Original Article

Efficacy of ultrasound-, computed tomography-, and magnetic resonance imaging-guided radiofrequency ablation for hepatocellular carcinoma

Chunwang Yuan*, Zhuhui Yuan*, Xiongwei Cui, Wenfeng Gao, Peng Zhao, Ning He, Shichang Cui, Yang Wang, Yonghong Zhang, Wei Li, Jiasheng Zheng

Center of Interventional Oncology and Liver Diseases, Beijing Youan Hospital, Capital Medical University, Beijing 100069, PR. China

For correspondence: Prof. Wei Li, Prof. Jiasheng Zheng, Center of Interventional Oncology and Liver Diseases, Beijing Youan Hospital, Capital Medical University 8 Xitoutiao, Youwai St, Fengtai Dist, Beijing 100069, PR. China. E-mail: vision988@126.com; zhengjiasheng6@sina.com

*Chunwang Yuan and Zhuhui Yuan contributed equally to this work

ABSTRACT

Purposes: This study aimed to investigate the efficacy of ultrasound (US)-, computed tomography (CT)-, and magnetic resonance imaging (MRI)-guided radiofrequency ablation (RFA) for the treatment of hepatocellular carcinoma (HCC).

Materials and Methods: This retrospective study included 141 patients with HCC who were treated with US-guided (n = 29), CT-guided (n = 50), or MRI-guided RFA (n = 62). The primary endpoint was progression-free survival (PFS). The secondary endpoints included overall survival (OS), technique success (TS), and technique efficacy (TE). Cox model and logistic regression were used to determine the risk factors for tumor recurrence and TE.

Results: The US, CT, and MRI groups did not show a significant difference in terms of baseline variables. The three groups did not differ significantly in PFS rate (P = 0.072) and OS rate (P = 0.231). The PFS rates at 3 years for the US, CT, and MRI groups were 40.90%, not reached, and 14.80%, respectively. The OS rates at 3 years were 94.70%, 97.50%, and 85.50% for US, CT, and MRI groups, respectively. No significant differences were observed between the three groups in terms of TS rate (P = 0.113) and TE rate (P = 0.682). In multivariate analysis, liver cirrhosis (P = 0.001), level of alpha-fetoprotein (AFP, P = 0.004), and number of tumors (P = 0.012) were independent risk factors for PFS. For TE, the level of AFP (P = 0.018) was an independent factor.

Conclusion: US-, CT-, and MRI-guided RFA was effective for treating HCC patients. Liver cirrhosis, AFP level, and tumor number were associated with tumor recurrence, and the level of AFP was an independent risk factor affecting TE.

KEY WORDS: Hepatocellular carcinoma, imaging guidance, radiofrequency ablation, risk factor

INTRODUCTION

Image guidance techniques play a critical role in radiofrequency ablation (RFA) of liver cancer. Ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) are the usual imaging modalities. US has the advantages of low cost, real-time imaging, and nonionizing radiation; however, there are dead spots, blind areas, and vaporization interference caused by ablation.[1,2] CT guidance is suitable for liver tumors of all sizes and locations. Contrast-enhanced CT (CECT) can be used to monitor the whole process of ablation, especially for tumors near dangerous sites.[3] However, it is a nonreal-time imaging, and repeat scans significantly increase radiation exposure. MRI has the advantages of high resolution of soft tissue, no bone, and metal artifacts. MRI also can perform multiplanar, thermal, and functional imaging, and it is currently the only imaging modality with well-validated techniques for real-time temperature monitoring.[4,5] Most importantly, there is nonionizing radiation for doctors and patients. However, magnetic resonance-compatible ablation applicators and auxiliary equipment are needed. In addition, there are other limiting factors, such as presence of a cardiac pacemaker, in which case MRI guidance is not suitable.

Several studies have investigated the efficacy and safety of different image guidance modalities. Lee *et al*.[6] demonstrated that US guidance was

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equivalent to CT guidance in terms of overall survival (OS) rate, local tumor recurrence rate, and complication rate for small hepatocellular carcinoma (HCC). Clasen *et al*.[7] found that both CT-guided RFA and MRI-guided RFA were locally effective for HCC; however, the latter could provide a higher primary technique efficacy (TE) rate (TER) and reducing the number of procedures required for complete ablation. However, there was no consensus about whether US, CT, and MRI are equivalent for percutaneous liver cancer ablation. Thus, this study aimed to investigate and compare the efficacy and safety of US-, CT-, and MRI-guided RFA for HCC.

MATERIALS AND METHODS

Patients

This retrospective study was performed at a single institution with the approval of the Institutional Ethics Committee and in accordance with the Helsinki Declaration. Written informed consent was obtained from all participants before treatment.

A total of 141 consecutive patients with HCC who underwent US-guided [Figure 1], CT-guided [Figure 2], or MRI-guided RFA [Figure 3] between April 2013 and July 2016 were included in the study [Table 1].

Patients were included based on the following inclusion criteria: (1) age 18–75 years; (2) CECT/contrast-enhanced MRI (CE-MRI) was performed within 2 weeks before ablation;[8] (3) Barcelona-Clinic Liver Cancer Stage 0–B1; (4) refusal to undergo hepatectomy or liver transplantation; (5) well-preserved liver function, i.e., Child–Pugh Class A/B and serum total bilirubin level ≤3 mg/dl; and (6) Eastern Cooperative Oncology Group performance status score ≤2. The exclusion criteria were as follows: (1) tumor thrombus in a major hepatic vessel; (2) extrahepatic metastases; (3) uncontrollable ascites, history of hepatic encephalopathy, or variceal bleeding that occurred before <1 month; (4) Child–Pugh Class C; (5) severe coagulation disorder (platelet count $<5 \times 10^3/\mu L$ or prothrombin activity <50%); (6) history of secondary malignancy; (7) severe dysfunction of the heart, brain, kidney, or other organs; (8) active infection (except viral hepatitis); and (9) refusal to undergo ablation. The choice of imaging guidance modality was mainly based on cost, ease of use, patient's needs, as well as the operator's wishes.

Radiofrequency ablation equipment

The RITA Model 1500X radiofrequency (RF) generator (RITA Medical Systems, Mountain View, CA, USA), with StarBurst™ XL RF electrode (RITA Medical Systems, Mountain View, CA, USA) and StarBurst™ MRI-compatible RF electrode (RITA Medical Systems, Mountain View, CA, USA), was used in this study. The RF generator with 460 kHz could provide a maximum output power of 200 W.

The MyLab™ Twice US system (Esaote, Genoa, Italy) was used for US guidance. For CT guidance, Aquilion™ CT scanner (Toshiba Medical Co., Tokyo, Japan) was used. A 0.35 T imaging system (Oper 0.35, XinGaoYi Co., Zhejiang, China) and a navigation system (IGS-MF, Symbow Medical Technology Co., Beijing, China) were used for guiding the ablation in the MRI group.

Transarterial chemoembolization procedure

A 5-French catheter was inserted into the trunk of the celiac artery using the Seldinger technique, and angiography was performed to identify the arterial blood supplying of the tumors, followed by superselective chemoembolization via a microcatheter (Asahi Intecc Co., Ltd., Japan) using

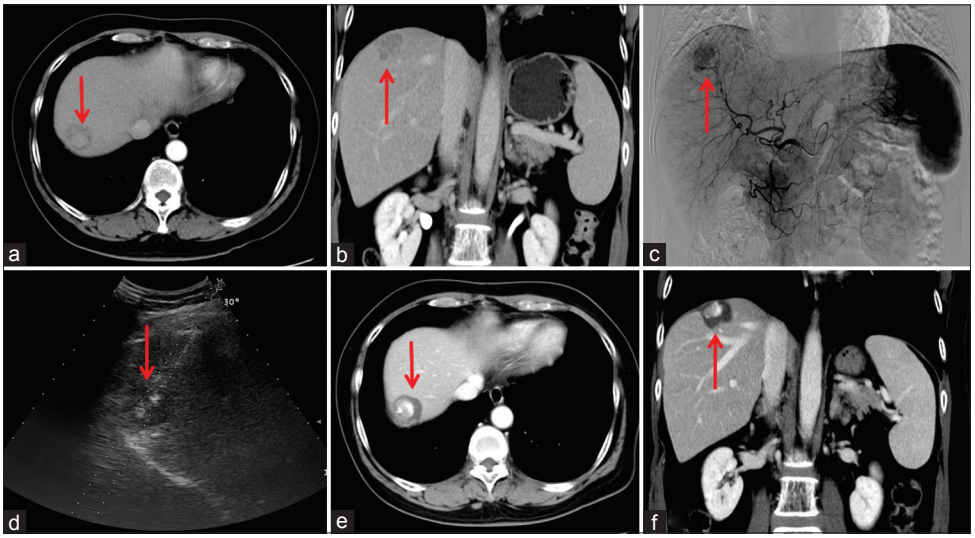

Figure 1: Ultrasound-guided radiofrequency ablation for liver cancer in a 65-year-old woman. (a) Axial and (b) coronal show a lesion located in segment VII, which exhibits fast wash-in in arterial phase and fast wash-out in portal venous phase; (c) the tumor exhibiting obvious staining. (d) The puncture of electrode. (e) Axial and (f) coronal show the unenhanced ablation zone, which covers the lesion completely on contrast-enhanced computed tomography 2 years later

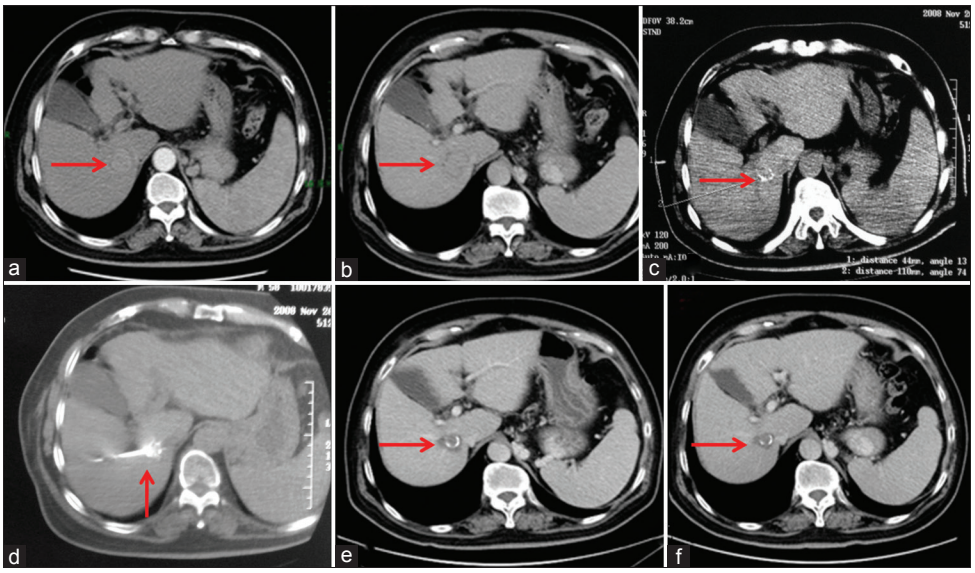

Figure 2: Computed tomography-guided radiofrequency ablation for liver cancer in a 57-year-old man. (a and b) A lesion located in the right lobe, which exhibits fast wash-in in arterial phase and fast wash-out in portal venous phase; (c) The puncture route design; (d) The insertion of the electrode into the tumor, and the multiple subneedle tips unfold and cover the tumor ideally. (e and f) The unenhanced ablation zone, which covers the lesion completely with an enough ablation margin on contrast-enhanced computed tomography 6 months and 1 year later, respectively

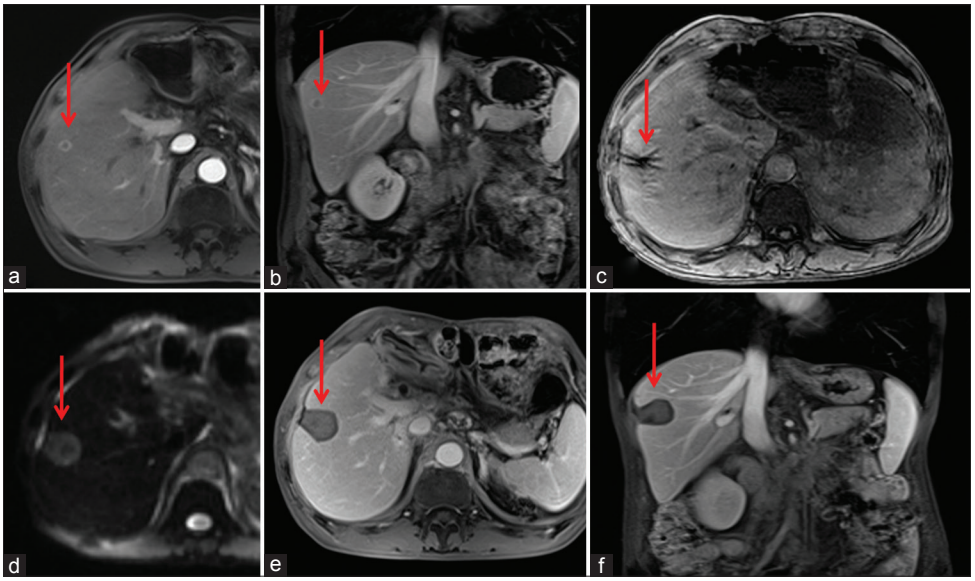

Figure 3: Magnetic resonance imaging-guided radiofrequency ablation for liver cancer in a 62-year-old man. (a) Axial and (b) coronal show a small tumor located in segment V, which exhibits fast wash-in in arterial phase and fast wash-out in portal venous phase; (c) The insertion of electrode, and the multiple subneedle tips unfold and cover the tumor ideally; (d) axial, (e) axial, and (f) coronal show the ablation zone with an enough ablation margin exhibiting high signal on diffusion-weighted imaging and no enhancement on contrast-enhanced magnetic resonance imaging 10 months later

20–40 mg of epirubicin mixed with 1–5 ml Lipiodol (Guerbet, Villepinte, Seine-Saint-Denis, France), and further embolization was performed with a 350–560 μm gelatin sponge granules (Hangzhou Alicon Pharmaceutical Technology Co., Ltd. Hangzhou, China).

Radiofrequency ablation procedures

CECT/CE-MRI was performed before RFA to assess the location, size, and number of the HCC nodules. RFA was performed by two physicians specializing in liver RFA (>5 years' experience). Patients were placed in an appropriate position (prone, supine, or lateral decubitus position) according to the tumor location. The procedure was performed under local anesthesia with 1% lidocaine, combined with 25–100 mg pethidine hydrochloride and 12.5–50 mg promethazine intravenous sedative analgesia.

US, CT, or MRI was used for imaging guidance. MRI-guided RFA was assisted with a navigation system which has

Table 1: Demographics and characteristics of hepatocellular carcinoma patients in the magnetic resonance imaging, computed tomography, and ultrasound groups

Demographics and characteristics (*n*=141)	Number of Patients	US group (*n*=29)	CT group (*n*=50)	MRI group (*n*=62)	*P*
Categorical variables					
Gender					
Male	124	26	43	55	0.892
Female	17	3	7	7	
Liver cirrhosis					
No	24	6	9	9	0.706
Yes	117	23	41	53	
HBsAg					
Negative	21	5	4	12	0.186
Positive	120	24	46	50	
HBeAg					
Negative	102	23	38	41	0.480
Positive	39	6	12	21	
Ascites					
No	132	26	47	59	0.602
Yes	9	3	3	3	
Child-Pugh score					
A	133	27	45	61	0.151
B	8	2	5	1	
Continuous variables and ranked data					
Age (years), mean±SD	57.56±9.55	57.48±11.90	58.13±10.41	57.43±7.50	0.851
ALT (U/L), median (range)	31.00 (7.30-182.50)	31.60 (11.60-182.50)	28.20 (7.30-138.20)	31.90 (9.00-173.20)	0.359
AST (U/L), median (range)	31.10 (9.40-133.10)	33.40 (18.40-114.8)	32.90 (9.40-133.10)	29.30 (15.60-132.90)	0.342
TBIL (μmol/L), mean±SD	16.90±8.02	17.90±8.18	16.30±7.83	18.14±7.66	0.933
Albumin (g/L), mean±SD	40.25±5.01	39.24±5.16	39.43±5.02	39.80±5.06	0.869
PT (s), median (range)	11.70 (9.00-18.00)	11.30 (10.00-17.00)	11.50 (9.00-15.00)	11.70 (10.00-18.00)	0.886
AFP (μg/L), median (range)	14.92 (0.60-6011.00)	8.23 (1.20-1052.00)	13.88 (1.00-6011.00)	18.96 (0.60-5337.00)	0.105
Number of ablation procedures, median (range)	1 (1-2)	1 (1)	1 (1-2)	1 (1)	0.410
Number of tumors, median (range)	1 (1-3)	1 (1-2)	1 (1-4)	1 (1-2)	0.243
Total number of tumors ablated	175	34	78	63	
Maximum diameter of tumor (cm), median (range)	1.8 (0.7-4.8)	1.7 (0.8-4.6)	1.6 (0.7-4.8)	2.0 (1.0-4.2)	0.221

US=Ultrasound, CT=Computed tomography, MRI=Magnetic resonance imaging, HCC=Hepatocellular carcinoma, EHD=Extrahepatic disease, ALT=Alanine aminotransferase, AST=Aspartate transaminase, TBIL=Total bilirubin, GGT=Gamma-glutamyl transferase, PT=Prothrombin time, AFP=Alpha-fetoprotein, SD=Standard deviation

characteristics of near real-time, three-dimensional navigation and multiple plane imaging. The electrode was adjusted according to the size and location of the tumor in order to achieve an ideal ablative margin of 0.5–1 cm. The range of power delivered to the HCC nodules was 100–200 W (maintained for 20–30 min). If the tumor was larger than 3 cm, multiple overlapping ablations were usually needed. At the end of the RFA procedure, the needle track was ablated to avoid bleeding and seeding metastasis.

Contrast-enhanced US, CECT, or CE-MRI was routinely applied immediately after the RFA procedure. If residual tumors were present, additional RFA would be performed immediately.

Assessment of treatment efficacy

The primary endpoint of this study was progression-free survival (PFS), which was defined as the time elapsed from the initial treatment completion to tumor progression or death. The secondary endpoints included OS rate, technique success rate (TSR), and TER. OS was defined as the time elapsed between the completion of initial treatment and death. technique success (TS) was defined as the tumor was treated according to protocol and was covered completely by the ablation zone. TE was defined as complete ablation of the target lesion achieved within 1–4 procedures, as evaluated 1 month after the last procedure by CECT/CE-MRI. The complete ablation was defined as uniform hypoattenuation or hypointense signal of the ablation zone in the arterial phase, which included the ablated tumor and the ablative margin of 0.5–1 cm around it.

Complications were recorded and classified based on the Society of Interventional Radiology classification.[9] Minor complication was described as an event that needed no therapy or nominal therapy. Major complication was an event that required major therapy and prolonged hospitalization (>48 h) and could lead to mortality or permanent adverse sequelae.

Follow-up

All of the patients underwent abdominal CECT or CE-MRI and laboratory tests, mainly including tests for measuring serum alpha-fetoprotein (AFP) level, liver function, blood biochemistry, and blood coagulation every 1 month during the first 3 months and every 3 months thereafter.

Statistical analysis

Data were analyzed using IBM SPSS, version 17.0 (IBM Corp., Armonk, NY, USA). The baseline and clinical characteristics were summarized as mean ± standard deviation (continuous variable with normal distribution), median ± range (continuous variable

with nonnormal distribution), or frequency (categorical variables). Chi-square test or Fisher's exact test was used to compare the baseline and clinical characteristics of categorical variables in the US, CT, and MRI groups, and ANOVA test or Mann–Whitney U-test was used to compare the differences of continuous variables. Chi-square test was used to examine differences in TER between the three groups in different subgroups: (1) number of tumors ≥2 or <2; (2) maximum diameter of tumor ≥2 or <2 cm; (3) liver cirrhosis; and (4) AFP level ≥400 or <400 μg/L.

OS and PFS were calculated and depicted using the Kaplan–Meier method and compared using the logrank test. Cox proportional hazards model and logistic regression were used to explore the risk factors for PFS and TE, with proportional hazard ratio (HR), calculating 95% confidence interval (CI). The univariate that had $P < 0.05$ and certain univariates ($P > 0.05$) with potential influence on PFS or TE based on realistic clinical experience were incorporated into multivariate analysis. $P < 0.05$ was defined as statistically significant.

RESULTS

Clinicopathologic characteristics of patients in the three groups

Twenty-nine, 50, and 62 patients were assigned to the US, CT, and MRI groups, respectively. Demographics and characteristics of the three groups are listed in Table 1.

Progression-free survival and overall survival in the three groups

The PFS rate and curves are shown in Table 2 and Figure 4. The 1-, 2-, and 3-year PFS of the US group was 57.10%, 46.70%, and 40.90%, respectively. The 1-, 2-, and 3-year PFS of the CT group was 55.10%, 39.40%, and not reached (NR), respectively. The 1-, 2-, and 3-year PFS of the MRI group was 64.30%, 39.60%, and 14.80%, respectively. No significant difference in PFS was observed between the three groups ($P = 0.072$).

The OS rate and curves are presented in Table 2 and Figure 5. The 1-, 2-, and 3-year OS rate of the US group was 94.70%, 94.70%, and 94.70%, respectively. The 1-, 2-, and 3-year OS rate of the CT group was 100%, 97.50%, and 97.50%, respectively. The 1-, 2-, and 3-year OS of the MRI group was 96.20%, 85.50%, and 85.50%, independently. No significant difference in cumulative OS was found between the three groups ($P = 0.231$).

Comparison of technique success and primary technique efficacy

The total TER and total TSR are presented in Table 2. TS was achieved in 24 patients (24/29, 82.80%) in the US group, 46 patients (46/50, 92%) in the CT group, and 48 patients (48/62, 77.40%) in the MRI group. No significant difference was detected between the groups ($P = 0.113$).

The TER was 93.10% (27/29), 94% (47/50), and 96.80% (60/62) in the US, CT, and MRI groups, respectively. No significant differences were observed between the three groups ($P = 0.184$).

Univariate and multivariate analyses of progression-free survival

The results of univariate and multivariate analyses are presented in Table 3. The univariate analysis showed that liver cirrhosis ($P = 0.004$), modality of imaging guidance (reference: US; $P = 0.078$), alanine aminotransferase ($P = 0.032$), AFP ($P = 0.023$), and the number of tumors ($P = 0.001$) were risk factors for PFS.

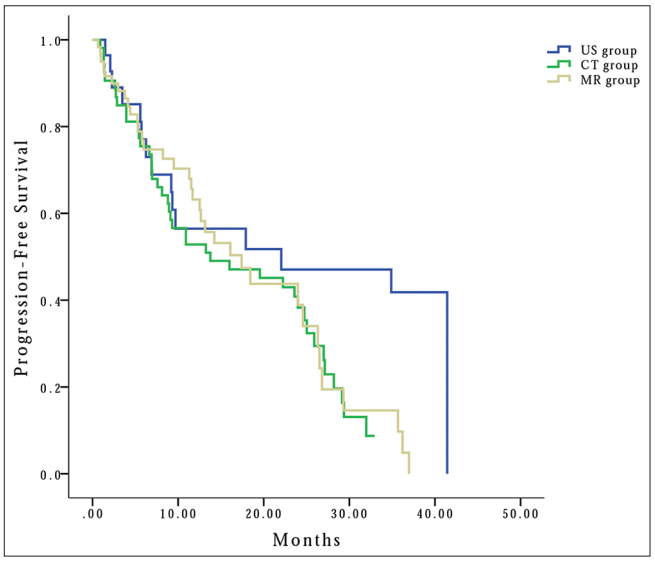

Figure 4: Progression-free survival of patients in the three groups. 1-, 2-, and 3-year progression-free survival of the ultrasound group was 57.10%, 46.70%, and 40.90%, respectively, that was 55.10%, 39.40%, and NR of the computed tomography group and 64.30%, 39.60%, and 14.80% of the magnetic resonance imaging group, respectively. Significant difference in cumulative progression-free survival was not observed among the three groups ($P = 0.072$)

Table 2: Technique success rate, technique efficacy rate, and 1-, 2-, and 3-year overall survival and progression-free survival

	TSR (%)	*P*	TER (%)	*P*	OS (%)				PFS (%)			
					1 year	2 years	3 years	*P*	1 year	2 years	3 years	*P*
US (*n*=29)	82.80 (24/29)	0.113	93.1 (27/29)	0.682	94.70	94.70	94.70		57.1	46.70	40.90	
CT (*n*=50)	92.00 (46/50)		94.00 (47/50)		100.00	97.50	97.50		55.10	39.40	NR	
MRI (*n*=62)	77.40 (48/62)		96.80 (60/62)		96.20	85.50	85.50		64.30	39.60	14.80	
ALL (*n*=141)	83.70 (118/141)	NA	95.04 (134/141)	NA	97.50	94.40	94.40	0.231	57.50	41.40	17.60	0.072

RFA=Radiofrequency ablation, OS=Overall survival, PFS=Progression-free survival, TSR=Technique success rate, TER=Technique efficacy rate, NR=Not reached, NA=Not available

In the multivariate analysis, liver cirrhosis (HR, 3.567; 95% CI, 1.668–7.630; $P = 0.001$), AFP (HR, 1.0004; 95% CI, 1.0001–1.0007; $P = 0.004$), and number of tumors (HR, 1.367; 95% CI, 1.070–1.747; $P = 0.012$) were the independent risk factors for PFS.

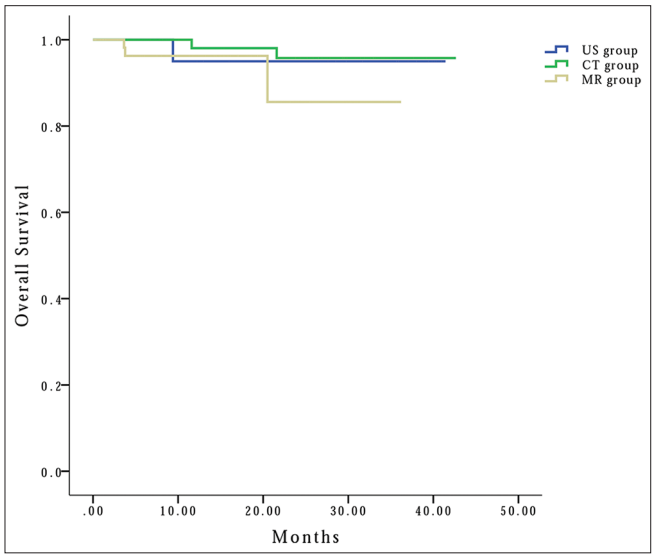

Figure 5: Overall survival rate of patients in the three groups. The 1-, 2-, and 3-year overall survival rate of the ultrasound group was 94.70%, 94.70%, and 94.70%, respectively, that was 100%, 97.50%, and 97.50% of the computed tomography group and 96.20%, 85.50%, and 85.50% of the magnetic resonance imaging group, respectively. No significant difference in cumulative overall survival was found among the three groups ($P = 0.231$)

Univariate and multivariate analyses of technique efficacy and subgroup analysis

The univariate and multivariate analyses of TE in logistic regression are presented in Table 4. Liver cirrhosis, HBsAg positivity, Child–Pugh score, total bilirubin, albumin, prothrombin time, AFP level, and the maximum diameter of the tumor were included in the multivariate analysis. It was found that only the AFP level (HR, 0.999; 95% CI, 0.998–1.000; $P = 0.018$) was an independent risk factor for TE.

The comparison of TER in different subgroups is presented in Table 5. According to the multiple variable analyses of TER in logistic regression and clinical experience, the TE of the three different methods of image-guided RFA was compared based on the maximum tumor diameter (≥2 or <2 cm), number of tumors (≥2 or <2), liver cirrhosis, and serum AFP level (≥400 or <400 μg/L). No significant differences were observed between the eight subgroups.

Complications in the ultrasound, computed tomography, and magnetic resonance imaging groups

Only one patient in the MRI-guided group (1/62) developed subcapsular hemorrhage after the procedure, which was classified as a major complication. The hemorrhage was cured by transarterial embolization immediately, and the patient was discharged on the 5th day after RFA. Minor complications included fever (34/141), vomiting (26/141), pain (47/141), and self-limiting intraperitoneal bleeding (5/141). There was no ablation-related death.

Table 3: Univariate and multivariate analyses of progression free survival in hepatocellular carcinoma patients using Cox proportional hazards model

Variates	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Categorical variates				
Gender	0.620 (0.286-1.346)	0.227		
Liver cirrhosis	2.664 (1.359-5.221)	0.004	3.567 (1.668-7.630)	0.001
HBsAg	2.019 (0.968-4.209)	0.061		
HBeAg	1.202 (0.751-1.924)	0.443		
Ascites	1.555 (0.715-3.381)	0.265		
Child-Pugh score	1.364 (0.592-3.143)	0.467		
TS	1.291 (0.740-2.254)	0.368		
TE	1.851 (0.575-5.963)	0.302		
Imaging guidance modality				
Reference: US	NA	0.078	NA	0.671
CT	2.121 (1.088-4.133)	0.027	1.276 (0.636-2.559)	0.492
MRI	1.950 (1.001-3.798)	0.050	1.369 (0.688-2.724)	0.372
Continuous variates and ranked data				
Age, years	1.016 (0.995-1.037)	0.132		
ALT, U/L	0.989 (0.980-0.999)	0.032	0.994 (0.983-1.004)	0.236
AST, U/L	0.991 (0.982-1.001)	0.068		
TBIL, μmol/L	1.015 (0.989-1.041)	0.256		
Albumin, g/L	0.983 (0.942-1.025)	0.418		
PT, s	1.051 (0.900-1.227)	0.529		
AFP, μg/L	1.0003 (1.00003-1.0005)	0.023	1.0004 (1.0001-1.0007)	0.004
Number of ablation procedures	3.176 (0.435-23.214)	0.255		
Length of stay, days	0.967 (0.902-1.038)	0.355		
Number of tumors	1.473 (1.167-1.861)	0.001	1.367 (1.070-1.747)	0.012
Maximum diameter of tumor, cm	0.987 (0.966-1.009)	0.256		

HCC=Hepatocellular carcinoma, EHD=Extrahepatic disease, ALT=Alanine aminotransferase, AST=Aspartate transaminase, TBIL=Total bilirubin, PT=Prothrombin time, PTA=Prothrombin time activity, AFP=Alpha-fetoprotein, NA=Not available, PFS=Progression-free survival, TE=Technique efficacy, TS=Technique success

Table 4: Univariate and multivariate analyses of technique efficacy in hepatocellular carcinoma patients using logistic regression

Variates	Univariate		Multivariate	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Categorical variates				
Gender	0.814 (0.092-7.200)	0.853		
Liver cirrhosis	4.036 (0.842-19.354)	0.081	8.827 (0.227-343.676)	0.244
HBsAg	2.379 (0.430-13.157)	0.321	6.708 (0.476-94.590)	0.159
HBeAg	0.902 (0.167-4.863)	0.905		
Ascites	98,654,952.2 (0.000-NA)	0.999		
Child-Pugh score	0.117 (0.019-0.733)	0.022	0.769 (0.021-28.350)	0.887
Modality of imaging guidance	1.012 (0.359-2.849)	0.982		
Continuous variates and ranked data				
Age (years)	2.197 (0.772-6.249)	0.140		
ALT (U/L)	1.009 (0.973-1.046)	0.627		
AST (U/L)	0.993 (0.965-1.022)	0.626		
TBIL (μmol/L)	0.954 (0.873-1.043)	0.301	1.121 (0.936-1.342)	0.215
Albumin (g/L)	1.212 (1.034-1.420)	0.017	1.429 (0.953-2.144)	0.084
PT (s)	0.654 (0.438-0.977)	0.038	0.566 (0.267-1.198)	0.137
AFP (μg/L)	0.999 (0.998-1.000)	0.002	0.999 (0.998-1.000)	0.018
Number of tumors	1.325 (0.279-6.284)	0.723		
Maximum diameter of tumor (cm)	0.908 (0.843-0.977)	0.010	0.949 (0.836-1.077)	0.417

HCC=Hepatocellular carcinoma, EHD=Extrahepatic disease, ALT=Alanine aminotransferase, AST=Aspartate transaminase, TBIL=Total bilirubin, PT=Prothrombin time, AFP=Alpha-fetoprotein, NA=Not available, OR=Odds ratio, CI=Confidence interval

Table 5: Technique efficacy rate of patient subgroups

Variates	Number of patients	US group (%)	CT group (%)	MRI group (%)	*P*
Number of tumors					
<2	119	92.6 (25/27)	94.90 (37/39)	96.20 (51/53)	0.865
≥2	22	100.00 (2/2)	90.90 (10/11)	100.00 (9/9)	1.000
Maximum diameter of tumor, cm					
<2.0	82	94.10 (16/17)	100.00 (32/32)	100.00 (33/33)	0.207
≥2.0	59	91.70 (11/12)	83.80 (15/18)	93.10 (27/29)	0.550
Liver cirrhosis					
No	24	100.00 (6/6)	77.80 (7/9)	88.90 (8/9)	0.760
Yes	117	91.30 (21/23)	97.60 (40/41)	98.10 (52/53)	0.332
AFP (μg/L)					
<400	122	92.30 (24/26)	95.65 (44/46)	98.00 (49/50)	0.440
≥400	19	100.00 (3/3)	75.00 (3/4)	91.70 (11/12)	0.614

US=Ultrasound, CT=Computed tomography, MRI=Magnetic resonance imaging, TER=Technique efficacy rate, AFP=Alpha-fetoprotein

DISCUSSION

In our study, the use of different image guidance modalities did not affect the TE or patients' outcomes. The rates of TS and TE were all satisfying in the three groups, and no significant differences were observed. A previous study showed that the rates of TE in US- and CT-guided RFA were 89.1% and 92.2%, respectively ($P = 0.54$).[6] Another study demonstrated that both US-guided RFA and CT-guided RFA were similar in terms of local recurrence rate, OS, and complete ablation.[10] Lin *et al*.[11] reported that the curative effect of MRI-guided RFA is better than that of US- and CT-guided ablation. When comparing the efficacy of CT- and MRI-guided RFA, the rate of local tumor progression after CT-guided RFA was 19.2% and 11.5% after MRI-guided RFA ($P = 0.44$).[7] The results for TS and TE in our study were similar to the above-mentioned results. When comparing the TSR and the TER between the three groups in the HCC ≥2 cm and <2 cm subgroup, no significant difference was found. This indicated that the maximum diameter of HCC nodules had no obvious influence on the selection of imaging guidance method. This finding is consistent with that of a previous literature report, which showed that TSR and TER were both 100% in US-guided RFA on small and medium HCC.[10]

The risk factors of PFS and TE have been analyzed in US-, CT-, and MRI-guided RFA. The percentage of patients with HCC who were HBsAg positive in our study was 83.68%, and liver cirrhosis accounted for 82.98%. Although HBV infection could directly progress to HCC without advanced hepatic fibrosis, 70%–80% of cases of HCC occur mainly from HBV infection with liver cirrhosis.[12] Patients with chronic HBV infection accounted for 50% of patients with HCC globally.[13] Liver cirrhosis is associated with early recurrence after RFA. Besides, the occurrence of liver cancer would conversely increase the load of virus and prolong the duration of infection, ultimately leading to oncogenesis.[14]

In this study, tumor number ≥2 was an independent risk factor for recurrence. Shiina *et al*.[15] found that the number of tumors was a predictive factor for distant recurrence. Tumor number ≥2 is associated with a high rate of local recurrence and distant metastasis. The reason for this may be that the

biological behavior of multiple HCCs is more aggressive than that of solitary HCC.

Some researchers suggested that the elevation of AFP would be a marker forecasting tumor aggressiveness and vascular invasion and intrahepatic metastasis.[16-18] In our study, the high level of serum AFP indicated a high risk of tumor recurrence. In addition, preoperative serum AFP level has considerable predictive value for the malignant feature and prognosis of HCC.[19]

Complete ablation is not as easily achieved in HCC nodules larger than 3 cm in diameter as it is in small HCC nodules (<3 cm).[20-25] In pathological examination after RFA, residual tumor was detected in 71% of patients with large HCC, and the rate was 37% in patients with small HCC.[26] Large tumors are usually hypervascular, and the heat sink effect is obvious during ablation. For residual tumors, supplemental ablations were usually required. Transarterial chemoembolization (TACE) could embolize tumor's feeding vessels, causing ischemic necrosis, shrinkage (downstage) of the tumor, and reduction of the heat sink effect.[27] Therefore, RFA combined with TACE for a large tumor is feasible for achieving complete ablation.[24]

There were several limitations in this study. First, it was a retrospective study and had a nonrandomized design, which can introduce flaws in this study. A randomized and controlled trial is considered the best way to validate the above results. Second, MRI-guided RFA was assisted with a navigation system, which was not used in the US- and CT-guided groups. Hence, we demonstrated that MRI combined with navigation system defined as MRI-guided group could achieve similar efficacy compared with US- and CT-guided RFA. However, the treatment efficacy under MRI guidance without the assistant of navigation system should be investigated in further studies.

CONCLUSION

US-, CT-, and MRI-guided RFA was effective for the treatment of HCC. It seems that the use of different imaging guidance modalities has no significant effect on the survival and the ablation efficacy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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