Initial radiofrequency ablation failure for hepatocellular carcinoma: repeated radiofrequency ablation versus transarterial chemoembolisation

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AIM: To compare the long-term therapeutic outcomes of repeated radiofrequency ablation (RFA) with that of transarterial chemoembolisation (TACE) in patients with local tumour progression (LTP) after initial RFA treatment for hepatocellular carcinoma (HCC).

MATERIALS AND METHODS: This retrospective study was approved by the institutional review board and the requirement for informed consent was waived. Between July 2006 and February 2012, 713 patients underwent RFA for single HCC as a first-line treatment. Fifty-eight patients who showed LTP as initial tumour recurrence post-RFA treatment were included. Patients were treated with either repeated RFA (n=33) or TACE (n=25). TACE was performed as an alternative therapeutic option when repeated RFA was not feasible based on the planning ultrasonography. Recurrence-free and overall survival rates were estimated using the Kaplan–Meier method. Prognostic factors for outcomes were evaluated using the Cox proportional hazards model.

RESULTS: Both groups did not show significant differences in terms of baseline characteristics, with the exception being the proportion of subphrenic tumours (p=0.031). The RFA and TACE groups did not differ significantly in their 5-year recurrence-free and overall survival rates (17% versus 10.7% and 72.7% versus 51.9%, respectively, with all p-values >0.05). In addition, multivariate analyses revealed that type of treatment was not associated with recurrence-free or overall survival in patients with post-RFA LTP.

CONCLUSION: TACE is an effective treatment, comparable to repeated RFA, in patients with LTP after initial RFA when repeated RFA is not feasible.

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Introduction

Radiofrequency ablation (RFA) has been added to the international hepatocellular carcinoma (HCC) management guidelines as a curative treatment modality for very early or early-stage HCCs1–4; however, despite recent advances in RFA technology,5 the risk of local tumour progression (LTP) following RFA treatment for HCC is still problematic. For patients subjected to RFA treatment, tumour recurrence at 5 year is 4–27%.6–8 This is due to the inherent limitations of the local thermal ablation method: it does not allow for the systemic removal of a hepatic segment to eliminate minute satellites around the main tumour,9,10 and it is difficult to evaluate the exact tumour-free margin during the RFA procedure.11

Recently, the utilisation of RFA as a treatment of HCC has markedly increased over time.12 Therefore the number of patients with post-treatment LTP would have increased. In clinical practice, LTP in patients who have undergone RFA as the first-line treatment for HCC due to difficulty of surgical treatment are usually treated with local-regional therapies such as repeated RFA or transarterial chemoembolisation (TACE) due to the same reason; however, treating LTP with RFA is difficult as LTP after RFA tends to occur in high-risk locations, such as subphrenic or perivascular areas, because such sites are often associated with technical difficulties during the initial RFA procedure. Therefore, the high-risk location would hamper the achievement of complete ablation with sufficient ablative margins.13,14 In these cases, treating LTP with RFA is often difficult and TACE could be an alternative treatment; however, few data exist for outlining an optimal protocol for the treatment of LTP after initial RFA.15 In addition, there have been no studies comparing the therapeutic efficacy of these two modalities for LTP treatment after initial RFA.

Therefore, the aim of the present study was to evaluate retrospectively the recurrence-free and overall survival of repeated RFA and TACE in LTP patients who had undergone RFA for HCC as a first-line treatment. A second aim was to analyse the prognostic factors for these outcomes.

Materials and methods

The institutional review board approved this retrospective study and waived the requirement for informed consent. The terminology used for the description of the RFA and TACE procedures followed the proposed guidelines.16,17

Patients

The inclusion criteria of RFA for patients with HCCs were identical to those described in previous studies6,14: (a) very early or early stage HCCs defined as a single tumour ≤5 cm in diameter, or 2–3 nodules ≤3 cm in diameter without extra-hepatic metastasis or any macro-vascular invasion (Barcelona Clinic Liver Cancer [BCLC] stage 0 or A); (b) Child–Pugh class A or B; and (c) a prothrombin time within the normal range and platelet count ≥50,000 cells/ml3. Between July 2006 and February 2012, 713 consecutive patients underwent RFA for single HCC as a first-line treatment at Samsung Medical Center, Sunkyunkwan University, Seoul, Korea. First-line treatment was defined as the absence of prior treatment during HCC diagnosis. Among them, 126 patients (17.7%) exhibited LTPs during follow-up after RFA treatment.

The LTP diagnosis was based on imaging results and indicated by a newly developed lesion, showing arterial enhancement and delayed wash-out around the previously treated zone.16,18 From these patients, 69 patients who exhibited LTPs as the initial tumour recurrence were selected to exclude patients with possible intrahepatic metastasis from other untreated tumours. Among these patients, 11 were excluded from the study for the following reasons: (a) patients who had been subjected to other treatments besides repeated RFA or TACE (n=6); (b) patients with tumour thrombus along with the LTP (n=2); (c) loss to follow-up at 1 month after treatment (n=1); and (d) the technical failure of repeated RFA or TACE to treat the LTP (n=2). The remaining 58 patients (37 men and 21 women; age range, 38–78 years) comprised the study cohort (Electronic Supplementary Material Fig. S1). TACE was performed as an alternative therapeutic option for LTP when repeated RFA was not feasible on planning ultrasonography (US) for the following reasons: poor sonic window or RF electrode path (n=19) and poor lesion conspicuity (n=6). Treatment technical failure was defined as the presence of an enhancing tumour on 1-month follow-up computed tomography (CT) after the initial treatment. Two patients (3.3%, 2/61) with incomplete treated tumours after initial treatment underwent surgical resection or RFA for tumour control and they were excluded from recurrence analysis.

Repeated RFA

The planning US for RFA was performed at an outpatient clinic to assess the feasibility of repeated RFA,19 When considered feasible, patients were treated with repeated RFA on an inpatient basis by four different radiologists (H.K.L., H.R., Y.S.K. and M.W.L.), each with at least 7 years of clinical experience in RFA before the starting point of this study.

All procedures were performed percutaneously under US guidance with local anaesthesia and conscious sedation. They were performed by using one of the following US systems: iU22 (Philips Medical Systems, Bothell, WA, USA), LOGIQ, E9 (GE Healthcare, Waukesha, WI, USA), and Acuson Sequoia 512 (Siemens Medical Solutions, Mountain View, CA, USA). The fusion imaging technique (Volume Navigation, GE Healthcare) was routinely used after July 2010.20 Commercially available internally cooled electrode systems: iU22 (Philips Medical Systems, Bothell, WA, USA), LOGIQ, E9 (GE Healthcare, Waukesha, WI, USA), and Acuson Sequoia 512 (Siemens Medical Solutions, Mountain View, CA, USA). The fusion imaging technique (Volume Navigation, GE Healthcare) was routinely used after July 2010.20
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