Original Article | Gastrointestinal Imaging

eISSN 2005-8330
https://doi.org/10.3348/kjr.2023.0022
Korean J Radiol 2023;24(8):761-771

Korean Journal of Radiology

Treatment Outcomes of Percutaneous Radiofrequency Ablation for Hepatocellular Carcinomas: Effects of the Electrode Type and Placement Method

Jiyeon Park[1], Min Woo Lee[1,2], Soo Hyun Ahn[3], Seungchul Han[1], Ji Hye Min[1], Dong Ik Cha[1], Kyoung Doo Song[1], Tae Wook Kang[1], Hyunchul Rhim[1,2]

[1]Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

[2]Department of Health Sciences and Technology, The Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, Seoul, Republic of Korea

[3]Department of Mathematics, Ajou University, Suwon, Republic of Korea

Objective: To investigate the association among the electrode placement method, electrode type, and local tumor progression (LTP) following percutaneous radiofrequency ablation (RFA) for small hepatocellular carcinomas (HCCs) and to assess the risk factors for LTP.

Materials and Methods: In this retrospective study, we enrolled 211 patients, including 150 males and 61 females, who had undergone ultrasound-guided RFA for a single HCC < 3 cm. Patients were divided into four combination groups of the electrode type and placement method: 1) tumor-puncturing with an internally cooled tip (ICT), 2) tumor-puncturing with an internally cooled wet tip (ICWT), 3) no-touch with ICT, and 4) no-touch with ICWT. Univariable and multivariable Cox proportional-hazards regression analyses were performed to evaluate the risk factors for LTP. The major RFA-related complications were assessed.

Results: Overall, 83, 34, 80, and 14 patients were included in the ICT, ICWT, no-touch with ICT, and no-touch with ICWT groups, respectively. The cumulative LTP rates differed significantly among the four groups. Compared to tumor puncturing with ICT, tumor puncturing with ICWT was associated with a lower LTP risk (adjusted hazard ratio [aHR] = 0.11, 95% confidence interval [CI] = 0–0.88, P = 0.034). However, the cumulative LTP rate did not differ significantly between tumor-puncturing with ICT and no-touch RFA with ICT (aHR = 0.34, 95% CI = 0.03–1.62, P = 0.188) or ICWT (aHR = 0.28, 95% CI = 0–2.28, P = 0.294). An insufficient ablative margin was a risk factor for LTP (aHR = 6.13, 95% CI = 1.41–22.49, P = 0.019). The major complication rates were 1.2%, 0%, 2.5%, and 21.4% in the ICT, ICWT, no-touch with ICT, and no-touch with ICWT groups, respectively.

Conclusion: ICWT was associated with a lower LTP rate compared to ICT when performing tumor-puncturing RFA. An insufficient ablation margin was a risk factor for LTP.

Keywords: Radiofrequency ablation; Hepatocellular carcinoma; Local tumor progression; Internally cooled tip; Internally cooled wet tip

INTRODUCTION

Radiofrequency ablation (RFA) is a curative treatment option for hepatocellular carcinomas (HCCs) measuring < 3 cm [1]. Although the efficacy and safety of RFA are well-established, the therapeutic performance of ablative treatments has continuously evolved over the last decade. Advanced RFA techniques, including centripetal RFA

Received: January 11, 2023 **Revised:** April 29, 2023 **Accepted:** May 23, 2023

Corresponding author: Min Woo Lee, MD, PhD, Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Republic of Korea
• E-mail: leeminwoo0@gmail.com

with multiple electrodes accompanied by the no-touch technique, are widely used to treat small HCCs [2,3].

Straight radiofrequency (RF) electrodes are positioned at the periphery or outside the tumor for centripetal RFA, and RF energy is delivered by switching bipolar and switching monopolar modes [4-8]. Internally cooled tips (ICTs) and internally cooled wet tips (ICWTs) are commercially available straight electrodes [9]. The ICWT electrode also provides an effusion of normal saline around the exposed tip. Therefore, the electrical conductivity around the ICWT increases, creating a larger ablation zone than that of the ICT electrodes. Thus, multiple ICWTs create a larger and more spherical ablation zone compared to ICT electrodes [10]. Therefore, the size and shape of the ablation zone appear to be affected by the combined electrode placement method (no-touch vs. tumor-puncturing) and type of RF electrode (ICT vs. ICWT).

No-touch RFA provides better local tumor control compared to tumor-puncturing RFA because it can achieve a large ablation zone [5,8,11,12]. However, to the best of our knowledge, therapeutic outcomes of RFA based on the electrode placement method in combination with the type of RF electrode have not been thoroughly explored. Therefore, this study was aimed at investigating the association of the electrode placement method with the electrode type and local tumor progression (LTP) following percutaneous RFA for small HCCs and assessing the risk factors for LTP.

MATERIALS AND METHODS

Compliance with Ethical Standards

This retrospective study was approved by the Institutional Review Board of Samsung Medical Center (IRB # 2022-12-003-001). The requirement for obtaining written informed consent was waived.

Patients

We retrospectively screened 264 consecutive patients from a longitudinal hospital registry who had undergone RFA for HCC from January 2017 to May 2021. Among them, 53 patients were excluded for the following reasons: 1) lack of pre-procedural laboratory data (n = 28); 2) more than two HCCs (n = 1); 3) combined transcatheter arterial chemoembolization (TACE) and RFA (n = 4); 4) tumor size < 1 cm (n = 15); 5) recurrent HCC after TACE or liver transplantation (LT; n = 3); and 6) follow-up loss immediately after RFA (n = 2). Finally, we enrolled 211 patients, including 150 males and 61 females, with a mean age of 60.9 ± 9.5 years, who had undergone ultrasound (US)-guided RFA for a single HCC < 3 cm (Fig. 1).

Percutaneous RFA

All RFA procedures were performed percutaneously under US guidance (LOGIQ E9 or LOGIQ E10, GE Healthcare) by five radiologists with at least three years of experience with RFA using a fusion imaging technique (volume navigation; GE Healthcare) [13]. The operators used various RFA systems

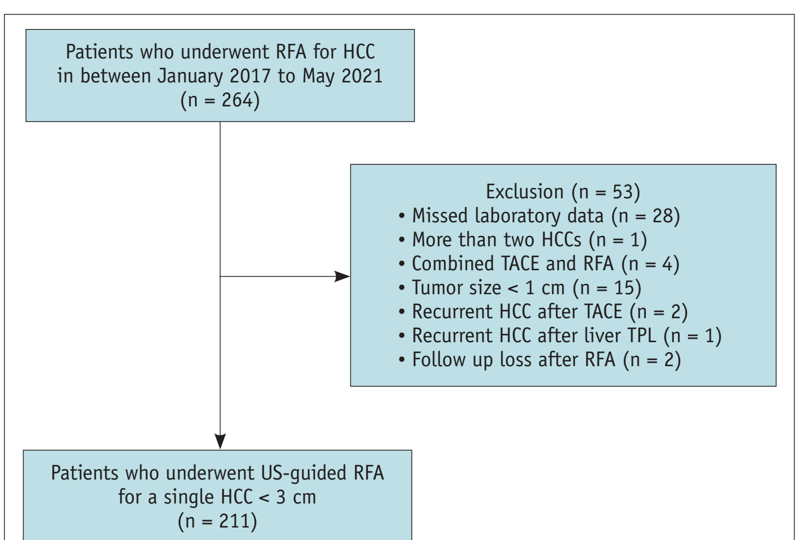

Fig. 1. Flow diagram showing the patient selection process with inclusion and exclusion criteria. Among 264 patients who underwent radiofrequency ablation (RFA) for hepatocellular carcinoma (HCC), 53 were excluded for various reasons. Finally, 211 patients were included in this study. TACE = transcatheter arterial chemoembolization, TPL = transplantation, US = ultrasonography

(VIVA RFA System, STARmed; Jet-tip RFA System, RF Medical). An active-tip length-adjustable tip (Proteus RF Electrode; STARmed) or clustered separable electrodes (Octopus Electrode, STARmed) were used. For ICWT, one (Jet-tip, RF Medical) or two (Twin electrodes, RF Medical) electrodes were used [10].

The operators used the tumor puncturing or no-touch method based on their preference, tumor location, and tumor shape [4]. Tumor-puncturing RFA refers to conventional RFA in which the operator places one electrode across the center of the tumor or multiple electrodes at the periphery of the tumor. In no-touch RFA, the operator positions multiple electrodes outside the tumor [12]. The RF energy is then delivered by switching monopolar, switching bipolar, and/or combined modes [5,8,11].

Assessment of the Treatment Response

The treatment was considered technically successful if the RFA zone entirely covered the index tumor on contrast-enhanced computed tomography (CT) performed within 12 h of the procedure [14]. The maximum (D_{max}) and minimum (D_{min}) diameters of the ablation zone were measured on axial CT scans in the portal phase, and the longest vertical diameter (D_v) was measured on sagittal or coronal images. The ablation volume was calculated using the following formula: ablation volume = π (D_{max} x D_{min} x D_v)/6 [10].

Follow-up CT was performed 1 month after the initial treatment, every 3–4 months during the first 2 years, and every 4–6 months thereafter. The technique efficacy was evaluated using a 1-month follow-up CT scan. The ablative margins were evaluated on immediate follow-up CT. A sufficient ablative margin was defined as a margin 5 mm from the tumor margin [5]. Major complications were defined as events that lead to substantial morbidity and disability that increase the level of care, result in hospital admission, or substantially lengthen the hospital stay, based on the standardization paper for terminology and reporting criteria [14].

Tumor recurrence after RFA was classified into four categories: LTP, intrahepatic distant recurrence (IDR), extrahepatic metastasis (EM), and aggressive intrasegmental recurrence (AIR). LTP was defined as recurrence at the margin of the ablation zone after treatment success [15,16]. IDR refers to the development of HCCs apart from the ablation zone in the liver. EM was defined as an HCC metastasis outside the liver [12]. AIR was defined as the simultaneous development of multiple nodules (at least three) or infiltrative tumor recurrence in the treated liver segment [17]. Overall survival (OS) was measured from the date of RFA to the date of death from any cause. The cutoff date for data collection was June 30, 2022. Patients who had undergone LT during the follow-up period were censored from the study on the date of LT.

Statistical Analyses

The patients were divided into four groups according to the electrode placement method and type of RF electrode: 1) tumor-puncturing with ICT, 2) tumor-puncturing with ICWT, 3) no-touch with ICT, and 4) no-touch with ICWT. Patient demographics and clinical characteristics were summarized using descriptive statistics and compared among the four groups using the Fisher's exact test for categorical data and the Kruskal–Wallis test for continuous data. Univariable and multivariable Cox proportional-hazards regression analyses were performed to evaluate factors associated with HCC recurrence and OS. In the multivariable analysis, variables with a *P*-value < 0.1 in the univariable analyses or comparisons of baseline characteristics among the four groups were included as potential confounders. A stepwise selection method was used to identify the independent confounding factors. Kaplan–Meier curves, log-rank tests, and z-tests were used to compare the cumulative rates of HCC recurrence and OS. Statistical analyses were performed using R version 3.5.0 (The R Foundation for Statistical Computing). Statistical significance was set at a *P*-value < 0.05.

RESULTS

Baseline Characteristics

Among the 211 patients, tumor puncturing with ICT, tumor puncturing with ICWT, no-touch with ICT, and no-touch with ICWT were performed in 83, 34, 80, and 14 patients, respectively. Table 1 summarizes the baseline characteristics. Among patient-related factors, the etiology and tumor size differed significantly among the four groups (P = 0.014 and 0.005, respectively). Liver function, including the albumin–bilirubin (ALBI) grade, prothrombin time-international normalized ratio, and albumin level, also differed significantly (P = 0.017, P = 0.003, and P < 0.001, respectively). Other variables, including tumor location and marker levels, did not differ significantly among the four groups.

Table 1 summarizes the characteristics of ablation

 https://doi.org/10.3348/kjr.2023.0022

Table 1. Demographic and clinical characteristics of the study patients

Variable	Tumor-puncturing with ICT (n = 83)	Tumor-puncturing with ICWT (n = 34)	No-touch with ICT (n = 80)	No-touch with ICWT (n = 14)	*P*
Age, yr	62.0 (43.0–84.0)	62.0 (42.0–80.0)	59.0 (35.0–79.0)	62.5 (43.0–79.0)	0.146
Sex					0.559
Male	55 (66.3)	24 (70.6)	61 (76.3)	10 (71.4)	
Female	28 (33.7)	10 (29.4)	19 (23.8)	4 (28.6)	
Etiology					0.014
HBV	51 (61.4)	24 (70.6)	67 (83.8)	8 (57.1)	
HCV	7 (8.4)	3 (8.8)	6 (7.5)	1 (7.1)	
Others	25 (30.1)	7 (20.6)	7 (8.8)	5 (35.7)	
Tumor size, cm	1.5 ± 0.4	1.6 ± 0.5	1.6 ± 0.4	1.2 ± 0.2	0.005
Tumor location					0.508
Segment I	1 (1.2)	1 (2.9)	0 (0)	0 (0)	
Segments II, III, and IV	15 (18.1)	3 (8.8)	11 (13.8)	3 (21.4)	
Segments V, VI, VII, and VIII	67 (80.7)	30 (88.2)	69 (86.3)	11 (78.6)	
Peri-portal venous location	8 (9.6)	1 (2.9)	7 (8.8)	1 (7.1)	0.696
Peri-hepatic venous location	10 (12)	2 (5.9)	4 (5)	0 (0)	0.309
Subcapsular location					0.550
Non-subphrenic subcapsular	17 (20.5)	9 (26.5)	18 (22.5)	6 (42.9)	
Subphrenic	12 (14.5)	3 (8.8)	8 (10.0)	0 (0)	
Non-subcapsular	54 (65.1)	22 (64.7)	54 (67.5)	8 (57.1)	
Pre-procedural laboratory results					
ALBI grade					0.017
Grade 1	28 (33.7)	10 (29.4)	44 (55.0)	6 (42.9)	
Grade 2 or 3	55 (66.3)	24 (70.6)	36 (45.0)	8 (57.1)	
MoRAL score	60.2 (38.6–186.7)	63.6 (46.2–145.9)	62.6 (38.9–265.4)	57.0 (38.6–90.1)	0.543
Platelet	113 (48–232)	113.5 (54–217)	132.5 (47–301)	129.5 (63–272)	0.103
PT-INR	1.1 (0.9–1.5)	1.1 (1–1.7)	1.0 (0.9–1.6)	1.1 (0.9–1.5)	0.003
Albumin, g/dL	4.2 (2.9–5)	4.0 (2.8–4.7)	4.4 (2.6–5)	4.4 (3.4–4.7)	< 0.001
Bilirubin, mg/dL	0.6 (0.2–2)	0.65 (0.2–3.7)	0.6 (0.2–2.4)	0.5 (0.3–1.6)	0.718
AFP, ng/mL	4.8 (1.3–998.4)	6.4 (0.9–156.3)	6 (1.2–636)	3.7 (1.3–60.3)	0.555
PIVKA-II, mAU/mL	23 (10–274)	24 (14–166)	25 (10–522)	22 (10–60)	0.592
Number of electrodes used					< 0.001
One	41 (49.4)	17 (50.0)	6 (7.5)	1 (7.1)	
Two or more	42 (50.6)	17 (50.0)	74 (92.5)	13 (92.9)	
Ablation zone volume, cm^3	13.0 (1.7–39.8)	11.9 (2.6–29.2)	20.1 (4.1–50)	14.3 (5.1–51.4)	< 0.001
Ablative margin					0.012
Sufficient	76 (91.6)	32 (94.1)	80 (100)	12 (85.7)	
Insufficient	7 (8.4)	2 (5.9)	0 (0)	2 (14.3)	

Values are presented as the median (range), number (%), or mean ± standard deviation unless otherwise indicated.
ICT = internally cooled tip, ICWT = internally cooled wet tip, HBV = hepatitis B virus, HCV = hepatitis C virus, ALBI = albumin-bilirubin, MoRAL = model for tumor recurrence after living donor liver transplantation, PT-INR = prothrombin time-international normalized ratio, AFP = alpha-fetoprotein, PIVKA-II = protein induced by vitamin K absence or antagonist-II

techniques. The number of electrodes used was higher in the no-touch RFA group than in the tumor-puncturing RFA group ($P < 0.001$). The ablation zone volume and margin differed significantly among the four groups ($P < 0.001$ and $P = 0.012$, respectively).

Treatment Outcomes and Complications

Technical success was achieved in all patients after a single RFA session. The median follow-up period for liver CT/magnetic resonance imaging (MRI) was 30.4 (0.0–65.7) months. During the follow-up period, LTP was observed in nine (9/83, 10.8%) patients in the tumor-puncturing RFA with ICT

Korean Journal of Radiology
KJR

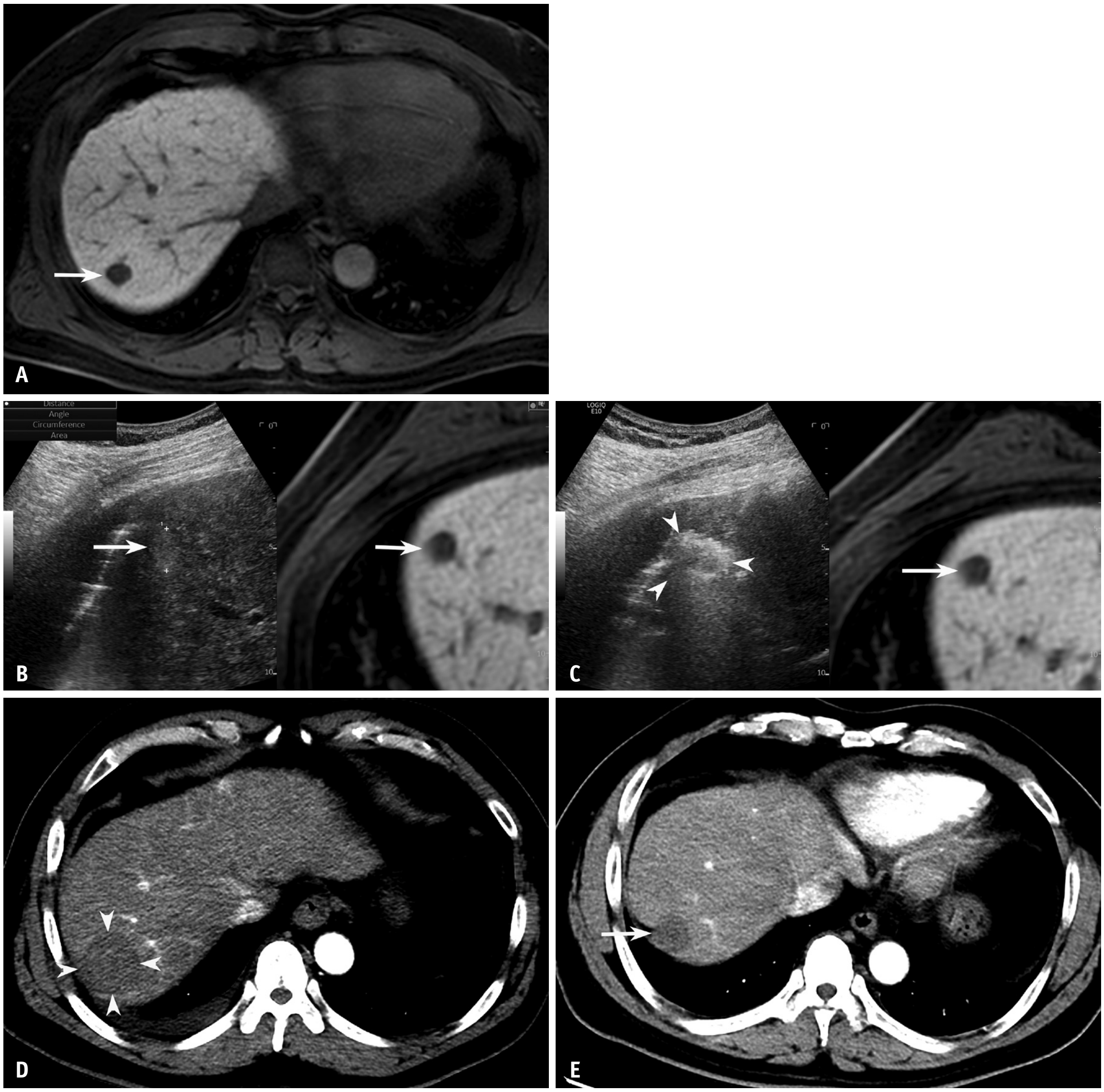

Fig. 2. A 58-year-old male with a 1.5 cm-sized hepatocellular carcinoma (HCC) and hepatitis B virus-related liver cirrhosis. **A:** Axial hepatobiliary phase magnetic resonance imaging (MRI) shows a 1.5-cm HCC (arrow) in the dome area of segment 7. **B:** Percutaneous radiofrequency ablation (RFA) was performed under the guidance of fusion imaging with real-time ultrasonography and pretreatment MRI after the introduction of artificial pleural effusion. The tumor is seen as a slightly hyperechoic lesion (arrows) on ultrasound at the corresponding site on the fused MRI. **C:** No-touch RFA was performed for 10 min using triple internally cooled tip electrodes. After RFA, an echogenic cloud (arrowheads) was created, which seemed to be sufficiently large to cover the tumor (arrow). **D:** The arterial-phase computed tomography (CT) scan obtained immediately after RFA shows that the tumor is completely covered with a sufficient ablative margin (arrowheads). **E:** The arterial-phase CT scan obtained 18 months after RFA shows that the ablation zone (arrow) is shrunken with no local tumor progression.

group and in one (1/80, 1.3%) patient in the no-touch RFA with ICT group (Figs. 2, 3). The cumulative LTP rates differed significantly among the four groups (P = 0.025, log-rank test; Fig. 4A). When tumor-puncturing RFA was performed, the cumulative LTP rates at 1, 3, and 5 years were higher in the ICT group than in the ICWT group (2.7%, 12.1%, and 18.8%, respectively; 0%, 0%, and 0%, respectively; P = 0.152, 0.006, and 0.002, respectively, in the z-test). However, the LTP rate did not differ significantly between no-touch RFA and tumor-puncturing RFA using ICT or ICWT electrodes. When ICT was used, the corresponding LTP rates were 2.7%, 12.1%, and 18.8% in the tumor-puncturing group and 0%, 5.0%, and 5.0% in the no-touch RFA group (P = 0.152, 0.280, and 0.077, respectively). When ICWT was used, no LTP was observed, regardless of the electrode placement method.

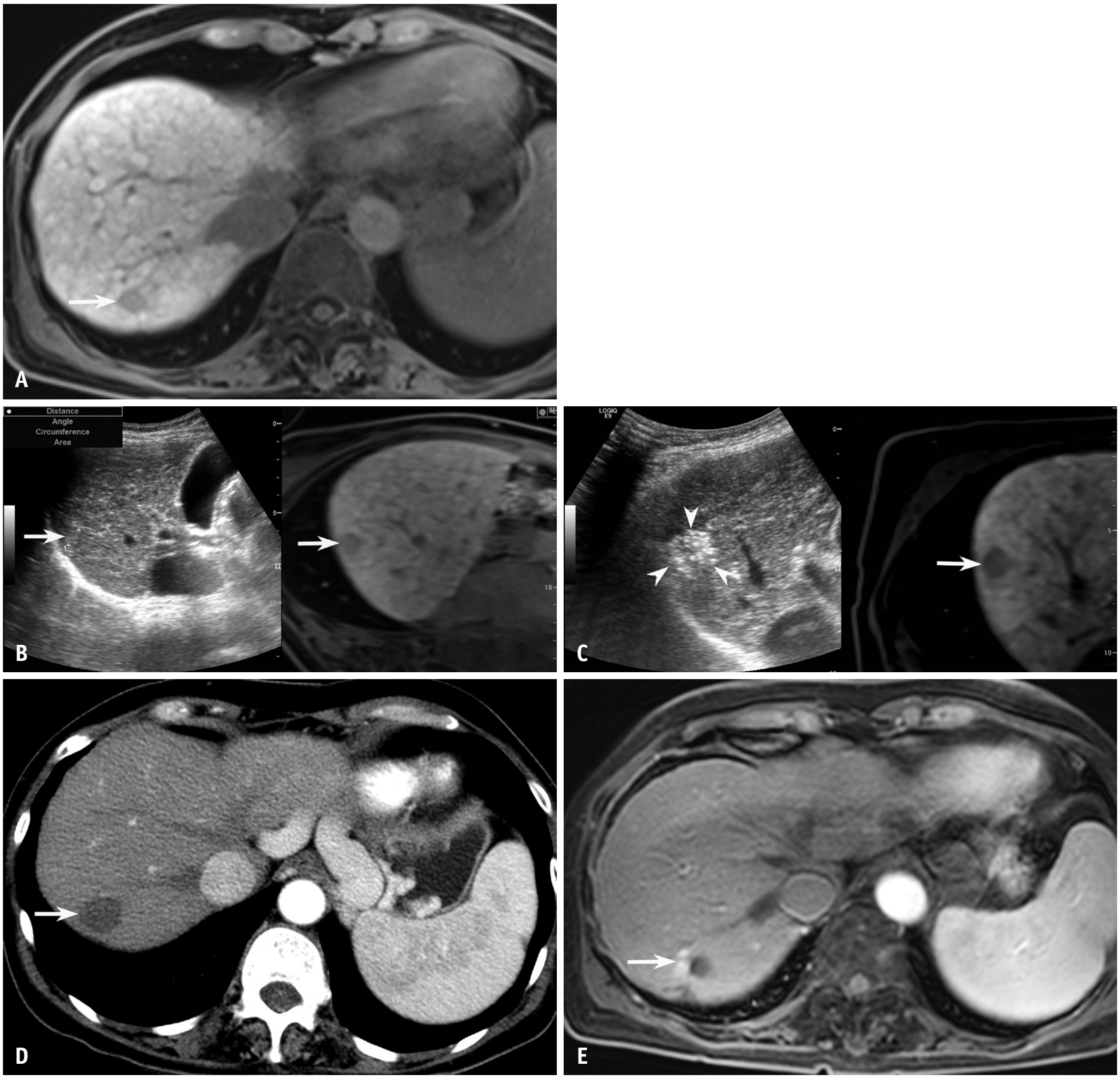

Fig. 3. A 56-year-old female with a 1.2-cm-sized hepatocellular carcinoma (HCC) and hepatitis B virus-related liver cirrhosis **A:** The axial hepatobiliary phase magnetic resonance imaging (MRI) scan shows an HCC (arrow) in the dome of segment 7. **B:** The fusion image shows a 1.2-cm-sized hyperechoic nodule (arrow in left image) in segment 7, where the tumor (arrow in right image) is located in the fused MRI. **C:** Tumor-puncturing radiofrequency ablation (RFA) was performed for 8.5 min by puncturing the center of the nodule with one electrode. After ablation, an echogenic cloud (arrowheads) was generated, which seemed sufficient to cover the tumor, when referring to the tumor (arrow) in the fused MR image. **D:** The arterial-phase computed tomography scan obtained immediately after RFA shows that the tumor is completely covered with a sufficient ablative margin (arrow). **E:** The axial arterial-phase MRI scan obtained 40 months after RFA shows local tumor progression (arrow) at the margin of the RFA zone. The patient underwent percutaneous RFA for the recurrent tumor.

IDR was observed in 35 (35/83, 42.2%), 11 (11/34, 32.4%), 15 (15/80, 18.8%), and three (3/14, 21.4%) individuals in the tumor puncturing ICT, tumor puncturing with ICWT, no-touch with ICT, and no-touch with ICWT groups, respectively. The cumulative IDR rates did not differ significantly among the four groups (P = 0.251, log-rank test) (Fig. 4B).

EM and AIR were observed only in the tumor-puncturing with ICT group, in two patients (2.4%) and one patient (1.2%), respectively. Recurrence was found in 39 (39/83, 47.0%), 11 (11/34, 32.4%), 16 (16/80, 20.0%), and three (3/14, 21.4%) patients in the four groups, respectively. However, the cumulative rates of any type of recurrence did not differ significantly among the four groups (P = 0.125, log-rank test) (Fig. 4C).

The median follow-up period for the survival analysis was 31.6 (1.0–65.9) months. During the follow-up, seven of the 211 (3.3%) patients died. For three patients, the cause of death was HCC progression and associated complications. For the other four patients, the cause of death was unrelated

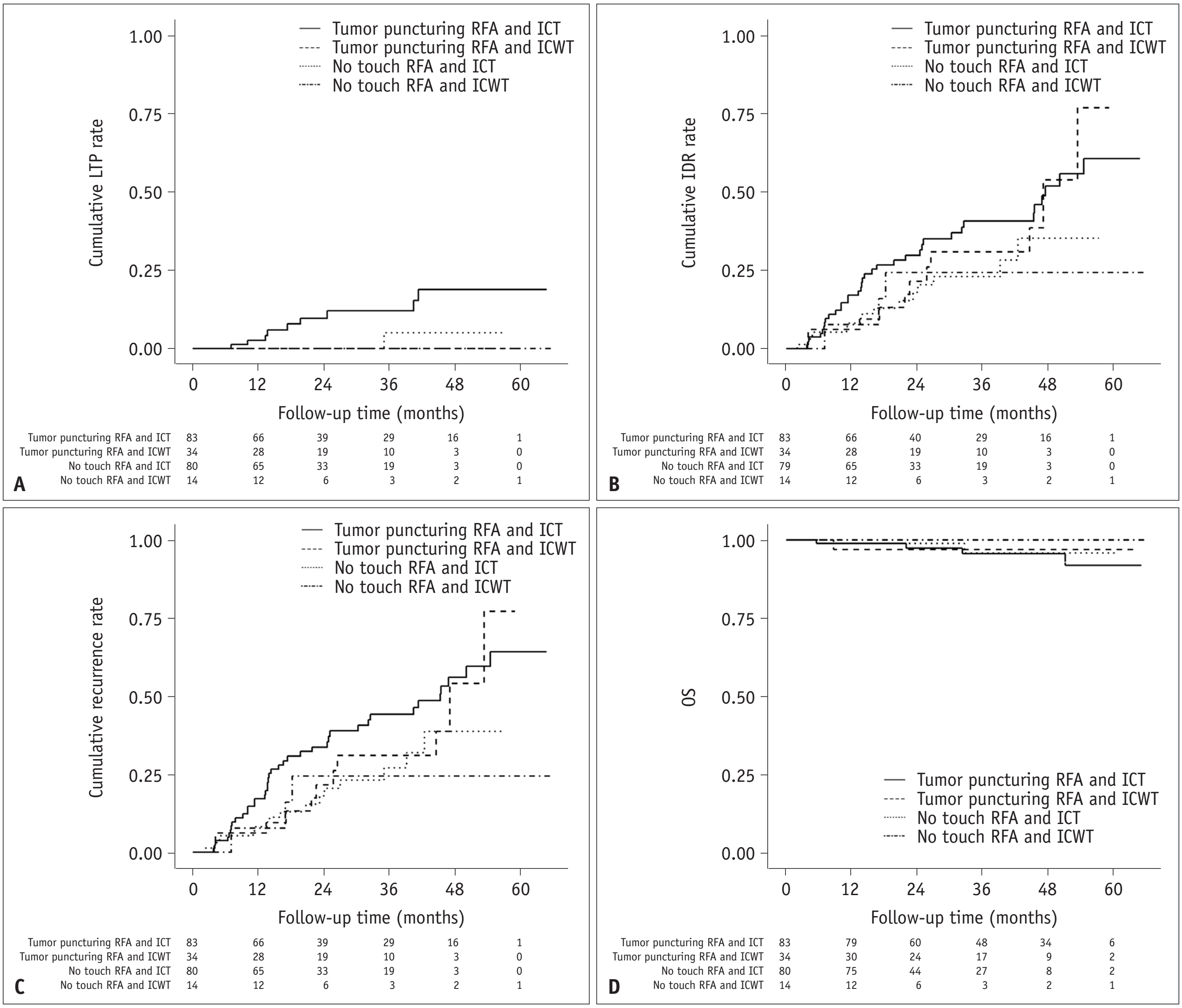

Fig. 4. The cumulative rate of local tumor progression (LTP; **A**), intrahepatic distant recurrence (IDR; **B**), any type of recurrence **(C)**, and overall survival (OS; **D**) according to the combination of the electrode placement method and type used during radiofrequency ablation (RFA). **A:** The cumulative LTP rate differed significantly among the combinations of the electrode placement method and type (P = 0.025 in the log-rank test). **B:** The cumulative IDR rate did not differ significantly among the combinations of the electrode placement method and type (P = 0.251 in the log-rank test). **C:** The cumulative rate of any type of recurrence did not differ significantly among the combinations of the electrode placement method and type (P = 0.125 in the log-rank test). **D:** OS did not differ significantly among the combinations of the electrode placement method and type (P = 0.914 in the log-rank test). ICT = internally cooled tip, ICWT = internally cooled wet tip

to HCC and included lung cancer (n = 1), interstitial lung disease (n = 2), or unknown cause (n = 1). The OS rates did not differ significantly among the four groups (P = 0.914 in the log-rank test) (Fig. 4D).

Major complications occurred in six (2.8%) of the 211 patients: a case of hepatic infarction (n = 1, 1.2%) in the tumor-puncturing with ICT group; no complication (0%) in the tumor-puncturing with ICWT group; a case of infection in the RFA zone with persistent fever (n = 2, 2.5%) in the no-touch with ICT group; and cases of abscess, hepatic infarction, and gallbladder perforation (n = 3, 21.4%) in the no-touch with ICWT group. All six patients recovered after conservative treatment.

Risk Factors for LTP

The univariable Cox proportional-hazards regression analysis revealed that a high albumin level, large ablation volume, and sufficient ablative margin were significantly associated with

 https://doi.org/10.3348/kjr.2023.0022

a lower risk of LTP (hazard ratio [HR] = 0.28, 95% confidence interval [CI] = 0.10–0.84, $P = 0.023$; HR = 0.89, 95% CI = 0.80–0.99, $P = 0.040$; and HR = 5.6, 95% CI = 1.43–21.88, $P = 0.013$; respectively]. Compared to tumor-puncturing RFA with ICT, tumor-puncturing RFA with ICWT and no-touch RFA with ICT were also associated with a lower risk of LTP (HR = 0.13, 95% CI = 0–0.99, $P = 0.049$ and HR = 0.2, 95% CI = 0.02–0.87, $P = 0.030$, respectively). The multivariable analysis revealed that an insufficient ablative margin was a risk factor for LTP (adjusted HR [aHR] = 6.13, 95% CI = 1.41–22.49, $P = 0.019$). Compared to tumor-puncturing RFA with ICT, tumor-puncturing RFA with ICWT had a lower LTP risk (aHR = 0.11, 95% CI = 0–0.88, $P = 0.034$). However, the cumulative LTP rate did not differ significantly between tumor-puncturing with ICT and no-touch RFA with ICT (aHR = 0.34, 95% CI = 0.03–1.62, $P = 0.188$) or ICWT (aHR = 0.28, 95% CI = 0–2.28, $P = 0.294$) (Table 2).

DISCUSSION

In this study, we evaluated the treatment outcomes of percutaneous RFA for HCCs < 3 cm in a cohort from the Samsung Medical Center. The cumulative LTP rate did not differ significantly between no-touch RFA and tumor-puncturing RFA using ICT or ICWT electrodes. When tumor-puncturing RFA was performed, the ICWT electrode provided a lower LTP rate compared to the ICT electrode. LTP was not observed when ICWT was used, regardless of the electrode placement method. However, major complications were frequently noted in 21.4% of the patients when no-touch RFA was performed using the ICWT electrode. These results imply that the electrode type and placement method affect treatment outcomes when performing RFA. Our results may be helpful to interventional oncologists in deciding which electrodes should be used during RFA.

No-touch RFA provides a lower LTP rate compared to conventional tumor-puncturing RFA [5,6,8,11]. However, in the present study, the LTP rate did not differ significantly between no-touch RFA and tumor-puncturing RFA using ICT or ICWT electrodes. With ICT, the cumulative LTP rates at 1, 3, and 5 years were lower in the no-touch RFA group than in the tumor-puncturing group, although without statistical significance (0%, 5.0%, and 5.0% vs. 2.7%, 12.1%, and 18.8%, respectively). The results differ between the present and previous studies because the operators in the present study may have employed a more aggressive treatment even during tumor-puncturing RFA to prevent LTP and improve OS [18]. In the present study, multiple electrodes were used for tumor-puncturing RFA, accounting for 50.4% (59/117) of the patients. This implies that tumor-puncturing RFA is occasionally performed with the centripetal approach, wherein multiple electrodes are placed in the peripheral portion of the tumor to create a larger ablation zone than when using a single electrode.

In general, the favorable outcomes of no-touch RFA are attributed to larger ablative margins [5]. Despite these advantages, fewer than half of the patients (44.5%, 94/211) in the present study underwent no-touch RFA. This could be because no-touch RFA is not always applicable. Previous prospective studies reported that conversion from no-touch RFA to tumor-puncturing RFA was unavoidable in 8.6%–10.8% of patients because of insufficient peritumoral liver parenchyma for multiple electrode placement [11,12]. In a randomized controlled trial that compared no-touch and conventional RFA [5], HCCs abutting the main hepatic vessels (≥ 5 mm in diameter) were excluded, possibly because of the technical difficulty of no-touch RFA. However, the feasibility of no-touch RFA remains debatable, as a few studies have reported that bipolar no-touch RFA is well suited, even for subcapsular tumors with little adjacent liver parenchyma [6,19].

In the present study, the patients in the no-touch RFA group had better liver function than those in the tumor-puncturing RFA group (Table 1). Considering that a large ablation zone is prone to complications after RFA [20], no-touch RFA may have been performed in patients with preserved hepatic function. Therefore, the difference in hepatic function between the no-touch and tumor-puncturing RFA groups may have affected the treatment outcomes in the present study.

As no-touch RFA is not always feasible, tumor-puncturing RFA continues to play a pivotal role in the management of small HCCs. In the present study, the insufficient ablative margin was a risk factor for LTP than a sufficient ablative margin, in close agreement with a previous study [21]. The ICWT electrode showed a lower LTP rate than the ICT electrode when tumor-puncturing RFA was performed. This result can be explained by the fact that RFA using multiple ICWT electrodes provides a larger and more circular ablation zone compared to ICT electrodes because of the increased electrical conductivity around the ICWT [10]. As obtaining an adequate ablative margin is occasionally challenging in tumor-puncturing RFA [5], ICWT electrodes may be a good solution. However, the major complication rate after no-touch

RFA with ICWT electrodes was significant (21.4%). Therefore, ICWT electrodes should be used cautiously when performing no-touch RFA. Instead, ICT electrodes may be sufficient for achieving local tumor control with no-touch RFA.

This study has several limitations. First, a selection bias was unavoidable because of the retrospective nature of the study. For example, the electrode placement method and type were determined according to each operator's preference

Table 2. Univariable and multivariable cox proportional hazard regression analyses of the risk factors for LTP

Variable	Hazard ratio (95% CI)	*P*
Univariable analysis		
Age	0.99 (0.93–1.05)	0.696
Sex (ref: male)	1.63 (0.46–5.77)	0.451
Etiology (ref: HBV)		
HCV	1.87 (0.22–15.67)	0.563
Others	1.99 (0.5–7.98)	0.331
Tumor size	0.65 (0.11–3.72)	0.628
Tumor location (ref: Segment I)		
Segments II, III, and IV	0.34 (0.02–49.24)	0.547
Segments V, VI, VII, and VIII	0.36 (0.04–46.01)	0.539
Peri-portal venous location	0.81 (0.01–6.5)	0.882
Peri-hepatic venous location	1.66 (0.21–13.26)	0.631
Subcapsular location (ref: non-subphrenic subcapsular)		
Subphrenic	2.17 (0.36–13.21)	0.401
Non-subcapsular	0.67 (0.16–2.81)	0.584
Pre-procedural laboratory result		
ALBI grade (ref: grade 1)	3.62 (0.76–17.19)	0.105
MoRAL score	1 (0.97–1.02)	0.901
Platelet	0.99 (0.98–1)	0.156
PT-INR	6.4 (0.11–359.87)	0.367
Albumin	0.28 (0.10–0.84)	0.023
Bilirubin	2.17 (0.81–5.81)	0.122
AFP	0.99 (0.96–1.02)	0.410
PIVKA-II	1 (0.99–1.01)	0.837
Ablation zone volume	0.89 (0.8–0.99)	0.040
Ablative margin (ref: sufficient)	5.6 (1.43–21.88)	0.013
Number of electrodes used (ref: One)	0.87 (0.24–3.1)	0.831
Electrode placement and type (ref: Tumor puncturing with ICT)		
Tumor puncturing with ICWT	0.13 (0–0.99)	0.049
No-touch with ICT	0.2 (0.02–0.87)	0.030
No-touch with ICWT	0.35 (0–2.79)	0.397
Multivariable analysis		
ALBI grade (ref: grade 1)	3.86 (1–21.26)	0.050
Subcapsular location (ref: non-subphrenic subcapsular)		
Subphrenic		
Non-subcapsular		
Ablative margin (ref: sufficient)	6.13 (1.41–22.49)	0.019
Electrode placement and type (ref: Tumor puncturing with ICT)		
Tumor puncturing with ICWT	0.11 (0–0.88)	0.034
No-touch with ICT	0.34 (0.03–1.62)	0.188
No-touch with ICWT	0.28 (0–2.28)	0.294

LTP = local tumor progression, CI = confidence interval, HBV = hepatitis B virus, HCV = hepatitis C virus, ALBI = albumin-bilirubin, MoRAL = model for tumor recurrence after living donor liver transplantation, PT-INR = prothrombin time-international normalized ratio, AFP = alpha-fetoprotein, PIVKA-II = protein induced by vitamin K absence or antagonist-II, ICT = internally cooled tip, ICWT = internally cooled wet tip based on tumor and patient factors. Nonetheless, the electrode placement method and type affected LTP. Second, the number of LTP and OS events was very low (10 LTPs in 211 tumors and seven deaths in 211 patients), reflecting improved treatment outcomes because of recent advances in the RFA technique. This might have led to biased estimates (infinite estimates or CIs) owing to the small number of events [22,23]. Third, this was a single-center study conducted at a tertiary cancer center. Therefore, further prospective studies are required to confirm these results.

In conclusion, when tumor-puncturing RFA was performed, the ICWT electrode provided a lower LTP rate compared to the ICT electrode. An insufficient ablation margin was a risk factor for LTP.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

Min Woo Lee, a contributing editor of the *Korean Journal of Radiology*, was not involved in the editorial evaluation or decision to publish this article. Min Woo Lee is a consultant for the STARmed company, however this does not affect to publish this manuscript. All remaining authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Min Woo Lee. Data curation: Jiyeon Park. Formal analysis: Jiyeon Park, Ji Hye Min. Funding acquisition: Min Woo Lee. Investigation: Jiyeon Park. Methodology: Min Woo Lee, Dong Ik Cha, Soo Hyun Ahn. Project administration: Min Woo Lee. Resources: Ji Hye Min, Seungchul Han, Tae Wook Kang, Dong Ik Cha, Kyoung Doo Song. Supervision: Hyunchul Rhim. Validation: Seungchul Han, Tae Wook Kang. Visualization: Jiyeon Park. Writing—original draft: Min Woo Lee, Jiyeon Park. Writing—review & editing: Seungchul Han, Tae Wook Kang, Dong Ik Cha, Kyoung Doo Song.

ORCID IDs

Jiyeon Park
https://orcid.org/0000-0002-0353-0109
Min Woo Lee
https://orcid.org/0000-0001-9048-9011
Soo Hyun Ahn
https://orcid.org/0000-0001-5016-5469
Seungchul Han
https://orcid.org/0000-0002-7276-0370
Ji Hye Min
https://orcid.org/0000-0002-8496-6771
Dong Ik Cha
https://orcid.org/0000-0003-3271-6532
Kyoung Doo Song
https://orcid.org/0000-0002-2767-3622
Tae Wook Kang
https://orcid.org/0000-0002-0725-8317
Hyunchul Rhim
https://orcid.org/0000-0002-9737-0248

Funding Statement

This work was supported by the Korea Medical Device Development Fund grant funded by the Korea government (the Ministry of Science and ICT) (Project Number: RS-2020-KD000303).

REFERENCES

1. Reig M, Forner A, Rimola J, Ferrer-Fàbrega J, Burrel M, Garcia-Criado Á, et al. BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. *J Hepatol* 2022;76:681-693
2. Lee MW, Lee JM, Koh YH, Chung JW. 2022 Korean Liver Cancer Association-National Cancer Center Korea practice cuidelines for local ablation therapy of hepatocellular carcinoma: what's new? *Korean J Radiol* 2023;24:10-14
3. Korean Liver Cancer Association (KLCA), National Cancer Center (NCC) Korea. 2022 KLCA-NCC Korea practice guidelines for the management of hepatocellular carcinoma. *Korean J Radiol* 2022;23:1126-1240
4. Cha DI, Lee MW, Song KD, Ko SE, Rhim H. Ablative outcomes of various energy modes for no-touch and peripheral tumor-puncturing radiofrequency ablation: an ex vivo simulation study. *Korean J Radiol* 2022;23:189-201
5. Park SJ, Cho EJ, Lee JH, Yu SJ, Kim YJ, Yoon JH, et al. Switching monopolar no-touch radiofrequency ablation using octopus electrodes for small hepatocellular carcinoma: a randomized clinical trial. *Liver Cancer* 2021;10:72-81
6. Hocquelet A, Aubé C, Rode A, Cartier V, Sutter O, Manichon AF, et al. Comparison of no-touch multi-bipolar vs. monopolar radiofrequency ablation for small HCC. *J Hepatol* 2017;66:67-74
7. Seror O, N'Kontchou G, Nault JC, Rabahi Y, Nahon P, Ganne-Carrie N, et al. Hepatocellular carcinoma within Milan criteria: no-touch multibipolar radiofrequency ablation for treatment-long-term results. *Radiology* 2016;280:611-621

8. Seror O. No touch radiofrequency ablation for hepatocellular carcinoma: a conceptual approach rather than an iron law. *Hepatobiliary Surg Nutr* 2022;11:132-135
9. Kim JH, Kim PN, Won HJ, Shin YM. Percutaneous radiofrequency ablation using internally cooled wet electrodes for the treatment of hepatocellular carcinoma. *AJR Am J Roentgenol* 2012;198:471-476
10. Cha DI, Lee MW, Jeong WK, Ha SY, Ahn SH, Rhim H, et al. Comparison of ablation performance between dual internally cooled wet tip and conventional dual internally cooled tip radiofrequency electrodes: an experimental study in ex vivo bovine liver. *Int J Hyperthermia* 2021;38:332-340
11. Suh YS, Choi JW, Yoon JH, Lee DH, Kim YJ, Lee JH, et al. No-touch vs. conventional radiofrequency ablation using twin internally cooled wet electrodes for small hepatocellular carcinomas: a randomized prospective comparative study. *Korean J Radiol* 2021;22:1974-1984
12. Lee DH, Lee MW, Kim PN, Lee YJ, Park HS, Lee JM. Outcome of no-touch radiofrequency ablation for small hepatocellular carcinoma: a multicenter clinical trial. *Radiology* 2021;301:229-236
13. Lee MW. Fusion imaging of real-time ultrasonography with CT or MRI for hepatic intervention. *Ultrasonography* 2014;33:227-239
14. Ahmed M, Solbiati L, Brace CL, Breen DJ, Callstrom MR, Charboneau JW, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria--a 10-year update. *Radiology* 2014;273:241-260
15. Lee MW, Rhim H. Research highlight: how to use technical and ncologic outcomes of image-guided tumor ablation according to guidelines by society of interventional oncology and DATECAN? *Korean J Radiol* 2022;23:385-388
16. Puijk RS, Ahmed M, Adam A, Arai Y, Arellano R, de Baère T, et al. Consensus guidelines for the definition of time-to-event end points in image-guided tumor ablation: results of the SIO and DATECAN initiative. *Radiology* 2021;301:533-540
17. Kang TW, Lim HK, Lee MW, Kim YS, Rhim H, Lee WJ, et al. Aggressive intrasegmental recurrence of hepatocellular carcinoma after radiofrequency ablation: risk factors and clinical significance. *Radiology* 2015;276:274-285
18. Lee MW, Kang D, Lim HK, Cho J, Sinn DH, Kang TW, et al. Updated 10-year outcomes of percutaneous radiofrequency ablation as first-line therapy for single hepatocellular carcinoma < 3 cm: emphasis on association of local tumor progression and overall survival. *Eur Radiol* 2020;30:2391-2400
19. Petit A, Hocquelet A, N'kontchou G, Varin E, Sellier N, Seror O, et al. No-touch multi-bipolar radiofrequency ablation for the treatment of subcapsular hepatocellular carcinoma ≤ 5 cm not puncturable via the non-tumorous liver parenchyma. *Cardiovasc Intervent Radiol* 2020;43:273-283
20. Jo MG, Lee MW, Ahn S, Kang TW, Song KD, Cha DI, et al. Percutaneous radiofrequency ablation of hepatocellular carcinoma in a recent cohort at a tertiary cancer center: incidence and factors associated with major complications and unexpected hospitalization events. *Ultrasonography* 2022;42:41-53
21. Nakazawa T, Kokubu S, Shibuya A, Ono K, Watanabe M, Hidaka H, et al. Radiofrequency ablation of hepatocellular carcinoma: correlation between local tumor progression after ablation and ablative margin. *AJR Am J Roentgenol* 2007;188:480-488
22. Austin PC, Allignol A, Fine JP. The number of primary events per variable affects estimation of the subdistribution hazard competing risks model. *J Clin Epidemiol* 2017;83:75-84
23. Ko SE, Lee MW, Min JH, Ahn SH, Rhim H, Kang TW, et al. Laparoscopic radiofrequency ablation of subcapsular hepatocellular carcinomas: risk factors related to a technical failure. *Surg Endosc* 2022;36:504-514