Research Square

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Percutaneous ablation for hepatocellular carcinoma: comparison between cryoablation and microwave ablation

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Abstract

Background

Microwave ablation (MWA) and cryoablation (CA) are both widely applied minimally invasive therapies for hepatocellular carcinoma (HCC). However, direct comparisons of their therapeutic efficacy and safety in HCC remain limited. This investigation compared the clinical effectiveness and safety profiles of CA and MWA in patients with HCC.

Methods

This retrospective analysis consecutively enrolled individuals with HCC treated with either CA or MWA between June 2020 and December 2024. Baseline characteristics, primary complete ablation rates, intraoperative pain scores, complication rates, and long-term outcomes were systematically compared between the two cohorts.

Results

The study included 82 patients, of whom 42 underwent CA and 40 received MWA. The groups were comparable in terms of baseline clinical and tumor characteristics. The primary complete ablation rates were 95.2% and 90.0% in the CA and MWA groups, respectively (P = 0.43). CA-treated patients experienced significantly less intraoperative pain than MWA-treated patients (P < 0.001). The rates of major complications (4.8% vs. 2.5%, P = 1.00) and minor complications (14.3% vs. 17.5%, P = 0.69) were comparable between the CA and MWA groups. Median progression-free survival (PFS) was 13 months in the CA group and 17 months in the MWA group (P = 0.53), while corresponding median overall survival (OS) rates were 32 months and 36 months, respectively (P = 0.92).

Conclusions

CA and MWA demonstrate similar therapeutic efficacy and safety for the treatment of HCC. However, CA is associated with significantly lower intraoperative pain compared with MWA.

Introduction

Hepatocellular carcinoma (HCC) represents over 90% of primary liver cancers worldwide [1]. Owing to the widespread use of surveillance imaging and advances in diagnostic techniques, a growing number of patients are now diagnosed at an early stage [2]. While surgical resection is the treatment of choice for less advanced HCC [3], many patients are not suitable candidates for surgery because of impaired liver function, comorbid conditions, or personal preference, making percutaneous image-guided ablation a critical alternative therapeutic option [4–6].

Currently, the most commonly employed ablation techniques for HCC are microwave ablation (MWA), radiofrequency ablation (RFA), and cryoablation (CA) [1, 7]. Both RFA and MWA are based on thermal energy. Compared with RFA, MWA offers several technical advantages, including shorter procedure times, higher intratumoral temperature, and more extensive ablation [8]. In a study by Sugimoto et al. [8], the 2-year local tumor progression rate was significantly lower in MWA-treated patients than in RFA-treated patients (16.4% vs. 30.4%, P = 0.007). In contrast, CA destroys tumor tissue through cycles of freezing and thawing [9]. A major advantage of CA is the real time visualization of the formation of the ice ball, allowing precise monitoring of the ablation zone and accurate adjustment of treatment margins. Despite these theoretical advantages, there remains a paucity of studies that have directly compared the effectiveness and safety of CA and MWA for HCC.

The objective of this study was a comparison of the clinical effectiveness and safety of CA and MWA in individuals with HCC.

Methods

Study description

This retrospective analysis received approval from the Ethics Committee of Xuzhou Cancer Hospital. Requirement for written informed consent was waived because this study was retrospective.

Individuals with HCC who underwent CA or MWA at our institutions from June 2020 to December 2024 were consecutively recruited. The inclusion criteria were: (a) Barcelona Clinic Liver Cancer (BCLC) stage ≤ A; (b) inability or refusal to undergo surgical resection; and (c) Child-Pugh class A or B. Exclusion criteria were: (a) aged < 18 years or > 80 years; (b) more than two tumors; (c) tumor diameter > 5 cm; (d) presence of another malignant tumor; or (e) prior receipt of anticancer therapy. American Association for the Study of Liver Diseases guidelines were used when diagnosing HCC [10].

Before treatment, we introduced the details of the advantages and disadvantages of the CA and MWA to each patients. Patients chose one of the 2 methods after discussing with their family members.

Baseline characteristics, complete ablation rates, intraoperative pain scores, complication profiles, and long-term outcomes were collected and compared between the two treatment groups.

Percutaneous ablation

All patients underwent transarterial chemoembolization (TACE) one week prior to ablation. CA and MWA were performed under computed tomography (CT) guidance with local anesthesia.

CA was carried out using an argon-helium CA system (CryoHit, Galil Medical, Israel). Cryoprobe number and positioning determinations were made according to the size and location of the target tumors. Each lesion was subjected to two freeze-thaw cycles consisting of 10 minutes of freezing followed by 3 minutes of thawing. Rapid expansion of argon gas within the probe generated temperatures as low as −

140°C within seconds, while helium gas was subsequently used to facilitate thawing. After completion of the procedure, CT scans were obtained to assess immediate tumor necrosis.

MWA was conducted using a KY-2450B microwave ablation system (Kangyou, Nanjing, China). Antennas were positioned in a manner analogous to cryoprobe placement in CA. Ablation was delivered at a power of 60–70 W for 4–8 minutes. Post-procedural CT imaging was conducted to confirm immediate ablation of the targeted lesions.

Definitions and assessments

Complete ablation was evaluated via contrast-enhanced CT and/or MRI one week after treatment and was determined by a lack of enhancement within the tumor and surrounding liver tissue. Intraoperative pain was assessed using a visual analog scale with scores between 0 and 10 [11]. The Clavien-Dindo system [12] was used for grading of complications, with grade III or higher events considered major complications. Progression-free survival (PFS) represented the time between treatment initiation and disease progression, death, or last follow-up, and overall survival (OS) was assessed as the interval between first treatment to death or last follow-up. Follow-up evaluations were undertaken at one and three months after treatment and every three months thereafter until December 2025, including physical examination, laboratory tests (liver and kidney indicators, electrolytes, and alpha-fetoprotein), and imaging.

Statistical analyses

SPSS 16.0 was used to analyze data. Continuous variables with normal distributions are presented as mean ± standard deviation and were compared using t-tests, while skewed variables are shown as median (interquartile range) and were analyzed via Mann-Whitney U tests. Categorical data were analyzed with χ^2 tests. Survival was assessed using Kaplan-Meier curves and log-rank tests, and multivariable Cox proportional hazards models were used to identify factors associated with PFS and OS. A two-sided $P < 0.05$ was considered significant.

Results

Patients

The patient enrollment process is summarized in Fig. 1. Eighty-two individuals with HCC were enrolled, of whom 42 underwent CA and 40 underwent MWA. As shown in Table 1, baseline demographic, clinical, and tumor characteristics were comparable in both groups between the two groups, indicating good comparability.

Table 1
Patients' baseline data.

Age (y)	**CA group (n = 42)**	**MWA group (n = 40)**	**P value**
	64.3 ± 6.7	**61.8 ± 7.9**	**0.12**
Gender			0.22
Male	36	30	
Female	6	10	
Types of hepatitis			0.22
None	4	9	
B	36	28	
C	2	3	
Child-Pugh grade			0.87
A	33	32	
B	9	8	
BCLC stage			0.53
0	13	15	
A	29	25	
Largest tumor size (cm)	2.3 ± 0.6	2.4 ± 0.8	0.56
Tumors' number			0.70
1	34	31	
2	8	9	
AFP value			0.69
< 20 ng/ml	28	25	
≥ 20 ng/ml	14	15	
ALBI grade			0.44
1	18	14	
2	23	26	
3	1	0	

AFP: alpha-fetoprotein; ALBI: Albumin-Bilirubin; BCLC: Barcelona Clinic Liver Cancer; CA: cyroablation; MWA: microwave ablation.

Ablation procedures

Primary complete tumor ablation was achieved in 95.2% and 90.0% of individuals in the CA and MWA groups, respectively; the difference was non-significant (P = 0.43, Table 2). Patients who failed to achieve complete ablation after the initial procedure received repeat CA or MWA, and secondary complete ablation was ultimately obtained in all cases. Intraoperative pain, as assessed by visual analog scale scores, was substantially lower in the CA group relative to the MWA group (P < 0.001, Table 2).

Table 2
Treatment effectiveness.

Initial complete ablation	**CA group (n = 42)**	**MWA group (n = 40)**	**P value**
	40 (95.2%)	**36 (90.0%)**	**0.43**
Secondary complete ablation	42 (100.0%)	40 (100.0%)	Not applicable
Intraoperative pain score	1.6 (1.0)	3.2 (0.9)	< 0.001
Local recurrence	11 (26.2%)	10 (25.0%)	0.90
Distant recurrence	21 (50.0%)	22 (55.0%)	0.65
PFS (months)	13 (10–17)	17 (12–21)	0.53
OS (months)	32 (29–34)	36 (33–39)	0.92
CA: cyroablation; MWA: microwave ablation; OS: overall survival; PFS: progression-free survival.			

Complication

The incidence of major complications was similar between the two groups (4.8% for CA vs. 2.5% for MWA, P = 1.00). In the CA group, major adverse events included one case of symptomatic pleural effusion and one case of pneumothorax, whereas the MWA group had one case of intrahepatic abscess.

Minor complications were observed in six individuals (14.3%) who underwent CA and in seven individuals (17.5%) who were treated with MWA (P = 0.69). In the CA group, minor events consisted of fever in four patients and asymptomatic pleural effusion in two patients. In the MWA group, fever occurred in six patients and asymptomatic pleural effusion in one patient.

Survival

Over a median 20-month follow-up (Q1-Q3: 16.8–20.3 months), local tumor recurrence occurred in 11 individuals (26.2%) following CA and in 10 (25.0%) following MWA (P = 0.90). Distant recurrence was documented in 21 patients (50.0%) treated with CA and 22 patients (55.0%) treated with MWA (P = 0.65). The median PFS values were 13 and 17 months in the CA and MWA groups, respectively, with no significant difference (P = 0.53, Fig. 2a). The 1- and 3-year PFS rates were 45.2% and 7.6% in the CA group and 44.7% and 18.6% in the MWA group, respectively. Multivariable Cox regression analysis

demonstrated that younger age (P < 0.001) and a worse albumin-bilirubin (ALBI) grade (P = 0.01) were independently associated with shorter PFS (Table 3).

Table 3
Cox-regression analysis of progression-free survival.

Variables	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
Age (y)	0.936	0.901–0.92	0.001	0.926	0.892–0.962	< 0.001
Gender						
Male	1					
Female	0.672	0.388–1.164	0.16			
Hepatitis						
None	1					
B	0.764	0.434–1.344	0.35			
C	0.610	0.178–2.091	0.43			
Child-Pugh grade						
A	1					
B	1.437	0.786–2.626	0.24			
BCLC stage						
0	1					
A	0.874	0.558–1.370	0.56			
AFP value	0.999	0.997–1.000	0.17			
ALBI grade	1.603	0.966–2.660	0.07	1.973	1.222–3.188	0.01
Largest tumor size	1.126	0.804–1.578	0.49			
Tumors number						
1	1					
2	1.010	0.639–1.597	0.97			
Treatment methods						
CA	1					

AFP: alpha-fetoprotein; ALBI: Albumin-Bilirubin; BCLC: Barcelona Clinic Liver Cancer; CA: cyroablation; MWA: microwave ablation.

Variables	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
MWA	0.859	0.521–1.415	0.55			

AFP: alpha-fetoprotein; ALBI: Albumin-Bilirubin; BCLC: Barcelona Clinic Liver Cancer; CA: cyroablation; MWA: microwave ablation.

During follow-up, five patients in each group died. The median OS values were 32 and 36 months in the CA and MWA groups, respectively (P = 0.92, Fig. 2b). The corresponding 1- and 3-year OS values were 97.6% and 73.0% for CA and 97.2% and 80.0% for MWA. No variables were found to be significantly predictive of OS in Cox regression analysis.

Subgroup analyses for survival

The subgroup analyses were conducted according to the BCLC stages. Thirteen and 15 patients with BCLC stage 0 in CA and MWA groups, respectively. The median PFS values were 15 and 13 months in the CA and MWA groups, respectively (P = 0.49, Fig. 3a). The median OS values were 28 and 35 months in the CA and MWA groups, respectively (P = 0.43, Fig. 3b).

Twenty-nine and 25 patients with BCLC stage A in CA and MWA groups, respectively. The median PFS values were 12 and 19 months in the CA and MWA groups, respectively (P = 0.22, Fig. 4a). The median OS values were 33 and 36 months in the CA and MWA groups, respectively (P = 0.59, Fig. 4b).

Discussion

HCC is still a major cause of cancer-related mortality worldwide. Timely detection and accurate diagnosis are essential for optimizing patient outcomes [2]. Although surgical resection is preferred for treating early-stage HCC, many patients are ineligible because of comorbid conditions, portal hypertension, compromised hepatic function, or insufficient liver reserve [13]. In these settings, percutaneous ablation has become an important alternative therapeutic strategy [2].

Previous studies have shown that, although surgical resection may provide superior overall and disease-free survival compared with RFA in early-stage disease, RFA and resection yield comparable long-term survival in patients with BCLC stage 0 tumors and in those with solitary lesions smaller than 3 cm [2]. Similarly, Zhu et al. [14] reported comparable PFS and OS between MWA and surgical resection in patients with early HCC and moderate to severe cirrhosis, while Min et al. [15] found no differences in disease-free survival or OS between CA and surgery in early-stage HCC. Despite these data, direct comparisons between different ablation techniques for HCC remain limited.

The present study specifically evaluated the relative safety and effectiveness of CA versus MWA. From a technical standpoint, CA offers the advantage of real-time visualization of ice-ball formation, which

allows precise monitoring of the ablation zone and dynamic adjustment of margins, potentially leading to more accurate tumor destruction than heat-based techniques such as RFA or MWA [7]. Nevertheless, in our cohort, the primary complete ablation rates did not differ significantly between CA and MWA, possibly due in part to the limited sample size.

Notably, patients undergoing CA experienced significantly less intraoperative pain than those treated with MWA. This finding is consistent with prior observations suggesting that cold-induced tissue injury is better tolerated than heat-related injury, representing a potential clinical advantage of CA [16]. Importantly, both techniques demonstrated favorable safety profiles, with low and comparable rates of major and minor complications, supporting the overall safety of both modalities.

In addition, no differences were noted between CA and MWA in terms of PFS, OS, or rates of local and distant recurrence, indicating similar oncologic effectiveness. However, the relatively high rates of distant recurrence in both groups (50.0% and 55.0%, respectively) highlight a key limitation of local ablative therapies, which cannot eradicate microscopic or disseminated disease outside the treated area.

The Cox-regression analysis demonstrated that younger age and a worse ALBI grade were independently associated with shorter PFS in this study. Younger age was found to be a predictor for worse HCC pathological grade [17], which may be associated with PFS. The worse ALBI grade also indicated the worse liver function.

However, the BCLC grade was not associated with PFS and OS in this study. Both BCLC grade 0 and A HCCs can be considered as early-stage HCCs [6], therefore, no significant difference in survival time between these 2 stages may be reasonable. The subgroup analyses also indicated that PFS and OS were comparable in both subgroups of BCLC grade 0 and A. These findings may indicate that the treatment effectiveness of CA and MWA was not influenced by different tumor stages.

Several limitations warrant acknowledgment. First, the retrospective design introduces the potential for selection bias, emphasizing the importance of prospective randomized trials. Second, the study involved two institutions, and differences in operator experience may have influenced outcomes. Third, the modest sample size restricts the generalizability of the results, and additional multicenter studies with larger samples are warranted to confirm the findings.

Conclusion

To summarize, despite the need for additional prospective studies, our findings suggest that CA and MWA provide comparable clinical efficacy and safety in the treatment of HCC. However, CA appears to be associated with significantly lower intraoperative pain compared with MWA, which may offer an important advantage in patient comfort during the procedure.

Abbreviations

AFP: alpha-fetoprotein;

ALBI: Albumin-Bilirubin;

BCLC: Barcelona Clinic Liver Cancer;

CA: cryoablation;

CT: computed tomography;

HCC: hepatocellular carcinoma;

MWA: microwave ablation;

OS: overall survival;

PFS: progression-free survival;

RFA: radiofrequency ablation.

Declarations

Ethics approval and consent to participate: This study was approved by Ethics Committee of Xuzhou Cancer Hospital. All methods were carried out in accordance with the 1964 **Declaration of Helsinki.** Requirement for written informed consent was waived because this study was retrospective.

Clinical trial number: Not applicable.

Consent for publication: Not applicable.

Availability of data and materials: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests: None.

Funding: None.

Authors' contributions: FG designed this work. SL, YBW, and YYW collected the clinical data. HH and TTA performed the statistical analyses. SL wrote this article. Final manuscript was approved by all authors.

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Figures

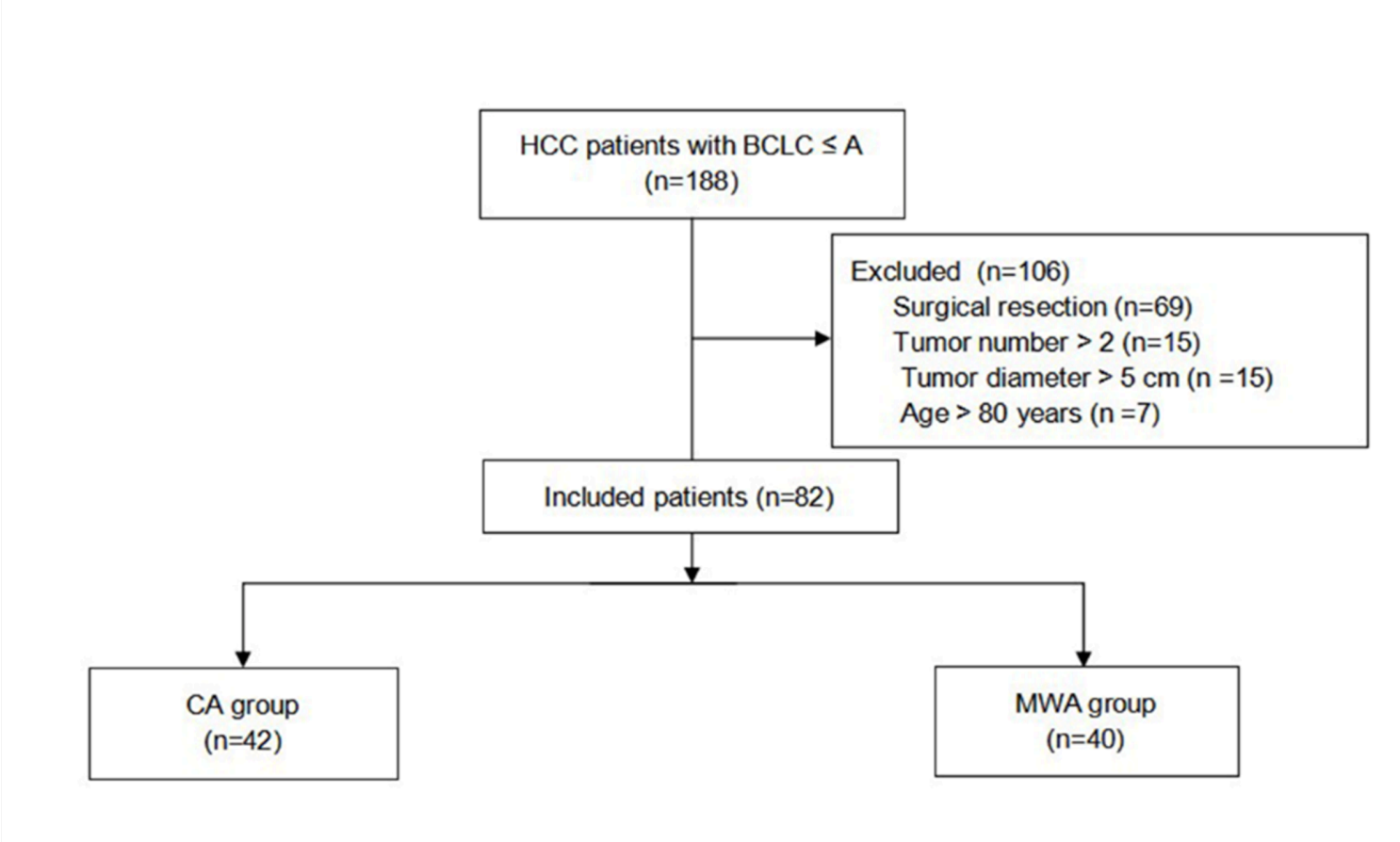
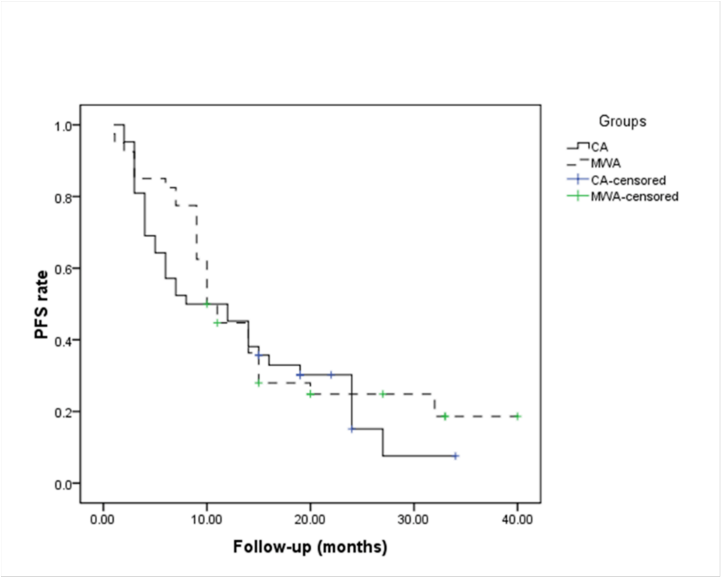
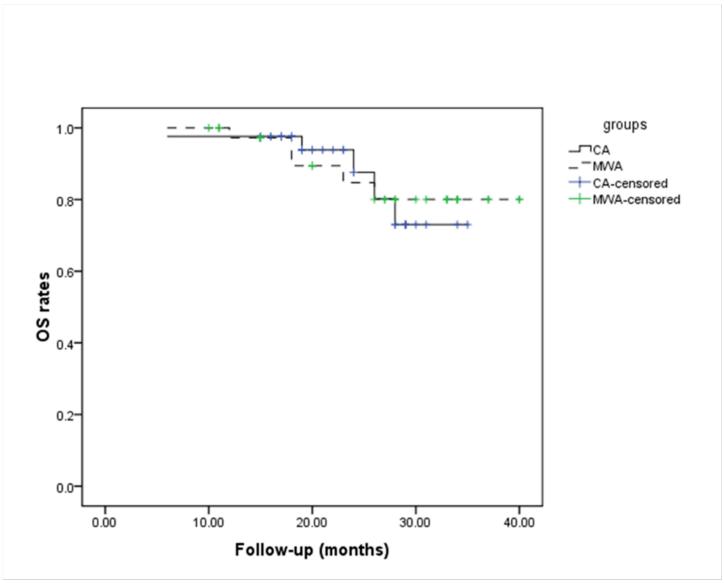


Figure 1

The flowchart of this study.



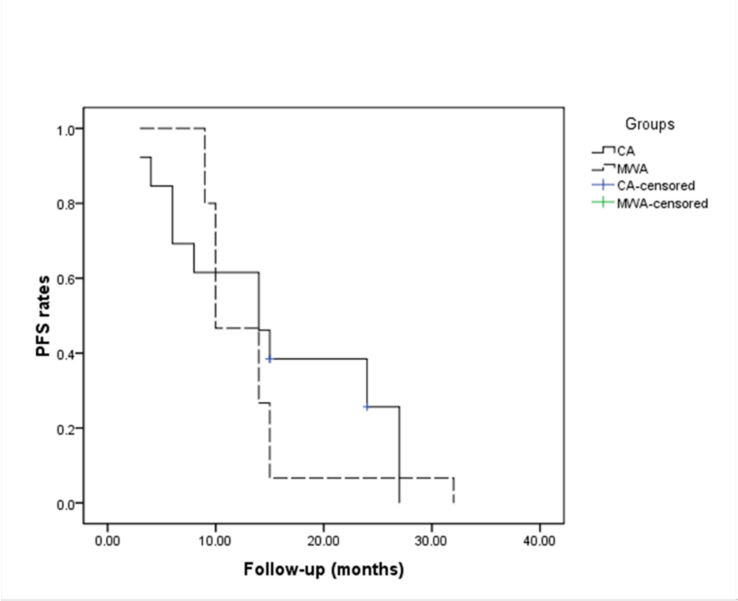
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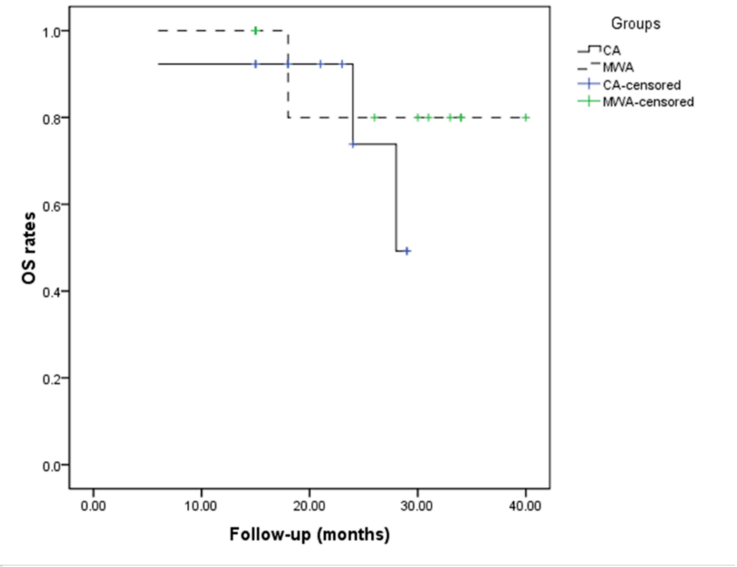
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Figure 2

The comparison of (a) PFS (P = 0.53) and (b) OS (P = 0.92) between CA and MWA groups.



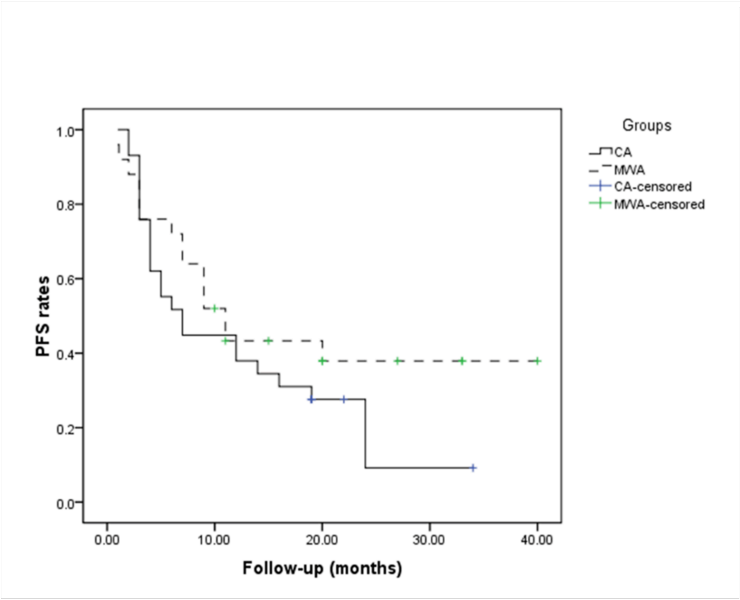
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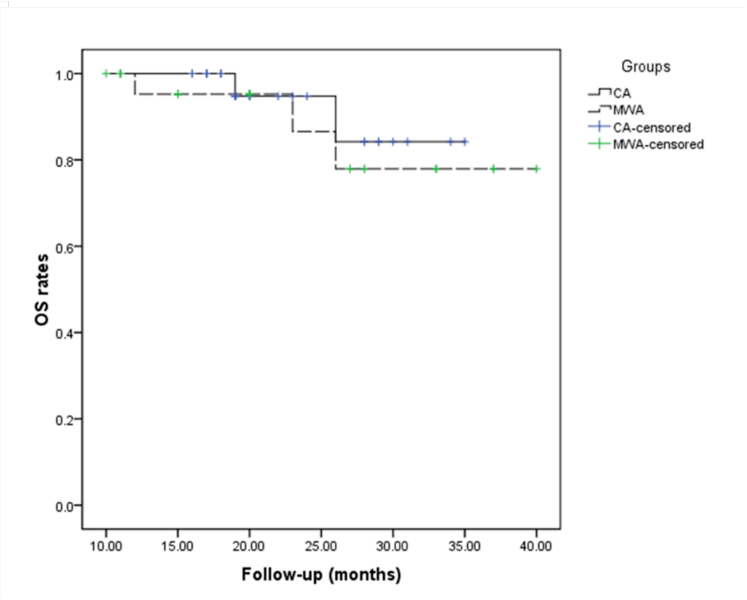
3b

Figure 3

The comparison of (a) PFS (P = 0.49) and (b) OS (P = 0.43) between CA and MWA groups based on the BCLC stage 0 patients.



4a



4b

Figure 4

The comparison of (a) PFS (P = 0.22) and (b) OS (P = 0.59) between CA and MWA groups based on the BCLC stage A patients.