Research Article

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Ten-year outcomes of percutaneous radiofrequency ablation as first-line therapy of early hepatocellular carcinoma: Analysis of prognostic factors

Young-sun Kim[1], Hyo Keun Lim[1,*,†], Hyunchul Rhim[1,*,†], Min Woo Lee[1], Dongil Choi[1], Won Jae Lee[1], Seung Woon Paik[2], Kwang Cheol Koh[2], Joon Hyeok Lee[2], Moon Seok Choi[2], Geum-Youn Gwak[2], Byung Chul Yoo[2]

[1]*Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea;* [2]*Department of Medicine and Digestive Disease Research Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea*

Background & Aims: The aim was to assess 10-year outcomes of radiofrequency ablation as a first-line therapy of early-stage hepatocellular carcinoma with an analysis of prognostic factors.
Methods: From April 1999 to April 2011, 1305 patients (male: female = 993:312; mean age, 58.4 years) with 1502 early-stage hepatocellular carcinomas (mean size, 2.2 cm) were treated with percutaneous radiofrequency ablation as a first-line option. Follow-up period ranged from 0.4 to 146.6 months (median, 33.4 months). We assessed the 10-year follow-up results of recurrences and survival with the analyses of prognostic factors.
Results: Recurrences occurred in 795 patients (1–17 times), which were managed with various therapeutic modalities. The cumulative local tumor progression rates were 27.0% and 36.9% at 5 and 10 years, respectively, for which the only significant risk factor was large tumor size (B = 0.584, $p = 0.001$). Cumulative intrahepatic distant and extrahepatic recurrence rates were 73.1% and 88.5%, and 19.1% and 38.2% at 5 and 10 years, respectively. Corresponding overall survival rates were 59.7% and 32.3%, respectively. Poor survival was associated with old age (B = 0.043, $p = 0.010$), Child-Pugh class B (B = −1.054, $p < 0.001$), absence of antiviral therapy during follow-up (B = −0.699, $p = 0.034$), and presence of extrahepatic recurrence (B = 0.971, $p = 0.007$).
Conclusions: Ten-year survival outcomes after percutaneous radiofrequency ablation as a first-line therapy of hepatocellular carcinoma were excellent despite frequent tumor recurrences. Overall survival was influenced by age, Child-Pugh class, antiviral therapy, or extrahepatic recurrence.

Keywords: Hepatocellular carcinoma; Radiofrequency ablation; Outcome analysis; Ten-year survival; Prognostic factor.
Received 30 January 2012; received in revised form 7 September 2012; accepted 13 September 2012; available online 27 September 2012
* Corresponding authors. Address: Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, #50, Irwon-dong, Gangnam-gu, Seoul 138-225, Republic of Korea. Tel: +82 2 3410 2518; fax: +82 2 3410 6368.
E-mail addresses: rfalim@skku.edu (H.K. Lim), rhimhc@skku.edu (H. Rhim).
† These authors contributed equally to this work.
Abbreviations: RFA, radiofrequency ablation; HCC, hepatocellular carcinoma; LTP, local tumor progression; IDR, intrahepatic distant recurrence; ER, extrahepatic recurrence; OS, overall survival; US, ultrasonography; CT, computed tomography; MRI, magnetic resonance imaging; AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer.

Introduction

Since the first clinical study in 1995 [1], clinical implications of percutaneous radiofrequency ablation (RFA) in the treatment of early-stage hepatocellular carcinoma (HCC) have expanded. Currently, RFA is recognized as a curative modality for early-stage HCC [2] whose outcomes are comparable to those of surgery, as evidenced by many studies [3–7]. Clinical roles of percutaneous RFA are actually more meaningful than those of surgery from the viewpoint that RFA could be applied to patients whose hepatic functional reserve is insufficient to endure surgery, and can be conducted repeatedly with the same patient [8]. Despite such a large potential, long-term (i.e., more than 10 years) follow-up results are rare [9] because of its relatively short history of clinical applications although there has been plenty of reports regarding 5-year outcomes [8,10–12].

During the last 12 years, our institution has performed percutaneous RFA of HCC in more than 3000 patients, and approximately more than 40% were performed as a first-line therapy. Through these clinical experiences, the best way to perform RFA has evolved toward developing an effective as well as safe treatment, for example, the use of artificial ascites techniques, multiple overlapping ablations with "switch box", or fusion image guidance. In addition, antiviral therapy has become more and more readily available, all of which seemingly affect therapeutic outcomes regarding not only recurrence but also overall survival (OS). These long-term changes raise the necessity for a new analysis of the longer-term outcomes.

Therefore, the purposes of our study were to evaluate 10-year follow-up results with regard to recurrences and OS after

Cancer

percutaneous RFA as a first-line therapeutic option for the treatment of early-stage HCC, and to assess factors significantly influencing survival.

Patients and methods

This study was approved by the institutional review board of our hospital, and informed consent from patients was waived because this was a retrospective clinical study. However, written informed consent for RFA procedures and the use of data for research purposes were obtained from patients prior to every treatment.

Study population

We reviewed the departmental database of RFA procedures and retrieved the following data. Between April 1999 and April 2011, a total of 10,334 planning ultrasonography (US) examinations were conducted by one of six radiologists (Y.S.K., H.K.L., H.R., M.W.L., D.C., and W.J.L.) on a referral basis, and among them, US-guided percutaneous RFAs were performed for the treatment of a total of 5097 HCC tumors in 3084 patients (male:female = 2402:682 mean age, 58.5 years; age range, 24–89). Out of 5097 HCC tumors, 1502 tumors (mean size, 2.2 cm; size range, 0.5–4.9 cm) in 1305 consecutive patients (male:female = 993:312; mean age, 58.4 years; age range, 28–86 years), which were initially diagnosed and treated with US-guided percutaneous RFA as a first-line option, were analyzed in this study (Fig. 1). Two hundred six tumors (206/1502, 13.7%) were confirmed as HCC by means of a US-guided core needle biopsy, and the remaining 1296 tumors (1296/1502, 86.3%) were considered to be HCC, based on one of two clinical criteria from the American Association for the Study of Liver Diseases according to the time of RFA procedures [2,13].

Our institutional inclusion criteria for percutaneous RFA procedures were as follows: (1) presence of a single nodular HCC <5 cm in maximum diameter; (2) presence of multinodular HCCs (⩽3 in number, each <3 cm in maximum diameter); (3) absence of portal venous thrombosis; (4) Child-Pugh class A or B; and (5) prothrombin time ratio >50% (prothrombin time with an international normalized ratio <1.7) and platelet count >50,000 cells/mm^3 (50 cells × 10^9/L). The decision to perform RFA was made by consensus of an interdisciplinary discussion. In cases of a single HCC in a Child-Pugh class A patient with neither portal hypertension nor hyperbilirubinemia, surgical resection was primarily considered. However, patients' age, co-morbidity and preference were also taken into account. The technical feasibility of RFA was assessed with planning US exam [14] by the radiologist who would perform the procedure. The presence of ascites was not either a relative or an absolute contraindication. Clinical characteristics of the patients and tumors analyzed in this study are summarized in Table 1.

RFA procedure

All RFA procedures were performed percutaneously under US guidance. Procedures were performed on an inpatient basis by one of six radiologists (Y.S.K., H.K.L., H.R., M.W.L., D.C., and W.J.L.), who had at least seven years of experience with this procedure, by the end of the study period. Details about RFA procedures are reported as Supplementary data.

Follow-up after RFA

For early evaluation of the therapeutic response or possible complications, either contrast-enhanced US (n = 199, 15.2%), CT (n = 1091, 83.6%), or MRI (n = 15, 1.5%) was performed within 24 h. Between July 2002 and December 2003, contrast-enhanced US using a microbubble contrast agent (SH U508A, Levovist; Bayer

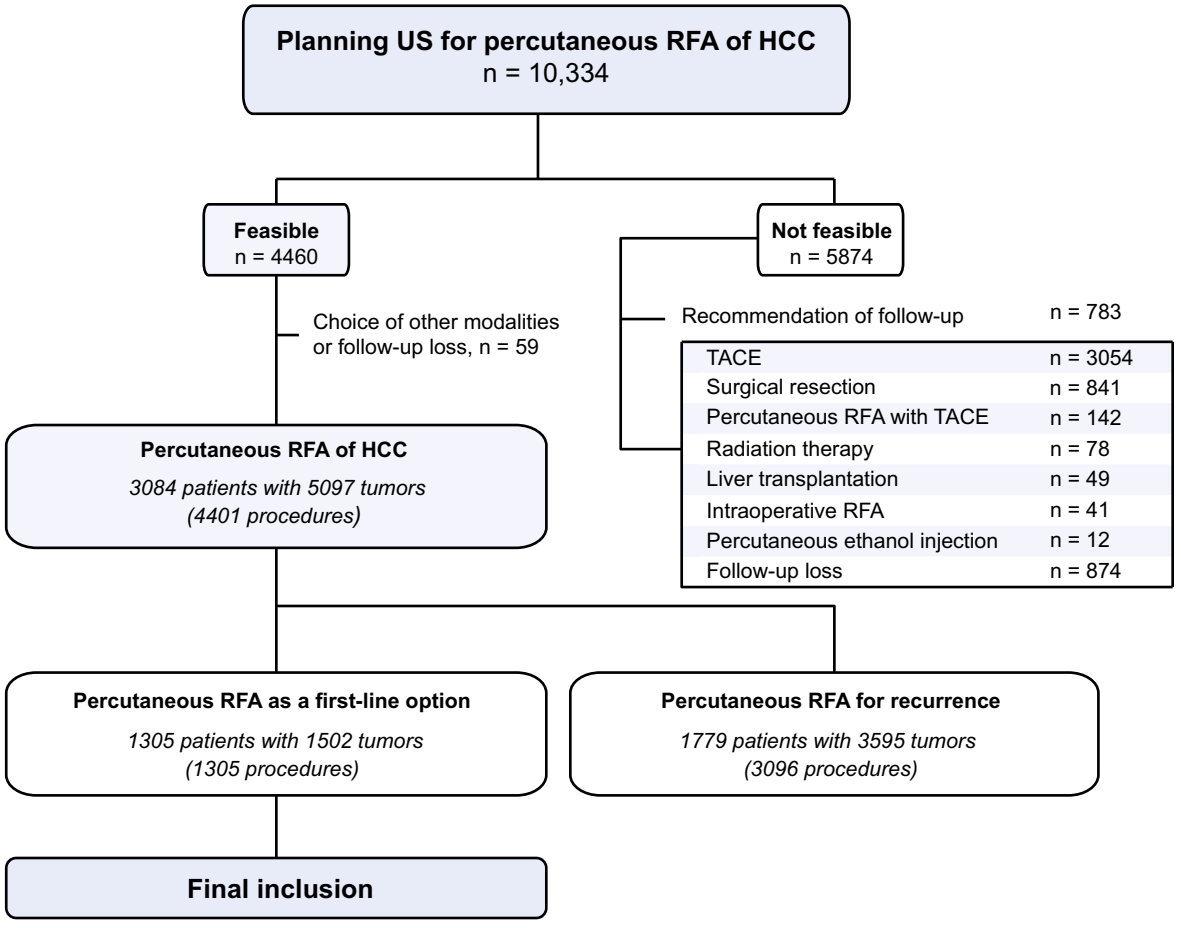

Fig. 1. Flow of study inclusion. A total of 10,334 patients were examined with planning US, and 1305 patients with 1502 HCC tumors, treated with percutaneous RFA as a first-line option, were finally included.