

Efficacy of microwave ablation for intrahepatic cholangiocarcinoma: a systematic review and meta-analysis

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Background: Data on overall survival (OS) and progression-free survival (PFS) after microwave ablation (MWA) for intrahepatic cholangiocarcinoma (ICC) are scarce. We conducted a systematic review of the safety and efficacy of MWA for ICC.

Methods: The PubMed, Embase, Web of Science, and Cochrane Library databases were searched for studies reporting the outcomes of MWA for ICC. Meta-analyses of the pooled OS, PFS, technical success, technical efficacy, and complication rates were conducted. Pooled hazard ratios (HRs) of common variables were calculated to identify the factors associated with OS.

Results: The analysis encompassed 168 entries, among which 8 observational studies comprising 423 patients were deemed eligible. The pooled results were as follows: The median OS was 22.0 months [95% confidence interval (CI): 15.1–28.9], with the 1-, 3-, and 5-year OS rates being 83.7% (95% CI: 75.8–91.6%), 51.0% (95% CI: 41.1–60.9%), and 33.3% (95% CI: 14.1–52.4%), respectively. The median PFS was 12.5 months (95% CI: 8.3–16.7), and the 1-year PFS rate was 61.2% (95% CI: 36.5–85.9%). The technical success, technical efficacy, and major complication rates were 100% (95% CI: 99.5–100%), 99% (95% CI: 92.1–100%), and 2.8% (95% CI: 1.1–5.2%), respectively. A cancer antigen 19-9 (CA 19-9) level >37 U/mL was associated with a shorter OS (HR =1.4; 95% CI: 1.2–1.7; P=0.001).

Conclusions: MWA is a safe and effective alternative to chemotherapy, radiotherapy, and radiofrequency ablation (RFA) treatments, especially for patients with a CA 19-9 level ≤37 U/mL, and potentially has advantages over RFA. However, further studies are required to validate these findings.

Keywords: Intrahepatic cholangiocarcinoma (ICC); microwave ablation (MWA); meta-analysis; review

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Introduction

Primary liver cancer can be classified as hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (ICC), or a mixed type according to the pathological classification. ICC, a highly aggressive primary malignancy arising from the epithelial cells of the bile ducts, is the second most common primary liver cancer, following only HCC in the spectrum of liver malignancies (1).

Only a minority of patients diagnosed with ICC meet the criteria for surgical resection, which is the sole curative option. The majority of patients with ICC are deemed ineligible for surgery due to factors such as extrahepatic disease, major large vessel invasion, and severe comorbidities. Furthermore, the likelihood of repeat resection is limited by pre-existing comorbidities acquired after the initial surgery or insufficient hepatic functional reserve predisposing patients to posthepatectomy liver failure (2-5). The primary systemic treatment for unresectable ICC continues to be the combination of gemcitabine and cisplatin chemotherapy, which yields a median overall survival (OS) of approximately 11.7 months. However, the occurrence of grade 3-4 toxicity in up to 70% of the patients is a notable concern (6). When standard firstline treatment has failed or when patients cannot tolerate its toxicity, second-line treatment with immunotherapies and immune-based combinations is a viable alternative (7,8).

The majority of deaths related to ICC are attributable to local disease progression rather than metastases (9). Therefore, locoregional treatments (LRTs) are becoming increasingly significant, especially for patients with unresectable ICC confined predominantly or exclusively to the liver. Current LRT options for ICC include radiofrequency ablation (RFA), microwave ablation (MWA), irreversible electroporation (IE), hepatic arterial infusion (HAI) of chemotherapy, transarterial chemoembolization (TACE), transarterial radioembolization (TARE), external beam radiotherapy (EBRT), stereotactic body radiotherapy (SBRT), selective internal radiation therapy (SIRT), and brachytherapy. These LRTs have shown encouraging initial outcomes with improved survival rates (10), and some have been endorsed in the relevant guidelines.

In recent years, neoadjuvant therapy has emerged as an attractive therapeutic approach, as it can target the micrometastatic disease that contributes to the high rates of recurrence after therapies such as radical surgery and local ablation. Although there is currently a dearth of data related to this therapeutic strategy in cholangiocarcinoma, it has nonetheless demonstrated its benefits in a limited number of case series in terms of reducing tumor volume, improving local and distant control, and thereby improving long-term survival (11,12).

MWA is a thermal ablation technique wherein electromagnetic waves induce the rotation of dipole water molecules, generating frictional heat and leading to tumor coagulation necrosis (13). Compared with RFA, the earliest developed thermal ablation technology, MWA offers advantages such as higher heat production efficiency, reduced influence from heat loss effects, and shorter surgical time. A growing body of evidence suggests that MWA provides a clinical efficacy for HCC comparable to that of surgical resection. However, the clinical evidence regarding MWA for the treatment of ICC is limited, possibly because oncologists are concerned about the potential for thermal ablation, including MWA, to damage bile ducts and cause infectious bile fistula (14,15). The aim of this systematic review and meta-analysis was thus to pool the data regarding the survival, efficacy, and safety of MWA and to investigate the effect of patient- and tumor-related factors on survival in patients with ICC. We present this article in accordance with the PRISMA reporting checklist (16) (available at https://qims.amegroups.com/article/ view/10.21037/qims-24-607/rc).

Methods

Search strategy and study selection

A computerized search of PubMed, Embase, Web of Science, and Cochrane Library databases was performed to identify relevant studies published from the inception of the databases to August 2023. The search term strategy used was as follows: (((((biliary(title/abstract))) OR (bile(title/abstract))) AND ((((carcinoma(title/abstract))) OR (tumor(title/abstract))) OR (neoplasms(title/abstract))) OR (tumor(title/abstract))) OR (cholangiocarcinoma(title/abstract))) AND (microwave ablation(title/abstract)).

Duplicates were removed, and the initially identified articles were screened by title and abstract. If the abstracts adhered to the inclusion and exclusion criteria, a full-text evaluation was performed. Two reviewers (X.Z. and Mengyao Song) independently performed the literature search and study selection using a standardized protocol. Discrepancies between authors were resolved via discussion.

The inclusion criteria were as follows: (I) (population)

patients with pathologically proven primary or postoperative recurrent ICC; (II) (intervention) MWA; (III) (outcomes) data available on least one of OS, progressionfree survival (PFS), technical success, technical efficiency, or complication rate; and (IV) (study design) an observational study design (retrospective or prospective). The exclusion criteria were as follows: (I) case reports/series with fewer than 10 patients, reviews, conferences, letters, or comments; (II) studies involving patients treated concurrently with other treatments (i.e., simultaneous chemotherapy); (III) studies with recurrent ICC from extrahepatic cholangiocarcinoma (ECC); (IV) studies of patients with ICC and other types of cancer in which the ICC data could not be isolated; (V) studies in which the relevant outcomes for patients under MWA treatment were not available or could not be extracted in isolation; and (VI) studies with partially overlapping patients and data.

Data extraction and quality assessment of studies

The following data were extracted from the selected studies by two authors (Mengyao Song and D.J.): (I) study characteristics, including author name, country, publication year, study design, and years of inclusion; (II) patient characteristics, including total number of patients, age, and sex; (III) tumor characteristics, including total number of tumors, sizes and whether they were primary or recurrent cases; (IV) treatment characteristics, including imaging-guided modalities for MWA; (V) survival outcomes, including OS, PFS, technical success rate, technical efficacy rate, complications, and hazard ratios (HRs) of common variables associated with OS.

The Joanna Briggs Institute (JBI) Quality Assessment Checklist was used to assess the quality of the included articles (17). Two independent reviewers (Mengyao Song and J.L.) evaluated each paper, and any disagreements were discussed and decided upon via consultation with a third author (D.J.).

Definitions

OS was defined as the time from the initial MWA to death due to any cause or to the last follow-up. PFS was defined as the time from MWA to disease progression or the last follow-up. Technical success was defined as complete ablation coverage of the tumor at the time of the procedure. Technical efficacy was considered to be complete ablation of the tumor as verified by imaging follow-up 1 month after

ablation (18). Major complications were defined as events that caused substantial morbidity or disability resulting in increased levels of care, hospital admission, or substantially prolonged hospital stays (19).

Data synthesis and statistical analysis

Statistical analyses were performed using STATA v. 12 software (StataCorp, College Station, TX, USA). Pooling meta-analyses was only performed when three or more studies were available. Heterogeneity was evaluated using the Cochran Q test and I^2 statistics. A random-effects model was used to combine effect indicators when $I^2 \ge 50\%$ and P<0.05; otherwise, a fixed-effects model was used. When 10 or more studies were included in the analysis, publication bias was examined. To identify the factors associated with OS, we combined the common variable HR analyzed in at least three studies.

Results

Literature selection

Figure 1 shows the literature search procedure that was employed in this study. The initial search yielded 168 results, among which 71 duplicate records were identified, 79 articles excluded based on their titles and abstracts, and 18 potentially eligible full-text articles assessed according to the inclusion and exclusion criteria.

After the full content was examined, 10 of these 18 articles were removed for the following reasons: (I) fewer than 10 patients (n=6); (II) unavailability of the full text (n=3); and (III) lack of sufficient details to separately extract the relevant MWA outcomes (n=1). Consequently, a total of 8 studies were used for the qualitative and quantitative analyses (20-27).

Study characteristics and quality

The characteristics of the eight studies that reported data from 423 patients are summarized in *Table 1*. All eight eligible articles were retrospective observational studies. Seven of them were from China (20,21,23-27) and one was from Italy (22), indicating that MWA is more widely used in China, with more published clinical data originating from this country. There was a predominance of men (n=311, 73.5%) compared to women (n=112, 26.5%). The median age ranged from 53.9 to 72.0 years. Six studies

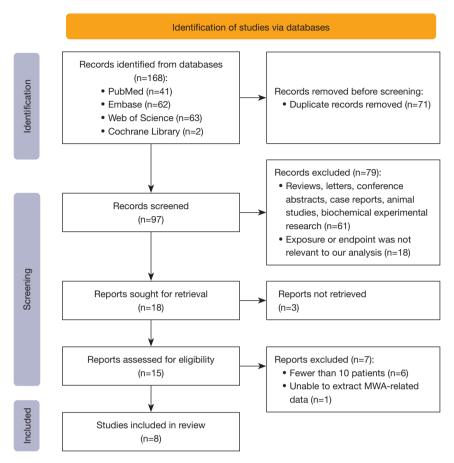


Figure 1 Study selection flowchart. MWA, microwave ablation.

used ultrasound (US)-guided modalities (20-22,24-26), one used computed tomography (CT) (23), and one used either US or CT (27). Four articles examined primary ICC (20,23,25,26), two examined recurrent ICC (24,27), and two examined both primary and recurrent ICC (21,22). A total of 251 patients had primary ICC (59.3%), and 172 had recurrent ICC (40.7%). Most studies (6/8, 75%) included patients with a single tumor with a maximum size smaller than 5 cm and a tumor number lesser than 3 according to the Milan criteria (21-25,27). The remaining two studies did not restrict the number or size of tumors (20,26).

According to the JBI quality assessment checklist, the quality of the included studies was assessed to be high, ranging from 9 to 10 points (*Table 2*).

Technical success and technical efficacy

Five studies reported technical success rates (range, 91.7–100%) and three reported technical efficiency rates

(range, 87.5–100%), with final pooled results of 100% [95% confidence interval (CI): 99.5–100%; I^2 =0] and 99% (95% CI: 92.1–100%; I^2 =80.5%), respectively (*Figure 2A,2B*).

Clinical outcomes

The median follow-up period ranged from 4 to 48 months among the six studies that provided the data. The 1-, 3-, and 5-year OS rates ranged from 60–95%, 39.6–75%, and 7.9–68%, respectively, with six studies providing data at 1 year and 3 at years and 5 providing data at 5 years. High degrees of heterogeneity were apparent in the 1-year OS (I^2 =71.3%; P=0.004), 3-year OS (I^2 =72.2%; P=0.003), and 5-year OS (I^2 =94.4%; P<0.001). Therefore, the randomeffects model was used, and the final pooled values for 1-, 3-, and 5-year OS were 83.7% (95% CI: 75.8–91.6%), 51.0% (95% CI: 41.1–60.9%), and 33.3% (95% CI: 14.1–52.4%), respectively (*Figure 3A-3D*).

Only three studies reported median PFS and 1-year PFS,

Table 1 Characteristics of the studies included in the meta-analysis

First Ye author	Year	Country	ry Study design	Years of inclusion	Primary vs. recurrent			Age (years)	Sex (M:F)	N of tumors	Tumor size (cm)	Follow-up period (months)	Median OS (months)	OS (%)			Median PFS (months)	1-year	Technical	Technical	Major
	rear	Country												1-year	3-year		Median PP3 (months)	PFS (%)	success (%)	efficacy (%)	complication (%)
Yu	2011	China	Retrospective	2006.5–2010.3	Primary	US	15	57.4±11.4 [33–75]	11:4	24	3.2±1.9 [1.3–9.9]	12.8±8.0 [4-31]	10	60.0	-	-	-	-	91.7	87.5	20
Zhang	2018	China	Retrospective	2009.1–2016.2	Mixed	US	107	58.0 [15–85]	78:29	171	-	20.1 [2.8–63.5]	28.0 (95% CI: 23.7–32.2)	-	39.6	7.9	8.9 (95% CI: 6.5–11.3)	41.5	100	100	1.9
Giorgio	2019	Italy	Retrospective	2008.1–2018.6	Mixed	US	35	72±10	18:17	-	_	48 [8–86]	_	95.0	75.0	68.0	-	79	-	-	0
Ni	2019	China	Retrospective	2011.4–2018.3	Primary	CT	78	59.6±10 [40-77]	57:21	106	3.1±0.7 [0.8–5.0]	22.7 [1–86.7]	_	89.5	52.2	35.0	-	-	100		3.8
Xu	2019	China	Retrospective	2011.4–2017.1	Recurrent	US	56	53.9±17.5	49:7	62	2.7±0.5 [0.8–5.0]	_	31.3 (3.8-62.9)	81.2	42.5	23.7	-	-	100	100	5.4
Yang	2021	China	Retrospective	2011.4–2018.3	Primary	US	52	59.6±10.0 [40-77]	39:13	74	3.1±0.7 [0.8–5.0]	21.2 [3.2–78.7]	_	87.4	51.4	35.2	-	-	100	-	3.8
Wang	2022	China	Retrospective	2012.3–2020.12	Primary	US	29	56.3±9.8 [33–75]	22:7	58	2.68±1.59 [0.5-8.1]	18.43 [4.17–93.13]	18.43 (95% CI: 18.33–33.61)	64.4	48.1	-	18.43 (95% CI: 18.33–33.61)	64.4	-	-	-
Wei	2023	China	Retrospective	2014.1–2021.3	Recurrent	US/CT	51	55.1±9.1	37:14	-	-	-	18.0 (95% CI: 16.3–19.7)	-	-	-	13.4 (95% CI: 11.6–15.2)	-	-	-	-

Data are presented as mean ± SD [range] or median [range]. -, not available. SD, standard deviation; M, male; F, female; OS, overall survival; PFS, progression-free survival; US, ultrasound; CI, confidence interval; CT, computed tomography.

Table 2 Risk of bias assessment according to the Joanna Briggs Institute Quality Assessment Checklist

First author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Total
Yu	1	1	1	U	1	1	1	1	1	1	9
Zhang	1	1	1	U	1	1	1	1	1	1	9
Giorgio	1	1	1	1	1	1	1	1	1	1	10
Ni	1	1	1	U	1	1	1	1	1	1	9
Xu	1	1	1	1	1	1	1	1	1	1	10
Yang	1	1	1	U	1	1	1	1	1	1	9
Wang	1	1	1	U	1	1	1	1	1	1	9
Wei	1	1	1	U	1	1	1	1	1	1	9

The checklist for the case series consisted of 10 questions: Q1: Were there clear criteria for inclusion in the case series? Q2: Was the condition measured in a standard and reliable manner for all the participants included in the case series? Q3: Were valid methods used to identify the conditions of all the participants included in the case series? Q4: Does the case series include consecutive participants? Q5: Did the case series include all participants? Q6: Was there clear reporting of the participants in the study? Q7: Was there clear reporting of the clinical information of the participants? Q8: Were the outcomes or follow-up results clearly reported? Q9: Was there clear reporting of the presenting site(s) and clinical and demographic information? Q10: Was the statistical analyses appropriate? Each item was answered with "Yes" [1], "No" [0], "Unclear" [U], or "Not applicable" [NA]. A score of 6 or higher indicated high methodological quality.

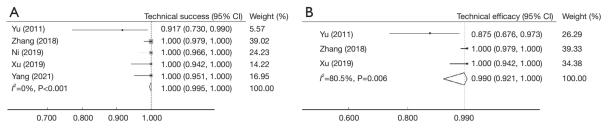


Figure 2 Forest plot analysis of technical success and technical efficacy. (A) Technical success. (B) Technical efficacy. CI, confidence interval.

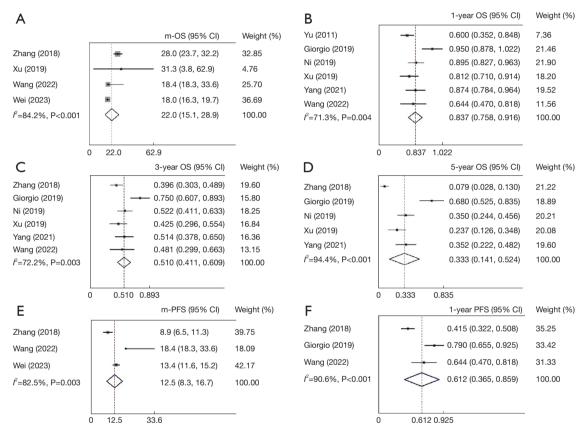


Figure 3 Forest plot analysis of the clinical outcomes. (A) m-OS (months). (B) One-year OS. (C) Three-year OS. (D) Five-year OS. (E) m-PFS (months). (F) One-year PFS. m-OS, median overall survival; CI, confidence interval; m-PFS, median progression-free survival.

with combined values of 12.5 months (95% CI: 8.3–16.7) and 61.2% (95% CI: 36.5–85.9%). Meta-analytic pooling of 3- and 5-year PFS rates was not performed because only one study reported a 3-year PFS rate (59%) and a 5-year PFS rate (55%) (*Figure 3E,3F*).

Prognostic factors associated with OS

Four studies analyzed the risk factors associated with OS, but only three studies reported HRs for cancer antigen 19-9

(CA 19-9) level and comorbidities, which could ultimately be combined. Both of them showed very low heterogeneity (CA 19-9: I²=0, P=0.613; comorbidity: I²=0, P=0.954), and so a fixed-effects model was used. Although none of the three studies were independently significant, meta-analysis revealed an increased HR for patients with a CA 19-9 level >37 U/mL (HR=1.4; 95% CI: 1.2–1.7; P=0.001) (*Figure 4*). In contrast, comorbidities (HR =0.75; 95% CI: 0.52–1.10; P=0.137) were not significantly associated with OS. Although the number of studies reporting age,

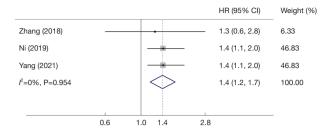


Figure 4 Forest plot analysis of HRs associated with OS. HR, hazard ratio; CI, confidence interval; OS, overall survival.

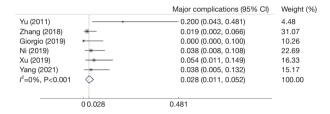


Figure 5 Forest plot analysis of major complications. CI, confidence interval.

Child-Pugh score, tumor number, tumor size, tumor differentiation, and hepatitis virus infection was sufficient, a meta-analysis was not performed due to inconsistencies in the classification across the literature.

Complications

In six studies, 13 out of 343 patients experienced serious complications, and the pooled incidence of major complications was 2.8% (95% CI: 1.1–5.2%) (*Figure 5*). Pleural effusions (n=4) and liver abscesses (n=8) were the most common complications.

Discussion

The prevalence of ICC is relatively low and geographically varied, with a predominance in Asian countries. However, epidemiology suggests that its global incidence is increasing, particularly in Western populations, with a steady rise from 0.1 per 100,000 cases to 0.6 per 100,000 (28). The available data are small-sample retrospective studies from single institutions, which limits their reliability and makes it difficult to establish associations between prognostic factors and OS, potentially explaining the heterogeneity exhibited by the studies in this meta-analysis. Nevertheless, our meta-analysis suggests that MWA has the potential to prolong the

OS of select patients with ICC.

Moreover, our meta-analysis showed that MWA had high technical success and efficiency rates (100% and 99%, respectively). The pooled median OS was 22.0 months, and the pooled 1-, 3-, and 5-year survival rates were 83.7%, 51.0%, and 33.3%, respectively. The pooled median PFS was 12.5 months, and the pooled 1-year PFS rate was 61.2%. The OS of patients with high preoperative CA 19-9 levels (>37 U/mL) was significantly worse than that of those with low preoperative CA 19-9 levels (≤37 U/mL), with an HR of 1.4 (95% CI: 1.2-1.7; P=0.001). This result highlights the significance of serum CA19-9 levels as a risk factor associated with the postoperative survival of patients with ICC, providing a basis for the prognostic value of MWA. This indicates that a CA 19-9 level ≤37 U/mL would be an optimal indication for MWA. MWA was found to be relatively safe, with a pooled major complication risk of 2.8%. These findings suggest that in certain patients, MWA can provide effective tumor control and a favorable safety profile when used to treat primary or recurrent ICC. Yu et al. observed the lowest technical success rate (91.7%), lowest technical efficiency rate (87.5%), shortest OS (median OS: 10 months; 1-year OS: 60.0%), and highest complication rate (20.0%), with two patients having liver abscesses and one patient undergoing needle seeding (20). There are probably two reasons for this: (I) the study was conducted in 2011, the earliest among the included studies, at a time when the MWA equipment and technology were not yet mature; (II) the study included ICC nodules of larger sizes (9.9 and 4.7 cm) located close to the stomach. Owing to the requirements of ablation technology, an ablation margin of 5–10 mm beyond the tumor is required. Therefore, when the tumor volume is too large, the ablation volume is proportionally larger, inevitably worsening the damage to the liver, especially the biliary system. The biliary system connects to the duodenum through the ampulla, and a patient with a compromised immune system is more prone to developing intrahepatic bile abscesses and abscesses due to intestinal bacterial translocation.

A meta-analysis comprising 57 studies and 4,756 cases reported that the median and 5-year OS for curative surgical resection of ICC were approximately 28 months (range, 9–53 months) and 30% (range, 5–56%), respectively, which is comparable to our results (29). Xu *et al.* (24) reported two cohorts treated with MWA and surgical resection. The 1-, 3-, and 5-year OS rates were 81.2% *vs.* 77.4%, 42.5% *vs.* 36.4%, and 23.7% *vs.* 21.8%, respectively; meanwhile, the 1-, 3-, and 5-year relapse-free survival (RFS) rates were 70.3% *vs.* 76.7,

33.1% vs. 30.6, and 0% vs. 0%, respectively, representing no statistically significant difference. However, the complication rate, cost, duration of hospitalization, blood loss, and procedure time were lower in the MWA group. These results suggest that MWA may be an effective alternative method with comparable clinical outcomes and fewer complications for both operable or inoperable patients.

RFA and MWA are both selective thermal ablation techniques for liver tumors in clinical practice (30,31). However, MWA has unique advantages and the potential to overcome a few limitations of RFA, including a shorter ablation and operative time, uniform heating achieving more predictable ablation zones, the ability to achieve higher temperatures in a short time resulting in larger ablation zones, less susceptibility to cooling heat-sink effects of the adjacent blood vessels, and effectiveness in high-impedance desiccated tissue for which RFA may not be successful (3,32); this suggests that MWA may be a more effective technique for tumor ablation.

Xu et al. (33) reported on two small cohorts of 12 patients treated with RFA and 6 with MWA. The median OS was 8 months and 13.5 months in the RFA and MWA groups, respectively, with no statistically significant difference (P=0.147). In contrast, Giorgio et al. (22) reported on two larger cohorts, indicating that MWA was superior to RFA in achieving better survival (1-year OS: 95% vs. 68%; 3-year OS: 75% vs. 53%; 5-year OS: 68% vs. 26%; P<0.005). Subgroup analysis revealed that OS was significantly better in the MWA group than in the RFA group when ICC nodules were ≤4 cm (P<0.0005); however, there was no significance for nodule diameters >4 cm (P=0.25). Regression analyses in a recent meta-analytic study indicated no significant difference in the 3-year OS between RFA and MWA (odds ratio =0.949; P=0.304). However, the authors stated that they were unable to perform multivariate regression analyses and adjust for other important factors related to OS due to discrepancies in the reporting of results and insufficient study details; therefore, firm conclusions could not be drawn (34). Nevertheless, the study identified large tumor size (>3 cm) (HR =2.12; 95% CI: 1.24-3.63), the presence of multiple tumors (HR =1.67; 95% CI: 1.17-2.39), and advanced age (>65 years: HR =1.67; 95% CI: 1.16–2.42) as factors predictive of shorter OS. However, in our study, we only evaluated the association between CA 19-9 levels, comorbidities, and OS. Other important factors could not be analyzed due to inconsistency in classifications and insufficient data from too few studies. Although none of the three studies were independently significant, the

meta-analysis showed that patients with a CA 19-9 level >37 U/mL had a shorter OS (HR =1.4; 95% CI: 1.2–1.7; P=0.001). After conducting a comprehensive search, we found that our study is the first to identify a correlation between CA 19-9 level and the OS in patients with ICC who have undergone ablation.

Despite conflicting outcomes, we recommend MWA as the first-choice of ablation method due to its potential benefits. Further randomized trials with more details are needed to definitively demonstrate the difference in efficacy between the two approaches and the predictors of superior OS.

This meta-analysis involved several limitations. (I) All the literature included consisted of retrospective, observational, single-arm studies, resulting in a relatively low level of evidence. Additionally, with different inclusion criteria for each study, patient selection bias was unavoidable. (II) MWA is not as widely used as RFA, so there were fewer studies on MWA included in this meta-analysis. This, along with the heterogeneity of outcome indicators reported by different studies, resulted in fewer endpoints that could be combined. (III) Despite the high heterogeneity in outcomes, publication bias and subgroup meta-analyses were not performed due to insufficient categorical detail and a limited number of available studies. Nonetheless, our meta-analysis, which included a sizable sample of 423 individuals who had MWA for ICC, may serve to direct present practices and future studies.

Conclusions

Our results suggest that MWA is a safe and effective treatment option for patients with ICC. Low levels of CA 19-9 (≤37 U/mL) are an optimal indication for MWA. However, further prospective studies with larger sample sizes are required to confirm our conclusions.

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Footnote

Reporting Checklist: The authors have completed the

PRISMA reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-24-607/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-607/coif). M.S., X.Z., and D.J. report funding support from the Science and Technology Research Project of Henan Province in 2023 (No. 232102311132) and the Joint Construction Project of Medical Science and Technology Research Program of Henan Province (No. LHGJ20220412). The other authors have no conflicts of interest to declare.

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

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