Pathology – Research and Practice 213 (2017) 824–830

Contents lists available at ScienceDirect

Pathology – Research and Practice

journal homepage: www.elsevier.com/locate/prp

Original article

Edmondson-Steiner grade: A crucial predictor of recurrence and survival in hepatocellular carcinoma without microvascular invasio

Li Zhou [a,*], Jing-An Rui [a], Wei-Xun Zhou [b], Shao-Bin Wang [a], Shu-Guang Chen [a], Qiang Qu [a]

[a] Department of General Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences/Peking Union Medical College, Beijing, China
[b] Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences/Peking Union Medical College, Beijing, China

ARTICLE INFO

Article history:
Received 26 October 2016
Accepted 4 March 2017

Keywords:
Hepatocellular carcinoma
Microvascular invasion
Recurrence
Survival
Edmondson-Steiner grade

ABSTRACT

Background: Microvascular invasion (MVI), an important pathologic parameter, has been proven to be a powerful predictor of long-term prognosis in hepatocellular carcinoma (HCC). However, prognostic factors in HCC without MVI remain unknown. The present study aimed to identify the risk factors of recurrence and poor post-resectional survival in this type of HCC.
Methods and methods: A total of 109 patients with MVI-absent HCC underwent radical hepatectomy were enrolled. The influence of clinicopathologic variables on recurrence and patient survival was assessed using univariate and multivariate analyses.
Results: Chi-square test found that Edmondson-Steiner grade and satellite nodule were significantly associated with recurrence, while the former was the single marker for early recurrence. Stepwise logistic regression analysis demonstrated the independent predictive role of Edmondson-Steiner grade for recurrence. On the other hand, Edmondson-Steiner grade, serum AFP level and satellite nodule were significant for overall and disease-free survival in univariate analysis, whereas tumor size was linked to disease-free survival. Of the variables, Edmondson-Steiner grade, serum AFP level and satellite nodule were independent indicators.
Conclusions: Edmondson-Steiner grade, a histological classification, carries robust prognostic implications for all the endpoints for prognosis, thus being potential to be a crucial prognosticator in HCC without MVI.

1. Introduction

Hepatocellular carcinoma (HCC) is a well acknowledged cancer with high incidence and mortality worldwide [1–3]. Although in patients underwent curative resection, high recurrence rate (up to 70% within 5 post-operation years) significantly worsens long-term prognosis of HCC [4]. Therefore, identification of factors predictive for recurrence and patient survival of HCC has been a hotspot of study. Except for clinical, pathologic and molecular markers that were previously reviewed [5], microvascular invasion (MVI), found by postoperative pathologic examinations, was also shown to serve as a strong predictor of tumor relapse and unfavorable survival in individuals suffering from HCC, following different therapy modalities with curative intent, such as liver resection and transplantation [6–11]. However, prognostic determinants of HCC without MVI, a subset without the influence of this significant outcome associated variable, have not been investigated.

The current study was designed to identify clinicopathological parameters that affect recurrence and survival of HCC without MVI after radical hepatectomy, using uni- and multi-variate statistical analyses in a Chinese cohort.

2. Patients and methods

2.1. Patients

Medical records of a total of 109 patients with HCC without MVI, following radical hepatectomy, were reviewed. Of them, 96 (88.1%) were males and 13 (11.9%) were females. Patient ages ranged from 24 to 78 years (mean ± SD, 54.8 ± 11.7 years). Ninety patients (82.5%) carried hepatitis B surface antigen (HBsAg) positivity, and hepatitis C virus (HCV) antibody was positive in 11 (10.1%). Liver cirrhosis was present in 87 cases (79.8%). Ninety-eight patients (89.9%) were classified as Child-Pugh grade A and 11 (10.1%) were grade B. Serum a-fetoprotein (AFP) level was higher than 20 ng/ml

* Corresponding author.
E-mail address: lizhou02@hotmail.com (L. Zhou).

http://dx.doi.org/10.1016/j.prp.2017.03.002
0344-0338/

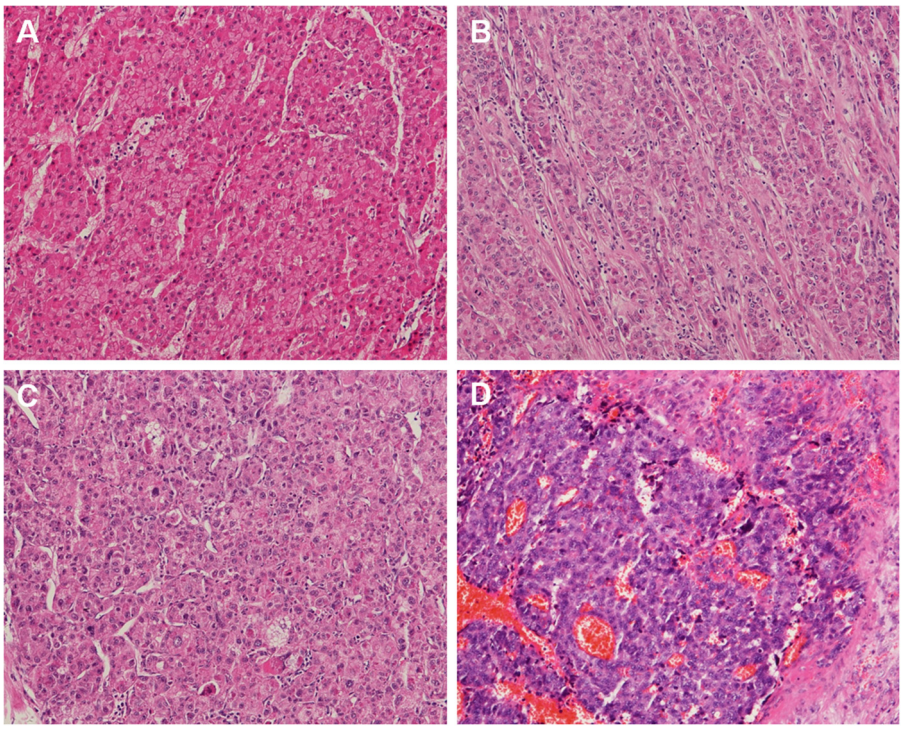

Fig. 1. Edmondson-Steiner grades of HCC. (**A**), Grade I; (**B**), Grade II; (**C**), Grade III; (**D**), Grade IV.

in 69 patients (63.3%). The mean tumor size was 7.0 cm (range: 0.7–20 cm). Satellite nodules were defined as macroscopic ones and found in 10 patients (9.2%), by postoperative gross observation. Histological grading, that was performed by a senior pathologist (WXZ) according to the Edmondson-Steiner criteria [12], showed that grade I, II, III and IV tumors were found in 16 (14.7%), 58 (53.2%), 32 (29.4%) and 3 (2.7%) patients, respectively (Fig. 1).

2.2. Endpoints and parameters

Overall/early recurrence (early recurrence: defined as recurrence within 1 year following radical hepatectomy) and overall/disease-free survival were designed to be endpoints of the study. A total of eleven parameters that might be prognostic in HCC were enrolled in statistical analyses, including those for general situation (age and sex), liver background and status (HBsAg, HCV, liver cirrhosis and Child-Pugh grade) and HCC-related factors (serum AFP value, tumor size, tumor number, satellite nodule and Edmondson-Steiner grade). TNM stage was not considered because MVI was a key factor of this staging system [13].

2.3. Follow-up

All the patients were follow-uped with intervals of 1–3 months. Serum AFP level and imaging examinations, such as B-type ultrasonography (BUS), computed tomography (CT), magnetic resonance imaging (MRI) and angiography, were applied for detection of local tumor recurrence and distant metastasis. The median follow-up term was 21 months (range: 3–108 months).

2.4. Statistical analyses

Risk factors of overall and early recurrence were determined by Chi-square (univariate) and stepwise logistic regression (multivariate or univariate) tests. Kaplan-Meier method and log-rank test were adopted for identifying univariate prognostic indicators. Multivariate survival analysis was performed by Cox regression (Proportional hazard model) test. Statistical software package SPSS11.5 (SPSS Inc, Chicago, IL) was used for all the analyses. The statistical significance was defined when a P value was less than 0.05.

3. Results

3.1. Risk factor analysis of overall recurrence in HCC without MVI

Overall post-operative recurrence was found in 66 patients (60.6%). Univariate Chi-square test showed that Edmondson-Steiner grade and satellite nodule were significantly linked to overall recurrence ($P < 0.05$, Table 1), whereas others were not of significance ($P > 0.05$, Table 1). The predictive value of Edmondson-Steiner grade, rather than satellite nodule, was further proven by multivariate stepwise logistic regression analysis (HR: 5.700, 95%CI: 1.951–-16.653, $P = 0.001$, Table 1).

3.2. Risk factor analysis of early recurrence in HCC without MVI

Early recurrence was detected in 23 patients (21.1%). Using Chi-square test, Edmondson-Steiner grade was the single risk factor of early recurrence in HCC without MVI ($P < 0.001$, Table 2), unlike other ones ($P > 0.05$, Table 2). In addition, univariate stepwise logistic regression analysis also identified Edmondson-Steiner grade as a risk factor of early recurrence (HR: 1.933, 95%CI: 1.418–2.636, $P < 0.001$, Table 2).

3.3. Markers of survival in HCC without MVI

Edmondson-Steiner grade, serum AFP level and satellite nodule were found by univariate analysis to be correlated with overall and disease-free survival in HCC without MVI, whereas tumor size was