

## Short-Term Outcomes of Ultrasound-Guided Microwave Ablation (USG-MWA) Versus Transarterial Chemoembolization (TACE) in Intermediate-Stage Hepatocellular Carcinoma (HCC)

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### Abstract

**Background:** Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality worldwide. For patients with intermediate-stage HCC, transarterial chemoembolization (TACE) is widely recommended as the standard locoregional treatment. However, its efficacy may be limited by incomplete tumour necrosis, recurrence, and transient impairment of liver function. Ultrasound-guided microwave ablation (USG-MWA) has emerged as a potential alternative locoregional therapy with promising tumour control. This study compared the short-term outcomes of USG-MWA and TACE in patients with intermediate-stage HCC. **Methods:** A retrospective comparative cohort study was conducted using medical records from Anshan Cancer Hospital, China, between 2018 and 2020. A total of 102 patients with intermediate-stage HCC were included, with 51 patients treated with USG-MWA and 51 treated with TACE. Tumour response was assessed at 1 month using modified Response Evaluation Criteria in Solid Tumours (mRECIST). Serial changes in alpha-fetoprotein (AFP), total bilirubin (TBIL), and alanine aminotransferase (ALT) were measured at baseline, 7 days, and 1 month after treatment using mixed-design repeated-measures analysis of variance. **Results:** Baseline demographic, clinical, and biochemical characteristics were comparable between the two groups. USG-MWA achieved a significantly higher complete response rate than TACE (68.6% vs. 31.4%,  $P < 0.001$ ). Partial response and stable disease were more frequently observed in the TACE group, while progressive disease was uncommon in both groups. AFP levels declined significantly over time in both groups, with a greater reduction observed in the USG-MWA group. No significant between-group differences were identified in TBIL or ALT trajectories during the 1-month follow-up period, although the transient biochemical fluctuations were more pronounced in the TACE group. **Conclusion:** In this retrospective single-center cohort, USG-MWA was associated with better short-term tumor response and greater AFP reduction than TACE in patients with intermediate-stage HCC, while short-term liver biochemical changes were broadly comparable between treatments. These findings support that USG-MWA is a potentially effective locoregional treatment option in selected patients with intermediate-stage HCC. Further prospective multicenter studies with longer follow-up are warranted to validate these results.

**Keywords:** hepatocellular carcinoma; ultrasound-guided microwave ablation; transarterial chemoembolization; alpha-fetoprotein; locoregional therapy

## Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and remains a leading contributor to cancer-related mortality worldwide. The disease burden is particularly high in East Asia and sub-Saharan Africa, where chronic hepatitis B virus and hepatitis C virus infections continue to represent major risk factors for hepatocarcinogenesis. Because HCC often develops in the background of chronic liver disease and cirrhosis, its management is often complex, and prognosis remains unfavorable, especially in patients diagnosed beyond the early stage.<sup>1-3</sup>

Treatment selection in HCC is primarily determined by tumor stage, underlying liver function reserve, and patient performance status, most guided by the Barcelona Clinic Liver Cancer (BCLC) staging system.<sup>4-6</sup> Patients with very early-stage or early-stage disease may be eligible for potentially curative interventions, including surgical resection, liver transplantation, or local ablative therapy. By contrast, intermediate-stage HCC (BCLC stage B) is generally characterized by multinodular disease without vascular invasion or extrahepatic spread, for which locoregional therapy remains the cornerstone of management.<sup>4-6</sup>

Among available locoregional treatment modalities, transarterial chemoembolization (TACE) is widely regarded as the standard treatment of intermediate-stage HCC. Its antitumour effect is achieved through targeted intra-arterial chemotherapy combined with embolization-induced ischemic necrosis.<sup>4-6</sup> Nevertheless, its clinical efficacy may be constrained by incomplete tumour necrosis, recurrence, and the need for repeated sessions, particularly in larger or more heterogeneous tumours.<sup>7,8</sup> These limitations have prompted growing interest in alternative or complementary treatment strategies that may improve local tumour control.

Microwave ablation (MWA) has emerged as an increasingly recognized technique for the treatment of HCC. Compared with radiofrequency ablation, MWA is capable of producing higher intratumoural temperatures, larger ablation zones, and reduced susceptibility to the heat-sink effect, which may offer potential advantages in selected tumors.<sup>9,10</sup> When performed under ultrasound guidance, MWA allows real-time visualization and procedural precision, with prior studies reporting encouraging clinical outcomes in patients with HCC.<sup>9-11</sup> Taken together, these findings highlight the potential role of ultrasound-guided microwave ablation (USG-MWA) as an alternative locoregional treatment option.

Despite the growing use of both TACE and USG-MWA, direct evidence comparing their short-term outcomes in intermediate-stage HCC remains limited.<sup>12-14</sup> Therefore, this study set out to evaluate the short-term outcomes of USG-MWA and TACE in patients with intermediate-stage HCC by focusing on tumour response, serum alpha-fetoprotein (AFP) levels, and liver function parameters, including total bilirubin (TBIL) and alanine aminotransferase (ALT). Specifically, this study evaluated short-term radiologic and

biochemical outcomes in patients with preserved liver function at a single tertiary cancer centre.

## Methods

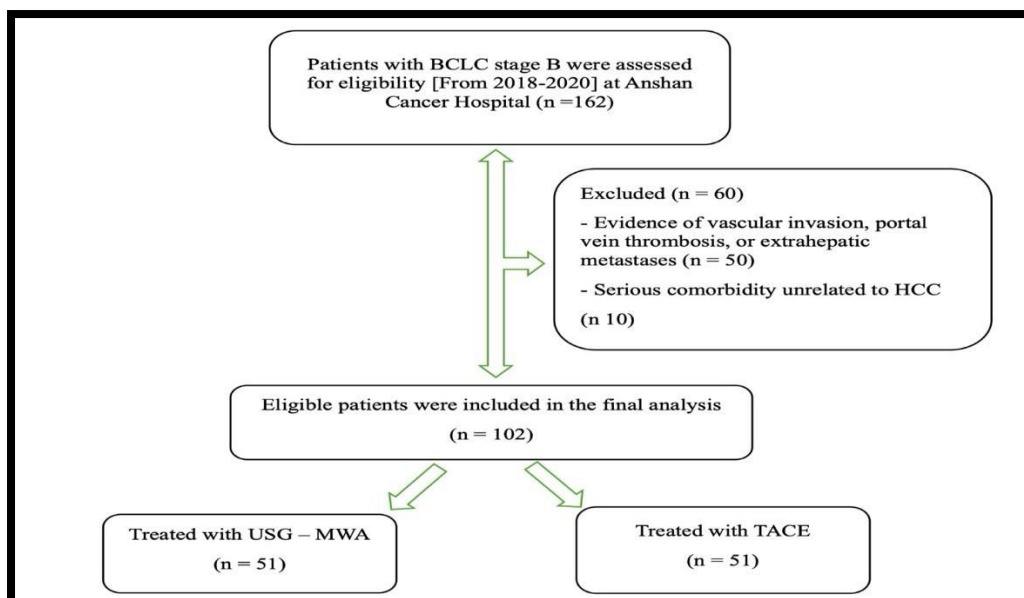
### Study design and setting

This retrospective comparative cohort study was conducted at Anshan Cancer Hospital, China, using medical records of patients with intermediate-stage hepatocellular carcinoma (HCC) treated between 2018 and 2020. Patients who underwent ultrasound-guided microwave ablation (USG-MWA) or transarterial chemoembolization (TACE) during the study period were identified and reviewed. Intermediate-stage HCC was defined according to the Barcelona Clinic Liver Cancer (BCLC) staging system and contemporary clinical practice guidelines.<sup>4-6</sup> The study protocol was approved by the Anshan Cancer Hospital and UniversitiTunku Abdul Rahman Scientific Ethical Review Committee (U/SERC/86/2022).

### Study population

A total of 162 patients with BCLC stage B HCC who underwent either USG-MWA or TACE at Anshan Cancer Hospital between 2018 and 2020 were screened for eligibility. Of these, 60 patients were excluded: 50 due to vascular invasion, portal vein thrombosis, or extrahepatic metastases, and 10 because of serious comorbidities unrelated to HCC. The final cohort comprised 102 eligible patients, with 51 patients assigned to the USG-MWA group and 51 patients to the TACE group. Clinical, radiological, and biochemical data were analyzed according to treatment modality. The study selection process is illustrated in Figure 1.

**Figure 1. Flow diagram of patient selection and study inclusion**



Eligible patients met the following inclusion criteria: Child–Pugh class A liver function, an Eastern Cooperative Oncology Group (ECOG) performance status of 0, presence of two tumour nodules, and tumour size between 3 and 5 cm. These criteria were selected to ensure enrollment of patients with preserved liver function, limited tumour burden, and good performance status who were suitable for locoregional treatment in intermediate-stage HCC.<sup>4–6</sup> Clinical, radiological, and laboratory data were collected from the medical records using a standardized data collection form.

### Sample size

The sample size calculation based on the expected proportion reported by Chen et al.<sup>12</sup> indicated that a minimum of 51 patients per group (giving a total  $n = 102$ ) was required to achieve 80% power.

### Treatment procedures

USG-MWA was performed using the KY-2000 microwave ablation system. Microwave energy of 40 to 60 W was delivered for 5 to 10 minutes per session. Contrast-enhanced ultrasound was used to evaluate the completeness of ablation, and additional ablation was performed when necessary to ensure adequate tumour coverage. This procedural approach is consistent with published evidence supporting microwave ablation as an effective locoregional treatment for selected HCC lesions.<sup>9–11</sup>

TACE was carried out through selective catheterization of the tumour-feeding artery using a 2.6-Fr microcatheter, followed by administration of doxorubicin hydrochloride mixed with iodized oil tailored to tumour size and vascularity. Embolization was then completed using gelatin sponge pledgets until angiographic stasis was achieved. As a well-established locoregional therapy, TACE remains a standard treatment option for appropriately selected patients with intermediate-stage HCC.<sup>4–6,8</sup>

### Outcome measures

The primary outcome was tumour response at one month following treatment, evaluated using the modified Response Evaluation Criteria in Solid Tumours (mRECIST) on contrast-enhanced computed tomography or magnetic resonance imaging.<sup>15</sup> Tumour response was classified into four categories: complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD).

Secondary outcomes included serial measurements of serum alpha-fetoprotein (AFP), total bilirubin (TBIL), and alanine aminotransferase (ALT), at baseline, 7 days, and 1 month after treatment. Post-procedural inflammatory syndromes, including post-ablation syndrome and post-embolization syndrome, as well as minor symptoms and major complications, were also recorded. Major complications were defined as adverse events resulting in significant morbidity, the need for unplanned additional treatment, or hospitalization.<sup>7</sup>

## Statistical analysis

Data were analyzed using IBM SPSS Statistics version 26.0. Categorical variables were summarized as frequencies and percentages, whereas continuous variables were expressed as mean  $\pm$  standard deviation. Baseline characteristics and tumour response rates between the two groups were compared using the chi-square test or Fisher's exact test, as appropriate. Longitudinal changes in AFP, TBIL, and ALT were analyzed using mixed-design repeated-measures analysis of variance. All statistical tests were two-sided, and a *P* value of less than 0.05 was considered statistically significant.

## Results

### Study population and baseline characteristics

Of the 162 patients with BCLC stage B hepatocellular carcinoma screened for eligibility, 102 were included in the final analysis after the exclusion of 60 patients. The study cohort consisted of 51 patients treated with ultrasound-guided microwave ablation (USG-MWA) and 51 treated with transarterial chemoembolization (TACE) (Figure 1). Baseline demographic, tumour, and biochemical characteristics were well balanced between the two groups, with no statistically significant differences observed in age, sex, hepatitis B status, tumour size, alpha-fetoprotein (AFP), alanine aminotransferase (ALT), or total bilirubin (TBIL) (Table 1).

**Table 1. Baseline characteristics**

Characteristic	TACE (n = 51) n (%), mean $\pm$ SD	USG-MWA (n = 51) n (%) mean $\pm$ SD	Test statistic	P value
<b>Gender,</b>			$\chi^2 = 0.927$	0.471
Male	38 (74.5)	42 (82.4)		
Female	13 (25.5)	9 (17.6)		
<b>Hepatitis B, n (%)</b>			$\chi^2 = 0.703$	0.577
Yes	42 (82.4)	45 (88.2)		
No	9 (17.6)	6 (11.8)		
<b>Age, years</b>	58.59 $\pm$ 10.38	60.55 $\pm$ 7.90	t = 1.152	0.286
<b>Baseline tumour size, mm</b>	42.61 $\pm$ 6.50	41.35 $\pm$ 5.99	t = 1.027	0.313
<b>Number of Tumour</b>	2	2	-	-
<b>Baseline AFP, ng/mL</b>	420.46 $\pm$ 325.43	387.35 $\pm$ 317.22	t = 0.271	0.604
<b>Baseline ALT, U/L</b>	54.84 $\pm$ 29.51	46.42 $\pm$ 24.63	t = 2.447	0.121
<b>Baseline TBIL, <math>\mu</math>mol/L</b>	24.63 $\pm$ 13.92	20.34 $\pm$ 12.13	t = 2.751	0.100

Data are presented as n (%) or mean  $\pm$  standard deviation. Categorical variables were compared using the chi-square test. Continuous variables were compared using the

independent samples *t*-test. AFP, alpha-fetoprotein; ALT, alanine aminotransferase; TBIL, total bilirubin; TACE, transarterial chemoembolization; USG-MWA, ultrasound-guided microwave ablation.

### Tumour Response after 1 month

Tumour response at 1 month according to mRECIST is summarized in Table 2. USG-MWA demonstrated a significantly higher complete response rate than TACE (68.6% vs. 31.4%,  $P < 0.001$ ). Partial response was observed in 23.5% of patients in the USG-MWA group and 47.1% of those in the TACE group. Stable disease was more frequent in the TACE group than in the USG-MWA group, while progressive disease was uncommon in both groups. Overall, these findings indicate superior short-term radiologic tumour response following USG-MWA compared with TACE.

**Table 2. Tumour response at 1 month according to mRECIST**

Tumour response category	TACE (n = 51)	USG-MWA (n = 51)
	n (%)	n (%)
<b>Complete response (CR)</b>	16 (31.4%)	35 (68.6%)
<b>Partial response (PR)</b>	24 (47.1%)	12 (23.5%)
<b>Stable disease (SD)</b>	9 (17.6%)	3 (5.9%)
<b>Progressive disease (PD)</b>	2 (3.9%)	1 (2.0%)

Data are presented as n (%). Overall comparison between groups was performed using the chi-square test or Fisher's exact test, as appropriate;  $P < 0.001$ . Abbreviations: mRECIST, modified Response Evaluation Criteria in Solid Tumours; TACE, transarterial chemoembolization; USG-MWA, ultrasound-guided microwave ablation.

### Changes in AFP, TBIL, and ALT over time

Longitudinal changes in AFP, TBIL, and ALT are summarized in Table 3. A significant time-by-group interaction was observed for AFP ( $F = 6.608$ ,  $P = 0.012$ ), indicating that the pattern of AFP decline over time differed significantly between the two treatment groups. By contrast, no significant interaction effects were found for TBIL ( $F = 0.000$ ,  $P = 0.985$ ) or ALT ( $F = 0.026$ ,  $P = 0.873$ ), suggesting similar overall temporal trends for these liver biochemical parameters in both groups.

In both treatment groups, AFP levels declined significantly from baseline to 7 days and from baseline to 1 month. In the USG-MWA group, reductions were evident at each interval with

mean differences baseline (mean difference [MD] = 229.37,  $P < 0.001$ ), from 7 days to 1 month (MD = 68.25,  $P < 0.001$ ), and from baseline to 1 month (MD = 232.72,  $P < 0.001$ ). Corresponding reductions were also seen in the TACE group (baseline to 7 days: MD = 102.59,  $P < 0.001$ ; 7 days to 1 month: MD = 76.14,  $P < 0.001$ ; baseline to 1 month: MD = 178.73,  $P < 0.001$ ). While both modalities achieved significant short-term reduction, the overall magnitude of AFP decline was greater in the USG-MWA group.

For TBIL, the TACE group demonstrated a transient increase from baseline to 7 days (MD = -5.99,  $P < 0.001$ ), followed by a decrease between 7 days and 1 month (MD = 9.00,  $P < 0.001$ ), with no significant overall difference between baseline and 1 month (MD = 3.02,  $P = 0.161$ ). In contrast, no significant changes in TBIL were observed across the assessed time points in the USG-MWA group.

**Table 3. Interaction Effects and within-group changes in AFP, TBIL, and ALT over time in the USG-MWA and TACE groups**

Characteristics	AFP	TBIL	ALT
	F	F	F
Interaction (period*group)	6.608**	0.000	0.026
	P = 0.012	P= 0.985	P= 0.873
	<b>Mean Difference</b>	<b>Mean Difference</b>	<b>Mean Difference</b>
<b>USG-MWA</b>			
Baseline to 7 Days	229.37**	0.41	-65.20**
7 Days to 1 Month	68.25**	2.55	61.12**
Baseline to 1 Month	232.72**	2.96	-4.08
<b>TACE</b>			
Baseline to 7 Days	102.59**	-5.99**	-107.01**
7 Days to 1 Month	76.14**	9.00**	104.13**
Baseline to 1 Month	178.73**	3.02	-2.88

(Values are presented as F-values for the time-by-group interaction and mean differences for within-group comparisons across time points. Longitudinal changes were analyzed using mixed-design repeated-measures analysis of variance.  $**P < 0.001$ .)

ALT showed a similar temporal pattern in both groups, with an increase from baseline to 7 days followed by a decline from 7 days to 1 month. In the USG-MWA group, ALT changed significantly from baseline to 7 days (MD = -65.20,  $P < 0.001$ ) and from 7 days to 1 month (MD = 61.12,  $P < 0.001$ ), but there was no significant net difference between baseline and 1 month (MD = -4.08). A comparable pattern was observed in the TACE group, with significant changes from baseline to 7 days (MD = -107.01,  $P < 0.001$ ) and from 7 days to 1 month (MD = 104.13,  $P < 0.001$ ), but no significant overall change between baseline and 1 month (MD = -2.88). These results indicate that although both groups experienced early post-treatment biochemical fluctuations, liver function markers at one month were broadly similar between the groups.

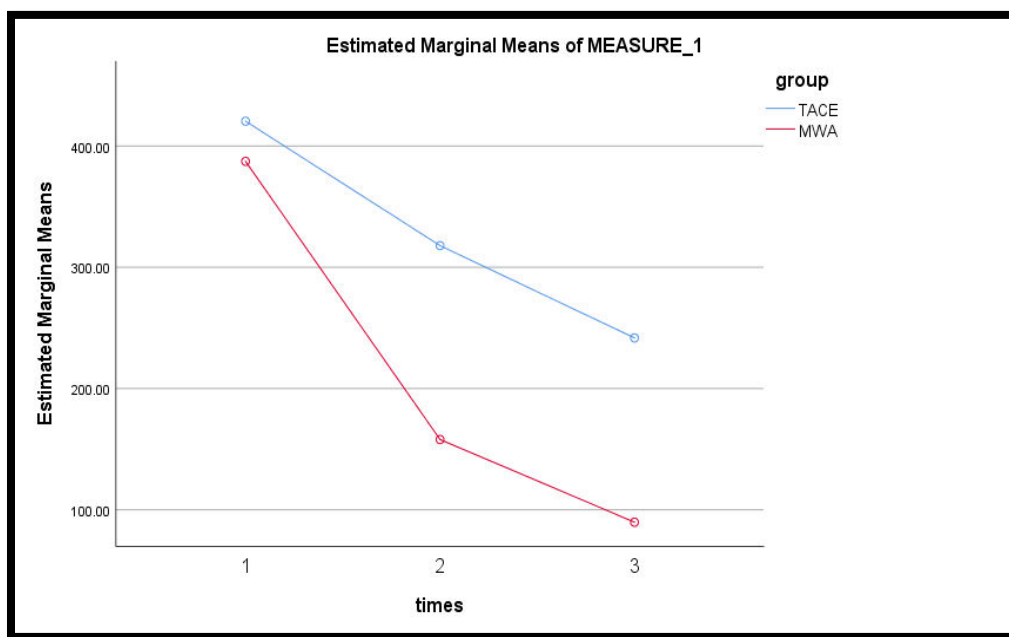


Figure 2. Interaction plot of AFP over time by treatment group

### Interaction plots

The interaction plot for AFP (Figure 2) shows a steeper, more sustained decline in estimated marginal mean AFP levels in the USG-MWA group than in the TACE group over the 1-month follow-up period. In contrast, the interaction plots for TBIL and ALT (Figures 3 and 4) show relatively similar overall temporal patterns between groups. However, greater short-term fluctuation was observed in the TACE group, particularly at 7 days after treatment.

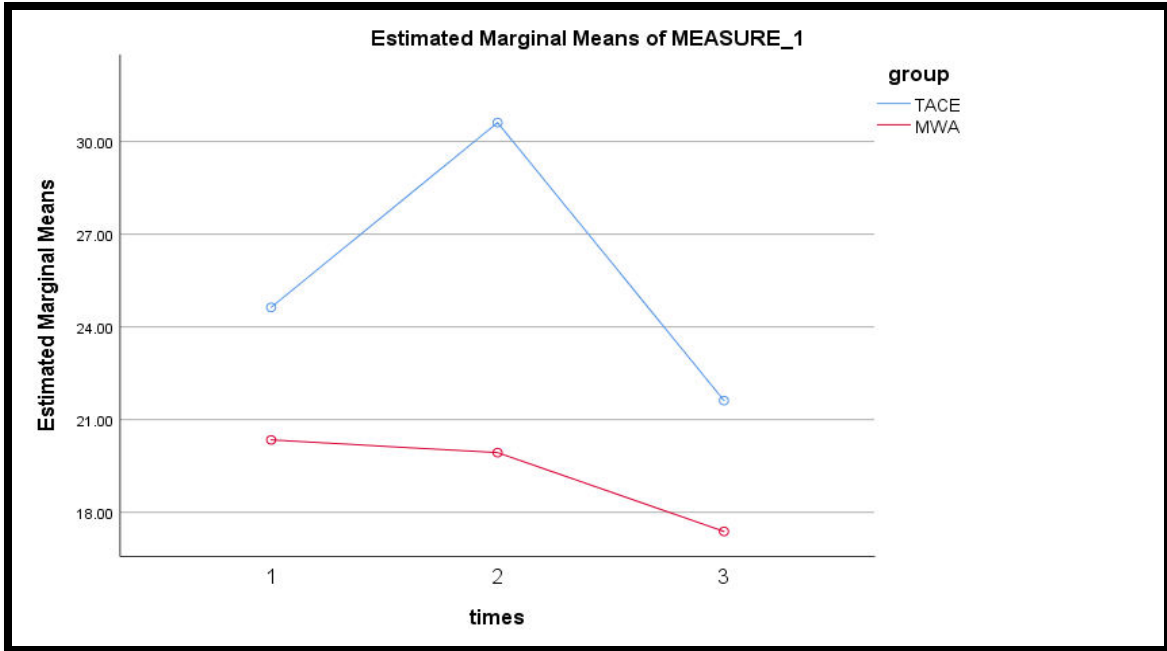


Figure 3. Interaction plot of TBILover time by treatment group

Figure 3 shows the temporal pattern of TBIL in both treatment groups. A transient increase at 7 days was observed in the TACE group, followed by a decline at 1 month, whereas TBIL remained relatively stable in the USG-MWA group.

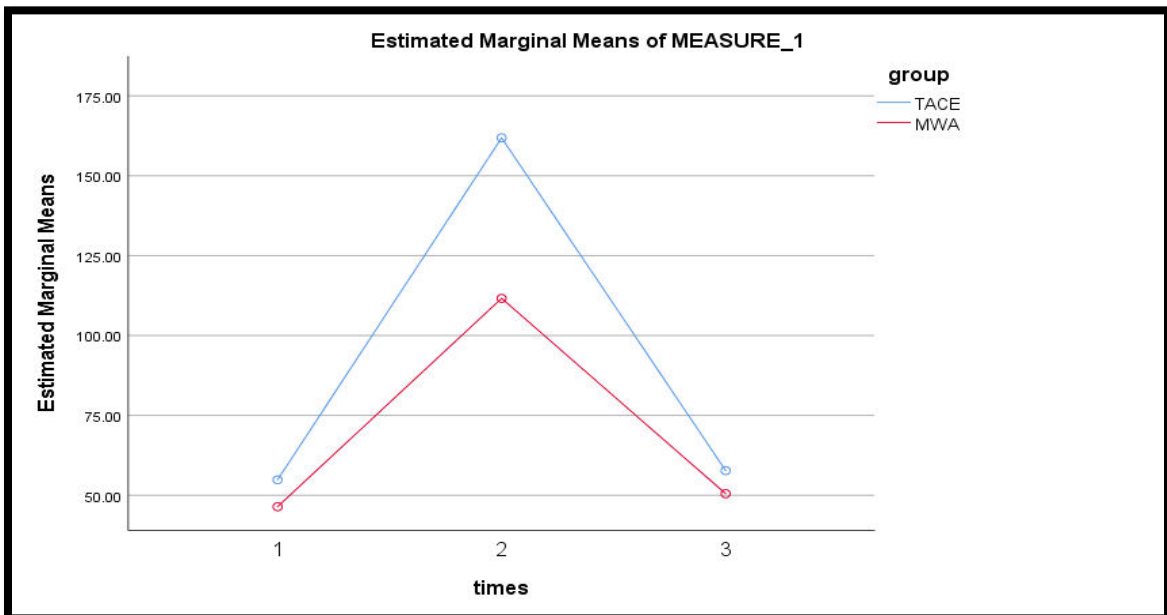


Figure 4. Interaction plot of ALT over time by treatment group

Figure 4 shows the temporal pattern of ALT in both treatment groups. ALT increased at 7 days and declined by 1 month in both groups, with greater short-term fluctuation observed in the TACE group.

**Table 4. Comparison of post-procedural symptoms (minor complications) within 7 days between the TACE and USG-MWA groups**

Symptom	TACE [n = 51], n (%)	Microwave Ablation [n = 51], n (%)	p-value
Low-grade fever	[28] (54.9%)	[25] (49.0%)	0.55
Nausea	[30] (58.8%)	[27] (52.9%)	0.55
Vomiting	[26] (51.0%)	[24] (47.1%)	0.69
Abdominal discomfort	[29] (56.9%)	[26] (51.0%)	0.55

Post-procedural symptoms were recorded from the medical notes. No statistically significant between-group differences were observed for any minor post-procedural symptoms (all  $P > 0.05$ ). No major complications were documented.

## Discussion

This study compared short-term outcomes of ultrasound-guided microwave ablation (USG-MWA) and transarterial chemoembolization (TACE) in patients with intermediate-stage hepatocellular carcinoma (HCC). The result showed that USG-MWA was associated with a higher complete response rate and a greater reduction in serum alpha-fetoprotein (AFP) over 1 month. In contrast, short-term changes in total bilirubin (TBIL) and alanine aminotransferase (ALT) were similar between the two treatment groups. These findings suggest that, in selected patients with intermediate-stage HCC, USG-MWA may provide better short-term local tumour control compared with TACE, without evidence of increased short-term hepatic biochemical deterioration.<sup>4-6,8-11</sup>

The primary objective of this study was to compare short-term tumour response between the two locoregional treatment modalities. In this study, the markedly higher complete response rate observed in the USG-MWA group supports the potential efficacy of microwave ablation in achieving short-term local tumour control. This outcome makes biological sense, as microwave ablation induces direct thermal destruction of tumour tissue and is capable of generating larger and more uniform ablation zones, with less susceptibility to the heat-sink effect than other local ablative techniques.<sup>9-11</sup> On the other hand, TACE exerts its antitumor

effect indirectly through selective arterial embolization combined with localized chemotherapy, which may result in incomplete tumour necrosis in some lesions.<sup>4-8</sup> The higher proportion of partial response and stable disease in the TACE group in this study is consistent with the fundamental differences in how the two treatment options act.

The results are also broadly consistent with previous literature reporting improved tumour response when microwave ablation is incorporated into locoregional treatment strategies for HCC. Chen et al. demonstrated better tumour response with TACE combined with microwave ablation than with TACE alone, while subsequent meta-analyses and propensity-matched studies also reported that the contribution of microwave ablation to improved local tumour control in selected patients.<sup>12-14</sup> Although prior investigations were conducted somewhat different treatment settings, the current findings similarly reinforce the role of USG-MWA as a potentially effective locoregional option in carefully selected patients with intermediate-stage HCC. However, these results should be interpreted cautiously because treatment allocation in the present study was not randomized and may have been influenced by lesion-specific characteristics, anatomical accessibility, and technical feasibility.

A secondary objective of this study was to compare the change in AFP after treatment. The AFP declined significantly in both groups, reflecting a treatment-related reduction in tumour activity. However, the USG-MWA group demonstrated a greater reduction in AFP levels, suggesting a stronger short-term effect. This is clinically relevant because AFP remains a widely used biomarker for monitoring treatment response and prognosis in HCC, particularly when interpreted together with imaging findings.<sup>16</sup> The steeper reduction in AFP after USG-MWA may reflect more immediate tumour destruction through direct thermal ablation. On the other hand, the gradual decline of AFP levels after TACE may be due to its ischemic and chemotherapeutic mechanisms. The AFP may not be elevated in every HCC patient and should not be used by itself to make a decision; the current findings support its role as an additional marker of early treatment response in this context.<sup>16</sup>

Regarding the liver biochemical results, no notable differences between groups were observed in the temporal trends of TBIL and ALT over the 1-month follow-up period. Nevertheless, descriptive analysis revealed a greater early fluctuation in the TACE group, with a temporary decline at 7 days before recovering by 1 month, while the USG-MWA group exhibited a more consistent biochemical profile. These observations might indicate a more targeted treatment effect with USG-MWA and reduced short-term injury to the adjacent non-tumorous liver tissue. In contrast, the transient biochemical disturbance observed after TACE might indicate post-embolization hepatic stress, which has been described in previous studies.<sup>7,11</sup> Notably, since the interaction effects for TBIL and ALT were not statistically significant, these biochemical results should be interpreted with caution and regarded as supportive rather than conclusive evidence of varying hepatic tolerance.

From a clinical standpoint, the present findings could influence treatment selection among the diverse BCLC stage B group. Current BCLC-, EASL, and AASLD-based recommendations still endorse TACE as a standard locoregional therapy for numerous patients with intermediate-stage HCC, while acknowledging that this stage includes a wide spectrum of tumour burden, liver reserve, and treatment appropriateness.<sup>4-6,8</sup> In specific patients with preserved liver function, limited tumour burden, and good performance status, USG-MWA may serve as a beneficial option when swift local control is essential. Concurrently, TACE remains clinically important, particularly in patients with multifocal disease or lesion distributions less amenable to ablative treatment. Consequently, the present results favour personalised, multidisciplinary treatment strategies instead of a uniform approach for all patients with intermediate-stage HCC.<sup>4-6,8</sup>

The present findings hold important clinical implications for treatment stratification within the heterogeneous BCLC stage B population. Although transarterial chemoembolization (TACE) remains the conventional standard of care for many patients in this stage, it is increasingly evident that intermediate-stage hepatocellular carcinomas (HCC) do not behave uniformly. Tumour characteristics such as size, distribution, vascularity, and accessibility for local therapy vary considerably, influencing both prognosis and therapeutic suitability.<sup>4,8</sup> In carefully selected patients with preserved liver function, limited tumour burden, and lesions technically amenable to percutaneous access, ultrasound-guided microwave ablation (USG-MWA) may provide distinct advantages. Specifically, it offers the potential for more immediate cytoreduction and a higher likelihood of complete local response, which may be particularly relevant when early tumour control is prioritized or when repeated embolization sessions are undesirable.<sup>8,11</sup> However, treatment selection must remain individualized, taking into account tumour number, anatomical location, proximity to critical structures, and institutional expertise. Rather than universally replacing TACE, these findings support the concept that USG-MWA represents a valuable alternative locoregional option for a carefully defined subgroup of intermediate-stage HCC patients, ideally within a multidisciplinary framework.

### Limitations

This study has several limitations. First, its retrospective, single-centre design restricts causal inference and generalisability. Second, treatment allocation was non-randomized and may have been influenced by factors such as lesion location, technical feasibility, and clinician preference, introducing potential selection bias. Third, the follow-up period was limited to one month, which precludes evaluation of long-term oncologic and hepatic outcomes. These limitations indicate that the current findings should be interpreted as short-term comparative data rather than definitive evidence of treatment dominance.<sup>4-8,11</sup> Future studies should address the limitations of the present study through larger prospective multicenter designs with extended follow-up periods.

**Conclusion:**

In this retrospective single-centre cohort, ultrasound-guided microwave ablation was associated with superior short-term radiological tumor response and a greater decline in alpha-fetoprotein than transarterial chemoembolization in selected patients with intermediate-stage hepatocellular carcinoma, while short-term liver biochemical outcomes were comparable for both groups. Prospective multicenter studies with long-term follow-up are needed to validate these findings.

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