

Intraoperative Radiofrequency Ablation for Hepatocellular Carcinoma: Long-Term Results in a Large Series

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Background: Intraoperative radiofrequency (RF) ablation with or without surgical resection currently plays one of important roles in modern hepatocellular carcinoma (HCC) therapy. We evaluated long-term follow-up results including prognostic factors of intraoperative RF ablation for HCC that was difficult to treat percutaneously.

Methods: A total of 133 patients (male, 22 female, mean age 55.8 years) underwent intraoperative RF ablations for 200 HCCs (follow-up period 3.0–79.7 months, median 22.3 months). Hepatic resection was also performed in 29 patients. Reasons for the intraoperative procedure included no safe electrode path ($n = 59$), excessive tumor burden ($n = 41$), nonvisualization of the HCC on ultrasonography ($n = 20$), and risk of collateral thermal damage to adjacent organs ($n = 13$). We evaluated the technique effectiveness rate at 1 month computed tomography (CT), cumulative local tumor progression rate, cumulative disease-free and overall survival rates, and complications. We also sought significant prognostic factors for overall survival.

Results: The technique effectiveness at 1 month was 94.7% (126/133). The cumulative local tumor progression rates at 1 and 3 years were 4.9% and 8.8%, respectively. The cumulative disease-free and overall survival rates at 1, 3 and 5 years were 51.8%, 21.3%, and 16.0% and 92.3%, 72.6%, and 46.5%, respectively. Major complications occurred in nine patients (6.8%). Procedure-related mortality was 1.5% (2/133). The patients treated for recurrent HCC ($P = 0.003$) or with high serum alpha-fetoprotein levels ($P = 0.009$) had poor survival by multivariate analysis.

Conclusion: The results of this study showed that intraoperative radiofrequency ablation with or without hepatic resection is a safe and effective treatment for hepatocellular carcinoma in patients who are not candidates for the percutaneous approach.

Key Words: Hepatocellular carcinoma—Radiofrequency ablation—Hepatectomy—Complication.

Radiofrequency (RF) ablation for hepatocellular carcinoma (HCC) had been regarded as complementary to surgical resection until recently. Initially, it was performed in patients who were not eligible for

surgery. However, its role in the treatment of small HCCs has been expanding. In fact, for small HCCs, percutaneous RF ablation is replacing surgery as the initial therapeutic modality at many treatment centers throughout the world. In one recently published study, the long-term follow-up results of percutaneous RF ablation, as a first-line therapy for small HCC, were comparable to the surgical outcomes in terms of the overall survival and complication rates.¹

Published online May 8, 2008.

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Published by Springer Science+Business Media, LLC © 2008 The Society of Surgical Oncology, Inc.

In addition, RF ablation preserves more of the hepatic parenchyma than surgical resection, which is very important especially in patients whose hepatic functional reserve is limited. These advantages have made RF ablation preferred to surgery in some patients.

The ultrasound (US)-guided percutaneous approach is the most widely used method to perform RF ablation; this is because of its versatility and the wide availability of US, in addition to the minimal invasiveness of the procedure. However, US-guided percutaneous RF ablation is not effective for all small HCCs encountered in clinical practice. One recent intention-to-treat analysis showed that 9% of HCCs could not be treated by US-guided percutaneous RF ablation due to an unfavorable location of the tumor.² The concerns in such cases include the risk of collateral thermal injury of the adjacent organs and no available safe electrode path due to, for instance, the large portal vein. In such cases, computed tomography (CT) guidance, use of artificial ascites³ or laparoscopy,⁴ or change to another therapeutic modality such as transcatheter arterial chemoembolization (TACE) may be more effective. However, these choices are not always available, not always as effective as RF ablation, or require special skills and experience to perform. Intraoperative RF ablation, although it no longer is a minimally invasive treatment, can solve some of the above-stated problems without unnecessary sacrifice of the hepatic parenchyma. It is sometimes the only solution, other than liver transplantation, to cure the disease in clinical practice.

On the other hand, combined resection and ablation should be considered in cases where neither sole resection nor sole ablation can provide complete treatment, such as in the case of bilobar distribution of the tumors. Hence, intraoperative RF ablation with or without hepatic resection currently plays an important role in modern HCC therapy.

The purpose of this study was to evaluate the clinical features, complications, long-term survival, and prognostic factors associated with curative intraoperative RF ablation for HCC performed in difficult cases that could not be treated percutaneously or cases where the standard surgical resection was not feasible in a large series at a single center.

MATERIALS AND METHODS

Patients

From October 1999 to April 2007, 187 patients underwent intraoperative RF ablation after laparot-

TABLE 1. Summary of clinical characteristics of patients (n = 133) treated with intraoperative radiofrequency ablation for hepatocellular carcinoma

Characteristics	Value
Sex (n)	
Male	111
Female	22
Age (years)	31–76
Parenchymal liver disease (n)	
None ^a	9
Chronic hepatitis	18
Liver cirrhosis	106
Cause of liver disease (n)	
None	4
Hepatitis B virus ^a	111
Hepatitis C virus	13
Hepatitis non-B, non-C virus	2
Alcohol	2
Budd–Chiari syndrome	1
Child–Pugh class (n)	
A	116
B	17
History of treatment for HCC (n)	
Absent	85
Present	48
Transcatheter arterial chemoembolization	26
Surgical resection	11
Percutaneous radiofrequency ablation	9
Percutaneous ethanol injection therapy	2
Serum alpha-fetoprotein level before treatment ^b (n)	1–13000 ng/mL
<20 ng/mL	10
>20 ng/mL, <400 ng/mL	92
>400 ng/mL	24

^a Five of these patients were healthy carriers of hepatitis B virus.

^b Available in 126 patients.

omy under general anesthesia with a curative intention. Among them, 133 patients, with 238 HCCs, whose follow-up period was more than 3 months, were enrolled in our study. The study population consisted of 111 men and 22 women (age 31–76 years, mean 55.8 years). Two hundred HCCs were treated with RF ablation, and 38 tumors in 29 patients were resected concurrently. The institutional review board of our hospital waived the requirement for approval and the need for informed consent from the patients because this was a retrospective clinical study.

The clinical characteristics of the patients and the tumor burden (size and number) per patient are summarized in Tables 1 and 2, respectively. Eighty-five tumors (42.5%) from 62 patients were confirmed by histopathology and the remaining 115 tumors (57.5%) from 71 patients were considered to be HCC based on the clinical criteria from the Barcelona 2000 EASL conference⁵ that included: imaging findings compatible with this diagnosis, an elevated serum alpha-fetoprotein (AFP) level greater than 400 ng/mL (n = 20) or satisfaction of at least two coincident

TABLE 2. Number and size of hepatocellular carcinoma treated with intraoperative radiofrequency ablation with/without surgical resection per patient

Tumor	Value ^a
Overall tumor (<i>n</i> = 133)	
Number	1.8 ± 0.9 (1–6)
Size	2.4 ± 1.4 cm (0.5–10 cm)
Radiofrequency-ablated tumor (<i>n</i> = 133)	
Number	1.5 ± 0.8 (1–6)
Size	2.2 ± 1.1 cm (0.5–6 cm)
Resected tumor (<i>n</i> = 29)	
Number	1.3 ± 0.6 (1–3)
Size	3.2 ± 2.2 cm (0.8–10.0 cm)

^a Mean ± standard deviation (range).

imaging findings (US, spiral CT, magnetic resonance image, and angiography) (*n* = 51).

RF Ablation and Surgical Procedures

All procedures were carried out under real-time US guidance by one of five experienced radiologists using the free-hand technique. Exclusion criteria for this procedure at our center were as follows: maximal tumor diameter over 6 cm, Child–Pugh class C, and presence of portal vein thrombosis or extrahepatic metastasis. There was no restriction on the number of tumors for treatment as long as complete ablation was reasonably achievable considering the procedure time required and the amount of preserved hepatic parenchyma after treatment.

We used an internally cooled electrode system (Cool-tip RF system, Valleylab, Boulder, CO, USA) for 150 tumors in 105 patients. Three different types of electrodes were used with 200-W RF generator: a single 17-gauge straight electrode with a 2-cm- and 3-cm active tip, and a cluster-type electrode with a 2.5-cm active tip. The multi-tined expandable electrode (Model 500 and 1500 series, RITA medical systems, Fremont, CA, USA; RF 2000 system, Boston Scientific Corp., Natick, MA) was also adopted for 39 tumors in 30 patients. For one tumor in one patient, a perfusion-mediated RF electrode was used (Elektronon 106 HiTT, Berchtold corporation, Tuttingen, Germany). The decision of RF ablation device was made depending on tumor size and availability of the devices.

Our strategy for complete necrosis of the tumor was to ablate at least 0.5–1.0 cm of normal hepatic parenchyma surrounding the tumor for a safety margin. Therefore, for tumors larger than 2.5 cm in diameter, we made use of a multiple overlapping ablation technique or a special form of electrode such as the cluster-type internally cooled electrode. The

overlapping ablation technique was used for 52 tumors in 42 patients (mean ± standard deviation [SD], 2.6 ± 1.1 times, range 2–6 times). The total ablation time varied from patient to patient (mean ± SD, 16.5 ± 9.4 min, range 6–60 min).

Hepatic resection was conducted after consideration of the resectability of the liver based on the indocyanine green (ICG) retention test [ICG-R₁₅ (ICG retention rate 15 min after injection of a 0.5-mg/kg dose) ≤ 10%—up to lobectomy; ICG-R₁₅ ≤ 20%—up to bisegmentectomy], the feasibility of curative treatment by a combination of therapeutic modalities, and the treatment efficiency. For instance, in cases where the tumors were in both hepatic lobes and the majority of the tumors, especially larger ones, were located in one hepatic lobe, hepatic lobectomy was performed and the remnant tumor(s) in the other lobe were treated by RF ablation as long as the hepatic functional reserve was not limited. In cases where a larger tumor was seen in the subcapsular area and a smaller one was noted deep in the hepatic parenchyma, a tumorectomy and RF ablation were carried out for each of the tumors. Hepatic resection was performed in 29 patients for 38 HCC tumors. The number and size of the resected tumors in the patients are listed in Table 2.

In four cases with four large tumors (mean 4.5 cm, range 3.5–5.5 cm), Pringle's maneuver was carried out by the surgeon to assure a large enough ablation zone to cover the tumor and an adequate safety margin.^{6,7} A cluster-type, internally cooled electrode was used in all cases and 3–6 ablations with overlap were carried out for the three tumors, except for a 3.5-cm tumor.

Follow-Up after Treatment

All patients were followed-up with contrast-enhanced three-phase CT. The first follow-up was performed 1 month after treatment and the technique effectiveness was evaluated at this time. If the RF ablation achieved a technical success, the follow-up CT was repeated every 3 months after this visit. However, the interval of follow-up was changed based on suspected complications or other clinical concerns.

Contrast-enhanced CT examinations were performed with one of five helical scanners (HiSpeed CT/i, LightSpeed QX/i, LightSpeed Ultra, LightSpeed 16, GE healthcare, Milwaukee, WI, USA; Brilliance 40, Philips Medical Systems, Best, the Netherlands). We used 120 mL nonionic contrast material (Ultravist 300 [300mg I/mL iopromide] Shering AG, Berlin, Germany) administered intravenously with an automatic injector (OP 100, Medrad, Indianola, PA, USA)

at a rate of 3 mL/s. The images were obtained at 25–35, 60–70, and 180 s after the initiation of contrast material injection, representing the hepatic arterial, portal venous, and equilibrium phases. Using a single-detector helical CT scanner, we obtained images in a craniocaudal direction with a 7 mm slice thickness and a 7 mm interval. The parameters for the multi-detector CT examination were 2.5–5.0 mm slice thickness and 2.5–5.0 mm intervals.

Clinical Features and Therapeutic Efficacy Analysis

We evaluated the reasons why an intraoperative procedure was performed instead of a percutaneous procedure. The postoperative clinical features included duration of the hospital stay, body temperature changes, and changes in laboratory findings (peak values within one month of aspartate aminotransferase [AST], alanine aminotransferase [ALT], and total bilirubin).

The technique effectiveness, in terms of the absence of residual unablated tumors, was assessed at the 1-month CT.⁸ Local tumor progression was diagnosed when a follow-up CT demonstrated tumor growth and enhancement along the margin of the ablation zone where the technique was considered to be completely effective (i.e., there was no evidence of residual tumor). Intrahepatic distant recurrence was defined when new tumor growth which met the previously mentioned criteria for diagnosing HCC appeared remote from the ablation zone. When we found residual unablated tumor or local tumor progression, we attempted additional RF ablations. Unless it was possible, TACE was the preferred procedure.

The cumulative local tumor progression, intrahepatic distant recurrence, disease-free survival, and overall survival rates were evaluated. Disease-free survival was defined by no local tumor progression, intrahepatic distant recurrence, extrahepatic metastasis, or death. Overall survival time was defined as the interval between RF ablation and either death or the last visit to the outpatient clinic up to April 31, 2007.

The major and minor complications, as defined by the standard terminology and reporting criteria of the Society of Interventional Radiology Technology Assessment Committee and the International Working Group on Image-Guided Tumor Ablation⁸ and procedure-related mortality, were assessed as well.

Statistical Analysis

The cumulative rates of local tumor progression, intrahepatic distant recurrence, disease-free survival,

and overall survival were assessed by the Kaplan–Meier method. Advanced age, presence of a treatment history for HCC, poor hepatic function (i.e., Child–Pugh class B), high AFP level, large number of tumors, large size of the largest tumor treated by RF ablation or resection, and accompanying hepatic resection were evaluated as potentially poor prognostic factors for overall survival. The statistical significance was determined using the multivariate stepwise Cox hazard model. Age, serum AFP level, tumor number, and diameter of the largest tumor were computed as continuous variables in the multivariate analysis (i.e., not using a cut-off value). A *P* value <0.05 was considered a significant difference. Data were analyzed using commercially available statistics software (SPSS for Windows, version 11.0, SPSS, Chicago, IL, USA).

RESULTS

Reasons for Intraoperative Procedure and Clinical Features

Intraoperative RF ablation was performed for several reasons as follows. The most common reason was that there was no available safe route for the electrode. This was due to organs blocking the electrode route: large portal or hepatic vein branches (*n* = 19), the right lower lung lobe (*n* = 17), the hepatic hilum, and cases where the tumor was located in the caudate lobe (*n* = 12), the gall bladder (*n* = 8), or the stomach (*n* = 3). There were 59 such patients (44.4%), in three of which a hepatic resection was also performed. The second most common reason was tumor burden too high to treat percutaneously (*n* = 41, 30.8%). The indications for percutaneous procedure with regard to tumor burden at our center are: single nodular HCC ≤5 cm in maximum diameter and multinodular (up to three) and HCCs ≤3 cm in maximum diameter each. The number of tumors in the patients in this group ranged from one to six, and the sizes of the largest tumors measured from 1.4 to 10 cm. Among 21 cases in this group, a part of the liver was resected simultaneously with the RF ablation and, in most cases, this was planned preoperatively. In 20 patients (15.0%), intraoperative RF ablation was performed due to poor visibility of the index tumor on US examination. This was usually due to unfavorable location of the tumor. Three of these cases required hepatic resection. Lastly, intraoperative RF ablation was performed because of the risk of collateral thermal injury to the adjacent organs (*n* = 13, 9.8%). Hepatic resection

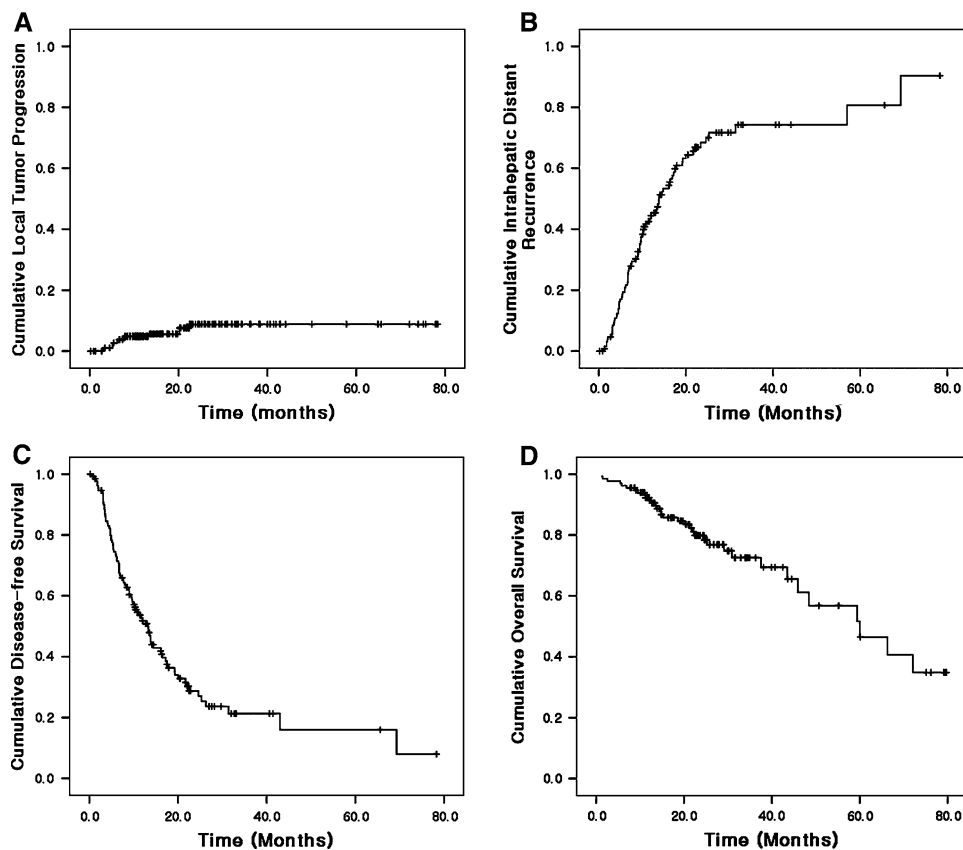


FIG. 1. The cumulative rates for (A) local tumor progression, (B) intrahepatic distant recurrence, (C) disease-free survival, and (D) overall survival of the 133 patients who underwent intraoperative RF ablation for 200 HCCs (follow-up period 1.2–79.7 months, mean 25.5 months, median 22.1 months; crosses indicate censored data).

was performed in two patients in this treatment group.

The duration of the hospital stay after surgery ranged from 5 to 45 days (mean \pm SD, 11.0 ± 5.9 days; median 9 days). In patients who required hepatic resection, hospital stay (range 7–45 days; mean \pm SD, 12.5 ± 7.7 days; median 10 days) was slightly longer than in the cases that did not require hepatic resection (range 5–35 days; mean \pm SD, 10.6 ± 5.3 days; median 9 days) without statistically significant difference ($P = 0.134$). The peak body temperature after surgery was 36.7 – 39.9°C (mean \pm SD, $37.9 \pm 0.5^\circ\text{C}$). The body temperature peaked from 1 to 10 days (mean \pm SD, 2.5 ± 2.0 days) after the day of surgery. Peak values of serum AST and ALT levels within 1 month were 390.3 ± 399.4 IU/L (9.9 ± 11.1 -fold increase) and 472.5 ± 1391.8 IU/L (12.4 ± 43.8 -fold increase), respectively. The serum total bilirubin level was 3.8 ± 5.3 mg/dL (4.7 ± 14.0 -fold increase).

Local Therapeutic Efficacy

Patients were followed up for 3.0–79.7 months (except two patients who expired within 3 months;

mean 25.6 months, median 22.3 months). The technique effectiveness rate evaluated at 1 month was 94.7% (126/133) on a per-treatment base and 96.0% (192/200) on a per-tumor base. Six patients with residual unablated tumors were treated with TACE and one patient was treated with an additional percutaneous RF ablation. Local tumor progression was identified in 6.7% of the tumors (13/192) from 3.1 to 22.5 months during the follow-up period. The cumulative local tumor progression rates estimated at 1, 2, and 3 year were 4.9%, 8.8%, and 8.8%, respectively (median not available) (Fig. 1A). Twelve (92.3%) locally progressed tumors were treated with TACE and the remaining one was controlled with an additional percutaneous RF ablation.

Long-Term Survival Results

Cumulative intrahepatic distant recurrence rates were estimated to be 44.4%, 68.4%, 74.3%, 74.3%, and 80.7% at 1, 2, 3, 4, and 5 years, respectively (median 13.8 months, standard error [SE] 1.8 months, 95% confidence interval [95%CI] 10.3–17.3 months). A disease-related event (i.e., local tumor progression, intrahepatic distant recurrence, extrahepatic

metastasis, and death) occurred in 66.8% (88/133) of the patients by the end of follow-up period. Cumulative disease-free survival rates at 1, 2, 3, 4, and 5 years were estimated as 51.8%, 28.7%, 21.3%, 16.0%, and 16.0%, respectively (median 13.2 months, SE 1.5 months, 95%CI 10.3–16.1 months). Estimated cumulative overall survival rates, which considered only death, at 1, 2, 3, 4, and 5 years were 92.3%, 79.9%, 72.6%, 61.2%, and 46.5%, respectively (median 60.0 months, SE 10.4 months, 95%CI 39.7–80.3 months). Thirty-four patients (25.6%) died during the follow-up period due to progression of HCC ($n = 21$), complications of cirrhosis ($n = 11$), and postoperative hepatic failure ($n = 2$) (Fig. 1B–D).

Among the potential risk factors, high serum AFP level ($P = 0.009$, odds ratio not available due to an attribute of a continuous variable) and the presence of a treatment history of HCC (i.e., recurrent HCC) ($P = 0.003$, odds ratio 2.185) were statistically significant for risk of a poor prognosis by the multivariate analysis.

Complications

Following 133 treatments, there were 17 complications (12.8%). Major complications were observed in nine patients (6.8%). There were three cases of hepatic lobar infarction, one of which progressed to hepatic failure. In two of three cases, complicated by lobar infarction (66.7%), Pringle's maneuver with a multiple overlapping ablation technique was used. Hepatic failure occurred in another two patients who underwent simultaneous RF ablation and hepatic resection. Two cases of peritoneal abscess (Fig. 2), one case of sepsis (without hepatic abscess), and one case with a large amount of ascites were also classified as major complications. Minor complications were reported in eight patients (6.0%). A biliary tree injury on CT was the most common and was detected in six patients (subsegmental biliary tree dilatation, $n = 4$; biloma, $n = 2$). Subsegmental infarction of the liver and a small perihepatic hematoma was noted in one patient.

Among three patients with hepatic failure, one patient survived after undergoing living-donor-related liver transplantation 6 days after the RF ablation. However, the remaining two patients died 1.2 months (infarction-induced) (Fig. 3) and 1.5 months later (resection-induced). The procedure-related mortality rate was 1.5% (2/133). The other patients that had major complications recovered after appropriate management.



FIG. 2. Intraperitoneal abscess developed after intraoperative RF ablation and hepatic resection. A 61-year-old man who had undergone simultaneous segmentectomy of S VIII for HCC measuring 4.2 cm and intraoperative RF ablation (white arrow) for HCC measuring 1.0 cm complained of fever and abdominal pain after surgery. Follow-up CT on the sixth postoperative day demonstrated a large intraperitoneal abscess cavity with an air-fluid level (black arrows). This abscess was managed by percutaneous catheter drainage.

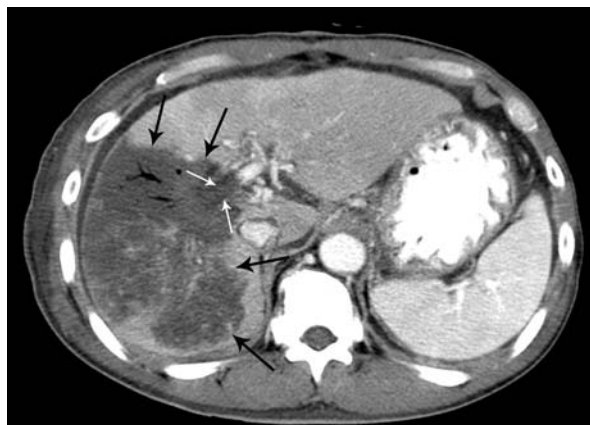


FIG. 3. Hepatic lobar infarction-induced hepatic failure after intraoperative RF ablation. A 65-year-old man had been treated with intraoperative RF ablation for HCC measuring 3.0 cm adjacent to the central portal vein using a cluster-type internally cooled electrode without Pringle's maneuver. The patient had clinical features of hepatic failure after surgery; the CT scan on the ninth postoperative day revealed an extensive right lobar infarction (black arrows) of the liver with portal vein thrombosis (white arrows) from the main to the segmental branches. He refused liver transplantation and expired 1.2 months after the RF ablation.

DISCUSSION

Several investigators have previously discussed intraoperative RF ablation for HCC. However, in most cases, the procedure was evaluated as a part of an entire RF ablation series; both the size of the study

population undergoing intraoperative RF ablation for HCC and the follow-up period were limited and therefore the reliability of the results related to the intraoperative RF ablation for HCC were also limited.⁹⁻¹⁴ Although Stella et al. and Tepel et al. reported on the results of intraoperative RF ablation for hepatic tumors, the tumors treated were mostly metastatic tumors to the liver.^{15,16} There has been no prior study where intraoperative RF ablation for HCC was solely evaluated. This study was the first large series to provide long-term results of intraoperative RF ablation for HCC.

As stated, there are several options for difficult cases where percutaneous RF ablation for HCC guided by US is not suitable. However, each method has its own drawbacks. In cases where the tumor is located beyond the scope of the sonic window or delineation of the tumor on the background hepatic parenchyma is difficult, changing the guiding modality to CT is one of the easiest and most efficient alternative approaches. However, because real-time monitoring of the tumor is impossible, due to the transient nature of contrast enhancement, the degree of technical difficulty is quite high, especially when a landmark for targeting is not available or overlapping ablation is needed. TACE is the most popular therapeutic modality used as an alternative to RF ablation. However, the rate of complete tumor remission after TACE is lower than RF ablation, and TACE usually requires multiple treatments to achieve a similar therapeutic efficacy as one RF ablation.^{17,18} Combination of TACE and subsequent RF ablation is sometimes helpful in the sense of that TACE reduces viable tumor size and accumulated iodized oil may improve the visibility of the tumor on US. Surgical alternatives including hepatectomy and liver transplantation are the best therapeutic modalities in terms of completeness. However, more often than not, hepatic resection cannot be performed in patients with hepatic decompensation, and liver transplantation requires a donor as well as special staff and facilities. Therefore, intraoperative RF ablation is often the most realistic alternative in difficult cases that cannot undergo percutaneous RF ablation for HCC.

Although intraoperative RF ablation is no longer a minimally invasive procedure, it has a number of advantages over the percutaneous procedure. First, intraoperative US imaging, which is performed directly on the surface of the hepatic capsule, improves visualization of the tumor and thus increases the procedure's diagnostic performance. Scaife et al. reported that intraoperative US examination of the li-

ver before surgical resection and/or RF ablation identified more hepatic tumors than were seen on the preoperative helical CT scan in 27% of the study patients.¹⁹ A laparotomy may provide a chance to detect a small tumor that was otherwise missed or to increase the diagnostic confidence about a tumor that was previously ambiguous. For this reason, the entire liver should be examined thoroughly with meticulous correlation with cross-sectional images before the initiation of the RF ablation. Unfortunately, we did not have specific data to assess this in our retrospective study. Second, a laparotomy can enable the combination of RF ablation with other therapies. Resection of the liver could be regarded as a combination therapy. Shen et al. attempted to combine intraoperative RF ablation for HCC with chemotherapy via the main portal vein and TACE. This group of patients demonstrated significantly better survival results than the percutaneous RF ablation-only group.²⁰ Furthermore, Pringle's maneuver can also be combined with the intraoperative RF ablation. Augmentation of the RF ablation zone by means of reducing the hepatic flow has been proven to be effective by an *in vivo* experimental model.^{6,7} This is explained by the elimination of the heat-sink phenomenon caused by the hepatic arterial and portal venous flow. However, our data, although the number of cases was not large enough to be evaluated statistically, suggests that the risk for hepatic infarction is elevated by combining RF ablation and Pringle's maneuver. We performed four cases of the Pringle's maneuver during intraoperative RF ablation for large HCCs. Two of them (50.0%) developed extensive lobar hepatic infarction on follow-up CT examination. In our entire study population, three hepatic lobar infarctions occurred, and Pringle's maneuver was used in two of them (66.7%). Although two patients with hepatic lobar infarction, caused by Pringle's maneuver, showed marked elevation of the serum hepatic enzyme levels, fortunately, both recovered. We would recommend a multiple overlapping ablation technique rather than the Pringle's maneuver, regardless of the size of the tumor.

Our exclusion criterion for performing intraoperative RF ablation with regard to tumor size was >6 cm in diameter. We set this size because 6.3 cm has been shown to be the largest tumor diameter (8.3 cm including a 1 cm safety margin) which we could theoretically expect complete necrosis by overlapping a 5-cm ablation sphere 14 times.²¹ However, this is affected by many factors such as the shape of the tumor and the ablation zone, the loca-

tion and direction of the RF electrode, the heat sink effect by the major vessels, and so on. Early in our practice, we adhered to this size criterion. However, over time, with increased experience, we realized that achievement of an 8-cm diameter of the ablation zone for a 6-cm tumor and a 1-cm safety margin was extremely difficult. Therefore, we lowered this criterion to a 5 cm diameter in mid 2002. In our study, there were two cases with a tumor diameter >5 cm. We adopted both Pringle's maneuver and the multiple overlapping techniques for the 5.5-cm tumor. For the other 6.0-cm HCC, the operator performed no more than three overlapping ablations because the tumor was ovoid and was sufficiently covered by an echogenic cloud after the three overlapping ablations.

Even though it was not included in the results of our study, there is one very important technical aspect that the operator of intraoperative RF ablation has to know. Because it is desirable to minimize the surgical manipulations such as the laparotomy incision and mobilization of the liver, the space in which the US transducer and the RF electrode operate is usually small; this results in a very limited range of motion for both the US transducer and electrode. Movements are sometimes hindered by the incised abdominal wall and even by the surgical traction devices. This is especially true when a surgical resection is not planned and/or the hepatectomy and RF ablation are not performed by the same physician; for example, the laparotomy may be performed by a surgeon and the RF ablation by a radiologist. For this reason, the smaller the size of the US transducer and the RF electrode, the easier the procedure. Even though we do not have experience with this device, a flexible electrode might help overcome this problem.

Comparing with the results of percutaneous RF ablation for HCC at our center that were published previously (674 HCCs in 570 patients),¹ the results of the intraoperative RF ablation were similar to or slightly worse than the percutaneous treatment. The technique effectiveness at 1 month and the cumulative local tumor progression rate at 3 years for the percutaneous and intraoperative RF ablation were 96.7% versus 94.7% and 11.8% versus 9.1%, respectively. The cumulative disease-free survival and overall survival rate at 5 years were 21.0% versus 16.0% and 58.0% versus 46.5%, respectively. The previous study differs from the current study in that the tumors included were initially diagnosed HCC tumors less than 3 cm in diameter and immediate follow-up CT evaluation and, if needed, subsequent additional treatment was performed. These differences in the study population and follow-up protocol

could explain the discrepancies in the results. However, the complication rates were quite dissimilar. The major complications for the intraoperative RF ablation occurred in 6.8% of patients compared with 1.9% of cases undergoing percutaneous treatment. Among the nine cases with major complications in this study, six (hepatic failure in patients with hepatic lobectomy $n = 2$, peritoneal abscess $n = 2$, sepsis without hepatic abscess $n = 1$, massive ascites $n = 1$; 66.7%) might be attributed to the surgical resection or laparotomy. After excluding these cases, the major complication rate directly related to the RF ablation was 2.3%, which is slightly higher than that of the percutaneous RF ablation. The minor complication rates were 4.2% versus 6.0%, respectively. These slightly higher complication rates could be explained by a relatively more aggressive treatment approach due to the larger sizes of the tumors and the patients' condition under general anesthesia.

Most of the patients in our study group (85.0%, 113/133) had an underlying liver disease associated with hepatitis B virus, which is dominant in the Asian population and distinct from the hepatitis C virus-dominant Western population. Because hepatitis B virus-related HCC has lower risk of recurrence after treatment than hepatitis C virus-related HCC,²² we need to consider the difference in the etiology of underlying liver disease should the results of this study be applied to Western population.

Throughout the study period, the decision-making process for the treatment modalities was not standardized and the decisions were made on a case-by-case basis. This is an inevitable limitation of a retrospective study design. However, we used criteria for both the percutaneous and intraoperative RF ablation techniques to minimize the subjectivity of the decision-making.

In conclusion, intraoperative RF ablation is an effective and safe therapeutic modality for HCC when conventional treatment was not effective. Therefore, curative treatment in such cases should not be abandoned just because the HCC tumor cannot be treated percutaneously or if there are tumors distributed in both hepatic lobes. However, the results of this study showed a higher rate of major complications and mortality with intraoperative RF compared with percutaneous RF ablation. In addition, although the amount of data was not large enough for us to be convinced, our findings suggest that use of Pringle's maneuver with intraoperative RF ablation may increase the risk of hepatic lobar infarction. Further studies are needed to confirm these findings.

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