Histopathologic Comparison of Monopolar versus No-Touch Multipolar Radiofrequency Ablation to Treat Hepatocellular Carcinoma within Milan Criteria

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ABSTRACT

Purpose: To compare histopathologically the completeness of radiofrequency (RF) ablation to treat hepatocellular carcinoma (HCC) with monopolar or multipolar technique.

Materials and Methods: Thirty-five consecutive patients (mean age, 59 y) with cirrhosis and HCC (n = 59) within Milan criteria received RF ablation and subsequently underwent liver transplantation (LT) for tumor progression or liver failure. Data were extracted retrospectively from a prospective database. Thirty nodules were treated with a monopolar device with internally cooled (n = 17) or perfused (n = 13) electrodes, and 29 were treated with a multipolar technique with internally cooled electrodes based on the "no-touch" concept. This consisted of inserting two or three straight electrodes around the nodule to avoid intratumor puncture to the greatest extent possible. Effectiveness of the three devices was compared by histopathologic examination of explants. Fisher exact and χ^2 tests and multivariate logistic regression analysis were performed.

Results: Mean sizes of nodules ablated (25, 22, and 21.6 mm) and median times from ablation to LT (11, 7.5, and 8.4 months) for patients treated with the monopolar internally cooled electrode device (MoICD), monopolar perfused electrode device (MoPED), and multipolar internally cooled electrode device (MuICD), respectively, were similar ($P = .8$ and $P = .9$, respectively). Pathologic examination showed complete necrosis for eight of 17 and six of 13 nodules treated with the MoICD and MoPED, respectively, versus 26 of 29 treated with the MuICD ($P = .0019$). In multivariate analysis, RF technique remained the predictive factor for complete necrosis ($P = .005$).

Conclusions: Ablation of small HCCs with multipolar RF ablation based on the no-touch concept improves the rate of complete necrosis during pathologic examination compared with monopolar techniques.

ABBREVIATIONS

AFP = α-fetoprotein, HE = hematoxylin/eosin, HCC = hepatocellular carcinoma, LT = liver transplantation, MoICD = monopolar internally cooled electrode device, MoPED = monopolar perfused electrode device, MuICD = multipolar internally cooled electrode device, RF = radiofrequency

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O.S. is a consultant for Olympus (Teltow, Germany). He was sponsored two times per year to allow him oral presentations in international scientific meetings. In the present work, he was not involved in the process of patient selection from the prospective database; pathologic analysis and reporting of explanted livers, which were used as a gold standard in assessing the effectiveness of three radiofrequency ablation techniques; data follow-up recording and collection; and data computation for statistical analysis. None of the other authors have identified a conflict of interest.

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For the past 10 years, radiofrequency (RF) ablation has been widely accepted as a potential curative treatment for small ($\leq$ 3 cm) hepatocellular carcinomas (HCCs) in patients with cirrhosis (1). After RF ablation of HCC, complete tumor necrosis rates lower than 50% have been reported on the basis of systematic pathologic examination of explanted livers of patients who subsequently underwent liver transplantation (LT) (2–6).

Remnants of tumors are frequently located at the periphery of ablation zones, corresponding to incomplete peripheral ablation of the nodule or to the presence of microsatellites or loci of micro- or macrovascular invasion in the margins of the targeted tumor (5,6).

These shortcomings of RF ablation have been reported with the use of monopolar devices with internally cooled linear (4) or expandable electrode technologies (3,5,6). The amount of RF energy delivered to tissues decreases approximately by the square of the distance from the electrode. Accordingly, with the monopolar device, the further the edge of a tumor from the electrode, the lower the probability of obtaining a tumor-free ablative margin. Moreover, the passive centrifugal diffusion of heat from the active RF energy heating zone accounts, by far, for most of the final ablation volume. Unfortunately, this passive heat diffusion is very sensitive to the cooling effect generated by tissue perfusion and macrovessel blood flow at the tumor and nontumor interface (7).

Multipolar RF ablaiton technology, which creates local high-density electrical fields between several pairs of independent electrodes, offers potential advantages over monopolar RF ablation (8). With multipolar RF ablation, tissue coagulation occurs first between the electrodes. Multipolar technology could allow RF probes to be inserted outside the parameters of target lesion and is feasible in a tumor as large as 4 cm in size depending on the limitations of the device. Such a "no-touch" technique allows ablation of the tumors from their margin to their center, which might better ensure the achievement of a free tumor margin while decreasing the risk of intraprocedure tumor cell seeding.

The purpose of the present study was to compare the efficacy of multipolar device using a no-touch technique versus that of monopolar devices by assessing the histopathologic specimens of patients with HCC treated with RF ablation before LT.

MATERIALS AND METHODS

Study Design

Our local review board approved this single-center cohort study, and informed consent was waived. Data of patients who received LT after RF ablation for HCC that met Milan criteria were extracted from a prospective database. Because of a shortage of cadaveric liver graft, the French guidelines (9) recommend LT for patients with HCC that meets Milan criteria but Child–Pugh class A cirrhosis only for salvage treatment if recurrence or liver failure occurs after curative local therapies (ie, RF ablation or resection).

Patients and Tumors

Between January 2001 and January 2010, 432 consecutive patients with cirrhosis were treated in a single institution by RF ablation for HCC according to the previously reported criteria (10). Among them, 35 patients with HCC that met Milan criteria and Child–Pugh class A cirrhosis (29 men; mean age, 60 y; age range, 36–65 y) received LT after RF ablation, which was the sole anti-HCC treatment before LT. The chart flow selection to select the patient study group is detailed in **Figure 1**. The diagnosis of HCC was histologically proven in 28 patients or established according to noninvasive criteria, as defined by the European Association for the Study of the Liver for seven patients (11).

During the first 30 months, 17 nodules (including seven cases of distant tumor progression after initial RF ablation) were treated with a monopolar internally cooled electrode device (MoICD; Cool-Tip; Covidien, Mansfield, Massachusetts). Over the subsequent 36 months, 13 nodules (including six cases of distant tumor progression after initial RF ablation) were treated with a monopolar perfused electrode device (MoPED; HITT Integra, Tubingen, Germany). Since January 2005, 29 nodules (including 10 cases of distant tumor progression after initial RF ablation) were treated with a multipolar internally cooled electrode device (MuICD; ProSurge; Celon AG Medical Instruments/Olympus, Teltow, Germany; **Table 1**). There was no crossover between the study groups. There were no significant differences between groups in terms of patient demographic characteristics (age, sex, etiology of cirrhosis, Child–Pugh class, and serum α-fetoprotein [AFP] level) or tumor characteristics (size, primary or recurrent nodule, location including the presence of large [diameter $\geq$ 3 mm] vessels abutting the nodule; **Table 1**). In the MuICD ablation group, one patient had a 5.5-cm HCC at the time of treatment because the tumor was growing since the initial staging performed 1 month before.

RF Ablation Procedure

A single operator (O.S.), with 5 years of experience in percutaneous ablation as of the beginning of the inclusion period, performed all procedures percutaneously under general anesthesia and with ultrasound guidance. All patients were treated by RF ablation with the aim of achieving a complete tumor ablation including at least a 10-mm margin. Needle-tract ablation was systematically performed during needle removals.

With MoICD and MoPED ablation, achievement of ablation procedures conformed to previously described