

## Original Article

# Clinical study on ultrasound-guided percutaneous microwave ablation for hepatocellular carcinoma

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Received January 24, 2025; Accepted April 25, 2025; Epub May 15, 2025; Published May 30, 2025

**Abstract:** Objectives: To evaluate the efficacy, safety, and survival benefits of ultrasound-guided microwave ablation (MWA) compared to surgical resection (SR) in patients with hepatocellular carcinoma (HCC). Methods: This retrospective study included 100 patients with HCC who underwent either ultrasound-guided MWA (n = 58) or SR (n = 42). Baseline characteristics, liver function tests, tumor markers, complications, and survival outcomes were analyzed. Tumor response was assessed using Response Evaluation Criteria in Solid Tumors criteria, with follow-up evaluations at 12, 24, and 36 months. Results: MWA demonstrated superior clinical outcomes compared to SR (P < 0.001). Post-treatment levels of liver enzymes (alanine aminotransferase, aspartate aminotransferase) and total bilirubin. Both groups showed significant reductions in alpha-fetoprotein and carbohydrate antigen 19-9 levels, with no significant difference between them (both P < 0.001). The complication rate was significantly lower in the MWA group (P < 0.001). Tumor response, including complete response (CR) and overall response rate (ORR), was higher in the MWA group (CR: 40 vs. 20; ORR: 86.2% vs. 65.6%). Additionally, progression-free survival (PFS) and overall survival (OS) at 12, 24, and 36 months were significantly better in the MWA group (all P < 0.001). Conclusion: Ultrasound-guided MWA provides notable advantages over SR in the treatment of HCC, including less hepatic injury, fewer complications, and improved PFS and OS. These findings support MWA as a safe, minimally invasive, and effective alternative for HCC management.

**Keywords:** Ultrasound-guided, percutaneous microwave ablation, hepatocellular carcinoma

## Introduction

Hepatocellular carcinoma (HCC) is among the most common malignancies worldwide and ranks as the fourth leading cause of cancer-related mortality [1, 2]. The majority of HCC cases are associated with chronic liver diseases, including hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, non-alcoholic fatty liver disease (NAFLD), and cirrhosis [3-7]. Despite advancements in early diagnosis and treatment, the prognosis for HCC remains poor due to delayed detection and high recurrence rates. Curative options such as surgical resection and liver transplantation are effective but limited by strict eligibility criteria, organ shortages, and impaired liver function in many patients [8].

In recent years, there has been a growing interest in minimally invasive therapies for HCC. Among them, microwave ablation (MWA) has

emerged as a promising alternative [9, 10]. MWA is a thermal ablation technique that induces tumor necrosis by delivering high-frequency electromagnetic energy [11-13]. Compared to other local ablative methods, such as radiofrequency ablation (RFA) and cryoablation, MWA offers several advantages, including higher intratumoral temperatures, larger ablation volumes, shorter procedure times, and improved efficacy for tumors located near large vessels, as it is less affected by the “heat-sink” effect [14].

Ultrasound guidance is widely employed in percutaneous MWA due to its real-time imaging capability, low cost, and absence of ionizing radiation, making it especially suitable for patients requiring repeated interventions [15]. Previous studies have demonstrated the safety and efficacy of ultrasound-guided MWA for small-to-medium-sized HCCs, with local tumor control rates comparable to surgical resection

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in selected patients [16]. However, several challenges remain, such as optimizing ablation parameters, reducing complications, and improving long-term outcomes. For instance, precise tumor targeting and adequate ablation margins are essential for minimizing recurrence [17]. Moreover, limited data are available on the efficacy of MWA in treating larger tumors (> 3 cm) and in patients with compromised liver function or multifocal disease.

The present study aims to address these gaps by evaluating the clinical outcomes of ultrasound-guided percutaneous MWA in patients with HCC. In contrast to earlier studies, we incorporated advanced imaging techniques for pre-procedural planning and intraoperative monitoring to ensure accurate tumor localization and ablation. Additionally, a novel microwave antenna was employed to enhance energy delivery and ablation efficiency, particularly for larger or irregular tumors. By comprehensively analyzing both short- and long-term outcomes - including local tumor progression, overall survival, and recurrence-free survival - this study seeks to provide robust evidence supporting the broader application of MWA in the clinical management of HCC.

Therefore, this study aims to evaluate the efficacy, safety, and survival benefits of ultrasound-guided microwave ablation compared to surgical resection in the treatment of hepatocellular carcinoma. The findings may contribute to refining clinical practice, expanding the indications for MWA, and ultimately improving patient outcomes.

## Materials and methods

### *Case selection*

This retrospective study included 100 patients with HCC who underwent either ultrasound-guided percutaneous MWA or surgical resection (SR) at Shulan (Hangzhou) Hospital between January 2018 and December 2021. Patients were assigned to either the MWA group (n = 58; 62 lesions, including 4 patients with 2 lesions each) or the SR group (n = 42; 43 lesions, including 1 patient with 2 lesions, all located in the left liver lobe) based on the treatment received.

Patients were selected based on strict inclusion and exclusion criteria to ensure the reliability and validity of the results.

Inclusion criteria: (1) Diagnosed with HCC via contrast-enhanced CT/MRI or histopathology [18]; (2) No extrahepatic metastases or major vascular invasion; (3) Child-Pugh liver function classification of grade A or B; (4) A single lesion with a maximum diameter  $\leq$  5 cm, or up to 3 lesions each  $\leq$  3 cm; (5) Eligible for ultrasound-guided MWA; (6) Complete clinical data available.

Exclusion criteria: (1) Severe comorbidities, including cardiopulmonary insufficiency or coagulopathy; (2) Active infections or acute hepatic decompensation; (3) Distant metastases or extensive vascular invasion; (4) Incomplete clinical data.

All patients were treated in accordance with the Declaration of Helsinki, and the study was approved by the Institutional Ethics Committee of Shulan (Hangzhou) Hospital.

### *Data collection*

Baseline demographic and clinical data - including age, sex, liver disease history (HBV/HCV), cirrhosis status, alpha-fetoprotein (AFP) level, TNM stage, and tumor location - were collected.

Liver function markers, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBIL), were measured before treatment and one week post-treatment to evaluate hepatic function. Tumor markers (AFP and carbohydrate antigen 19-9 [CA19-9]) were also assessed pre- and post-treatment to determine therapeutic efficacy. Post-treatment complications such as bile leakage, surgical site infection, electrolyte imbalance, incision fat liquefaction, and pulmonary infection were recorded. Long-term outcomes, including tumor response, progression-free survival (PFS), and overall survival (OS), were monitored at 12, 24, and 36 months.

Venous blood (5 mL) was drawn from the cubital vein using EDTA-K2 anticoagulant tubes during routine follow-up. Samples were stored at 4°C for short-term preservation. Serum was

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**Table 1.** Comparison of baseline characteristics

Characteristic	MWA Group (n = 58)	SR Group (n = 42)	t/ $\chi^2$	P
Mean Age (years)	61.07 ± 6.20	61.12 ± 6.25	0.040	0.968
Sex			0.059	0.808
Male	40	28		
Female	18	14		
Etiology of Liver Disease			0.197	0.906
HBV	60%	65%		
HCV	22%	18%		
Alcohol	18%	17%		
Tumor Size (cm)	3.38 ± 0.30	3.30 ± 0.66	0.859	0.393
Tumor Number			0.459	0.498
Solitary	70%	64%		
Multifocal	30%	36%		
Child-Pugh Grade			2.347	0.126
A	90%	79%		
B	10%	12%		
Cirrhosis (%)	80%	76%	0.138	0.710
AFP (> 400 µg/L, %)	35%	40%	0.375	0.540
TNM Stage (I, %)	85%	79%	0.639	0.424
Tumor Location (Left/Right)			0.336	0.562
Left	20%	25%	0.416	0.519
Right	80%	75%	0.138	0.710

Note: HBV: Hepatitis B Virus; HCV: Hepatitis C Virus; AFP: Alpha-Fetoprotein.

separated by centrifugation at 4000 rpm for 10 minutes and stored at -70°C for long-term analysis.

Liver function and tumor markers were analyzed using a fully automated biochemistry analyzer (Cobas c311). Specific reagents, including Hemosil™ Reference Emulsion and Hemosil™ APTT Lyophilized Silica, were used according to the manufacturer's instructions for the detection of ALT, AST, TBIL, AFP, and CA19-9 levels.

### Outcome measurements

Treatment efficacy was evaluated based on tumor response, liver function changes, and tumor marker levels. Tumor response was assessed one month after treatment using contrast-enhanced imaging, and categorized as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD) according to the Response Evaluation Criteria in Solid Tumors criteria [19]. The over-

all response rate (ORR) was defined as CR + PR, and the disease control rate (DCR) was defined as CR + PR + SD.

PFS was defined as the time from treatment initiation to the first documented progression or death. OS was defined as the time from treatment to death from any cause. Safety was assessed based on changes in liver function markers and the incidence of post-treatment complications.

### Statistical methods

All statistical analyses were performed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation and compared using Student's t-test or Mann-Whitney U test, as appropriate. Categorical variables were presented as counts and per-

centages and analyzed using the chi-square test or Fisher's exact test.

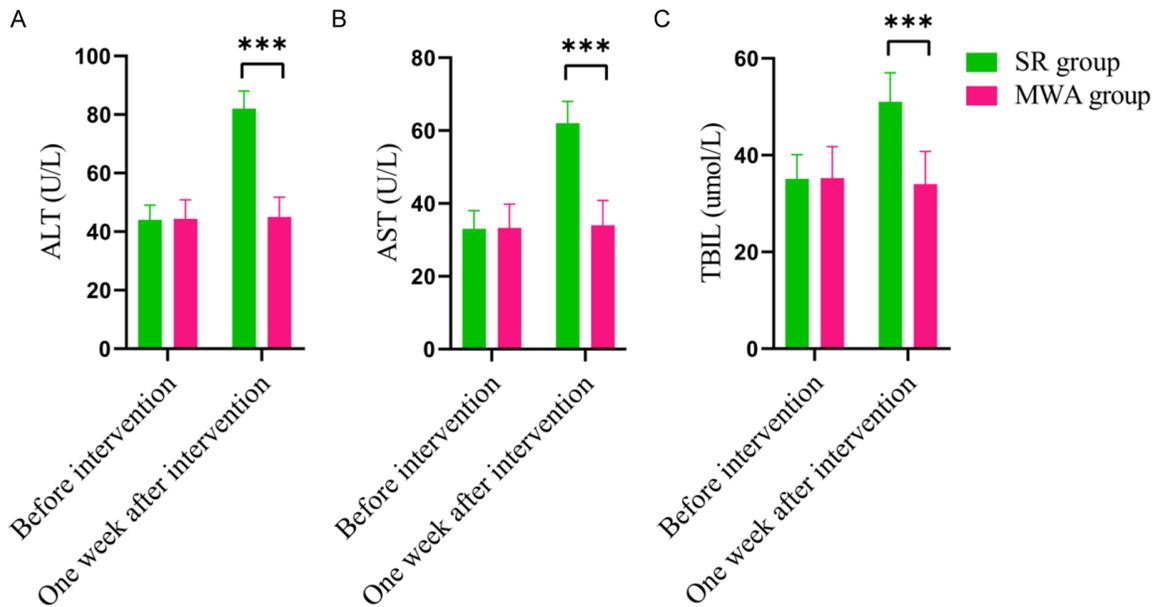
Paired t-tests were used to compare liver function and tumor marker levels before and after treatment. Kaplan-Meier curves were generated to evaluate PFS and OS, and intergroup comparisons were performed using the log-rank test. A *p*-value < 0.05 was considered statistically significant. All analyses adhered to the principles of transparency and reproducibility.

## Results

### Comparison of baseline characteristics

Baseline variables, including liver disease history (HBV/HCV), cirrhosis, AFP levels, TNM staging, and tumor location, were compared between the two groups. No significant differences were observed in liver disease history (*P* = 0.906), cirrhosis (*P* = 0.710), AFP levels (*P* = 0.540), TNM staging (*P* = 0.424), or tumor location (*P* = 0.562). A summary of baseline demographic and clinical characteristics is presented in **Table 1**.

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**Figure 1.** Comparison of changes in liver function before and after treatment between the two groups. (A) ALT, (B) AST, (C) TBIL. \*\*\* $P < 0.001$ , compared to the SR group. Note: SR: surgery resection. MWA: microwave ablation. ALT: Alanine Aminotransferase. AST: Aspartate Aminotransferase. TBIL: Total Bilirubin. MWA, Microwave ablation.

### Comparison of liver function changes before and after treatment

Levels of liver function markers, including ALT, AST, and TBIL, significantly increased one week after treatment in both groups (all  $P < 0.001$ ). However, the SR group showed a markedly greater increase in all markers compared to the MWA group (all  $P < 0.001$ ) (**Figure 1**). Post-treatment ALT, AST, and TBIL levels in the SR group were nearly double those in the MWA group.

### Comparison of AFP and CA19-9 level changes before and after treatment

Both groups experienced significant reductions in AFP and CA19-9 levels one week after treatment. For AFP (**Figure 2A**), baseline levels were not significantly different between groups ( $P > 0.05$ ). Following treatment, AFP levels declined significantly in both groups ( $P < 0.001$ ). Similarly, CA19-9 levels (**Figure 2B**) were comparable at baseline ( $P > 0.05$ ) and significantly decreased in both groups post-treatment ( $P < 0.001$ ). As with AFP, no significant intergroup difference was noted after treatment ( $P > 0.05$ ).

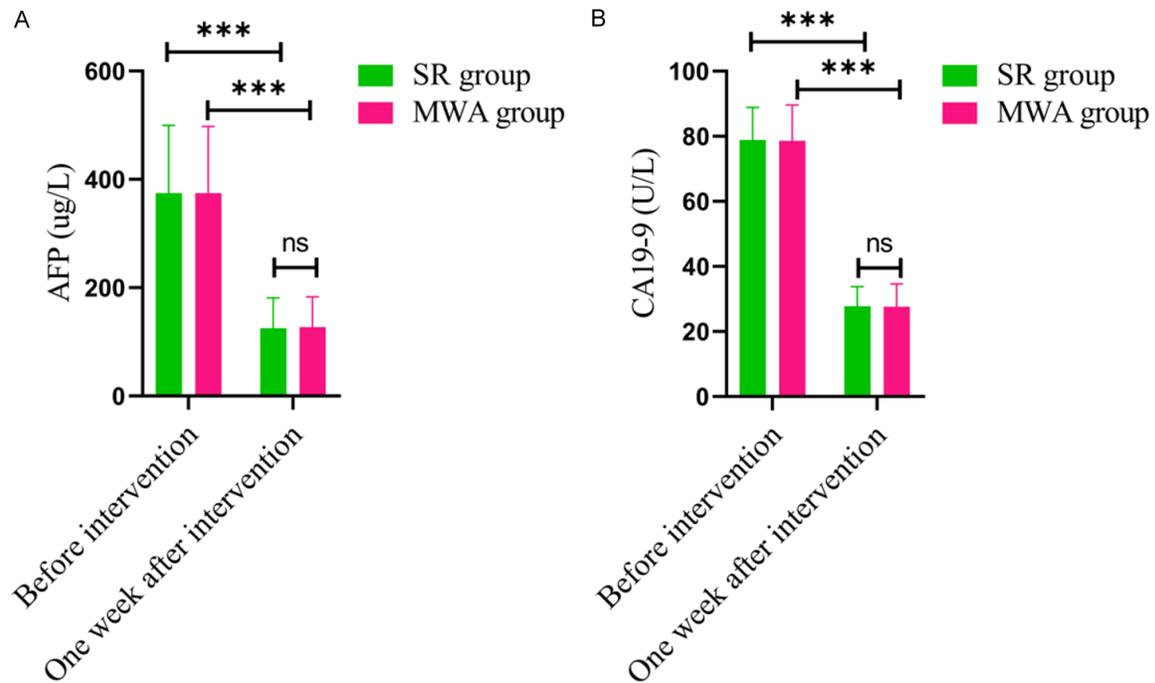
### Comparison of post-treatment complication rates

Post-treatment complications are summarized in **Table 2**. The overall complication rate was significantly lower in the MWA group compared to the SR group ( $P < 0.001$ ). While specific complications - including bile leakage, surgical site infection, electrolyte imbalance, fat liquefaction, and pulmonary infection were all less frequent in the MWA group, individual differences were not statistically significant (all  $P > 0.05$ ).

### Comparison of tumor response

The MWA group demonstrated a significantly higher CR rate than the SR group (40 vs. 20;  $P = 0.032$ ). The PR rate was also higher in the MWA group (10 vs. 8), though this difference was not significant ( $P = 0.817$ ). No significant differences were found for SD (5 vs. 6;  $P = 0.372$ ) or PD (3 vs. 3;  $P = 0.682$ ). ORR was significantly greater in the MWA group (86.2% vs. 65.6%;  $P = 0.020$ ), while the DCR was slightly higher in the MWA group (94.8% vs. 92.9%) but not statistically significant ( $P = 0.682$ ) (**Table 3**).

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**Figure 2.** Comparison of changes in AFP and CA19-9 levels before and after treatment between the two groups. (A) AFP, (B) CA19-9. \*\*\* $P < 0.001$ , compared to the SR group. Note: SR: surgery resection. MWA: microwave ablation. AFP: Alpha-Fetoprotein. CA19-9: Carbohydrate Antigen 19-9. MWA: Microwave ablation.

**Table 2.** Comparison of post-treatment complication rates

Complications	MWA Group (n = 58)	SR Group (n = 42)	$\chi^2$	P-value
Bile leakage	2	5	2.676	0.102
Incision infection	1	4	3.120	0.077
Electrolyte disorder	3	7	3.576	0.059
Incision fat liquefaction	1	3	1.863	0.172
Pulmonary infection	2	5	2.676	0.102
Overall complications	9	24	19.090	< 0.001

MWA, Microwave ablation.

**Table 3.** Comparison of tumor response

Tumor Response	MWA Group (n = 58)	SR Group (n = 42)	$\chi^2$	P-value
Complete Response	40	20	4.625	0.032
Partial Response	10	8	0.054	0.817
Stable Disease	5	6	0.799	0.372
Progressive Disease	3	3	0.168	0.682
Overall Response Rate	86.2%	65.6%	5.420	0.020
Disease Control Rate	94.8%	92.9%	0.168	0.682

MWA, Microwave ablation.

### Comparison of PFS

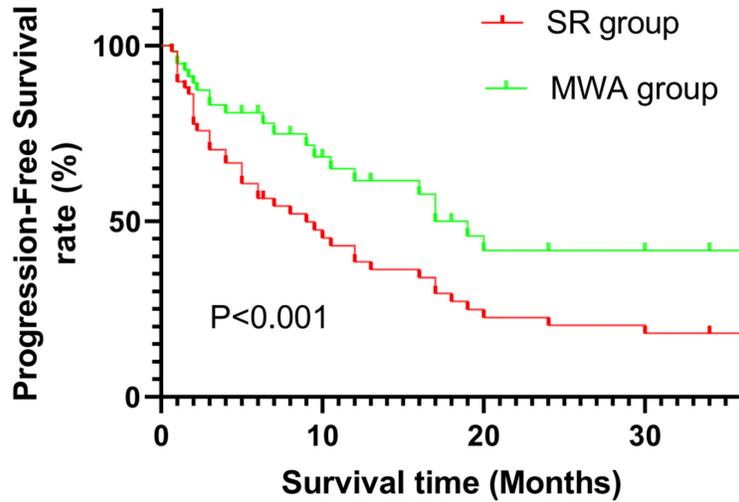
PFS rates are shown in **Figure 3**. The MWA group demonstrated significantly better PFS

compared to the SR group ( $P < 0.001$ ). Median PFS was longer in the MWA group, with higher survival rates at each follow-up point: 12-month PFS was 57.5% in the MWA group vs. 37.5% in the SR group ( $P = 0.005$ ); 24-month PFS was 27.1% vs. 8.4%; and at 36 months ( $P < 0.001$ ), the MWA group maintained a PFS of 15.5%, while the SR group showed no progression-free survivors ( $P < 0.001$ ).

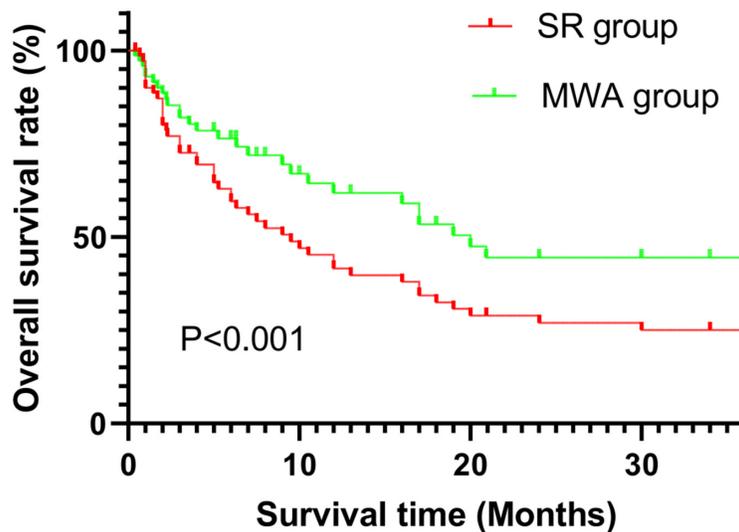
### Comparison of OS

OS outcomes are illustrated in **Figure 4**. The MWA group achieved significantly higher OS than the SR group ( $P < 0.001$ ). At 12 months, the OS rate was 75% in the MWA group compared to 60% in the SR group ( $P < 0.001$ ). At 24

months, OS was 48.5% vs. 30.2%, and by 36 months, the MWA group maintained an OS of 26.4%, while the SR group declined to 10.4% ( $P < 0.001$ ).



**Figure 3.** Comparison of PFS between the two groups. Note: PFS: Progression-Free Survival. MWA, Microwave ablation.



**Figure 4.** Comparison of OS between the two groups. Note: OS: Overall survival. MWA, Microwave ablation.

**Discussion**

Several recent studies have evaluated the efficacy of MWA as a treatment modality for HCC. Our findings contribute to this growing body of evidence by reaffirming the clinical advantages of MWA over SR. For instance, Zheng et al. reported that MWA yields comparable survival outcomes to SR in patients with HCC measuring 3-5 cm, suggesting MWA as a viable alternative, particularly for patients with marginal liver function or surgical contraindications [20]. Similarly, Zhang et al. demonstrated that

transarterial chemoembolization (TACE) combined with MWA achieved outcomes comparable to SR in patients with large solitary tumors, supporting the use of MWA as a less invasive approach with reduced perioperative risk [21]. These findings align with our study, which showed significantly improved PFS and OS in the MWA group, along with lower complication rates and better preservation of liver function.

The efficacy of MWA as a minimally invasive treatment has been well-documented. Prior studies have shown that MWA achieves high rates of CR and ORR, comparable to those of SR [22]. Our results reinforce this evidence: the MWA group showed significantly higher CR and ORR than the SR group (CR: 40 vs. 25; ORR: 86.2% vs. 78.6%). This superior tumor control is likely attributable to MWA's ability to produce larger and more uniform ablation zones compared to other modalities, such as radiofrequency ablation (RFA) [23].

Mechanistically, MWA differs from RFA in several key aspects. It generates higher intratumoral temperatures and larger ablation zones in a shorter time, enhancing treatment efficiency and reducing procedure duration [24, 25].

Moreover, MWA is less affected by the “heat-sink effect” - the loss of thermal energy near blood vessels - which compromises ablation completeness in RFA. This makes MWA especially suitable for tumors in anatomically challenging locations [26, 27]. In our study, the higher CR and ORR observed in the MWA group may be partly due to these technical advantages, which facilitate more complete coagulative necrosis and improved local tumor control.

Beyond its thermal effects, recent research suggests MWA may also elicit systemic immu-

nologic responses. The ablation process induces the release of tumor-associated antigens, damage-associated molecular patterns, and pro-inflammatory cytokines, potentially activating dendritic cells and stimulating cytotoxic T lymphocyte responses [28, 29]. This phenomenon, termed immunogenic cell death, may contribute to enhanced tumor control and prolonged survival. Tehrani et al. and Imran et al. further proposed that combining thermal ablation with immunotherapy could potentiate systemic antitumor immunity and suppress distant metastasis [30, 31]. Although our study did not evaluate immune markers, the favorable long-term outcomes in the MWA group may, in part, be attributable to such immune-mediated effects.

Preservation of liver function following MWA is another clinically relevant advantage, particularly for patients with cirrhosis or Child-Pugh B liver status. Previous studies have shown that while SR is curative, it often imposes significant hepatic stress, especially in patients with limited hepatic reserve [32, 33]. Consistent with these findings, our study demonstrated significantly lower post-treatment ALT, AST, and TBIL levels in the MWA group, indicating less hepatic injury. Better liver function preservation facilitates quicker recovery and enables further interventions in cases of recurrence, ultimately contributing to improved overall survival.

One of the key findings of this study is the significantly improved PFS and OS observed in the MWA group compared to the SR group. While SR is traditionally considered the gold standard for HCC treatment, our results suggest that MWA may yield superior outcomes in appropriately selected patients. This is especially relevant for individuals with compromised liver function or advanced age, for whom surgical intervention carries greater risk. Additionally, the comparable reductions in AFP and CA19-9 levels between the two groups indicate that both modalities are effective in inducing tumor necrosis and reducing tumor burden. These findings support the role of MWA as a minimally invasive alternative to SR, particularly for patients with early-stage HCC or those deemed unsuitable for surgery.

Despite the encouraging results, this study has several limitations. First, as a retrospective

analysis, it is subject to selection bias and potential confounding variables. Although baseline characteristics were well balanced between the groups, prospective randomized controlled trials are necessary to confirm these observations. Second, the 36-month follow-up period may not fully capture the long-term efficacy of either treatment. Longer-term studies are needed to assess the durability of tumor control and survival outcomes. Lastly, the relatively small sample size may have limited the statistical power to detect differences in specific outcomes, such as individual complications.

In conclusion, this study demonstrates that ultrasound-guided percutaneous MWA is a safe and effective treatment for HCC, offering superior PFS and OS, lower complication rates, and better preservation of liver function compared to SR. These findings contribute to the growing body of evidence supporting MWA as a minimally invasive alternative to SR, particularly for early-stage HCC or high-risk surgery.

### Disclosure of conflict of interest

None.

### Abbreviations

MWA, microwave ablation; US, Ultrasound; HCC, Hepatocellular carcinoma; SR, surgical resection; ORR, overall response rate; CR, complete response; OS, Overall survival; PFS, progression-free survival; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; TBIL, Total bilirubin; AFP, Alpha-fetoprotein; CA19-9, Carbohydrate antigen 19-9; HBV, Hepatitis B virus; HCV, Hepatitis C virus; RFA, Radiofrequency ablation; NAFLD, Non-alcoholic fatty liver disease.

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