Image-Guided Microwave Ablation of Hepatocellular Carcinoma (≤5.0 cm): Is MR Guidance More Effective Than CT Guidance?

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Abstract

Background

Percutaneous tumor ablation is usually performed using computed tomography (CT) or ultrasound (US) guidance, although reliable visualization of the target tumor may be challenging. MRI guidance can provide more reliable visualization of the target tumor and allow for multiplanar capabilities, making it the modality of choice. Due to the lack of comparative studies of microwave ablation(MWA) guided by different images. This study retrospectively compared the effectiveness of computed tomography (CT)-guided versus magnetic resonance (MR)-guided MWA for hepatocellular carcinoma (HCC≤5.0 cm).

Methods

In this retrospective study, 47 patients and 54 patients received MWA under the guidance of CT and MR, respectively. The inclusion criteria were a single HCC≤5.0 cm or a maximum of three. The local tumor progression (LTP), overall survival (OS), prognostic factors for local progression, and safety of this technique were assessed.

Results

All procedures were technically successful. The complication rates of the two groups were significantly different with respect to liver abscess and pleural effusion ($P<0.05$). The mean LTP was 44.264 months in the CT-guided group versus 47.745 months in the MR-guided group of HCC ($P = 0.629$, log-rank test). The mean OS was 56.772 months in the patients who underwent the CBCT-guided procedure versus 58.123 months in those who underwent the MR-guided procedure ($P = 0.630$, log-rank test). Multivariate Cox regression analysis further illustrated that tumor diameter (<3 cm) and the number of lesions (single) were important factors affecting LTP and OS.

Conclusions

CT-guided and MR-guided MWA are safe and effective in the treatment of HCC with a diameter of less than 5 cm. Furthermore, MR-guided MWA could reduce the incidence of complications.

Background

The optimal treatment choice for hepatocellular carcinoma (HCC ≤ 5 cm) is a very complex issue, as the selection of treatment requires careful consideration of multiple factors, including tumor location, liver function, and physical status[1, 2]. The treatments for early HCC include liver transplantation, surgical resection, and local ablation. However, due to the high cost and shortage of donor livers, many patients are not candidates for these radical treatment options. Therefore, most centers regard thermal ablation as the main treatment for early-stage HCC[3, 4, 5]. Of note, the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) also use local ablation as the first-line guide for early HCC when patients are not eligible for surgical treatments or as a bridge to transplantation. At present, CT-guided thermal ablation is generally accepted by most clinical centers[6, 7, 8, 9]. However, unenhanced CT during the ablation process cannot clearly demonstrate the boundary of ablated lesions, and multiple uses of contrast agents will undoubtedly increase the burden on the kidneys. Therefore, magnetic resonance imaging (MR) is a promising MWA guidance method that has excellent tissue resolution, no ionizing radiation during treatment, and imaging capabilities in any direction.

This study retrospectively analyzed and summarized the results of MWA for HCC ($\leq$ 5.0 cm) under the guidance of CT and MR, and Cox's regression model was used to analyze the factors affecting LPT and OS. The results are summarized as follows.

Methods

Patients

This was a retrospective cohort study conducted in a single center approved by the institutional review board. In this retrospective study, we included 47 patients (55.8 ± 8.9 years; range 41–69 years) who received CT-guided MWA for HCC and 54 patients (53.2 ± 6.5, range 43–67 years) who received MWA under MR guidance (median age 56 years; range 36–69 years). The patient characteristics are shown in (Table 1). The inclusion and exclusion criteria are listed in (Table 2).

Table 1
Patient characteristics

Characteristics	**CT-guided (*n* = 47)**	**MR-guided (*n* = 54)**	***P* value**
Age (y)†	55.8 ± 8.9	53.2 ± 6.5	0.367[‡]
Sex			0.176[*]
Male	31	43	
Female	16	11	
ECOG performance status			0.230[*]
0	29	26	
1	18	28	
Etiology			0.086[§]
Hepatitis B	32	44	
Hepatitis C	4	6	
Alcohol	9	2	
Unknown	2	2	
Child–Pugh class			0.217[*]
A	33	31	
B	14	23	
Location of tumor			0.245[*]
Ordinary locations	23	33	
Hepatic dome	12	7	
Close to the heart/diaphragm/hepatic hilum	12	14	
a-Fetoprotein level (ng/mL)			0.407[*]
□200	28	37	
□200	19	17	

Note.—Unless indicated, data are numbers of patients, and numbers in parentheses are percentages. ECOG = Eastern Cooperative Oncology Group.*Pearson χ2 test was used. †Data are mean ± standard deviation. ‡Independent-samples t test was used. §Fisher exact test was used.

Characteristics	CT-guided (*n* = 47)	MR-guided (*n* = 54)	*P* value
Tumor diameter(cm)			0.163*
3	28	24	
3⩾,<5	19	30	
Tumor number			0.686*
Single(1)	26	33	
2–3	21	21	
Duration of ablation (min)	11.2 ± 5.4	9.7 ± 3.2	0.003‡
Generator power (watts)	57.3 ± 8.5	54.5 ± 6.3	0.047‡

Note.—Unless indicated, data are numbers of patients, and numbers in parentheses are percentages. ECOG = Eastern Cooperative Oncology Group.*Pearson χ2 test was used. †Data are mean ± standard deviation. ‡Independent-samples t test was used. §Fisher exact test was used.

Table 2
Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
1 Age range: 18–75 years	Age < 18 or > 75 years
2 HCC diagnosed according to EASL standards	No pathology or image evidence
3 Child–Pugh grade A or B	Child–Pugh grade C
3 BCLC grades are A and B	BCLC grades are C
4 ECOG score ≦ 2	ECOG score2
4 Liver lesions ≤ 3	The liver lesions number3
5 Single tumor diameter < 5 cm	Single tumor diameter ≥ 5
6 The expected survival time3 months	The expected survival time ≤ 3 months
7 No portal vein thrombus	Portal vein thrombus
8 No extrahepatic metastases	Extrahepatic metastases
9 PLT 40 × 109/L or PT ≤ 25 s	PLT ≤ 40 × 109/L or PT 25 s

European Association for the Study of the Liver, EASL; Eastern Cooperative Oncology Group, ECOG; platelet, PLT; prothrombin time: PT; HCC, small hepatocellular carcinoma

Preparation before treatment

All procedures were performed by an alternating team of two trained interventional radiologists with 8–10 years of experience in ablation procedures. The patient's position was determined according to the preoperative puncture plan on CT/MR. All patient treatment procedures were performed under local anesthesia.

CT-guided ablation procedure protocol

Under the guidance of CT, follow the predesigned procedure for lesion site puncture. The microwave ablation probe (ECO-100AI10, ECO Microwave System Co, Nanjing, China) was inserted after achieving the best insertion angle and depth, and 57.3 ± 8.5 (watts) of ablation was used. The time settings were typically 11.2 ± 5.4 minutes. After completing the ablation, immediately use enhanced CT to assess the ablation area, to provide supplementary treatment for the residual tumor after ablation, and to evaluate immediate complications.

MR-guided ablation procedure protocol

In this study, the MR-compatible MWA apparatus (2450 MHz, ECO Medical Instrument Co., Ltd. Nanjing, China) was used, and the MWA procedure was guided by a 3.0 T dual gradient MR scanner (Magnetom Verio 3.0T scanner, Siemens Healthineers, Germany) with a closed bore (inner diameter, 70 cm). After marking with the cod liver oil capsule matrix on the body surface, a standard MR protocol was carried out to locate intrahepatic lesions. Under the guidance of MR, a microwave probe (ECO-100AI13, 1.8 mm, 15 cm, Co., Ltd. Nanjing, China) was inserted into the tumor center, and multiple scans were carried out to confirm that the applicator tip was beyond the distal tumor 0.5–1 cm. Additionally, tumors at each site were ablated at 54.5 ± 6.3 watts for 9.7 ± 3.2 minutes **(Fig. 1/2)**. During ablation, a series of monitoring T2 Haste and T1 Vibe sequences were performed continuously to monitor the ablated scope every 16 s. If MR showed that the ablation area did not cover 110% of the lesion, the probe was requisitioned, and multiple overlapping ablations were needed. The MR scanning sequences and parameters used in our study are listed in (Table 3**).**

Table 3
MR scanning sequences and parameters

Section	Sequence	TE (ms)	TR (ms)	Slice thicknes (mm)	Matrix	Flip angle	Band Width (Hz/pixel)
Transverse section	T1 Vibe	1.93	4.56	3.3	216 × 288	9.0	400
Transverse section	T2 Haste	106	1000	4.5	137 × 256	180	781
Transverse section	Diffusion	83	7100	5.0	192 × 144	90	1670
Coronal section	T1 vibe	2.46	6.11	3.0	179 × 256	9.0	410
Sagittal	T2 Haste	106	1000	4.0	137 × 256	180	781

Definitions and Evaluation of Data

The study endpoints were OS, LTP, and radiological response. OS was defined as the interval between initial treatment and death from any cause. LTP was defined as the detection of nodular enhancement in the adjacent ablation area, based on follow-up imaging data. Radiological response was evaluated according to the modified response evaluation criteria in solid tumors (mRECIST; 2020 edition) 4 weeks after MWA.

Follow-up

One month after MWA, laboratory tests including tumor markers, i.e., alpha-fetoprotein (AFP) and liver function test, as well as imaging studies, i.e., enhanced CT or enhanced MR, were performed. Subsequently, the patients were followed-up every 3 months to monitor the recurrence/ residual after MWA. Treatment response was evaluated using the mRECIST (2020 edition). When the patient did not achieve complete response (CR), additional treatment was performed until the achievement of CR according to the physicians' discretion.

Statistical analysis

Statistical analysis was conducted using the statistical software SPSS 22.0 (SPSS Inc., Chicago, IL, USA). To determine significant differences between the two groups, continuity correction and independent-samples t, Pearson $\chi 2$, and Fisher exact tests were used. Categorical variables are expressed as numbers or percentages (%), and continuous variables are expressed as the mean ± standard deviation (SD). Comparisons between two groups were conducted using a chi-square test or Wilcoxon rank-sum test.

Kaplan–Meier survival curves were used for survival analysis. Univariate and multivariate Cox proportional hazards regression analyses were used to predict prognostic factors of LTP and OS. A $P < 0.05$ was considered for significant differences.

Results

Patient characteristics

A total of 235 patients with HCC underwent CT-guided MWA or MR-guided MWA during the study period. A total of 134 patients were excluded from the study because they met the exclusion criteria. As a result, 101 patients with HCC ≤ 5.0 cm were included in the present study (CT-guided, n = 47; MR-guided, n = 54) **(Fig. 3)**. There were no significant differences in age, sex, ECOG score, etiology, Child–Pugh classification, tumor location, or tumor diameter between the two types of guidance. For patients in the CT-guided group and in the MR-guided group, the mean energy of each tumor was 57.3 ± 8.5 watts and 54.5 ± 6.3 watts, respectively, and the difference between the two groups was statistically significant ($P = 0.047$). Additionally, the mean ablation duration of each tumor in the two MWA process groups was 11.2 ± 5.4 and 9.7 ± 3.2, respectively ($P = 0.003$).

Safety of CT guidance versus safety of MR guidance

Postoperative pain and fever (with/without treatment) were the most common adverse events after treatment (Table 4). With four exceptions, all adverse events and complications were CTCAE grade 1 or 2 (mild symptoms, no or local/noninvasive intervention indicated) or interventional radiology society grade A or B (no or nominal treatment, no consequences). Of the exceptions, the incidences of liver abscess, asymptomatic perihepatic fluid, pleural effusion and subcapsular hepatic hemorrhage under CT guidance were 9 (6%), 2 (4%), 8 (6%) and 3 (4%), respectively. The corresponding MR-guided complication rates were 2 (9%), 1 (2%), 1 (2%) and 1 (2%). Of note, there were significant differences in the incidence of liver abscess ($P = 0.022$) and pleural effusion ($P = 0.011$) between the two guidance methods. Second, patients with subhepatic hemorrhage need to undergo interventional embolization; patients with pleural effusion need to be treated with auxiliary thoracic drainage, and these complications will undoubtedly prolong the patient's hospital stay. None of the patients had life-threatening complications during or after treatment.

Table 4
Adverse events and complications

Categories	**CT-guided(n = 47)**		**MR-guided(n = 54)**		***P* Value**
	Grades				
Adverse events	**CTCAE**		**CTCAE**		
Fever, maximum 38 °C, no treatment		17(36)		23(43)	0.546*
Fever, 38 °C,treatment		13(28)		21(39)	0.293*
Nausea or vomiting		7(15)		6(11)	0.767*
Mild pain, requiring nonopioid oral analgesic treatment		24(51)		31(57)	0.553*
Moderate pain, requiring opioid oral analgesic treatment		18(38)		21(39)	1.000*
Mild liver dysfunction, requiring conservative treatment		32(68)		43(80)	0.254*
complications					
Liver abscess		9(6)		2(9)	0.022*
Asymptomatic perihepatic fluid		2(4)		1(2)	0.596§
Pleural effusion		8(6)		1(2)	0.011*
Subcapsular liver hemorrhage		3(4)		1(2)	0.336§
National Cancer Institute Common Terminology Criteria for Adverse Event (CTCAE version 4.03)					
Data are numbers of events. Data in parentheses are percentages.					

Survival between two groups

Kaplan–Meier local tumor progression (LTP) and overall survival (OS) of the CT-guided group versus the MR-guided group. The mean LTP was 44.264 months (95% CI: 39.484, 49.043) in the CT-guided group versus 47.745 months (95% CI: 43.840, 51.650) in the MR-guided group ($P = 0.629$, log-rank test). The mean OS was 56.772 months (95% CI: 53.858, 59.889) in the patients who underwent CT-guided procedures versus 58.123 months (95% CI: 56.375, 59.889) in those who underwent MR-guided procedures ($p = 0.630$, log-rank test). The 1-, 3-, and 5-year LTP rates in patients who underwent CT-guided procedures were 93.6%, 69.5% and 30.7%, respectively, and the 1-, 3- and 5-year OS rates were 100.0%, 91.3% and 75.8%, respectively. The 1-, 3-, and 5-year LTP rates in MR-guided procedures were 96.3%, 81.2% and 28,7%, respectively, and the 1-, 3- and 5-year OS rates were 100.0%, 96.2% and 79.4%, respectively. **(Fig. 5)**

Factors affecting OS and LTP

Univariate Cox proportional hazard regression indicated that MWA under CT guidance and MR guidance ($P = 0.632$ and $P = 0.633$, respectively) was not associated with longer LTP or OS, while tumor diameter (3⩾, < 5) (both $P < 0.05$), tumor location (challenging locations) (both $P < 0.005$) and the number of lesions (2–3 lesions) (both $P < 0.001$) were all related to shorter LTP and OS (Table 5). Additionally, multivariate Cox regression revealed that the guiding method of MWA therapy did not have a significant impact on the patient's LTP or OS, and the regression model further showed that the tumor diameter (< 3 cm) and the number of lesions (single) could independently predict better LTP and OS (both $P < 0.05$). More specifically, the mean LTP was 52.574 months (95% CI: 50.025, 55.124) in the patients with a single tumor versus 36.604 months (95% CI: 31.464, 41.743) in the 2–3 lesions of HCC ($P = 0.000$, log-rank test). The mean OS was 59.934 months (95% CI: 59.847, 60.021) in patients with a single tumor versus 53.787 months (95% CI: 50.053, 57.520) in patients with 2–3 lesions of HCC ($P = 0.000$, log-rank test). The mean LTP was 50.944 months (95% CI: 50.025, 55.124) in the patients with tumor diameter (< 3 cm) versus 41.042 months (95% CI: 31.464, 41.743) in the tumor diameter (3⩾, < 5) ($P = 0.000$, log-rank test). The mean OS was 59.232 months (95% CI: 58.052, 60.413) in the patients with tumor diameter (< 3 cm) versus 55.653 months (95% CI: 52.602, 58.705) in the tumor diameter (3⩾, < 5) ($P = 0.023$, log-rank test) **(Fig. 5 and Fig. 6).**

Table 5
Factors affecting PFS and OS

Parameters	LTP			*P*	OS			*P*
	HR	*95%*CI			HR	*95%*CI		
		Lower	Higher			Lower	Higher	
Univariate Cox's regression								
Age (> 60 vs ≤ 60)	0.217	0.836	2.197	1.356	2.825	1.085	7.356	0.033
AFP (> 200 vs ≤ 200 ng/mL)	0.138	0.887	2.371	1.451	1.496	0.619	3.613	0.371
Tumor diameter (3⩾,<5 vs < 3 cm)	2.644	1.596	4.380	**0.000**	2.865	1.100	7.460	**0.031**
Tumor location (challenging locations vs ordinary locations)	3.399	2.065	5.593	**0.000**	4.604	1.759	12.050	**0.002**
Number of lesion (single VS 2–3 lesions)	3.282	1.995	5.399	**0.000**	9.109	3.029	27.395	**0.000**
Child–Pugh stage (B vs A)	1.180	0.723	1.923	0.508	1.337	0.554	3.228	0.519
Guidance system (CT vs MR)	0.888	0.547	1.443	0.632	0.808	0.336	1.941	0.633
Multivariate Cox's regression								
Age (> 60 vs ≤ 60)	1.006	0.606	1.672	0.980	2.337	0.846	6.454	0.101
AFP (> 200 vs ≤ 200 ng/mL)	1.312	0.775	2.220	0.312	0.971	0.387	2.434	0.950
Tumor diameter (3⩾,<5 vs < 3 cm)	2.869	1.621	5.081	**0.000**	3.388	1.100	10.431	**0.033**
Tumor location (challenging locations vs ordinary locations)	2.848	1.621	5.273	**0.001**	2.646	0.868	8.070	0.087
Number of lesion (single VS 2–3 lesions)	1.890	1.053	3.391	**0.033**	9.287	2.649	32.567	**0.000**
Child–Pugh stage (B vs A)	1.429	0.816	2.505	0.212	2.393	0.843	6.789	0.111
Guidance system (CT vs MR)	0.824	0.487	1.393	0.470	0.419	0.143	1.223	0.101
Note—general anesthesia (GA) and local anesthesia (LA) ; challenging locations(Hepatic dome, Close to the heart/diaphragm/hepatic hilum)								

Discussion

In the field of therapeutics, HCC in the early stage has three major types of curative treatment: hepatectomy, liver transplantation, and percutaneous ablation. Each method has limitations that need to be partially overcome to provide curative treatment for the highest number of patients and avoid premature use of palliative treatment for HCC. According to the guidelines of the EASL and the AASLD [10, 11, 12], local thermal ablation has been considered to be the first-line treatment option for patients with small HCC when the patient has comorbidities, liver dysfunction or limited surgical resources. Percutaneous ablation includes a vast range of techniques that have changed over the last 10 years, enabling treatment of an increasing number of patients, with improved efficacy in local control. Of note, RFA and MWA are the most commonly used thermal ablation methods for hepatic malignancies[13, 14, 15]. In comparison with RFA, MWA is a new method that has similar benefits of the RFA, such as a larger volume of cellular necrosis, procedure time reduction, and bring the target lesion to a higher temperature in a shorter period of time, and is less susceptible to variation in the morphology of the treatment zone because of heat-sink effects from adjacent vasculature[16]. Additionally, a matching analysis of the propensity score between hepatic resection (HRN) and MWA therapy for single HCC $\leq$ 5 cm confirmed that the 5-year and 10-year OS rates of HRN were 76% and 47%, respectively, and the corresponding OS rates of MWA were 77% and 48% (P = 0.865)[17]. Another meta-analysis revealed that MWA may be superior to HRN, as it is as effective as HRN in terms of overall survival, disease-free survival, and tumor recurrence and is associated with fewer complications[18]. Therefore, MWA has high value for the treatment of HCC.

Rempp et al observed that all tumor progression occurred at the edge of the ablation zone[19], and previous research has repeatedly dealt with the importance of the safety margin of tumor ablation[20, 21, 22]. Although the mean safety margin based on the measured tumor diameter and ablation zone seemed to be sufficient, insufficient focal margins were detected in various cases, which may be the cause of local progression. Worth noting, although CT can meet the treatment requirements of MWA and provide accurate imaging, the differentiation between vital tumor tissue and the ablation zone is only possible for a limited time after application of a contrast agent. Recently, MR-guided MWA has been commonly used as a minimally invasive therapy for the treatment of liver malignancies, which can clearly obtain the boundary between the burn range and normal tissue without the use of contrast agents[19, 23, 24, 25]. Unfortunately, controlled studies on MR-guided MWA with HCC are extremely rare. Clasen et al. retrospectively compared the technical effects of CT-guided and MR-guided RFA in the treatment of HCC and found that these two sets of guidance are both locally effective methods for the treatment of HCC, and research further revealed that MR-guided RFA may reduce the number of required sessions for complete tumor treatment[26]. In this research, univariate Cox proportional hazard regression indicated that MWA under CT guidance and MR guidance (P = 0.632 and P = 0.633, respectively) had no correlation with longer LTP and OS. However, tumor diameter (3⩾, < 5), tumor location (challenging locations) and the number of lesions (2–3 lesions) were all related to shorter LTP and OS (both $P < 0.05$). In addition, multivariate Cox regression further revealed that MR-guided MWA had no significant effect on patients'

LTP or OS (both $P < 0.05$), but the incidence of complications in the MR-guided procedure was relatively lower ($P < 0.05$).

There are several limitations of our research. First, the real-time MR thermometry technique was not used in this study due to software limitations. In addition, the duration of MR-guided MWA is relatively longer than that of conventional CT-guided treatment. However, we have already used more optimized sequences to reduce the duration of the procedures and improve treatment efficiency. Finally, this is a single-center retrospective study involving a small number of cases, which may have led to biased results. Thus, further studies need to be combined with prospective multicenter studies and extend the follow-up period to reduce the risk of bias.

Conclusion

In short, we have shown that both CT-guided and MR-guided MWA can safely and successfully treat HCC (≤5.0 cm) with high technical efficiency, but MR-guided MWA could reduce the occurrence of complications.

Abbreviations

MR Magnetic resonance

CT Computed tomography

MWA Microwave ablation

HCC Hepatocellular carcinoma

EASL European Association for the Study of the Liver

AASLD American Association for the Study of Liver Diseases

LTP A local tumor progression

OS Overall survival

RFA Radiofrequency ablation

CA Cryoablation

AFP Alpha-fetoprotein

HRN hepatic resection

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the institutional review board of the First Affiliated Hospital of Zhengzhou University. All participants gave written informed consent that their data can be used for scientific purposes.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated for this study are available on request to the corresponding author.

Competing interests

The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

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Author Contributions

ZL: primary investigator, involved in study planning, data collection, data analysis and interpretation, and manuscript writing. CW, XZ, GS, YL, and JL: involved in study planning, data collection, data analysis and interpretation, and proofreading of manuscript. DC and XH: involved in study planning, data collection, data analysis and interpretation, manuscript writing, and proofreading of manuscript. All authors provided approval for publication of the content.

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Tables

Table 1. Patient characteristics

Characteristics	CT-guided (n=47)	MR-guided (n=54)	P value
Age (y)†	55.8±8.9	53.2±6.5	0.367‡
Sex			0.176*
Male	31	43	
Female	16	11	
ECOG performance status			0.230*
0	29	26	
1	18	28	
Etiology			0.086§
Hepatitis B	32	44	
Hepatitis C	4	6	
Alcohol	9	2	
Unknown	2	2	
Child–Pugh class			0.217*
A	33	31	
B	14	23	
Location of tumor			0.245*
Ordinary locations	23	33	
Hepatic dome	12	7	
Close to the heart/diaphragm/hepatic hilum	12	14	
a-Fetoprotein level (ng/mL)			0.407*
□200	28	37	
□200	19	17	
Tumor diameter(cm)			0.163*
□3	28	24	
3⩾,<5	19	30	
Tumor number			0.686*

Single(1)	26	33	
2-3	21	21	
Duration of ablation (min)	11.2 ± 5.4	9.7 ± 3.2	0.003‡
Generator power (watts)	57.3 ± 8.5	54.5 ± 6.3	0.047‡

Note.—Unless indicated, data are numbers of patients, and numbers in parentheses are percentages. ECOG = Eastern Cooperative Oncology Group.*Pearson $\chi 2$ test was used. †Data are mean ± standard deviation. ‡Independent-samples t test was used. §Fisher exact test was used.

Table 2: Inclusion and exclusion criteria

Inclusion criteria	***Exclusion criteria***
1 Age range: 18–75 years	Age <18 or >75 years
2 HCC diagnosed according to EASL standards	No pathology or image evidence
3 Child–Pugh grade A or B	Child–Pugh grade C
3 BCLC grades are A and B	BCLC grades are C
4 ECOG score≦2	ECOG score□2
4 Liver lesions ≤3	The liver lesions number□3
5 Single tumor diameter <5 cm	Single tumor diameter ≥5
6 The expected survival time□3 months	The expected survival time ≤3 months
7 No portal vein thrombus	Portal vein thrombus
8 No extrahepatic metastases	Extrahepatic metastases
9 PLT □40 × 109/L or PT ≤25 s	PLT ≤ 40 × 109/L or PT □25 s

European Association for the Study of the Liver, EASL; Eastern Cooperative Oncology Group, ECOG; platelet, PLT; prothrombin time: PT; HCC, small hepatocellular carcinoma

Table 3: MR scanning sequences and parameters

Section	*Sequence*	*TE (ms)*	*TR (ms)*	*Slice thicknes (mm)*	*Matrix*	*Flip angle*	*Band Width (Hz/pixel)*
Transverse section	T1 Vibe	1.93	4.56	3.3	216×288	9.0	400
Transverse section	T2 Haste	106	1000	4.5	137×256	180	781
Transverse section	Diffusion	83	7100	5.0	192×144	90	1670
Coronal section	T1 vibe	2.46	6.11	3.0	179×256	9.0	410
Sagittal	T2 Haste	106	1000	4.0	137×256	180	781

Table 4. Adverse events and complications

Categories	CT-guided（n=47）		MR-guided（n=54）		*P Value*
	Grades				
Adverse events	**CTCAE**		**CTCAE**		
Fever, maximum 38°C, no treatment	[illegible]	17(36)	[illegible]	23(43)	0.546*
Fever, ≥ 38°C,treatment	[illegible]	13(28)	[illegible]	21(39)	0.293*
Nausea or vomiting	[illegible]	7(15)	[illegible]	6(11)	0.767*
Mild pain, requiring nonopioid oral analgesic treatment	[illegible]	24(51)	[illegible]	31(57)	0.553*
Moderate pain, requiring opioid oral analgesic treatment	[illegible]	18(38)	[illegible]	21(39)	1.000*
Mild liver dysfunction, requiring conservative treatment	[illegible]	32(68)	[illegible]	43(80)	0.254*
complications					
Liver abscess	[illegible]	9(6)	[illegible]	2(9)	0.022*
Asymptomatic perihepatic fluid	[illegible]	2(4)	[illegible]	1(2)	0.596§
Pleural effusion	[illegible]	8(6)	[illegible]	1(2)	0.011*
Subcapsular liver hemorrhage	[illegible]	3(4)	[illegible]	1(2)	0.336§

National Cancer Institute Common Terminology Criteria for Adverse Event (CTCAE version 4.03)

Data are numbers of events. Data in parentheses are percentages.

Note.—Data are numbers of events. Data in parentheses are percentages. *Pearson $\chi 2$ test was used. §Fisher exact test was used.

Table 5: Factors affecting PFS and OS

Parameters	LTP			*P*	OS			*P*
	HR	*95%*CI			***HR***	*95%**CI***		
		Lower	Higher			*Lower*	*Higher*	
Univariate Cox's regression								
Age (>60 vs ≤ 60)	*0.217*	0.836	2.197	1.356	*2.825*	*1.085*	*7.356*	*0.033*
AFP (>200 vs ≤ 200ng/mL)	0.138	0.887	2.371	1.451	*1.496*	*0.619*	*3.613*	*0.371*
Tumor diameter (3⩾,<5 vs <3cm)	*2.644*	1.596	4.380	**0.000**	*2.865*	*1.100*	*7.460*	***0.031***
Tumor location (challenging locations vs ordinary locations)	*3.399*	2.065	5.593	**0.000**	*4.604*	*1.759*	*12.050*	***0.002***
Number of lesion (single VS 2-3 lesions)	*3.282*	1.995	5.399	**0.000**	*9.109*	*3.029*	*27.395*	***0.000***
Child–Pugh stage (B vs A)	*1.180*	0.723	1.923	0.508	*1.337*	*0.554*	*3.228*	*0.519*
Guidance system (CT vs MR)	*0.888*	0.547	1.443	0.632	*0.808*	*0.336*	*1.941*	*0.633*
Multivariate Cox's regression								
Age (>60 vs ≤ 60)	1.006	0.606	1.672	0.980	2.337	0.846	6.454	0.101
AFP (>200 vs ≤ 200ng/mL)	1.312	0.775	2.220	0.312	0.971	0.387	2.434	0.950
Tumor diameter (3⩾,<5 vs <3cm)	2.869	1.621	5.081	**0.000**	3.388	1.100	10.431	**0.033**
Tumor location (challenging locations vs ordinary locations)	2.848	1.621	5.273	**0.001**	2.646	0.868	8.070	0.087
Number of lesion (single VS 2-3 lesions)	1.890	1.053	3.391	**0.033**	9.287	2.649	32.567	**0.000**
Child–Pugh stage (B vs A)	1.429	0.816	2.505	0.212	2.393	0.843	6.789	0.111
Guidance system (CT vs MR)	0.824	0.487	1.393	0.470	0.419	0.143	1.223	0.101

Note—general anesthesia (GA) and local anesthesia (LA) ; challenging locations(Hepatic dome, Close to the heart/diaphragm/hepatic hilum)

Figures

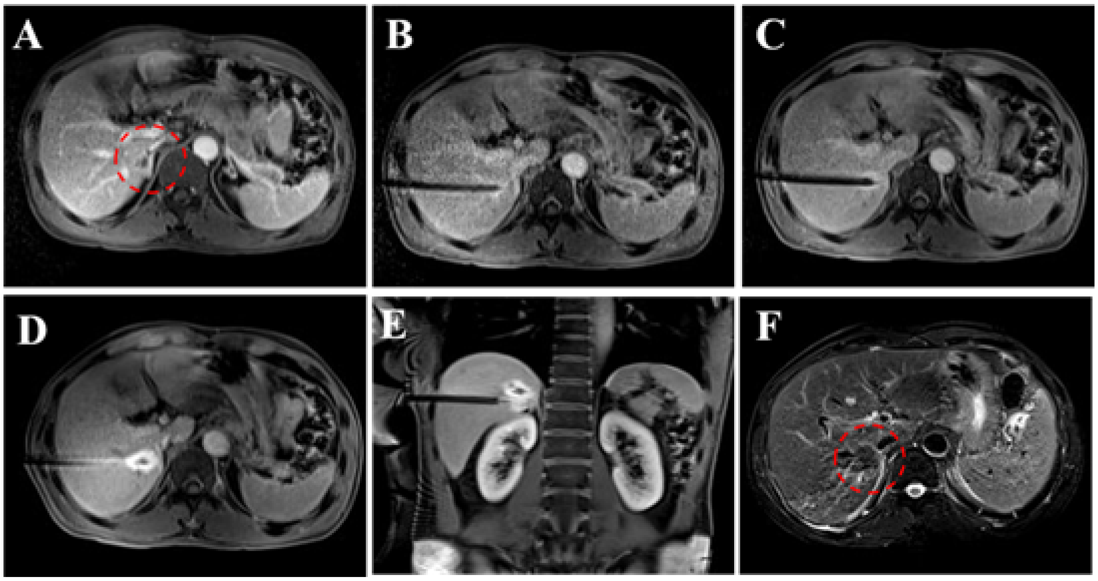

Figure 1

Images of a 58-year-old patient with a small HCC (8.8 mm) in the caudate lobe (A; dashed circle). The image shows that the probe has been accurately inserted into the target lesion and the ablation process has been completed (B, C). The thermal-induced damage zone estimated as hyperintensity on T1 high signal range completely covers the tumor after during ablation (D). A typical "target sign" (dashed circle) is clearly shown in the ablated area of T1WI (E), and a low point appears in T2WI immediately after MWA. (F; dashed circle).

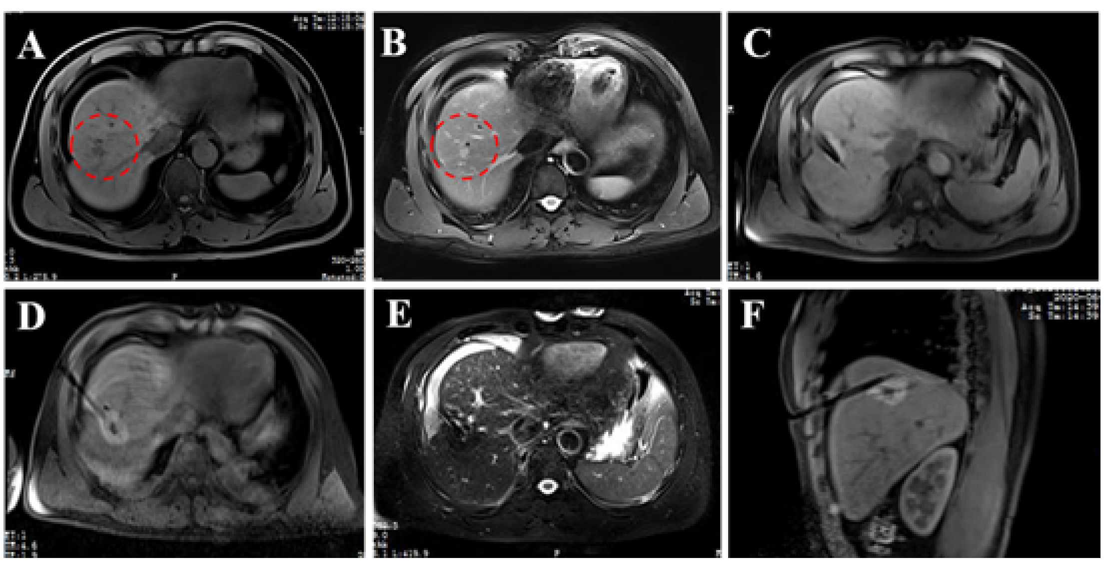

Figure 2

Small HCC in the hepatic of a 48-year-old man treated with MR-guided MWA. Nodules with a diameter of 12 mm are located in the right lobe of the liver. Before MWA, the nodules appear low in signal on the T1WI (A; dashed circle) and appear with hyper-intensity on the T2WI (B; dashed circle). Correct the puncture path in the T1WI sequence, and reconfirm it through the T1WI traverse after reaching the tumor target (C).

A typical "target sign" is clearly shown in the ablated area of T1WI (D,F), and a low point appears in T2WI immediately after MWA(E).

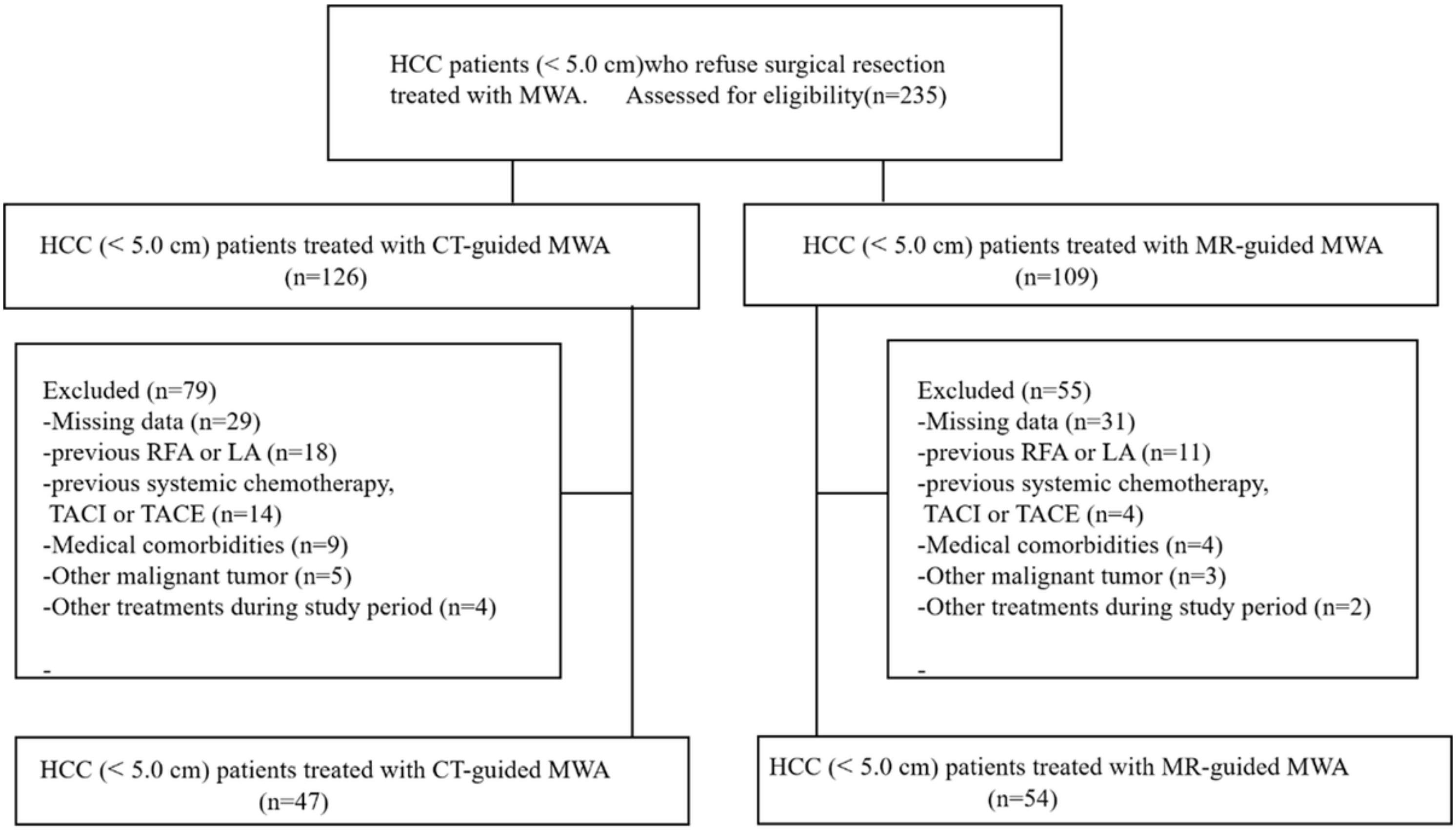

Figure 3

Flow diagram shows exclusion criteria.RFA = radiofrequency ablation;LR = liver resection; LT = liver transplantation;TACI = transarterial chemoinfusion;TACE = transarterial chemoembolization.

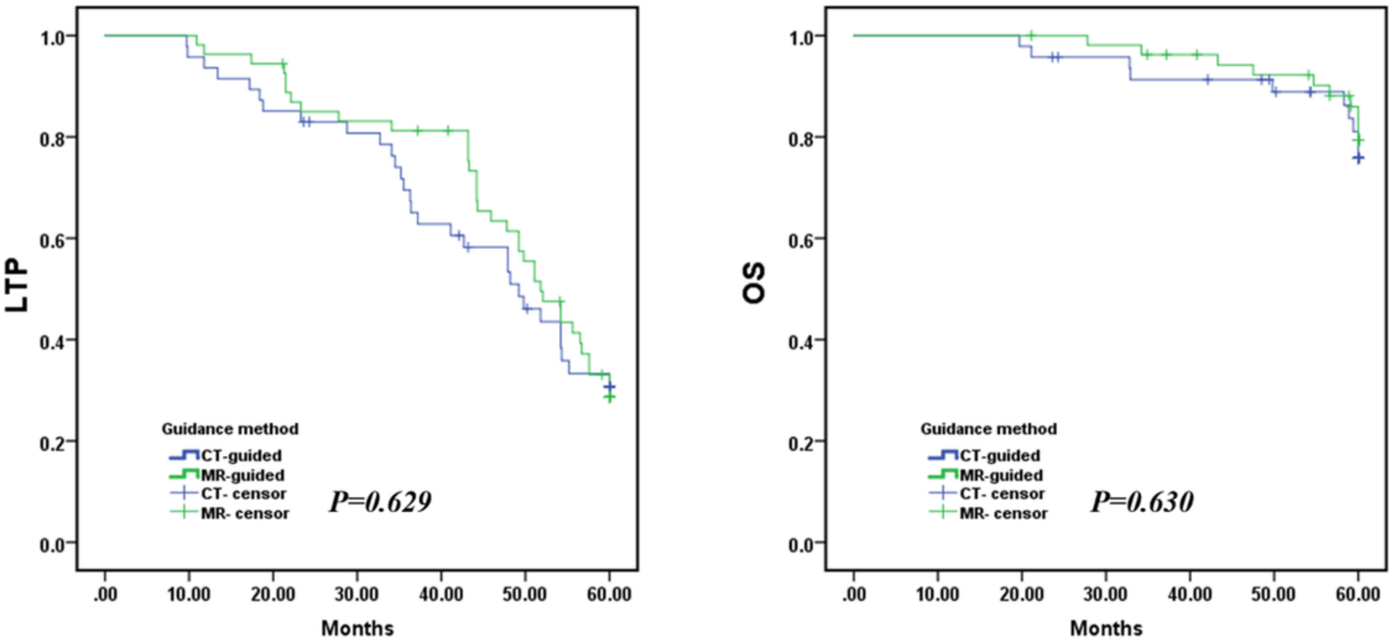

Figure 4

Kaplan–Meier local tumor progression (LTP) with CT-guided group versus MR-guided group. Mean LTP was 44.264 months (95% CI:39.484, 49.043) in CT-guided group versus 47.745 months (95% CI: 43.840, 51.650) in MR-guided group of HCC (p = 0.629, log-rank test). Kaplan–Meier Overall survival (OS) with CT-guided group versus MR-guided group. Mean OS was 56.772 months (95% CI:53.858, 59.889) in the patients with CT-guided group versus 58.123 months (95% CI: 56.375, 59.889) in the MR-guided group (p = 0.630, log-rank test). The 1-, 3-, and 5-year LTP rates in patients with CT-guided group were 93.6%, 69.5% and 30.7% , respectively; and the 1-, 3- and 5-year OS rates were 100.0%, 91.3% and 75.8%, respectively. The 1-, 3-, and 5-year LTP rates in MR-guided group were 96.3%, 81.2% and 28,7% , respectively; and the 1-, 3- and 5-year OS rates were 100.0%, 96.2% and 79.4%, respectively.

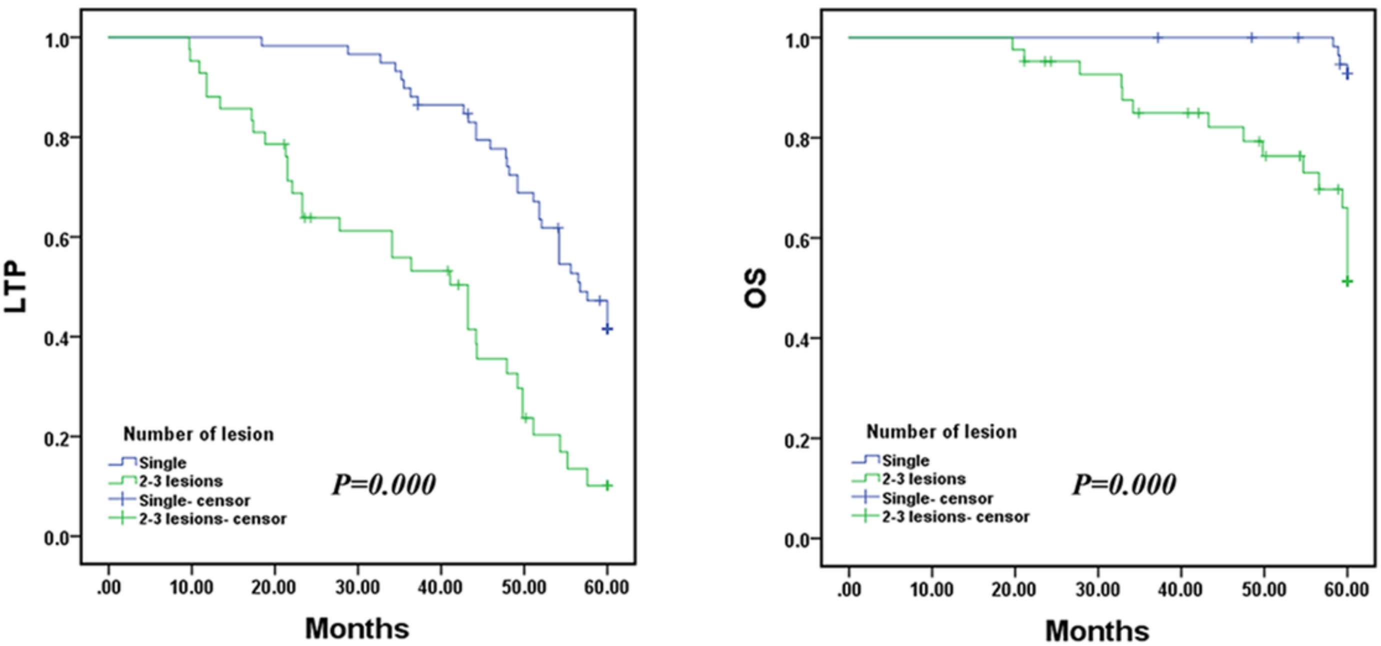

Figure 5

Kaplan–Meier local tumor progression (LTP) with single tumor versus 2-3lesions of HCC. Mean LTP was 52.574 months (95% CI:50.025, 55.124) in the patients with single tumor versus 36.604 months (95% CI: 31.464, 41.743) in the 2-3lesions of HCC (p = 0.000, log-rank test). Kaplan–Meier Overall survival (OS) with single tumor versus 2-3lesions of HCC. Mean OS was 59.934 months (95% CI:59.847, 60.021) in the patients with single tumor versus 53.787 months (95% CI: 50.053, 57.520) in the 2-3lesions of HCC (p = 0.000, log-rank test). The 1-, 3-, and 5-year LTP rates in single tumor were 100.0%, 89.8% and 41.6% , respectively; and the 1-, 3- and 5-year OS rates were 100.0%, 100.0% and 92.8%, respectively. The 1-, 3-, and 5-year LTP rates in the 2-3 lesions of HCC were 88.1%%, 55.9% and 10.2% , respectively; and the 1-, 3- and 5-year OS rates were 100.0%, 84.9% and 51.4%, respectively.

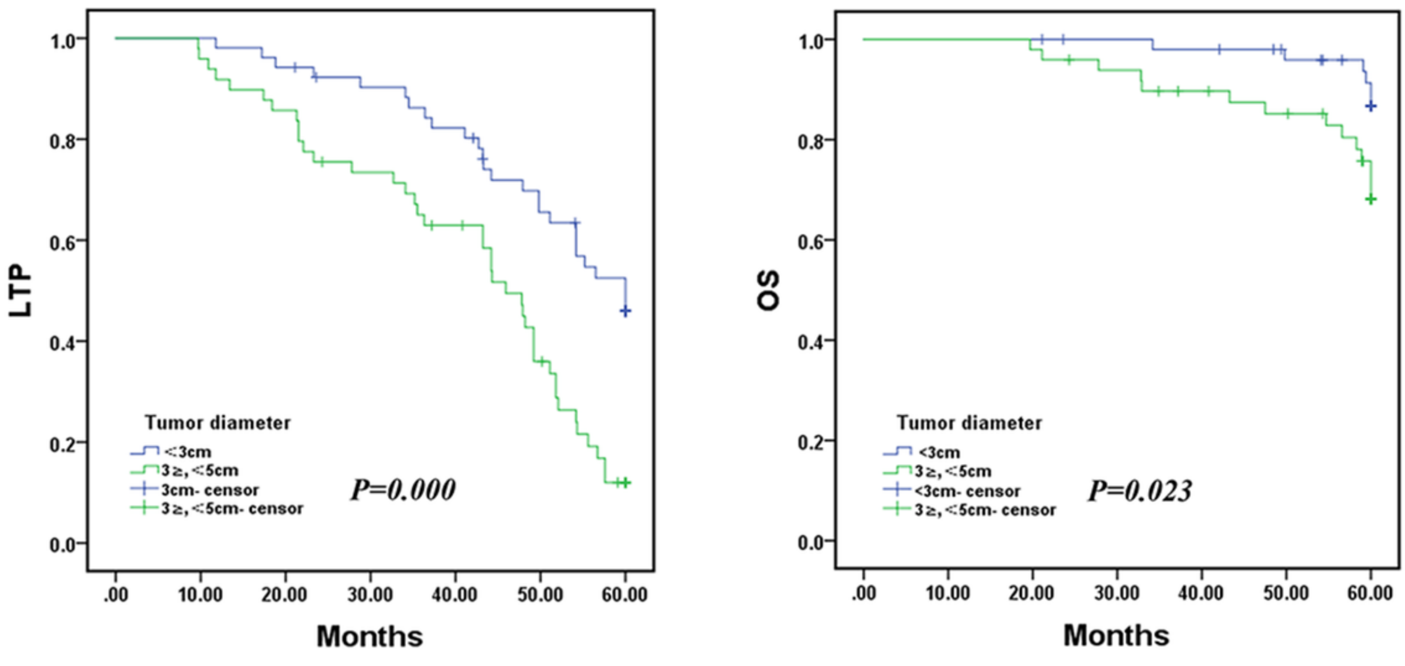

Figure 6

Kaplan–Meier local tumor progression (LTP) with tumor diameter (3cm) versus tumor diameter (3cm⩾,<5cm). Mean LTP was 50.944 months (95% CI:50.025, 55.124) in the patients with tumor diameter (3cm) versus 41.042 months (95% CI: 31.464, 41.743) in tumor diameter (3cm, ≤5cm) of HCC (p = 0.000, log-rank test). Kaplan–Meier Overall survival (OS) with tumor diameter (3cm) versus tumor diameter (3cm⩾,<5cm). Mean OS was 59.232 months (95% CI:58.052, 60.413) in the patients with tumor diameter (3cm) versus 55.653 months (95% CI: 52.602, 58.705) in the tumor diameter (3cm⩾,<5cm) of HCC (p = 0.023, log-rank test). The 1-, 3-, and 5-year LTP rates in patients with tumor diameter (3cm) were 100.0%, 89.8% and 41.6% , respectively; and the 1-, 3- and 5-year OS rates were 100.0%, 98.0% and 86.7%, respectively. The 1-, 3-, and 5-year LTP rates in tumor diameter (3cm⩾,<5cm) were 91.8%, 65.0% and 12.0% , respectively; and the 1-, 3- and 5-year OS rates were 100.0%, 89.7% and 68.1%, respectively.