

Guidewire-catheter induced hydrodissection to assist radiofrequency ablation for subcapsular hepatocellular carcinoma with iodized oil retention in patients with failed artificial ascites due to perihepatic adhesion

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PURPOSE

We aimed to evaluate the usefulness of guidewire-catheter induced hydrodissection (GIH) to assist radiofrequency ablation (RFA) for subcapsular hepatocellular carcinoma (HCC) with iodized oil retention in patients with failed artificial ascites due to perihepatic adhesion.

METHODS

This retrospective study included 17 patients with small subcapsular HCC ineligible for ultrasonography-guided RFA who received RFA under guidance of fluoroscopy and cone-beam computed tomography immediately after iodized oil transarterial chemoembolization (TACE) between April 2011 and January 2016. In the study patients, creation of artificial ascites to protect the perihepatic structures failed due to perihepatic adhesion and GIH was attempted to separate the perihepatic structures from the ablation zone. The technical success rate of GIH, technique efficacy of RFA with GIH, local tumor progression (LTP), peritoneal seeding, and complications were evaluated.

RESULTS

The technical success rate of GIH was 88.24% (15 of 17 patients). Technique efficacy was achieved in all 15 patients receiving RFA with GIH. During an average follow-up period of 48.1 months, LTP developed in three patients. Cumulative LTP rates at 1, 2, 3, and 5 years were 13.3%, 20.6%, 20.6%, and 20.6%, respectively. No patient had peritoneal seeding. Two of the 15 patients receiving RFA with GIH had a CIRSE grade 3 liver abscess, but none had complications associated with thermal injury to the diaphragm or abdominal wall near the ablation zone.

CONCLUSION

GIH can be a useful method to assist RFA for subcapsular HCC with iodized oil retention in patients with failed artificial ascites due to perihepatic adhesion.

Radiofrequency ablation (RFA) is widely accepted as a curative treatment for patients with small (≤ 3 cm) hepatocellular carcinoma (HCC) not suitable for surgery (1, 2). However, when the tumor is located close to the liver surface, RFA carries a risk of unintended collateral thermal injury to the perihepatic structures (i.e., diaphragm and abdominal wall). To overcome this problem, adjunctive techniques such as introduction of artificial ascites or pleural effusion have been applied (3–8). Nonetheless, patients with perihepatic peritoneal adhesion may still be at risk of collateral thermal injury as adhesion prevents separation of the perihepatic structures by artificial ascites from the ablation zone (6, 9, 10). Some investigators have used an alternative technique making localized hydrodissection by using an 18–22 G needle at the contact point between the index tumor and perihepatic structure (9, 11). However, this also seems to be not applicable when the lung or bowel interposes on the access route.

Prior iodized oil transarterial chemoembolization (TACE) enhances the feasibility of subsequent RFA for small tumors with poor conspicuity (12, 13). This is because intratumoral retention of radio-opaque iodized oil provides radiographic contrast to the index tumor. As the index tumor with iodized oil retention is clearly seen on fluoroscopy and the perihepatic peritoneal space is easily accessed by traditional methods of making artificial ascites (6, 9, 14), an angiographic catheter and guidewire system can reach the region near the tumor through the perihepatic space under fluoroscopic guidance. Therefore, in patients with

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perihaptic adhesion, if forceful advancement of the catheter and guidewire system could dissect the adhesion, introduction of fluid via the catheter tip at the region near the tumor may protect the perihaptic structures from thermal injury during RFA for subcapsular HCC.

The aim of this study was to evaluate the usefulness of guidewire-catheter induced hydrodissection (GIH) to assist RFA for subcapsular HCC with iodized oil retention in patients with failed artificial ascites due to perihaptic adhesion.

Methods

Our institutional review board approved this retrospective study, and the requirement for patient informed consent was waived (SMC 2021-01-079). In our institution, treatment for naïve HCC is generally determined according to the Korean Liver Cancer Association-National Cancer Center guidelines (15). For recurrent HCC, appropriate treatment option was selected according to the recurrence pattern and underlying liver function, with discussion on multidisciplinary tumor board for complex cases. In our routine practice, patients with small HCC ineligible for ultrasonography (US)-guided RFA were referred for combined TACE and RFA treatment.

Study population

Based on our interventional radiology database, 225 patients with small (≤ 3 cm) HCC ineligible for US-guided RFA received iodized oil TACE and immediately subsequent RFA treatments between April 2011 and January 2016. Artificial ascites or pleural effusion to assist RFA was made when a tumor was in the subcapsular location with a minimum distance of <1 cm from the vulnerable perihaptic structures. GIH to separate the perihaptic structures from the ablation zone was attempted in patients with failed artificial ascites due to perihaptic

adhesion. A review of the procedural reports found 18 patients in whom creation of artificial ascites failed due to suspected perihaptic adhesion. One of them was excluded because he received RFA with creation of artificial pleural effusion instead of attempting GIH. This study included the

other 17 patients with failed artificial ascites due to perihaptic adhesion, in whom GIH was attempted to assist RFA (Fig. 1).

Details of patient demographics and tumor characteristics are shown in Tables 1 and 2. All patients had a history of initial HCC treatment with liver resection ($n=12$) or RFA

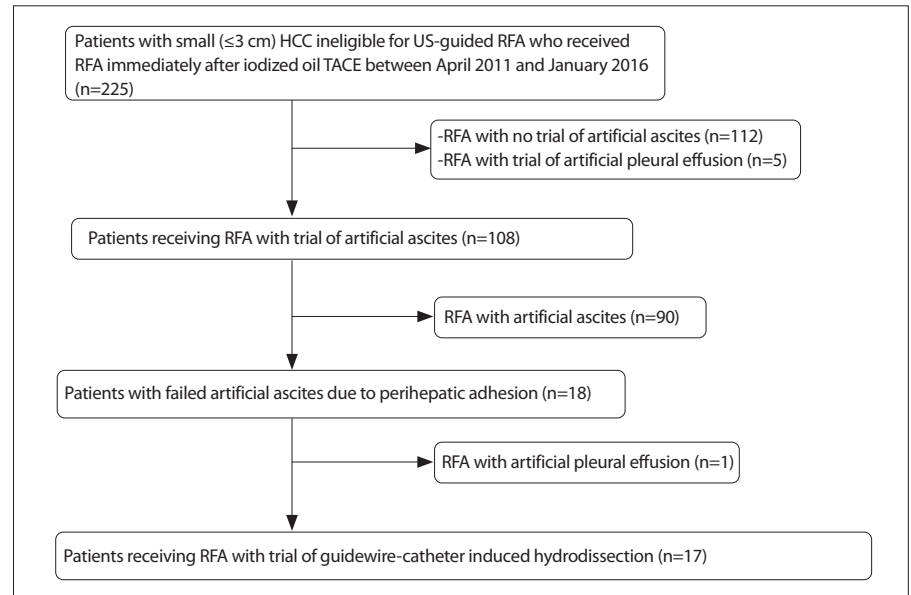


Figure 1. A flow diagram showing study group enrollment. HCC, hepatocellular carcinoma; US, ultrasonography; RFA, radiofrequency ablation; TACE, transarterial chemoembolization.

Table 1. Baseline patient and tumor characteristics ($n=17$)

Age (years), mean \pm SD	63.6 \pm 9.62
Male/female, n (%)	16 (94.12) / 1 (5.88)
Etiology, n (%)	
Hepatitis B virus	16 (94.12)
Nonviral	1 (5.88)
Child-Pugh score, n (%)	
A5 / A6	16 (94.12) / 1 (5.88)
Serum α -fetoprotein (ng/mL), median (min-max)	3.1 (1.3 – 175.4)
History of previous treatment, n (%)	
Yes	17 (100)
No	0 (0)
Tumor size (cm), mean \pm SD	1.4 \pm 0.52
Tumor location, n (%)	
Segment IV	2 (11.8)
Segment VI	1 (5.9)
Segment VII	4 (23.5)
Segment VIII	10 (58.8)
Perihaptic structure around the tumor, n (%)	
Diaphragm	15 (88.24)
Abdominal wall	2 (11.76)
SD, standard deviation.	

Main points

- Guidewire-catheter induced hydrodissection is a safe and feasible method.
- Radiofrequency ablation (RFA) with GIH for subcapsular hepatocellular carcinoma (HCC) appears to be effective and safe.
- GIH can be a useful method to assist RFA for subcapsular HCC with iodized oil retention in patients with failed artificial ascites due to perihaptic adhesion.

Table 2. Details of patients with trial of GIH to assist RFA for subcapsular HCC with iodized oil retention

Case no	Age/sex	No of previous TACEs	No of previous RFAs	Type of previous surgery	Tumor size (cm)	Tumor location (segment)	Perihepatic structure	Distance between tumor and perihepatic structure (mm)
1	68/M	2	1	-	1.5	IV	Diaphragm	5
2	67/M	1	3	Left HHT	1.0	VIII	Abdominal wall	5
3	60/M	3	2	-	2.4	VII	Diaphragm	0
4	69/M	1	1	S6 SMT, S7 WR	1.2	VIII	Diaphragm	0
5	66/M	-	1	Cholecystectomy	2.2	VIII	Diaphragm	0
6	53/M	-	-	Left HHT	1.2	VII	Diaphragm	0
7	65/M	1	1	Left HHT, S8 WR	0.8	VII	Diaphragm	3
8	67/M	-	-	S5 SMT	0.9	VIII	Diaphragm	0
9	78/M	-	-	Left lateral SCT	1.5	VIII	Diaphragm	0
10	55/F	-	-	S8 WR	1.2	VIII	Diaphragm	0
11	58/M	-	-	S6 SMT	1.5	VIII	Diaphragm	0
12	51/M	2	1	-	2.0	IV	Diaphragm	0
13	66/M	-	2	Left lateral SCT	0.9	VIII	Diaphragm	0
14	63/M	7	1	S7 WR + cholecystectomy	1.9	VI	Abdominal wall	2
15	43/M	-	-	S8 WR	0.8	VIII	Diaphragm	0
16	81/M	-	2	-	2.0	VII	Diaphragm	0
17	72/M	2	3	S5 SMT	1.0	VIII	Diaphragm	0

GIH, guidewire-catheter induced hydrodissection; RFA, radiofrequency ablation; HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization; M, male; F, female; HHT, hemihepatectomy; SMT, segmentectomy; WR, wedge resection; SCT, sectionectomy.

(n=5). The index tumor in subcapsular location abutted the diaphragm (n=13) or had a distance of 5 mm or less from the diaphragm (n=2) or abdominal wall (n=2). All HCCs were diagnosed based on the Asian Pacific Association of the Study of the Liver guidelines (16): a typical vascular pattern (arterial enhancement with portal venous/delayed washout) on dynamic computed tomography (CT) or magnetic resonance imaging (MRI).

Guidewire-catheter induced hydrodissection

All procedures were performed by one of three interventional radiologists with at least 5 years of experience. Creation of artificial ascites or GIH was attempted just before RFA procedure. The selected needle puncture site was the right intercostal space for a tumor in the right lobe and segment IV of the liver and the epigastric area for a tumor in the left lateral segment. Similar to techniques described in previous studies (6, 9), creation of artificial ascites was first attempted as follows. With patient's inhalation to displace the liver downward, an 18 G sheathed needle was advanced into the subcapsular portion of the liver parenchyma under real-time US guidance.

After removing the inner stylet out of the sheathed needle, the tip of the sheath usually remained in the perihepatic peritoneal space with full expiration because it retracted from the displaced hepatic parenchyma moving upward. At this moment, a guidewire of 45 cm length was inserted through the sheath under fluoroscopic guidance and then a 5 F angiosheath (Radiofocus introducer, Terumo) was placed over the guidewire. After placing the angiosheath in the peritoneal space, 5% dextrose in water (D5W) solution was infused. If perihepatic fat was abundant in the patient, the needle was introduced into the perihepatic fat without making a direct liver puncture. Failure of artificial ascites was considered when the guidewire accessed into the perihepatic peritoneal space was not advanced freely on fluoroscopy or when localization of the fluid around the infusion site was observed on US. As a technical error (i.e., poor needle placement) could be a cause of the failure, final decision on the failure was made after repeating the attempt to create artificial ascites three times. If a patient had a history of prior treatment (surgery, TACE, or RFA), perihepatic adhesion was considered as the cause of the failed artificial ascites.

In patients with failed artificial ascites due to perihepatic adhesion, creation of GIH was attempted as follows (Fig. 2). A 0.035-inch regular or stiff shaft hydrophilic guidewire of 150 cm length (Glidewire, Terumo) was introduced via the angiosheath or the needle sheath used for creation of artificial ascites. Then, a 5 F angled tip catheter of 40 cm length (Kumpe, Cook) was advanced into the perihepatic space over the guidewire. On both anteroposterior and lateral projections of fluoroscopy, the location relationship between the guidewire-catheter system and the tumor with iodized oil retention was checked. Under real-time fluoroscopic guidance, the guidewire-catheter system was manipulated toward the tumor, the guidewire with a support of the catheter was forcefully pushed to make dissection of the adhesion, and then the catheter was advanced over the guidewire. In order to make appropriate dissection toward the region near the tumor with iodized oil retention, the location and direction of the guidewire-catheter system were frequently checked and adjusted on both anteroposterior and lateral projections of fluoroscopy. This dissection process was repeated until the catheter tip reached the region near the

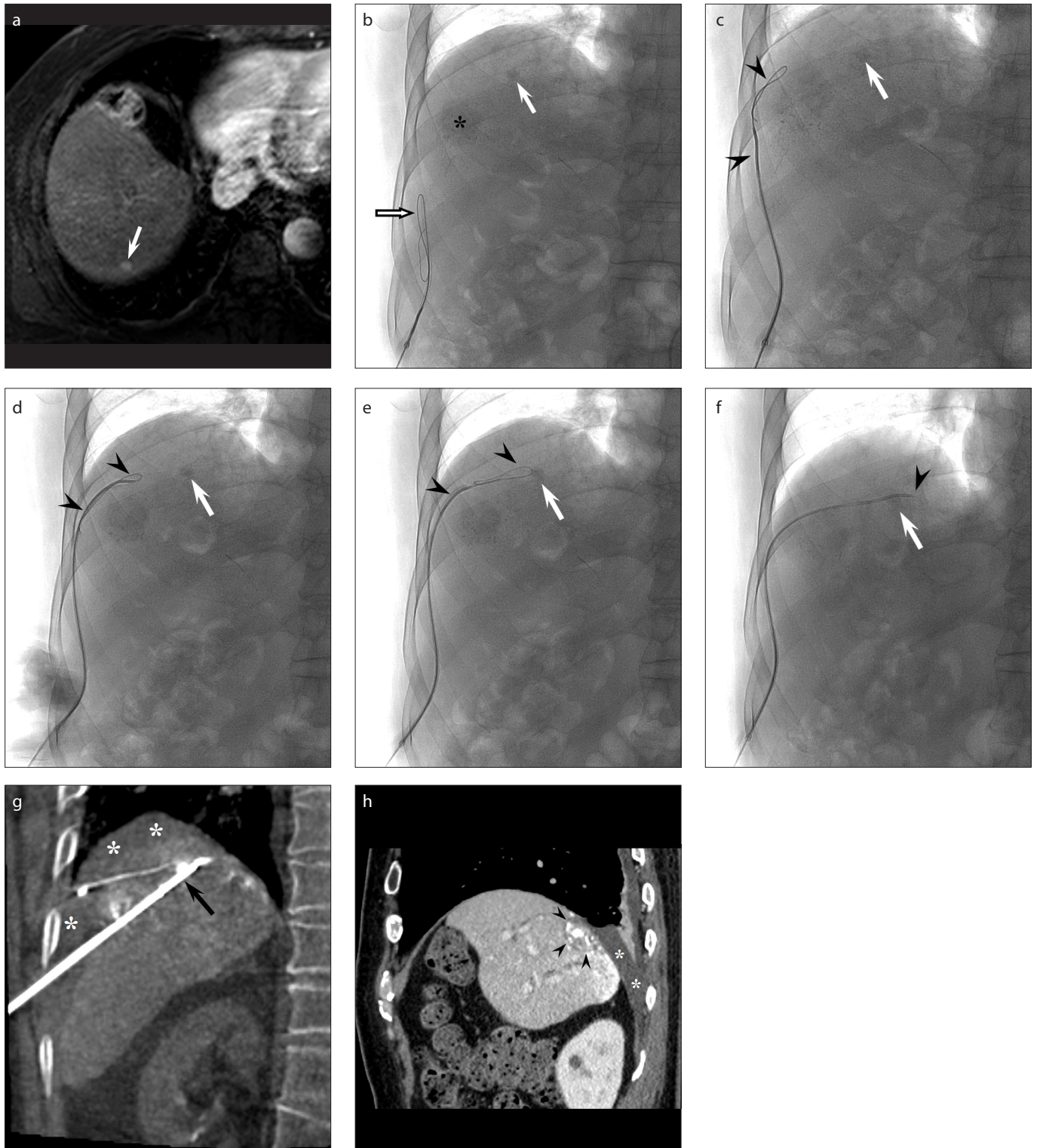


Figure 2. a–h. Creation of GIH to assist RFA for subcapsular HCC in a 65-year-old man with failed artificial ascites due to perihepatic adhesion (case No. 7). Arterial phase axial magnetic resonance image (a) demonstrates a 0.8 cm diameter HCC in hepatic segment VII (arrow), at a 3 mm distance from the diaphragm. Spot image (b) obtained when attempting creation of artificial ascites immediately after iodized oil TACE for the tumor (arrow) shows looping of the guidewire (open arrow) accessed into the perihepatic peritoneal space due to perihepatic adhesion. Also, a previously treated lipiodolized tumor (asterisk) is noted. To create GIH, a 5 F angled tip catheter was advanced into the perihepatic space over the guidewire. Serial spot images of anteroposterior projection (c–f) show sequential advancement of the guidewire–catheter system (arrowheads) with dissection of the perihepatic adhesion to the region near the index tumor with iodized oil retention (arrow). To make appropriate dissection toward the region near the index tumor, the location and direction of the guidewire–catheter system were frequently checked and adjusted on both anteroposterior and lateral projections of fluoroscopy. After reaching the region near the index tumor, D5W was instilled via the catheter tip to make hydrodissection of the perihepatic space near the index tumor. Oblique coronal cone-beam CT (CBCT) image (g) obtained to confirm the final position of RFA electrode tip (arrow) before ablation clearly shows the fluid (asterisks) introduced via the catheter tip. Portal phase sagittal CT image obtained 1 day after RFA with GIH (h) demonstrates complete ablation of the index tumor with iodized oil retention (arrowheads) and no thermal injury to the adjacent diaphragm. Right pleural effusion (asterisks) may represent transdiaphragmatic shifting of the fluid introduced for GIH.

Table 3. Therapeutic results and complications of RFA with GIH for subcapsular HCC with iodized oil retention in patients with failed artificial ascites due to perihepatic adhesion

Case No	Tumor size (cm)	Location (segment)	Technical success of GIH	Ablation time (min)	Technical success of RFA	Technique efficacy of RFA	Complications	LTP	Peritoneal seeding	Disease progression (progression type)	Follow-up duration (months)
1	1.5	IV	Yes	10	Yes	Yes	Gr 3 liver abscess	No	No	Yes (IRR)	100
2	1.0	VIII	Yes	12	Yes	Yes	No	No	No	No	95
3	2.4	VII	Yes	18	Yes	Yes	Gr 3 liver abscess	No	No	Yes (IRR, EM)	22
4 ^a	1.2	VIII	No	7	Yes	Yes	Gr 3 hemothorax	No	No	No	28
5	2.2	VIII	Yes	16	Yes	Yes	No	No	No	No	53
6	1.2	VII	Yes	8	Yes	Yes	No	No	No	No	52
7	0.8	VII	Yes	8	Yes	Yes	No	No	No	No	47
8 ^b	0.9	VIII	No	7	Yes	Yes	No	No	No	No	52
9	1.5	VIII	Yes	6	Yes	Yes	No	No	No	Yes (IRR)	52
10	1.2	VIII	Yes	10	Yes	Yes	No	Yes	No	Yes (LTP)	21
11	1.5	VIII	Yes	12	Yes	Yes	No	No	No	Yes (IRR)	46
12	2.0	IV	Yes	14	Yes	Yes	No	No	No	Yes (IRR)	46
13	0.9	VIII	Yes	12	Yes	Yes	No	Yes	No	Yes (LTP)	45
14	1.9	VI	Yes	8	Yes	Yes	No	Yes	No	Yes (LTP, IRR, EM)	10
15	0.8	VIII	Yes	12	Yes	Yes	No	No	No	No	43
16	2.0	VII	Yes	17	Yes	Yes	No	No	No	No	40
17	1.0	VIII	Yes	7	Yes	Yes	No	No	No	Yes (IRR, EM)	49

^aRFA without any adjunctive technique to protect the perihepatic structure; ^bRFA with artificial pleural effusion.

RFA, radiofrequency ablation; GIH, guidewire-catheter induced hydrodissection; HCC, hepatocellular carcinoma; LTP, local tumor progression; IRR, intrahepatic remote recurrence; EM, extrahepatic metastasis.

tumor. When the catheter tip reached the region near the tumor, 500 or 1000 mL of D5W in a bag was completely instilled via the catheter to make hydrodissection of the perihepatic space near the tumor. Technical success of GIH was defined when separation of the perihepatic space near the tumor was observed on cone-beam CT (CBCT) obtained for guidance of RFA electrode.

Treatment procedures and follow-up

Both TACE and immediately subsequent RFA were performed under conscious sedation with 50 mg remifentanyl (Ultiva, GlaxoSmithKline). After performing TACE by infusing an emulsion of iodized oil (Lipiodol, Laboratoire Andre Guerbet) and doxorubicin hydrochloride (Adriamycin, Dong-A Pharm) and sequentially embolizing the tumor feeding artery with gelatin sponge pledgets (Cutanplast, Mascia Brunelli) as in previous studies (13, 17), CBCT was obtained to check anatomical information of the index tumor with iodized oil retention and to determine best electrode access route. For RFA procedure, a 22 G needle (Chiba needle, Cook) as a reference needle

was first introduced near the tumor under fluoroscopic and CBCT guidance. When the course and position of the reference needle was considered appropriate, a 17 G cooled-tip electrode (Cool-tip, Valley Lab) or a 17 G internally cooled electrode with a manually adjustable active tip (VIVA, Starmed) was advanced in parallel with the reference needle. After confirming the electrode position by CBCT acquisition, RFA was performed with a 200 W generator. Active tip length was selected or adjusted according to the tumor size. Average ablation time was 10.8 ± 3.75 min. Overlapping ablation technique was applied in 5 patients to achieve sufficient ablation margin. After tumor ablation, RFA electrode tract was cauterized while the electrode was retracted to prevent bleeding and tumor seeding. The end point was complete ablation of the visible tumor with an ablative margin of at least 5 mm. The fluid infused to make hydrodissection was not drained or aspirated after the ablation procedure.

Contrast-enhanced CT scan was obtained on the following day to evaluate immediate therapeutic response and post-procedural

complications. Patients were followed by contrast-enhanced dynamic CT or MRI at one month after the procedure and thereafter at every 3 months.

Assessment

The technical success rate of GIH, technique efficacy of RFA with GIH, local tumor progression (LTP), peritoneal seeding, disease progression, and complications were evaluated. Technique efficacy of RFA was defined as absence of residual tumor enhancement on 1-month follow-up CT (18). LTP was defined as any tumor recurrence abutting the ablation zone that was previously considered to be completely ablated (18). LTP was calculated with Kaplan-Meier method using statistical software (SPSS for Windows release 25.0, SPSS Inc.). Peritoneal seeding was defined as the appearance of enhancing nodular or thick irregular-shaped lesions with interval increments, attached to the peritoneum or in the peritoneal cavity. Disease progression was considered when LTP, intrahepatic remote recurrence, peritoneal seeding, or extrahepatic metastasis was observed.

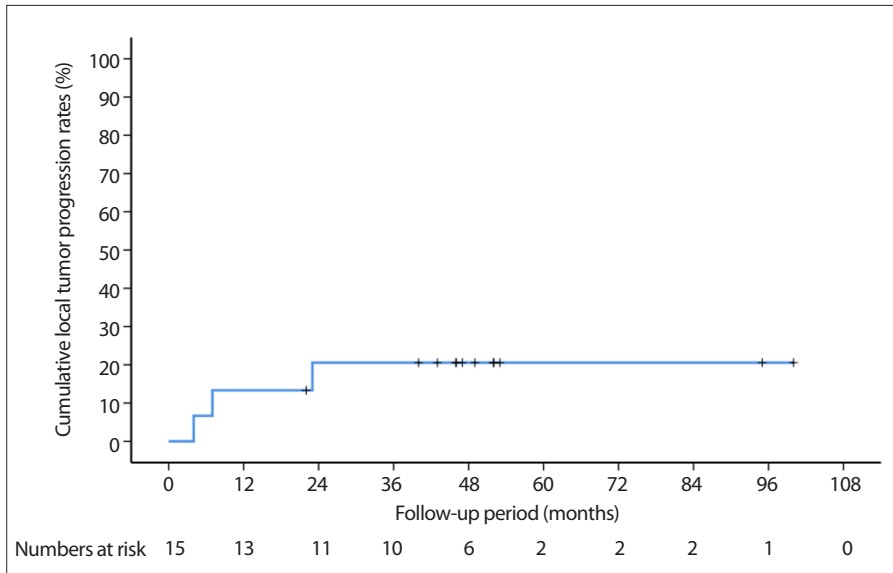


Figure 3. Kaplan-Meier curve of local tumor progression.

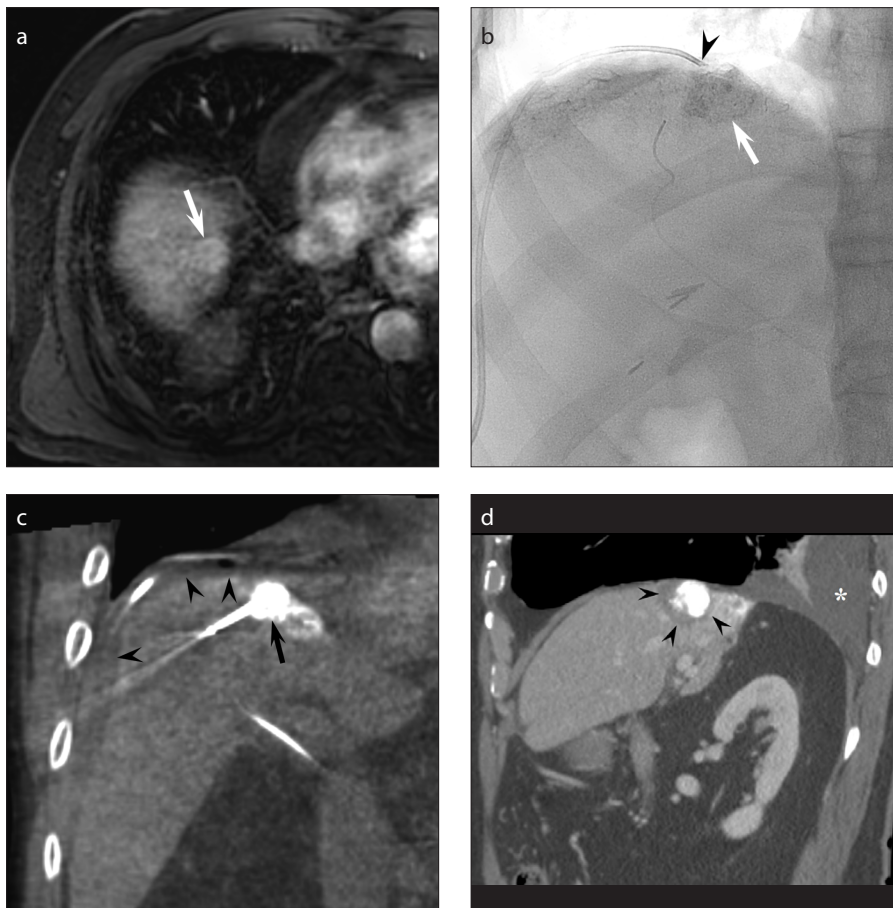


Figure 4. a–d. RFA with GIH for subcapsular HCC in a 66-year-old man with failed artificial ascites due to perihepatic adhesion (case No. 5). Arterial phase axial magnetic resonance image (a) demonstrates a 2.2 cm diameter HCC in hepatic segment VIII (arrow), abutting the diaphragm. Spot image obtained during creation of GIH after TACE (b) shows the catheter tip (arrowhead) in the perihepatic space near the tumor with iodized oil retention (arrow). Coronal CBCT image (c) obtained before ablation confirms the final position of RFA electrode tip in the tumor (arrow). The fluid introduced for GIH (arrowheads) is also seen. Portal phase sagittal CT image obtained 1 day after RFA with GIH (d) demonstrates an ablation zone surrounding the tumor (arrowheads) and no thermal injury to the adjacent diaphragm. Right pleural effusion (asterisk) may represent transdiaphragmatic shifting of the fluid introduced for GIH.

Complications were assessed following the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) classification (19).

Results

GIH succeeded in 15 of 17 patients (88.24%) with failed artificial ascites due to perihepatic adhesion. In the other two patients, the guidewire-catheter system failed to reach the region near the tumor. One of them received RFA without any adjunctive technique (i.e., artificial pleural effusion) to protect the perihepatic structure and the other received RFA with creation of artificial pleural effusion. Therapeutic results and complications of RFA with GIH for subcapsular HCC with iodized oil retention in patients with failed artificial ascites due to perihepatic adhesion are presented in Table 3. Technique efficacy was achieved in all 15 patients who received RFA with GIH. During an average follow-up period of 48.1 ± 23.8 months (range, 10–100 months), three of the 15 patients (20%) had LTP at 4, 7, and 23 months, respectively. Cumulative LTP rates at 1, 2, 3, and 5 years were 13.3%, 20.6%, 20.6%, and 20.6%, respectively (Fig. 3). No patients had peritoneal seeding. Disease progression was observed in 9 of 15 patients (60%). As for complications, two patients receiving RFA with GIH had a CIRSE grade 3 liver abscess at the ablation zone, managed with antibiotics treatment. No complications associated with thermal injury to the diaphragm or abdominal wall near the ablation zone developed in the 15 patients receiving RFA with GIH (Fig. 4). One patient with failed GIH who received RFA without any adjunctive technique to protect the diaphragm had CIRSE grade 3 hemothorax probably related to adjacent diaphragm and lung injury, which was managed with percutaneous drainage.

Discussion

Thermoprotective effect of artificial ascites for subcapsular HCC, except for a tumor in the bare area, is well-established (3, 6, 8). A major obstacle in creating artificial ascites is peritoneal adhesion due to prior treatments (surgery, TACE, or thermal ablation) (6, 9). Creation of artificial pleural effusion can be an alternative method for tumors in subphrenic location (4). However, creating GIH may have an advantage by providing more complete insulating effect from thermal injury than artificial pleural effusion.

The technical success rate of GIH in this study was 88% (15/17), which is similar to the success rates (84%–88%) of artificial ascites in previous studies (6, 9). Two cases of GIH failure developed because the guidewire-catheter system did not reach the region near the tumor. Given that the two patients had perihepatic adhesion resulting from previous hepatic resection, the failure may be attributed to the hardness or extent of the adhesion. Thus, instead of a 5 F catheter, use of a device with more rigid shaft (i.e., a dilator) or with more supportive power (i.e., a guiding sheath) might enhance the feasibility of GIH.

There may be two major concerns about creating GIH. One concern is that GIH might increase the risk of peritoneal seeding after RFA. To reduce peritoneal seeding after RFA, direct puncture of a subcapsular tumor without interposing normal liver parenchyma should be avoided (20, 21). This is because, with the direct puncture, some tumor cells can spill into the peritoneal space. In this study, although GIH was created via the peritoneal space, we could not assure that only the peritoneal space was involved with the dissection. In theory, it might be possible that forceful advancement of a guidewire-catheter system in hard peritoneal adhesion could make separation of the hepatic subcapsular space as well as the peritoneal space. Separation of the hepatic subcapsular space might result in direct contact with the subcapsular tumor and raise the risk of peritoneal seeding. Despite these presumptions, no peritoneal seeding was observed in any of the 15 patients receiving RFA with GIH in this study. The other concern is that forceful dissection of the peritoneal space by the guidewire-catheter system might cause perihepatic bleeding. However, this study showed no peritoneal bleeding at CT scan one day after treatment. A possible explanation for the result may be the tamponade effect of the perihepatic adhesion. In addition, no complications associated with thermal injury to the diaphragm or abdominal wall near the ablation zone developed in all the 15 patients receiving RFA with GIH. Altogether, results in this study suggest that creating GIH is a safe method and makes RFA safe for subcapsular HCC in patients with perihepatic adhesion.

As for the efficacy, RFA with GIH is believed to be effective for subcapsular HCC in patients with perihepatic adhesion. RFA

with GIH for subcapsular HCC with iodized oil retention achieved 100% technique efficacy. The 5-year cumulative LTP rate in this study was 20.6%, which seems to be slightly higher than that of combined TACE and RFA for small HCC in previous studies (9.6%–17%) (22, 23). However, due to the small case number and the selected group of subcapsular location in this study, validation on the difference is required.

GIH can be attempted only for a tumor evident on fluoroscopy, therefore, iodized oil TACE seems to be a prerequisite for RFA with GIH. In view of creating GIH, the time interval between iodized oil TACE and RFA may be of no importance because GIH can be applied as long as the tumor with iodized oil retention is seen on fluoroscopy. On the other hand, prior TACE and subsequent RFA in the combination therapy have been performed in a single session without time delay as in this study or separately with a time interval of up to 4 weeks between them (13, 24–26). An animal study investigating the ablation zone according to the time interval between transarterial embolization and RFA revealed that a single-session combination could create a larger ablation zone, but induce more severe acute hepatic damage than a dual-session with a 5-day interval (27). However, due to lack of evidence, the best time interval between TACE and RFA in the combination therapy has not yet been established.

This study has several limitations. First, there is an inherent limitation of the retrospective observational study. Second, the number of study group is small. Therefore, the results of the current study should be validated in a large case series. Third, the decision on attempting GIH was determined at the discretion of an operator performing the procedure. Therefore, there could be a selection bias. Fourth, this study did not evaluate the true thermal injury to the diaphragm or abdominal wall near the ablation zone. Instead, complications associated with thermal damage to the perihepatic structures were evaluated based on clinical and CT findings. This could be a weakness of this study. Fifth, the procedure time of GIH creation should have been evaluated for ideal study design. However, as it was not recorded, we could not provide the data. In our experience, it usually took 10–15 minutes for the catheter to reach the region near the tumor from the decision of creating GIH. Sixth, perihepatic adhesion was suspected with a history of previous

treatments. As it was not confirmed, there could be a selection bias.

In conclusion, GIH can be a useful method to assist RFA for subcapsular HCC with iodized oil retention in patients with failed artificial ascites due to perihepatic adhesion.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Bruix J, Sherman M, American Association for the Study of Liver D. Management of hepatocellular carcinoma: an update. *Hepatology* 2011; 53:1020–1022. [Crossref]
2. Omata M, Cheng AL, Kokudo N, et al. Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. *Hepatol Int* 2017; 11:317–370. [Crossref]
3. Garnon J, Cazzato RL, Caudrelier J, et al. Adjunctive thermoprotection during percutaneous thermal ablation procedures: review of current techniques. *Cardiovasc Intervent Radiol* 2019; 42:344–357. [Crossref]
4. Inoue T, Minami Y, Chung H, et al. Radiofrequency ablation for hepatocellular carcinoma: assistant techniques for difficult cases. *Oncology* 2010; 78 Suppl 1:94–101. [Crossref]
5. Knuttinen MG, Van Ha TG, Reilly C, Montag A, Straus C. Unintended thermal injuries from radiofrequency ablation: organ protection with an angioplasty balloon catheter in an animal model. *J Clin Imaging Sci* 2014; 4:1. [Crossref]
6. Rhim H, Lim HK. Radiofrequency ablation for hepatocellular carcinoma abutting the diaphragm: the value of artificial ascites. *Abdom Imaging* 2009; 34:371–380. [Crossref]
7. Uehara T, Hirooka M, Ishida K, et al. Percutaneous ultrasound-guided radiofrequency ablation of hepatocellular carcinoma with artificially induced pleural effusion and ascites. *J Gastroenterol* 2007; 42:306–311. [Crossref]
8. Wang CC, Kao JH. Artificial ascites is feasible and effective for difficult-to-ablate hepatocellular carcinoma. *Hepatol Int* 2015; 9:514–519. [Crossref]
9. Kang TW, Lee MW, Hye MJ, et al. Percutaneous radiofrequency ablation of hepatic tumours: factors affecting technical failure of artificial ascites formation using an angiosheath. *Clin Radiol* 2014; 69:1249–1258. [Crossref]
10. Song I, Rhim H, Lim HK, Kim YS, Choi D. Percutaneous radiofrequency ablation of hepatocellular carcinoma abutting the diaphragm and gastrointestinal tracts with the use of artificial ascites: safety and technical efficacy in 143 patients. *Eur Radiol* 2009; 19:2630–2640. [Crossref]
11. Kondo Y, Yoshida H, Shiina S, Tateishi R, Teratani T, Omata M. Artificial ascites technique for percutaneous radiofrequency ablation of liver cancer adjacent to the gastrointestinal tract. *Br J Surg* 2006; 93:1277–1282. [Crossref]
12. Hyun D, Cho SK, Shin SW, et al. Combined transarterial chemoembolization of the right inferior phrenic artery and radiofrequency ablation for small hepatocellular carcinoma near the diaphragm: its efficacy and safety. *Abdom Radiol (NY)* 2018; 43:2851–2858. [Crossref]

13. Hyun D, Cho SK, Shin SW, et al. Early stage hepatocellular carcinomas not feasible for ultrasound-guided radiofrequency ablation: comparison of transarterial chemoembolization alone and combined therapy with transarterial chemoembolization and radiofrequency ablation. *Cardiovasc Intervent Radiol* 2016; 39:417–425. [\[Crossref\]](#)
14. Kim J, Yoon CJ, Seong NJ, Jeong SH, Kim JW. Fluoroscopy-guided radiofrequency ablation for small hepatocellular carcinoma: a retrospective comparison with ultrasound-guided ablation. *Clin Radiol* 2015; 70:1009–1015. [\[Crossref\]](#)
15. Korean Liver Cancer Study G, National Cancer Center K. 2014 Korean Liver Cancer Study Group-National Cancer Center Korea practice guideline for the management of hepatocellular carcinoma. *Korean J Radiol* 2015; 16:465–522. [\[Crossref\]](#)
16. Omata M, Lesmana LA, Tateishi R, et al. Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma. *Hepatol Int* 2010; 4:439–474. [\[Crossref\]](#)
17. Song YG, Shin SW, Cho SK, et al. Transarterial chemoembolization as first-line therapy for hepatocellular carcinomas infeasible for ultrasound-guided radiofrequency ablation: a retrospective cohort study of 116 patients. *Acta Radiol* 2015; 56:70–77. [\[Crossref\]](#)
18. Ahmed M, Solbiati L, Brace CL, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria—a 10-year update. *J Vasc Interv Radiol* 2014; 25:1691–1705 e1694. [\[Crossref\]](#)
19. Filippidis DK, Binkert C, Pellerin O, Hoffmann RT, Krajina A, Pereira PL. CIRSE Quality Assurance Document and Standards for Classification of Complications: The Cirse Classification System. *Cardiovasc Intervent Radiol* 2017; 40:1141–1146. [\[Crossref\]](#)
20. Shirai K, Tamai H, Shingaki N, et al. Clinical features and risk factors of extrahepatic seeding after percutaneous radiofrequency ablation for hepatocellular carcinoma. *Hepatol Res* 2011; 41:738–745. [\[Crossref\]](#)
21. Filippousis P, Sotiropoulou E, Manataki A, Konstantinopoulos O, Thanos L. Radiofrequency ablation of subcapsular hepatocellular carcinoma: single center experience. *Eur J Radiol* 2011; 77:299–304. [\[Crossref\]](#)
22. Kim JW, Kim JH, Won HJ, et al. Hepatocellular carcinomas 2-3 cm in diameter: transarterial chemoembolization plus radiofrequency ablation vs. radiofrequency ablation alone. *Eur J Radiol* 2012; 81:e189–193. [\[Crossref\]](#)
23. Lee SY, Hyun D, Cho SK, Shin SW, Jung SH, Chi SA. Iodized oil transarterial chemoembolization and radiofrequency ablation for small periportal hepatocellular carcinoma: comparison with nonperiportal hepatocellular carcinoma. *Cardiovasc Intervent Radiol* 2018; 41:120–129. [\[Crossref\]](#)
24. Fujimori M, Takaki H, Nakatsuka A, et al. Survival with up to 10-year follow-up after combination therapy of chemoembolization and radiofrequency ablation for the treatment of hepatocellular carcinoma: single-center experience. *J Vasc Interv Radiol* 2013; 24:655–666. [\[Crossref\]](#)
25. Kang SG, Yoon CJ, Jeong SH, et al. Single-session combined therapy with chemoembolization and radiofrequency ablation in hepatocellular carcinoma less than or equal to 5 cm: a preliminary study. *J Vasc Interv Radiol* 2009; 20:1570–1577. [\[Crossref\]](#)
26. Shibata T, Isoda H, Hirokawa Y, Arizono S, Shimada K, Togashi K. Small hepatocellular carcinoma: is radiofrequency ablation combined with transcatheter arterial chemoembolization more effective than radiofrequency ablation alone for treatment? *Radiology* 2009; 252:905–913. [\[Crossref\]](#)
27. Lee IJ, Kim YI, Kim KW, et al. Radiofrequency ablation combined with transcatheter arterial embolisation in rabbit liver: investigation of the ablation zone according to the time interval between the two therapies. *Br J Radiol* 2012; 85:e987–994. [\[Crossref\]](#)