Original Article

Radiofrequency ablation versus microwave ablation for hepatocellular carcinoma with cirrhosis: a propensity score analysis

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Background: Radiofrequency ablation (RFA) and microwave ablation (MWA) are the most frequently used percutaneous ablation techniques for the treatment of liver cancer. The aim of our study was to identify the ablation method that had a better long-term prognosis for patients with cirrhotic hepatocellular carcinoma (HCC).

Methods: This retrospective study consisted of HCC patients with cirrhosis who underwent RFA and MWA between January 2014 to December 2021 at Beijing You'an Hospital. Patients were divided into two groups according to the therapeutic approaches: the RFA group and the MWA group. The prognosis was compared before and after 1:1 propensity score matching (PSM).

Results: A total of 800 HCC patients with cirrhosis who received interventional treatment from January 2014 to December 2021 were prospectively enrolled. After PSM, there were 268 patients in each of the RFA and MWA groups. The statistically significant differences in recurrence-free survival (RFS) and overall survival (OS) between RFA and MWA groups can be observed, both before and after PSM. Besides, 1-, 3-year RFS, and 5-year OS rates were higher in those the RFA group than in the MWA group. Age, tumor size, gamma glutamyl transferase (GGT), and hepatitis B surface antigen (HBsAg) were independent risk factors for RFS. Child-Pugh, lymphocyte (Lym), GGT, and treatment modality were independent risk factors for OS.

Conclusions: For patients with HCC associated with cirrhosis, RFA can provide a better prognosis than MWA, with lower recurrence and mortality rate.

Keywords: Hepatocellular carcinoma (HCC); radiofrequency ablation (RFA); microwave ablation (MWA); prognosis; propensity score matching analysis (PSM analysis)

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Introduction

Primary liver cancer is the sixth most prevalent malignancy and the third leading cause of cancer-related death, with the growing incidence globally (1,2). It is estimated that by 2025, more than one million individuals will suffer from liver cancer each year (3). China is the country with the highest hepatocellular carcinoma (HCC) occurrence, accounting for over 50% of new cases and deaths worldwide. At present, HCC often occurs in the context of chronic liver disease caused by hepatitis B virus (HBV) infection in China (4). 80–90% of HCCs develop in cirrhotic liver and 2–4% of persons with cirrhosis progress to HCC annually (5,6). Due to the lack of symptoms,

only 40% of HCC patients are diagnosed within the early stage (7,8). According to current HCC clinical guidelines, curative therapeutic options for patients with early-stage HCC are surgical resection, liver transplantation, and local ablation. It has been proven in studies that ablation is as effective as surgery and has fewer complications (9,10).

Radiofrequency ablation (RFA) has been the most widely used and studied image-guided thermal ablation technique for HCC (10). However, new ablation technologies continue to emerge, including microwave ablation (MWA), cryoablation (CRA), irreversible electroporation, and high-intensity focused ultrasound (HIFU), of which MWA is the most commonly used (11). Although both of RFA and MWA are high-temperature-based modalities, leading to coagulation necrosis in tumor tissues, the heat production principles of RFA and MWA are different. Randomized controlled trials (RCTs) comparing RFA and MWA have also demonstrated similar safety and efficacy in small HCC (12-14).

However, the properties of the liver parenchyma may vary with the disease, which can affect the ablation area and efficacy. Cirrhosis is the consequence of chronic liver inflammation, followed by diffuse liver fibrosis and the normal liver structures are replaced by regenerative liver nodules that result in distorted blood vessels (15-17). Furthermore, the prognosis of HCC combined cirrhosis is worse. A multicenter case-control study found that >70% of patients with cirrhosis had a postoperative recurrence, compared with <40% of patients with normal liver parenchyma (18-20). Because of the specific liver histology and worse prognosis, the aim of our study was to determine and compare the therapeutic efficacy of minimally invasive therapies (RFA and MWA) in the treatment of cirrhotic HCC and utilized propensity score matching (PSM) to minimize selection bias. We present this article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1939/rc).

Highlight box

Key findings

- For patients with hepatocellular carcinoma (HCC) associated with cirrhosis, radiofrequency ablation (RFA) can provide a better prognosis than microwave ablation (MWA), with lower recurrence and mortality rate.

What is known and what is new?

- Although both of RFA and MWA are high-temperature-based modalities, leading to coagulation necrosis in tumor tissues, the heat production principles of RFA and MWA are different. Randomized controlled trials comparing RFA and MWA have also demonstrated similar safety and efficacy in small HCC.
- For patients with HCC associated with cirrhosis, RFA can provide a better prognosis than MWA.

What is the implication, and what should change now?

- In clinical practice, RFA can be prioritized for HCC patients with cirrhosis.

Methods

Patient selection

Our retrospective study evaluated 800 patients with cirrhotic HCC who received RFA and MWA from January 2014 to December 2021 at Beijing Youan Hospital. During the diagnosis of HCC, the American Association for the Study of Liver Diseases (ASSLD) was followed (2,21). The inclusion criteria of patients were as follows: (I) aged 18–75 years; (II) early-stage HCC patient accepted ablation (RFA and MWA) and achieved complete response; (III) Child-Pugh score was class A or B; (IV) received no other therapeutics prior to ablation. Exclusion criteria were listed as follows: (I) with second primary malignant tumors; (II) clinical follow-up data incomplete; (III) advanced HCC (*Figure 1*).

This study was approved by the Ethics Committee of Beijing You'an Hospital, Capital Medical University, and was conducted in accordance with the standards of the Declaration of Helsinki (No. 2022/111). A waiver of patient informed consent was granted since the Ethics Committee considered the study to be low-risk.

Ablation procedure

Ablation was performed under the guidance of computed tomography (CT) and magnetic resonance imaging (MRI) by a qualified interventionalist. The size of the tumor decided the number of electrodes. Routine disinfection and local anesthesia were applied around the puncture points, combined with intravenous analgesia, and monitored anesthesia care. The radiofrequency needle follows the puncture path of the puncture needle to the tumor site. During RFA, after measuring the baseline impedance, the power was gradually increased from 80 to 160 W to reach the maximum impedance. For MWA, after inserting the

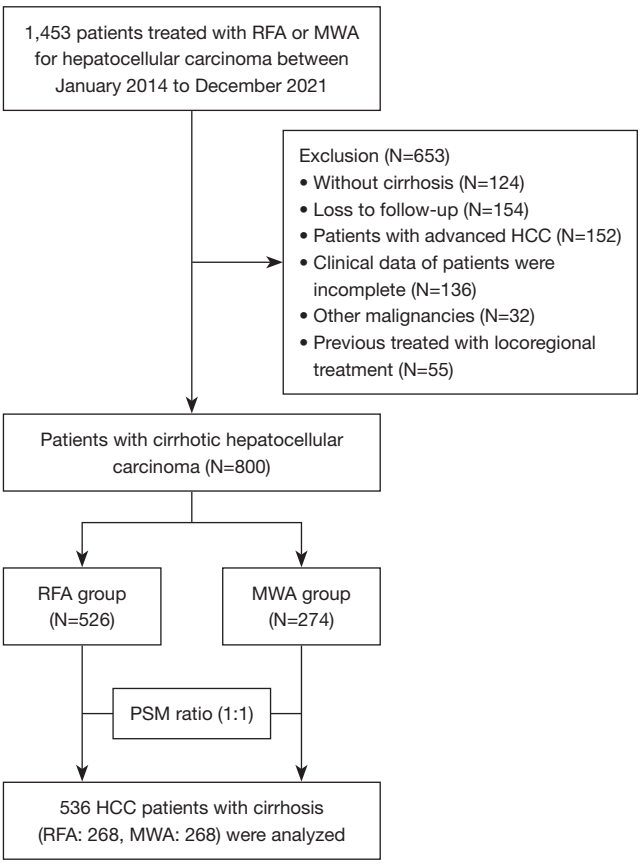

Figure 1 Screening flow chart of enrolled patients. A total of 1,453 HCC patients were treated with RFA or MWA between January 2014 from December 2021. After the exclusion of 653 patients, 800 patients were finally enrolled, including 526 in the RFA group and 274 in the MWA group. After PSM, 268 patients remained in each of the two groups. RFA, radiofrequency ablation; MWA, microwave ablation; HCC, hepatocellular carcinoma; PSM, propensity score matching.

MWA needle (Nanjing Ruibo Medical Technology Co., China) into the tissue, the ablation power was 30–60 W, and the time setting was 5–8 minutes. Cold saline was injected into the electrode cavity using a pump to keep the tip temperature below 20 ℃ at all times. In addition, to achieve complete ablation, the safe margin for complete ablation of the tumor was 0.5–1.0 cm. In order to prevent postoperative bleeding and tumor implantation, a thermocoagulation was performed along the needle track when the ablation finished. Arteriography-enhanced CT was performed immediately after treatment to evaluate the success of the procedure and its complications.

Follow-up

All patients underwent regular follow-up in the outpatient department. Therapeutic response was evaluated at 4–6 weeks after ablation by using CT and MRI. Complete tumor ablation was defined as the absence of enhancement on enhanced images at 1-month after thermal ablation. Patients with viral hepatitis were treated with entecavir or tenofovir. Patients were examined once every three months during the first year and once every 6 months thereafter. Follow-up assessment included blood tests, liver function, and imaging examination to detect tumor recurrence. Recurrence-free survival (RFS) and overall survival (OS) were the primary endpoint in this study. RFS was defined as the time from the start of ablation to the first relapse or death from any cause, and OS was estimated as the period from the receipt of the ablation to death or the last follow-up.

Statistical analysis

Differences between the two groups were compared through the *t*-test, chi-squared test, and Mann-Whitney *U* test, with the purpose of providing median or counts and percentages to summarize baseline variables. Survival and recurrence were calculated using the Kaplan-Meier method, and the log-rank test was used for comparison. Univariate and multivariate Cox regression analyses were performed to identify the independent risk factors for survival and recurrence in HCC with cirrhosis.

To reduce the potential selection bias, 1:1 PSM was conducted, which the matching tolerance was 0.1. Matches were made in baseline variables that were previously considered clinically relevant in the literature, comprising age, sex, antiviral, Child-Pugh classification, Barcelona Clinic Liver Cancer (BCLC) stage, tumor size, tumor number, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alpha fetoprotein (AFP), AFP classification and etiology.

All the statistical data were analyzed with SPSS software (version 26.0, IBM, Armonk, NY, USA) and R software (version 4.1.2), and P value of less than 0.05 was considered statistically significant ($P<0.05$).

Results

Patient characteristics

A total of 800 HCC patients combined with cirrhosis from

January 2014 to December 2021 were retrospectively analyzed, containing 526 (65.7%) in the RFA group and 274 (34.3%) in the MWA group. After PSM, 268 patients were included in each group (*Figure 1*). The last follow-up was conducted on July 1, 2023, and the median follow-up time was 4.05 years (interquartile range, 2.68–7.05 years).

Before PSM, baseline data showed that compared to MWA group, the RFA group had a higher proportion of patients with diabetes (24.0% *vs.* 17.5%, P=0.03), BCLC stage 0 (35.6% *vs.* 20.4%, P<0.0001), solitary tumors (71.1% *vs.* 63.1%, P=0.02), tumor with a size of <3 mm (73.2% *vs.* 49.6%, P<0.0001), and lower fibrous protein levels (2.70±0.82 *vs.* 2.89±1.01 g/L, P=0.003). After PSM, all clinical and pathological characteristics were well balanced between the two treatment arms (*Table 1*).

Efficacy

Prior to PSM, median recurrence-free survival (mRFS) was significantly longer in the RFA groups than in the MWA group (24.4 *vs.* 17.9 months, P=0.0048), and the same result was observed in median overall survival (mOS) (not reached *vs.* 86.0 months, P=0.0016) (*Figure 2*). The 1-, 3-, and 5-year OS rates for the RFA group were 95%, 84%, and 55%, respectively, and the 1-, 3-, and 5-year RFS rates were 50%, 34%, and 16%. For the MWA group, the 1-, 3-, and 5-year OS and RFS rates were 95%, 85%, 39%, 40%, 24%, and 12%, respectively. There were statistical differences in the 1-year RFS rate (P=0.008), 3-year RFS rate (P=0.004), and 5-year OS rate (P<0.0001).

After PSM, mPFS and mOS remained longer in the RFA group than in the MWA group (24.4 *vs.* 18.4 months, P=0.03; not reached *vs.* 85.3 months, P=0.01; *Figure 3*). The 1-, 3-, and 5-year OS rates of the RFA group were 94%, 88%, and 53%, while the 1-, 3-, and 5-year RFS rates were 51%, 33%, and 15%, respectively. The 1-, 3-, and 5-year OS of MWA group were 95%, 85%, and 39%. And the 1-, 3-, and 5-year RFS rates of the MWA group were 41%, 24%, and 13% (*Table 2*). The same results were found after comparative analysis. The 1-year RFS rate (P=0.01), 3-year RFS (P=0.01), and 5-year OS rate (P=0.001) were higher in the RFA group than in the MWA group.

Independent prognostic factors of RFS and OS

To investigate the independent risk factors for RFS and OS, univariate and multivariate Cox regression analyses were performed. Before PSM, univariate and multivariate Cox regression analyses showed that age [hazard ratio (HR): 1.02, 95% confidence interval (CI): 1.01–1.03, P<0.0001], gender (HR: 0.78, 95% CI: 0.61–0.99, P=0.04), BCLC (0 *vs.* B) stage (HR: 0.57, 95% CI: 0.36–0.91, P=0.01), BCLC (A *vs.* B) stage (HR: 0.69, 95% CI: 0.50–0.95), tumor number (HR: 1.36, 95% CI. 1.03–1.80, P=0.02), tumor size (HR: 1.29, 95% CI: 1.03–1.63, P=0.02), gamma glutamyl transferase (GGT) (HR: 1.00, 95% CI: 1.00–1.01), and

Table 1 Demographics and clinical characteristics before and after PSM

Characteristic	Before PSM			After PSM		
	RFA (N=526)	MWA (N=274)	P value	RFA (N=268)	MWA (N=268)	P value
Age (years)	56.6±8.5	57.2±9.5	0.329	56.26±8.85	57.26±9.47	0.207
Sex			0.519			0.428
Male	418 (79.5)	223 (81.4)		224 (83.6)	217 (81.0)	
Female	108 (20.5)	51 (18.8)		44 (16.4)	51 (19.0)	
Antiviral			0.058			0.665
Yes	317 (60.3)	146 (53.3)		148 (55.2)	143 (53.4)	
No	209 (39.7)	128 (46.7)		120 (44.8)	125 (46.6)	
Diabetes			0.036			0.911
Yes	126 (24.0)	48 (17.5)		49 (18.3)	48 (17.9)	
No	400 (76.0)	146 (82.5)		219 (81.7)	220 (82.1)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristic	Before PSM			After PSM		
	RFA (N=526)	MWA (N=274)	P value	RFA (N=268)	MWA (N=268)	P value
ALD			0.28			0.91
Yes	121 (23.0)	54 (19.7)		52 (19.4)	53 (19.8)	
No	405 (77.0)	220 (80.3)		216 (80.6)	215 (80.2)	
Child-Pugh class			0.24			0.42
A	379 (72.1)	208 (75.9)		195 (72.8)	203 (75.7)	
B	147 (27.9)	66 (24.1)		73 (27.2)	65 (24.3)	
BCLC stage			<0.0001			0.26
0	187 (35.6)	56 (20.4)		65 (24.2)	55 (20.5)	
A	276 (52.5)	152 (55.5)		154 (57.5)	150 (56.0)	
B	63 (12.0)	66 (24.1)		49 (18.3)	63 (23.5)	
Tumor number			0.02			0.85
Single	374 (71.1)	173 (63.1)		173 (64.6)	171 (63.8)	
Multiple	152 (28.9)	101 (36.9)		95 (35.4)	97 (36.2)	
Tumor size (mm)			<0.0001			0.04
<30	385 (73.2)	136 (49.6)		157 (58.6)	134 (50.0)	
≥30	141 (26.8)	138 (50.4)		111 (41.4)	134 (50.0)	
Etiology			0.23			0.62
HBV	470 (89.4)	252 (92.0)		249 (92.9)	19 (7.1)	
Coinfection	56 (10.6)	22 (8.0)		19 (7.1)	22 (8.2)	
Neu (10^9/L)	3.11±1.75	3.36±1.81	0.05	3.21±1.87	3.37±1.83	0.31
Lym (10^9/L)	1.26±0.67	1.21±0.60	0.28	1.26±0.69	1.20±0.59	0.29
PLT (10^9/L)	117.00±59.21	121.80±62.15	0.28	118.49±61.76	121.58±62.78	0.56
TBIL (μmol/L)	20.46±10.73	19.42±9.83	0.18	20.20±10.87	19.47±9.91	0.41
GGT (U/L)	67.89±59.60	72.99±65.00	0.26	72.89±60.39	72.91±64.84	0.99
Fib (g/L)	2.70±0.82	2.89±1.01	0.003	2.75±0.87	2.89±1.01	0.08
HBsAg	3,485±3,173	3,890±2,894	0.08	3,605±3,267	3,872±2,884	0.32
ALT (U/L)	30.01±16.87	32.22±18.91	0.09	31.56±18.38	32.13±19.04	0.72
AST (U/L)	32.49±15.05	31.89±14.37	0.59	33.58±14.92	31.79±14.47	0.15
AFP (μmol/L)	278.67±1,403.9	502.18±2,600.9	0.11	419.91±1,899.9	502.18±2,600.9	0.67
AFP level (μmol/L)			0.13			0.20
<7	220 (41.8)	94 (34.3)		112 (41.8)	94 (35.1)	
7–200	222 (42.2)	132 (48.2)		107 (39.9)	126 (47.0)	
>200	84 (16.0)	48 (17.5)		49 (18.3)	48 (17.9)	

Data are presented as No. (%) or mean ± standard deviation. PSM, propensity score matching; RFA, radiofrequency ablation; MWA, microwave ablation; ALD, alcoholic liver cancer; BCLC, Barcelona Clinic Liver Cancer; HBV, hepatitis B virus; Neu, neutrophil; Lym, lymphocyte; PLT, platelet; TBIL, total bilirubin; GGT, gamma glutamyl transferase; Fib, fibrous protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AFP, alpha fetoprotein.

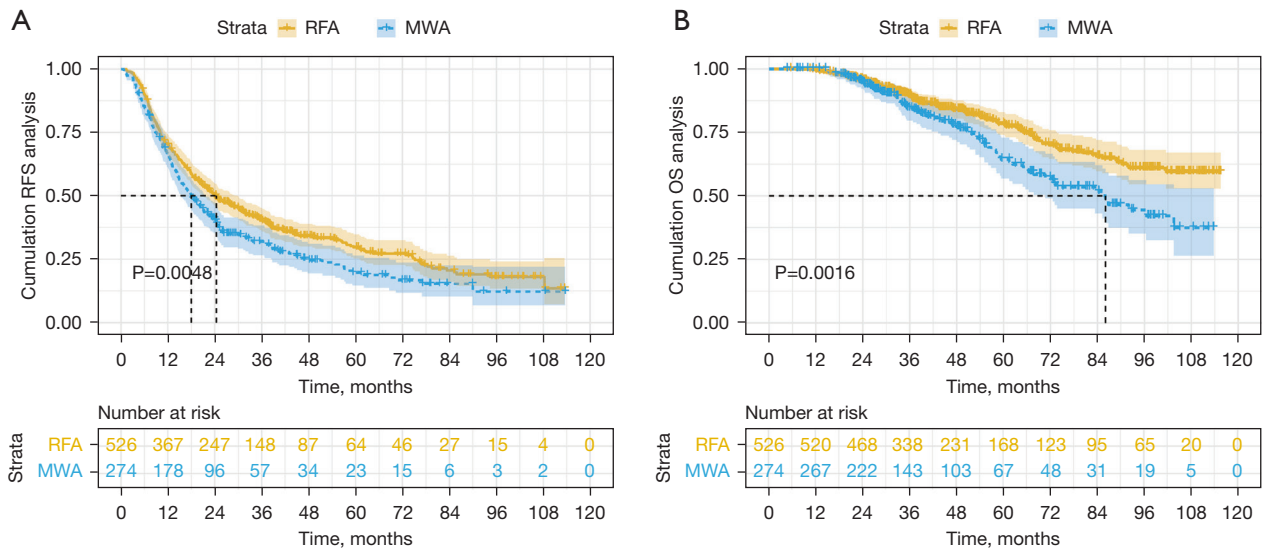

Figure 2 Kaplan-Meier plots of RFS and OS in cirrhotic HCC patients treated with RFA or MWA before PSM. (A) Kaplan-Meier plot of RFS in cirrhotic HCC patients treated with RFA or MWA before PSM; (B) Kaplan-Meier plot of OS in cirrhotic HCC patients treated with RFA or MWA before PSM. HCC, hepatocellular carcinoma; RFS, recurrence-free survival; RFA, radiofrequency ablation; MWA, microwave ablation; OS, overall survival; PSM, propensity score matching.

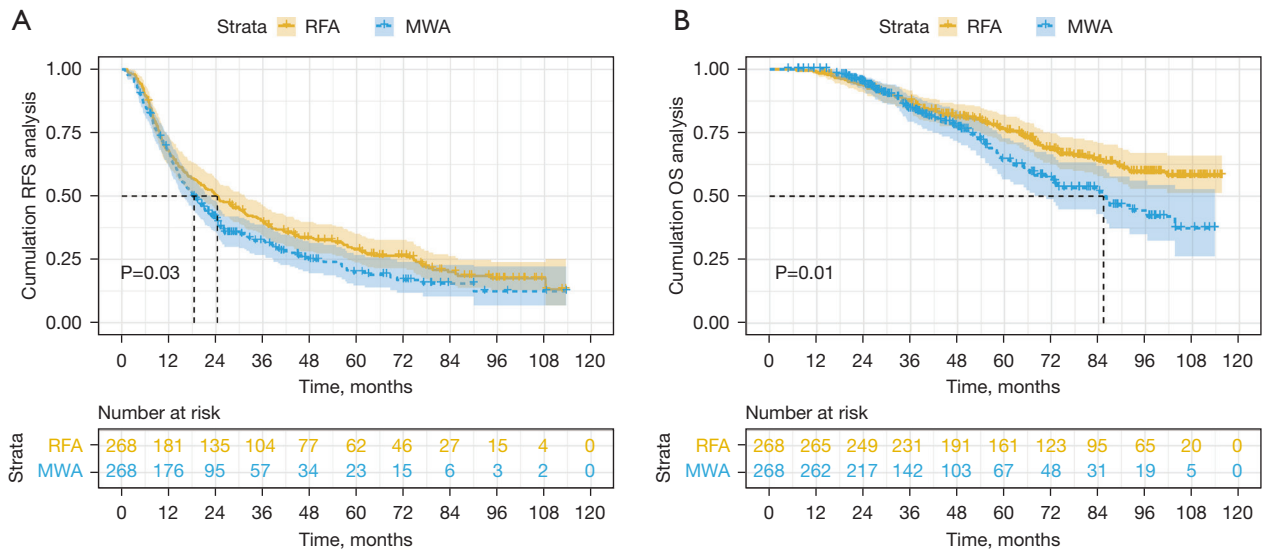

Figure 3 Kaplan-Meier plots of RFS and OS in cirrhotic HCC patients treated with RFA or MWA after PSM. (A) Kaplan-Meier plot of RFS in cirrhotic HCC patients treated with RFA or MWA after PSM; (B) Kaplan-Meier plot of OS in cirrhotic HCC patients treated with RFA or MWA after PSM. RFA, radiofrequency ablation; MWA, microwave ablation; RFS, recurrence free survival; OS, overall survival; HCC, hepatocellular carcinoma; PSM, propensity score matching.

hepatitis B surface antigen (HBsAg) (HR: 1.00, 95% CI: 1.00–1.00) were independent risk factors for RFS (*Table 3*). While independent risk factors for OS included Child-Pugh classification (HR: 1.47, 95% CI: 1.08–2.01, P=0.01), GGT (HR: 1.00, 95% CI: 1.00–1.01, P=0.014) and treatment modality (HR: 0.71, 95% CI: 0.52–0.97, P= 0.02) (*Table 4*). Following the PSM, age (HR: 1.01, 95% CI: 1.00–1.03, P=0.01), tumor size (HR: 1.33, 95% CI: 1.01–1.75, P=0.04),

Table 2 1-, 3-, and 5-year RFS and OS rate before and after PSM

Time	Before PSM			After PSM		
	RFA	MWA	P value	RFA	MWA	P value
RFS rate, %						
1-year	50	40	0.008	51	41	0.01
3-year	34	24	0.004	33	24	0.01
5-year	16	12	0.13	15	13	0.53
OS rate, %						
1-year	95	95	0.91	94	95	0.56
3-year	84	85	0.81	88	85	0.31
5-year	55	39	<0.0001	53	39	0.001

RFS, recurrence-free survival; OS, overall survival; PSM, propensity score matching; RFA, radiofrequency ablation; MWA, microwave ablation.

GGT (HR: 1.00, 95% CI: 1.00–1.01, P<0.0001), HBsAg (HR: 1.00, 95% CI: 1.00–1.00, P=0.02) were independent risk factors for RFS (*Table 5*). Moreover, independent risk factors for OS were Child-Pugh (HR: 1.52, 95% CI: 1.09–2.12, P=0.01), lymphocyte (Lym) (HR: 0.73, 95% CI: 0.57–0.95, P=0.02), GGT (HR: 1.00, 95% CI: 1.00–1.00, P=0.01) and treatment modality (HR: 0.69, 95% CI: 0.50–0.96, P=0.02) (*Table 6*).

Discussion

HCC remains a global health challenge with increasing morbidity and mortality rates (1,2,22). 80–90% of patients with HCC develop from cirrhosis, and the presence of cirrhosis also worsens the prognosis of HCC (5,23). Consequently, further study is needed in cirrhotic HCC patients. Ablation is one of the preferred treatments for early-stage HCC, and the effectiveness and safety have been well demonstrated in clinical trials (24-26). RFA is well-established while MWA is gaining popularity (27,28). With the use of 1:1 PSM, our study revealed that RFA had a lower recurrence rate and a higher survival rate compared to MWA in patients with HCC associated with cirrhosis.

The most common cause of cirrhotic HCC is hepatitis B infection in China (29). Viral infections lead to exposure of the liver to environmental risk factors that induce chronic inflammation. Besides, inflammation is further aggravated by the dysbiosis of intestinal flora, the accumulation of extracellular matrix, and hepatic fibrosis, which destroys the normal physiological structure of the liver. Eventually, cirrhosis develops in the liver, and cirrhosis is the soil in which HCC occurs (22,30,31). Additionally, cirrhosis itself is the eleventh most common cause of death in the world, and its decompensation and tumor recurrence lead to an increased mortality rate, even though radical treatment of early-stage HCC has been achieved (32).

Previous studies have proved that MWA and RFA have equivalent efficacy, local recurrence, and survival rate (33-35). Nevertheless, it is inconclusive whether there is a variance in efficacy between RFA and MWA in patients with cirrhotic HCC. The gold standard for assessing treatment is the RCT which can be difficult in clinical realities. Hence, PSM, which can reduce the confounding bias of baseline characteristics, was applied in our study, making the two groups more comparable after PSM. Survival analyses before PSM suggested that RFA was superior to MWA in terms of both RFS and OS, and results after PSM further supported our view. Moreover, we found that there was a difference in RFS rates between RFA and MWA at 1- and 3-year (P<0.05) and a concordant RFS rate at 5-year. What's more, OS was consistent at 1- and 3-year and higher at 5-year for RFA than for MWA (P<0.001), which might be due to the fact that MWA is highly dependent on tissue properties (water content) and does not control heat propagation as well as RFA (36,37). In patients with cirrhosis, as a consequence of liver fibrosis, the tissue properties are altered in contrast with normal liver, and the water content decreases, leading to a decrease in the efficacy of MWA and an increase in the relapse rate. For the increase in long-term mortality, it might be because of the

Table 3 Univariate and multivariate Cox hazards analysis for RFS before PSM

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.02 (1.01–1.03)	0.002	1.02 (1.01–1.03)	<0.0001
Sex	0.67 (0.54–0.84)	0.001	0.78 (0.61–0.99)	0.04
Antiviral	0.82 (0.69–0.97)	0.21		
Diabetes	1.15 (0.94–1.40)	0.17		
ALD	1.29 (1.05–1.57)	0.01	1.12 (0.91–1.38)	0.29
Child-Pugh	1.10 (0.91–1.33)	0.30		
BCLC (0 *vs.* B)	0.30 (0.24–0.39)	<0.0001	0.57 (0.36–0.91)	0.01
BCLC (A *vs.* B)	0.48 (0.39–0.59)	<0.0001	0.69 (0.50–0.95)	0.02
Tumor number	1.86 (1.56–2.21)	<0.0001	1.36 (1.03–1.80)	0.02
Tumor size	1.77 (1.49–2.10)	<0.0001	1.29 (1.03–1.63)	0.02
Etiology	0.99 (0.92–1.06)	0.76		
Neu	0.99 (0.95–1.04)	0.66		
Lym	0.94 (0.83–1.07)	0.33		
PLT	1.00 (0.99–1.00)	0.55		
TBIL	1.00 (0.99–1.00)	0.92		
GGT	1.00 (1.00–1.00)	<0.0001	1.00 (1.00–1.01)	<0.0001
Fib	1.03 (0.94–1.13)	0.31		
HBsAg	1.00 (1.00–1.00)	0.005	1.00 (1.00–1.00)	0.008
ALT	1.00 (0.99–1.00)	0.10		
AST	1.00 (1.00–1.01)	0.03	0.99 (0.99–1.01)	0.68
AFP	1.00 (1.00–1.00)	0.30		
Ablative modality (RFA/MWA)	0.78 (0.66–0.93)	0.005	0.96 (0.79–1.16)	0.66

RFS, recurrence-free survival; PSM, propensity score matching; ALD, alcoholic liver cancer; BCLC, Barcelona Clinic Liver Cancer; Neu, neutrophil; Lym, lymphocyte; PLT, platelet; TBIL, total bilirubin; GGT, gamma glutamyl transferase; Fib, fibrous protein; HBsAg, hepatitis B surface antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AFP, alpha fetoprotein; RFA, radiofrequency ablation; MWA, microwave ablation; HR, hazard ratio; CI, confidence interval.

fact that the actual ablation area of MWA may be larger as tissue shrinkage increases, yet it is not apparent on imaging immediately after ablation (37-39). To achieve complete ablation, the ablation border was larger than the tumor border by 0.5 cm. Since MWA is not apparent on imaging immediately after ablation, the unnecessary ablation area was increased. Beyond, the MWA ablation region is more elongated and elliptical than RFA [which has a lower short-to-long diameter ratio (ALR)]. Within the rugby ball ablation zone, additional areas of healthy tissue are similarly ablated unnecessarily, which gives rise to larger ablation volumes and higher complication rates. In patients with cirrhotic HCC, especially in the decompensated stage with insufficient hepatic functional reserve, the more normal liver tissue is ablated, and the relative reduction in the volume of the normal liver may accelerate hepatic failure and result in increased mortality. In-depth studies are needed to demonstrate the underlying mechanisms.

Within PSM, age, tumor size, GGT, and HBsAg were found to be independent risk factors for RFS, whereas Child-Pugh, lymphocyte, GGT, and treatment modality (RFA/MWA) were independent risk factors for

Table 4 Univariate and multivariate Cox hazards analysis for OS before PSM

Characteristic	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.02 (1.01–1.03)	0.04	1.02 (0.99–1.03)	0.06
Sex	0.72 (0.58–1.07)	0.10		
Antiviral	0.70 (0.52–0.93)	0.01	0.78 (0.58–1.04)	0.09
Diabetes	1.20 (0.84–1.68)	0.32		
ALD	1.40 (0.99–1.99)	0.05		
Child-Pugh	1.56 (1.15–2.12)	0.004	1.47 (1.08–2.01)	0.01
BCLC (0 *vs.* B)	0.30 (0.19–0.48)	<0.0001	0.55 (0.25–1.24)	0.15
BCLC (A *vs.* B)	0.69 (0.49–0.97)	0.03	0.97 (0.59–1.60)	0.91
Tumor number	1.90 (1.43–2.54)	<0.0001	1.45 (0.91–2.29)	0.11
Tumor size	1.61 (1.20–2.15)	0.001	1.16 (0.79–1.72)	0.45
Etiology	1.06 (0.94–1.19)	0.33		
Neu	0.96 (0.88–1.04)	0.95		
Lym	0.74 (0.58–0.94)	0.01	0.78 (0.61–1.01)	0.05
PLT	0.99 (0.99–1.00)	0.21		
TBIL	1.00 (0.99–1.02)	0.38		
GGT	1.00 (1.00–1.01)	<0.0001	1.00 (1.00–1.01)	0.01
Fib	1.01 (0.86–1.19)	0.92		
HBsAg	1.00 (1.00–1.00)	0.64		
ALT	1.00 (0.99–1.01)	0.28		
AST	1.01 (1.00–1.02)	0.002	1.00 (0.99–1.01)	0.33
AFP	1.00 (1.00–1.00)	0.96		
Ablative modality (RFA/MWA)	0.63 (0.47–0.84)	0.002	0.71 (0.52–0.97)	0.02

OS, overall survival; PSM, propensity score matching; ALD, alcoholic liver cancer; BCLC, Barcelona Clinic Liver Cancer; Neu, neutrophil; Lym, lymphocyte; PLT, platelet; TBIL, total bilirubin; GGT, gamma glutamyl transferase; Fib, fibrous protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBsAg, hepatitis B surface antigen; AFP, alpha fetoprotein; RFA, radiofrequency ablation; MWA, microwave ablation; HR, hazard ratio; CI, confidence interval.

OS. Age is associated with liver functional reserve and risk of postoperative complications (40,41). Tumor size is a feature of tumor burden. One study displayed that tumor size was associated with hypofractionation and higher survival rates (42,43). The level of serum GGT, a metabolite of glutathione, elevates with the process of liver hepatocarcinogenesis and promotes tumor progression in animal HCC models (44,45). HBsAg can promote the proliferation of HCC cells through the Sec/pi3k/Akt pathway, and HBsAg negative patients have better OS and RFS than positive patients (46,47). Previous researches have shown that the lower Child-Pugh score, the higher rate of postoperative complications in advanced cirrhosis, with mortality rates of 10%, 17%, and 63% in patients with cirrhotic HCC in Child-Pugh A, B, and C grades after surgery, respectively (48,49). As we all know, inflammation promotes poor prognosis of HCC through inducing lymphopenia (50,51).

Limitations of our study have to be noted. First, our study was a single-center retrospective study that the

Table 5 Univariate and multivariate Cox hazards analysis for RFS after PSM

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.01 (1.00–1.02)	0.01	1.01 (1.00–1.03)	0.01
Sex	0.67 (0.50–0.88)	0.004	0.81 (0.60–1.09)	0.16
Antiviral	0.80 (0.65–0.97)	0.02	0.88 (0.71–1.08)	0.21
Diabetes	1.18 (0.92–1.51)	0.20		
ALD	1.42 (1.11–1.80)	0.004	1.20 (0.93–1.56)	0.16
Child-Pugh	0.99 (0.79–1.25)	0.94		
BCLC (0 *vs.* B)	0.58 (0.49–0.69)	<0.0001	0.80 (0.60–1.08)	0.14
BCLC (A *vs.* B)	0.93 (0.82–1.07)	0.31	0.95 (0.82–1.09)	0.45
Tumor number	1.73 (1.42–2.16)	<0.0001	1.30 (0.91–1.86)	0.14
Tumor size	1.76 (1.44–2.15)	<0.0001	1.33 (1.01–1.75)	0.04
Etiology	0.96 (0.87–1.01)	0.38		
Neu	1.02 (0.97–1.07)	0.45		
Lym	1.00 (0.87–1.16)	0.98		
PLT	1.00 (0.99–1.00)	0.31		
TBIL	1.00 (0.99–1.01)	0.89		
GGT	1.00 (1.00–1.00)	<0.0001	1.00 (1.00–1.01)	<0.0001
Fib	1.04 (0.93–1.16)	0.49		
HBsAg	1.00 (1.00–1.00)	0.008	1.00 (1.00–1.00)	0.02
ALT	1.00 (0.99–1.00)	0.13		
AST	1.01 (1.00–1.01)	0.02	0.99 (0.99–1.01)	0.87
AFP	1.00 (1.00–1.00)	0.32		
Ablative modality (RFA/MWA)	0.81 (0.67–0.99)	0.03	0.91 (0.74–1.12)	0.35

RFS, recurrence-free survival; PSM, propensity score matching; ALD, alcoholic liver cancer; BCLC, Barcelona Clinic Liver Cancer; Neu, neutrophil; Lym, lymphocyte; PLT, platelet; TBIL, total bilirubin; GGT, gamma glutamyl transferase; Fib, fibrous protein; HBsAg, hepatitis B surface antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AFP, alpha fetoprotein; RFA, radiofrequency ablation; MWA, microwave ablation; HR, hazard ratio; CI, confidence interval.

selection bias inevitably exists. Subsequently, the main cause of cirrhosis in China is hepatitis B infection, and it is not clear whether this conclusion can be extrapolated to patients with HCC of other etiologies. Besides, we did not monitor the specifics of tumor recurrence, which will have to be further explored in future studies. Yet, there are few studies on minimally invasive treatment options for patients with cirrhotic HCC so far. We established a large cohort (N=800) of cirrhotic HCC that used ablation therapy with up to eight follow-up to find the appropriate minimally invasive treatment for HCC patients with cirrhosis.

Conclusions

For patients with HCC associated with cirrhosis, RFA can provide a better prognosis than MWA, with lower recurrence and mortality rate. Therefore, RFA should be the preferred treatment modality of the choice for cirrhotic HCC patients who require minimally invasive therapy.

Table 6 Univariate and multivariate Cox hazards analysis for OS after PSM

Characteristic	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.01 (0.99–1.03)	0.12		
Sex	0.71 (0.46–1.10)	0.12		
Antiviral	0.73 (0.54–0.99)	0.04	0.79 (0.58–1.09)	0.16
Diabetes	1.22 (0.83–1.80)	0.30		
ALD	1.40 (0.95–2.05)	0.08	1.23 (0.82–1.83)	0.31
Child-Pugh	1.62 (1.17–2.25)	0.003	1.52 (1.09–2.12)	0.01
BCLC (0 *vs.* B)	0.49 (0.36–0.68)	<0.0001	0.42 (0.17–1.03)	0.05
BCLC (A *vs.* B)	1.19 (0.96–1.48)	0.11		
Tumor number	1.84 (1.35–2.16)	<0.0001	1.22 (0.73–2.03)	0.44
Tumor size	1.51 (1.12–2.49)	0.009	1.03 (0.68–1.56)	0.90
Etiology	1.07 (0.93–1.23)	0.33		
Neu	0.98 (0.90–1.07)	0.66		
Lym	0.72 (0.55–0.93)	0.01	0.73 (0.57–0.95)	0.02
PLT	0.99 (0.99–1.00)	0.45		
TBIL	1.00 (0.99–1.02)	0.36		
GGT	1.00 (1.00–1.00)	<0.0001	1.00 (1.00–1.01)	0.01
Fib	0.98 (0.83–1.17)	0.84		
HBsAg	1.00 (1.00–1.00)	0.75		
ALT	1.00 (0.99–1.01)	0.22		
AST	1.02 (1.01–1.02)	0.001	1.00 (0.99–1.02)	0.14
AFP	1.00 (1.00–1.00)	0.94		
Ablative modality (RFA/MWA)	0.67 (0.49–0.92)	0.01	0.69 (0.50–0.96)	0.02

OS, overall survival; PSM, propensity score matching; ALD, alcoholic liver cancer; BCLC, Barcelona Clinic Liver Cancer; Neu, neutrophil; Lym, lymphocyte; PLT, platelet; TBIL, total bilirubin; GGT, gamma glutamyl transferase; Fib, fibrous protein; HBsAg, hepatitis B surface antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AFP, alpha fetoprotein; RFA, radiofrequency ablation; MWA, microwave ablation.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1939/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1939/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1939/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Beijing You'an Hospital, Capital Medical University (No. 2022/111). A waiver of patient informed consent was granted since the Ethics Committee considered the study to be low-risk.

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