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Intermittent Hepatic Vein Balloon Occlusion During Radiofrequency Ablation in the Liver

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Abstract

The purpose of the study was to assess the feasibility of *intermittent* hepatic vein balloon occlusion during percutaneous radiofrequency (RF) ablation. Eight non-anticoagulated patients who had primary ($n = 2$) and metastatic ($n = 6$) liver tumors with a mean diameter of 4.2 cm (range 2.4–6.5 cm) were treated, resulting in a mean ablation diameter of 6.3 cm (range 4.3–9.3 cm). Six of 9 (67%) of the balloon-occluded hepatic veins were patent. No clinical sequelae of thrombosis were noted. Mean length of follow-up with CT and/or MRI was 12 months. Local tumor control was achieved in 5 of 8 patients. Intermittent hepatic vein balloon occlusion could potentially be a low-risk adjunctive maneuver for thermal ablation therapy in the treatment of large tumors and tumors adjacent to large vessels.

Keywords

Hyperthermia; Liver neoplasms; Oncology; Radiofrequency (RF) ablation; Vascular occlusion

For years the standard of treatment of hepatocellular carcinoma (HCC) and secondary liver metastases has involved surgery, despite often unsuccessful outcomes or recurrence of tumor. More recently, several newer treatment options such as chemoembolization, percutaneous ethanol injection, and radiofrequency (RF) ablation are available for HCC depending on the size of the tumor, stage of disease, and hepatic function [1]. Since the first report of RF ablation for the treatment of HCC by Rossi et al. in 1993, various techniques have sought to improve deficiencies in RF ablation and to minimize local recurrence of residual tumor [2–4]. One of the major limitations is the perfusion-mediated tissue cooling that results from both dissipation of heat in that portion of the tumor closest to large blood vessels as well as capillary level microperfusion [3].

Previous studies have shown that mechanical and pharmacologic strategies aimed at lowering hepatic perfusion can increase the volume of coagulation necrosis [5,6]. Temporarily occluding selective hepatic veins during RF ablation should reduce the local portal venous inflow and therefore minimize the heat sink effect sufficiently to increase the area of ablation [6]. More importantly, balloon occlusion may allow the tumor tissue immediately adjacent to the vessel wall to be heated to lethal temperatures (Fig. 1). While some authorities recommend combining maneuvers to decrease blood flow with RF ablation for patients with lesions that are greater

than 5 cm in diameter or abut major intrahepatic vessels, it is uncertain whether this technique has sufficient clinical benefit to warrant a change in the standard of RF ablation practice.

The purpose of this study was to assess the feasibility of *intermittent* hepatic vein balloon occlusion during percutaneous RF ablation. Intermittent balloon occlusion was performed to not only minimize all perfusion-mediated tissue cooling but also to potentially maintain vessel patency.

Materials and Methods

Patients and Tumor Characteristics

All patients were on an Institutional Review Board approved protocol and informed consent was obtained from all patients (Table 1). The mean tumor size was 4.2 cm (range 2.4–6.5 cm) and the mean distance of the peritumoral vessels from the lesion was 1.56 mm (range 0–6.50 mm). The mean diameter of balloon-occluded vessels was 7.1 mm (range 4.1–9.0 mm).

Techniques

The Radionics Cool Tip Coagulator 200 watt, 480 kHz generator ablation system (Valleylab, Boulder, CO, USA) was used for ablation with an internally cooled cluster electrode. Grounding was achieved with four dispersive pads to the patient's thighs. Regional hepatic balloon occlusion via right internal jugular vein was performed with a 9 Fr 10 cm sheath (Boston Scientific, Natick, MA, USA) prior to insertion of the RF electrode. In 1 patient, an additional 9 Fr sheath was placed in the left internal jugular vein for placement of a second balloon occlusion catheter. A hepatic venogram was obtained and the hepatic vein closest to the tumor being ablated was occluded with an 11.5 mm occlusion balloon (Boston Scientific, Natick, MA, USA).

Once hepatic vein occlusion was tested under angiographic guidance, the patient was either treated in the angiography suite under ultrasound guidance ($n = 2$) (HDI 5000 SonoCT; Philips Medical Systems) (Fig. 2), or taken to the adjacent CT room ($n = 6$) where CT and ultrasound-guided RF ablation ensued. The balloon was placed prior to RF ablation and imaged with ultrasound to confirm that the appropriate hepatic vein had been catheterized. No anticoagulation was given.

Balloons were placed adjacent to the tumor or at the origin of the nearby vein (Fig. 3). Due to the location of the tumor in the dome of the liver, 1 patient underwent subphrenic 5% Dextrose infusion to separate the diaphragm from the dome of the liver and possibly minimize thermal damage to the diaphragm and heart [7] (Fig. 1). An internally cooled triple cluster RF electrode was percutaneously placed in the liver under sonographic guidance. The balloon was then inflated simultaneously with onset of RF ablation current. Intermittent balloon occlusion (maximum temperature range during cooling phase 57–99°C) was performed for 12 min per needle location. During this time, the balloon was inflated for an arbitrarily selected time of 3 min to impede hepatic venous flow and then deflated for 1 min to maintain patency of the hepatic vein and perfusion to normal liver tissue, in cycles throughout the RF ablation. One patient had the balloon inflated for the full 12 min ablation due to tumor invasion of vein and the desire to thrombose and coagulate the vein.

Upon completion of the procedure, CT (Mx 8000 IDT; Philips Medical Systems) was used to evaluate the treated areas for completeness of treatment and to exclude early complications. Follow-up imaging with CT and/or MRI (1.5T; GE Healthcare) was performed in the first week in cases where there was reasonable concern for residual disease. This in turn was followed by additional CT/MRI studies typically at 4–6 weeks, 3 months, 6 months, and 1 year post-ablation. The patient's clinical course was closely monitored by both the primary service and

the interventional radiology service prior to discharge. Standard criteria defining complete and incomplete coagulation were used [8].

Results

The 9 balloon-occluded hepatic veins consisted of 1 left hepatic vein, 3 middle hepatic veins, 4 right hepatic veins, and 1 accessory hepatic vein. Six of 9 (67%) of the balloon-occluded hepatic veins were patent. Although 2 right hepatic veins and 1 left hepatic vein were found to be thrombosed, the left hepatic vein was intentionally ablated and thrombosed with continuous balloon occlusion during the procedure due to the vein invading the tumor.

In all 3 patients, the 3 hepatic vein thromboses were evident at first imaging follow-up within 1 week of the procedure, and no evidence of recanalization was noted in subsequent follow-up imaging. No clinical sequelae of hepatic vein thrombosis were noted. Imaging performed 1–6 months post-ablation showed no evidence of perfusion abnormalities, focal hepatic swelling, or atrophy. Balloon occlusion resulted in ablations with a mean diameter of 6.3 cm (range 4.3–9.3 cm). The mean length of follow-up with CT and/or MRI was 12 months (range 3–38 months).

Local tumor control was achieved in 5 of 8 patients, despite large vessel proximity. Five of 8 tumors touched or encased a hepatic vein, while 3 tumors ranged from 2.70 to 6.50 mm in proximity to a hepatic vein. One patient had tumor encasing the inferior vena cava and right hepatic vein. Two of 3 patients without local control had tumors touching the portal vein (Table 2).

Discussion

The purpose of percutaneous ablative hepatic therapies is to offer treatment for patients who might otherwise not be candidates for surgical interventions. The bioheat transfer equation below governs the amount of energy deposited in tissue [9]:

$$\rho c(\partial T/\partial t) = \nabla \cdot k \nabla T + Q_2$$

where ρ is the tissue density (kg/m³), c is the specific heat (J/kg·K), k is the thermal conductivity (W/m·K), and Q_2 is a heat sink or source.

The extent of the coagulation necrosis is directly proportional to current density and is inversely related to the blood flow [10]. Other determinants of the size of the thermal lesion include the total heat deposition in the tissue, which depends on the exposed active electrode surface, the total amount of RF energy delivered, the temperatures achieved in the tissue and the exposure time, as well as the thermal conductivity of the tissue [11,12]. The diameter of coagulation necrosis also depends partly on the type of electrode used during the procedure. Single internally cooled electrodes have been reported to induce a mean coagulation diameter up to 4.5 cm in liver ex vivo, in contrast to the 2.4 cm ± 0.2 of coagulation seen in normal liver *in vivo* [13]. Similarly, the use of a cluster of three RF electrodes can produce a mean coagulation of 7.3 cm ± 0.2 in liver ex vivo in contrast to a mean coagulation diameter of 3.1 cm ± 0.2 observed in normal liver *in vivo* [14].

The discrepancy in coagulation necrosis diameter between liver *in vivo* versus ex vivo may be explained by the heat sink effect that is seen in perfused liver *in vivo*. Due to the extensive vascularity of the liver, hepatic blood flow causes dissipation of heat via convection from those areas of tissue nearest to large blood vessels. Convective heat loss may occur globally but may be most pronounced immediately adjacent to vessels greater than 3 mm in diameter [4]. Therefore, areas of tumor in close proximity to large vessels may not reach the temperature

needed for coagulation necrosis to occur, which can result in smaller diameter, irregular shapes, suboptimal ablation, and residual tumor. In fact, regardless of the tumor size, perivascular location of a tumor is an independent predictor for treatment failure [15].

Various methods of decreasing blood flow in the liver have been used in conventional surgery for trauma, liver resections, creation of portosystemic shunts, etc. Some of these techniques have also been employed in RF ablation studies to minimize hepatic blood flow and decrease the heat sink effect. One of the most common surgical techniques is the Pringle maneuver that involves occlusion of the portal vein and hepatic artery [16,17]. While several studies have investigated the role of blood flow occlusion in RF ablation *in vivo*, the question remains as to the best way to achieve blood flow occlusion in humans. Chang et al. demonstrated that complete vascular occlusion resulted in the greatest area of necrosis as well as more spherical ablative areas than the Pringle maneuver and hepatic vein occlusion, respectively [16]. There is a trend toward greater size uniformity of ablation zones with vessel embolization or clamping in the pig kidney RF ablation model [17]. It is unclear whether this holds true with hepatic vein occlusion in liver RF ablation. There is a potential benefit of a uniformly larger ablative area with lethal temperatures in tumor tissue near large blood vessels. Miyamoto et al. [18] showed that balloon occlusion of both the hepatic artery and hepatic vein resulted in an ablation diameter of 50–60 mm using a single electrode. However, by drastically reducing if not removing the heat sink effect, total vascular occlusion may leave large vessels and bile ducts open to injury.

Using balloon occlusion of only the common hepatic artery, Yamasaki et al. similarly showed a significant difference in the diameter of coagulation necrosis between the balloon-occluded versus standard RF ablation treatment groups (36.6 ± 3.8 mm in balloon-occluded vs. 26.7 ± 6.4 mm in standard RF). Although it is unclear what effect balloon-occluded RF ablation has on complication rates, the rate of minor complications (localized warmth and pain and transient fever) was higher with hepatic artery balloon-occluded RF ablation compared with standard RF ablation [6].

de Baere et al. [19] treated 10 tumors with either hepatic vein or portal vein occlusion during liver RF ablation for large tumor size or for proximity to vessels, and showed larger devascularized zones after RF ablation compared with the zones in a control group without vein occlusion. de Baere et al. occluded the hepatic vein for the duration of the RF ablation, without mention of deflating the balloon until the end of the RF ablation. With immediate color and Doppler ultrasound, this resulted in three vessel occlusions and four vessels with slow flow, although they reported no vascular abnormalities on the follow-up imaging. Exactly how this technique of continuous occlusion compares to intermittent balloon occlusion (in terms of treatment volumes and occlusion rates) is unknown. It is also unclear whether the possible gain in tumor volumes with continuous occlusion can be maintained along with low vein thrombosis rates.

We chose to further investigate the effects of hepatic flow cessation on coagulation necrosis by using *intermittent* balloon occlusion of hepatic vein(s). Because the hepatic artery contributes approximately 20% of blood flow to the liver and the portal system provides the remaining 80% of hepatic flow, cessation of portal blood flow might produce a greater reduction of the heat sink effect [20]. However, portal vein thrombosis has been reported with RF ablation [21]. Access for hepatic vein occlusion is less invasive than portal vein access, and hepatic vein occlusion likely carries less risk for thrombosis. While Yamasaki et al. [6] believed the diseased liver to be more reliant on hepatic arterial circulation and thus performed hepatic artery occlusion, we hypothesized that occlusion of hepatic venous outflow would sufficiently hamper blood flow to decrease the heat sink effect. As a result, occlusion of the right, left, or middle hepatic veins or a combination thereof was performed in 8 patients, and

short local control was achieved in 5 of the 8, despite tumor being in very close proximity to or touching the large vessels. Failure to locally control tumor in 2 of the 3 patients may have been due to the tumor hypervascularity often seen with renal cell cancer metastases.

RF ablation is well known for the treatment of tumors at multiple organ sites. The minimal invasiveness of the procedure combined with the reduced patient discomfort and medical costs compared with traditional open surgery and shorter length of hospital stay suggest that RF ablation will only increase in popularity in the coming years. At this time, RF ablation is being used for the treatment of small tumors until an optimal way to increase the size and efficacy of ablation can be consistently achieved. While many studies have focused on ways to reduce blood flow in highly vascular organs to improve the quality of ablation, a consensus has yet to be reached as to the best way to achieve this effect. The type and number of vessels to be occluded will need further investigation, especially in those cases involving tumors extending into both lobes. Different tumors might require different strategies (balloon occlusion or embolization). Other balloon occlusion schemes are possible (continuous, intermittent, intermittent during application of pulsed RF energy).

Exactly how the technique of continuous occlusion compares with intermittent balloon occlusion (in terms of treatment volumes and occlusion rates) is unknown. In comparison with de Baere et al.'s continuous occlusion study [19], the technique of intermittent occlusion resulted in a similar but slightly larger mean ablation diameter of 6.3 cm (vs. 5.1 cm by de Baere et al.); however, direct comparison is not possible. The small sample sizes in both studies preclude a conclusion as to whether one technique is more efficacious than the other. Although a further study may be useful to determine how this technique compares with results in patients who have not undergone vascular occlusion, a better approach may be to study various intermittent occlusion periods (e.g., 3, 5, and 10 min) and their effects on ablation diameter in an animal model. Furthermore, the rationale for intermittent balloon occlusion was an attempt to balance the risk for thrombosis with the benefit of the maneuver. With a hepatic vein thrombosis rate of 40%, the potential role of anticoagulation prior to and during the procedure is unclear and warrants investigation, as there must be a balance between the risk of thrombosis and bleeding. The optimal methodology of achieving large ablation diameters is as yet unknown, and the pathophysiology of balloon occlusion requires further investigation.

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References

1. Kooby DA, Jarnagin WR. Surgical management of hepatic malignancy. *Cancer Invest* 2004;22:283–303. [PubMed: 15199611]
2. Rossi S, Fornari F, Buscarini L. Percutaneous ultrasound-guided radiofrequency electrocautery for the treatment of small hepatocellular carcinoma. *J Interv Radiol* 1993;8:97–103.
3. Rhim H, Goldberg SN, Dodd GD, et al. Essential techniques for successful radiofrequency thermal ablation of malignant hepatic tumors. *RadioGraphics* 2001;XX:S17–S39. [PubMed: 11598245]
4. Lu DS, Raman SS, Vodopich DJ, et al. Effect of vessel size on creation of hepatic radiofrequency lesions in pigs: Assessment of the “heat sink” effect. *AJR Am J Roentgenol* 2002;178:47–51. [PubMed: 11756085]
5. Goldberg SN, Hahn PF, Halpern EF, et al. Radiofrequency tissue ablation: Effect of pharmacologic modulation of blood flow on coagulation diameter. *Radiology* 1998;209:761–767. [PubMed: 9844671]
6. Yamasaki T, Kurokawa F, Shirahashi H, et al. Percutaneous radiofrequency ablation therapy for patients with hepatocellular carcinoma during occlusion of hepatic blood flow. *Cancer* 2002;95:2353–2360. [PubMed: 12436442]

7. Kapoor BS, Hunter DW. Injection of subphrenic saline during radiofrequency ablation to minimize diaphragmatic injury. *Cardiovasc Intervent Radiol* 2003;26:302–304. [PubMed: 14562984]
8. Goldberg SN, Grassi CJ, Cardella JF, et al. Image-guided tumor ablation: Standardization of terminology and reporting criteria. *Radiology* 2005;235:728–739. [PubMed: 15845798]
9. Wren J, Karlsson M, Loyd D. A hybrid equation for simulation of perfused tissue during thermal treatment. *Int J Hyperthermia* 2001;17:483–449. [PubMed: 11719965]
10. Strohbehn JW. Temperature distributions from interstitial RF electrode hyperthermia systems: Theoretical predictions. *Int J Radiat Oncol Biol Phys* 1983;9:1655–1667. [PubMed: 6643161]
11. Cosman ER, Nashold BS, Badenbaugh P. Stereotactic radiofrequency lesion making. *Appl Neurophysiol* 1983;46:160–166. [PubMed: 6367642]
12. Organ LW. Electrophysiologic principles of radiofrequency lesion making. *Appl Neurophysiol* 1976;39:69–76. [PubMed: 1052287]
13. Goldberg SN, Gazelle GS, Solviati I, et al. Radiofrequency tissue ablation: Increased lesion diameter with a perfusion electrode. *Acad Radiol* 1996;3:636–644. [PubMed: 8796727]
14. Goldberg SN, Solbiati L, Hahn PF, et al. Large-volume radiofrequency tissue ablation by using a clustered internally cooled electrode technique: Laboratory and clinical experience in liver metastases. *Radiology* 1998;209:371–379. [PubMed: 9807561]
15. Lu DSK, Raman SS, Limanond P, et al. Influence of large peritumoral vessels on outcome of radiofrequency ablation of liver tumors. *J Vasc Interv Radiol* 2003;14:1267–1274. [PubMed: 14551273]
16. Chang CK, Hendy MP, Smith JM, et al. Radiofrequency ablation of the porcine liver with complete hepatic vascular occlusion. *Ann Surg Oncol* 2002;9:594–598. [PubMed: 12095977]
17. Chang I, Mikityansky I, Wray-Cahen D, et al. Effects of perfusion on radiofrequency ablation in swine kidneys. *Radiology* 2004;231:500–505. [PubMed: 15128994]
18. Miyamoto N, Tsuji K, Sakurai Y, et al. Percutaneous radiofrequency ablation for unresectable large hepatic tumors during hepatic blood flow occlusion in four patients. *Clin Radiol* 2004;59:812–818. [PubMed: 15351246]
19. de Baere T, Bessoud B, Dromain C, et al. Percutaneous radiofrequency ablation of hepatic tumors during temporary venous occlusion. *AJR Am J Roentgenol* 2002;178:53–59. [PubMed: 11756087]
20. Lauth WW, Greenway CV. Conceptual review of the hepatic vascular bed. *Hepatology* 1987;7:952–963. [PubMed: 3308669]
21. Francica G, Marone G, Solbiati L, et al. Hemobilia, intrahepatic hematoma and acute thrombosis with cavernomatous transformation of the portal vein after percutaneous thermoablation of a liver metastasis. *Eur Radiol* 2000;10:926–929. [PubMed: 10879704]

Fig. 1.

A–C. RF ablation of liver tumor with balloon occlusion and saline infusion. **A** Contrast-enhanced CT scan before RF ablation shows a 4.2 cm lesion directly invading the left hepatic vein (arrow). **B** Unenhanced CT scan during RF ablation shows needle placement (white arrow) after left hepatic vein balloon occlusion (black arrow) and saline infusion (arrowhead) for diaphragmatic and cardiac protection. **C** Contrast-enhanced CT scan after RF ablation shows thrombosis of the left hepatic vein (arrow) and coagulation diameter extending to the thrombosed vein.

Fig. 2.
Ultrasound monitoring of the occlusion balloon (large arrow) in the hepatic vein just proximal to the tumor (small arrow).

Fig. 3.
Angiogram showing two balloon occlusion catheters in the middle (arrowhead) and right (arrow) hepatic veins.

Table 1

Patient demographics

Case no.	Age (years)	Sex	Diagnosis	Underlying liver disease	Previous treatment
1	49	F	Adrenocortical with metastasis	None	Chemo/OR
2	57	M	Renal cancer with metastasis	None	Chemo/Rad/OR
3	77	M	Renal cancer with metastasis	None	Chemo/Rad
4	49	F	Renal cancer with metastasis	None	Chemo/Rad
5	52	F	HCC	HBV	COE/OR
6	59	M	HCC	HDV	None
7	55	F	Renal cancer with metastasis	None	OR
8	56	F	Pelvic sarcoma with metastasis	None	Chemo/Rad/OR

HCC < hepatocellular carcinoma; Chemo, chemotherapy; OR, surgery; Rad, radiation; COE, chemoembolization; HBV, hepatitis B; HDV, hepatitis D

Table 2

Summary of the results of balloon-occluded RF ablation

Case no.	Tumor size (cm)	Ablation diameter (cm)	Occluded vein	Proximity to occluded vessel (mm)	Vessel size (mm)	Vessel patent	Follow-up (months)	Local Control
1	2.4	5.0	RHV	2.70	7.0	-	38	+
2	3.4	6.3	MHV	3.30	8.0	+	13	+
3	6.2	9.3	RHV	Around IVC and touching RHV	9.0	-	5	+
4	6.5	7.0	RHV	6.50 and touching portal vein	5.3	+	14	-
5	3.0	6.5	MHV	Encasing MHV	7.0	+	12	+
6	3.7	6.4	MHV and RHV	Touching portal vein, MHV and RHV	8.0, 8.0	+	3	-
7	4.3	5.2	AHV	Touching AHV	4.1	+	6	-
8	4.2	4.3	LHV	Invading LHV	8.0	-	5	+

RHV, right hepatic vein; MHV, middle hepatic vein; LHV, left hepatic vein; IVC, inferior vena cava; AHV, accessory hepatic vein