



ORIGINAL ARTICLE

High pre-operative serum aminotransferase levels predict local recurrence after curative resection of hepatocellular carcinoma



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KEYWORDS

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Summary Background: Hepatocellular carcinoma is a common cancer with an increasing incidence worldwide because of the dissemination of hepatitis B and hepatitis C virus infection. Surgical resection is the most important therapeutic option with a curative intent. Early tumor detection through screening and improvements in surgical techniques have significantly improved the outcome of patients with hepatocellular carcinoma. However, local recurrence after curative hepatic resection is common and is the most frequent cause of death in these patients.

Patients and Methods: In an attempt to identify the risk factors that predict tumor recurrence, we conducted this retrospective study in a single institution for a 6-year period. Of the 100 consecutive patients who underwent curative tumor resection, we analyzed age, sex, viral etiology (hepatitis B virus vs. hepatitis C virus), preoperative levels of aspartate aminotransferase and alanine aminotransferase, the α -fetoprotein level, underlying liver disease status (chronic hepatitis vs. cirrhosis), number and size of tumors, type of resection, and presence of microvascular invasion. **Results:** In the median follow-up period of 36 months (range, 12–85 months), the 1-year, 3-year, and 5-year overall survival rates were 90%, 84%, and 73%, respectively; tumor recurrence occurred in 38 (38%) patients and was the leading cause of death among the patients who died (15 of 17 patients; 88%). On univariate analysis, the only factor significantly associated with a higher incidence of tumor recurrence was preoperative levels of aspartate aminotransferase greater than twice the upper normal value ($p < 0.01$) and this factor remained significant with multivariate analysis. Subgroup analysis of the risk factor of early tumor recurrence (≤ 2 years) and late tumor recurrence

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(>2 years) was conducted and a preoperative aspartate aminotransferase level greater than twice the upper normal value was still significant in both groups ($p = 0.02$ and $p = 0.044$, respectively). *Conclusion:* Although this is a small-scale study, our findings could be easily applied clinically and used as readily available indicators to help the follow-up algorithm. We also suggest antiviral management as soon as possible for patients with hepatocellular carcinoma undergoing curative resection, especially those with a high preoperative aspartate aminotransferase level.

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Introduction

Hepatocellular carcinoma (HCC) is one of the most common cancers in Asia and Africa and its incidence is increasing worldwide because of the dissemination of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection [1]. It is prevalent in Taiwan with around 10,000 new cases each year and has been the leading cause of cancer death, accounting for approximately 8000 deaths annually [2]. Recent advances in screening, such as ultrasonography, dynamic computed tomography, and magnetic resonance imaging, have made early diagnosis possible and thus improved survival [3,4]. Surgery is the most important therapeutic option for patients with HCC [5,6]. With the progress in early diagnosis and operative techniques, the outcome of patients with HCC after tumor resection have significantly improved, with median survival rates of 80% (range, 63–97%) at 1 year and 50% (range, 17–69%) at 5 years, with a surgical mortality rate of less than 2% [5,7–9]. The wide ranges of survival rates are attributed mainly to differences in the HCC stage among various studies, with an obvious survival advantage in early-stage tumors [10]. However, a significant proportion of patients cannot achieve a cure or a sustained tumor-free survival and the long-term outcome after initial treatment remains unsatisfactory because of a high recurrence rate, ranging from 43% to 100% at 5 years [6,7,11–15].

HCC recurrence has been classified as early (within 2–3 years) or late. Early recurrence is usually due to metastasis from the primary tumor (dissemination from the primary tumor), whereas late recurrence is often due to *de novo* second primary tumors occurring in a cirrhotic or HBV-infected liver [16]. Many factors have been identified to be associated with tumor recurrence after surgical resection, including: the accompanying chronic viral hepatitis status (Ishak activity score); serum levels of albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), α -fetoprotein, and HBV DNA; the extent of hepatectomy; and various tumor factors [12,13,16–21]. Among these, the most powerful predictors of recurrence are the presence of microvascular invasion or additional tumor sites besides the primary lesions, or both [12]. In this retrospective study we aimed to identify the risk factors for recurrence in patients undergoing curative surgical resection in a single institution.

Methods

We retrospectively searched the database of the Chi-Mei Medical Center in southern Taiwan for patients diagnosed

with HCC who underwent curative liver resection from March 2002 to March 2008. The institutional review board approved this study. We used either ultrasonography and abdominal computed tomography (CT) scan or magnetic resonance imaging (MRI) to determine the anatomical location of HCC; the operative procedures were defined according to Couinaud's classification of hepatic segments [22]. Curative resection referred to a complete resection of all macroscopic tumors with tumor clearance along the parenchymal transection line.

We reviewed the medical records of the patients for the underlying causes of hepatitis and coexisting liver diseases. Those patients with cirrhosis were classified according to the Child–Pugh scheme [23]. The clinicopathological variables evaluated included age at surgery, sex, etiology of hepatitis, α -fetoprotein level, microvascular invasion,

Table 1 Clinicopathological features of patients in this study.

Variable	n (%)
Sex	
Male	69 (69)
Female	31 (31)
Etiology of liver disease	
Hepatitis B	52 (52)
Hepatitis C	32 (32)
Hepatitis B + C	6 (6)
Alcohol	7 (7)
Other	3 (3)
Non-neoplastic liver disease	
Liver cirrhosis	79 (79)
Chronic hepatitis	21 (21)
Diameter of main nodule (cm)	
<3	51 (51)
≥3	26 (26)
≥5	23 (23)
Number of nodules	
Single	91 (91)
Multiple	9 (9)
BCLC stage	
Stage 0	25 (25)
Stage A	59 (59)
Stage B	16 (16)
Microvascular invasion	
Positive	2 (2)
Negative	98 (98)

BCLC = Barcelona Clinic Liver Cancer classification.

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