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Outcome of No-Touch Radiofrequency Ablation for Small Hepatocellular Carcinoma: A Multicenter Clinical Trial

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Conflicts of interest are listed at the end of this article.

See also the editorial by Soulen and García-Mónaco in this issue.

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Background: Recently introduced no-touch radiofrequency ablation (RFA) of hepatocellular carcinoma (HCC) has the potential to improve local tumor control.

Purpose: To evaluate midterm clinical outcomes of monopolar no-touch RFA in single HCCs 2.5 cm or smaller.

Materials and Methods: In this multicenter clinical trial (*ClinicalTrials.gov*: NCT03375281), participants were evaluated for eligibility from November 2017 to January 2019. Patients with single HCCs 2.5 cm or smaller planning to be treated with no-touch RFA were enrolled. The rate of successful no-touch RFA, defined as performing RFA without violation of the tumor itself, was recorded. Multivariable logistic regression analysis was used to determine associated factors for failure of no-touch RFA. Development of major complication after no-touch RFA was also recorded. Cumulative incidence of local tumor progression (LTP) and recurrence-free survival were estimated by using the Kaplan-Meier method.

Results: A total of 140 participants (mean age, 62 years ± 9 [standard deviation]; 106 men) were evaluated. No-touch RFA was successfully performed in 128 participants (128 of 140; 91.4%), and conversion to tumor puncture RFA was undertaken in 12 participants because of the lack of a safe access route. By using either no-touch RFA or conversion to tumor puncture RFA, all participants achieved technical success of RFA, which was defined as complete coverage of target tumor by ablation zone. Insufficient peritumoral parenchyma (<5 mm width around more than half portion of tumor; odds ratio, 74; 95% CI: 18, 309; $P < .001$) was the only significant predictive factor for failure of the no-touch technique. Among the 140 participants, LTP developed in two participants, and the estimated 1- and 2-year cumulative incidence of LTP was 0.7% and 1.6%, respectively. The estimated 1- and 2-year recurrence-free survival was 82.8% and 74.1%, respectively.

Conclusion: No-touch radiofrequency ablation was an effective and safe treatment method for small hepatocellular carcinomas (≤2.5 cm), with 1.6% of cumulative incidence of local tumor progression at 2 years.

Online supplemental material is available for this article.

Radiofrequency ablation (RFA) is a widely accepted curative treatment method for early-stage hepatocellular carcinoma (HCC) that provides comparable overall survival to hepatic resection (1–3). The recently updated HCC management guideline proposed by the European Association for the Study of the Liver recommended both RFA and hepatic resection as first-line treatment modalities for early-stage HCC (4). However, one of the most important drawbacks of RFA compared with hepatic resection is the higher rate of local tumor progression (LTP) because satellite nodules around the main tumor are not covered by the ablation zone. Traditionally, RFA has been performed by using the conventional tumor puncture method, in which a radiofrequency electrode is inserted into the central portion of the tumor to maximize the efficacy of thermal energy delivery to the target tumor. The reported cumulative incidence of LTP after RFA with this method for HCC was reported to be as high as 27% at 5 years in retrospective studies (2). Even in recent clinical trials that compared the therapeutic efficacy of RFA with that of other treatment modalities, the reported 2-year cumulative incidence of LTP after performance of RFA with the conventional tumor puncture method ranged from 11% to 16.1% (5–7). This is higher than the typically lower than 3% LTP rate after hepatic resection (8,9).

The concept of no-touch RFA was recently introduced to clinical practice for further improvement of local therapeutic efficacy. In no-touch RFA, multiple electrodes are inserted outside the tumors and then sequentially activated to create an ablation zone (10). Therefore, the tumor itself is not violated during no-touch RFA, providing the potential to reduce the incidence of LTP. In previous in vivo animal studies,

Abbreviations

HCC = hepatocellular carcinoma, LTP = local tumor progression, RFA = radiofrequency ablation

Summary

No-touch radiofrequency ablation was a safe and effective treatment method for hepatocellular carcinomas 2.5 cm or smaller, providing 1.6% of cumulative incidence of local tumor progression at 2 years.

Key Results

- In a multicenter clinical trial with 140 participants with hepatocellular carcinoma (HCC) 2.5 cm or smaller, all participants achieved technical success of radiofrequency ablation (RFA) by using either no-touch (n = 128) or conversion to tumor puncture (n = 12), indicating planned no-touch technique success rate of 91.4% (128 of 140).
- No-touch RFA provided 1.6% local tumor progression rate at 2 years for HCC 2.5 cm or smaller.
- Insufficient peritumoral parenchyma ($P < .001$) was the only important predictive factor for failure of no-touch technique.

no-touch RFA provided good local tumor control and a lower rate of recurrence (11,12). Several clinical studies have also reported that no-touch RFA may provide an LTP rate as low as 6% at 5 years and that it also has the potential to prevent intrasubsegmental recurrence (10,13). Moreover, in their multicenter retrospective case-matched study, Hocquelet et al (14) reported that no-touch RFA provided better local tumor control compared with conventional tumor puncture RFA. Prospective studies are warranted to accurately evaluate the clinical outcomes of treatment methods such as no-touch RFA. Several prospective studies evaluating clinical potential of no-touch RFA in the HCC treatment were recently published that reported good local tumor control (15,16). However, to our knowledge, both the rate and predictive factors of successful no-touch RFA technique when it is planned for HCC treatment have not been fully evaluated (15,16). Therefore, our study aimed to evaluate the clinical outcomes of no-touch RFA by using separable clustered electrodes in switching monopolar mode for the treatment of small HCCs (≤2.5 cm) in a multicenter prospective setting. The primary end point of our study was cumulative incidence of LTP.

Materials and Methods

In our study, five university-affiliated tertiary referral hospitals in Seoul, South Korea (Seoul National University Hospital; Asan Medical Center; Samsung Medical Center, Seoul St Mary's Hospital, and Konkuk University Hospital) participated, with each center treating their own participants. The institutional review boards at each center approved this prospective study, and written informed consent was obtained from all participants (*clinicaltrial.gov* identifier: NCT03375281). This study was financially supported by STARmed (Goyang, Kyunggi, South Korea). However, participant enrollment, data collection, data analysis, and interpretation were performed solely by the authors without any input from the funding source. All data generated during the study are available from the corresponding author by request.

Study Sample

This study was designed as a single-arm prospective multicenter study. The detailed information about the sample size estimation is in Appendix E1 (online). From November 2017 to January 2019, all five university-affiliated participating tertiary referral centers prospectively evaluated participants with small single nodular HCCs to determine their eligibility for study enrollment. The inclusion criteria for this study were as follows: single HCC 1.0–2.5 cm in size, Child-Pugh class A liver function, and untreated HCC or intrahepatic recurrent HCC that developed more than 2 years after initial curative treatment. The exclusion criteria for this study were as follows: tumors with macrovascular invasion and/or distant metastasis, invisible tumors even at real-time fusion US with MRI or CT because no-touch RFA could not be guaranteed for these invisible tumors, presence of bleeding tendency defined as a platelet count less than 50 000 mm^3, or prothrombin time international normalized ratio greater than 1.5 (ie, more than 50% prolongation of prothrombin time). When peritumoral parenchymal width was less than 5 mm around the more than half portion of tumor, we considered it to be insufficient peritumoral parenchyma.

RFA Procedures and Follow-up

We used noninvasive imaging criteria according to the Korean Liver Cancer Association-National Cancer Center Korea guideline (17) to diagnose the HCCs in this study. All RFA procedures were performed percutaneously with conscious sedation by six radiologists with experience in imaging-guided liver tumor ablation (J.M.L., with 25 years of experience; P.N.K., with 30 years of experience; M.W.L., with 15 years of experience; Y.J.L., with 19 years of experience; H.S.P., with 12 years of experience; and D.H.L., with 5 years of experience). Real-time fusion US with MRI or CT was chosen as the guidance modality for all study participants. Separable clustered electrodes (Octopus electrodes; STARmed), which contain three separable electrodes in a single unit and a 200-W multichannel generator (VIVA RF System; STARmed), were used for the RFA procedures. All HCCs were intended be treated with no-touch RFA (Figs 1, 2). However, when the operator judged that there was no safe access route of multiple electrodes insertion required for no-touch RFA, conversion to conventional tumor puncture RFA was undertaken to treat HCC. The rate of successful no-touch RFA, defined as performing RFA without violation of the tumor during the procedure, was also recorded. In addition, technical success of RFA was de-

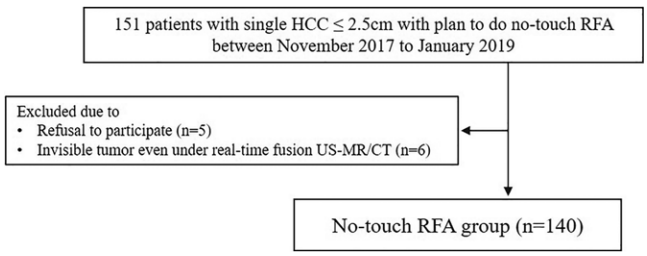

Figure 1: Patient enrollment process. HCC = hepatocellular carcinoma, RFA = radiofrequency ablation.

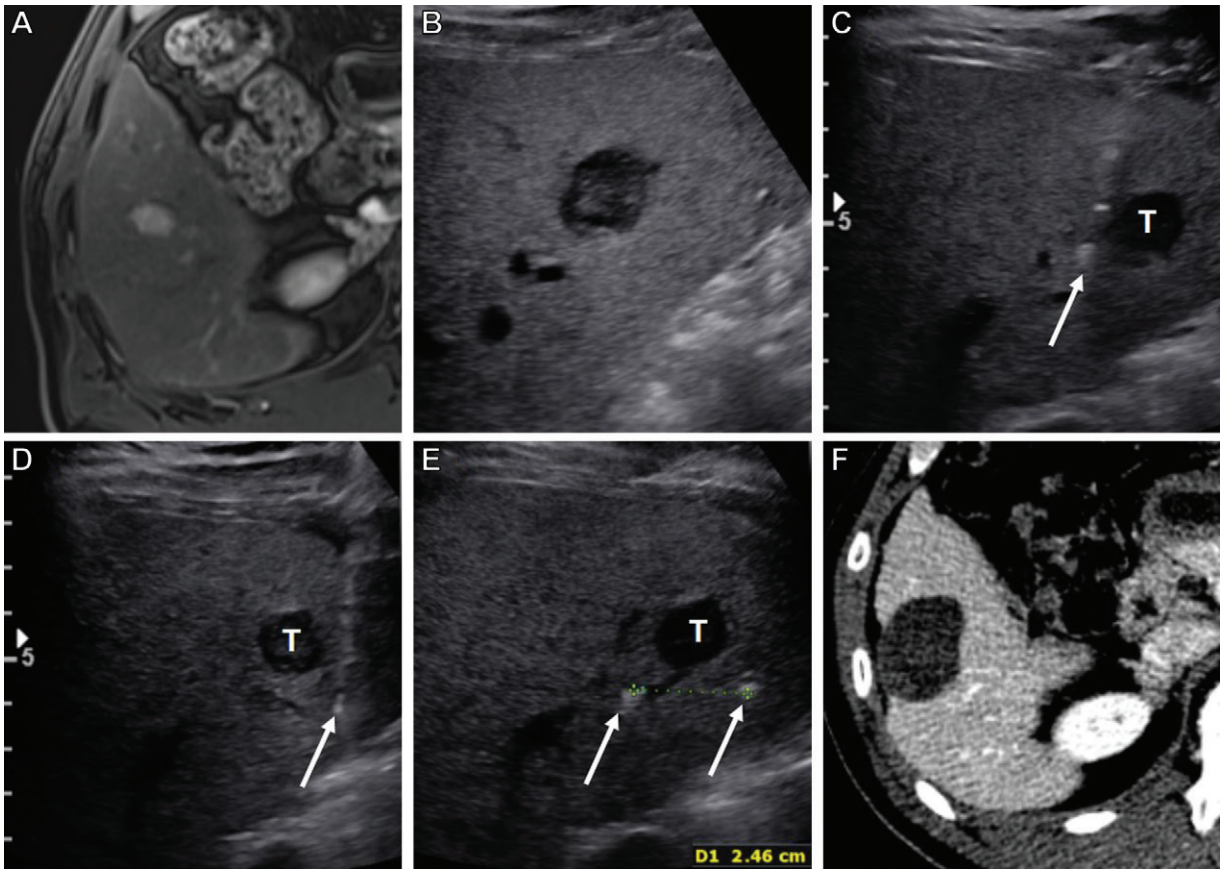

Figure 2: No-touch radiofrequency ablation in a 52-year-old man with 2-cm hepatocellular carcinoma (HCC) and hepatitis B–related cirrhosis. **(A)** Arterial phase axial gadoxetic acid–enhanced MRI shows a 2-cm enhancing nodular lesion in segment VI of the liver, indicating HCC. **(B)** Target tumor appeared as low echoic nodular lesion at B-mode US. **(C, D)** Three internally cooled separable clustered electrodes were inserted outside the tumor boundary, and two of them were shown (*T* indicates the target tumor; arrow indicates the electrode tip). **(E)** The interelectrode distance was about 2.5 cm for this participant (*T* indicates the target tumor; arrows indicate the electrode tip). After 12 minutes of ablation, the ablation zone (mean size, 4.2 cm) completely encompassing the target tumor was created. **(F)** There was no local tumor progression on the 24-month follow-up CT image.

fined as complete coverage of the target tumor by the ablation zone achieved by either no-touch RFA or conversion to tumor puncture RFA. The detailed information regarding the RFA procedure is provided in Appendix E1 (online).

One month after RFA, all participants underwent follow-up imaging studies by using either contrast-enhanced multiphasic liver CT or MRI, and measurements of serum α-fetoprotein levels and liver function tests were performed. Treatment success or failure was evaluated by using 1-month follow-up imaging studies. Treatment failure was defined as incomplete coverage of the target tumor as observed at CT or MRI performed before RFA by the ablation zone (18,19). In cases of treatment failure, various treatment methods including repeat ablation, hepatic resection, liver transplantation, transarterial chemoembolization, and external radiation therapy were considered to treat the residual tumor. Treatment success was defined as complete coverage of the target tumor by the ablation zone assessed at 1-month follow-up imaging. For participants who were successfully treated, follow-up contrast-enhanced liver CT or MRI together with a measurement of α-fetoprotein levels were performed every 3 months until June 30, 2020 (ie, the end of the study). Tumor recurrence after RFA was further classified into three categories: LTP, intrahepatic distant recurrence, and extrahepatic metastasis. LTP was defined as the reappearance of enhancing tumor foci adjacent to the ablation zone after the achievement of treatment success (18,19). Intrahepatic distant recurrence was defined as the occurrence of HCC in the liver apart from the ablation zone. When metastatic tumor foci were found outside of the liver, we considered them to be the appearance of extrahepatic metastasis.

End Points

The primary end point of our study was the cumulative incidence of LTP at 2 years, measured from the RFA treatment date to the first occurrence of LTP. Secondary end points included overall survival after RFA treatment, recurrence-free survival, and cumulative incidence of intrahepatic distant recurrence and extrahepatic metastasis. Overall survival was measured from the RFA treatment date to the date of death from any cause. The cutoff date for data collection was June 30, 2020.

Statistical Analysis

Continuous variables were compared by using the Mann-Whitney *U* test and categorical variables were compared by using the χ^2 test for univariable analysis. To determine the factors significantly associated with the conversion from no-touch RFA to conventional tumor puncture RFA, mixed lo-

gistic regression analysis was performed and all variables with a *P* value less than .05 at univariable analysis were included for multivariable analysis. The following cumulative incidences of each type of recurrence were estimated by using the Kaplan-Meier method: LTP; intrahepatic distant recurrence; and extrahepatic metastasis, overall survival, and recurrence-free survival after RFA treatment for HCCs. Analyses were performed in an intention-to-treat manner. *P* values less than .05 were considered to indicate significant difference. Statistical analyses were performed by using a commercially available software program (SPSS version 25.0; IBM).

Results

Participant Characteristics

Initially, 151 potentially eligible participants were screened for study enrollment. Among them, 11 participants were excluded for refusal to participate in the study (n = 5) and for invisible tumors even at real-time fusion US with MRI or CT guidance (n = 6). Therefore, 140 participants were finally enrolled in our study and were scheduled to undergo no-touch RFA in HCC treatment (Fig 1). Baseline characteristics of the participants are summarized in Table 1.

Table 1: Baseline Participant Characteristics

Characteristic	Data at Baseline
Age (y)	62 ± 9
Sex	
No. of men	106
No. of women	34
Etiologic cause	
HBV	110 (78.8)
HCV	16 (11.2)
Alcoholism	7 (5.0)
Others	7 (5.0)
Tumor size (cm)	1.69 ± 0.45
Albumin (mg/dL)	4.03 ± 0.43
Total bilirubin (mg/dL)	0.70 ± 0.34
Prothrombin activity (INR)	1.06 ± 0.10
AFP (ng/mL)	60.7 ± 267.9
Platelet count (K/mm^3)	135.8 ± 49.9
Initial HCC	92
Recurrent HCC	48
Tumor location, segment	
Right anterior segment	61 (43.6)
Right posterior segment	54 (38.6)
Left medial segment	13 (9.3)
Left lateral segment	12 (8.5)
Ablation zone size (cm)	3.75 ± 0.62

Note.—There were a total of 140 participants. Unless otherwise noted, data are number of participants. Data in parentheses are percentages. Mean data are ± standard deviation. AFP = α-fetoprotein, HBV = hepatitis B virus, HCC = hepatocellular carcinoma, HCV = hepatitis C virus, INR = international normalized ratio.

Rate of Successful No-Touch RFA and Complications

Among the 140 study participants, no-touch RFA was successfully performed in 128 participants, resulting in a success rate of 91.4% (128 of 140) (Fig 2). In the remaining 12 participants, no-touch RFA could not be performed because there was no safe access route for multiple radiofrequency electrodes insertion in the peritumoral region, and thus conversion to conventional tumor puncture RFA was performed for HCC treatment (Fig 3). After RFA treatment with either no-touch RFA or conversion to tumor puncture RFA, all participants achieved technical success assessed at immediate contrast-enhanced multiphasic liver CT. Factors associated with successful no-touch RFA are summarized in Table 2. At multivariable logistic regression analysis, insufficient peritumoral parenchyma, defined as parenchyma smaller than 5-mm width around the half portion of tumor (odds ratio, 74; 95% CI: 18, 309; $P < .001$), was the only factor significantly associated with the failure of no-touch RFA technique and conversion to conventional tumor puncture RFA. The mean ablation zone size was 3.75 cm, and the mean ablation time was 12.3 minutes. All participants in the study group including those who were converted to conventional tumor puncture RFA achieved treatment success assessed at the 1-month follow-up imaging study.

Three participants (2.1%; three of 140) experienced major complications: bleeding requiring angiographic embolization (n = 1) and segmental infarction with fever (n = 2). These three participants with major complication recovered completely after treatment, and there was no procedure-related mortality in this study.

Recurrence Outcomes after RFA

During the mean and median follow-up period of 17.3 months and 18.0 months (range, 3–31 months), respectively, LTP developed in two of 140 participants of the study group and they were treated by repeated RFA (n = 1) and transarterial chemoembolization (n = 1). In these two participants who developed LTP, no-touch RFA had originally failed because the lack of a safe assess route, and conversion to conventional tumor puncture RFA was undertaken to treat HCC. Thus, when no-touch RFA was successfully performed, there were no incidences of LTP. The estimated cumulative incidences of LTP in the intention-to-treat no-touch RFA group at 1 and 2 years were 0.7% and 1.6%, respectively (Fig 4A).

The cumulative incidences of intrahepatic distant recurrence and extrahepatic metastasis after no-touch RFA at 2 years were 22.3% and 2.4%, respectively. Considering all kind of recurrence, the estimated recurrence-free survival rates at 1 and 2 years after no-touch RFA in single HCCs 2.5 cm or smaller were 82.8% and 74.1%, respectively, (Fig 4B).

Survival Outcomes after RFA

During the follow-up, one participant in the study group died of HCC progression. The estimated overall survival rates in the no-touch RFA group were 100% and 98.3% at 1 and 2 years, respectively.

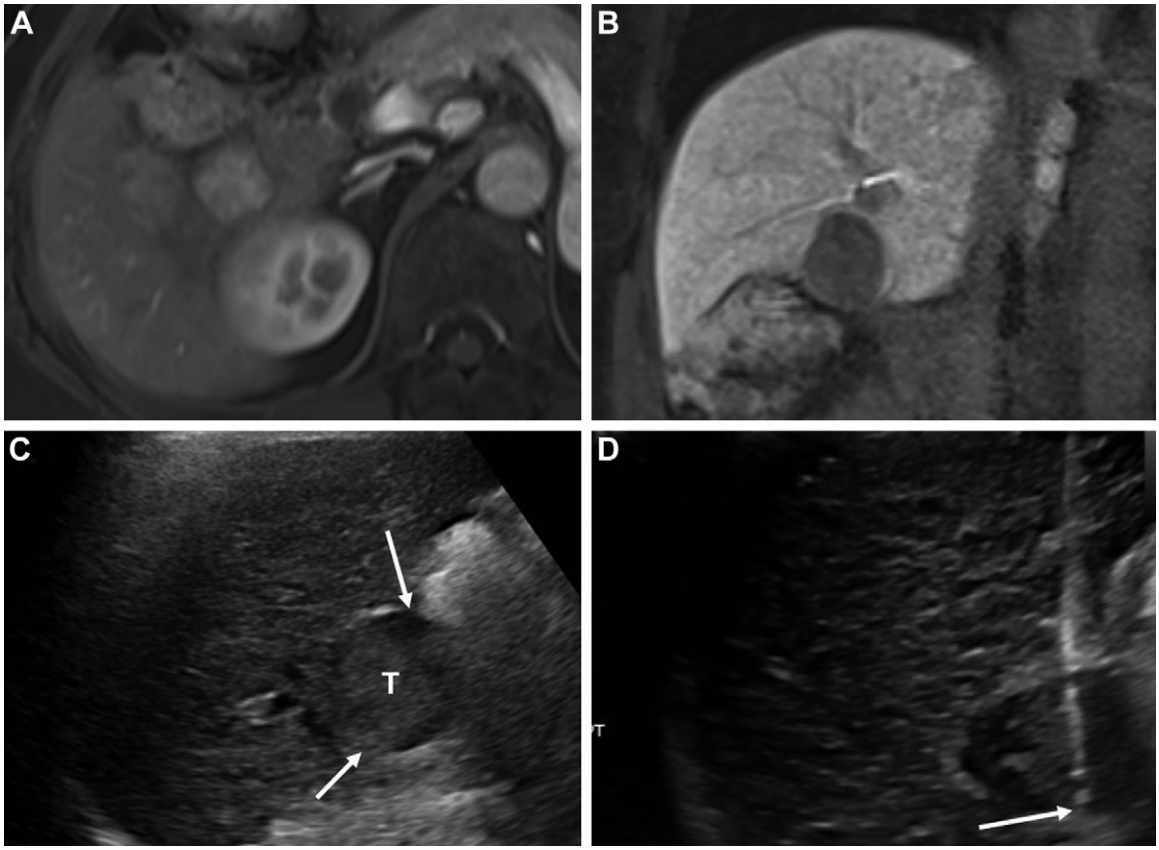

Figure 3: Conversion to tumor puncture radiofrequency ablation (RFA) in a 59-year-old woman with 2.5-cm hepatocellular carcinoma (HCC) and hepatitis B–related cirrhosis. **(A)** Arterial phase axial gadoxetic acid–enhanced MRI shows a 2.5-cm enhancing nodular lesion in segment VI subcapsular portion of the liver, indicating HCC. **(B)** On a coronal hepatobiliary phase image, the tumor shows low signal intensity abutting to hepatic flexure colon. **(C)** Target tumor appeared as low echoic nodular lesion on B-mode US. The half of tumor is not covered by liver parenchyma, indicating insufficient peritumoral liver parenchyma (*T* indicates the target tumor; arrows indicate the margin of target tumor). **(D)** Because of the lack of a safe access route for multiple radiofrequency electrodes insertion in the peritumoral region, conversion to tumor puncture RFA was done to treat HCC (arrow indicates the electrode tip within target tumor).

Table 2: Predictive Factors for Failure to Perform No-Touch RFA Technique and Conversion to Tumor Puncture RFA

	Univariable Analysis of No-Touch RFA			Mixed Logistic Regression Analysis	
Parameter	Success (n = 128)	Failure (n = 12)	*P* Value	Odds Ratio	*P* Value
Age (y)	62 ± 9	66 ± 9	.23		
Sex			.13		
No. of men	99	7			
No. of women	29	5			
Platelet (10^3/mm^3)	137 ± 49	123 ± 63	.30		
PT-INR	1.06 ± 0.11	1.06 ± 0.07	.58		
Albumin (g/L)	4.0 ± 0.4	3.9 ± 0.4	.16		
AFP (ng/mL)	34.1 ± 146.9	340.3 ± 745.2	.22		
Bilirubin (mg/dL)	0.7 ± 0.3	0.8 ± 0.4	.26		
Tumor size ≥ 2 cm			.001	2.4 (0.4, 14)	.32
Yes	38	9			
No	90	3			
Insufficient peritumoral parenchyma*			<.001	74 (18, 309)	<.001
Yes	1	6			
No	127	6			

Table 2 (*continues*)

Table 2 *(continued)*: Predictive Factors for Failure to Perform No-Touch RFA Technique and Conversion to Tumor Puncture RFA

	Univariable Analysis of No-Touch RFA			Mixed Logistic Regression Analysis	
Parameter	Success (n = 128)	Failure (n = 12)	P Value	Odds Ratio	P Value
Tumor location			>.99		
Right anterior segment	55	5			
Right posterior segment	49	5			
Left medial segment	12	1			
Left lateral segment	12	1			

Note.—Data in parentheses are 95% CIs. Tumor size and insufficient peritumoral parenchyma were included in multivariate mixed logistic regression analysis because these two variables had P values less than .05 at univariate analysis. AFP = α-fetoprotein, PT-INR = prothrombin time international normalized ratio, RFA = radiofrequency ablation.

*Insufficient peritumoral parenchyma is equivalent to less than 5-mm width of peritumoral parenchyma around more than half portion of tumor.

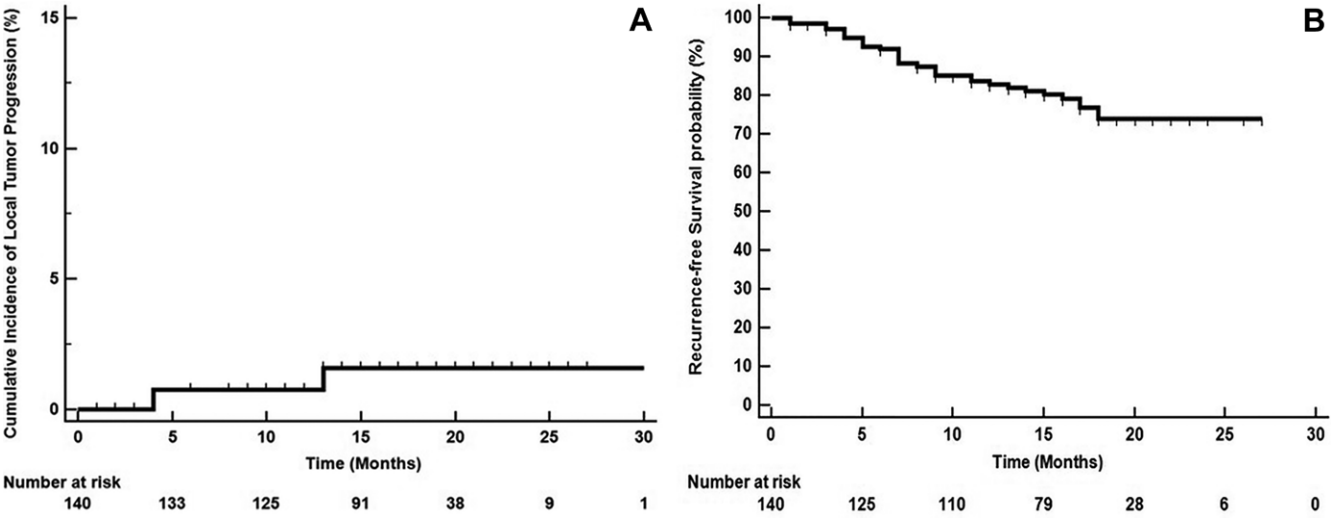

Figure 4: Kaplan-Meier estimation of the cumulative incidence of **(A)** local tumor progression and **(B)** recurrence-free survival after no-touch radiofrequency ablation in single hepatocellular carcinoma 2.5 cm or smaller.

Discussion

In this multicenter clinical trial with 140 study participants, no-touch radiofrequency ablation (RFA) in small hepatocellular carcinoma (HCC) 2.5 cm or smaller was safe and effective, resulting in good local tumor control. The rate of successful no-touch RFA technique was 91.4% (128 of 140), and conversion to conventional tumor puncture RFA was undertaken in 8.6% (12 of 140) of participants because of the lack of a safe access route for multiple electrode insertion. Local tumor progression (LTP) developed in two participants and the estimated cumulative incidence of LTP was 1.6% at 2 years in the study group. At evaluation, we found that no-touch RFA technique had failed in these two participants with LTP, and conversion to conventional tumor puncture RFA was undertaken to treat the HCC. Thus, no participants developed LTP after successful no-touch RFA for the treatment of HCC during the median follow-up of 18 months. Insufficient peritumoral parenchyma (odds ratio, 74; $P < .001$) was the only significant predictive factor for failure of no-touch RFA technique. The estimated 1- and 2-year recurrence-free survival was 82.8% and 74.1%, respectively. Three participants experienced major complications (three of 140; 2%).

Given that the reported LTP rates after no-touch RFA in HCCs have ranged from 4% to 8% at 3 years in previous retrospective cohort studies (10,14), our prospective study results regarding the LTP rate aligns with those studies. Moreover, considering that the reported LTP rate after conventional tumor puncture RFA was more than 11.0% at 2 years even in prospective clinical trials (5–7), there would be a possibility that no-touch RFA technique provides better local tumor control than conventional tumor puncture RFA. Further prospective studies with a double-arm design and a large number of participants are warranted to confirm our study results. In addition to no-touch RFA technique, smaller tumor size might contribute to the lower LTP rate in this study; the mean tumor size of this study was 1.69 cm and seemed to be smaller than that of previous studies (3,10,14). The use of real-time fusion US with MRI or CT guidance, which is better than B-mode US alone, to identify target tumor and the use of immediate

contrast-enhanced liver CT to assess technical success in our study may also have had a positive influence on the study results.

During the no-touch RFA technique, multiple electrodes are inserted outside of the tumor boundary and sequentially activated. Therefore, thermal energy is first deposited outside the tumor margin, and energy is thereafter delivered centripetally to the target tumor. Because of this energy delivery method, a sufficient ablation margin can be obtained with the use of no-touch RFA (10). Thermal energy deposition in the tumor periphery is another potential advantage of no-touch RFA. Tumor feeding vessels and draining veins are mainly located in the tumor periphery. Thus, no-touch RFA could obliterate the tumor feeding and draining vessels in the early period of ablation. This would reduce intratumoral perfusion during early treatment, resulting in more homogeneous necrosis and avoiding tumor dissemination through the draining vein during the procedure. This may explain our study results regarding the lower cumulative incidence of LTP with no-touch RFA.

A disadvantage of no-touch RFA compared with conventional tumor puncture RFA is that it is necessary to insert multiple electrodes outside the target tumor, which may be challenging with US guidance (14). Real-time fusion US with MRI or CT guidance can show the target tumor and adjacent vascular structures or organs more clearly than conventional B-mode US guidance. Thus, real-time fusion US with MRI or CT guidance may help overcome the technical difficulties of no-touch RFA (20–22). Nevertheless, because of this technical difficulty, no-touch RFA may not be able to be performed in all candidates with small HCCs, particularly in participants who lack a safe access route. In our study, conversion to conventional tumor puncture RFA was undertaken in 8.6% of participants who did not undergo no-touch RFA technique because of the lack of safe access route for multiple electrode insertion. Regarding the risk factor for failure of no-touch RFA technique, insufficient peritumoral parenchyma was the only significant predictive factor. In this regard, Petit et al (23) performed no-touch RFA in subcapsular HCC with sufficient peritumoral nontumorous liver parenchyma and reported good local tumor control with a 2-year LTP rate of 6%. Furthermore, because the insertion of multiple electrodes is required for no-touch RFA and the ablation zone would be larger than with conventional tumor puncture RFA, an increased risk of complications in no-touch RFA may be possible. However, in our study, the major complication rate of no-touch RFA was 2.1%, which is similar to that of conventional tumor puncture RFA. Therefore, despite the technical difficulty of no-touch RFA, no-touch RFA in small HCC was as safe as conventional tumor puncture RFA, as reported in a previous study (14).

Our study had limitations. First, our study had a multicenter prospective design, but it was not a randomized controlled trial. Therefore, we could not directly compare the cumulative incidence of LTP after no-touch RFA with that of conventional tumor puncture RFA. However, performing a randomized controlled trial by using an interventional procedure such as RFA would be difficult, and inevitably open labeled. Also, we only used monopolar RFA with switching system for no-touch RFA procedures. Multibipolar RFA can also be used for no-touch RFA and has reported promising results (10,14). In addition, because microwave ablation can provide a larger ablation zone in a given time with the use of single antenna than can RFA, further studies comparing the therapeutic efficacy of no-touch RFA with that of microwave ablation for HCC are warranted. Second, because the median follow-up period of our study was only 18 months, we only evaluated the short to midterm clinical outcomes of no-touch RFA.

In conclusion, we demonstrated that no-touch radiofrequency ablation (RFA) is a safe and effective treatment method for small hepatocellular carcinomas (HCCs) that were 2.5 cm or smaller and provided 1.6% of cumulative incidence of local tumor progression at 2 years. Further prospective studies with larger numbers of participants and longer follow-up terms that include various RFA systems (such as multibipolar) or microwave ablation are warranted to generalize our results and to assess the therapeutic efficacy of no-touch RFA in HCCs.

Author contributions: Guarantor of integrity of entire study, P.N.K.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, D.H.L., J.M.L.; clinical studies, all authors; statistical analysis, D.H.L., M.W.L.; and manuscript editing, all authors

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