Aktueller Stand der Radiofrequenz-Ablation bei hepatozellulärem Karzinom


Methodik: Diese kritische Übersicht konzentriert sich auf den gegenwärtigen Stand der RFA bei HCC mit besonderer Beachtung ihrer Indikationen, der Methodik, der Risiken, des lokalen Therapieversagens und der Verbesserung der Überlebenszeit.


Schlussfolgerungen: Bis vor kurzem gab es keine ausreichenden Beweise dafür, dass die RFA andere Behandlungsmethoden des HCC ersetzen kann. Überzeugendere Daten aus randomisierten Studien sind notwendig, um ein Behandlungsprotokoll für die RFA bei Patienten mit HCC zu etablieren.

Schlüsselwörter: Radiofrequenz-Ablation, hepatozelluläres Karzinom.

Summary. Background: Radio-frequency ablation (RFA) is the latest developed and widely practised local ablation therapy for liver tumours. It has the merit of effective tumour ablation and preservation of the maximal normal liver parenchyma. In the past few years, there has been tremendous expansion in the application of RFA for hepatocellular carcinoma (HCC) patients. However, the therapeutic effect of this local-ablation treatment needs to be balanced against its risks and possible local failure.

Methods: This review focuses on the current status of RFA for HCC, with attention to its indications, approaches, risks, local failure, and survival benefit.

Results: Although the results of most clinical studies of RFA seem optimistic, the associated complication and tumour recurrence should not be overlooked. Careful patient selection, meticulous RFA techniques, and prompt treatment of residual and recurrent tumours are necessary to ensure a better outcome after RFA.

Conclusions: Until recently, there has been no strong evidence showing that RFA can replace any treatment modalities in the management of HCC. Nonetheless, more convincing evidence by randomised trials is required for the establishment of a treatment protocol of RFA for HCC patients.

Key words: radio-frequency ablation, hepatocellular carcinoma.

Introduction

Hepatocellular carcinoma (HCC) is the fifth most common malignancy in the world [2]. Although it occurs predominantly in Asia and Africa, its incidence is rising in western countries where hepatitis C infection is common [16]. Hepatic resection and liver transplantation are regarded as the curative treatment options for HCC. However, the prognosis of most patients with HCC remains poor because of the low resectability rate (20–37%) and shortage of liver grafts [20, 22, 60]. Different locoregional therapies have been developed for unresectable HCC with an attempt to control the tumour locally, thus prolonging patients' survival. These include transarterial chemoembolisation (TACE), percutaneous ethanol injection (PEI), and thermal ablation therapies. Each of these treatment modalities has its own advantages and limitations [19, 53, 65].

Radio-frequency ablation (RFA) is the latest developed and widely practised thermal ablation therapy for HCC. It is based on the interaction of high-frequency al-
ternating current (460–480 kHz) with living tissues to heat energy by ionic vibration. At lethal temperature (60–100 °C), there is instantaneous protein coagulation with irreversible damage of key intracellular enzymes, which contributes to coagulative necrosis of the target lesion [24]. RFA causes effective local tumour ablation, while the maximal normal liver parenchyma can be preserved. There are four types of radio-frequency (RF) electrodes in clinical practice, namely, the multitined expandable electrode, the internally cooled electrode, the perfusion electrode, and the bipolar electrode [23]. The purpose of using this variety of electrode devices is to enlarge the size of coagulation necrosis in order to extend the limit of ablation volume for the liver tumour. Following favourable outcomes of RFA in initial clinical series [10, 42, 72], there seems to be an uncontrolled expansion in the application of RFA for malignant liver tumours. However, one should be meticulous in dealing with this situation by striking a balance between the benefits and limitations of RFA in clinical trials. This article aims to review the current status of RFA in the management of HCC regarding its indications, approaches of ablation, risks, and long-term survival benefit. A MEDLINE literature search from January 1990 to July 2004 was undertaken, with additional pertinent references extracted from bibliographies of the articles.

**Indications for RFA**

RFA is indicated in patients with unresectable HCC, which is caused by multifocal tumours, poor liver function, and/or proximity of the tumour to major intrahepatic vasculature precluding margin-negative resection. In addition, there should be no extrahepatic metastasis. Curley et al. [11] performed RFA on 110 patients with unresectable HCC, among whom 55% had Child’s B or C cirrhosis. Complete tumour ablation was achieved in 95% of the patients with a low complication rate (12.7%) and zero treatment-related death.

Large HCC seems to be an obstacle for RFA because the maximal size of tissue necrosis achieved by RFA is limited to 5 cm. Nevertheless, several studies have demonstrated that multiple RF ablation processes with overlap of ablation zones are feasible for large HCC. Livraghi et al. [41] studied the efficacy of percutaneous RFA for medium and large HCC (mean diameter, 5.4 cm) in 114 patients. Complete tumour necrosis was attained in 78% of the tumour nodules. In study by Bowles et al. [3], 76 patients with locally advanced liver tumours (25 had HCC and 39 had colorectal liver metastases) underwent RFA. The mean tumour size was 3 cm, ranging from 0.4 cm to 18 cm. Local recurrence was 9% at a mean follow-up of 15 months. By using a mathematic model to calculate the optimal number of RF ablation processes for the target tumour, Chen et al. [5] have achieved a complete tumour ablation rate of 87.6% in 110 patients with large HCC. Our group has studied the safety and efficacy of RFA in 35 patients with medium and large HCC with diameters ranging from 3 cm to 8 cm [66]. There was no significant difference in the complete tumour ablation rates (91 vs. 94%) between medium and large HCC and small HCC (<3 cm in diameter).

The anatomical location of the HCC is another concern for RFA. Llovet et al. [44] have shown that tumour seeding along the RF needle-track was significant (12.5%) after percutaneous RFA for HCC, and this was associated with the subcapsular location of the tumour. The underlying mechanism could be related to the iatrogenic tumour dissemination during puncture of the RF electrode into the tumour. In contrast, by indirect puncture of the tumour through the nontumourous liver during RFA and complete coagulation of the RF needle-track, our group reported no needle-track tumour seeding in 48 patients with subcapsular HCC [67]. The presence of large intrahepatic blood vessels (≥3 mm) contiguous to the liver tumour may contribute to the incomplete tumour ablation by RFA due to the flow-related “heat sink” effect. The perivascular location of the liver tumour was identified as the independent prognostic factor for local recurrence after RFA [45]. Nevertheless, an experimental study has revealed that complete ablation around the main portal vein branch could be achieved after RFA without hepatic inflow occlusion [55]. In fact, our group has shown that the clinical outcome after RFA was similar between 58 patients with perivascular HCC and 104 patients with nonperivascular HCC in terms of treatment morbidity (19 vs. 27.6%), mortality (3.4 vs. 0%), complete-ablation rate (86.2 vs. 95.1%), and local recurrence rate (10 vs. 7%). RFA for tumours situated at the liver hilum is potentially dangerous because of the risk of bile duct injury [49, 81]. Elias et al. [15] advocated a novel way of using the intraductal chilled saline irrigation to minimise the central bile duct injury by RFA. A subsequent study by the same group of authors confirmed the efficacy of this approach in 13 patients with liver tumours close to the central bile duct [18]. There was no biliary stenosis in all except one patient after a median follow-up of 19.7 months. The protective effect of intraductal chilled saline irrigation against RF thermal injury has been further investigated experimentally with a porcine model [69]. The degree of thermal injury to the biliary epithelium and subepithelial glands by RFA was significantly reduced after chilled saline irrigation of the bile duct when compared with the control group.

Intrahepatic recurrence after curative resection for HCC is common (40–60%) because of either intrahepatic metastasis from the primary tumour or multicentric occurrence of the tumour [52, 63, 82]. Repeated hepatic resection has been accepted as the treatment of choice for recurrent HCC provided that the liver function reserve is satisfactory and the recurrent tumour is anatomically resectable. However, the re-resection rate among patients with recurrent HCC remains low, ranging from 10 to 48% [21, 30, 51, 63]. In recent years, RFA has been used as an alternative to surgery for recurrent HCC. Kainuma et al. [34] reported the first case of recurrent HCC treated successfully by RFA. Thereafter, RFA has been shown to be effective for recurrent HCC by several case series [6, 17, 58]. Choi et al. [6] have reported the largest series of percutaneous RFA for recurrent HCC in 45 patients. A complete ablation rate of 87% was achieved after single or repeated RFA with no death or complication. The overall survival rates at 1, 2, and 3 years were 82, 72 and 54%, respectively.