Percutaneous Radiofrequency Ablation for the Hepatocellular Carcinoma Abutting the Diaphragm: Assessment of Safety and Therapeutic Efficacy

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Materials and Methods: We retrospectively assessed 80 patients who underwent a percutaneous RF ablation for a single nodular (< 4 cm) HCC over the last four years. Each patient underwent an ultrasound-guided RF ablation using internally cooled electrodes for the first-line treatment. We divided patients into two subgroups based on whether the index tumor was abutting (less than 5 mm) the diaphragm or not: group A (abutting; n = 31) versus group B (non-abutting; n = 49). We compared the two subgroups for complications and therapeutic efficacy using image and the review of medical records. The statistical assessment included an independent t-test, Fisher's exact test, and chi-square test.

Results: The assessment of the diaphragmatic swelling at CT immediately following the procedure was more severe in group A than group B (mean thickness change:1.44 vs. 0.46 mm, p = 0.00). Further, right shoulder pain was more common in group A than B (p = 0.01). Although minor complications (hemothorax 1 case, pleural effusion 1 case) were noted only in group A, no major thoracic complication occurred in either group. The technical success rate was lower in group A than group B (84% vs. 98%, p = 0.03). As well, the primary and secondary technique effectiveness rates in group A and group B were 90% versus 98% (p = 0.29) and 79% versus 91% (p = 0.25), respectively. The local tumor progression rate was higher in group A than in group B (29% vs. 6%, p = 0.02).

Conclusion: We found that the percutaneous RF ablation for the HCC abutting the diaphragm is a safe procedure without major complications. However, it is less effective with regard to technical success and local tumor control.

adiofrequency (RF) ablation is one of the most effective techniques for local treatment of hepatocellular carcinoma (HCC) and hepatic metastasis (1, 2). Recent clinical studies on the RF ablation of hepatic tumors have reported low rates of morbidity and favorable local tumor control rates. Although the RF ablation has been accepted as a safe procedure, potential complications can arise including bleeding, infection, and collateral thermal injury (3–6).

Unintended thermal injury may occur in the structures close to the tumor ablation zone, including the gastrointestinal region, biliary tracts, and the diaphragm. If an index tumor abuts one of these organs, the operator must consider the balance between two conflicting factors: safe ablation versus complete ablation (7–10). If the index tumor is located in the hepatic dome, the tumor frequently abuts the diaphragm and has a limited sonic window due to overlapped lung or ribs. Therefore, due to these

difficulties the percutaneous ablation of hepatic tumors abutting the diaphragm may result in poor clinical outcomes with high morbidity and low local tumor control (11, 12).

To our knowledge, several reports of thoracic complications such as diaphragmatic perforation, right shoulder pain, pleural effusion, and other problems following an RF ablation of subcapsular tumors abutting the diaphragm have been reported (5, 9, 10, 13–16, 21–23). However, no comparative studies have been performed using a control group to focus on the occurrence of thermal injury of the diaphragm. The purpose of this study was to retrospectively evaluate the safety (by focusing on the occurrence of thermal injury of the diaphragm) and the therapeutic efficacy of the percutaneous RF ablation for the HCC abutting the diaphragm, compared to a non-abutting control group.

MATERIALS AND METHODS

Patient Selection

Written informed consent was obtained from every patient prior to treatment. From August 2000 to March 2006, 627 patients with HCC were treated with 944 RF ablation procedures at our institution. The 627 patients included 469 men and 158 women ranging in age from 20 to 88 years (mean: 58.52 years). Among them, 80 patients were included in the study group. All patients included in the study met the following criteria for a percutaneous RF ablation: a single nodular HCC with a tumor size not exceeding 4 cm in maximum diameter, tumors located in liver segments 4, 7, and 8 above the portal bifurcation, and at least 4 follow-ups (immediately after, 1, 4, and 7 months). Other conditions for inclusion in this study include: no cases of portal vein thrombosis or extrahepatic metastases, use of an internally cooled electrode system for the procedure, a Child-Pugh classification of A or B for liver cirrhosis, normal coagulation data, no prior treatment for HCC, tumor visible on planning sonography, and tumor accessibility by the percutaneous approach.

For the diagnosis of HCC, pre-procedural imaging studies using combined sonography and CT or sonography, CT, and enhanced MRI were performed on all patients. All tumors were considered to be HCCs based on imaging findings (newly developed tumor on a follow-up sonography in patients with chronic liver disease and characteristic enhancement pattern on contrast-enhanced multiphase helical CT or dynamic contrast-enhanced MRI). Among them, 18 patients had elevated serum tumor markers (afetoprotein > 200 ng/mL) and another 13 patients had a confirmed diagnosis via a percutaneous needle biopsy.

We defined patients with tumors abutting the diaphragm when tumors were near the diaphragm (< 5 mm) on axial CT scan imaging. All tumors in this study were located in liver segment 4, 7, and 8 for an easy and accurate assessment of diaphragm thickness. Eighty patients were divided into two groups depending on whether the tumor was abutting the diaphragm or not: group A (abutting: n = 31), group B (non-abutting; n = 49). No statistically significant differences in the baseline characteristics of the group A and group B were found, except the distance from the diaphragm. The distance from diaphragm was defined as the nearest distance between tumor and diaphragm (Table 1).

Radiofrequency Ablation Procedure

Descriptions of the RF ablation procedure in this study follow the proposed standardization of terminology and reporting criteria (17). Vital signs and pain were continuously monitored during the procedure. All procedures were performed under conscious sedation using 50 mg of pethidine hydrochloride, intravenously (Samsung Pharmaceutical; Korea). Next, local anesthesia was provided by injecting an anesthetic (lidocaine; Kwang Myung Pharmaceutical; Korea) from the skin to the liver capsule along the planed RF electrode path. To avoid puncture of the tumor along the exposed liver surface, indirect access through the intervening non-tumorous liver parenchyma was used all cases. The RF ablation was performed under real-time US guidance (HDI 3000 or 5000, ATL) by one of three experienced radiologists (9, 10, 7 years experience with local ablation therapy, respectively). We used an internally cooled electrode system (Cool-tip; Valleylab; Boulder, CO). This system includes an electrode with an internally cooled tip (by chilled saline). The device was equipped with a 200-W generator and uses either a single 17-gauge straight electrode or a cluster electrode consisting of three electrodes mounted on a common handle in a triangular fashion. The algorithm of energy deposition followed the manufacturer's recommended protocol for the device. The therapeutic strategy of the radiofrequency ablation consisted of including a peripheral margin of at least 0.5 cm of normal hepatic parenchyma surrounding the tumor and the entire tumor itself as soon as possible. We cauterized the electrode path during retraction of the electrode to minimize bleeding after ablation and to avoid track seeding. We performed single or multiple overlapping ablations (mean: 1.21 ablations / tumor) to destroy the entire tumor (including the ablative margin). The mean duration of a complete RF ablation during the initial session was 16.32 min (8-36 min) in group A and 13.10 min (8-20 minutes) in group B.

We did not use artificial ascites and pleural effusion for the RF ablation procedure. After the procedure, a physician evaluated each patient for right shoulder pain for the approximate location and duration in a ward.

Follow-up Imaging

For the initial evaluation of procedure-related complications and therapeutic response, all patients immediately contrast-enhanced a three phase CT within two hours after the RF ablations. If residual tumor or unablated therapeutic margin was detected, additional RF ablation was repeated for a second session on the following day. We used a helical scanner (HiSpeed Advantage, GE Healthcare, Milwaukee, WI) with a 5-mm slice thickness as in the pre-procedural imaging study. A total of 120 mL of nonionic contrast material (Ultravist 300 [iopromide, 300 mg I/mLl, Schering, Berlin, Germany) was administered at a rate of 3 mL/sec with an automatic power injector. The scan images were acquired at pre-injection, 30, 70, and 180 sec after IV contrast material injection. Correspondingly, these represent the non-enhanced, hepatic arterial, portal venous, and equilibrium phases, respectively. All scans were obtained by using a 0.625 mm collimation beam at 200 mA and 120 kVp.

To evaluate the response to each of the RF ablations, scheduled follow-up contrast-enhanced CT scans, with the same parameters as the pre and immediately after scanning were performed on the day following treatment to assess the outcome at 1, 4, and 7 months, as well as one year or more after treatment. All follow-up CT scans were evaluated by the consensus of two abdominal radiologists.

Assessment of Safety and Therapeutic Efficacy

For the assessment of safety, we evaluated whether any thoracic complications occurred; including collateral thermal injury at the diaphragm adjacent to the RF ablation zone. In addition, we assessed the change in the diaphragm thickness at the initial and follow-up CT scans. Diaphragmatic thickness was defined as the thickest measurable portion of the diaphragm when that portion abutted the ablation zone on axial CT scanning (immediately after an RF ablation). Two radiologists measured the diaphragm thickness independently using a magnification view of the picture archiving and communication system (GE PACS, GE Healthcare). The results of each radiologist were averaged. The measurements of the initial and follow-up CT scans were compared at the same level as soon as possible. Each case was adjusted for CT window level optimization to delineate the diaphragm. One radiologist reviewed the electronic medical records of all patients for levels of pain medication as well as the presence and duration of persistent right shoulder pain after the RF ablation. We excluded transient and tolerable right shoulder pain during the RF ablation procedure without the administration of pain medication.

The description of complications and therapeutic efficacy in this study follow the proposed standardization of terminology and reporting criteria (17). Major complications are described as conditions that may lead to death if untreated, as well as conditions resulting in substantial morbidity and disability or a lengthened hospital stay. All other complications were considered to be of minor complications.

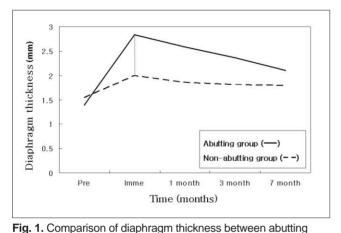
Table 1. Comparison of Baseline Characteristics of Patients between Group A and Group B

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Characteristic ——	Group		
	A (n = 31)	B (n = 49)	- P value
Mean age (yr)	59.25 ± 9.80	60.00 ± 10.46	0.32
Sex (M:F)	20:11	37:12	0.75
Mean follow-up period (month) †	18.48 ± 12.51	17.71 ± 9.77	0.76
Cause			
HBV	17	35	0.24
HCV	10	12	
NBNC	4	2	
Child class			
A	25	40	0.91
В	6	9	
Mean tumor size (cm) [†]	2.39 ± 0.69	2.13 ± 0.58	0.06
Mean α-FP (ng/mL) [†]	87.02 ± 170.32	88.11 ± 779.09	0.98
Mean distance from diaphragm (cm) [†]	0.21 ± 0.25	2.06 ± 1.12	< 0.01

Note.— Group A = abutting diaphragm, Group B = non-abutting diaphragm, HBV = hepatitis B virus, HCV = hepatitis C virus, NBNC = non-hepatitis B virus and non-hepatitis C virus.

 $^{^{\}dagger}$ Data are expressed as means \pm standard deviations.

To assess the therapeutic efficacy, we evaluated the technical success rate, primary technique effectiveness rate, secondary technique effectiveness rate, and local tumor progression rate. Technical success was defined by tumor treatment according to protocol and the achievement of complete tumor ablation after one session immediate as well as after a follow-up CT scan of the first RF ablation session. The primary technique effectiveness rate is defined as the percentage of tumors that were successfully eradicated at the one month follow-up CT. Secondary technique effectiveness rate was determined by a 1-year or later follow-up CT and included cases that underwent successful repeated percutaneous RF ablations following the identification of local tumor progression. Local tumor progression was diagnosed with the identification of untreated disease foci in tumors that were previously



group A and non-abutting group B. Graph shows changes in diaphragmatic thickness in two groups after radiofrequency ablation. Mean increase in diaphragmatic thickness between pre- and immediately after radiofrequency ablation on CT scanning was 1.44 mm for abutting group A and 0.46 mm for non-abutting group B. This difference was statistically significant (p < 0.01). Diaphragmatic thickness sponta-

considered to be completely ablated. These tumors had to be considered completely ablated by the definition used for primary effectiveness. The mean follow-up period was 18 months (7–67 mos). We found was no statistically significant differences between the both groups.

Statistical Analysis

A comparison between the two groups using independent t-test for continuous variables was carried out. A Fisher's exact test and chi-square test were used to analyze differences in the complication rate and therapeutic efficacy. All statistical tests were two-tailed and a p < 0.05 was considered statistically significant. All statistical analyses were performed with SPSS 10.0 (SPSS Inc., Chicago, IL).

RESULTS

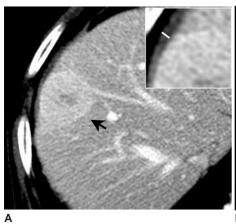
Safety

Collateral Thermal Injury of the Diaphragm

The mean increase in diaphragmatic thickness between pre and immediately after RF ablations on CT scans were 1.44 mm for group A and 0.46 mm for group B. These differences were statistically significant (p < 0.01). The mean diaphragm thickness was measured for its maximum value for the immediate follow-up CT for group A (2.84 mm) and group B (2.00 mm). The sequential diaphragmatic thickness change was observed to determine the decrease in diameter with time in both groups (Figs. 1, 2).

Mortality and Major Complications

There were no deaths related to the RF ablation procedures. Six patients died during the follow-up period. The causes of the deaths were aggravation of underlying liver cirrhosis in five patients and brain infarction in one patient. No major complications leading to substantial morbidity and disability, or extension of the hospital stay



neously decreased over time.

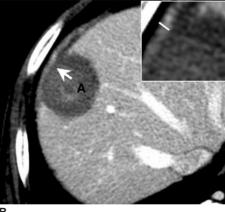


Fig. 2. 76-year-old man with hepatocellular carcinoma showing diaphragm swelling and enhancement.

A. Portal phase CT scan obtained prior to radiofrequency ablation shows enhancing nodule (black arrow) in segment VIII. White line = diameter of diaphragm thickness.

B. Portal phase CT scan obtained immediately after radiofrequency ablation shows ablation zone (A) with minimal amount of fluid collection. Swelling and enhancement of diaphragm is noted as thermal injury for abutting ablation zone (white arrow). White line = diameter of diaphragm thickness.

was noted in either group (Table 2).

Minor Complications

In the group A, eight patients had right shoulder pain after the RF ablation compared with two patients in the group B. Only two of these patients needed analgesics to control the pain in group A. The mean duration of right shoulder pain after RF ablation was 1.75 days for group A (0–2 days), and 1 day for group B (0–1 day).

Other minor complications for group A included one patient with asymptomatic pleural effusion and another with a small sized hemothorax after the ablation procedure. For the hemothorax case, the patient had two therapeutic sessions due to the detection of residual tumor for the immediate follow-up CT after the first session (Fig.

3). Neither of these two patients had respiratory symptoms and received only conservative treatment without transfusion or pleural tapping. For group A, seven patients had abnormal parenchymal densities detected in the right lower lobe for the CT immediately after the RF ablation. However, these patients had no respiratory symptoms. In the follow-up serial CT scans, the abnormal parenchymal densities spontaneously resolved without specific treatment (Fig. 4). We considered these imaging findings transient lung injury. By contrast, there were no thoracic complications in the group B (Table 2).

Therapeutic Efficacy

Technical Success

The technical success rate (84%, 26/31) in group A was

Table 2. Thoracic Complications following Percutaneous Radiofrequency Ablation of Hepatocellular Carcinoma between Group A and Group B

Thoracic Complications —	Gro	oup	<i>P</i> value
	A (n = 31)	B (n = 49)	
Major complication	0	0	
Minor complications and side effects			
Hemothorax	1 (3%)	0	0.39
Pneumothorax	0	0	
Pleural effusion	1 (3%)	0	0.39
Right shoulder pain	8 (26%)	2 (4%)	0.01
Transient lung injury	7 (23%)	0	< 0.01

Note.— Group A = abutting diaphragm, Group B = non-abutting diaphragm

 $^{^{*}}P$ values were calculated by using Fisher's exact test.

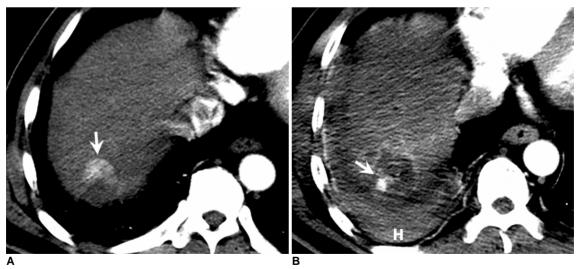


Fig. 3. 67-year-old man with hepatocellular carcinoma showing incomplete ablation and hemothorax.

A. Arterial phase CT scan obtained immediately after first session of radiofrequency ablation shows residual enhancing lesion (white arrow) at central portion of index tumor.

B. Second radiofrequency ablation session of residual tumor was performed on next day. However, persistent enhancing viable portion at ablation margin is noted immediately after radiofrequency ablation (white arrow). Hemothorax (H) at right lung is associated with diaphragmatic thermal injury. At that time, patient's vital signs were stable and resulted in use of conservative treatments only.

significantly lower than that group B (98%, 48/49) for the initial session (p = 0.03) (Table 3).

Primary and secondary technique rate of efficacy. At the one month follow-up CT, the primary technique rate of efficacy rate was 90% (28/31) for group A, compared to 98% (48/49) for group B (p = 0.29). As mentioned above, five patients in group A failed to undergo a complete

ablation of the tumor during the first session. These patients required additional tumor ablations in additional sessions. However three patients in group A continued to have viable portions of the tumor identified at the immediate follow-up CT after additional sessions, which was due to the difficulty of targeting a tumor adjacent to the diaphragm. These cases were treated by transarterial

Table 3. Comparison of Therapeutic Efficacy of Percutaneous Radiofrequency Ablation for Removal for Hepatocellular Carcinoma between Group A and Group B

Therapeutic Efficacy (%)	Group		D. chuc*
	A (n = 31)	B (n = 49)	— Pvalue*
Technical success rate	84 (26/31)	98 (48/49)	0.03
Primary technique effectiveness rate	90 (28/31)	98 (48/49)	0.29
Secondary technique effectiveness rate	79 (19/24)	91 (32/35)	0.25
Local tumor progression rate	29 (8/28)	6 (3/48)	0.02

Note.—Group A = abutting diaphragm, Group B = non-abutting the diaphragm

^{*}P values were calculated by using Fisher's exact test and chi-square test.

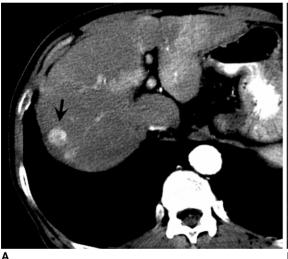






Fig. 4. 69-year-old man with hepatocellular carcinoma showing transient lung injury.

A. Arterial phase CT scan obtained prior to radiofrequency ablation shows enhancing nodule abutting diaphragm in liver segment VII (black arrow).

B. In lung window setting obtained immediately after radiofrequency ablation indicated abnormal parenchymal density at right lower lobe (white arrow). Patient was asymptomatic at time.

C. Without any specific treatment, lesion resolved at one month follow-up CT scan.

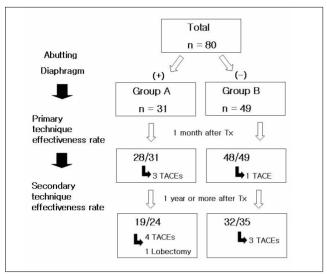


Fig. 5. Flow diagram showing primary and secondary technique effectiveness rates in this study. At one month follow-up CT, primary technique effectiveness rates was 90% (28/31) in group A, compared to 98% (48/49) in group B (p = 0.29). Among 80 patients, secondary technique effectiveness rates was evaluated in 59 patients who had one year or more of follow-up with CT. Secondary technique effectiveness rates was 79% (19/24) in group A, compared to 91% (32/35) in group B (p = 0.25). Both primary and secondary technique effectiveness rates showed no statistically measurable difference. Group A = abutting diaphragm, group B = non-abutting diaphragm

chemoembolization (TACE). One patient in the group B had an enhancing lesion adjacent to the ablated margin detected at the 1-month follow-up CT and was also treated by TACE.

Among the 80 study patients, the secondary technique effectiveness rates was evaluated in 59 patients who had a one year or more follow-up with CT. The secondary technique effectiveness rates was 79% (19/24) in group A, compared to 91% (32/35) in the group B (p = 0.25) (Fig. 5, Table 3).

Local Tumor Progression

On the follow-up CT, local tumor progression was observed in 29% (8/28) at the ablation margin in Group A and 6% (3/48) in group B. This difference was significant (p = 0.02) (Table 3). On the other hand, the mean detection time for local tumor progression on follow-up CT was 9.5 months for group A and 10.25 months for group B. This difference was not statistically significant (p = 0.09).

DISCUSSION

The diaphragm is innervated by both phrenic nerves arising from the nerve roots (C3, 4, and 5), which

represent the same dermatome as in shoulder skin. Thus, diaphragmatic irritation is referred to the shoulder and irritation of the diaphragm can cause right shoulder pain (18). Further, thermal injury to tissue causes increase in tissue volume and water content and has been demonstrated experimentally (19, 20). Hence, we considered an increase in the diaphragmatic thickness and right shoulder pain (referred pain) as the representative indicators of diaphragmatic thermal injury.

Our study demonstrated that changes in diaphragmatic thickness after an RF ablation for CT images in the abutting group were significantly greater than the non-abutting group. Also, the mean distance from the diaphragm in the non-abutting group was greater than the abutting group (2.06 vs. 0.21 cm, p < 0.01). Moreover, the mean total RF ablation time during the first session, was longer in the abutting group than the non-abutting group (16.32 vs. 13.10 min, p = 0.02). Therefore, the distance between the index tumor and diaphragm as well as the ablation time could be an important factor for the risk of collateral thermal injury of the diaphragm.

Although the degree of thermal injury to the diaphragm and basal lungs at the immediate CT scan was more severe in the abutting group, these changes spontaneously improved without substantial mortality or significant morbidity in either group. Thus, we suggest that hepatic tumors abutting the diaphragm can safely be treated by a percutaneous RF ablation without significant morbidity. In comparison to the recent study by Head et al. (21), our data have show a lower incidence, duration of right shoulder pain, and local tumor recurrence rate. These differences may be due to the definition of "abutting the diaphragm" and "tumor size" because their study included larger sized tumors, which were on average at a closer proximity to the diaphragm.

Our study demonstrated that the percutaneous RF ablation for HCC was more effective in the non-abutting group compared to abutting group in terms of technical success and local tumor progression. In three of five patients in the abutting group with technical failure after the first session of ablation, complete ablation was not achieved; even after a second session of ablation on the following day. The main reason for the technical failure in the abutting group was attributed to the difficulty in targeting the tumor by the RF electrode. This is a well-known problem in US-guided interventions of hepatic focal lesions in the hepatic dome. If the index tumor is located in the hepatic dome, the boundary of the tumor is usually only partially visible due to overlap of the lungs, even at a deep inspiration state. Another reason for technical failure in our series of patients was the use of the straight type RF

electrodes. These can be dislocated by expiration during the ablation, especially if the index tumor is targeted during deep inspiration.

We found that the local tumor progression rate was significantly higher in the abutting group compared to the non-abutting group. The reasons for these differences may be similar to those for the differences outlined in the technical success rate. The most probable explanation for the difference in local tumor progression rate is the accessibility of the tumor for the RF ablation. The operator's concern of thermal injury to the adjacent diaphragm may lead to incomplete (suboptimal) ablation because it is very difficult to monitor the RF ablation zone and the diaphragm in the subphrenic area with a poor sonic window and an ill-defined hyperechoic zone during the ablation.

Recently, Teratani et al. (16) reported the clinical results of the use of RF ablations for HCC at high-risk locations. They reported that HCC nodules adjacent to a large vessel or extrahepatic organ were treated with RF ablations without compromising safety or therapeutic efficacy. The reason for the differences with our study is that they routinely used artificial pleural effusion for cases with tumors abutting the diaphragm or artificial ascites in cases when tumors abutted the gastrointestinal tract. In addition, our results for the local tumor progression rate were contrary to recent studies using a control group by Kim et al. (13), Cho et al. (22), and Sartori et al. (23). Kim et al. reported no significant difference in the local tumor progression rate between subcapsular HCCs and nonsubcapsular HCCs. However, their study groups showed that they included cases such that significantly larger tumor sizes were included in the subcapsular HCCs group compared to the nonsubcapsular HCCs group. The Cho et al. study population included patients with multiple HCCs. Moreover, their total study population was relatively low. Further, Satorini et al. included study patients with hepatic metastatic lesions; and our definition of a subcapsular tumor was closer to that of a tumor. These differences may account for the differences in study outcome. Their studies reported better therapeutic efficacy including local tumor progression in subcapsular HCCs compared with our study.

Currently, the only way to achieve safe and complete ablation with an ablative margin, is to separate the RF ablation zone from organs in danger of being injured. To separate between the index tumor and adjacent organs, several studies have evaluated the use of artificial materials between the index tumor and abutting organs for the percutaneous RF ablation. Various methods such as the injection of artificial ascites, pleural effusion, and intra-

abdominal carbon dioxide insufflation are reported to minimize diaphragmatic thermal injury during percutaneous RF ablation (15, 24–30). These studies are based on the hypothesis that the RF ablation of tumors adjacent to the organs poses a substantial risk of thermal injury. The results of our comparative study may support the previous studies which use artificial ascites and pleural effusion during an RF ablation for lesions that abut the diaphragm (with regard to therapeutic efficacy). Further, these additional techniques may be supportive in preventing technical failure and may also reduce the rate of local tumor progression.

Our study did have certain limitations. First, we evaluated the thermal injury of the diaphragm by indirect methods (using diaphragm thickness and right shoulder pain) because we could not assess the pathologic grading of the thermal injury [as in the animal study by Raman et al. (28, 29)]. We also had to measure the change in diaphragmatic thickness on CT as a quantitative assessment of the degree of diaphragmatic thermal injury. In addition, we performed axial CT scan images without multi-planar reconstruction images (31). Further the respiratory movement during CT scanning influences the evaluation of diaphragm thickness. As well, we only reviewed for the presence of right shoulder pain without a validated pain assessment tool (such as a pain scale score). Lastly, we could not objectively consider the variability of experience and therapeutic planning associated with the three interventional radiologists or use exclusively the internally cooled electrode system for RF ablation.

In conclusion, our results suggest that the percutaneous RF ablation of HCC abutting the diaphragm is safe without major complications. However, it is less effective with regard to the technical success and local tumor control and it is associated with a higher rate of right shoulder pain and transient lung injury.

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