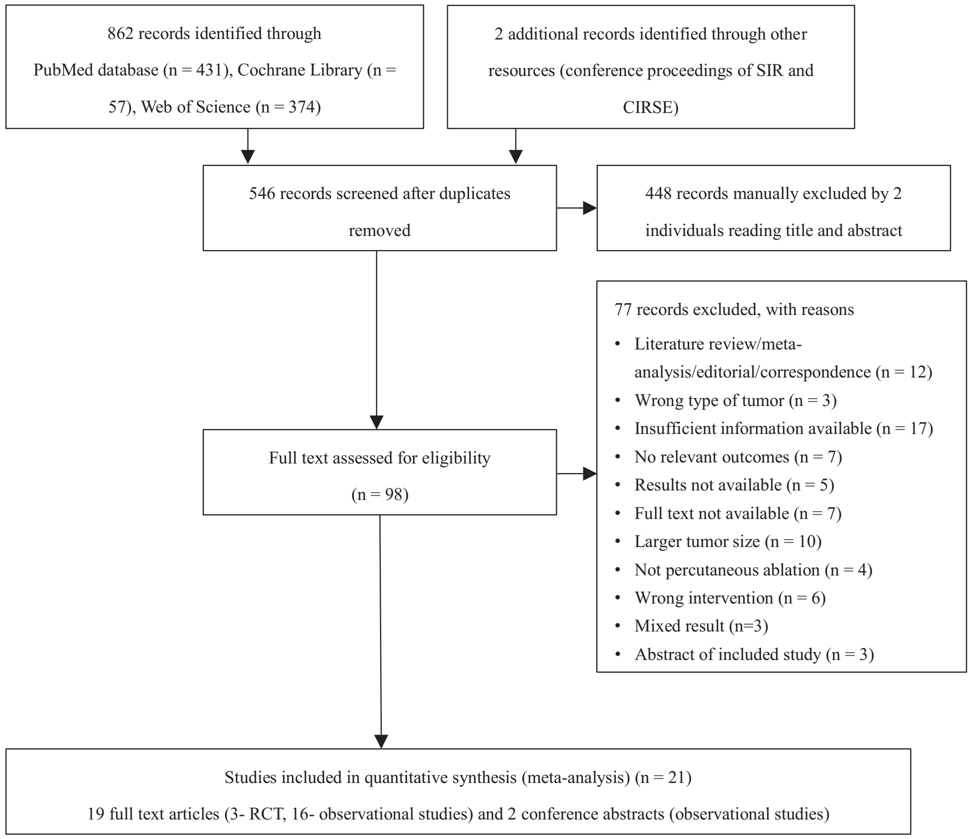


Figure 1. Study flow diagram. CIRSE = Cardiovascular and Interventional Radiology Society of Europe, RCT = randomized controlled trial, SIR = The Society of Interventional Radiology.

3.2. Network meta-analysis and rank probability

The network of treatment comparison showed no closed loop for all outcomes (Fig. 2). At 1 month, the NMA demonstrated that the multiple-antenna MWA group was associated with a significantly greater (4.7%) likelihood of CA (RR: 1.047, 95% CI 1.001, 1.111) compared to RFA with 0% heterogeneity. The absolute probabilities of CA for the multiple-antenna MWA group and RFA group were 94.4% and 90.2%, respectively. CA was similar between multiple-and single-antenna MWA groups (Table 2A). The rank probability indicated that the multiple-antenna MWA group had the highest probability of being ranked the best treatment arm for CA (93.6%) (Fig. 3A).

LTPF rate assesses the reappearance of the ablated tumor over time. The results showed the multiple-antenna MWA group and single-antenna MWA group had similar LTPF rates, whereas the multiple-antenna MWA group increased the LTPF incidence compared with RFA (RR: 1.12, 95% CI 1.032, 1.234) (Table 2B), with the absolute probability of 86.9% and 77.6% for the multiple-antenna MWA group and RFA, respectively. The heterogeneity between studies was 9%. Using the rank probability, the results were consistent with the relative treatment effect, suggesting that multiple-antenna MWA was the best treatment with a probability of 96.1% of being ranked first (Fig. 3B). Table 1 shows that studies reported LTPF rates at different follow-up periods, which might have influenced the intervention outcomes. However, a network meta-regression analysis revealed no significant impact of the follow-up period on the treatment effects (see Table S7, Supplemental Digital Content, http://links.lww.com/MD/I142, which presents the meta-regression results).

The OS analysis was divided into one- and three-year OS. For the one-year OS, similar effects were seen in multiple-antenna MWA, single-antenna MWA, and RFA groups (Table 2C). The rank probabilities indicated that the single-antenna MWA group had the highest probability of being the best treatment arm (52.0%) (Fig. 3C). For three-year OS, similar to the result in one-year OS, the three treatment arms were similar with respect to the three-year OS (Table 2D). In the rank probability, however, multiple-antenna MWA group was found to rank the best in the comparison of three-year OS (52.2%) (Fig. 3D).

The risk of major complications was not significantly different among the single-antenna MWA, multiple-antenna MWA, and RFA groups (Table 2E). The rank probability showed that the multiple-antenna MWA group had the lowest risk of complications (Fig. 3E). The meta-regression found that the follow-up period had no impact on the risk of major complications (see Table S7, Supplemental Digital Content, http://links.lww.com/MD/I142, which presents the meta-regression results).

3.3. Subgroup analysis

Table 3A shows that the advantage of multiple-antenna MWA in CA was mainly driven by the synchronous multiple-antenna MWA, which increased the CA rate by 6.9% (98.0% vs 91.6%; RR: 1.069, 95% CI 1.005, 1.195) compared to RFA with not significant heterogeneity (I^2= 2%). Results also showed that synchronous multiple-antenna MWA was the best treatment for liver cancer for LTPF rates with the highest probability of freedom from LTP (85.9%). The MWA with synchronized multi-antenna was associated with significant increases in LTPF by 24.5% (RR: 1.245, 95% CI 1.104, 1.428), 22% (RR: 1.22, 95% CI 1.068, 1.421), and 21.4% (RR: 1.214, 95% CI 1.035, 1.449) with not significant heterogeneity (I^2 = 6%) compared with RFA, single-antenna MWA, and asynchronous multiple-antenna MWA, respectively (Table 3D). For the outcome of OS and major complications, the differences were not

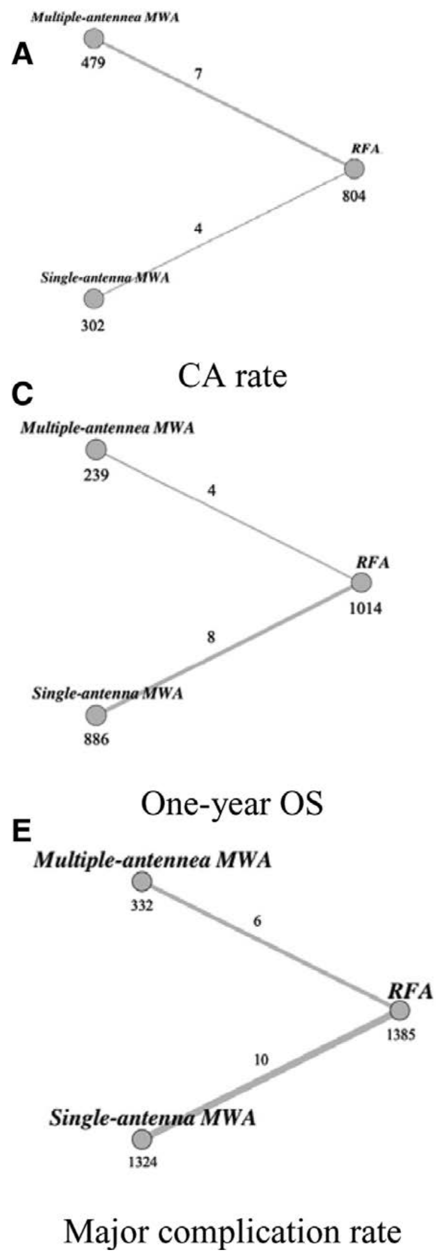


Figure 2. Networks of treatment comparisons for the interventions evaluated in the study. (A) Complete ablation rate, (B) Local tumor progression-free rate, (C) 1-year overall survival rate, (D) 3-year overall survival rate, (E) Major complication rate. The nodes represent the interventions evaluated. The thickness of the lines connecting the nodes is proportional to the number of studies. The number of studies is mentioned on the lines. CA = complete ablation, LTPF = local tumor progression-free, MWA = microwave ablation, OS = overall survival, RFA = radiofrequency ablation.

significant among MWA subgroups (see Table S8, Supplemental Digital Content, http://links.lww.com/MD/I143, which shows the league table presenting subgroup network meta-analysis results for OS at 1 year and 3 years and major complication rate). Heterogeneity of the follow-up period did not have significant impact on outcomes when assessed by meta-regression (see Table S7, Supplemental Digital Content, http://links.lww.com/MD/I142, which presents the meta-regression results).

In the subgroup analysis for groups with tumors ≥ 2 cm, the CA rate in synchronous multi-antenna MWA group was 24.2% higher (98.3% vs 79.2%; RR: 1.242, 95% CI 1.013, 1.846), and 23.9% higher (98.3% vs 79.4%; RR: 1.239, 95% CI 1.027, 1.826) compared with single-antenna MWA and RFA, respectively (Table 3C). The issue of heterogeneity was not significant (I^2 = 10%). Synchronous multi-antenna MWA was associated with the greatest likelihood of freedom from LTP compared to asynchronous multiple-antenna MWA (88.6% vs 73.5%; RR: 1.205, 95% CI 1.027, 1.49), single-antenna MWA (88. 6% vs 70.6%; RR: 1.254, 95% CI 1.081, 1.552), and RFA (88.6% vs 71.7%; RR: 1.236, 95% CI 1.089, 1.469) with low heterogeneity (I^2 = 7%) (Table 3F). The differences were not found to be significant among patients with tumors <2 cm (Table 3B and 3E). The network meta-regression analysis revealed that the variation in the follow-up period did not significantly affect the treatment effects (see Table S7, Supplemental Digital Content, http://links.lww.com/MD/I142, which presents the meta-regression results).

3.4. Publication bias

Funnel plots showed symmetric distributions (Figure S2, Supplemental Digital Content, http://links.lww.com/MD/I145) and low risk of bias for all comparison outcomes for single- and multiple-antenna CA, LTPF, and one- and three-year OS. No evidence of asymmetric distribution was noted for the pairwise

Table 1

Study characteristics.

Study, year	Country, type	Disease type	Treatment	Subject, n (Tumor, n)	Follow-up (mo)	Males (%)	Mean age, (yr)	Mean/Median tumor size (range, cm)
Ding et al, 2013[37]	China, RCS	HCC	RFA	85 (98)	27.69	80.0%	58.64	2.38 (1.0–4.8)
			Single-antenna MWA	113 (131)	18.32	75.2%	59.06	2.55 (0.8–5.0)
Durrani et al, 2016[51]	US, RCS	HCC	RFA + TACE	49	15.9	–	–	2.0 (1.3–2.5)
			Multiple-antenna MWA (synchrony) + TACE	119	11.3	–	–	2.0 (1.3–2.4)
Han et al, 2021[38]	China, RCS	HCC	RFA	150	36.6	85.3%	54.90	2.14 (0.7–4.8)
			Single-antenna MWA	51	36.8	84.3%	56.71	2.21 (0.8–5)
Kamal et al, 2019[39]	Egypt, RCT	HCC	RFA	28 (34)	12	–	55	3.28 (1.7–4.5)
			Single-antenna MWA	28 (34)	12	–	55	3.25 (2.0–5.0)
Kuroda et al, 2021[40]	Japan, RCS, PSM	HCC	RFA	150	12.97	74.7%	72.3	2.46
			Single-antenna MWA	150	13.67	72.7%	71.6	2.68
Liu et al, 2018[33]	China, RCS, PSM	HCC	RFA	123	34.1	88.6%	54.00	2.30 (1.8–3.0)
			Single-antenna MWA	123	36.8	90.2%	53.00	2.25 (1.7–2.9)
Liu et al, 2013[52]	China, RCS	Liver metastases	RFA	54 (70)	32.2	61.1%	53.1	2.5 (1.0–5.0)
			Multiple-antenna MWA (asynchrony)	35 (62)	32.2	60	53.4	2.3 (0.8–5.0)
Ohmoto et al, 2009[41]	Japan, RCS	HCC	RFA	34 (37)	48	73.5	67	1.6 (0.7–2.0)
			Single-antenna MWA	49 (56)	48	83.7	64	1.7 (0.8–2.0)
Potretzke et al, 2016[46]	US, RCS	HCC	RFA	55 (68)	31	72.7	62	2.2 (2.0–2.3)
			Multiple-antenna MWA (synchrony)	99 (136)	24	81.8	61	2.4 (2.2–2.6)
Qian et al, 2012[42]	China, PCS	HCC	RFA	20	5.1	95	56.0	2.0 (1.2–2.9)
			Single-antenna MWA	22	5.1	90.9	52.0	2.1 (1.2–3.0)
Shady et al, 2018[53]	USA, RCS	Liver Metastases	RFA	62 (85)	56	61	–	1.8 (0.6–4.5)
			Multiple-antenna MWA (synchrony)	48 (60)	29	73	–	1.7 (0.7–3.7)
Shibata et al, 2002[47]	Japan, RCT	HCC	RFA	36 (48)	18	72.2	63.6	2.3 (1.0–3.7)
			Multiple-antenna MWA (asynchrony)	36 (46)	18	66.7	62.5	2.2 (0.9–3.4)
Suwa et al, 2021[32]	Japan, RCS	HCC	RFA	72 (86)	24	68.1	74.40	1.76
			Single-antenna MWA	72 (86)	24	65.3	74.90	1.77
Suwa et al, 2020[43]	Japan, RCS	HCC	RFA	55 (70)	12	80.0	73.2	1.77
			Single-antenna MWA	44 (52)	12	68.2	73.4	1.72
Tamai et al, 2021[34]	Japan, RCS	HCC	RFA	174 (214)	36	70.1	74	1.5 (0.7–3.0)
			Single-antenna MWA	339 (416)	36	71.4	75	1.5 (0.5–3.0)
Thornton et al, 2017[48]	US, RCS	HCC	RFA + TACE	15	18	73.3	62	2.43 (1.2–3.6)
			Multiple-antenna MWA (synchrony) + TACE	20	14	90.0	66.6	2.78 (1.6–4.1)
Vietti Violi et al, 2018[44]	France, Switzerland, RCT	HCC	RFA	73 (104)	25	84.9	65	1.8
			Single-antenna MWA	71 (98)	26	83.1	68	1.8
Virk et al, 2014[50]	US, RCS	HCC	RFA	52 (56)	6	67.3	63	2.1 (0.7–4.1)
			Multiple-antenna MWA (synchrony)	50 (54)	6	74.0	65	2.1 (0.6–4.4)
Vogl et al, 2015[49]	Germany, RCS	HCC	RFA	25 (32)	12	76.0	57	3.2 (0.8–4.5)
			Multiple-antenna MWA (asynchrony)	28 (36)	12	82.1	60	3.6 (0.9–5)
Xu et al, 2017[45]	China, RCS	HCC	RFA	159	62	83.1	54.0	1.7
			Single-antenna MWA	301	53	78.1	54.2	1.7
Zhang et al, 2013[17]	China, RCS	HCC	RFA	78 (97)	26.3	82.1	54	2.3 (0.8–5.0)
			Multiple-antenna MWA (asynchrony)	77 (105)	24.5	87.0	54	2.2 (0.9–5.0)

HCC = hepatocellular carcinoma, MWA = microwave ablation, PCS = prospective cohort study, PSM = propensity score-matching, RCS = retrospective cohort study, RCT = randomized controlled trail, RFA = radiofrequency ablation, TACE = trans-arterial chemoembolization.

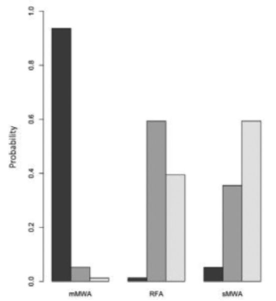
comparisons, even though the number of studies for multiple-antenna MWA versus RFA was small.

4. Discussion

Advanced thermal ablation technologies are continually emerging; however, head-to-head studies comparing existing features and energy delivery modalities for the treatment of liver cancer are lacking. Our study compared the efficacy and safety of various MWA antenna and generator capabilities using RFA as a common comparator. Results indicated that RFA, single/multiple-antenna mixed MWA, and single-antenna MWA had similar rates of complications and efficacy regarding one- and three-year OS. However, single/multiple-antenna mixed MWA performed better than RFA and single-antenna MWA for CA and LTPF rates. Furthermore, the probability analysis ranked multiple-antenna MWA as the best thermal ablation technology for CA, LTPF rate, three-year OS, and major complications. The subgroup analysis revealed that synchronous multiple-antenna MWA was associated with higher CA and LTPF rates compared to RFA and other MWA, and was the optimal technology for tumors ≥2 cm in diameter.

Our observation of better LTPF rates with the use of single/multiple-antenna mixed MWA, especially synchronous

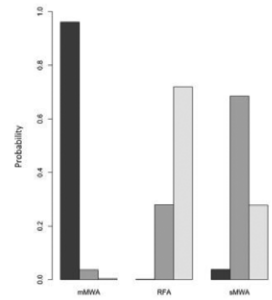
A



	1^{st}	2^{nd}	3^{rd}
mMWA	93.565%	5.250%	1.185%
sMWA	5.195%	35.475%	59.330%
RFA	1.240%	59.275%	39.485%

CA rate

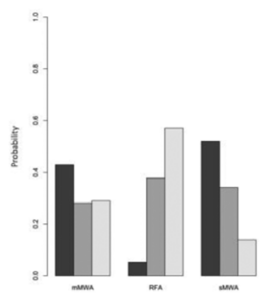
B



	1^{st}	2^{nd}	3^{rd}
mMWA	96.075%	3.605%	0.320%
sMWA	3.775%	68.480%	27.745%
RFA	0.150%	27.915%	71.935%

LTPF rate

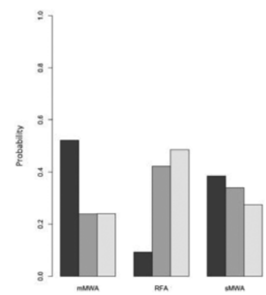
C



	1^{st}	2^{nd}	3^{rd}
mMWA	42.925%	28.035%	29.040%
sMWA	51.965%	34.190%	13.845%
RFA	5.110%	37.775%	57.115%

1-year OS

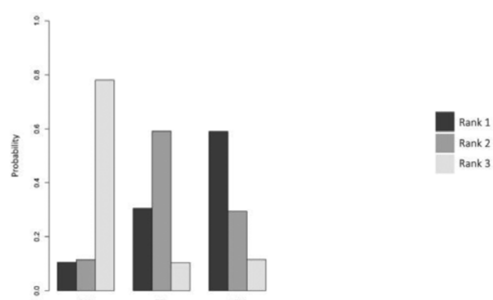
D



	1^{st}	2^{nd}	3^{rd}
mMWA	52.19%	23.83%	23.98%
sMWA	38.51%	34.03%	27.46%
RFA	9.30%	42.14%	48.56%

3-year OS

E



	1^{st}	2^{nd}	3^{rd}
mMWA	10.500%	11.445%	78.055%
sMWA	59.015%	29.405%	11.580%
RFA	30.485%	59.150%	10.365%

Major complication rate

Figure 3. Rank probability tests. Black column demonstrated rank 1, dark column gray demonstrated rank 2, light gray column demonstrated rank 3. CA = complete ablation, LTPF = local tumor progression-free, mMWA = multiple-antenna MWA, OS = overall survival, RFA = radiofrequency ablation, sMWA = single-antenna MWA.

multiple-antenna MWA, may be due to the simultaneous activation of antennas that creates high, uniform temperatures and more confluent ablations, as previously shown in comparison studies of sequential and simultaneous RFA.[54,55] Previous studies have also found that inadequate ablation zone (ablative margins less than 5 mm) is a primary cause of local tumor recurrence.[56,57] When using single-antenna MWA, the center of the ablation zone displays the highest temperature, which gradually decreases toward the zone's periphery. However, when using simultaneous multiple-antenna MWA, temperature is higher at the periphery.[19,21] Therefore, the more consistent heat distribution and confluent ablations observed with the use

Table 2

League table presenting NMA results on the RR along with 95% CI for CA rate and LTPF rate for all pairwise comparisons.

A: CA rates (RR): $I^2 = 0\%$		
Multiple-antenna MWA		
1.051 (0.987, 1.138)	Single-antenna MWA	
1.047 (1.001, 1.111)	0.996 (0.947, 1.044)	Radiofrequency ablation
B: LTPF rates (RR): $I^2 = 9\%$		
Multiple-antenna MWA		
1.099 (0.991, 1.246)	Single-antenna MWA	
1.12 (1.032, 1.234)	1.019 (0.948, 1.086)	Radiofrequency ablation
C: 1-year OS (OR): $I^2 = 9\%$		
Multiple-antenna MWA		
0.9803 (0.6772, 1.449)	Single-antenna MWA	
1.081 (0.7984, 1.495)	1.102 (0.8881, 1.357)	Radiofrequency ablation
D: 3-year OS (OR): $I^2 = 6\%$		
Multiple-antenna MWA		
1.046 (0.615, 1.851)	Single-antenna MWA	
1.127 (0.738, 1.755)	1.08 (0.749, 1.489)	Radiofrequency ablation
E: Major complications rates (RR): $I^2 = 8\%$		
Multiple-antenna MWA		
0.605 (0.193, 1.628)	Single-antenna MWA	
0.671 (0.275, 1.526)	1.109 (0.615, 2.188)	Radiofrequency ablation

CA = complete ablation, CI = confidence interval, LTPF = local tumor progression-free, MWA = microwave ablation, NMA = network meta-analysis, OR = odds ratio, OS = overall survival, RFA = radiofrequency ablation, RR = relative risk.

of simultaneous multiple-antenna MWA may result in lower local tumor recurrence and increased efficacy as clefting (i.e., sunken tissue between two sequential ablation zones), often observed when repositioning a single antenna, is reduced.[21] Additionally, multi-antenna synchronized delivery of microwave energy enables in-phase waves generated from multiple antennas being activated simultaneously to create a more uniform heating zone,[20–22,58] whereas electromagnetic waves generated by asynchronous multiple-antenna systems may be either amplified or canceled.[22] Therefore, synchronous multiple-antenna systems are more effective at creating consistent MWA zones than asynchronous multiple-antenna systems that use multiple independent generators to deliver electromagnetic energy in the microwave frequency range.

OS was not significantly different between the MWA and RFA arms, which is expected given the high recurrence risk caused by the underlining liver status (poor liver function, liver cirrhosis, hepatic virus infection) of the HCC population and the multimodal therapy for liver cancer. Therefore, local tumor control is generally considered a better indicator of treatment efficacy for ablative therapies than OS.[59] What's more, the results of OS should be interpreted with caution. Previous studies have demonstrated that the OS after thermal ablation is greatly influenced by the tumor microenvironment, a factor that has often been neglected in clinical studies.[60,61] It has also been proven that a low lymphocyte-to-monocyte ratio (LMR), indicating higher monocyte/macrophage over lymphocytes in the tumoral stroma, is associated with poor survival outcomes after thermal ablation for liver cancer.[60,61] As none of the included studies in this NMA has considered the impact of pre-operative LMR, in light of the abovementioned evidence, there might be heterogeneity in OS outcomes between studies. This issue is unavoidable until the pre-operative LMR is widely reported.

Despite the overall improvement in LTPF and CA achieved by the synchronous single/multiple-antenna mixed MWA approach compared to other MWA techniques and RFA, the risk of major complications was not significantly different. This suggests that the larger total amount of microwave energy applied by synchronous multiple-antenna MWA did not increase the risk of major complications.

In a nutshell, this study demonstrates that multiple-antenna MWA and synchronous multiple-antenna MWA have

Table 3

League Table presenting subgroup NMA results on the RR along with 95% CI for CA rate and LTPF rate.

A: Classification by both number of antenna and number of generators during the ablation: CA rates (RR) $I^2 = 2\%$			
Synchronous multiple-antenna MWA			
1.048 (0.942, 1.209)	Asynchronous multiple-antenna MWA		
1.075 (0.996, 1.22)	1.028 (0.931, 1.136)	Single-antenna MWA	
1.069 (1.005, 1.195)	1.023 (0.94, 1.113)	0.995 (0.942, 1.049)	Radiofrequency ablation
B: Tumor size < 2 cm: CA rates (RR) $I^2 = 9\%$			
Synchronous multiple-antenna MWA			
–	Asynchronous multiple-antenna MWA		
1.049 (0.982, 1.138)	–	Single-antenna MWA	
1.042 (0.997, 1.106)	–	0.995 (0.943, 1.046)	Radiofrequency ablation
C: Tumor size ≥ 2 cm: CA rates (RR) $I^2 = 10\%$			
Synchronous multiple-antenna MWA			
1.215 (0.982, 1.804)	Asynchronous multiple-antenna MWA		
1.242 (1.013, 1.846)	1.023 (0.899, 1.166)	Single-antenna MWA	
1.239 (1.027, 1.826)	1.021 (0.927, 1.126)	0.998 (0.915, 1.091)	Radiofrequency ablation
D: Classification by both number of antenna and number of generators during the ablation: LTPF rates (RR) $I^2 = 6\%$			
Synchronous multiple-antenna MWA			
1.214 (1.035, 1.449)	Asynchronous multiple-antenna MWA		
1.220 (1.068, 1.421)	1.004 (0.888, 1.142)	Single-antenna MWA	
1.245 (1.104, 1.428)	1.025 (0.918, 1.145)	1.021 (0.956, 1.081)	Radiofrequency ablation
E: Tumor size < 2 cm: LTPF rates (RR) $I^2 = 13\%$			
Synchronous multiple-antenna MWA			
–	Asynchronous multiple-antenna MWA		
1.186 (0.845, 1.666)	–	Single-antenna MWA	
1.245 (0.897, 1.707)	–	1.05 (0.937, 1.157)	Radiofrequency ablation
F: Tumor size ≥ 2 cm: LTPF rates (RR) $I^2 = 7\%$			
Synchronous multiple-antenna MWA			
1.205 (1.027, 1.49)	Asynchronous multiple-antenna MWA		
1.254 (1.081, 1.552)	1.04 (0.904, 1.216)	Single-antenna MWA	
1.236 (1.089, 1.469)	1.024 (0.915, 1.146)	0.986 (0.887, 1.077)	Radiofrequency ablation

CA = complete ablation, CI = confidence interval, LTPF = local tumor progression-free, MWA = microwave ablation, NMA = network meta-analysis, OR = odds ratio, RFA = radiofrequency ablation, RR = relative risk.

significantly lower recurrence rate in the treatment of primary HCC and liver metastases. However, only a minority of patients with HCC can have curative treatments, among patients who are no longer considered as candidates for curative treatments, other loco-regional therapies, such as TACE or trans-arterial radioembolization can be considered.[62] TACE has become the standard of care in patients with intermediate-stage HCC,[63,64] and trans-arterial radioembolization has also appears to be a viable treatment option for intermediate-advanced stage HCC.[65]

There are several limitations of this NMA. First, observational studies were included in the analysis as only a small number of RCTs were available. Also, due to the nature of thermal ablation, blinding of participants' assigned intervention during the trial could not be achieved in RCTs. In light of this limitation, the results may be biased because of the confounding or selection of participants in the included studies. These concerns, however, are partly eased from two aspects. From the aspect of the bias assessment in this study, most of the studies have low risk in the selection of the study groups, the comparability of the groups, and the ascertainment of the exposure and outcome of interest. From the aspect of the study design of the included studies, most were well-balanced for baseline covariates, especially for the tumor size (see more details in Supplemental Digital Content (Table S4, http://links.lww.com/MD/I139)), and some of the studies used matching to control for differences or reported regression analyses, showing the minimal impact of potential effect modifiers on treatment outcomes. Second, multiple antennas were used only for some tumors in the multiple-antenna MWA group while, for the other tumors in this group, single antennas were used. In the ablation procedure, the number of antennas usually depends on the tumor size. For tumors larger than the cutoff size in diameter (usually 2 cm[17,49,52], sometimes 3 cm[47]), overlapping ablations were conducted; for others, single-antenna MWA was performed. Since no studies discussed the results separately in the purely multiple-antenna ablations, it is impossible to isolate the multiple-antenna results in the NMA. However, a subgroup analysis was conducted according to tumor size and found an increased performance of multiple-antenna MWA over single-antenna MWA mainly in tumors ≥ 2 cm.

5. Conclusion

This systematic review and NMA demonstrated that single/multiple-antenna mixed MWA has the best local tumor control rate (LTPF rate) in the treatment of HCC and liver metastasis, particularly so for synchronous multiple-antenna MWA in patients with tumors ≥2 cm. The efficacy and clinical benefits of new emerging technologies in the field of MWA should be investigated in a systematic manner and compared regularly to current standard therapies.

Acknowledgments

The authors would like to thank Erin Prifogle-Meyers, Bogdan Ilie, and Hector De Leon (employees of Ethicon, Inc. (Raritan, New Jersey, USA)) for general and medical writing support.

Author contributions

Conceptualization: Yi Han, Wangyang Zhao, Yingjun Qian.
Data curation: Wangyang Zhao, Min Wu, Yingjun Qian.
Formal analysis: Yi Han, Min Wu.
Funding acquisition: Yi Han, Yingjun Qian.
Investigation: Yi Han, Min Wu, Wangyang Zhao.
Methodology: Yi Han, Wangyang Zhao.
Project administration: Wangyang Zhao, Yingjun Qian.
Resources: Yi Han, Yingjun Qian.
Software: Wangyang Zhao.
Supervision: Yingjun Qian.
Validation: Yi Han, Yingjun Qian.
Visualization: Wangyang Zhao.
Writing – original draft: Yi Han, Wangyang Zhao, Yingjun Qian.
Writing – review & editing: Yi Han, Wangyang Zhao, Yingjun Qian.

References

[1] Collaboration GBoDC. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2017: a systematic analysis for the global burden of disease study. JAMA Oncol. 2019;5:1749–68.
[2] El–Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterology. 2007;132:2557–76.
[3] Horn SR, Stoltzfus KC, Lehrer EJ, et al. Epidemiology of liver metastases. Cancer Epidemiol. 2020;67:101760.
[4] Bruix J, Sherman M; American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: an update. Hepatology. 2011;53:1020–2.
[5] Xu J, Fan J, Qin X, et al.; China CRLM Guideline Group. Chinese guidelines for the diagnosis and comprehensive treatment of colorectal liver metastases (version 2018). J Cancer Res Clin Oncol. 2019;145:725–36.
[6] Lai EC, Lau WY. The continuing challenge of hepatic cancer in Asia. Surgeon. 2005;3:210–5.
[7] Chen QF, Li W, Yu SC, et al. Consensus of minimally invasive and multidisciplinary comprehensive treatment for Hepatocellular Carcinoma - 2020 Guangzhou recommendations. Front Oncol. 2021;11:621834.
[8] Ren L, Zhu D, Benson AB, 3rd, et al.; SINCE (Shanghai International Consensus Expert Group on Colorectal Liver Metastases) Group. Shanghai international consensus on diagnosis and comprehensive treatment of colorectal liver metastases (version 2019). Eur J Surg Oncol. 2020;46:955–66.
[9] Raees A, Kamran M, Özkan H, et al. Updates on the diagnosis and management of hepatocellular carcinoma. Euroasian J Hepatogastroenterol. 2021;11:32–40.
[10] Brace CL, Ziemlewicz TJ, Schefelker R, et al. Microwave tumor ablation: cooperative academic-industry development of a high-power gas-cooled system with early clinical results. Proc SPIE Int Soc Opt Eng. 2013;8584:05.
[11] Han J, Fan YC, Wang K. Radiofrequency ablation versus microwave ablation for early stage hepatocellular carcinoma: a PRISMA-compliant systematic review and meta-analysis. Medicine (Baltim). 2020;99:e22703.
[12] Facciorusso A, Abd El Aziz MA, Tartaglia N, et al. Microwave ablation versus radiofrequency ablation for treatment of hepatocellular carcinoma: a meta-analysis of randomized controlled trials. Cancers. 2020;12:3796.
[13] Nault JC, Sutter O, Nahon P, et al. Percutaneous treatment of hepatocellular carcinoma: state of the art and innovations. J Hepatol. 2018;68:783–97.
[14] Glassberg MB, Ghosh S, Clymer JW, et al. Microwave ablation compared with hepatic resection for the treatment of hepatocellular carcinoma and liver metastases: a systematic review and meta-analysis. World J Surg Oncol. 2019;17:98.
[15] Ricci AD, Rizzo A, Bonucci C, et al. The (Eternal) debate on microwave ablation versus radiofrequency ablation in BCLC-A hepatocellular carcinoma. In Vivo. 2020;34:3421–9.
[16] Zhao J, Wu J, He M, et al. Comparison of transcatheter arterial chemoembolization combined with radiofrequency ablation or microwave ablation for the treatment of unresectable hepatocellular carcinoma: a systemic review and meta-analysis. Int J Hyperthermia. 2020;37:624–33.
[17] Zhang L, Wang N, Shen Q, et al. Therapeutic efficacy of percutaneous radiofrequency ablation versus microwave ablation for hepatocellular carcinoma. PLoS One. 2013;8:e76119e76119.
[18] Loriaud A, Denys A, Seror O, et al. Hepatocellular carcinoma abutting large vessels: comparison of four percutaneous ablation systems. Int J Hyperthermia. 2018;34:1171–8.
[19] Laeseke PF LF, Jr., van der Weide DW, Brace CL. Multiple-antenna microwave ablation: spatially distributing power improves thermal profiles and reduces invasiveness. J Interv Oncol. 2009;2:65–72.
[20] Wright AS, Jr., Lee FT, Mahvi DM. Hepatic microwave ablation with multiple antennae results in synergistically larger zones of coagulation necrosis. Ann Surg Oncol. 2003;10:275–83.

[21] Brace CL, Laeseke PF, Sampson LA, et al. Microwave ablation with multiple simultaneously powered small-gauge triaxial antennas: results from an in vivo swine liver model. Radiology. 2007;244:151–6.

[22] Harari CM, Magagna M, Bedoya M, et al. Microwave ablation: comparison of simultaneous and sequential activation of multiple antennas in liver model systems. Radiology. 2016;278:95–103.

[23] Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann Intern Med. 2015;162:777–84.

[24] Villanueva A. Hepatocellular Carcinoma. N Engl J Med. 2019;380:1450–62.

[25] Liver. EAftSot. EASL clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol. 2018;69:182–236.

[26] Brace CL. Microwave ablation technology: what every user should know. Curr Probl Diagn Radiol. 2009;38:61–7.

[27] Ahmed M, Solbiati L, Brace CL, et al.; International Working Group on Image-Guided Tumor Ablation. Image-guided tumor ablation: standardization of terminology and reporting criteria – a 10-year update. J Vasc Interv Radiol. 2014;25:1691–705.e4.

[28] Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.

[29] Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp [access date May 16, 2022].

[30] Higgins J, Green S. Cochrane handbook for systematic reviews of interventions version 6.2. Available at: http://handbook.cochrane.org [access date May 16, 2022].

[31] Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. Res Synth Methods. 2012;3:80–97.

[32] Suwa K, Seki T, Aoi K, et al. Efficacy of microwave ablation versus radiofrequency ablation for hepatocellular carcinoma: a propensity score analysis. Abdom Radiol. 2021;46:3790–7.

[33] Liu W, Zheng Y, He W, et al. Microwave vs radiofrequency ablation for hepatocellular carcinoma within the Milan criteria: a propensity score analysis. Aliment Pharmacol Ther. 2018;48:671–81.

[34] Tamai H, Okamura J. New next-generation microwave thermosphere ablation for small hepatocellular carcinoma. Clin Mol Hepatol. 2021;27:564–74.

[35] Higgins JP, Jackson D, Barrett JK, et al. Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies. Res Synth Methods. 2012;3:98–110.

[36] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315:629–34.

[37] Ding J, Jing X, Liu J, et al. Comparison of two different thermal techniques for the treatment of hepatocellular carcinoma. Eur J Radiol. 2013;82:1379–84.

[38] Han X, Ni JY, Li SL, et al. Radiofrequency versus microwave ablation for hepatocellular carcinoma within the Milan criteria in challenging locations: a retrospective controlled study. Abdom Radiol (NY). 2021;46:3758–71.

[39] Kamal A, Elmoety AAA, Rostom YAM, et al. Percutaneous radiofrequency versus microwave ablation for management of hepatocellular carcinoma: a randomized controlled trial. J Gastrointest Oncol. 2019;10:562–71.

[40] Kuroda H, Nagasawa T, Fujiwara Y, et al. Comparing the safety and efficacy of microwave ablation using thermosphere (TM) technology versus radiofrequency ablation for hepatocellular carcinoma: a propensity score-matched analysis. Cancers. 2021;13:1295.

[41] Ohmoto K, Yoshioka N, Tomiyama Y, et al. Comparison of therapeutic effects between radiofrequency ablation and percutaneous microwave coagulation therapy for small hepatocellular carcinomas. J Gastroenterol Hepatol. 2009;24:223–7.

[42] Qian GJ, Wang N, Shen Q, et al. Efficacy of microwave versus radiofrequency ablation for treatment of small hepatocellular carcinoma: experimental and clinical studies. Eur Radiol. 2012;22:1983–90.

[43] Suwa K, Seki T, Tsuda R, et al. Short term treatment results of local ablation with water-cooled microwave antenna for liver cancer: comparison with radiofrequency ablation. Mol Clin Oncol. 2020;12:230–6.

[44] Vietti Violi N, Duran R, Guiu B, et al. Efficacy of microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma in patients with chronic liver disease: a randomised controlled phase 2 trial. Lancet Gastroenterol Hepatol. 2018;3:317–25.

[45] Xu Y, Shen Q, Wang N, et al. Microwave ablation is as effective as radiofrequency ablation for very-early-stage hepatocellular carcinoma. Chin J Cancer. 2017;36:14.

[46] Potretzke TA, Ziemlewicz TJ, Hinshaw JL, et al. Microwave versus radiofrequency ablation treatment for hepatocellular carcinoma: a comparison of efficacy at a single center. J Vasc Interv Radiol. 2016;27:631–8.

[47] Shibata T, Iimuro Y, Yamamoto Y, et al. Small hepatocellular carcinoma: comparison of radio-frequency ablation and percutaneous microwave coagulation therapy. Radiology. 2002;223:331–7.

[48] Thornton LM, Cabrera R, Kapp M, et al. Radiofrequency vs microwave ablation after neoadjuvant transarterial bland and drug-eluting microsphere chembolization for the treatment of hepatocellular carcinoma. Curr Probl Diagn Radiol. 2017;46:402–9.

[49] Vogl TJ, Farshid P, Naguib NN, et al. Ablation therapy of hepatocellular carcinoma: a comparative study between radiofrequency and microwave ablation. Abdom Imaging. 2015;40:1829–37.

[50] Virk J, Dayan E, Cohen SL, et al. Comparison of microwave vs. radiofrequency ablation of HCC when combined with DEB-TACE: safety and mid-term efficacy. J Vasc Interv Radiol. 2014;25:S33.

[51] Durrani RJ, Biederman DM, Virk J, et al. Comparison of microwave vs. Radiofrequency ablation of HCC when combined with DEB-TACE: progression-free and overall survival analysis. Cardiovasc Intervent Radiol. 2016;39:S277.

[52] Liu Y, Li S, Wan X, et al. Efficacy and safety of thermal ablation in patients with liver metastases. Eur J Gastroenterol Hepatol. 2013;25:442–6.

[53] Shady W, Petre EN, Do KG, et al. Percutaneous microwave versus radiofrequency ablation of colorectal liver metastases: ablation with clear margins (A0) provides the best local tumor control. J Vasc Interv Radiol. 2018;29:268–275.e1.

[54] Brace CL, Sampson LA, Hinshaw JL, et al. Radiofrequency ablation: simultaneous application of multiple electrodes via switching creates larger, more confluent ablations than sequential application in a large animal model. J Vasc Interv Radiol. 2009;20:118–24.

[55] Lee JM, Han JK, Kim HC, et al. Multiple-electrode radiofrequency ablation of in vivo porcine liver: comparative studies of consecutive monopolar, switching monopolar versus multipolar modes. Invest Radiol. 2007;42:676–83.

[56] Nakazawa T, Kokubu S, Shibuya A, et al. Radiofrequency ablation of hepatocellular carcinoma: correlation between local tumor progression after ablation and ablative margin. AJR Am J Roentgenol. 2007;188:480–8.

[57] Liu CH, Arellano RS, Uppot RN, et al. Radiofrequency ablation of hepatic tumours: effect of post-ablation margin on local tumour progression. Eur Radiol. 2010;20:877–85.

[58] Oshima F, Yamakado K, Nakatsuka A, et al. Simultaneous microwave ablation using multiple antennas in explanted bovine livers: relationship between ablative zone and antenna. Radiat Med. 2008;26:408–14.

[59] Glassberg MB, Ghosh S, Clymer JW, et al. Microwave ablation compared with radiofrequency ablation for treatment of hepatocellular carcinoma and liver metastases: a systematic review and meta-analysis. Onco Targets Ther. 2019;12:6407–38.

[60] Ali MAM, Harmsen WS, Morsy KH, et al. Prognostic utility of systemic inflammatory markers and chronic hepatitis C virus infection status in hepatocellular carcinoma patients treated with local ablation. BMC Cancer. 2022;22:221.

[61] Facciorusso A, Del Prete V, Crucinio N, et al. Lymphocyte-to-monocyte ratio predicts survival after radiofrequency ablation for colorectal liver metastases. World J Gastroenterol. 2016;22:4211–8.

[62] Zane KE, Makary MS. Locoregional therapies for hepatocellular carcinoma with portal vein tumor thrombosis. Cancers (Basel). 2021;13:5430.

[63] Abdelrahim M, Victor D, Esmail A, et al. Transarterial Chemoembolization (TACE) plus sorafenib compared to TACE alone in transplant recipients with hepatocellular carcinoma: an institution experience. Cancers (Basel). 2022;14:650.

[64] Forner A, Reig M, Bruix J. Hepatocellular carcinoma. Lancet. 2018;391:1301–14.

[65] Rognoni C, Ciani O, Sommariva S, et al. Trans-arterial radioembolization in intermediate-advanced hepatocellular carcinoma: systematic review and meta-analyses. Oncotarget. 2016;7:72343–55.