



ORIGINAL ARTICLE

Better prognosis of hepatic resection combined with antiviral therapy for HBV-related hepatocellular carcinoma with BCLC Stage B/C



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Summary *Background:* Whether hepatic resection (HR) could be performed for patients with Barcelona Clinic Liver Cancer (BCLC) B/C stage hepatocellular carcinoma (HCC) is controversial, and the safety and clinical value of HR combined with antiviral therapy for hepatitis B virus (HBV)-related HCC with BCLC-B/C stage remain to be investigated.

Methods: We retrospectively evaluated 126 patients with BCLC stage B/C HCC who underwent HR. These patients were divided into the antiviral group (Group A, $n = 86$) and the control group (Group B, $n = 40$). The operative indications and prognosis of 126 patients were analyzed.

Results: The 1-year, 3-year, and 5-year disease-free survival (DFS) rates for Group A and Group B were 55.4%, 36.1%, 33.7% and 53.8%, 28.2%, 23.1%, respectively. The corresponding overall survival (OS) rates for the two groups were 89.2%, 61.4%, 45.8% and 82.1%, 48.7%, 33.3%, respectively. The DFS and OS for Group A were better than for Group B ($p = 0.013$, and $p = 0.038$, respectively). Antiviral therapy was an independent protective factor of late tumor recurrence [hazard ratio (HR) = 0.391, 95% confidence interval (CI): 0.190–0.806, $p = 0.011$] but not of early tumor recurrence.

Conflicts of interest: All authors declare no conflicts of interest.

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Conclusion: It is safe and feasible to perform HR combined with antiviral therapy for HBV-related HCC with BCLC stage B/C.

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1. Introduction

Hepatocellular carcinoma (HCC) is the fifth most common malignancy in the world, and its incidence is increasing in some countries.^{1,2} In the past few decades, although several novel treatment options have been applied in the clinical practice, curative hepatic resection (HR) predominates in the treatment for HCC. However, the prognosis of HCC patients is discouraging, largely due to a high incidence of intrahepatic recurrence.

According to the Barcelona Clinic Liver Cancer (BCLC) staging system, HR is recognized as a first-line treatment for patients who have well-preserved liver function and HCC satisfying the BCLC A stage.³ In such patients, the 5-year survival rate after HR remains > 50%.^{4–7} Recently, a large-scale multicenter retrospective study demonstrated that HR is a safe and effective treatment for HCC outside BCLC A stage. HR can provide a survival benefit over transarterial chemoembolization (TACE) for patients with BCLC B/C stage HCC on condition that such patients have good liver function.⁸

In most Asia-Pacific countries, 75–80% of HCC are related to chronic hepatitis B virus (HBV) infection. In a retrospective study, researchers showed that antiviral therapy effectively improved safety for HBV-related large HCC patients who underwent major hepatectomy.⁹ Furthermore, ample evidence indicates that continuous treatment with nucleos(t)ide analogues (NAs) in HBV-related HCC patients after HR reduces the risk of HCC recurrence and significantly improves overall survival (OS).^{10,11} In China, the Chinese Medical Association recommends that NAs should be applied to HBV-related HCC patients with detectable levels of HBV DNA, regardless of alanine aminotransferase levels.¹² Nevertheless, there is little study of whether HR combined with antiviral therapy can reduce postoperative recurrence and improve long-term survival for patients with BCLC B/C stage HCC.

In this retrospective study, we described the clinical and pathologic data of patients with BCLC B/C stage HCC, and compared the therapeutic value of HR with the combination therapy of HR plus antiviral treatment.

2. Patients and methods

This study was approved by the ethics committees of the third affiliated hospital of Sun Yat-Sen University, and it was conducted in accordance with the Declaration of Helsinki.

2.1. Patients

In this retrospective study, a total of 283 patients were identified who were diagnosed with HBV-related HCC and

underwent HR between January 2006 and March 2010 at the Department of Hepatic Surgery, The Third Affiliated Hospital of Sun Yat-Sen University, China. The diagnosis of HCC was based on histopathological study of the resected specimens. All intraoperative and postoperative complications were recorded retrospectively.

2.2. Preoperative investigations

All patients were examined with preoperative evaluation protocol, including chest radiography, ultrasonography of the abdomen, contrast enhanced computed tomography or magnetic resonance imaging of the abdomen, and laboratory blood tests. The serum HBV-deoxyribonucleic acid (HBV-DNA) levels were detected using the real-time polymerase chain reaction (PCR) method (HBV PCR Kit, Da An Gene Co., Ltd. of Sun Yat-Sen University, Guangzhou, China). The lower limit of detection was 100 IU/mL. The preoperative diagnosis of HCC was based on the diagnostic criteria for HCC used by the European Association for the Study of the Liver (EASL).¹³

2.3. Surgical procedure

In our study, HR should not be carried out in patients with a small liver remnant or severe cirrhosis and with Child-Pugh C liver function. A bilateral subcostal incision was used. Intraoperative ultrasonography routinely was used to assess resectability of the tumor, and to assess the relationship of the tumor to vascular structures. Pringle maneuver was applied to occlude the blood inflow of the liver. Liver parenchymal transection was performed with the clamp-crushing method. Curative resection was defined as the removal of the entire tumor with a histologically proved tumor-free surgical margin and no tumor thrombus in the major branches of the veins and bile duct. Liver resection as potentially curative therapy was performed in selected patients in BCLC stage B/C, as well as in patients with portal hypertension (PHT).

2.4. Inclusion criteria

Patients who met all of the following criteria were included in the study: (1) positive test for hepatitis B surface antigen and negative test for antibodies to hepatitis C; (2) HBV-DNA level > 100 IU/mL; (3) BCLC B or C; (4) no lymph nodes and/or distant metastasis; (5) no previous treatment of HCC; (6) no previous history of antiviral therapy; and (7) detailed and precise follow-up records.

In this study, the 147 consecutive HCC cases that received HR were classified into two groups according to whether or not they used antiviral therapy to treat hepatitis B-related BCLC B/C stage HCC. Patients in Group A

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