Diagn Interv Radiol 2026; DOI: 10.4274/dir.2025.253308

INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Combined therapy with microwave ablation and conventional transarterial chemoembolization for hepatocellular carcinoma tumors larger than five centimetres: a prospective study

Hui Liu[1]*
Zhuoyang Fan[2]*
Ranying Zhang[1]
Xingwei Zhang[1]
Jianhua Wang[2]

[1]Fudan University Zhongshan Hospital, Department of Radiology, Shanghai, China

[2]Fudan University Zhongshan Hospital, Department of Interventional Radiology, Shanghai, China

*Joint first authors

Corresponding author: Jianhua Wang

E-mail: wjh1953a@163.com

Received 21 February 2025; revision requested 13 April 2025; last revision received 12 May 2025; accepted 18 May 2025

Epub: 07.07.2025

Publication date: 02.01.2026

DOI: 10.4274/dir.2025.253308

PURPOSE

This study aimed to compare the safety and efficacy of a combined therapy involving microwave ablation (MWA) and transarterial chemoembolization (TACE) versus only TACE for the treatment of hepatocellular carcinoma (HCC) tumors ≥5 cm.

METHODS

This prospective study enrolled 186 patients with HCC tumors ≥5 cm. Patients were divided into a test group (TACE + MWA) and a control group (TACE only). The average tumor size was 9.2 ± 3.7 cm, ranging from 5 to 19 cm. Forty-five patients (27.4%) had Barcelona Clinic Liver Cancer class A disease, and 119 (72.6%) had class B disease. The viable tumor volume was quantified utilizing ITK-SNAP, a free and open-source software package for medical image segmentation and visualization, along with contrast-enhanced magnetic resonance imaging. The tumor response was assessed according to the modified response evaluation criteria in solid tumors rules. Serum alpha-fetoprotein (AFP) levels were monitored, and the tumor necrosis ratio and AFP variation rate were calculated.

RESULTS

The final analysis of 164 patients (median age 57 years, range 26–80 years; 19 women, 145 men) showed that the test group exhibited a significantly higher tumor necrosis ratio than the control group (87.5% vs. 76.1%, $P = 0.002$). The serum AFP levels were markedly reduced in the test group relative to the control group 30 days after surgery ($P = 0.001$). The AFP variation rate in the test group (79.5%) was significantly greater than that observed in the control group (47.5%) ($P < 0.001$). A significant positive correlation existed between the tumor necrosis ratio and AFP variation rate ($P < 0.001$). Compared with the control group, the test group demonstrated a significantly higher partial response rate (68.6% vs. 51.3%, $P < 0.05$), a lower rate of progressive disease (17.4% vs. 35.9%, $P < 0.05$), an increased overall response rate (70.9% vs. 55.1%, $P = 0.036$), and an enhanced disease control rate (82.6% vs. 64.1%, $P = 0.007$). Post-MWA, 3 patients experienced hemorrhage and 2 developed arteriovenous fistulae, all of which were treated with embolization.

CONCLUSION

The combination of TACE and MWA demonstrated safety, good tolerability, and greater efficacy compared with TACE alone for HCC tumors ≥5 cm.

CLINICAL SIGNIFICANCE

The combination of TACE and MWA offers new possibilities for improving tumor necrosis rates, reducing AFP levels, and enhancing short-term prognosis. These findings not only provide new treatment options for clinical doctors but also promote the application of three-dimensional quantitative assessment technology and provide important references for future research and clinical practice.

KEYWORDS

Hepatocellular carcinoma, microwave ablation, therapeutic evaluation, three-dimensional, transarterial chemoembolization

You may cite this article as: Liu H, Fan Z, Zhang R, Zhang X, Wang J. Combined therapy with microwave ablation and conventional transarterial chemoembolization for hepatocellular carcinoma tumors larger than five centimetres: a prospective study. *Diagn Interv Radiol.* 2026;32(1):96-103.

Primary liver cancer is the sixth most frequently occurring cancer worldwide and is the third most common cause of death related to cancer.[1] Hepatocellular carcinoma (HCC) is the predominant form of liver cancer. More than 70% of patients received a diagnosis during the intermediate to advanced stages and were limited to non-invasive treatment options.[2] For patients with intermediate to advanced HCC, transarterial chemoembolization (TACE) is the initial treatment choice.[3] However, the effectiveness of TACE is restricted for large HCC lesions, often leading to TACE-refractoriness and deteriorating liver function with repeated treatments.[4,5]

Recent studies indicate that combining TACE with ablative methods is increasingly recognized for improving tumor response and patient survival.[6-9] However, the majority of these studies have concentrated on sequential combination therapy. Only a small number of studies have dealt with TACE plus concurrent ablation.[7,10] A retrospective study found that microwave ablation (MWA) immediately followed by TACE was a reliable and efficient therapy for large HCC tumors.[11] However, prospective studies on the topic have not been reported.

Therapeutic response in HCC was mainly assessed by measuring the target lesion's diameter through contrast-enhanced imaging.[12] Indeed, most large HCC tumors exhibit irregular morphology and significant internal heterogeneity pre-and post-treatment. Numerous studies have found that three-dimensional (3D) quantitative assessment is more precise than diameter-based measurements.[13-15] Precise delineation and quantitative assessment of the complete tumor active lesion are essential for an accurate evaluation of therapeutic efficacy. Few studies have evaluated the treatment efficacy on large HCC tumors by measuring viable tumor volumes using contrast-enhanced magnetic resonance imaging (MRI). Furthermore, although dynamic changes in serum alpha-fetoprotein (AFP) levels have been shown to correlate with treatment efficacy and patient outcomes,[16,17] the relationship between viable tumor volume and AFP dynamics remains unexplored.

Main points

- The transarterial chemoembolization (TACE) + microwave ablation (MWA) group exhibited a significantly higher viable tumor necrosis ratio than the TACE group.
- Post-treatment serum alpha-fetoprotein (AFP) levels were significantly lower in the TACE + MWA group than in the TACE group. The AFP variation rate was significantly higher in the TACE + MWA group than in the TACE group.
- A positive correlation was found between tumor necrosis ratio and AFP variation rate.
- The TACE + MWA group demonstrated superior partial response, overall response rate, and disease control rate relative to the TACE group.

Therefore, we performed a prospective study to assess changes in viable tumor volume and AFP levels before and after treatment, aiming to precisely analyze short-term efficacy differences between TACE alone and TACE combined with MWA in treating large HCC tumors.

Methods

Study design

A prospective, randomized controlled trial was performed at a single center for this research. The study was registered on ClinicalTrials.gov (NCT04721470). Before being enrolled, all patients gave their written informed consent. The study protocol received approval from all relevant institutional review boards, adhering to the Declaration of Helsinki and local regulations. The study was approved by the Ethics Committee of Zhongshan Hospital Affiliated to Fudan University (protocol number: B2018-146R, date: 17.11.2018). Participants were randomly assigned to either the TACE-only group or the TACE plus MWA group between December 2018 and December 2021. Demographic and clinical data, such as age, gender, tumor diameter, Child–Pugh class, hepatitis B virus (HBV) infection status, and serum AFP levels, for patients with HCC were obtained from medical records.

The main inclusion criteria were as follows: (1) age ≥18 years; (2) nodular and hypervascular HCC diagnosis was established using either non-invasive methods or pathological examination; (3) large (≥5 cm) HCC lesions confined to the liver as determined by contrast-enhanced MRI before treatment; (4) Barcelona Clinic Liver Cancer (BCLC) stage A or B; and (5) eastern cooperative oncology group performance status score of ≤2. Participants were excluded if they satisfied any of the following conditions: (1) having more than three HCC lesions (3 patients); (2) were involved in other clinical research treatments simultaneously (5 patients); (3) showed extrahepatic metastasis or significant vascular invasion (11 patients); (4) did not undergo MRI enhancement assessment 30 days after treatment (3 patients); or (5) had a platelet concentration <3 x 10^9/L and prothrombin activity <40%, which excluded 22 patients. Randomization occurred within 1 week following the verification of eligibility, with treatment protocols commencing in the subsequent week. Figure 1 depicts the study population inclusion process flowchart. Three interventional radiologists, each with >10 years of experience, conducted all treatment procedures at the study's onset.

Transarterial chemoembolization group

Angiography of the hepatic artery was conducted through the right common femoral access with a 5-F catheter (RH; Terumo, Tokyo, Japan) to evaluate the tumor's burden, localization, and blood supply. A 2.7-F microcatheter (Progreat; Terumo) was precisely manipulated to access the tumor's supplying arteries. A mixture of 5–20 mL iodized oil (lipiodol) and 50 mg epirubicin (Farmorubicin; Pfizer, Wuxi, China) was used for chemoembolization. The tumor's vascular characteristics, size, and number primarily dictated the dosage of ethiodized oil. The tumor's blood supply was cut off by fully embolizing all its arterial branches for optimal devascularization. Embolization was performed using a lipiodol emulsion mixed with gelatin sponge particles (350–560 mm; Ailikang Medicine Co., Ltd.).

Transarterial chemoembolization plus microwave ablation group

A right common femoral approach was used for hepatic artery angiography to assess tumor burden, localization, and blood supply. Ultrasound-guided percutaneous MWA (IPC–1530; Aloka, Tokyo, Japan) was performed, followed immediately by chemoembolization.

The MWA utilized a water-cooled microwave system (ECO-100C; Nanjing, Jiangsu, China) featuring a 2.45 GHz generator with adjustable power of 0–100 W. The antenna placement, power, and emission duration were customized according to the tumor's characteristics. Power was set between 60–100 W for 5–15 minutes per session, as per guidelines. Multiple overlapping ablations were monitored via real-time ultrasound. A 14-gauge antenna–or two if necessary–was placed into the target tumor to cover the tumor's margin. The session was ended if the deep region of the

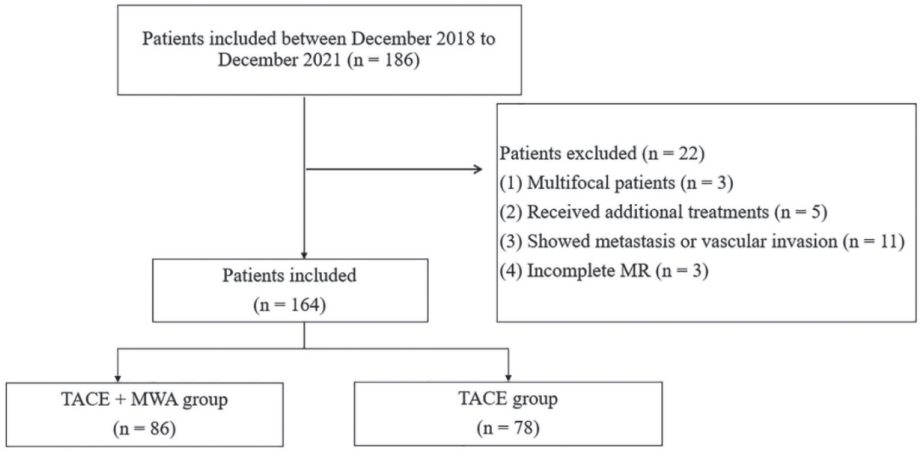

Figure 1. Flowchart of the study. TACE, transarterial chemoembolization; MWA, microwave ablation; MR, magnetic resonance.

lesion was covered by hyperechoic regions on ultrasound. Subsequently, the antenna was withdrawn gradually, and microwave emission was restarted. The end of the procedure was signaled when the entire tumor was hyperechoic on ultrasound. Post-ablation, needle pathway coagulation was performed to reduce bleeding or the spread of the tumor.

After MWA, hepatic angiography was quickly performed to evaluate ablation results, check for remaining tumor vascularity, and detect complications, such as arteriovenous fistula or bleeding. A mixture of 2–20 mL iodized oil (lipiodol) and 20–50 mg epirubicin (Farmorubicin; Pfizer, Wuxi, China) was used for chemoembolization until the tumor's blood supply was saturated. Gelatin sponge particles, sized 350–510 μm (Ailikang Medicine, Hangzhou, China) and combined with a contrast medium, were then injected to reduce any remaining blood flow. In cases of arteriovenous fistula or hemorrhage, arterial embolization was performed utilizing gelatin sponge particles or a Tornado embolization coil (Cook, Bloomington, Indiana). Patients were monitored with an electrocardiograph for 24 hours afterward.

Magnetic resonance imaging protocol

All participants underwent contrast-enhanced MRI using a 1.5 T scanner (Magnetom Aera, Siemens Healthcare, Germany). Liver protocols included T1-weighted imaging in-phase and opposed-phase, T2-weighted imaging, diffusion-weighted imaging with b values of 0, 50, and 500 s/mm^2, and dynamic contrast-enhanced imaging. The MR units automatically calculated the apparent diffusion coefficient. Gadopentetate dimeglumine was administered at 2 mL/s with a 0.1 mmol/kg dose, followed by a saline flush. Images for arterial, portal, and delayed phases were captured at 20–25, 70–90, and 150–180 seconds, respectively.

Viable tumor volume segmentation

The MRI were processed using open-source software (ITK-SNAP, version 3.8.0, www.itksnap.org) for segmentation and quantification by a radiologist with 12 years of experience. The free ITK-SNAP package provides the capabilities of semi-automatic segmentation as well as image navigation. Regions of interest were placed on arterial phase images to measure viable tumor volume (Figure 2), unless no lesion enhancement was detected, indicating inactivity (Figure 3). Another radiologist with 15 years of experience verified all segmented images.

Definition and evaluation of data

The viable tumor necrosis ratio was calculated as follows:

$$\text{Tumor necrosis ratio} = \frac{\text{VOLUME pretherapy} - \text{VOLUME posttherapy}}{\text{VOLUME pretherapy}} \times 100\%$$

Patients underwent contrast-enhanced MR examinations 7 days before and 30 days after the surgery. The volume of the viable tumor was calculated using ITK-SNAP. Patients were then followed up with contrast-enhanced MRI or computed tomography (CT). Routine laboratory tests, including AFP level evaluations, were conducted within 30 days post-treatment and subsequently every 6–8 weeks. Six months after initial treatment, local tumor response was assessed using the modified response evaluation criteria in solid tumors rules, categorizing outcomes as complete response (CR), partial response (PR), stable disease, or progressive disease (PD).[12] The disease control rate (DCR) and objective response rate (ORR) were also evaluated. The approach was evaluated by two radiologists with >10 years of specialization in abdominal imaging. The AFP variation rate was calculated 30 days after treatment as follows:

$$\text{AFP variation rate} = \frac{\text{AFPpretherapy} - \text{AFPposttherapy}}{\text{AFPpretherapy}} \times 100\%$$

Possible complications during treatment include contrast agent extravasation (indicating bleeding) or arteriovenous fistula. The most common short-term complication was postembolization syndrome, including mild to moderate pain, fever, nausea, and vomiting.

Statistical analysis

Statistical analysis was performed using GraphPad Prism 9.0 (GraphPad Software, San Diego, CA, USA) and SPSS Version 24 (IBM Corporation, Armonk, NY, USA). Continuous variables with a normal distribution were presented as mean ± standard deviation and analyzed using either the Student's t-test or the Mann–Whitney U test, based on their distribution. Spearman tests assessed correlations between pre-therapy viable tumor volume and post-therapy necrosis rate, as well as post-therapy viable tumor volume necrosis rate and AFP decline rate. Chi-squared tests were used for categorical variables, with significance set at $P < 0.05$.

Results

The study included 164 patients (median age 57 years, range 26–80 years; 19 women, 145 men), divided into TACE (n = 78) and TACE + MWA (n = 86) groups. The primary HCC lesions had a median size of 8.6 cm (range 5–17 cm), with 62.2% of patients having elevated AFP levels (≥20 ng/mL) and 62.8% having HBV infection. Table 1 shows there were no notable differences in clinical characteristics or laboratory results between the treatment groups.

Table 2 shows there were no significant differences in viable tumor volume between the two groups, both pre- and post-treatment. The MRI 30 days post-treatment indicated a significantly higher tumor necrosis ratio in the TACE + MWA group (87.5%) than in the TACE group (76.1%) (Figure 4).

Before treatment, both groups exhibited comparable elevated AFP levels, with no significant difference ($P = 0.137$). The AFP levels declined in all patients (Table 3), with the TACE + MWA group showing significantly lower levels (46.7 vs. 601.3, $P < 0.001$) than

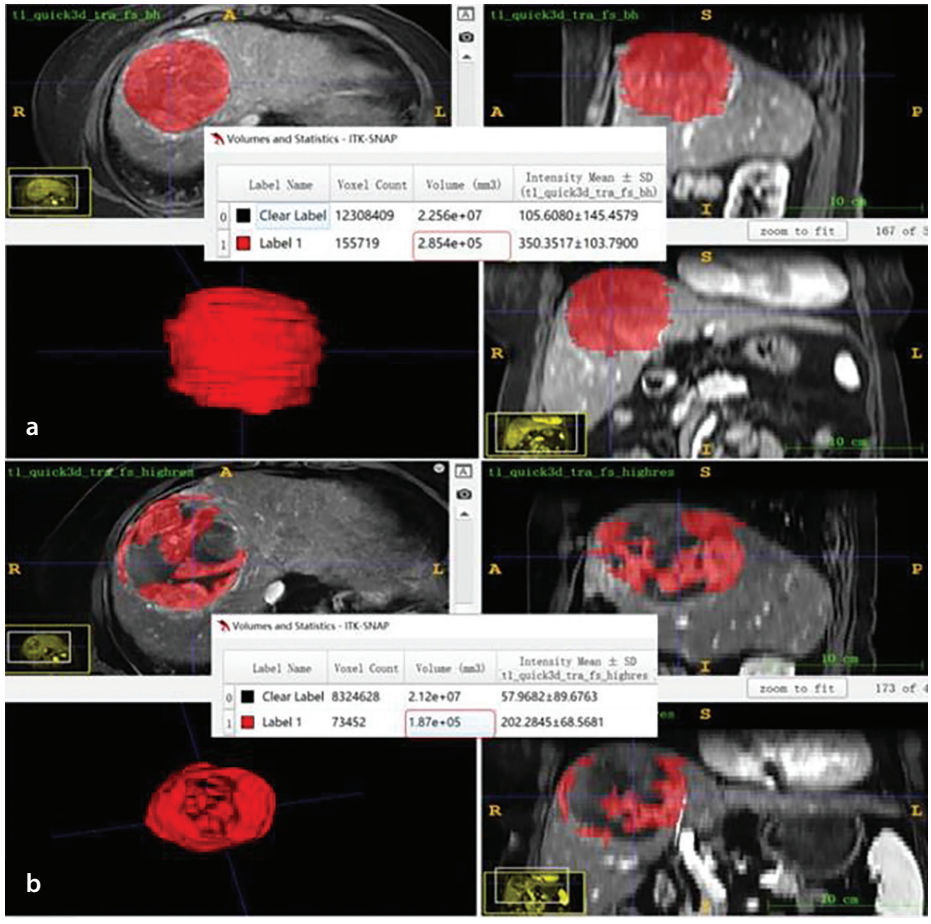

Figure 2. Images of a 76-year-old female patient with hepatocellular carcinoma. Arterial phase contrast-enhanced T1-weighted imaging before transarterial chemoembolization (TACE) revealed a tumor with a volume of 285,400 mm^3 in the right liver lobe **(a)**. Contrast-enhanced T1-weighted imaging in the arterial phase revealed heterogeneous enhancement 30 days after TACE. The volume of tumor enhancement (viable tissue) was 187,000 mm^3 **(b)**.

Table 1. Clinical characteristics of patients (n = 164)

Characteristic	TACE + MWA (n = 86)	TACE (n = 78)	*P* value
Age (y)			
≥60	38 (44.2%)	36 (46.2%)	0.8
<60	48 (55.8%)	42 (53.8%)	
Sex			
Male	78 (90.7%)	67 (85.9%)	0.34
Female	8 (9.3%)	11 (14.1%)	
Tumor diameter (cm)			
5-10	51 (59.3%)	52 (66.7%)	0.33
>10	35 (40.7%)	26 (33.3%)	
Child-Pugh class			
A	67 (77.9%)	61 (78.2%)	0.96
B	19 (22.1%)	17 (21.8%)	
Hepatitis B virus infection			
Yes	52 (60.5%)	51 (65.4%)	0.52
No	34 (39.5%)	27 (34.6%)	
AFP level (ng/mL)			
>20	52 (60.5%)	50 (64.1%)	0.63
≤20	34 (39.5%)	28 (35.9%)	

TACE, transarterial chemoembolization; MWA, microwave ablation; AFP, alpha-fetoprotein.

those in the TACE group after treatment (Figure 5). The AFP variation rate in the TACE + MWA group was significantly higher than that in the TACE group (Figure 6) ($P < 0.001$). Furthermore, a positive correlation was identified between tumor necrosis ratio and AFP variation rate (r = 0.46, $P < 0.001$) (Figure 7).

In the TACE + MWA group, the CR, PR, SD, and PD rates were 2.3%, 68.6%, 11.6%, and 17.4%, respectively, whereas in the TACE group, they were 3.8%, 51.3%, 8.9%, and 35.9%, respectively. Both PR and PD significantly differed between the groups ($P < 0.05$). The TACE + MWA group had a DCR of 82.6% and an ORR of 70.9%, both significantly higher than the TACE group's DCR of 64.1% ($P = 0.007$) and ORR of 55.1% ($P = 0.036$) (Table 4).

The treatment was well-tolerated, with no major complications or procedure-related fatalities. Post-MWA, 3 patients experienced hemorrhage and 2 developed arteriovenous fistulae, all of which were treated with embolization. Post-embolization syndrome was the most frequent short-term complication, treated with medication and supportive care. Alanine aminotransferase (150.3 ± 82.8 U/L) and aspartate aminotransferase (135.2 ± 25.6 U/L) levels were transiently increased on the third day after treatment compared with baseline levels (42.3 ± 7.6 U/L and 67.3 ± 6.3 U/L, respectively). The respective aminotransferase levels decreased to 39.8 ± 9.9 U/L and 60.1 ± 4.7 U/L at 1 month after treatment.

Discussion

This study assessed the effectiveness of combining TACE with MWA versus TACE alone for treating HCC tumors ≥5 cm. The results indicated that the combination treatment led to better short-term outcomes, including greater tumor volume reduction and lower serum AFP levels. The combined therapy showed promise in controlling tumor progression and improving patient outcomes for large HCC tumors.

For patients with BCLC stage A and B tumors ≥5 cm who are ineligible for surgical resection, TACE is generally preferred. However, complete tumor necrosis is difficult to achieve. TACE with drug-eluting beads achieves precise delivery and sustained release of drugs through drug-loaded microspheres, which may reduce systemic toxicity and improve local efficacy. In contrast, conventional TACE relies on iodized oil as a chemotherapy carrier, which is suitable for a wider range of clinical scenarios. Recent studies indicated that combining TACE with ablation was more effective for liver cancer

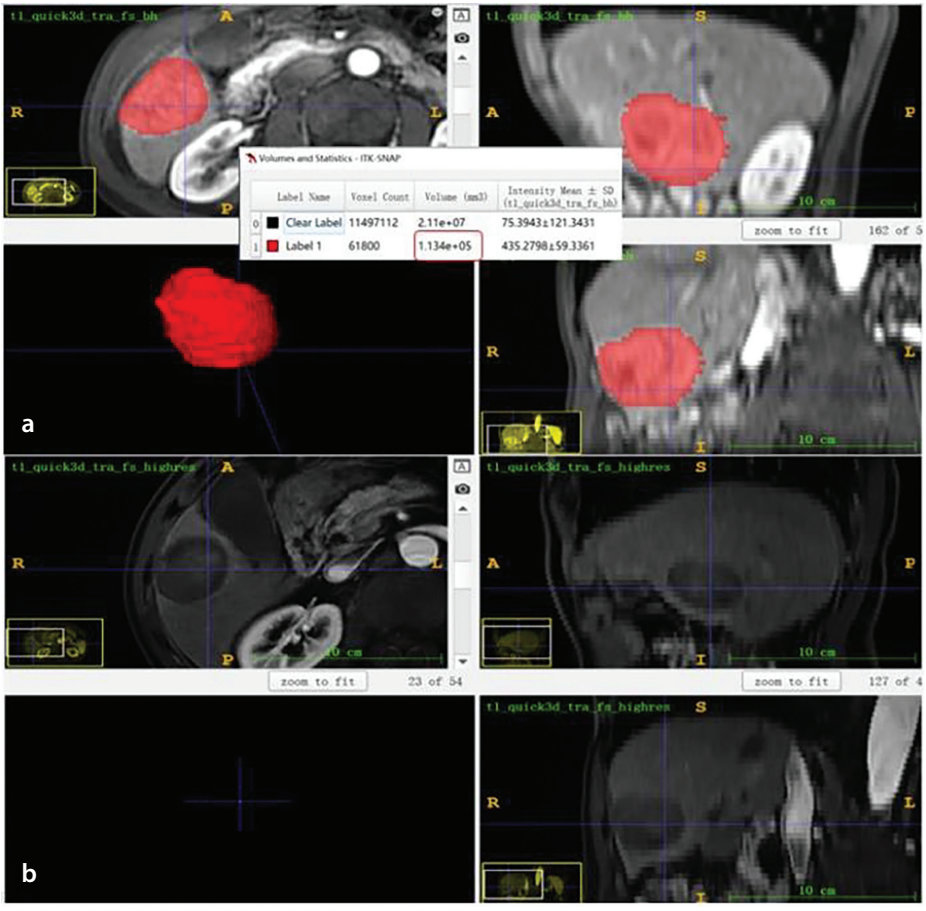

Figure 3. Images of a 62-year-old male patient with hepatocellular carcinoma. An arterial phase contrast-enhanced T1-weighted image revealed a tumor with a volume of 113,400 mm^3 in the right liver lobe before treatment **(a)**. No enhancement was observed in the tumor (complete necrosis) 30 days after transarterial chemoembolization + microwave ablation **(b)**.

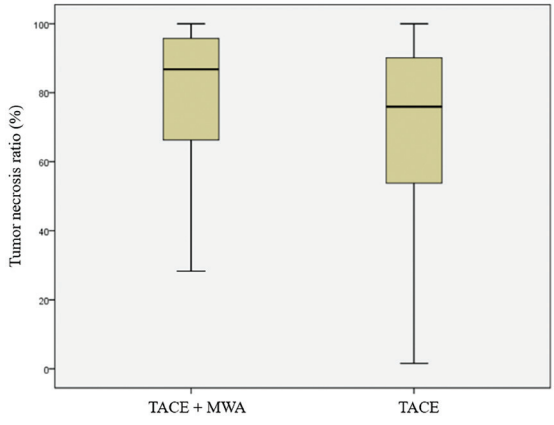

Figure 4. Boxplot of tumor necrosis ratio. TACE, transarterial chemoembolization; MWA, microwave ablation.

treatment than TACE alone.[7,18,19] The meta-analysis evaluated TACE combined with MWA versus TACE alone for BCLC stage A or B patients with HCC tumors ≥5 cm. The findings indicated notable enhancements in CR, PR, and ORR with the combined TACE and MWA treatment.[8] Another study demonstrated that combined therapy significantly improved ORR and DCR compared with TACE alone.[20] These findings are similar to our study. Our prospective study revealed that combined therapy significantly improved PR, ORR, and DCR compared with TACE alone. These findings may be attributed to the direct ablative effect of MWA on the lesion core, whereas TACE demonstrates a more pronounced therapeutic impact on the hypervascularized peripheral regions of the lesion. However, those investigations presented results for combination treatments on tumors exhibiting heterogeneous size ranges, stages, and tumor burden. This study focused mainly on tumors ≥5 cm.

Traditional liver cancer treatment evaluation relied on measuring the target lesion's diameter during arterial phase enhancement.[12] However, this method may not accurately reflect the true condition of the tumor, as it only considers changes in a single dimension and overlooks variations in volume and shape. Recent research suggested that 3D quantitative analysis offered a more comprehensive assessment of tumor response.[21-24] Pandey et al.[21] found that it can more precisely assess the tumor response and patient prognosis after treatment by accurately measuring tumor volume. Fleckenstein et al.[22] found that 3D quantitative analysis can be used to evaluate early responses in patients with liver cancer following local therapy, which is crucial for the timely adjustment of treatment plans. These findings support our study. The TACE + MWA cohort showed a greater necrosis ratio than the TACE cohort ($P < 0.05$), suggesting greater efficacy of the combined treatment. Additionally, another study pointed out that changes in tumor volume enhanced by 3D imaging significantly correlated with overall patient survival.[23,24] However, this aspect was not addressed in our study.

CT can evaluate the morphological and hemodynamic changes of tumors, but it is not as effective as MRI in displaying viable lesions. For patients with renal insufficiency or allergies to CT/MRI contrast agents, contrast-enhanced ultrasound can be used as a useful complementary technique.[25] The ITK-SNAP interactive software package allows manual and semi-automatic 3D medical image segmentation on computers.[26] Compared with traditional methods that require specific workstations, ITK-SNAP is more flexible and suitable for various clinical and research environments. The use of ITK-SNAP is not limited to image "omics" research but is also widely applied in clinical practice for precise tumor volume measurement. In clinical applications, the semi-automatic segmentation function of ITK-SNAP has been proven to reduce the time required for manual segmentation significantly while maintaining high accuracy.[26]

In patients with HCC, AFP levels were often used as a biomarker for diagnosis and prognosis assessment. Studies have shown that the dynamic changes in AFP levels can reflect the effectiveness of treatment and patient outcomes.[16,27,28] Previous studies have

shown that a notable reduction in AFP levels may suggest increased tumor necrosis and improved treatment outcomes.[16,17,28] Guo et al.[20] found that AFP levels significantly decreased in both groups after treatment, with the test group showing a greater reduction than the control group. This is in agreement with our results. Additionally, there was a significant positive correlation between the necrosis ratio and AFP variation rate after treatment in the present study, indicating that treatment has led to the death of tumor cells, thereby reducing AFP production. In addition, the decline in AFP levels can help identify patients who respond well to treatment, guiding subsequent treatment decisions.[28]

To date, numerous investigations have explored the application of transcutaneous thermal ablation in conjunction with TACE for the management of HCC. Nevertheless, the majority of existing reports on combination therapy described sequential treatment regimens with diverse temporal intervals (from 1–42 days).[6,29-31] Recent studies have validated the safety and efficacy of TACE combined with thermal ablation, showing no significant impairment of liver function.[9-11,17] In this prospective study, MWA combined with simultaneous TACE was a safe treatment for HCC tumors ≥5 cm without increasing the risk of major complications. These findings were consistent with previous studies.[11] Immediate TACE after MWA was considered to increase tumor necrosis by exposing sublethal heat-damaged tumor tissues to high drug concentration, potentially reducing the dosage of iodinated oil and chemotherapy drugs in subsequent TACE. Severe complications related to MWA, including arteriovenous fistula and hemorrhage, can be promptly identified and treated.[9,11] In addition, immediate TACE after MWA can reduce hospitalizations and costs. Hence, this method has a high potential for popularization in clinical applications. In studies on performing TACE prior to MWA, the accuracy of needle punctures into lesions is improved, and the "thermal settling effect" during the ablation process is reduced. Previous studies have not compared the two operation sequences, nor have they indicated a clear optimal sequence.

Our study had several limitations. First, some HCC tumors were diagnosed using clinical criteria, including contrast-enhanced MRI findings and AFP level, rather than histopathological confirmation. Second, this investigation assessed the effectiveness of the treatment over a short period and did not include an analysis of long-term efficacy, which is inadequate to establish conclusively

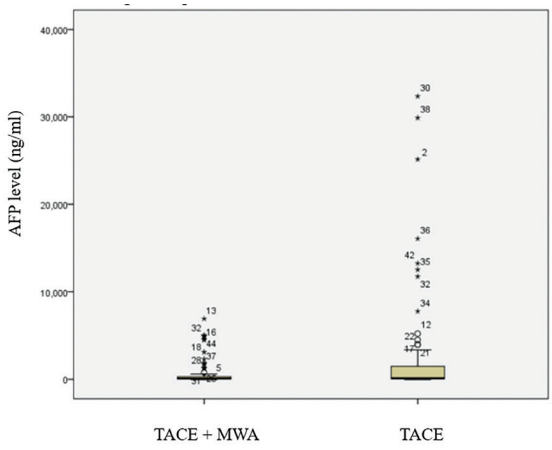

Figure 5. Boxplot of alpha-fetoprotein level after treatment. TACE, transarterial chemoembolization; MWA, microwave ablation; AFP, alpha-fetoprotein.

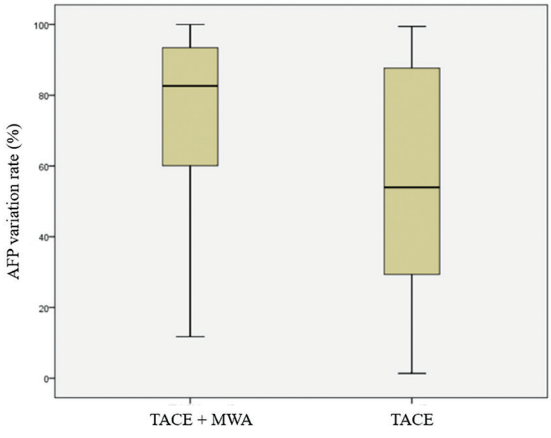

Figure 6. Boxplot of alpha-fetoprotein variation rate. TACE, transarterial chemoembolization; MWA, microwave ablation; AFP, alpha-fetoprotein.

Table 2. Measurements of viable tumor before and after treatment (n = 164)

Characteristic	TACE + MWA (n = 86)	TACE (n = 78)	*P* value
Pretherapy viable tumor volume	275,700 mm^3	250,000 mm^3	0.683
Posttherapy viable tumor volume	32,245 mm^3	54,995 mm^3	0.085
Tumor necrosis ratio	87.5%	76.1%	0.002*

*Data are statistically significant results. TACE, transarterial chemoembolization; MWA, microwave ablation.

Table 3. Alpha-fetoprotein level before and after treatment (n = 102)

	TACE + MWA (n = 52)	TACE (n = 50)	*P* value
AFP level before treatment (ng/mL)	978.7	2,178.5	0.137
AFP level after treatment (ng/mL)	46.7	601.3	0.001*
AFP variation rate	79.5%	47.5%	<0.001*

*Data are statistically significant results. TACE, transarterial chemoembolization; MWA, microwave ablation; AFP, alpha-fetoprotein.

Table 4. Assessment of target lesion response according to the modified response evaluation criteria in solid tumors rules (n = 164)

	TACE + MWA (n = 86)	TACE (n = 78)	*P* value
CR	2 (2.3%)	3 (3.8%)	0.572
PR	59 (68.6%)	40 (51.3%)	0.024*
SD	10 (11.6%)	7 (8.9%)	0.578
PD	15 (17.4%)	28 (35.9%)	0.007*
ORR	61 (70.9%)	43 (55.1%)	0.036*
DCR	71 (82.6%)	50 (64.1%)	0.007*

*Data are statistically significant results. CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate; DCR, disease control rate; TACE, transarterial chemoembolization; MWA, microwave ablation.

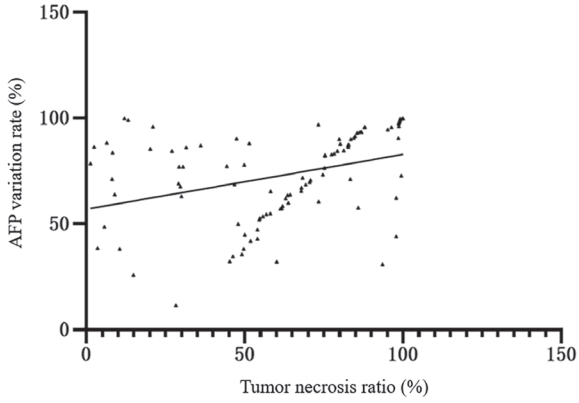

Figure 7. Scatter plot of the correlation between the tumor necrosis ratio and the alpha-fetoprotein variation rate. AFP, alpha-fetoprotein.

the superiority of combination therapy. Finally, as a single-center study, it was limited by a small sample size and a unique patient setting. Therefore, larger sample sizes in multicenter studies are necessary to further validate the treatment protocol's efficacy and safety.

In conclusion, TACE combined with MWA was more effective for treating HCC tumors ≥5 cm than TACE alone, as it significantly reduced AFP levels and enhanced tumor necrosis. This suggested that the combined therapy could be a viable treatment option for larger HCC tumors. However, larger multicenter studies are needed to confirm these benefits.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229-263. [Crossref]
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin*. 2015;65(1):5-29. [Crossref]
3. Raoul JL, Forner A, Bolondi L, Cheung TT, Kloeckner R, de Baere T. Updated use of TACE for hepatocellular carcinoma treatment: how and when to use it based on clinical evidence. *Cancer Treat Rev*. 2019;72:28-36. [Crossref]
4. Lencioni R, de Baere T, Soulen MC, Rilling WS, Geschwind JF. Lipiodol transarterial chemoembolization for hepatocellular carcinoma: a systematic review of efficacy and safety data. *Hepatology*. 2016;64(1):106-116. [Crossref]
5. Hiraoka A, Kumada T, Kudo M, et al. Hepatic function during repeated TACE procedures and prognosis after introducing sorafenib in patients with unresectable hepatocellular carcinoma: multicenter analysis. *Dig Dis*. 2017;35(6):602-610. [Crossref]
6. Li HZ, Tan J, Tang T, An TZ, Li JX, Xiao YD. Chemoembolization plus microwave ablation vs chemoembolization alone in unresectable hepatocellular carcinoma beyond the milan criteria: a propensity scoring matching study. *J Hepatocell Carcinoma*. 2021;8:1311-1322. [Crossref]
7. Özen Ö, Boyvat F, Zeydanlı T, Kesim Ç, Karakaya E, Haberal M. Transarterial chemoembolization combined with simultaneous thermal ablation for solitary hepatocellular carcinomas in regions with a high risk of recurrence. *Exp Clin Transplant*. 2023;21(6):512-519. [Crossref]
8. Liu C, Li T, He JT, Shao H. TACE combined with microwave ablation therapy vs. TACE alone for treatment of early- and intermediate-stage hepatocellular carcinomas larger than 5 cm: a meta-analysis. *Diagn Interv Radiol*. 2020;26(6):575-583. [Crossref]
9. Floridi C, Cacioppa LM, Rossini N, et al. Microwave ablation followed by cTACE in 5-cm HCC lesions: does a single-session approach affect liver function? *Radiol Med*. 2024;129(8):1252-1264. [Crossref]
10. Wu M, Gao S, Song H, et al. Percutaneous thermal ablation combined with simultaneous transarterial chemoembolization for hepatocellular carcinoma ≤5 cm. *J Cancer Res Ther*. 2019;15(4):766-772. [Crossref]
11. Si ZM, Wang GZ, Qian S, et al. Combination therapies in the management of large (≥ 5 cm) hepatocellular carcinoma: microwave ablation immediately followed by transarterial chemoembolization. *J Vasc Interv Radiol*. 2016;27(10):1577-1583. [Crossref]
12. Lencioni R, Llovet JM. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. *Semin Liver Dis*. 2010;30(1):52-60. [Crossref]
13. Bonekamp S, Li Z, Geschwind JF, et al. Unresectable hepatocellular carcinoma: MR imaging after intraarterial therapy. Part I. Identification and validation of volumetric functional response criteria. *Radiology*. 2013;268(2):420-430. [Crossref]
14. Chapiro J, Wood LD, Lin M, et al. Radiologic-pathologic analysis of contrast-enhanced and diffusion-weighted MR imaging in patients with HCC after TACE: diagnostic accuracy of 3D quantitative image analysis. Radiology. 2014;273(3):746-758. [Crossref]
15. Tacher V, Lin M, Duran R, et al. Comparison of existing response criteria in patients with hepatocellular carcinoma treated with transarterial chemoembolization using a 3D quantitative approach. *Radiology*. 2016;278(1):275-284. [Crossref]
16. Masior Ł, Krasnodębski M, Kuncewicz M, et al. Alpha-fetoprotein response after first transarterial chemoembolization (TACE) and complete pathologic response in patients with hepatocellular cancer. *Cancers (Basel)*. 2023;15(15):3962. [Crossref]
17. Zaitoun MMA, Elsayed SB, Zaitoun NA, et al. Combined therapy with conventional transarterial chemoembolization (cTACE) and microwave ablation (MWA) for hepatocellular carcinoma >3-<5 cm. *Int J Hyperthermia*. 2021;38(1):248-256. [Crossref]
18. Yan L, Ren Y, Qian K, et al. Sequential transarterial chemoembolization and early radiofrequency ablation improves clinical outcomes for early-intermediate hepatocellular carcinoma in a 10-year single-

center comparative study. *BMC Gastroenterol*. 2021;21(1):182. [Crossref]

19. Zhu ZY, Yuan M, Yang PP, et al. Single medium-sized hepatocellular carcinoma treated with sequential conventional transarterial chemoembolization (cTACE) and microwave ablation at 4 weeks versus cTACE alone: a propensity score. *World J Surg Oncol*. 2022;20(1):192. [Crossref]
20. Guo JY, Zhao LL, Cai HJ, Zeng H, Mei WD. Radiofrequency ablation combined with transcatheter arterial chemoembolization for recurrent liver cancer. *World J Gastrointest Surg*. 2024;16(6):1756-1764. [Crossref]
21. Pandey A, Pandey P, Aliyari Ghasabeh M, et al. Unresectable intrahepatic cholangiocarcinoma: multiparametric MR imaging to predict patient survival. *Radiology*. 2018;288(1):109-117. [Crossref]
22. Fleckenstein FN, Schernthaner RE, Duran R, et al. Renal cell carcinoma metastatic to the liver: early response assessment after intraarterial therapy using 3D quantitative tumor enhancement analysis. *Transl Oncol*. 2016;9(5):377-383. [Crossref]
23. Hajkova M, Andrasina T, Ovesna P, et al. Volumetric analysis of hepatocellular carcinoma after transarterial chemoembolization and its impact on overall survival. *In Vivo*. 2022;36(5):2332-2341. [Crossref]
24. Onur İD, Akdur PÖ, Çamöz ES, Çiledağ N, Yıldız F. Evaluation of the prognostic effectiveness of liver metastasis volume by volumetric measurement in colorectal cancer. *Future Oncol*. 2024;20(38):3133-3140. [Crossref]
25. Moschouris H, Malagari K, Papadaki MG, et al. mRECIST criteria and contrast-enhanced US for the assessment of the response of hepatocellular carcinoma to transarterial chemoembolization. *Diagn Interv Radiol*. 2014;20(2):136-142. [Crossref]
26. Yushkevich PA, Pashchinskiy A, Oguz I, et al. User-guided segmentation of multi-modality medical imaging datasets with ITK-SNAP. *Neuroinformatics*. 2019;17(1):83-102. [Crossref]
27. Paul SB, Sahu P, Sreenivas V, et al. Prognostic role of serial alpha-fetoprotein levels in hepatocellular carcinoma treated with locoregional therapy. *Scand J Gastroenterol*. 2019;54(9):1132-1137. [Crossref]
28. Chen IH, Hsu CC, Yong CC, et al. AFP response to locoregional therapy can stratify the risk of tumor recurrence in HCC patients after living donor liver transplantation. *Cancers (Basel)*. 2023;15(5):1551. [Crossref]
29. Zhang TQ, Huang ZM, Shen JX, et al. Safety and effectiveness of multi-antenna microwave ablation-oriented combined therapy for large hepatocellular carcinoma. *Therap Adv Gastroenterol*. 2019;12:1756284819862966. [Crossref]
30. Smolock AR, Cristescu MM, Hinshaw A, et al. Combination transarterial chemoembolization and microwave ablation improves local tumor control for 3- to 5-cm hepatocellular carcinoma when compared with transarterial chemoembolization alone. *Abdom Radiol (NY)*. 2018;43(9):2497-2504. [Crossref]
31. Zhu ZY, Qian Z, Qin ZQ, et al. Effectiveness and safety of sequential transarterial chemoembolization and microwave ablation for subphrenic hepatocellular carcinoma: a comprehensive evaluation. *World J Gastrointest Oncol*. 2024;16(7):2941-2951. [Crossref]