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ORIGINAL ARTICLE

Combination of intraoperative radiofrequency ablation and surgical resection for treatment of cholangiocarcinoma: feasibility and long-term survival

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PURPOSE
Most patients with intrahepatic cholangiocarcinoma (ICC) are not eligible for surgical resection due to advanced stage. We aimed to evaluate the feasibility, local tumor control, and long-term survival of intraoperative radiofrequency ablation (IORFA) with surgical resection to treat unresectable intrahepatic cholangiocarcinoma (ICC).

METHODS
From 2009 to 2016, 20 consecutive patients (12 primary ICC, 8 recurrent ICC) underwent curative IORFA with hepatic resection for surgically unresectable ICC. Patients were not qualified to undergo surgical resection due to multiple lesions causing postoperative hepatic insufficiency and undesirable tumor locations for surgical resection or percutaneous RFA. Of the 51 treated tumors (mean, 2.6±0.9 tumors/patient), 24 were treated by IORFA and 27 were surgically removed. The technical success and effectiveness, overall survival, progression-free survival (PFS), and complications were assessed retrospectively. The overall survival and PFS rates were estimated by the Kaplan-Meier method.

RESULTS
The technical success and effectiveness of IORFA were 100%. The overall survival rates at 6 months, 1, 3, and 5 years were 95%, 79%, 27%, and 14%, respectively. The median overall survival time was 22.0±3.45 months. The PFS rates at 6 months, 1, 3, and 5 years were 70%, 33%, 13%, and 13%, respectively. The median PFS was 9.0±1.68 months. The prognosis was significantly worse for patients with recurrent ICC than for patients with primary ICC. One patient (5%) had major complications due to IORFA such as liver abscess and biliary stricture.

CONCLUSION
IORFA with surgical resection can be a feasible option for ICC cases that are not amenable to treatment with surgical resection alone. This strategy provides acceptable local tumor control and overall survival.

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver malignancy after hepatocellular carcinoma and its global incidence and mortality are increasing (1). Although hepatic resection may be curative, most patients with ICC cannot undergo curative resection, owing to the presence of advanced cancer at the initial presentation, insufficient function of the remaining liver, or underlying patient's comorbidities (2). The prognosis for patients with untreated unresectable cholangiocarcinoma is poor, with a median survival time of 3.9 months (3). Although most patients with ICC receive palliative therapy, including systemic chemotherapy, radiation therapy, transarterial chemoembolization, and radioembolization, these options generally do not improve the chance of survival compared with supportive therapy alone, because ICC responds poorly to such therapies (4–6).

Percutaneous radiofrequency ablation (RFA) is reportedly safe and effective for the local control of hepatic malignancies in patients considered unsuitable for surgical resection (7–9). Moreover, several studies have shown the utility of percutaneous RFA for primary and recurrent ICC (10, 11). However, intraoperative RFA (IORFA) is more advantageous than percutaneous RFA in terms of broadening the surgical indications (12). Since the surgeon can resect larger tumors with the belonging segment or lobe, while ablating smaller resid-

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ual tumors with the belonging segment or lobe, combining IORFA with resection can qualify more patients to undergo surgical treatment (13). Indeed, applying a combination therapy consisting of IORFA and surgical resection has potential benefits in some cases; however, only few reports have addressed the long-term survival and expansion of surgical indication (14).

Herein, we evaluated the feasibility of using IORFA with surgical resection to treat unresectable ICC.

Methods

Patient population

The institutional review board approved this retrospective study, and the requirement to obtain informed consent was waived. This study was conducted in accordance with the World Association Declaration of Helsinki principles. Twenty consecutive patients (15 men, 5 women; mean age, 59.8±11.8 years) underwent curative IORFA with hepatic resection for ICC from June 2009 to August 2016. The ICCs were mass-forming type based on macroscopic appearance (15). Patients with histologically confirmed ICC were included. The feasibility and benefits of surgical resection for patients with multiple ICCs were discussed by a multidisciplinary team comprised of surgeons, oncologists, and interventional radiologists. Inoperable ICC (e.g., hepatic insufficiency can occur when intrahepatic metastasis of other lobe is surgically resected) was considered for IORFA.

The inclusion criteria for IORFA were as follows: 1) an ICC deemed completely resectable via surgery with additional IORFA after discussion by the multidisciplinary team; 2) ICC nodules less than 3 cm in diameter, three or fewer in number; 3) excessive resection of all tumor foci may pose a high risk of hepatic insufficiency; 4) tumors in unfavorable locations for surgical resection (e.g., central region of liver); 5) tumors in unfavorable locations for percutaneous RFA (e.g., subcapsular region); 6) for the recurrent ICC, no imaging evidence of vascular invasion by the tumor and no evidence of extrahepatic disease. Exclusion criteria for IORFA were as follows: 1) large size (maximum diameter, >3 cm) and number (> 3); 2) target tumors abutting a major vessels or bile duct; and 3) distant metastases. The feasibility of IORFA and surgical resection was determined by computed tomography (CT) and magnetic resonance imaging (MRI) within one month.

Among the 20 patients, 12 patients had primary ICC and eight patients had recurrent ICC after previous surgical hepatic resection. For patients with recurrent ICC, the median time to recurrence was 15.4 months (range, 8.4–51.2 months). Of the 20 patients, the tumor stage was II in 16 patients and IVA in four patients. The patients with stage IVA were able to undergo surgery due to the presence of only regional lymph node metastasis. Tumors were staged according to the American Joint Committee on Cancer Staging system, also known as tumor, node, and metastasis staging (16). The characteristics of the patients and tumors are summarized in Table 1.

Imaging techniques

Various CT scanners were used during the 8-year follow-up period, including the Sensation 16, Somatom Definition, Somatom Definition flash, and Somatom Definition AS + scanners (Siemens Medical Systems) and the LightSpeed 16, LightSpeed Plus, and LightSpeed VCT scanners (GE Healthcare). The intravenous contrast medium (120–150 mL of 300–370 mg I/mL non-ionic contrast; Iopromide, Ultravist 300 or Ultravist 370, Bayer Healthcare) was administered at a rate of 2–3 mL/s. The scanning protocol included unenhanced, arterial phase (determined by using a bolus-triggering method), portal venous phase (72 s), and delayed phase (3 min). The images were reconstructed in the axial and coronal planes, ranging from a 3 mm thickness at 3 mm intervals to 5 mm thickness at 5 mm intervals.

MRI examinations were performed using 1.5T (Magnetom Avanto; Siemens Medical Solutions) or 3T (Magnetom Skyra, Siemens Medical Solutions) systems. After unenhanced T1- and T2-weighted MRI, gadoxetic acid-enhanced T1-weighted 3D gradient-echo imaging was performed in arterial phase (5 s after peak aortic enhancement, which was determined by using a 1 mL test-bolus injection), portal venous phase (50 s), transitional phase (3 min), and hepatobiliary phase (20 min) after a bolus injection of gadoxetic acid (0.1 mL/kg) at a rate of 1.0 mL/s and a subsequent 20 mL saline flush.

Surgical resection

Intraoperative ultrasonography (US) was done to evaluate the tumor character (e.g., size, number, location) during laparotomy. The relationship between ICC and surrounding structures determined if a conventional resection was to be performed. The extent of surgery was determined by the predicted hepatic functional reserve. Type of surgical resection were categorized as segmentectomy, hemihepatectomy, or extended hepatectomy (more than five segments) (17). The policy regarding lymph node dissection in ICC surgery at our institution is to perform lymph node dissection of the hepatoduodenal ligament.

IORFA

IORFA was performed by an interventional radiologist with 18 years of clinical experience. Before the surgical resection of main hepatic tumors, an intraoperative US was done to evaluate other metastatic tumors in comparison with preoperative image findings. The visualization of the target lesion sometimes fails because of coarse parenchymal echogenicity in cirrhotic liver. Sonazoid (GE Healthcare) was used to clear delineation of the lesions. After surgically removing the resectable tumors, a single 17-gauge internally cooled electrode (Proteus; STARmed Co.) was inserted into the center of the tumor under US guidance using a 7 MHz convex probe (Avius, Hitachi Aloka Ltd.). RFA was performed using a 200 W generator (Viva RF system; STARmed Co.) in automatic impedance mode for 12 minutes. The endpoint of RFA was identifying the total ablation with 5 mm circumferential safety margins.

Follow-up, definitions, and data evaluation

All patients underwent contrast-enhanced CT and/or MRI at 1, 3, 6, 12 months, and annually after IORFA. The reporting standards of the Society of Interventional Radiology were used with respect to terminology and reporting criteria (18). Technical

Main points

- Intraoperative radiofrequency ablation (IORFA) with surgical resection is an effective treatment modality for unresectable ICC due to multiplicity and unfavorable location.
- IORFA can broaden the surgical indications, offering acceptable survival rate and tumor control, with minimal complications.
- At mean follow-up of 24.7 months, the median overall and progression-free survival were 22.0±3.45 months and 9.0±1.68 months.

success was defined as a target tumor was completely ablated with a sufficient margin. Technical effectiveness was defined as complete ablation of the tumor shown on imaging follow-up 1 month after IORFA. Disease progression was classified as local tumor progression or new tumor recurrence. Local tumor progression referred to the appearance of tumor foci at the edge of ablation zone on any follow-up image obtained more than 1 month after IORFA. New tumor recurrence referred to the remote intrahepatic recurrence or extrahepatic metastatic tumor relapse that was identified by imaging (CT or MRI) or verified by histological examination. The overall survival period was defined as the interval, in months, between the initial IORFA and the patient's death. The progression-free survival (PFS) was defined as the time interval between treatment initiation and disease progression. Major complications referred to any events that resulted in substantial morbidity and disability or hospital admission, or that substantially lengthened the hospital stay. All other complications were classified as minor.

Statistical analysis

The overall survival and PFS rates were estimated using the Kaplan-Meier method. The overall survival and PFS curves of primary and recurrent ICCs were compared using the log-rank test. The primary endpoints were the time from the initial IORFA to the time of disease progression (PFS) and ICC-related death (overall survival). All statistical analyses were performed using SPSS for Windows, version 21.0 (SPSS, Inc.). Differences were considered statistically significant at $P < 0.05$.

Results

Out of total 51 treated tumors (mean, 2.6±0.9 tumors/patient), 27 were surgically resected (mean, 1.4±0.8 tumors/patient; mean size, 4.4±2.9 cm) and 24 underwent IORFA (mean, 1.2±0.4 tumors/patient; mean size, 1.3±0.6 cm) (Figs. 1, 2). Out of the 20 patients, four underwent IORFA on multiple foci in different segments and 16 underwent single IORFA. The hepatic resection type was hemihepatectomy in three patients, bi-segmentectomy in nine patients, segmentectomy in six patients, and wedge resection in two patients (Table 1).

The technical success and effectiveness rates were both 100%. Technical effectiveness was confirmed at 1 month of follow-up CT after IORFA in all patients. Out of the 20 patients, ICC recurred in 16 patients (80%) and 31 sites after IORFA. Local tumor progression occurred in two patients (patient 13 and 17) at 9 months and 16 months, respectively, after IORFA, and new tumor recurrence occurred in 16 patients, including patients 13 and 17. The dominant pattern of new tumor recurrence was remote intrahepatic recurrence (15/31, 49%). Intrahepatic site without extrahepatic site occurred in three patients. Thirteen patients had extrahepatic recurrence in 16 sites. The sites

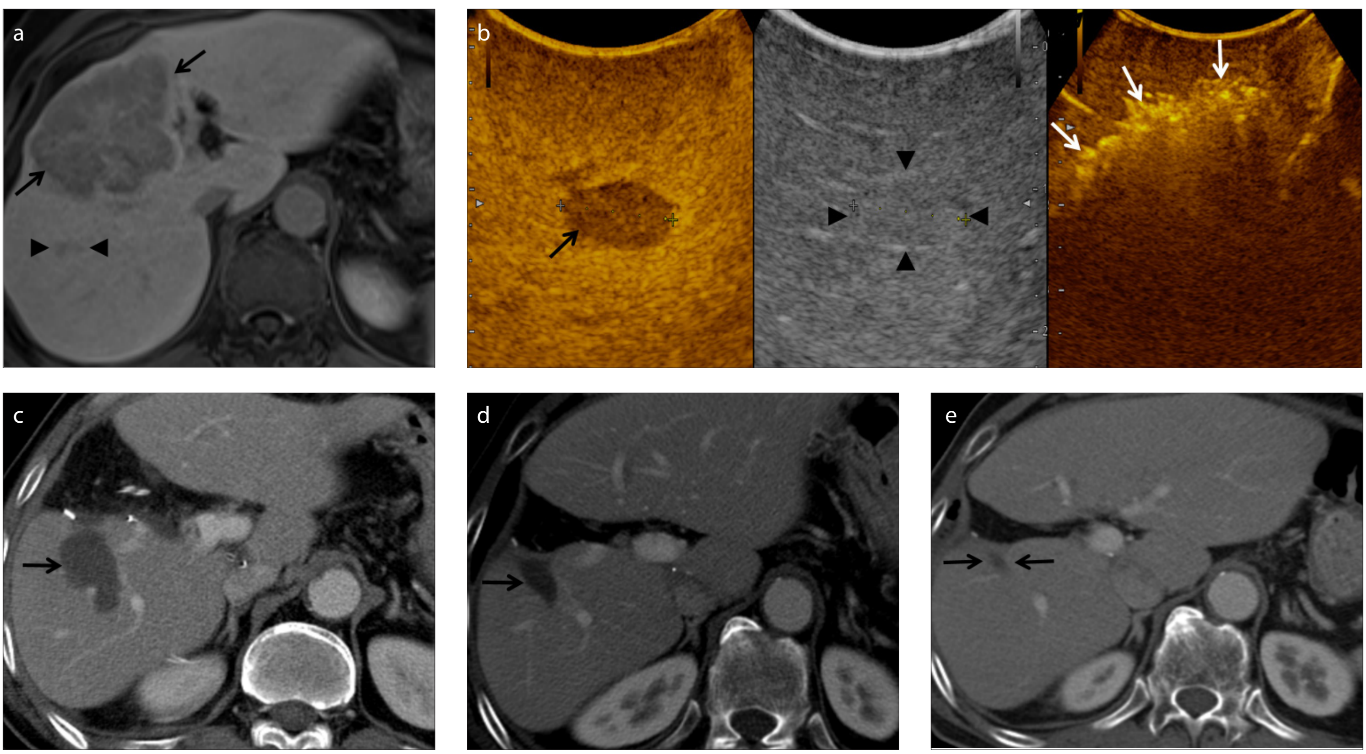

Figure 1. a–e. A 71-year-old man presented with intrahepatic cholangiocarcinoma (ICC). Gadoxetic acid-enhanced image **(a)** during hepatobiliary phase using a T1 VIBE sequence shows an 8.2 cm, soft tissue mass *(arrows)* in the hepatic segments IV, V, and VIII. A 2.1 cm, hypointense daughter nodule *(arrowheads)* is also found in segment VII. Extended right hemihepatectomy was planned, but central bisegmentectomy with intraoperative radiofrequency ablation (IORFA) was performed because of high risk of hepatic insufficiency for isolated resection. During IORFA, Sonazoid-enhanced US image **(b)** shows a clearly delineated nodule *(arrow)* in the liver that had a correlation with an ill-defined isoechoic nodule *(arrowheads)* on gray-scale ultrasound. Intraoperative ultrasound image obtained 12 minutes after the RFA shows successful ablation with sufficient margin *(white arrows)*. Contrast-enhanced axial CT image **(c)** in portal phase obtained 1 month after the central bisegmentectomy with IORFA shows surgical removal of the main mass and complete ablation of the daughter nodule *(arrow)*. CT image **(d)** obtained 10 months after IORFA shows reduced RFA zone *(arrow)* without a viable portion. CT image **(e)** 7 years following IORFA shows no suspicious enhancement within the extremely reduced ablated zone *(arrows)*. The patient has been doing well for 96 months without tumor recurrence or distant metastasis.

Table 1. Patients' characteristics and treatment details

No.	Age (years)	Sex	Primary or recurrent ICC	TNM (stage)	Child-Pugh class	IORFA No.	IORFA Location (segment)	IORFA Size (cm)	Hepatic resection Type	Hepatic resection No.	Hepatic resection Size* (cm)	Adjuvant treatment
1	57	M	Primary	200 (II)	A	1	5	1.6	Lt lat biseg	1	3.5	(+)
2	54	M	Primary	200 (II)	A	1	4	1.2	Lt lat biseg	1	3.2	(+)
3	43	M	Primary	200 (II)	A	1	2	1.0	Seg	1	2.5	(+)
4	75	M	Primary	200 (II)	A	1	8	1.0	Seg	1	4.7	(+)
5	37	F	Primary	200 (II)	B	1	3	0.7	Hemi	4	12.8	(+)
6	67	F	Primary	210 (IVA)	A	1	4	1.7	Hemi	3	8.8	(+)
7	71	M	Primary	210 (II)	A	2	6 7	1.2 2.1	Central biseg	1	8.2	(-)
8	53	M	Primary	200 (II)	A	1	6	1.0	Rt ant biseg	1	6.0	(+)
9	58	M	Primary	200 (II)	A	2	8 4	1.0 0.7	Seg	1	5.0	(+)
10	77	M	Primary	200 (II)	A	1	8	0.8	Biseg (3, 6)	2	1.5	(-)
11	53	M	Primary	210 (IVA)	A	1	6	0.8	Lt lat biseg	1	5.2	(-)
12	52	M	Primary	200 (II)	B	1	5	1.1	Seg	1	2.2	(-)
13	54	M	Recurrent	200 (II)	A	1	6	1.6	Lt lat biseg	1	1.0	(-)
14	72	M	Recurrent	200 (II)	A	1	7	2.3	Hemi	1	1.3	(+)
15	64	F	Recurrent	200 (II)	A	1	3	1.9	Wedge	1	2.0	(-)
16	70	M	Recurrent	210 (IVA)	B	1	3	1.0	Seg	1	2.2	(-)
17	73	M	Recurrent	210 (IVA)	B	1	8	1.9	Seg	1	1.6	(-)
18	40	F	Recurrent	200 (II)	A	2	5 6	2.7 2.4	Wedge	1	2.1	(+)
19	68	F	Recurrent	200 (II)	A	2	7 8	0.9 1.0	Lt lat biseg	2	4.2	(-)
20	57	M	Recurrent	200 (II)	A	1	6	0.6	Biseg (4, 8)	1	5.0	(+)

No., number; ICC, intrahepatic cholangiocarcinoma; TNM, tumor, node, and metastasis; IORFA, intraoperative radiofrequency ablation; M, male; F, female; Lt, left; lat, lateral; Rt, right; ant, anterior; Hemi, hemihepatectomy; Seg, segmentectomy; Biseg, bisegementectomy; Triseg, trisegementectomy.
* The largest diameter of all tumors.

of extrahepatic recurrence were the lungs (5/31, 16%), bones (4/31, 13%), adrenal gland (1/31, 3%), spleen (1/31, 3%), pancreas (1/31, 3%), and peritoneal seeding (4/31, 13%). Tumor recurrence was treated with a combined session of chemotherapy (n=7), irradiation (n=6), percutaneous RFA (n=2), IORFA (n=1), ethanol injection (n=1), and transarterial chemoembolization (n=1). The 11 patients with positive resection margins or nodal invasion received adjuvant therapy (chemotherapy and/or irradiation). The treatment results and clinical outcomes are summarized in Table 2.

Four patients (20%) had major complications due to the surgical resection or the IORFA. Patient 15 underwent IORFA for a 1.9 cm tumor of hepatic segment 3 and presented with symptomatic biliary stenosis and hepatic abscess at 1 month postoperatively. The hepatic abscess was successfully treated with percutaneous drainage and antibiotic therapy. However, the biliary stricture required repeated percutaneous transhepatic biliary drainage during the follow-up. The other three complications were attributed to surgical resection. Patient 11 had active bleeding at the removal site of the Jackson-Pratt drainage tube, which was successfully treated with endovascular embolization. Other major complications included hepatic abscess and hematoma at the resection margin (patient 8) and peritonitis (patient 16). No procedure-related deaths were identified.

The overall survival rate at 6 months, 1 year, 3 years, and 5 years after treatment were 95%, 79%, 27%, and 14%, respectively, and the median overall survival time was 22.0±3.45 months (Fig. 3). For patients with primary ICC, the overall survival rates at 1, 3, and 5 years post-treatment were 91%, 49%, and 24%, respectively, and the median overall survival time was 34.0±5.87 months. For patients with recurrent ICC, the overall survival rates at 6, 12, and 18 months post-treatment were 88%, 63%, and 25%, respectively, and the median overall survival time was 17.0±4.11 months. The PFS rates at 6 months, 1 year, 3 years, and 5 years after treatment were 70%, 33%, 13%, and 13%, respectively, and the median PFS was 9.0±1.68 months (Fig. 3). Recurrent ICC was associated with poor survival. The overall survival and PFS rates were significantly higher in patients with primary ICC than in patients with recurrent ICC (P = 0.001 and P = 0.031, respectively; Fig. 4). Out of the 20 patients, six patients were alive, whereas 14 patients died of disease progression. The mean follow-up was 24.7±20.0 months (range, 5–96 months). All surviving patients were followed up for at least 10 months af-

Table 2. Treatment results and clinical outcomes after IORFA

No.	TS	TE	Major complication	Recurrence	Progression free survival (months)	Overall survival period (months)	Survival
1	Yes	Yes	-	-	37	37	Alive
2	Yes	Yes	-	+	22	42	Dead
3	Yes	Yes	-	+	6	15	Dead
4	Yes	Yes	-	+	16	29	Alive
5	Yes	Yes	-	+	9	34	Dead
6	Yes	Yes	-	+	12	29	Dead
7	Yes	Yes	-	-	96	96	Alive
8	Yes	Yes	Hepatic abscess, hematoma	+	10	22	Dead
9	Yes	Yes	-	+	4	38	Alive
10	Yes	Yes	-	-	10	10	Alive
11	Yes	Yes	Abdominal wall bleeding	+	2	11	Dead
12	Yes	Yes	-	-	11	11	Alive
13	Yes	Yes	-	+	9	23	Dead
14	Yes	Yes	-	+	2	20	Dead
15	Yes	Yes	*Hepatic abscess, biliary stricture	+	7	11	Dead
16	Yes	Yes	Peritonitis	+	7	8	Dead
17	Yes	Yes	-	+	16	17	Dead
18	Yes	Yes	-	+	10	18	Dead
19	Yes	Yes	-	+	3	5	Dead
20	Yes	Yes	-	+	4	17	Dead

IORFA, intraoperative radiofrequency ablation; No., number; TS, technical success; TE, technical efficacy.
* Complications related to IORFA.

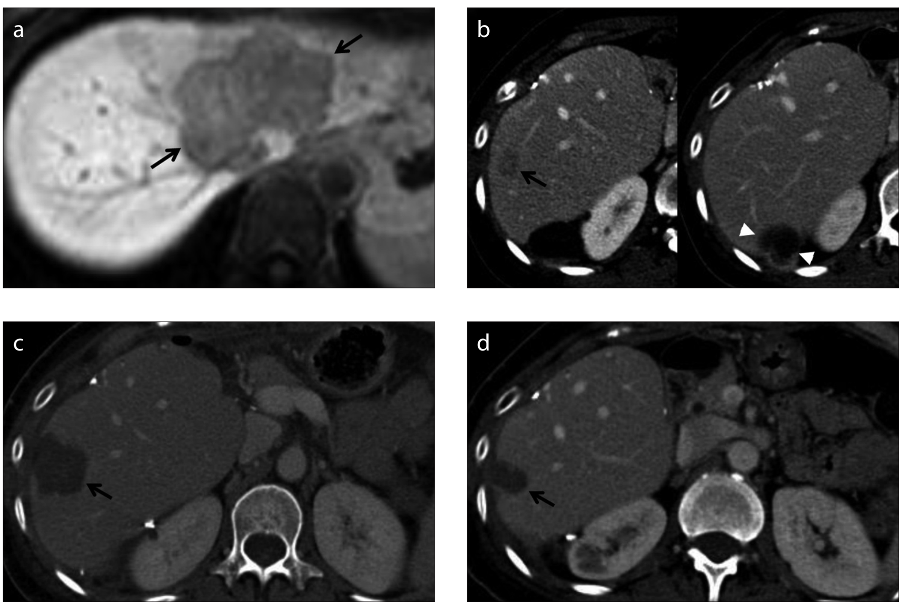

Figure 2. a–d. A 40-year-old woman presented with recurrent ICC. Gadoxetic acid-enhanced axial T1-weighted image **(a)** during hepatic biliary phase shows a 7 cm, lobulated mass *(arrows)* with hypointense rim in left hepatic lobe, which was histologically confirmed cholangiocarcinoma. The patient underwent hemihepatectomy of the left hepatic lobe. After 17 months, contrast-enhanced axial CT image **(b)** in portal phase shows three recurrent tumors in the hepatic segment VI *(arrow)*, segment VII *(arrowheads)*, and segment V (not shown). CT image **(c)** obtained 1 month after second operation shows complete ablation *(arrow)* and surgical resection. CT image **(d)** 1 year after IORFA shows reduced RFA zone *(arrow)* without tumor recurrence. Progression-free survival and overall survival periods of the patient were 10 months and 18 months, respectively. The patient had no intrahepatic recurrence, but died due to distant metastasis in the lungs and bones.

ter IORFA. Out of the six living patients, one (patient 7) was considered a long-term survivor (>60 months).

Discussion

Treating unresectable cholangiocarcinoma is challenging for oncologists and surgeons due to the poor prognosis (3, 19). Moreover, the postoperative ICC recurrence rate remains as high as 86% after curative resection (20–22). Unfortunately, only a few patients with ICC are surgical candidates due to poor remnant liver function and multifocal recurrence (20, 23). In the present study, we performed IORFA and surgical resection for the surgically unresectable ICC.

Surgical resection of ICC is considered the optimal treatment, with a 5-year survival rate ranging from 14% to 31% (24–26). Although most patients with unresectable ICC receive palliative therapies, the prognosis for patients who do not undergo curative resection is not significantly improved by such therapies, with the median survival time being between 6 and 12 months (5, 27). In this study, the patients who received IOR-

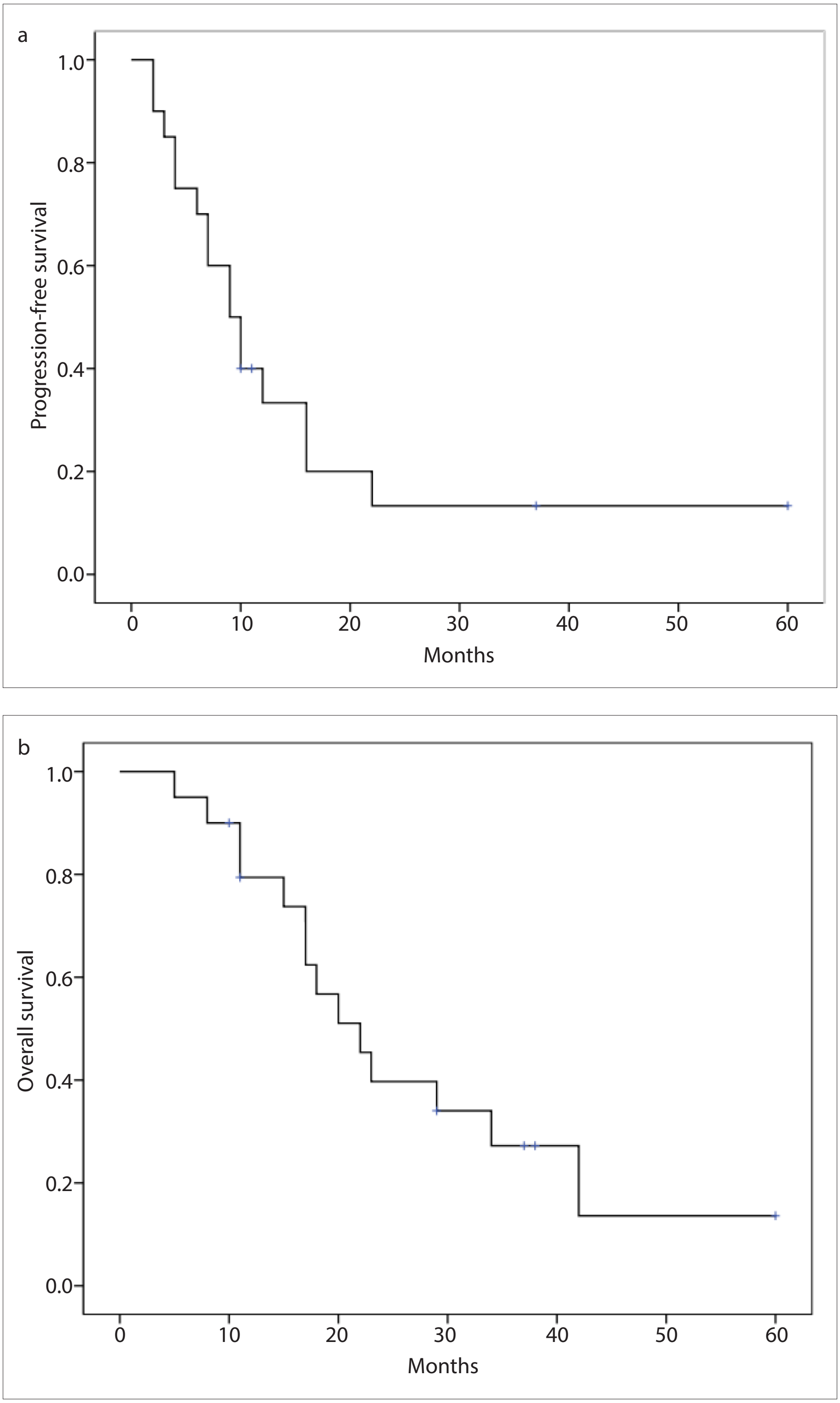

Figure 3. a, b. Graphs show progression-free survival **(a)** and overall survival **(b)** after IORFA of all 20 patients.

FA and hepatic resection likely had a higher risk of a poor prognosis. None of the patients were candidates for surgical resection without IORFA, due to the presence of multiple lesions that would have caused hepatic insufficiency after surgical resection and unfavorable location of the tumors for surgical resection or percutaneous RFA. Nonetheless, the 5-year survival rate after IORFA for our patients was 14%, which is comparable to that of surgical resection. Although, several reports stated that the combination of hepatic resection and IORFA improves the likelihood of survival for patients with various hepatic tumors and metastases (13, 24), to our knowledge, this study was the first to evaluate the long-term survival of patients with unresectable ICC. These preliminary results demonstrated that IORFA might increase the long-term survival, even in patients with advanced-stage ICC.

In previous reports, the prognosis of patients with unresectable recurrent ICC is poor with median overall survival time being about 7 months (23, 28). This study's analysis showed that the survival outcome of primary ICC was more favorable than that of recurrent ICC, with median overall survival of 34.0±5.87 months and 17.0±4.11 months, respectively. Although a few reports have stated that aggressive surgical treatment significantly improves the prognosis, repeat hepatectomy was feasible in only 13%–18% of patients (23, 29). However, this study's results show that for patients with unresectable recurrent ICC, using IORFA permitted them to undergo surgical resection, potentially prolonging survival.

Here, the technical success and effectiveness rates were both 100%. Previous studies reported that the technical effectiveness of percutaneous RFA for ICC ranged from 60% to 97% (10, 11, 30, 31). This study has several explanations for the high technical effectiveness. First, the sizes of the ablated ICCs may be important. Several studies reported that RFA was technically ineffective for large ICCs (>5 cm) (10, 31). In this study, the mean size of the ablated tumors was 1.3 cm (range, 0.6–2.7 cm). Moreover, the indication of <3 cm might have improved the technical effectiveness. Second, the intraoperative US guidance during IORFA may have played a role. Intraoperative US allows for improved visualization of the tumor compared to that of percutaneous RFA because of direct contact with the targeted organ (32). Moreover, using contrast-enhanced US with Sonazoid (GE Healthcare) aids in differentiating tumors that are not clearly detected on conventional US. It also provides better contrast and spatial resolution, which improves the sensitivity and specificity (33). Third, during IORFA, adequate mobilization of the liver creates a separate space between the tumor and surrounding structures to avoid injuries to the major vessels and surrounding organs (34), which increases the technical success of IORFA.

In the current study, local tumor progression occurred in two patients (10%) and in

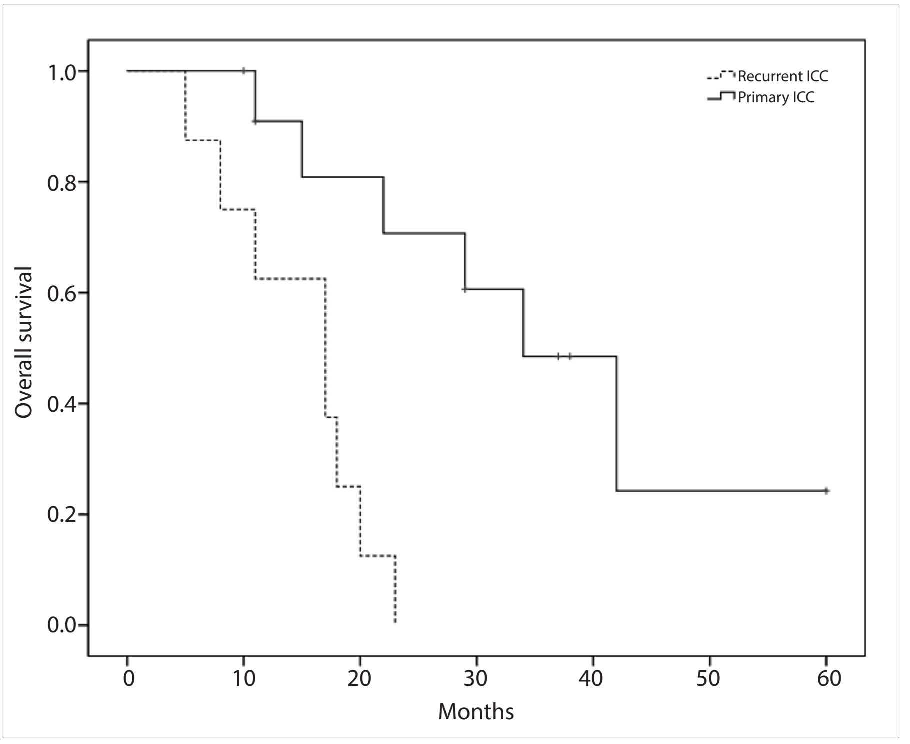

Figure 4. Graph shows overall survival curves of primary and recurrent ICC, respectively.

two individual tumors (8.3%). New tumor recurrence occurred in 16 patients (80%), including the patients with local tumor progression. A previous study reported that tumor size and number were significantly associated with local tumor progression when RFA was used to treat hepatic malignancies (9). Additionally, recurrence rates at the RFA site are reportedly <10% after RFA, with most treatment failures occurring in larger tumors (>3–4 cm in diameter) (35). As mentioned above, the mean tumor size in this study was 1.3 cm, and the mean number of tumors targeted for IORFA was 1.2. Since only two patients exhibited local tumor progression, the relationship between tumor size or number and local tumor progression could not be evaluated. However, considering the small size of the ablated tumors and the low local progression rate, this study's findings support that tumor size is the dominant factor influencing local tumor progression for ICCs after IORFA. Regarding new tumor recurrence, the most common site of recurrence was the liver. Similarly, Casavilla et al. (36) reported that the remnant liver was the most common site of recurrence, followed by the abdominal lymph node, lungs, bones, and other uncommon sites including the peritoneum, kidney, and adrenal gland. Recurrence following curative resection of ICC is common, with rates ranging from 52% to 86% (20–22). This study's data on disease progression with particularly acceptable local tumor progression were comparable to those from previous reports.

Only one major complication was found (biliary stenosis and hepatic abscess) after IORFA for 24 ICCs (4%). The incidence of hepatic abscess-associated RFA was similar to that (2%–6%) of previous studies (10, 37, 38). RFA can induce thermal injury to the bile duct and cause an inadvertent connection between the biliary tree and the ablation zone. The ablation zone is prone to contamination with enteric bacteria through the bilioenteric anastomosis, which produces hepatic abscess (39).

The major limitations of this study were its retrospective design and the lack of a control group (e.g., patients who underwent only surgical resection). Furthermore, the small number of patients in this single-center study limits its generalizability. Although ICC is a rare primary hepatic cancer and most patients are not qualified to undergo resection, randomized controlled trials on patients with unresectable ICC may confirm that IORFA can broaden the surgical indications. Despite these limitations, the results support that IORFA with surgical resection is an effective alternative treatment for unresectable ICC. In particular, considering that surgical resection is the only curative treatment and offers the best chance for long-term survival, the addition of IORFA may play an important role in ICC treatment by expanding the indication for surgical removal.

In conclusion, for surgically unresectable ICC, combining IORFA with surgical resection can be a feasible therapeutic modality, as it yields acceptable overall survival and local tumor control, with minimal complications.

Financial disclosure

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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