



Original Article

Treatment results and prognostic factors in resectable hepatocellular carcinoma—Results from a local general hospital



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ARTICLE INFO

Article history:

Received 7 March 2014

Received in revised form

15 May 2014

Accepted 26 May 2014

Keywords:

Adjuvant therapy

Hepatocellular carcinoma

Surgical margin

Vascular invasion

ABSTRACT

Objective: Hepatocellular carcinoma (HCC) is a common cause of cancer mortality. Resection is the best choice for HCC. Our objective was to evaluate the impact of various factors that affected survival in patients with resectable HCC.

Materials and methods: Between January 1, 2007 and December 31, 2013, 107 patients with a diagnosis of HCC who underwent surgery were enrolled retrospectively. The analysis was carried using *t* tests, the Kaplan–Meier method, and Cox proportional hazard regression model to identify potential confounding and predicting variables.

Results: The 3-year overall survival rates in patients with surgical margins >1 mm and ≤ 1 mm were 79% and 59% ($p = 0.02$), respectively, and those in patients with and without vascular invasion were 57% and 93% ($p < 0.001$), respectively. Based on multivariate analysis, postoperative pathological vascular invasion (hazard ratio, 6.25; 95% confidence interval, 2.01–19.37) and surgical margin (hazard ratio, 0.37; 95% confidence interval, 0.14–0.96) remained independent predictors of an adverse long-term outcome.

Conclusion: Patients with vascular invasion combined with surgical margins ≤ 1 mm are at risk of poor survival and have a worse locoregional control rate. Further studies are warranted to identify the optimal strategy for the prevention and management of intrahepatic recurrence in order to further improve the prognosis of HCC after resection.

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1. Introduction

Hepatocellular carcinoma (HCC) is one of the most common causes of cancer mortality in Taiwan. The 5-year survival rate of individuals is low, and there is an increasing mortality rate [1]. Several modalities, including surgical resection, transcatheter arterial chemoembolization, arterial infusion chemotherapy, percutaneous ethanol injection therapy, microwave coagulation therapy, radiotherapy, and liver transplantation, have been used

to treat HCC [2–4]. The traditional approach to the treatment of HCC has been hepatic resection, because resection can be performed without delay and it is associated with low mortality [4]. However, the rate of intrahepatic recurrence has been high [5].

The main causes of late death after hepatectomy are related to intrahepatic cancer recurrence or progressive liver insufficiency due to cirrhosis. Various factors, such as patient age, size and number of tumors, presence of a tumor capsule, vascular invasion, histological grading, pathological stage, and surgical margins, have all been demonstrated to influence recurrence postoperatively [6,7]. Importantly, improved survival after hepatectomy for HCC has been attributed mainly to the prevention of recurrence. The aim of this study was to evaluate the results after surgical treatment of 107 patients with HCC in the same institution; a range of prognostic factors were also analyzed.

Conflicts of interest: none.

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2. Materials and methods

2.1. Patients

Between January 1, 2007 and December 31, 2013, 107 patients with the diagnosis of HCC, who underwent partial hepatectomy with complete gross resection of the disease, were enrolled retrospectively. The study was approved by the Institutional Review Boards of the respective institutions [DTCRD101(2)-I-18]. All patients were evaluated based on a baseline history and physical examination, serum laboratory tests, and a computed tomography or magnetic resonance imaging scan of the abdomen and pelvis.

2.2. Follow-up

Postoperatively, patients were followed up by physical examinations, serial computed tomography scans or ultrasonography, and alpha-fetoprotein levels at 3–6-month intervals for the 1st year and every 6 months thereafter. All patients in this analysis had a minimum of a 6-month follow-up examination. Recurrence of HCC was identified by new lesions on imaging, with an appearance typical of HCC, or by a rising alpha-fetoprotein level. Lesions that were not typical of HCC were confirmed by biopsy. Pathological specimens were reviewed for the following tumor characteristics: number and size of tumors, tumor grade, vascular invasion, and microscopic margins. A margin of >1 mm was considered a negative margin, whereas a margin between 0 mm and ≤1 mm was considered a close margin. A positive margin indicated histological involvement. Pathological vascular invasion was defined as encroachment into blood vessels by a pathological process. Macrovascular involvement was defined as histological involvement of the lobar or segmental branches of portal or hepatic veins, or gross invasion of the right or left main branches of the portal or hepatic veins.

2.3. Analysis

Patient demographics, tumor, operative treatment, and treatment characteristics were evaluated. The following variables were analyzed: age, sex, Child–Pugh classification of cirrhosis, alpha-fetoprotein level, hepatitis serological condition, and extent of resection. Stage was determined by the seventh American Joint Commission on Cancer (AJCC) system.

Comparisons between groups were performed using the Chi-square test for categorical variables and *t* test for continuous variables. Time to recurrence (disease-free survival) and time to death were determined by Kaplan–Meier analysis, and the results for subgroups of patients were compared with a log-rank test (SPSS software version 17.0; SPSS Inc., Chicago, IL, USA). All variables that appeared to be associated significantly with survival ($p < 0.05$) were entered into a Cox proportional hazards model to test for significant effects and adjustment for multiple factors simultaneously. A probability value of <0.05 was considered to be statistically significant.

3. Results

Demographics of this cohort are shown in Table 1. Of the patients, 49.5% were <60 years of age and 76.7% were male. Most patients had Barcelona-clinic liver cancer (BCLC) stages 0 and A (67%), based on clinical and laboratory evaluation. Nine patients were classified as BCLC stage C. Most of the tumors were AJCC T-stage 1/2 (85%) and Stage I/II (84%). Twenty-three patients (21.5%) had close (≤0.1 cm) margins, 10 of whom had positive margins

Table 1
Characteristics of 107 patients with hepatocellular carcinoma.

Variable	Number of patients	%
Age (y)		
<60	53	49.5
≥60	54	50.5
Sex		
Male	82	76.6
Female	25	23.4
pT		
pT 1–2	91	85.0
pT 3–4	16	15.0
Vascular permeation		
No	52	48.6
Yes	55	51.4
Tumor size		
<4.5	68	63.6
≥4.5	39	36.4
Surgical margin		
(+)	10	9.3
(–)	97	90.7
≤1(mm)	23	21.5
>1	84	78.5
Stage		
I	39	36.4
II	51	47.7
III	17	15.9
BCLC stage		
0	25	23.4
A	47	43.9
B	26	24.3
C	9	8.4
HBV carrier	48	44.8
HCV carrier	38	35.5
Non-HBV and non-HCV carriers	14	13.1
Concurrent with HBV and HCV carriers	7	6.5%

BCLC = Barcelona-clinic liver cancer; HBV = hepatitis B virus; HCV = hepatitis C virus; pT = pathological T.

(9.3%). Pathological vascular invasion was common and found in 55 patients (51%). In 39 patients (63%), the tumors were larger than 4.5 cm in size. Fifty-seven patients (53.3%) had liver cirrhosis. Forty-eight patients (44.8%) and 38 patients (35.5%) were hepatitis B virus (HBV) and hepatitis C virus (HCV) carriers, respectively. The number of non-HBV and non-HCV HCC patients was 14 (13.1%). Seven patients (6.5%) had concurrent HBV and HCV infections.

The median follow-up time was 22.3 months. The 3-year overall survival (OS), disease-free survival, disease-specific survival, locoregional recurrence-free, and distant metastasis-free rates were 68%, 35%, 73%, 36%, and 93%, respectively. The 3-year OS rates for Stages I, II, and III were 91%, 71%, and 49%, respectively ($p = 0.001$). The 3-year OS rates for surgical margins of >1 mm and ≤1 mm were 79% and 59%, respectively ($p = 0.02$; Fig. 1A); however, no differences were observed in these rates for surgical margins of >2 mm and ≤2 mm ($p = 0.1$; Fig. 1B). The 3-year OS rates in patients with or without vascular invasion were 57% and 93%, respectively ($p < 0.001$). Moreover, pathological T (pT) stage and cirrhosis status also influenced the OS rates (Table 2).

The median time to recurrence was 8.8 months (range, 2–43 months); 44 patients (41%) had recurrent cancer. Among these patients, initial tumor recurrence was confined to the original segment of the liver in 12 patients (11%) or to different segments of the liver in 36 patients (34%). Two patients had both distant lung and brain failure.

Based on univariate analysis, the factors with the greatest influence on the OS rate were tumor diameter, vascular permeation, stage, margin, sex, and BCLC status. Stage, pT stage, BCLC status, and vascular invasion also affected locoregional recurrence significantly, whereas a positive surgical margin did not affect the time to recurrence ($p = 0.28$).

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