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ORIGINAL ARTICLE

Microvascular invasion and positive HB e antigen are associated with poorer survival after hepatectomy of early hepatocellular carcinoma: A retrospective cohort study

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KEYWORDS
Early hepatocellular carcinoma;
Microvascular invasion;
HBeAg;
Hepatectomy;
Survival

Summary
Background: We aimed to identify the independent predictive factors of microvascular invasion (MVI) for curative resection of HCC and to investigate the impacts of MVI and HBeAg on long-term recurrence and survival after resection.
Methods: The clinicopathological parameters of 237 patients with HCC with MVI who underwent hepatic resection from April 2005 to November 2010 were investigated. Clinical features and factors associated with the clinical outcomes of 386 patients with HCC without MVI were used for comparison.
Results: Multivariate stepwise logistic regression analysis revealed that alpha-fetoprotein level > 100 μg/L, positive HBeAg, and tumour size were independent prognostic factors in patients with HCC with MVI. The overall survival (OS) of patients in the HCC with MVI group was significantly poorer compared with the HCC without MVI group ($P < 0.001$). However, patients with HCC without MVI group exhibited a significantly better recurrence-free survival rate (RFS) ($P < 0.001$). While the HCC with positive HBeAg group exhibited significantly lower OS compared with the HCC with negative HBeAg group ($P = 0.007$).

Abbreviations: HCC, hepatocellular carcinoma; TNM, Tumor-Node-Metastasis; BCLC, Barcelona clinic liver cancer; RFS, recurrence-free survival; OS, overall survival; ALT, alanine aminotransferase; AFP, alpha-fetoprotein; HR, hazard ratio; CI, confidence interval.

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Conclusions: AFP level > 100 μg/L, positive HBeAg, and tumour size > 2 cm are independent indicators of poorer prognosis for HCC with MVI. The present study confirmed that microvascular invasion itself had a negative impact on patient survival; moreover, HBeAg was an independent risk factor influencing OS, while not RFS of patients with HCC underwent hepatectomy. It is important to predict the presence of MVI before hepatic resection to determine treatment strategies.

Background

Hepatocellular carcinoma (HCC) is one of the leading aetiologies of global cancer-related mortalities and is especially common in China [1—4]. Although wide regional disparity in distribution and aetiology of HCC exists, the prevalence of hepatitis B virus (HBV) and/or hepatitis C virus (HCV) can strongly predispose to chronic liver disease, cirrhosis and subsequent HCC development [5]. The incidence and mortality of liver cirrhosis in HCC patients undergoing hepatic resection varies [6]. The development of techniques for tumour staging and improved criteria for selection of patients different therapies have led to improved survival in carefully selected HCC patients [7,8]. However, the factors impacting postoperative survival remains a major concern, especially when patients have early HCC concomitant with microvascular invasion.

Early HCC generally exhibits a good prognosis after surgical resection, and these patients are regularly reported as a homogeneous group [9]. However, prognosis following hepatic resection in those patients with early HCC concomitant with microvascular invasion (MVI) may vary. Our previous study demonstrated that tumour size > 2 cm, multifocality, non-anatomic resection and vascular invasion may be used to stratify HBV-related cirrhotic patients with early HCC after resection [10]. Similarly, several factors are responsible for possible reduced survival after hepatic resection for early HCC [9,11]. Cirrhotic patients with HCC exhibited increased survival as a consequence of improved management of the tumour and cirrhosis [6]. Clinicopathological factors may exists that can enable better prognostic stratification of patients with early HCC concomitant with MVI. In addition, although tumour parameters, such as tumour size, have been investigated in HCC patients with cirrhosis [12], the interplay between tumour size and other prognostic factors, such as multifocality in a cohort of patients exclusively with early HCC concomitant with MVI, has not been specifically investigated.

Liver transplantation (LT) and liver resection are both curative therapeutic modalities. LT is best reserved for patients with compromised liver function and multifocal disease, whereas patients with solitary tumors and well-preserved liver function are good candidates for hepatectomy. Partial hepatectomy is a well-validated treatment strategy for early HCC, which has become more feasible with satisfactory safety and efficacy profiles due to more advanced surgical techniques and perioperative care. Meanwhile, partial hepatectomy is an effective treatment for early HCC; however, long-term survival may vary in early HCC patients [13,14]. Partial hepatectomy should be performed when technically feasible (following embolization or other procedures). However, short- and long-term outcomes of patients undergoing partial hepatectomy due to MVI and HBeAg of HCC have not been addressed to date [3].

The objective of this study was to identify the independent predictive factors of MVI for curative resection of HCC and to investigate the impacts of MVI and HBeAg on long-term recurrence and survival after resection.

Patients and methods

Patients and study design

This is a retrospective study of consecutive patients who underwent partial hepatectomy for HCC between April 2005 and November 2010 at the Department of Hepatic Surgery, Eastern Hepatobiliary Surgery Hospital, Shanghai, China. Data were prospectively collected in a computer database. Data analysis was performed retrospectively. Additional data were obtained by reviewing medical records. All HCC participants were divided into two groups based on the presence of MVI. Informed consent was obtained from all participants. The research protocol of this study was discussed and approved by the Clinical Research Ethics Committee of the Eastern Hepatobiliary Surgery Hospital.

Early HCC was defined as HCC with tumor size $\leq$ 5 cm and absence of nodal involvement, metastases, or major vascular invasion. Strict inclusion criteria were used in this study: histopathologically demonstrated HCC; cirrhosis based on specimen pathology (grade 4 fibrosis); tumours less than 5 cm in size and absence of nodal involvement, metastases, or major vascular invasion; patient underwent hepatic resection (not ablation or transplantation); no history of any other malignancy; no previous anticancer treatment; and complete resection of macroscopic liver tumours. The following exclusion criteria were employed: without microscopic confirmation of HCC; presence of HCV-positive serology or human immunodeficiency virus (HIV) infection; tumours of undetermined origin; mixed type of primary liver cancer that was confirmed histopathologically; perioperative mortality; extrahepatic tumour extension and/or major vascular invasion and/or early recurrence (1 month) and/or early loss to follow-up (6 months); with nodal disease (N1) or unknown N classification and with metastatic disease (M1) or unknown M classification.

Moreover, a cohort of consecutive patients, as the validation cohort of this study, who underwent hepatic resection for early HCC were prospectively investigated using the same inclusion and exclusion criteria.

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