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Differences in Survival Between First-Line Radiofrequency Ablation versus Surgery for Early-Stage Hepatocellular Carcinoma: A Population Study Using the Surveillance, Epidemiology, and End Results Database

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The first-line therapy for early-stage hepatocellular carcinoma (HCC) is unclear. This study was conducted to assess and compare survival after surgery *vs.* after radiofrequency ablation (RFA) for early-stage HCC.

Material/Methods: Data from HCC patients with a single tumor measuring 31–50 mm were extracted from the Surveillance, Epidemiology, and End Results (SEER) database from 2004 to 2015. Overall survival (OS) and cancer-specific survival (CSS) were assessed and compared between surgery and RFA treatment. Propensity score matching was performed. Multiple imputations were used to create 5 sets of complete data. Fine and Gray competing risk multivariate regression models were used to control biases.

Results: This study included 839 patients: 339 (40.41%) received RFA and 500 (59.59%) underwent surgery. Surgery improved the 5-year OS (63.95% *vs.* 37.13%, $p<0.01$) and CSS (64.01% *vs.* 38.29%, $p<0.01$) compared with RFA after propensity score matching. The competing risk regression models revealed that, compared with RFA, surgery resulted in better survival in the unmatched cohort with an adjusted sub-distribution hazard ratio of 0.689 (95% confident interval [CI], 0.562–0.868; $p=0.001$) and in the propensity-matched cohort with an adjusted sub-distribution hazard ratio of 0.642 (95% CI, 0.514–0.801; $p<0.001$).

Conclusions: Surgery appears to be a better therapy choice than RFA for patients with early-stage HCC with a single tumor measuring 31–50 mm.

MeSH Keywords: Carcinoma, Hepatocellular • Catheter Ablation • General Surgery

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Background

Hepatocellular carcinoma (HCC) is the sixth most common cancer and the third leading cause of cancer death worldwide [1]. The incidence of HCC has increased in Western countries in the last decade [2]. Moreover, it is expected to increase rapidly because of infections with hepatitis viruses and due to alcohol abuse [3]. With improvements in diagnosis, the incidence of early-stage HCC has greatly increased.

Surgery provides favorable treatment outcomes for early-stage HCC patients [3]. Unfortunately, some early-stage HCC patients are contraindicated for surgery due to comorbid conditions, insufficient remnant liver after surgery, and high-risk anatomic location [4]. Radiofrequency ablation (RFA) is an alternative therapeutic option for early-stage HCC, which offers treatment outcomes similar to those from surgery [5]. To date, surgery and RFA are the main treatment options for patients with early-stage HCC [5]. However, it is unclear which therapy provides better outcomes for early-stage HCC patients. Our study aimed to assess and compare survival after surgery or RFA for early-stage HCC.

Material and Methods

Patients

HCC patients were identified from the Surveillance, Epidemiology, and End Results (SEER) database from 2004 to 2015. Inclusion criteria were as follows: (1) pathology-confirmed HCC (International Classification of Diseases for Oncology, 3rd Edition [ICD-O-3] code 8170); (2) first-line treatment was either surgery (SEER code: 20–26, 30, 36–38, 50–52, 59, 60, 66, and 90) or RFA (SEER code: 16); (3) a single tumor measuring 31–50 mm; and (4) age ≥18 years. Exclusion criteria were: (1) macroscopic vascular invasion or metastasis, and (2) survival time < 30 days. Clinical variables, including age, sex, race, marital status, tumor grade, and alpha-fetoprotein (AFP) levels, were extracted from the SEER database.

Treatment and endpoints

Patients were divided into the surgery group and the RFA group. The primary endpoint was overall survival (OS), defined as the time interval from diagnosis to death attributed to any cause. The secondary endpoint was cancer-specific survival (CSS), defined as the time interval from diagnosis to death because of HCC.

Statistical analyses

We assessed the clinical variables for any significant difference between the 2 groups. Age was compared using the *t* test. Race, sex, marital status, tumor grade, and AFP levels were compared using Fisher's exact test or chi-square test. We estimated survival using the Kaplan-Meier method and compared the 2 groups statistically using the log rank test. To assess the simultaneous impact of potential confounders, Cox proportional hazards regression analysis was performed.

Selection bias existed in this retrospective study due to unbalanced baseline characteristics. A matched case-control analysis was performed to reduce the influence of selection bias on the efficacy comparison between RFA and surgery using propensity score matching (PSM). A logistic regression model was established, with treatment as the dependent variable. Patients were matched using a greedy nearest neighbor matching algorithm at 1: 1 fixed ratio. The absolute value <0.1 was used to compare the similarity of the 2 groups, which indicated that these covariates were well balanced in the 2 groups.

Using the mice package in R, multiple imputations were performed to identify the complete set of patients for regression analysis. Different bootstrap resamples were used for each imputation by fitting a flexible parametric additive regression model on a sample with replacement from the original data. This model was conducted to predict all of the original missing and non-missing values for the target variable for the current imputation. Five sets of complete data were generated for regression analysis.

We constructed a multivariable Fine-Gray model to estimate sub-distribution hazard ratios (sdHRs). The rates of HCC-related and non-HCC-related death were evaluated using Fine and Gray multivariate regression models. R software (version 3.4.4) and SPSS 24.0 for Windows (SPSS, Chicago, IL, USA) were used to perform statistical analyses. Two-tailed $p<0.05$ was considered statistically significant.

Results

Patient characteristics

Our study assessed the data of 97 118 HCC patients extracted from the SEER database from 2004 to 2015. Eventually, 839 patients were included based on the inclusion and exclusion criteria. Among the 839 patients, 339 (40.41%) were treated with RFA and 500 (59.59%) with surgery. Table 1 shows the patients' characteristics before PSM and after PSM. Before PSM, the AFP levels were higher in the RFA group, while patients were more likely to be classified as having moderately differentiated tumor grade in the surgery group. After PSM, the clinical variables were well balanced between the 2 groups.

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Table 1. Patients characteristics in the unmatched and propensity-matched cohorts.

	The unmatched cohort			The propensity-matched cohort (1: 1)		
	RFA (n=339)	Surgery (n=500)	P	RFA (n=227)	Surgery (n=227)	P
Age (years)			0.129			<0.001
≤65	186 (54.87%)	306 (61.20%)		136 (59.91%)	136 (59.91%)	
>65	153 (45.13%)	194 (38.80%)		91 (40.09%)	91 (40.09%)	
Sex			0.058			0.062
Male	260 (76.70%)	371 (74.20%)		176 (77.53%)	168 (74.00%)	
Female	79 (23.30%)	129 (25.80%)		51 (22.47%)	59 (26.00%)	
Race			0.181			0.091
White	201 (59.29%)	261 (52.20%)		131 (57.71%)	148 (65.20%)	
Black	43 (12.68%)	59 (11.80%)		28 (12.33%)	14 (6.17%)	
Others	95 (28.03%)	180 (36.00%)		68 (29.96%)	65 (28.63%)	
Marital status			0.096			0.021
Married	203 (59.88%)	302 (60.40%)		133 (58.59%)	131 (57.71%)	
Unmarried	130 (38.35%)	182 (36.40%)		89 (39.21%)	86 (37.88%)	
Unknown	6 (1.77%)	16 (3.20%)		5 (2.20%)	10 (4.41%)	
Tumor grade			0.896			0.063
Well differentiated	98 (28.91%)	111 (22.20%)		71 (31.28%)	75 (33.04%)	
Moderately differentiated	86 (25.37%)	258 (51.60%)		86 (37.89%)	84 (37.00%)	
Poorly differentiated	32 (9.44%)	86 (17.20%)		30 (13.22%)	30 (13.22%)	
Undifferentiated	2 (0.59%)	8 (1.60%)		2 (0.88%)	3 (1.32%)	
Unknown	121 (35.69%)	37 (7.40%)		38 (16.73%)	35 (15.42%)	
AFP			0.241			0.055
Positive	184 (54.28%)	225 (45.00%)		125 (55.07%)	119 (52.42%)	
Negative	102 (30.09%)	152 (30.40%)		68 (29.96%)	73 (32.16%)	
Unknown	53(15.63%)	123 (24.60%)		34 (14.97%)	35 (15.42%)	

Survival analysis in the original data

The median follow-up times of the RFA and surgery groups were 28 months (interquartile range [IQR]: 14–52) and 34 months (IQR: 15–59), respectively, before matching. After matching, the median follow-up times were 28 months (IQR: 14–55) for the RFA group and 33 months (IQR: 16–60) for the surgery group.

In the unmatched cohort, surgery improved the 5-year OS (59.18% *vs.* 29.35%, $p<0.01$) (Figure 1) and CSS (67.53% *vs.* 36.25%, $p<0.01$) (Figure 2) compared with RFA. In the propensity-matched cohort, surgery also had a better 5-year OS (63.95% *vs.* 37.13%, $p<0.01$) (Figure 3) and a more favorable CSS (64.01% *vs.* 38.29%, $p<0.01$) (Figure 4) than RFA. In the multivariate analysis, surgery was still an independent prognostic factor for OS ($p<0.001$) and CSS ($p<0.001$) (Table 2).

In the matched cohort, surgery also revealed a more favorable OS (HR=0.569, 95% CI: 0.396–0.743; $p<0.01$) and a more favorable CSS (HR=0.576, 95% CI: 0.379–0.773; $p<0.01$) compared with RFA (Table 3).

Survival analysis after multiple imputations

After multiple imputations, 5 sets of complete data were generated. Table 4 shows the results of univariate and multivariable

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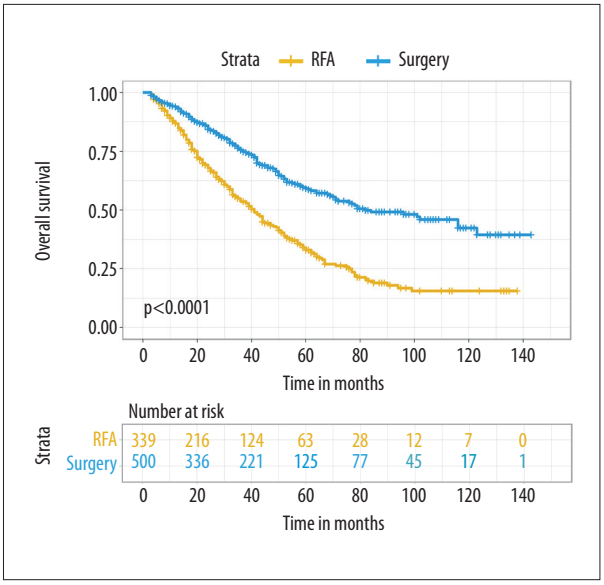

Figure 1. Overall survival following radiofrequency ablation (RFA) versus surgery for early-stage hepatocellular carcinoma in the unmatched cohort.

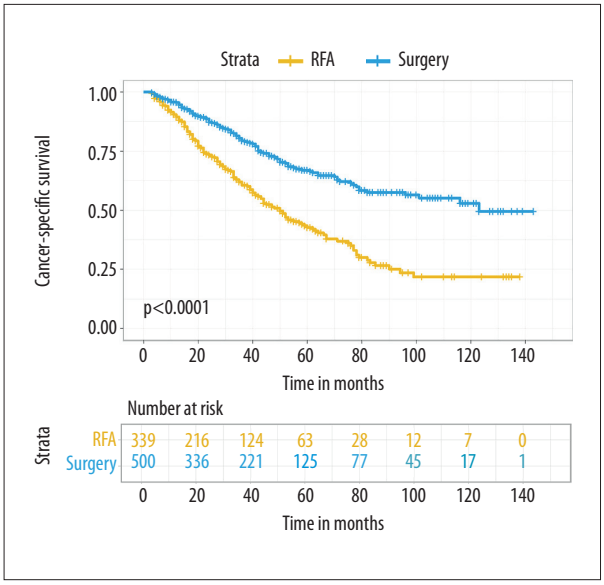

Figure 2. Cancer-specific survival following radiofrequency ablation (RFA) versus surgery for early-stage hepatocellular carcinoma in the unmatched cohort.

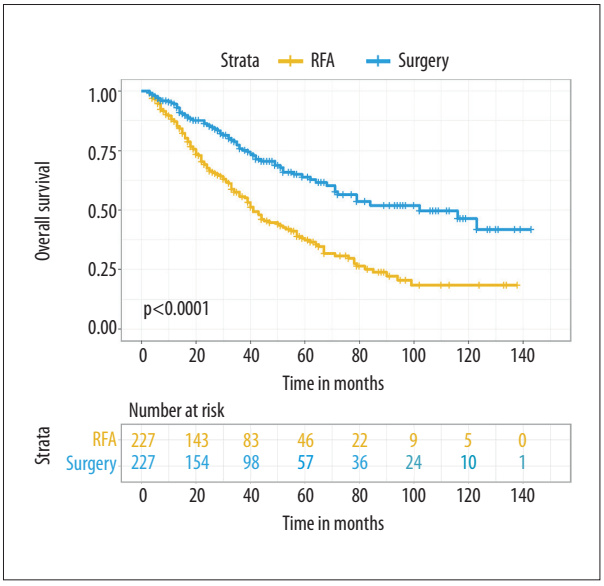

Figure 3. Overall survival following radiofrequency ablation (RFA) versus surgery for early-stage hepatocellular carcinoma in the propensity-matched cohort.

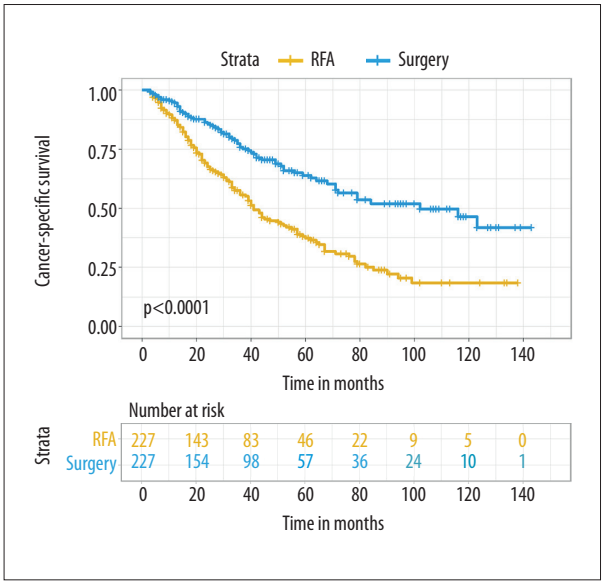

Figure 4. Cancer-specific survival following radiofrequency ablation (RFA) versus surgery for early-stage hepatocellular carcinoma in the propensity-matched cohort.

analyses of prognostic factors. After adjusting for confounding factors, surgery revealed a better OS (HR=0.561, 95% CI: 0.420–0.702; $p<0.01$) and a better CSS (HR=0.552, 95% CI: 0.291–0.712; $p<0.01$) compared with RFA in multivariate analysis.

Furthermore, Fine and Gray multivariate regression models revealed that, compared with RFA, surgery had a better survival in the unmatched cohort with an adjusted sdHR of 0.689 (95% CI, 0.562–0.868; $p=0.001$) and in the propensity-matched cohort with an adjusted sdHR of 0.642 (95% CI, 0.514–0.801; $p<0.001$) (Table 5).

Discussion

The incidence of HCC is rising in developed countries because of alcohol abuse, and in developing countries because

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Table 2. Univariate and multivariable analyses of prognostic factors in the unmatched cohort.

	Overall survival				Cancer-specific survival			
	Univariate analysis HR (95% CI)	*P*	Multivariate analysis HR (95% CI)	*P*	Univariate analysis HR (95% CI)	*P*	Multivariate analysis HR (95% CI)	*P*
Age (years)								
≤65* *vs.* >65	1.358 (1.218–1.498)	<0.001	1.507 (1.344–1.671)	<0.001	1.344 (1.184–1.504)	<0.001	1.364 (1.137–1.592)	0.007
Gender								
Female* *vs.* Male	1.119 (0.960–1.278)	0.167			1.134 (0.951–1.317)	0.176		
Race								
White	Reference		Reference		Reference		Reference	
Black	1.157 (0.956–1.357)	0.154	1.078 (0.847–1.308)	0.524	1.137 (0.905–1.369)	0.275	1.068 (0.739–1.396)	0.695
Others	0.589 (0.424–0.755)	<0.001	0.610 (0.419–0.800)	<0.001	0.614 (0.426–0.801)	<0.001	0.617 (0.352–0.882)	<0.001
Marital status								
Married* *vs.* unmarried	1.303 (1.164–1.443)	<0.001	1.276 (1.116–1.436)	0.003	1.357 (1.197–1.516)	<0.001	1.357 (1.132–1.582)	0.007
Tumor grade								
Well differentiated	Reference				Reference		Reference	
Moderately differentiated	0.784 (0.624–1.012)	0.056			0.789 (0.578–0.998)	0.027	0.864 (0.618–1.110)	0.245
Poorly differentiated	1.058 (0.817–1.299)	0.646			1.262 (0.993–1.530)	0.089	1.219 (0.901–1.537)	0.222
Undifferentiated	1.915 (0.823–2.842)	0.071			2.697 (1.986–3.408)	0.006	2.191 (1.287–3.095)	0.013
AFP								
Negative* *vs.* positive	1.404 (1.241–1.567)	<0.001	1.448 (1.279–1.617)	<0.001	1.533 (1.343–1.722)	<0.001	1.513 (1.275–1.751)	<0.001
Therapy								
RFA* *vs.* surgery	0.544 (0.405–0.684)	<0.001	0.582 (0.422–0.743)	<0.001	0.538 (0.379–0.698)	<0.001	0.659 (0.440–0.878)	<0.001

RFA – radiofrequency ablation; AFP – alpha-fetoprotein; HR – hazard ratio; CI – confidence interval. * Represents reference.

of hepatitis B virus infection [2]. Because of the poor treatment outcomes for advanced-stage HCC, mortality rates for HCC increased faster than those for any other cancer [1]. In contrast, survival in early-stage HCC improved. The 5-year OS of this subgroup of patients ranged from 32% to 70%, varying greatly between studies [6,7]. However, the proportion of early-stage HCC has increased because of the development of screening programs for early-stage HCC and improvement of imaging technology [1]. Thus, it is important to identify the best treatment option for early-stage HCC.

HCC tumors measuring 31–50 mm are very important in clinical practice, because many patients are diagnosed at this size of the tumor [8,9]. Although a cut-off value below 30 mm was recommended for RFA by the Americas Hepato-Pancreato-Biliary Association [10] and the Barcelona Clinic Liver Cancer (BCLC) staging algorithm [11], some reports have revealed that tumors measuring 31–50 mm could be safely ablated [12,13]. Regarding tumors measuring 31–50 mm, some studies reported that OS was worse following RFA compared to that after surgery [14–16]. However, several studies showed conflicting results that RFA provided similar outcomes compared

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Table 3. Univariate analysis of prognostic factors in the propensity-matched cohort.

	Overall survival			Cancer-specific survival		
	HR (95% CI)		*P*	HR (95% CI)		*P*
Age						
≤65* *vs.* >65	1.377	(1.204–1.550)	<0.001	1.361	(1.164–1.557)	0.002
Sex						
Female* *vs.* Male	1.077	(0.882–1.272)	0.455	1.132	(0.908–1.356)	0.277
Race						
White	Reference			Reference		
Black	1.040	(0.791–1.290)	0.756	1.121	(0.843–1.400)	0.420
Others	0.616	(0.412–0.820)	<0.001	0.655	(0.425–0.884)	<0.001
Marital status						
Married* *vs.* unmarried	1.206	(1.033–1.379)	0.034	1.251	(1.055–1.447)	0.025
Grade						
Well differentiated	Reference			Reference		
Moderately differentiated	0.875	(0.671–1.079)	0.200	0.917	(0.680–1.155)	0.479
Poorly differentiated	1.104	(0.820–1.389)	0.495	1.280	(0.961–1.599)	0.129
Undifferentiated	1.565	(0.423–2.707)	0.442	2.183	(1.037–3.329)	0.002
AFP						
Negative* *vs.* positive	1.317	(1.117–1.517)	0.007	1.437	(1.206–1.668)	0.002
Therapy						
RFA* *vs.* surgery	0.569	(0.396–0.743)	<0.001	0.576	(0.379–0.773)	<0.001

RFA – radiofrequency ablation; AFP – alpha-fetoprotein; HR – hazard ratio; CI – confidence interval. * Represents reference.

with surgery [9,12,17–19]. Our study revealed that surgery improved OS and CSS compared to RFA for HCC with a single tumor measuring 31–50 mm from the SEER database. Thus, surgery might be a better therapeutic option for early-stage HCC.

However, RFA becomes the first-line therapy for patients with BCLC stages 0–A who are not suitable for surgery and for patients with significant underlying parenchymal disease [20,21]. Moreover, RFA is widely used as first-line therapy for early-stage HCC, especially in Asia [22]. Possible explanations for this phenomenon may be: (1) several studies reported that RFA provided similar OS compared with surgery [9,12,17–19], while RFA provides a better quality of life and less morbidity [15,17,23]; and (2) HCC patients in high-incidence regions are more likely to be hepatitis B virus-positive. Hepatitis B virus-positive patients are more likely to have significant underlying parenchymal disease, like severe cirrhosis and liver dysfunction. The morbidity might increase in patients with a diseased liver following surgery [24].

This study has certain methodological advantages compared to previous studies [14,16]. We used PSM to reduce selection bias in the original data. Moreover, multiple imputations were performed to create 5 sets of complete data. Finally, a multivariable Fine-Gray model was used to assess the rates of HCC-related and non-HCC-related death. These methodological advantages can provide a more credible result.

However, there were some limitations in our study. First, liver function and fibrosis were not assessed. The missing data regarding liver function and fibrosis might lead to biases. Patients with severe cirrhosis were more likely to receive RFA than surgery [16]. As a result, patients who received RFA might have worse OS and CSS compared to patients who underwent surgery. Unfortunately, data regarding liver function and fibrosis were not recorded for many patients in the SEER database, so these data were not included in statistical analyses. To control this bias, our study generated 5 sets of complete data for regression analysis, which was conducted to predict all of the original missing and non-missing data values regarding liver function and fibrosis. Moreover, we performed PSM to control for potential biases, including age, sex, race, marital status, tumor grade, and AFP levels. The results revealed that RFA showed worse OS and CSS compared to surgery. Thus, the missing data regarding liver function and fibrosis might not have influenced the main conclusion of our study.

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Table 4. Univariate and multivariable analyses of prognostic factors after multiple imputations.

	Overall survival				Cancer-specific survival			
	Univariate analysis HR (95% CI)	*P*	Multivariate analysis HR (95% CI)	*P*	Univariate analysis HR (95% CI)	*P*	Multivariate analysis HR (95% CI)	*P*
Age (years)								
≤65* *vs.* >65	1.358 (1.219–1.497)	<0.001	1.449 (1.306–1.592)	<0.001	1.344 (1.184–1.505)	<0.001	1.428 (1.263–1.592)	<0.001
Gender								
Female* *vs.* Male	1.119 (0.960–1.277)	0.167			1.134 (0.952–1.317)	0.177		
Race								
White	Reference		Reference		Reference		Reference	
Black	1.159 (0.956–1.360)	0.153	1.101 (0.898–1.306)	0.351	1.139 (0.906–1.372)	0.272	1.062 (0.827–1.297)	0.618
Others	0.591 (0.426–0.756)	<0.001	0.594 (0.423–0.764)	<0.001	0.616 (0.428–0.804)	<0.001	0.620 (0.426–0.814)	<0.001
Marital status								
Married* *vs.* unmarried	1.301 (1.162–1.440)	<0.001	1.139 (0.996–1.282)	0.075	1.353 (1.194–1.511)	<0.001	1.192 (1.028–1.357)	0.036
Tumor grade								
Well differentiated	Reference				Reference			
Moderately differentiated	0.825 (0.633–1.017)	0.056			0.854 (0.623–1.085)	0.185		
Poorly differentiated	1.009 (0.764–2.280)	0.946			1.195 (0.928–1.461)	0.196		
Undifferentiated	1.467 (0.653–2.280)	0.361			2.024 (1.199–2.849)	0.100		
AFP								
Negative* *vs.* positive	1.354 (1.187–1.521)	0.001	1.365 (1.200–1.529)	<0.001	1.467 (1.280–1.653)	<0.001	1.478 (1.292–1.664)	<0.001
Therapy								
RFA* *vs.* surgery	0.544 (0.405–0.684)	<0.001	0.561 (0.420–0.702)	<0.001	0.538 (0.380–0.697)	<0.001	0.552 (0.291–0.712)	<0.001

RFA – radiofrequency ablation; AFP – alpha-fetoprotein; HR – hazard ratio; CI – confidence interval. * Represents reference.

Furthermore, data regarding tumor recurrence were not available because of the limitations of the SEER database. The impact of surgery or RFA on local-regional-free survival and distant metastasis-free survival could not be assessed. Thus, whether the unfavorable OS and CSS of RFA were due to the higher tumor recurrence remains unclear. The answer to this question is important for deciding treatment options for patients with early-stage HCC in clinical practice. We are going to conduct a prospective cohort study to investigate the efficacy of RFA in recurrence-free survival for early-stage HCC. We hope the results will provide useful evidence on the associations between OS and recurrence-free survival.

Conclusions

Surgery might be more appropriate than RFA for early-stage HCC patients with a single tumor measuring 31–50 mm. Due to the limitations of the SEER database, these results should be verified in a prospective randomized controlled trial.

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Table 5. Univariate and multivariable analyses of prognostic factors based on the competing risk model.

	The unmatched cohort				The propensity-matched cohort (1: 1)			
	Univariate analysis HR (95% CI)	*P*	Multivariate analysis HR (95% CI)	*P*	Univariate analysis HR (95% CI)	*P*	Multivariate analysis HR (95% CI)	*P*
Age (years)								
≤65* *vs.* >65	1.290 (1.100–1.510)	0.002	1.291 (1.025–1.625)	0.030	1.300 (1.070–1.580)	0.008	1.377 (1.091–1.737)	0.007
Gender								
Female* *vs.* Male	1.120 (0.890–1.350)	0.210			1.140 (0.913–1.430)	0.250		
Race								
White	Reference		Reference		Reference		Reference	
Black	1.091 (0.867–1.372)	0.460	0.997 (0.722–1.378)	0.990	1.134 (0.868–1.481)	0.360	0.911 (0.662–1.253)	0.570
Others	0.662 (0.551–0.796)	<0.001	0.667 (0.512–0.868)	0.002	0.711 (0.566–0.894)	0.004	0.666 (0.512–0.867)	0.003
Marital status								
Married* *vs.* unmarried	1.320 (1.130–1.550)	<0.001	1.361 (1.088–1.704)	0.007	1.230 (1.020–1.500)	0.033	1.389 (1.112–1.736)	0.004
Tumor grade								
Well differentiated	Reference		Reference		Reference			
Moderately differentiated	0.810 (0.657–0.998)	0.047	0.893 (0.698–1.142)	0.370	0.941 (0.745–1.190)	0.610		
Poorly differentiated	1.300 (0.992–1.710)	0.057	1.251 (0.908–1.722)	0.170	1.304 (0.944–1.800)	0.110		
Undifferentiated	2.920 (1.364–6.234)	0.006	2.402 (0.945–6.105)	0.066	2.362 (0.941–5.930)	0.067		
AFP								
Negative* *vs.* positive	1.490 (1.240–1.800)	<0.001	1.439 (1.136–1.823)	0.003	1.410 (1.120–1.770)	0.003	1.535 (1.207–1.953)	<0.001
Therapy								
RFA* *vs.* surgery	0.582 (0.497–0.681)	<0.001	0.698 (0.562–0.868)	0.001	0.623 (0.514–0.757)	<0.001	0.642 (0.514–0.801)	<0.001

RFA – radiofrequency ablation; AFP – alpha-fetoprotein; HR – hazard ratio; CI – confidence interval. * Represents reference.

Conflicts of interest

None.

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References:

1. Bray F, Ferlay J, Soerjomataram I et al: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. Cancer J Clin, 2018; 68(6): 394–424
2. Rahbari NN, Mehrabi A, Mollberg NM et al: Hepatocellular carcinoma: Current management and perspectives for the future. Ann Surg, 2011; 253(3): 453–69
3. Forner A, Reig M, Bruix J: Hepatocellular carcinoma. Lancet, 2018; 391(10127): 1301–14
4. Poon RT, Fan ST, Tsang FH, Wong J: Locoregional therapies for hepatocellular carcinoma: A critical review from the surgeon's perspective. Ann Surg, 2002; 235(4): 466–86
5. Wang CH, Wey KC, Mo LR et al: Current trends and recent advances in diagnosis, therapy, and prevention of hepatocellular carcinoma. Asian Pac J Cancer Prev, 2015; 16(9): 3595–604
6. Silva MF, Sapisochin G, Strasser SI et al: Liver resection and transplantation offer similar 5-year survival for Child-Pugh-Turcotte A HCC-patients with a single nodule up to 5 cm: a multicenter, exploratory analysis. Eur J Surg Oncol, 2013; 39(4): 386–95
7. Iida H, Aihara T, Ikuta S, Yamanaka N: Comparative study of percutaneous radiofrequency ablation and hepatic resection for small, poorly differentiated hepatocellular carcinomas. Hepatol Res, 2014; 44(10): E156–62
8. Akoad ME, Pomfret EA: Surgical resection and liver transplantation for hepatocellular carcinoma. Clin Liver Dis, 2015; 19(2): 381–99
9. Gory I, Fink M, Bell S et al: Radiofrequency ablation versus resection for the treatment of early stage hepatocellular carcinoma: A multicenter Australian study. Scand J Gastroenterol, 2015; 50(5): 567–76
10. Munene G, Vauthey JN, Dixon E: Summary of the 2010 AHPBA/SSO/SSAT Consensus Conference on HCC. Int J Hepatol, 2011; 2011: 565060
11. European Association For The Study Of The Liver, European Organisation For Research And Treatment Of Cancer: EASL-EORTC clinical practice guidelines: Management of hepatocellular carcinoma. J Hepatol, 2012; 56(4): 908–43
12. Tohme S, Geller DA, Cardinal JS et al: Radiofrequency ablation compared to resection in early-stage hepatocellular carcinoma. HPB (Oxford), 2013; 15(3): 210–17
13. Ogihara M, Wong LL, Machi J: Radiofrequency ablation versus surgical resection for single nodule hepatocellular carcinoma: Long-term outcomes. HPB (Oxford), 2005; 7(3): 214–21
14. Kutlu OC, Chan JA, Aloia TA et al: Comparative effectiveness of first-line radiofrequency ablation versus surgical resection and transplantation for patients with early hepatocellular carcinoma. Cancer, 2017; 123(10): 1817–27
15. Cucchetti A, Piscaglia F, Cescon M et al: Cost-effectiveness of hepatic resection versus percutaneous radiofrequency ablation for early hepatocellular carcinoma. J Hepatol, 2013; 59(2): 300–7
16. Jiang YQ, Wang ZX, Deng YN et al: Efficacy of hepatic resection *vs.* radiofrequency ablation for patients with very-early-stage or early-stage hepatocellular carcinoma: A population-based study with stratification by age and tumor size. Front Oncol, 2019; 9: 113
17. Kang TW, Kim JM, Rhim H et al: Small hepatocellular carcinoma: Radiofrequency ablation versus nonanatomic resection – propensity score analyses of long-term outcomes. Radiology, 2015; 275(3): 908–19
18. Ni JY, Xu LF, Sun HL et al: Percutaneous ablation therapy versus surgical resection in the treatment for early-stage hepatocellular carcinoma: A meta-analysis of 21,494 patients. J Cancer Res Clin Oncol, 2013; 139(12): 2021–33
19. Feng K, Yan J, Li X et al: A randomized controlled trial of radiofrequency ablation and surgical resection in the treatment of small hepatocellular carcinoma. J Hepatol, 2012; 57(4): 794–802
20. Raza A, Sood GK: Hepatocellular carcinoma review: Current treatment, and evidence-based medicine. World J Gastroenterol, 2014; 20(15): 4115–27
21. N'Kontchou G, Aout M, Laurent A et al: Survival after radiofrequency ablation and salvage transplantation in patients with hepatocellular carcinoma and Child-Pugh A cirrhosis. J Hepatol, 2012; 56(1): 160–66
22. Thandassery RB, Goenka U, Goenka MK: Role of local ablative therapy for hepatocellular carcinoma. J Clin Exp Hepatol, 2014; 4(Suppl. 3): S104–11
23. Huang G, Chen X, Lau WY et al: Quality of life after surgical resection compared with radiofrequency ablation for small hepatocellular carcinomas. Br J Surg, 2014; 101(8): 1006–15
24. Liu PH, Hsu CY, Hsia CY et al: Surgical resection versus radiofrequency ablation for single hepatocellular carcinoma </= 2 cm in a propensity score model. Ann Surg, 2016; 263(3): 538–45

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