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Comparison of Combination Therapies in the Management of Hepatocellular Carcinoma: Transarterial Chemoembolization with Radiofrequency Ablation versus Microwave Ablation

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Abstract

Purpose—To compare retrospectively the outcomes and complications of transcatheter arterial chemoembolization with drug-eluting embolic agents combined with radiofrequency (RF) ablation or microwave (MW) ablation in treatment of hepatocellular carcinoma (HCC).

Materials and Methods—From 2003–2011, 89 patients with HCC received a combination therapy—transcatheter arterial chemoembolization plus RF ablation in 38 patients and transcatheter arterial chemoembolization plus MW ablation in 51 patients. Local tumor response, tumor progression-free survival (PFS), overall PFS, overall survival (OS), and complications were compared. Overall PFS and OS were compared between the two treatment groups in multivariate analysis controlling for Child-Pugh class, Barcelona Clinic Liver Classification stage, and index tumor size.

Results—Complete local tumor response was achieved in 37 (80.4%) of the tumors treated with transcatheter arterial chemoembolization plus RF ablation and 49 (76.6%) of the tumors treated with transcatheter arterial chemoembolization plus MW ablation ($P = .67$). The median tumor PFS and overall PFS were 20.8 months and 9.3 months ($P = .72$) for transarterial chemoembolization plus RF ablation and 21.8 months and 9.2 months for transarterial chemoembolization plus MW ablation ($P = .32$). The median OS of the transcatheter arterial chemoembolization plus RF ablation group was 23.3 months, and the median OS of the transcatheter arterial chemoembolization plus MW ablation group was 42.6 months, with no significant difference in the survival experience between the two groups (log-rank test, $P = .10$). In the multivariate analysis, Barcelona Clinic Liver Classification stage was the only factor associated with overall PFS and OS. One patient in the transcatheter arterial chemoembolization plus RF ablation cohort (3%) and two patients in the transcatheter arterial chemoembolization plus MW ablation cohort

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(4%) required prolonged hospitalization (< 48 h) for pain management after the procedure ($P = 1.00$).

Conclusions—Based on similar safety and efficacy outcomes, both combination therapies, transcatheter arterial chemoembolization plus RF ablation and transcatheter arterial chemoembolization plus MW ablation, are effective treatments for HCC.

In recent years, a combination therapy of transcatheter arterial chemoembolization and percutaneous ablation has been gaining traction as a treatment option for hepatocellular carcinoma (HCC), with the goals of achieving better overall survival (OS) and improving prognosis (1–6). Several previous studies suggested that the effectiveness of transcatheter arterial chemoembolization combined with radiofrequency (RF) ablation is better than monotherapy and may have a synergistic effect in treating HCC (1–5). These results were further confirmed by a meta-analysis of randomized controlled trials by Ni et al (2), which demonstrated that the combination of transcatheter arterial chemoembolization and RF ablation has better effectiveness than either transcatheter arterial chemoembolization or RF ablation monotherapy alone. Although the evidence for combining transcatheter arterial chemoembolization and microwave (MW) ablation compared with monotherapy is less robust, a few more recent investigations also demonstrated improved efficacy of transcatheter arterial chemoembolization and MW ablation combination therapy (3,5).

Although combining transcatheter arterial chemoembolization with either RF ablation or MW ablation has shown survival benefits compared with monotherapy, the question of whether one of these percutaneous ablation combination modalities has a survival benefit advantage over the other is yet to be answered. The aim of this study was to investigate differences in local tumor response, progression-free survival (PFS), OS, and potential complications for combined treatment of HCC with transcatheter arterial chemoembolization with drug-eluting embolic agents plus RF ablation versus transcatheter arterial chemoembolization with drug-eluting embolic agents plus MW ablation.

MATERIALS AND METHODS

This retrospective study was conducted with institutional review board approval and adherence to Health Insurance Portability and Accountability Act guidelines. Written informed consent was obtained from each patient before treatment.

Patients

Consecutive patients with HCC who underwent transcatheter arterial chemoembolization with drug-eluting embolic agents in conjunction with RF ablation or MW ablation at our institution from November 1, 2003, through November 1, 2011, were included in the present analysis. The demographic and baseline disease characteristics of both cohorts are summarized in Table 1. The transcatheter arterial chemoembolization plus RF ablation treatment group preceded the transcatheter arterial chemoembolization plus MW ablation treatment group because the interventional radiology department transitioned from using RF ablation to MW ablation at a mid-time point in 2009.

There were 38 patients treated with transcatheter arterial chemoembolization plus RF ablation (12 with multiple tumors) and 51 patients treated with transcatheter arterial chemoembolization plus MW ablation (17 with multiple tumors). There was no statistically significant difference between the two groups in patient demographics, including age, sex, and etiology of liver cirrhosis, and no significant difference in tumor characteristics, including tumor size, number of tumors, and Barcelona Clinic Liver Classification (BCLC) staging. The transplantation rate was 37% in the transcatheter arterial chemoembolization plus RF ablation group and 22% in the transcatheter arterial chemoembolization plus MW ablation group ($P = .11$). However, there were differences between the two groups based on Child-Pugh Classification and follow-up time. Three patients in the transcatheter arterial chemoembolization plus RF ablation group and one patient in the transcatheter arterial chemoembolization plus MW ablation group had unknown Child-Pugh scores because of loss of outside charts. Among the remaining patients, 17 of 35 (49%) and 8 of 50 (16%) were Child-Pugh B in the transcatheter arterial chemoembolization plus RF ablation and transcatheter arterial chemoembolization plus MW ablation groups, respectively ($P = .001$). The median follow-up time among all survivors was 32.6 months (range, 14–82 mo). Among survivors in the transcatheter arterial chemoembolization plus RF ablation group, the median follow-up time was 55.6 months. Among survivors in the transcatheter arterial chemoembolization plus MW ablation group, the median follow-up time was 28.1 months ($P = .001$).

Evaluation and Staging

HCC was diagnosed by the presence of a hypervascular liver mass > 1 cm with arterial uptake followed by “washout” of contrast in the venous-delayed phases on either multiphase computed tomography (CT) or magnetic resonance (MR) imaging in accordance with the American Association for the Study of Liver Diseases guidelines (7). The only exclusion criterion was evidence of distant metastasis.

Before consideration for intervention, patients were assessed with either MR imaging or triphasic CT imaging and evaluated for baseline liver function, hematology, coagulation studies, and serum alpha fetoprotein. Underlying disease burden was staged with the Child-Pugh criteria, United Network for Organ Sharing, and the BCLC Classification. Patient demographics, histologic analysis, and assessment of portal venous hypertension and its sequelae were also taken into consideration before intervention.

Combination Therapy

Transcatheter arterial chemoembolization plus RF ablation and transcatheter arterial chemoembolization plus MW ablation were performed at a single tertiary care center by six physicians with certificates of added qualification for vascular interventions and 4–15 years of experience in performing the procedure. To ensure consistency in reporting of results, this article follows the Society of Interventional Radiology (SIR) reporting standards on transcatheter therapy for hepatic malignancy (8). During both procedures, patients were given moderate sedation with intravenous midazolam and fentanyl. Patients underwent transcatheter arterial chemoembolization with drug-eluting embolic agents first, followed by RF ablation or MW ablation on the subsequent day.

Transcatheter Arterial Chemoembolization with Drug-Eluting Embolic Agents

Common femoral arterial access was obtained with a 5-F vascular sheath (Pinnacle; Terumo Medical Corp, Elkton, Maryland). Selective arteriography of the celiac and superior mesenteric arteries was performed to assess hepatic blood supply and tumor blood supply. A 2.7-F microcatheter system (ProGlide; Terumo, Tokyo, Japan; or Renegade HI-FLO; Boston Scientific, Marlborough, Massachusetts) was used for distal superselective angiography of the hepatic artery branches targeted for chemoembolization.

Embolization of target lesions was performed with a solution containing 50 mg of superabsorbent polymer drug-eluting spheres (QuadraSphere [50–100 μ m diameter, 25 mg dry weight per vial]; Merit Medical Systems, Inc, South Jordan, Utah) that were loaded with either 50 mg of epirubicin (Farmorubicin, Pfizer, Inc, New York, New York) or 50–100 mg of doxorubicin (Pfizer, Inc) and then reconstituted in 20 mL of 0.9% saline, depending on national pharmaceutical availability. After 2 hours of loading the chemotherapeutic agents into the spheres, the mixture was diluted with 20 mL of nonionic contrast medium before administration. Of 38 patients in the transcatheter arterial chemoembolization plus RF ablation group, 7 received epirubicin, and of 51 patients in the transcatheter arterial chemoembolization plus MW ablation group, 11 received epirubicin; 31 and 40 patients received doxorubicin, respectively ($P = .72$). Chemoembolization material was administered under continuous fluoroscopic guidance until the visible stasis of flow to the subselected hepatic artery.

RF Ablation

A commercially available RF ablation system (RF 3000 Radiofrequency Ablation System; Boston Scientific) was used to generate up to 200 W of energy to cause adequate coagulation necrosis of the target tissue and a 1-cm margin. A 10-tine monopolar electrode needle with 15-gauge cannula (LeVein Needle [3–5 cm array]; Boston Scientific) was advanced under ultrasound or CT guidance. Appropriate positioning was confirmed by CT before expansion of the tines. Treatment began at a 50-W level, with wattage increasing 10 W every 2 minutes until tissue impedance increased and the prevention of further current flow or for 10 minutes. For some larger lesions, additional overlapping RF ablation treatments were performed when needed to attain adequate ablation margins.

MW Ablation

A commercially available MW ablation system with a 915-MHz generator and a maximum output of 45 W of energy (Evident Microwave Ablation System; Covidien, Boulder, Colorado) was used for MW ablation. A 13-gauge transcutaneous, water-cooled dipole antenna was placed under ultrasound guidance into the target lesion. The positioning was confirmed by CT. Lesions were treated for 10 minutes at 40 W to ensure adequate coagulative necrosis of the target lesion and a 1-cm margin of tissue. For some larger lesions, additional overlapping treatment or additional antennae were required to attain adequate ablation margins.

Clinical and Imaging Follow-up

Patients were followed using triphasic CT or contrast-enhanced MR imaging, clinical examination, and serum biochemistry 1 month after treatment and at subsequent 3-month intervals for the first year and then biannually, with coinciding clinical and imaging follow-up.

Response Assessment and Survival Analysis

Tumor response was assessed using European Association for the Study of the Liver necrosis criteria and evaluated both per patient and per each lesion individually (8,9). Local tumor response was classified as complete response, partial response, stable disease, or progressive disease.

Both tumor and overall PFS time (ie, the period between ablation and either progression or death, whichever comes first) was estimated with a conservative methodology adopted from Memon et al (10), where the date of progression was defined as 1 day after the last nonprogression scan before the scan showing disease progression. Patients whose tumors had not progressed or who had died were censored on the date they were last known to be progression-free (for overall PFS, this was the transplant date for transplant recipients). Patients were followed until death. OS was defined as the interval from the date of ablation until either the date of death or last known follow-up.

Statistical Analysis

Demographic and disease characteristics were compared between the two treatment cohorts using χ^2 tests or Fisher exact tests for categorical variables and two-sample t tests or Wilcoxon rank sum tests for continuous variables. Survival analyses were performed using the Kaplan-Meier method, log-rank test, and univariate and multivariate Cox proportional hazards regression. In addition to treatment group, other covariates were included in the multivariate model if they had a P value $\leq .1$ in univariate analysis for OS or overall PFS. For the tumor PFS analysis, a univariate Cox regression model with a gamma shared frailty component, to account for the within-patient correlation, was used to compare treatment groups. A secondary analysis of OS was also performed, with censoring at transplantation, which confirmed the robustness of the primary OS analysis (data not shown). Local tumor response was compared between treatment groups using ordinal or standard logistic regression with robust standard errors to account for the clustering of tumors within patient. A P value $< .05$ was considered statistically significant. Analyses were performed using Stata Version 13 (Stata-Corp LP, College Station, Texas).

RESULTS

Local Tumor Response and PFS

There were 46 total tumors in 34 patients in the transcatheter arterial chemoembolization plus RF ablation cohort and 64 total tumors in 48 patients in the transcatheter arterial chemoembolization plus MW ablation cohort. Four patients in the transcatheter arterial chemoembolization plus RF ablation group and three patients in the transcatheter arterial chemoembolization plus MW ablation group did not have sufficient baseline data for the per

tumor analysis. On initial treatment, complete response was seen in 37 (80.4%) of the tumors treated with transcatheter arterial chemoembolization plus RF ablation and 49 (76.6%) of the tumors treated with transcatheter arterial chemoembolization plus MW ablation ($P = .67$) (Fig 1). Per tumor analysis of the initial treatment response (complete response, partial response, stable disease, or progressive disease) also did not show a significant difference between the two cohorts ($P = .72$). In addition, there was no evidence for a differential treatment effect based on initial tumor size (< 3 cm vs ≥ 3 cm; $P = .55$ from the treatment group by size interaction). Among tumors with complete response initially, the transcatheter arterial chemoembolization plus RF ablation group had a higher complete response maintenance rate ($P = .059$), regardless of initial tumor size. In a secondary per patient analysis, assigning each patient his or her worst tumor response, no statistically significant difference was seen between the groups' initial outcomes ($P = .53$). The median tumor PFS was 20.8 months for transcatheter arterial chemoembolization plus RF ablation and 21.8 months for transcatheter arterial chemoembolization plus MW ablation ($P = .72$).

Overall PFS

The combined median overall PFS was 9.2 months (95% confidence interval [CI], 7.0–16.6). The median PFS for the transcatheter arterial chemoembolization plus RF ablation group was 9.3 months (95% CI, 5.9–15.8) and for the transcatheter arterial chemoembolization plus MW ablation group was 9.2 months (95% CI, 6.4–19.7), with no statistically significant difference in overall PFS between the two cohorts (log-rank, $P = .32$) (Fig 2). In further univariate analyses, BCLC stage was significantly associated with PFS with weaker evidence for Child-Pugh and index tumor size (Table 2). All of these variables were then considered in multivariate analysis.

In a multivariate Cox regression model adjusting for Child-Pugh, BCLC stage, and index tumor size (< 3 cm vs 3 – 5 cm vs > 5 cm), the hazard ratio for transcatheter arterial chemoembolization plus MW ablation versus transcatheter arterial chemoembolization plus RF ablation was 0.76 (95% CI, 0.41–1.41; $P = .39$) with only BCLC stage reaching statistical significance (Table 2). To determine whether the effect of treatment group on overall PFS varied based on other clinically important factors, the following interactions were tested and dropped from the multivariate model because of nonsignificance: treatment by Child-Pugh ($P = .40$) (Fig 3), treatment by BCLC stage (A/B) ($P = .67$) (Fig 4), and treatment by index tumor size ($P = .81$) (Fig 5).

Overall Survival

The combined median OS was 39.0 months (95% CI, 23.3–57.3). The median survival for the transcatheter arterial chemoembolization plus RF ablation group was 23.3 months (95% CI, 18.2–39.0) and for the transcatheter arterial chemoembolization plus MW ablation group was 42.6 months (95% CI, 41.3–not estimable) (log-rank, $P = .10$) (Fig 6). BCLC stage, Child-Pugh, and index tumor size were significantly associated with OS, as expected, in univariate analyses (Table 3). All of these variables were then considered in multivariate analysis.

In a multivariate Cox regression model adjusting for Child-Pugh, BCLC stage, and index tumor size, the hazard ratio for transcatheter arterial chemoembolization plus MW ablation versus transcatheter arterial chemoembolization plus RF ablation was 0.81 (95% CI, 0.41–1.62; $P = .56$) (Table 3). In this multivariate analysis, Child-Pugh ($P = .09$) and index tumor size ($P = .19$) were not statistically significant, whereas BCLC stage was statistically significant ($P = .008$). To determine whether the effect of treatment group on OS varied based on other clinically important factors, the following interactions were tested and dropped from the multivariate model because of nonsignificance: treatment by Child-Pugh ($P = .38$) (Fig 7), treatment by BCLC stage (A/B) ($P = .10$) (Fig 8), and treatment by tumor size ($P = .57$) (Fig 9).

Complications

Overall, transcatheter arterial chemoembolization plus RF ablation and transcatheter arterial chemoembolization plus MW ablation procedures were well tolerated without serious complications in both cohorts. Only three patients experienced complications consisting of pain that required therapy and prolonged hospitalization (< 48 h from the expected date of discharge) and that were classified as major complications (grade C) based on the SIR clinical practice guidelines (8,11,12). Of these three patients, one was in the transcatheter arterial chemoembolization plus RF ablation cohort (3%), and two were in the transcatheter arterial chemoembolization plus MW ablation cohort (4%) ($P = 1.00$).

DISCUSSION

Combination therapy of transcatheter arterial chemoembolization with percutaneous thermal ablation is evolving as an accepted treatment option for patients with unresectable HCC, with growing evidence that combination therapy improves therapeutic outcomes and prognosis (1–6). In many scenarios, the choice between ablative modalities depends on institutional preference, operator expertise, and available equipment. However, when both options are available, a clear consensus has not yet been delineated. This retrospective study found no statistically significant difference in local tumor response, tumor and overall PFS, OS, or complications between using RF ablation or MW ablation in combination with transcatheter arterial chemoembolization with drug-eluting embolic agents.

When used alone, no significant difference in OS has been demonstrated in the literature between RF ablation and MW ablation for the treatment of HCC (13,14). Two studies were identified that retrospectively evaluated transcatheter arterial chemoembolization plus RF ablation and transcatheter arterial chemoembolization plus MW ablation combination therapies. Fan et al (4) retrospectively analyzed the efficacy, PFS, and OS of conventional transcatheter arterial chemoembolization with RF ablation versus conventional transcatheter arterial chemoembolization with MW ablation in the treatment of HCC, demonstrating safety and efficacy of combination therapy for unresectable large HCCs (> 5.0 cm). However, this study was limited by sample size and did not directly compare the outcomes between the two groups. A recently published abstract by Virk et al (15) compared the local tumor progression and complications of MW ablation with RF ablation in the treatment of HCC when combined with transcatheter arterial chemoembolization with drug-eluting

embolic agents, but the study was limited by its short follow-up period and lack of PFS and OS comparison. This study analyzed BCLC A patients only and found a trend for better local tumor control with the MW ablation cohort compared with the RF ablation cohort. In contrast, no significant differences in local tumor response or tumor PFS between the two cohorts were seen in our study.

In theory, the combination of transcatheter arterial chemoembolization with percutaneous thermoablation has complementary effects because the heat sink effect is diminished by the embolization of intratumoral and adjacent parenchymal blood vessels, ultimately allowing for higher ablation temperatures (16). Used in isolation, there are hypothesized benefits to MW ablation, having demonstrated higher average intratumoral temperatures, larger ablation zones, and less susceptibility to the heat sink effect (17) compared with RF ablation. However, in this study, such theoretical technical advantages were not demonstrated in practice. It is possible that combination therapy lessens the advantage that MW ablation has over RF ablation on the heat sink effect because transcatheter arterial chemoembolization would mitigate such an advantage at least theoretically. Additionally, combination therapy with the two different ablative modalities had no significant differences in safety, with low complication rates for both groups. Three major complications were encountered, according to the SIR clinical practice guidelines, that required prolonged hospitalization (< 48 h) for pain management after the procedure; one (3%) patient was in the transcatheter arterial chemoembolization plus RF ablation cohort, and two (4%) patients were in the transcatheter arterial chemoembolization plus MW ablation cohort ($P = 1.00$). This documentation of three major complications is in line with the major complications rate of 3.7% reported by Ni et al (2) in their meta-analysis of randomized controlled trials comparing combined transcatheter arterial chemoembolization and RF ablation with transcatheter arterial chemoembolization or RF ablation monotherapy and compares favorably with the reported rates of pneumothorax requiring chest tube (6% and 2%) and portal vein thrombosis (6% and 15%) for MW ablation and RF ablation, respectively, reported by Virk et al (15).

This study has some limitations. The relatively small sample size and retrospective nature of the study with multiple confounding factors and complexity of underlying liver disease made multivariate analysis a challenging task. The two groups differed based on follow-up time and Child-Pugh class, with shorter median follow-up time and more patients classified as Child-Pugh A in the transcatheter arterial chemoembolization plus MW ablation group. However, Child-Pugh class (along with BCLC stage and index tumor size) was controlled for in multivariate analysis of PFS and OS, and no significant differences were found between the two treatment groups. An additional limitation involves the transition in ablative technology at a mid-time point in 2009. Because the transcatheter arterial chemoembolization plus RF ablation treatment group preceded the transcatheter arterial chemoembolization plus MW ablation treatment group, with the same censor date applied for both treatment cohorts, the patients in the transcatheter arterial chemoembolization plus MW ablation group had a shorter median follow-up time compared with the patients in the transcatheter arterial chemoembolization plus RF ablation group. Such differences in follow-up time limited the accurate evaluation of long-term efficacy. Despite the relatively close

periods in time of the two treatment groups, there was potential for increasing operator proficiency and improvements in medical care.

The order and timing of therapeutic intervention in combination therapy are still a matter of debate. For this study, transcatheter arterial chemoembolization was always followed by percutaneous ablation on the subsequent day to take advantage of the embolic effect during the ablation and for patients' convenience because both procedures were performed during one hospitalization. However, there are also theoretical advantages of the reverse order because hyperemia following ablation may bolster deposition of the transcatheter arterial chemoembolization chemotherapy. The findings of equivalence between thermoablation modalities cannot be inferred for ablative-first combination therapy.

In conclusion, the results of our study add to the growing body of literature that suggests combination therapy of transcatheter arterial chemoembolization plus RF ablation or plus MW ablation is a safe and effective treatment option for HCC. It is unclear if there are true advantages to either combination therapy regimen. Nevertheless, this retrospective analysis found no significant differences in efficacy or safety between transcatheter arterial chemoembolization plus RF ablation and transcatheter arterial chemoembolization plus MW ablation and suggests the two combination therapies are safe and may be used interchangeably.

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ABBREVIATIONS

BCLC	Barcelona Clinic Liver Classification
CI	confidence interval
HCC	hepatocellular carcinoma
MW	microwave
OS	overall survival
PFS	progression-free survival

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Figure 1.

Local tumor response initially (1 mo) and at the end of the study in both treatment cohorts, all tumors combined. CR = complete response; PD = progressive disease; PR = partial response; SD = stable disease.

Figure 2.
Kaplan-Meier curves showing PFS by treatment cohort.

Figure 3.
Kaplan-Meier curves showing PFS by treatment cohort and Child-Pugh score.

Figure 4.
Kaplan-Meier curves showing PFS by treatment cohort and BCLC stage.

Figure 5.
Kaplan-Meier curves showing PFS by treatment cohort and tumor size categories.

Figure 6.
Kaplan-Meier curves showing OS by treatment cohort.

Figure 7. Kaplan-Meier curves showing OS by treatment cohort and Child-Pugh score. NE = not estimable.

Figure 8. Kaplan-Meier curves showing OS by treatment cohort and BCLC stage. NE = not estimable.

Figure 9.
Kaplan-Meier curves showing OS by treatment cohort and tumor size categories.

Table 1

Demographic and Baseline Disease Characteristics of Two Treatment Cohorts

Variables	Transcatheter Arterial Chemoembolization + RF Ablation, N (%)	Transcatheter Arterial Chemoembolization + MW Ablation, N (%)	P Value
Gender			.51
Male	16 (42)	18 (35)	
Female	22 (58)	33 (65)	
Age (y)			.42
Median	63	67	
Range	48–84	34–89	
Cause of liver disease			
HBV	4 (11)	5 (10)	1.00
HCV	25 (66)	25 (49)	.12
Alcohol	8 (21)	8 (15)	.51
NASH	3 (8)	9 (18)	.22
Child-Pugh			.001
A	18 (51)	42 (84)	
B	17 (49)	8 (16)	
BCLC stage			1.00
A	28 (74)	36 (73)	
B	8 (21)	10 (20)	
C	2 (5)	4 (8)	
No. Tumors			.77
1	26 (68)	34 (67)	
2	10 (26)	12 (24)	
3	1 (3)	4 (8)	
4	1 (3)	1 (2)	
Maximum tumor size (cm)			.47
Median	3.1	2.9	
Range	1.8–12.5	1.6–10	

BCLC = Barcelona Clinic Liver Classification; HBV = hepatitis B virus; HCV = hepatitis C virus; MW = microwave; NASH = nonalcoholic steatohepatitis; RF = radiofrequency.

Table 2

Progression-Free Survival Analysis of Two Treatment Cohorts

	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	P Value	HR	95% CI	P Value
Treatment			.32			.39
Transcatheter arterial chemoembolization plus RF ablation	Referent			Referent		
Transcatheter arterial chemoembolization plus MW ablation	0.77	0.45–1.30		0.76	0.41–1.41	
Age (per year)	1.01	0.98–1.04	.43			
Child-Pugh			.11			.16
A	Referent			Referent		
B	1.65	0.90–3.02		1.65	0.83–3.28	
BCLC stage						
A	Referent			Referent		
B	1.55	0.79–3.02	.20	1.44	0.61–3.37	.41
C	16.75	6.04–46.46	< .001	19.58	5.30–72.32	< .001
			Overall $P < .001$			Overall $P < .001$
Gender			.59			
Female	Referent					
Male	1.16	0.67–1.99				
No. tumors			.75			
1	Referent					
> 1	1.09	0.62–1.93				
Tumor size						
3 cm	Referent			Referent		
3.1–5 cm	1.15	0.64–2.08	.65	1.05	0.51–2.15	.90
> 5 cm	2.32	1.13–4.74	.02	1.17	0.44–3.16	.75
			Overall $P = .07$			Overall $P = .95$

Note.—Results are from Cox regression models.

BCLC = Barcelona Clinic Liver Classification; CI = confidence interval; HR = hazard ratio; MW = microwave; RF = radiofrequency.

Table 3

Overall Survival Analysis of Two Treatment Cohorts

	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	P Value	HR	95% CI	P Value
Treatment			.10			.56
Transcatheter arterial chemoembolization plus RF ablation	Referent			Referent		
Transcatheter arterial chemoembolization plus MW ablation	0.60	0.33–1.11		0.81	0.41–1.62	
Age (per year)	1.01	0.98–1.04	.44			
Child-Pugh			.02			.09
A	Referent			Referent		
B	2.08	1.11–3.89		1.85	0.91–3.74	
BCLC stage						
A	Referent			Referent		
B	1.81	0.91–3.60	.09	1.47	0.61–3.55	.39
C	9.94	3.85–25.64	< .001	5.92	1.93–18.11	.002
			Overall $P < .001$			Overall $P = .008$
Gender			.70			
Female	Referent					
Male	0.89	0.49–1.61				
No. tumors			.61			
1	Referent					
> 1	1.17	0.64–2.16				
Tumor size						
3 cm	Referent			Referent		
3.1–5 cm	1.37	0.70–2.66	.36	1.36	0.59–3.09	.47
> 5 cm	3.90	1.78–8.54	.001	2.46	0.93–6.50	.07
			Overall $P = .003$			Overall $P = .19$

Note.—Results are from Cox regression models.

BCLC = Barcelona Clinic Liver Classification; CI = confidence interval; HR = hazard ratio; MW = microwave; RF = radiofrequency.