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Postoperative prognostic nutritional index change is an independent predictor of survival in patients with small hepatocellular carcinoma

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Abstract

BACKGROUND: There is limited information concerning the postoperative prognostic nutritional index change (ΔPNI) in hepatocellular carcinoma (HCC). This study was designed to evaluate the prognostic value of ΔPNI in patients with small HCC who underwent liver resection.

METHODS: A retrospective cohort study was performed to analyze 243 patients with small HCC who underwent liver resection. Patients were divided into prognostic nutritional index (PNI)–increased group (n = 161) and PNI-decreased group (n = 82) according to postoperative PNI change. Clinical data, overall survival (OS), and recurrence-free survival (RFS) were statistically compared between the 2 groups, and a multivariate analysis was used to identify prognostic factors.

RESULTS: Multivariable analysis revealed that ΔPNI as independent predictors of OS and RFS in patients with small HCC after liver resection ($P < .01$ for both).

CONCLUSIONS: Decreased PNI, but not low preoperative PNI was an independent risk factor for OS and RFS in patients with small HCC who underwent liver resection.

Hepatocellular carcinoma (HCC) is one of the most common malignancies and the 3rd leading cause of cancer-related death worldwide.[1] Liver resection remains one of the standard treatment methods for small HCC patients who meet the Milan criteria.[2,3] Despite the development in diagnostic techniques and advances in perioperative management, overall survival (OS) remains unsatisfactory because of the high recurrence rate in HCC patients.[4] Further efforts to identify the prognostic factors to better stratify those patients who are likely to benefit from treatments remain necessary. It is widely perceived that survival in HCC depends on tumor morphology, tumor histopathology, underlying liver function, and perhaps, general condition.[5–9]

Prognostic nutritional index, with the advantage of being readily available from routine tests of blood cell counts and liver function, was one of the various markers used to evaluate systemic inflammation and nutritional status, which was calculated based on serum albumin concentration and total lymphocyte count in the peripheral blood[10–12]

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Furthermore, low preoperative prognostic nutritional index (PNI) has been shown to be related with poor survival of patients with HCC.[13–15] The exact mechanism by which PNI is related to prognosis remains incompletely understood. Several potential mechanisms have been reported. First, albumin is widely used to evaluate the nutritional aspect of patients undergoing surgery and was reported to correlate with postoperative complications.[16–18] Esper and Harb[19] suggested that a decrease of albumin is driven by a potential systemic inflammatory response. Besides, lymphocytes play a significant role in cancer immune surveillance, which prevents tumor development and recurrence via cytotoxic cell death and cytokines production.[20] Patients with a low PNI value might have relative lymphocytopenia, which might weaken the ability to inhibit proliferation and metastatic activity of tumor cells.[21] When together, PNI acts as an indicator that reflects host systemic inflammatory response.

However, many studies focused on the preoperative PNI, postoperative PNI change (ΔPNI), which may represent the change of systemic inflammatory response after tumor removal, remains unclear.

The present study was designed to evaluate the prognostic value of ΔPNI in patients with hepatitis B virus related (HBV related) small HCC who underwent liver resection.

Patients and Methods

Patients

The study was approved by the Ethics Committee of West China Hospital, Sichuan University. Patients who went liver resection with presenting to the Department of Liver Surgery & Liver Transplantation Center of West China Hospital, Sichuan University (Chengdu, China) between February 2007 and April 2013 were identified from our prospectively maintained database. The patient was diagnosed with small HCC meeting Milan criteria when either 2 types of imaging examination showed the typical features of HCC or positive findings were found on 1 imaging examination together with an alpha fetoprotein (AFP) level greater than 400 ng/mL. In addition, the diagnosis of HCC was confirmed by postoperative histopathologic examination. Clinical variables, including demographic data, complete blood counts differentiation assessments, liver function tests, AFP, HBV markers, staging of the tumor, including the number of focal hepatic lesions, maximum diameter detected, and degree of intrahepatic spread were collected.

Our inclusion criteria were as follows: (1) primary small HCC (solitary tumor <5 cm in diameter or ≤ 3 nodules that were ≤ 3 cm in diameter); (2) receiving liver resection as the initial treatment; (3) HBV positive but hepatitis C virus (HCV) negative; and (4) appropriate liver reserve function (Child-Pugh grade A) and renal function (serum creatinine <124 mmol/L).

Exclusion criteria included the following: (1) recurrent HCC; (2) clinical symptoms or signs of sepsis or infection at the time of blood sampling for PNI; (3) loss to follow-up within 3 months after liver resection; and (4) poor data integrity.

Definition and calculation of prognostic nutritional index

All preoperative blood samples were taken 2 days before the operation. The PNI was calculated using the following formula: serum albumin concentration (g/L) + .005 $\times$ lymphocyte count (number/mm^3) in peripheral blood.[22] Postoperative PNI was obtained at the 1st follow-up visit, 1 month after the operation. Postoperative PNI change (ΔPNI) was calculated by subtracting the preoperative PNI from the postoperative PNI. If the value was greater than or equal to 0, ΔPNI was defined as increased; otherwise, ΔPNI was defined as decreased.

Follow-up visits

All patients were regularly followed up at the 1st, 3rd, and 6th months in the 1st half year after the operation, every 3 months throughout the following 3 years, and every 6 months thereafter.

Physical examination, blood cell and differential counts, AFP levels, liver function tests, HBV markers and HBV-DNA levels (if the patient was diagnosed with HBV infection), and imaging examinations were included when necessary in the follow-up examinations. The causes of death and sites of recurrence were determined by death certificates, medical interviews, and imaging examinations. OS time was defined as the interval between the operation and death or the last follow-up. Recurrence-free survival (RFS) time was defined as the time interval between the operation and the 1st incidence of detectable recurrence. The last follow-up date was the end of April 2014.

Statistical analysis

Statistical analysis was conducted with SPSS software, version 21.0 (SPSS Company, Chicago, IL). Categorical data were compared by the chi-square test or Fisher exact test. Continuous variables were compared by the independent sample t test. The OS and RFS were analyzed by the Kaplan-Meier method, and the differences were analyzed by a log-rank test. Variables with significant prognostic value on univariate analysis were further evaluated with multivariate Cox proportional hazards regression analysis. All P values were 2 sided, and a significant difference was considered when the P value was less than .05.