CLINICAL STUDY

# Transarterial Chemoembolization versus Radiofrequency Ablation for Recurrent Hepatocellular Carcinoma after Resection within Barcelona Clinic Liver Cancer Stage 0/A: A Retrospective Comparative Study

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## ABSTRACT

**Purpose:** To compare outcomes of transarterial chemoembolization with radiofrequency (RF) ablation in treatment of recurrent hepatocellular carcinoma (HCC) after resection within Barcelona Clinic Liver Cancer (BCLC) stage 0/A.

**Materials and Methods:** From January 2007 to December 2011, 110 consecutive patients with recurrent HCC meeting BCLC stage 0/A criteria underwent transarterial chemoembolization (n = 78; mean tumor size, 1.9 cm ± 1.0) or RF ablation (n = 32; mean tumor size, 1.9 cm ± 0.6) as initial treatment. The primary outcome was overall survival (OS). Kaplan-Meier method was used to construct survival curves, which were compared by log-rank test. Prognostic factors for OS were analyzed using univariate and multivariate Cox proportional hazard models.

**Results:** No significant differences between baseline clinical characteristics of the 2 treatment groups were identified. The 1-, 3-, and 5-year OS rates were 89.7%, 61.0%, and 36.6% for the transarterial chemoembolization group and 90.1%, 72.8%, and 60.0% for the RF ablation group. There was no significant difference in OS rates between the groups ($P = .159$). Subgroup analysis indicated that RF ablation achieved better survival than transarterial chemoembolization among patients ≤ 55 years old and patients with BCLC stage 0 ($P = .036$ and $P = .045$). Multivariate analysis revealed that serum albumin (≤ 35 g/L) (hazard ratio = 2.797; 95% confidence interval, 1.366–2.726; $P = .005$) and α-fetoprotein (> 400 ng/mL) (HR = 2.336; 95% CI, 1.210–4.508; $P = .011$) levels before treatment were 2 significant risk factors for poor prognosis.

**Conclusions:** Transarterial chemoembolization might provide a similar OS as RF ablation in patients with recurrent BCLC stage A HCC. However, RF ablation could provide better OS in patients with recurrent BCLC stage 0 HCC.

## ABBREVIATIONS

AFP = α-fetoprotein, BCLC = Barcelona Clinic Liver Cancer, HCC = hepatocellular carcinoma, OS = overall survival, RECIST = Response Evaluation Criteria In Solid Tumors

Hepatic resection is a well-accepted therapy to achieve long-term survival in patients with hepatocellular carcinoma (HCC). However, > 70% of patients experience tumor recurrence often isolated to the liver within 5 years after resection, which is the major cause of death in long-term evaluations (1,2). This high rate of HCC recurrence presents an important clinical challenge, and appropriate treatment is crucial in improving long-term outcome after hepatectomy. At the present time, consensus treatment strategies regarding recurrent HCC are lacking. Repeat resection and radiofrequency (RF)

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ablation are good options for treating localized recurrent HCC, attaining similar survival benefits (5-year overall survival [OS], 35.2% and 29.1%) (3). However, in practice, some patients with localized intrahepatic recurrence are ineligible for local ablation therapy or repeat liver resection because of difficult tumor location, limited hepatic reserve unsuitable for repeat resection, medical comorbidities, or other causes. In these settings, transarterial chemoembolization is used as an alternative option. Although transarterial chemoembolization is generally accepted as a palliative treatment for intermediate to advanced HCC, several retrospective cohort studies demonstrate that transarterial chemoembolization can offer acceptable survival outcomes for patients with treatment-naïve early HCC (5-year OS, 30%–74.2%), which is comparable to hepatic resection or RF ablation (5-year OS, 56%–93.6%) (4–7). However, it is unclear whether transarterial chemoembolization could produce equivalent therapeutic results for solitary or localized recurrence after resection, especially when curative treatment is unfeasible. To define the role of transarterial chemoembolization in localized recurrent HCC after resection, we compared the outcomes of patients with recurrent HCC fulfilling Barcelona Clinic Liver Cancer (BCLC) stage 0/A criteria who underwent transarterial chemoembolization or RF ablation as the initial treatment.

## MATERIALS AND METHODS

### Patient Selection

This single-center, retrospective study was approved by the institutional review board. The study participants included patients who received either transarterial chemoembolization or RF ablation as the initial treatment for recurrent HCC after resection at our hospital between January 2007 and December 2011. Patients' demographic and clinicopathologic data, response to treatment, and survival were retrieved and analyzed retrospectively from the maintained HCC database.

The diagnosis of HCC was made on the basis of pathology or noninvasive American Association for the Study of Liver Diseases radiologic criteria of typical imaging features (arterial enhancement followed by portal or delayed washout) on dynamic contrast-enhanced computed tomography (CT) and/or magnetic resonance (MR) imaging. Patients who met the following criteria were included: diagnosis of recurrent HCC after resection; recurrent tumor or tumors with a single tumor $\leq$ 5 cm or tumor number $\leq$ 3, each $\leq$ 3 cm; Child-Pugh class A or B; Eastern Cooperative Oncology Group performance status 0–2; albumin level $>$ 25 g/L; alanine aminotransferase and aspartate aminotransferase levels $<$ 5 times upper normal limit; total serum bilirubin level $<$ 51.5 μmol/L; serum creatinine level $<$ 180 μmol/L; prothrombin time $<$ 18 seconds; adequate bone marrow (leukocyte count $> 3 \times 10^9$/L, platelet count $\geq 50 \times 10^9$/L). Exclusion criteria were as follows: tumor stage BCLC C at initial liver resection; previous treatment with chemotherapy, hepatic arterial infusion, or radiation; treated with liver transplantation; evidence of coagulopathy; septicemia; and second primary malignancy.

The choice of treatment was determined by the consultant physicians (all with at least 10 years of experience in hepatic interventions). Written informed consent was obtained from each patient before the treatment procedure. Transarterial chemoembolization was chosen as an alternative treatment for recurrent BCLC stage 0/A HCC unsuitable for RF ablation for various reasons mainly including challenging tumor locations in proximity to critical structures, difficult-to-reach lesions, poorly visualized lesions on ultrasonography, inadequate safety margin, patient desire, and cost.

In this study, 162 patients underwent transarterial chemoembolization, and 36 patients underwent RF ablation for recurrent HCC after resection. Based on the inclusion and exclusion criteria, 78 patients who underwent transarterial chemoembolization and 32 patients who underwent RF ablation as the initial treatment for recurrent HCC meeting BCLC stage 0/A criteria were included in the final analyses (Fig 1). The study comprised 99 men and 11 women, with a median age of 55 years (range, 24–77 y). Among these patients, 90.0% (99 of 110) were found to be positive for hepatitis B surface antigen. The mean tumor diameter for the transarterial chemoembolization group was 1.9 cm ± 1.0 and for the RF ablation group was 1.9 cm ± 0.6 ($P$ = 0.958). Demographic and baseline data of patients were similar across both groups (Table 1).

### Transarterial Chemoembolization

Transarterial chemoembolization was performed by experienced physicians who had at least 10 years of experience in transarterial chemoembolization according to our institutional protocol as described previously (8,9). Briefly, visceral arteriograms were obtained to ascertain hepatic artery anatomy, tumor staining, and the tumor feeding arteries. A 5-F RH catheter (Cook, Inc, Bloomington, Indiana) was advanced into the desired hepatic artery as close as possible to the tumor. Microcatheters (2.7-F PROGREAT Microcatheter; Terumo, Tokyo, Japan) were used to superselect the feeding artery if needed. Chemotherapeutic agents including fluorouracil 1.0 g and cisplatin 80 mg (or oxaliplatin 150 mg) were infused followed by an emulsion of mitomycin C 10 mg and ethiodized oil (Lipiodol Ultra-Fluide; Guerbet, Villepinte, France) 5–10 mL. The dose of chemoembolization was adjusted according to liver function and peripheral leukocyte and platelet levels. The dose of Lipiodol was adjusted according to tumor blood supply and tumor sizes. When embolization with Lipiodol mixture alone was insufficient to block tumor-feeding arteries, additional embolization with 1- to 2-mm gelatin sponge