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Albumin-bilirubin grade predicts the outcomes of liver resection versus radiofrequency ablation for very early/early stage of hepatocellular carcinoma

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ABSTRACT

Background and purpose: Whether liver resection or ablation should be the first-line treatment for very early/early hepatocellular carcinoma (HCC) in patients who are candidates for both remains controversial. The aim of this study was to determine if the newly-developed Albumin-Bilirubin (ALBI) grade might help in treatment selections and to evaluate the survival of patients treated with liver resection and radiofrequency ablation (RFA).
Methods: Patients with BCLC stage 0/A HCC who were treated with curative liver resection and RFA from 2003 to 2013 were included. Baseline clinical and laboratory parameters were retrieved and reviewed from the hospital database. Liver function and its impact on survival was assessed by the ALBI score. Overall and disease-free survivals were compared between the two groups.
Results: 488 patients underwent liver resection (n = 318) and RFA (n = 170) for BCLC stage 0/A HCC during the study period. Liver resection offered superior survival to RFA in patients with BCLC stage 0/A HCC in the whole cohort. After propensity score matching, liver resection offered superior overall survival and disease-free survival to RFA in patients with ALBI grade 1 (P = 0.0002 and P < 0.0001 respectively). In contrast, there were no significant

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differences in overall survival and disease-free survival between liver resection and RFA in patients with ALBI grade 2 (P = 0.7119 and 0.3266, respectively).
Conclusions: Liver resection offered superior survival to RFA in patients with BCLC stage 0/A HCC. The ALBI grade could identify those patients with worse liver function who did not gain any survival advantage from curative liver resection.

Introduction

The clinical outcome of patients with hepatocellular carcinoma (HCC) depends on not only tumour burden but also hepatic function, performance status and treatment modality. Among more than 10 different staging systems for HCC, the Barcelona Clinic Liver Cancer (BCLC) system is currently the most widely accepted staging system to provide prognostic information and, simultaneously, guide therapeutic options.[1–3] It is the only staging system for HCC endorsed by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL).[4,5] Curative treatments, including surgical resection, transplantation and ablation, are recommended for patients with very early/early stage (BCLC 0/A) disease.[5,6] Despite being an effective treatment which offers good long-term survival, the transplantation option is limited by organ shortage, especially in Asian-Pacific countries.[7] Liver resection and ablation are therefore the mainstay of curative therapeutic options in Asian-Pacific countries.[8]

Liver resection is recommended for patients with BCLC stage 0 disease (single tumour smaller than 2 cm and Child-Pugh grade A) and a subset of BCLC stage A disease (a single tumour without portal hypertension or hyperbilirubinemia). On the other hand, patients with another subset of BCLC stage A disease (portal hypertension, hyperbilirubinemia or multiple tumour nodules) are recommended for ablation.[5,6] Recently, the BCLC group has suggested that ablation should be the first-line treatment for BCLC stage 0 disease because case-control and modeling studies show that ablation is comparably effective and more cost-effective than liver resection at this early stage HCC.[6,9]

The aim of the present study was to evaluate the extent to which the newly developed albumin-bilirubin (ALBI) grade might help in patient selection for liver resection or ablation. We also evaluate the survival of patients who were treated with liver resection or radiofrequency ablation (RFA).

Methods and materials

Patients

This retrospective cohort recruited patients who received potentially curative treatment (liver resection and RFA) for primary HCC from January 2003 to December 2013 at the Prince of Wales Hospital, Hong Kong.

The study was approved by the institutional review board. Baseline clinical and laboratory parameters were retrieved and reviewed from the hospital database. All parameters investigated were measured within 1 week before treatment. The ALBI score was computed by the formula, $-0.085 \times (\text{albumin g/l}) + 0.66 \times \log(\text{bilirubin } \mu\text{mol/l})$. Patients were stratified into 3 groups according to previously described cut-offs resulting in 3 grades: ALBI grade 1 (≤ -2.60), grade 2 (> -2.60 to -1.39) and grade 3 (> -1.39).[10]

Portal hypertension was defined according to AASLD/EASL guidelines as the presence of esophageal varices or thrombocytopenia (platelet count $< 100 \times 10^9$/l) associated with splenomegaly.[5] The blood tests, except viral serology, were taken within 1 week before treatment. All patients were staged according to the BCLC, CLIP and CUPI systems.[11–13] Only patients with BCLC stage 0/A disease were included. Among BCLC stage A, patients were further classified into A1 (a single tumour with Child-Pugh grade A, no portal hypertension and normal serum bilirubin), A2 (a single tumour with Child-Pugh grade A, portal hypertension and normal serum bilirubin), A3 (a single tumour with Child-Pugh grade A, portal hypertension and hyperbilirubinemia) and A4 (2 or 3 tumours less than 3 cm, Child-Pugh grade A or B).

After treatment, all patients were followed up according to institutional practice including serum alpha-fetoprotein (AFP) measurement at every visit and ultrasound or contrast computed tomography every 6–12 months. The duration of follow-up was measured from the date of operation to the date of the last follow-up before we analyzed the data or the date of death. Overall survival was measured from the time of liver resection to the time of HCC-related death or last follow-up if death had not occurred. Disease-free survival was measured from the time of liver resection to the time of radiological evidence of tumour relapse.

Statistical analyses

Continuous variables were expressed in mean ± standard deviation (SD) or median with interquartile range (IQR). Comparison between groups was analyzed by chi-square test or Fisher's exact test for categorical variables, and Student's t test or Mann–Whitney test for continuous variables as appropriate. Correlation was evaluated by the Spearman correlation test. The Kaplan–Meier method was used to estimate the survival rates for different groups. The equivalences of the survival curves were tested by log-rank statistics. The Cox proportional hazards model was employed for univariate and multivariate survival analyses. Propensity score matching

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