Abstract

Thermal ablation; radiofrequency ablation (RFA) and microwave coagulation therapy (MCT) has spread widely as a less invasive and curative treatment for hepatocellular carcinoma (HCC). “Thermal ablation program in Kumamoto University” has been continued for over 20 years. From 1994 to 2010, thermal ablation was applied for 807 HCC patients; percutaneous, endoscopic and open ablation were applied for 420 patients (52%), 298 (37%) and 89 (11%), respectively. Long-term survival was excellent; 3-, 5-, and 10-year cumulative overall survival rates were 68%, 52% and 29%, respectively. In contrast, there observed some adverse events in thermal ablation mainly in the early period. Complication rates in 200 MCT and 230 RFA were 10% and 5%, respectively. In this paper, we introduced several complications and its management and preventive method Thermal ablation has a dark side of providing severe complications for a couple of patients, therefore observance of strict indication is always required.

Abbreviations: HCC, hepatocellular carcinoma; RFA, radiofrequency ablation; MCT, microwave coagulation therapy; TACE, transarterial chemoembolization; PEIT, percutaneous ethanol injection therapy; OS, overall survival

Key words: thermal ablation, hepatocellular carcinoma, microwave coagulation therapy, radiofrequency ablation

Accepted on Feb. 29, 2012
Introduction

Thermal ablation, including radiofrequency ablation (RFA) and microwave coagulation therapy (MCT) has spread widely as a less invasive and curative treatment mainly for hepatocellular carcinoma (HCC). Thermal ablation is used for unresectable small-sized HCC patients with poor liver function reserve, but sometimes applied even for large-size or resectable HCC.

We started “Thermal ablation program in Kumamoto University” in 1991 and continued for over 20 years. Percutaneous, endoscopic and open approaches have been selected according to the size, number and location of the tumor.

In this article, we summarize not only advantages but also adverse effects of thermal ablation for HCC. This paper was presented in the evening seminar at the “30th Annual Meeting of Microwave Surgery in 2011”.

Bright side of thermal ablation

We have developed various new therapeutic modalities for HCC in the Department of Gastroenterological Surgery, Kumamoto University (Fig. 1). MCT and RFA were applied in 1991 and 1999, respectively. Initially, we started percutaneous and open thermal approach followed by endoscopic approach in 1994. Indeed, the cumulative overall survival (OS) of unresectable HCC patients significantly improved as time became newly: 5-year OS were 17% in 97 patients treated with solitary transarterial chemoembolization (TACE), 35% in 355 with TACE and partial applied thermal ablation, and 52% in 231 with completely performed with thermal ablation (Fig. 2).

From 1994 to 2010, thermal ablation was applied for 807 HCC patients in our department. Percutaneous, endoscopic and open ablation were applied for 420 patients (52%), 298 (37%) and 99 (11%) respectively. We have demonstrated that the 3-, 5-, and 10-year cumulative OS rates were 68%, 52% and 29%, respectively (Fig. 3A). Moreover, thermal ablation was quite useful for patients with poor liver function of liver damage B and C. Cumulative 5-year OS rates were 63%, 51% and 20% in liver damage A, B and C patients, respectively. Liver damage A and B patients showed equivalent OS and were superior to liver damage C patients (Fig. 3B).

We have summarized the data of the literatures: the cumulative OS were exactly equivalent between RFA and MCT, according to the analysis of 238 patients treated with MCT and 1321 patients treated with RFA. Actually, 3-and 5-year cumulative OS rates were 80-81% and 43-78% for MCT, and 62-78% and 33-55% for RFA, respectively.

Dark side of thermal ablation

1. Morbidity and mortality

The authors have demonstrated the adverse events in thermal ablation therapy in the early period: 430 patients underwent including 200 MCT and 230 RFA. The number of tumors treated with RFA was greater (average: 2.5, max: 10) compared to MCT (average: 1.9, max: 6, p<0.01). Complica-
Complications in MCT included intraabdominal dissemination in 2, hepatic failure in 2, bleeding in 1, liver abscess in 8, biliary fistula in 1, biloma in 2, massive effusion collection in 2, and acute respiratory distress syndrome in 2. Complications in RFA included hepatic failures in 2, bleeding in 1, biloma in 2, skin burn in 1, port-site hernia in 2, and massive effusion collection in 2. Liver abscess was never observed in RFA treated patients. But liver abscess was also not observed in the recent 50 MCT patients because we avoided concomitant non-sterile operation and ablation for patients with uncontrolled diabetes mellitus or infectious bile juice.

Mulier et al. reported that the 0.5% of mortality rate and the 8.9% of morbidity rate in 3670 patients treated with RFA. Livraghi et al. demonstrated that the mortality rate was 0.3%, the major complication rate was 2.2%, and the minor complication rate was less than 5% in 2320 RFA-treated patients. An extremely high rate of tumor seeding (12.5%) was reported by Llovet et al. In contrast, Livraghi et al. concluded that the rate of tumor seeding was low (0.9%) in
1314 patients, and the risk factor for tumor seeding is a prior tumor biopsy.

2. Case presentation

We will present several complicated cases after thermal ablation.
Bile duct dilatation

Figure 7 Delayed liver abscess formation after thoracoscopic MCT
A: Enhanced CT (pre MCT), B: Enhanced CT (6M after), C: Enhanced CT (15M after), D: Enhanced CT (17M after), E: Liver abscess-imaging, F: Autopsy findings

Solitary HCC (arrow), 4.5 cm in diameter, in liver damage C was treated with thoracoscopic MCT. Bile duct dilatation was already existed near the targeted tumor (A). Coagulated area was relatively large, 6 cm in diameter (B). Fifteen to seventeen months later, patients developed delayed liver abscess containing the gas with hepato-pulmonary fistula (C, D). Liver abscess was drained percutaneously but the patient died of septic condition with no recurrence of HCC (E, F).

Case 1 Spillage of tumor cells during laparoscopic RFA (Fig. 4)
If superficial HCC was directly punctured and ablated by percutaneous approach, neoplastic seeding may occur in some cases. To avoid neoplastic seeding, endoscopic ablation is especially useful. If tumor cells begin to spillage, then suction, peritoneal lavage, or dispersion of anticancer agent can be achieved promptly under direct vision.

Case 2 Thermal injury of the stomach after percutaneous RFA (Fig. 5)
The recurred tumor at the therapeutic site was located in the thin liver parenchyma in the left lateral segment. Endoscopic ablation was intended and found the thermal injury of the stomach due to a previous percutaneous RFA in referred hospital. To avoid such thermal injury of stomach, diaphragm or heart, laparoscopic RFA should be done in direct vision under lifting of the liver.

Case 3 Biloma formation after percutaneous RFA (Fig. 6)
Immediately after 8th TACE, percutaneous RFA was performed. Bile duct dilatation was already detected in enhanced CT before RFA. Two months after RFA, biloma formation was observed at the treating sites in segment 7 and 8. Many times of TACE and bile duct dilatation is a risk factor for biloma formation after RFA.

Case 4 Delayed liver abscess formation after thoraco-
Figure 8 Biliary hemorrhage after percutaneous RFA
A: Enhanced CT (after TACE and RFA), B: Ultrasoundography, C: DSA/arterial phase, D: DSA/venous phase.
Percutaneous RFA was applied for 4 tumors (A, arrows). After several hours, hematoma formation in the gallbladder was observed by ultrasoundography (B, arrow). Digital subtraction angiography (DSA) clearly demonstrated a cholangiogram after intra-arterial administration of contrast medium (C, D, arrow).

Figure 9 Biliary stricture after hand-assisted laparoscopic RFA
A: Enhanced CT (pre), B: Laparoscopic view, C: Enhanced CT (1W after), D: Enhanced CT (2M after).
Unresectable solitary HCC (arrow), 4 cm in diameter, was located in paracaval portion of caudate lobe (A). After 4 times of TACE, tumor is quite viable. Hand-assisted laparoscopic RFA was intended carefully using intraoperative US, and Dimon/guide needle (B). Tumor was completely ablated (C) and tumor markers were decreased to normal range, but dilatation of left bile duct was appeared after 2 months after RFA (D).

Thoracoscopic MCT (Fig. 7)  
Thoracoscopic MCT was applied for solitary HCC, 4.5 cm in diameter, in liver damage C patients. The patient developed delayed abscess formation. Bile duct dilatation and large tumor (>4 cm in diameter) is a risk factor for abscess formation after thermal ablation (refs. 1, 2, 3, 7).

Case 5 Biliary hemorrhage after percutaneous RFA (Fig. 8)
Biliary hemorrhage was observed after percutaneous RFA because of suspicious injury of Glissonian capsule. Acute pancreatitis occurred caused by intra-biliary bleeding, but the patient promptly recovered with conservative therapy.

Case 6 Biliary stricture after hand-assisted laparoscopic RFA (Fig. 9)
Solitary 4 cm HCC located in paracaval portion was
treated with hand-assisted laparoscopic RFA \(^{16}\). Although the tumor was very carefully ablated, dilatation of left bile duct appeared after 2 months after RFA. HCC located adjacent to major bile duct is contraindicative for RFA \(^{1,3,7}\).

**Case 7** Rapid tumor recurrence after laparoscopic RFA (Fig. 10)

A patient with hypovascular and large HCC \((\geq 5 \text{ cm})\) was treated with laparoscopic RFA. Tumor biopsy after RFA showed poorly differentiated HCC. Poor differentiation has been described as one of the risk factors of tumor seeding \(^{13,17}\). After the experience of this case, we never do thermal ablation for such large and strongly suggestive of poorly differentiated type HCC.

**3. Intrahepatic dissemination**

Recently, rapid and aggressive recurrence patterns after thermal ablation have been reported \(^{18-21}\). These unusual recurrences are serious problems resulting in poor prognosis. We have already reported the risk factors of intrahepatic dissemination \(^{20}\). Among 192 HCC patients underwent hepatic resection between 1992 and 2005, 8 patients were diagnosed as intrahepatic dissemination after thermal ablation including ethanol injection. Thermal ablation for HCCs (even those \(\leq 3\) cm in diameter) adjacent less than 5 mm to the main or sectional portal vein can promotes intrahepatic dissemination. The representative patient was demonstrated (Fig. 11) \(^{21}\).

**Conclusions**

Thermal ablation with MCT and RFA can result in a favorable long-term prognosis with low complication rates for HCC patients even with poor liver functional reserve. However, thermal ablation has a dark side of providing severe complications in a few cases, therefore observance of strict indication is always required.
Figure 11 Intrahepatic dissemination after RFA

A: Ultra-sonography (pre), B: Enhanced CT (pre), C: Enhanced CT (1W after RFA), D: Enhanced CT (23 M after RFA), E: Enhanced CT (post PVE), F: Macroscopic findings, G: Histological findings

The tumor was located in segment 5 and well-enhanced in arterial phase of contrast-CT and in contact with the sectional Glisson’s capsule (A, B). Percutaneous RFA was performed, but the surgical margin was insufficient (C). Twenty-three months after the RFA, a recurrence was detected as portal vein tumor thrombus of the right portal branch (D). Portal vein embolization (PVE) was performed to achieve a safe hepatic resection. The embolized right portal vein was detected as a linear unenhanced area (E: arrowheads). A right tri-sectionectomy was successfully completed. Numerous sectional metastases and massive portal vein tumor thrombus continuing from the ablated area (arrow) were observed in the resected specimen (F). Microscopic examination of countless intrahepatic metastases demonstrated poorly differentiated HCC (G, H, E; × 40).

References

3) Beppu T, Ishiko T, Sugiyama S, Baba H: Radio-frequency Ablation (RFA) and Microwave Coagulation Therapy (MCT) for Hepatocellular Carcinoma. Low Temp Med 31: 22-24, 2005
Bright side and dark side of thermal ablation for hepatocellular carcinoma


