Comparison between Disease Free Survival of Hepatocellular Carcinoma after Hepatic Resection in Chronic Hepatitis B Patients with or without Cirrhosis

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Background: *Hepatocellular carcinoma (HCC) in chronic hepatitis B (CHB) patients can develop in those with cirrhotic and non-cirrhotic liver. Not only impairment of liver status, but also the extension of tumor and difference of pathogenesis may also affect characteristics of patient and tumor including survival and recurrence.*
Objective: *To evaluate the disease free survival, prognostic factors and features of HCC after hepatic resection in CHB patients with and without cirrhosis.*
Material and Method: *Two hundred fifteen HBV-related HCC patients underwent hepatic resection and were analyzed. Cirrhotic and non-cirrhotic groups were compared for differences in patient and tumor characteristics, disease-free survival including prognostic factors.*
Results: *In comparison with cirrhotic patients, non-cirrhotic patients had more family history of HCC, more preserved liver function, were less HBeAg positive, and had lower HBV viral load. HCC characteristics in non-cirrhotic groups showed significantly larger (5.8±3.7 vs. 4.9±3.9 cm, p = 0.036) and operative data revealed that non-cirrhotic patients underwent more major surgery (50.7 vs. 18.3%, p<0.001), and had shorter hospital stay (10.8±8.9 vs. 8.1±4.3 days, p = 0.006) than cirrhotic ones. Operative time, blood loss and requirement of PRC transfusion were similar in both groups. Pathological profiles of HCC and liver parenchyma were comparable in both cirrhotic and non-cirrhotic patients. The disease-free survival of non-cirrhotic patients was longer than cirrhotic patients (Median disease free survival were 21 and 11 months respectively, p = 0.022). The independent predictive factor of lower disease-free survival of non-cirrhotic CHB patients who underwent hepatic resection was lymph node involvement (Hazard ratio (HR), 4.598. 95% confidence interval (CI), 1.1-19.212; p = 0.037) while of cirrhotic patients, factors were age >50 years old (HR, 2.998; 95% CI, 1.298-6.925; p = 0.01), multifocal tumor (HR, 5.835; 95% CI, 1.122-30.342; p = 0.036) and portal vein involvement (HR, 3.722; 95% CI, 1.121-12.353; p = 0.032). HBV treatment after HCC diagnosis was a significant predictor in the cirrhotic group by univariate analysis (p = 0.04).*
Conclusion: *Imaging and histological findings of HCC in cirrhotic and non-cirrhotic CHB patients were not different, except for larger tumor size in non-cirrhotic patients. Lymph node involvement is the predictor of HCC recurrence in non-cirrhotic CHB patients. Age >50 year old and multifocal tumor and portal vein involvement are the predictors of HCC recurrence in cirrhotic CHB patients. These groups may need surveillance that is more intensive after hepatic resection. Antiviral therapy may lower the risk of HCC recurrence among CHB cirrhotic patients.*

Keywords: *HCC, Hepatic resection, Hepatitis B, Cirrhosis, Survival*

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Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide and is the third most common cause of death from cancer[1]. In Thailand, it is the most common cancer in male and the third in female[2]. The important risk factor of HCC is cirrhosis from any causes, and 80-90% of HCC is found in patients with cirrhosis. Common causes of cirrhosis in Thailand are chronic viral hepatitis B and C, chronic alcohol use and non-alcoholic fatty liver disease.

According to the recent World Health Organization estimate, two billion people worldwide have serologic evidence of past or present hepatitis B virus (HBV) infection, and 360 million are chronically

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infected and at risk for HBV-related liver disease[3,4]. In Thailand, prevalence of HBV infection is 6 million and related to HCC 60-70%[5,6]. In the HBV infected patient, HCC can develop in both patient with cirrhosis or those without cirrhosis. Mechanisms of HCC development are multiple stages and multiple factors, beginning with chronic inflammation of hepatocyte and chronic hepatocyte destruction. Then the liver progresses to fibrosis, cirrhosis and develop regenerative nodules. Destruction-regeneration process provides a favorable ground for emergence of genetic and epigenetic alteration leading to hepatocyte transformation. Dysplastic cells and dysplastic nodules are precancerous lesions. By another pathway, HBV can be hepatocarcinogenetic without development of cirrhosis by integrating HBV DNA into human chromosomes, which causes major genetic alteration, DNA deletions, duplications and translocations. In addition, HBx protein has been designated a viral oncoprotein that is involved in liver cell transformation, cell cycle regulation, signaling pathways, DNA repair and which activates other oncogenes, c-myc and c-jun[7,8].

There are many options to treat HCC depending on tumor mass, liver function, and patient performance status. In early stage of HCC, hepatic resection is the treatment of choice and potential to be curative treatment[9]. However, recurrence after surgery is frequent, about 50-80% in 5 years[10], and that affects patient survival. Risk factors of recurrence and HCC related death in cirrhotic patient have been described in many studies[11-13], but in the non-cirrhotic patient there were only a few studies and these had heterogeneity of patients and causes of chronic hepatitis[14-17]. Poon et al[17] studied long-term prognosis after resection of HCC associated with HBV cirrhosis, and showed that preoperative aspartate aminotransferase (AST), perioperative blood transfusion, and vascular invasion of tumor are adverse prognostic factors.

In the past decade, significant improvement of overall and disease-free survival results after resection of HCC has been achieved as a result of advances in the diagnosis and surgical management of HCC[11,18,19]. Wide use of antivirals for HBV has been increasing, and some data revealed improvement of survival in HBV-related HCC who was treated with lamivudine[20,21]. The present study, the authors aimed to evaluate disease-free survival and recurrence of HCC after hepatic tumor resection in chronic hepatitis B patients with cirrhosis and without cirrhosis. The authors also assessed the differences of patient and tumor characteristics in radiological and pathological aspects in both groups, and of risk factors on disease free survival and recurrence of HCC.

Material and Method

Patients

Between January 2001 and December 2011, 251 HBV-related HCC patients underwent hepatic resection at the faculty of medicine Siriraj Hospital, Mahidol University. All of patients had been diagnosed hepatitis B by positive for hepatitis B surface antigen (HBsAg). Co-infection of hepatitis C (HCV) and human immunodeficiency virus (HIV) were excluded. Among the 215 available pathological data HBV-related HCC patients, 142 had cirrhosis and 73 had non-cirrhosis confirmed by histologic examination.

Hepatic resection was indicated when the complete removal of the tumor was consider possible, in accordance with the future liver remnant, the surgical technique and the pre-operative liver function.

All patients were recorded baseline characteristics, including hepatitis B status and prior or current treatment. Preoperative liver function assessed by Child-Turcotte-Pugh (CTP) score. HCC characteristics were available in radiologic picture archiving and communication system and radiologic reports were reviewed. Surgical specimens were sent for pathological exam for both tumor and non-tumor parenchyma. All specimens were reviewed by only one pathologist (AP).

After the operation, patients were followed-up regularly with serum alpha-fetoprotein (AFP) and hepatic imaging, computer tomography (CT) or magnetic resonance imaging (MRI) every 3 months. In case of recurrence, patients were managed with a multimodality approach according to standard guidelines that included resection for resectable recurrence, radiofrequency ablation (RFA) or transarterial chemoembolization (TACE) or systemic treatments for unresectable cases. Disease-free survival was defined as the duration of patients did not have any HCC recurrence after hepatic resection. In case of death, we defined as mortality either liver-related death or non-liver related death.

Statistical analysis

Descriptive statistics used to characterize the population, categorical variables are presented as frequencies and percentages, while continuous variables presented with mean and standard deviation if the data have a normal distribution. Non-normally

distributed data will be presented with the median, minimum and maximum.

Comparison between the factors that affect HCC recurrence and cirrhotic or non-cirrhotic groups was done using Chi-square statistics or Fisher's exact test for categorical variables and using independent t-test or the Mann-Whitney U test for continuous variables. The Kaplan-Meier method was used for the analysis of survival and disease-free survival rates. Survival curves were compared using the log rank test. Variables achieving statistical significance at the univariate analysis of survival were put in the multivariate analysis, performed with the Cox's proportional hazard model. The p-value <0.05 was considered statistically significant. Statistical analysis was carried out with the SPSS 20.0 software packaging (SPSS, Chicago, IL, USA).

Results

Clinical and laboratory profiles

Patients with cirrhosis and non-cirrhosis were comparable as regards gender, BMI, smoking, alcohol use and comorbid diseases. Non-cirrhotic patients had more family history of HCC (12.3 vs. 4.9%, $p = 0.05$) and trend to be younger than cirrhotic patients (53±12 vs. 56±10 years old, $p = 0.065$) (Table 1).

Cirrhotic group had higher laboratory parameters including total bilirubin, aminotransferase, prothrombin time (PT); however, it had lower albumin, white blood cell and platelet count. Renal function was comparable in both groups. When assessing liver status, cirrhotic group had more CTP than the non-cirrhotic group, significantly. However, all patients in this study were CTP child A. As for viral status, cirrhotic patients were more HBeAg positive than non-cirrhotic patients (32.1 vs. 10.6%, $p = 0.006$). HBV viral load and AFP were higher in cirrhotic group (Table 2).

Radiologic and pathologic profiles

No significant difference in number, lobar involvement, dynamic pattern of HCC in imaging, portal vein, nor lymph node involvement (4.5% in non-cirrhosis group and 8.6% in cirrhotic group, $p = 0.395$) was indicated in either groups, but non-cirrhotic patients had significantly larger tumor sizes than cirrhotic patient (5.8±3.7 vs. 4.9±3.9 cm, $p = 0.036$). On pathological examination, tumor differentiation, tumor border, resection margin and vascular invasion were similar in both groups (Table 3). Non-tumoral pathological examination were comparable in both groups, as were inflammation Metavir score), steatosis, type of steatosis, and steatohepatitis (Table 4).

Table 1. Clinical profile of patients with and without cirrhosis

Clinical profiles	Non-cirrhosis (n = 73)	Cirrhosis (n = 142)	p-value
Age (year)	53±12	56±10	0.065
Gender male	52 (71.2)	103 (72.5)	0.840
BMI (kg/m^2)	23.2±3.2	24.1±3.6	0.086
Smoking			0.491
Non-smoker	43/72 (59.7)	96 (67.6)	
Current smoker	3/72 (4.2)	4 (2.8)	
Alcohol drinking			0.775
Never	46/72 (63.9)	94 (66.2)	
Previous drinking	22/72 (30.6)	43 (30.3)	
Current drinking	4/72 (5.6)	5 (3.5)	
Family history of HCC	9 (12.3)	7 (4.9)	0.050
HBV treatment after diagnosis of HCC*	53 (72.6)	102 (71.8)	0.905
Comorbid diseases	39 (53.4)	69 (48.6)	0.502
Presentation			0.614
HCC surveillance	46 (63.0)	93/140 (66.4)	
Symptomatic	23 (31.5)	43/140 (30.7)	
Incidental	4 (5.5)	4/140 (2.9)	

BMI = body mass index; HCC = hepatocellular carcinoma; HBV = hepatitis B virus

* Lamivudine 66.7%, Adefovir 11.1%, Entecavir 17.5%, Telbivudine 1.6%, Multiple 3.2%

Data was presented as mean ± SD or n (%)

Table 2. Laboratory profile of patients with and without cirrhosis

Laboratory profiles	Non-cirrhosis (n = 73)	Cirrhosis (n = 142)	*p*-value
Total bilirubin (mg/dL)	0.6±0.3	0.9±0.7	0.004
AST (U/L)	43±30	57±49	0.002
ALT (U/L)	46±55	50±41	0.040
Albumin (g/dL)	4.2±0.4	3.9±0.5	0.001
Creatinine (mg/dL)	0.9±0.2	0.9±0.3	0.842
PT (second)	12.0±0.9	13.0±1.3	<0.001
Hct (%)	40±5	38±6	0.165
WBC (/ul)	6,607±2,213	5,541±1,973	<0.001
Platelet ($x10^3$/ul)	218±71	154±78	<0.001
HBeAg positive	5/47 (10.6%)	26/81 (32.1%)	0.006
HBV viral load (log IU/mL)	1.6 (0-8.1)	3.29 (0-8.1)	0.019
Alpha-fetoprotein (IU/mL)	14.5 (0-105)	41.0 (1.6-105)	0.009
Child-Turcotte-Pugh score	5.1±0.4	5.4±0.7	<0.001

AST = aspartate aminotransferase; ALT = alanine aminotransferase; PT = prothrombin time; Hct = hematocrit; WBC = white blood cell; HBeAg = hepatitis B e antigen
Data was presented as mean ± SD or median (range)

Table 3. Tumoral pathologic profile of patients with and without cirrhosis

Pathologic profiles	Non-cirrhosis (n = 73)	Cirrhosis (n = 142)	*p*-value
Differentiation			0.212
Well	5/68 (7.4%)	4/130 (3.1%)	
Moderate	59/68 (86.8%)	122/130 (93.8%)	
Poor	4/68 (5.9%)	4/130 (3.1%)	
Tumor border			1.000
Well circumscribed	72/72 (100%)	131/132 (99.2%)	
Infiltrative	0/72 (0%)	1/132 (0.8%)	
Resection margin			0.759
Free	66/72 (91.7%)	117/134 (87.3%)	
Microscopic involvement	5/72 (6.9%)	15/134 (11.2%)	
Macroscopic involvement	1/72 (1.4%)	2/134 (1.5%)	
Vascular invasion			0.961
No	49/72 (68.1%)	90/131 (68.7%)	
Microvascular	21/72 (29.2%)	36/131 (27.3%)	
Macrovascular	2/72 (2.8%)	5/131 (3.8%)	

Operative data

Non-cirrhotic patients significantly underwent more major surgery than cirrhotic patients (50.7 vs. 18.3%, $p<0.001$) but operative time, blood loss and perioperative blood transfusion were not significantly different. The cirrhotic group had longer hospital stays (10.8±8.9 vs. 8.1±4.3 days, $p = 0.006$) while ICU stays were not different.

Patient survival and disease free survival

The cumulative overall survival was not significant different among cirrhotic and non-cirrhotic patients, median survival was 33 months in cirrhotic patients and 35 months in non-cirrhotic patients, $p = 0.312$. The 1-, 3- and 5-year overall survival rates were 82.6%, 44% and 22% in cirrhotic group, and 87.3%, 43.6%, and 23.6% in non-cirrhotic group respectively.

Disease-free survival, as shown in Fig. 1, was significantly lower in cirrhotic than non-cirrhotic patients. Median disease-free survival was 11 and 21 months respectively, $p = 0.022$. The 1-, 3- and 5-year disease free survival rates were 45.6%, 20% and 8% in the cirrhotic group, and 62.5%, 25%, and 15.6% in the non-cirrhotic group.

Table 4. Non-tumoral pathologic profile of patients with and without cirrhosis

Pathologic profiles	Non-cirrhosis (n = 73)	Cirrhosis (n = 142)	*p*-value
Fibrosis (Metavir score)			
0	3 (4.1%)		
1	5 (6.8%)		
2	16 (21.9%)		
3	49 (67.1%)		
Inflammation (Metavir score)			0.898
0	6 (8.2%)	10 (7.0%)	
1	35 (47.9%)	62 (43.7%)	
2	25 (34.2%)	55 (38.7%)	
3	7 (9.6%)	15 (10.6%)	
Steatosis			0.493
<5%	49 (67.1%)	98 (69.0%)	
5-33%	17 (23.3%)	37 (26.1%)	
34-66%	5 (6.8%)	6 (4.2%)	
>66%	2 (2.7%)	1 (0.7%)	
Type of steatosis			0.635
Macrosteatosis	42 (64.4%)	96 (67.6%)	
Microsteatosis	0 (0%)	0 (0%)	
Mixed	26 (35.6%)	46 (32.4%)	
Steatohepatitis	9 (12.3%)	12 (8.5%)	0.364

Prognostic factors for disease free survival

On univariate analysis, three factors were identified as significant predictive factors for disease free survival in non-cirrhotic patients, including age >50 years old, serum albumin <3.5 g/dL, and lymph node involvement. In cirrhotic patients, age, BMI, treatment of HBV after HCC resection, Hct, bilateral lobar involvement and portal vein involvement in imaging study, tumor size, and vascular invasion in pathology were significant predictive factors.

By multivariate analysis, only lymph node involvement was independently correlated to disease-free survival in non-cirrhotic patients. Age >50 years old, multifocal tumor, and portal vein involvement were found as the independent predictive factors of lower disease-free survival of cirrhotic patients (Table 5, 6).

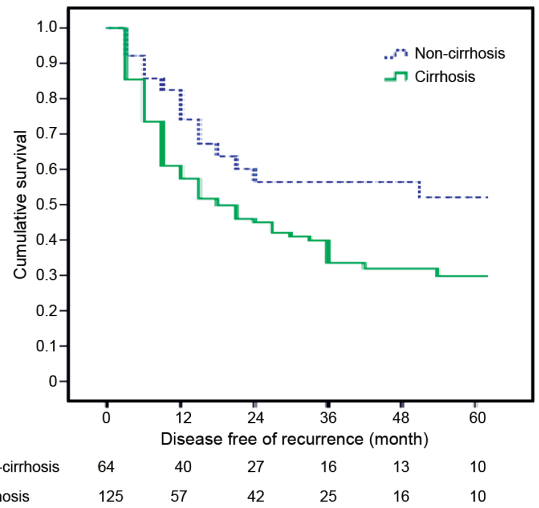

Fig. 1 Cumulative disease free survival after HCC resection in HBV patient with and without cirrhosis.

Discussion

There has been a variety of results in prognosis and prognostic factors for HCC between patients with and without cirrhosis. In cirrhotic patients, multiple factors contribute poorer prognosis than non-cirrhotic such as liver function status, portal hypertension. Multiple data showed that outcome in patients with HCC with cirrhosis who underwent HCC resection were worse than non-cirrhotic patients, but in some studies results were similar in both groups. In non-cirrhotic patient, HCC most developed in patients with hepatitis B and is rare with other causes, and usually under recognized in HBV status and never found through HCC surveillance. HCC in this group may be the first presentation, for a tumor usually is advanced and less likely suitable for curative treatment. For this reason, it may affect the prognosis and recurrence comparable with cirrhotic patients.

Table 5. Univariate and multivariate analysis of factors affecting disease free survival after HCC resection in non-cirrhotic HBV patients

Variables	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	*p*-value	Hazard ratio	95% CI	*p*-value
Age >50 years old	2.161	1.022-4.570	0.044	1.612	0.656-3.963	0.298
Albumin ≤3.5 g/dL	8.619	1.810-41.041	0.007	4.299	0.686-26.949	0.119
Lymph node involvement	9.038	2.392-34.151	0.001	4.598	1.100-19.212	0.037
Non-free resection margin	3.032	0.903-10.178	0.073	1.470	0.365-5.925	0.588
Tumor size >5 cm	1.913	0.881-4.152	0.101	1.411	0.552-3.604	0.472
Vascular invasion	1.702	0.767-3.778	0.191	1.755	0.673-4.579	0.250

Table 6. Univariate and multivariate analysis of factors affecting disease free survival after HCC resection in cirrhotic HBV patients

Variables	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	*p*-value	Hazard ratio	95% CI	*p*-value
Age >50 years old	2.338	1.431-3.821	0.001	2.998	1.298-6.925	0.010
BMI ≥25 kg/m^2	1.693	1.065-2.692	0.026	1.935	0.905-4.139	0.089
HBV treatment after resection	1.664	1.014-2.668	0.044	0.695	0.209-2.307	0.552
Hct <30%	2.186	1.044-4.577	0.038	2.573	0.633-10.456	0.186
HBeAg positive	1.801	0.995-3.261	0.052	1.608	0.730-3.541	0.239
Multifocal tumor	1.548	0.908-2.638	0.108	5.835	1.122-30.342	0.036
Bilateral lobar involvement	2.291	1.171-4.482	0.015	5.459	0.779-38.238	0.087
Tumor size >5 cm	2.821	1.680-4.737	<0.001	1.347	0.550-3.298	0.515
Non-free resection margin	1.815	0.898-3.667	0.097	1.039	0.237-4.558	0.960
Portal vein involvement	2.428	1.298-4.545	0.006	3.722	1.121-12.353	0.032
Vascular invasion	1.787	1.101-2.901	0.019	1.721	0.821-3.607	0.150

This study aims to assess the patients and HCC characteristics including survival, disease-free survival difference between the groups of patients with and without cirrhosis. The authors found that non-cirrhotic patients had more family history of HCC and tended to be younger; this may be due HBV endemic, and usually vertical transmission in our area compatible with reports in Asian countries[15,16]. In a previous study Grazi et al[14] showed that non-cirrhotic patients more often presented with tumor-related symptoms that may reflect under surveillance in this group. However, presentation of our patients was comparable in both groups according to symptomatic and surveillance data and may be influenced by development of HCC management guidelines in the past decade and studies conducted in a medical school. However, this result may not reflect overall HCC due to selection bias, we selected only the patient in early stage that could undergo surgery. Many studies showed HCC in patients without cirrhosis exhibiting more aggressive behavior, having a larger diameter, a poorer differentiation and high incidence of vascular invasion[14,22]. The authors also demonstrated larger tumor in non-cirrhotic group but tumor pathology was similar in differentiation and vascular invasion. Even though, larger tumor size in the non-cirrhotic group might be affected by selection bias from the surgeon who considered treatment modalities for the patients. According to HBV status, our data showed that the cirrhotic patient had more HBeAg positive and higher viral load and AFP level that was consistent with the natural history of more replicative HBeAg positive virus. By size of tumor, larger in the non-cirrhotic group and with liver function preserve, patients underwent significantly more extensive resection than in the cirrhotic group. Even though more major surgery occurred in the non-cirrhotic patient, operative time, blood loss, peri-operative blood transfusion were similar. Moreover, there were shorter hospital stays and lower ICU admission in this group. These finding indicate that

hepatic resection had to be performed on carefully selected patients if cirrhosis was presented.

The present study showed that disease-free survival periods are shorter in cirrhotic than non-cirrhotic patients, like many previous reports[14-16,23] but as for overall survival, we showed comparable results in both groups, that is consistent with Poon et al[17] data which included only HBV patients, as did our study. A lower survival and a higher recurrence were expected in patient with fibrotic liver compared to those with chronic hepatitis of less advanced fibrosis[13]. The disease free survival periods in our study are shorter than Chang et al reports[16] which included all causes of cirrhosis but are comparable with Poon et al[17] these results showed that mean disease-free survival after HCC resection are 18.3 and 12.4 months in non-cirrhotic and cirrhotic patients, respectively. The different populations may cause the discrepancy in results between our patients and the Poon et al study that included only HBV population that had the potential to develop HCC without occurrence of cirrhosis causing more HCC recurrence.

The independent predictive factors for disease free survival identified in this study included age >50 years old, multifocal tumor, and portal vein involvement in cirrhotic patients, while there was only lymph node involvement in non-cirrhotic patients. As in the previous study, Grazi et al[14] showed multiple HCC nodules are tumor recurrence predictors. Other factors tending to affect prognosis are albumin ≤3.5 mg/dL, non-free resection margin, major surgery, large HCC, portal vein and vascular involvement (which probably reflected liver status) complexity of operation and advance of tumor[18,19]. Treatment of HBV also tends to be a positive predictive factor for disease-free survival that is reflected by decreased recurrence of tumors, which supports the hypothesis about the benefit of viral suppression on HCC development[20,21].

In conclusion, imaging and histologic finding of HCC including non-tumoral pathology in cirrhotic and non-cirrhotic chronic hepatitis B (CHB) patients are not different, except for larger tumor size in non-cirrhotic patients. Lymph node involvement is the predictor of HCC recurrence in non-cirrhotic CHB patients. Age >50 years old, multifocal HCC and portal vein involvement are the predictors of HCC recurrence in cirrhotic CHB patients. These groups may need more intensive surveillance after hepatic resection. Antiviral therapy may lower risk of HCC recurrence among CHB cirrhotic patients.

What is already known on this topic?

HCC is one of the most common malignancies and one of major risk factors for development of HCC is chronic hepatitis B infection.

HCC can develop in chronic hepatitis B patients with cirrhosis and those without cirrhosis.

Disease-free survival in cirrhosis tends to be shorter than in non-cirrhotic patients.

What this study adds?

Imaging and histologic finding of HCC in cirrhosis and non-cirrhosis are not different, only larger tumor size is significantly found in non-cirrhotic patients.

Age more than 50 years, multifocal tumor and portal involvement are predictors of HCC recurrence in cirrhotic patients; whereas, lymph node involvement is on predictor for non-cirrhotic patients.

Antiviral treatment may lower risk of HCC recurrence in CHB with cirrhotic patients.

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Potential conflicts of interest

None.

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การเปรียบเทียบอัตราการรอดชีวิตที่ไม่มีโรคหลังได้รับการผ่าตัดเพื่อรักษาโรคมะเร็งตับในผู้ป่วยโรคไวรัสตับอักเสบ บี ที่มีภาวะตับแข็งและไม่มีภาวะตับแข็งร่วมด้วย

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ภูมิหลัง: โรคมะเร็งตับชนิด hepatocellular carcinoma (HCC) ในผู้ป่วยโรคไวรัสตับอักเสบ บี เรื้อรัง สามารถเกิดได้ในผู้ป่วยที่มีสภาพตับที่เป็นตับแข็งหรือไม่มีตับแข็งก็ได้ ลักษณะต่าง ๆ ได้แก่ ลักษณะการทำงานของตับ ขนาดของก้อนมะเร็ง และพยาธิสภาพกำเนิดที่แตกต่างกัน อาจมีผลต่อลักษณะของผู้ป่วย ลักษณะของก้อนมะเร็ง รวมถึงอัตราการรอดชีวิต และการเกิดโรคซ้ำได้

วัตถุประสงค์: ต้องการประเมินอัตราการรอดชีวิตที่ไม่มีโรค (disease free survival, DFS) ปัจจัยที่มีผลต่อการพยากรณ์โรคและลักษณะของก้อนมะเร็ง HCC หลังจากผู้ป่วยได้รับการผ่าตัดโรคมะเร็งตับแล้ว ในผู้ป่วยที่มีโรคไวรัสตับอักเสบ บี ที่มีมะเร็งชนิด HCC โดยเปรียบเทียบในกลุ่มที่มีภาวะตับแข็งร่วมด้วย และกลุ่มที่ไม่มีภาวะตับแข็ง

วัสดุและวิธีการ: ผู้ป่วยทั้งหมด 215 ราย ที่เป็นโรคมะเร็งตับชนิด HCC ร่วมกับเป็นโรคไวรัสตับอักเสบ บี ซึ่งได้รับการผ่าตัดโรคมะเร็งตับได้นำเข้าการศึกษานี้เพื่อวิเคราะห์ข้อมูลโดยแบ่งเป็น 2 กลุ่มหลัก คือ กลุ่มที่ผู้ป่วยมีภาวะตับแข็งร่วมด้วย และอีกกลุ่มไม่มีภาวะตับแข็งร่วมด้วยจากนั้นนำมาเปรียบเทียบดูความแตกต่างในด้านลักษณะของผู้ป่วย ลักษณะโรคมะเร็งค่า DFS และปัจจัยต่าง ๆ ที่มีผลต่อการพยากรณ์ของโรค

ผลการศึกษา: ผลการเปรียบเทียบผู้ป่วยที่มีภาวะตับแข็งและผู้ป่วยที่ไม่มีภาวะตับแข็ง พบว่ากลุ่มผู้ป่วยที่ไม่มีภาวะตับแข็งมีจำนวนมากกว่าที่มีประวัติคนในครอบครัวเป็นโรคมะเร็งชนิด HCC การทำงานของตับดีกว่า มีผู้ป่วยที่มี HBeAg เป็นผลบวกน้อยกว่าและปริมาณไวรัสตับอักเสบ บี ในเลือดน้อยกว่า ลักษณะของมะเร็ง HCC ในผู้ป่วยที่ไม่มีภาวะตับแข็งพบว่ามีขนาดใหญ่กว่า (5.8±3.7 เซนติเมตร vs. 4.9±3.9 เซนติเมตร, p = 0.036) และข้อมูลขณะผ่าตัดพบว่าผู้ป่วยที่ไม่มีสภาวะตับแข็งมักได้รับการผ่าตัดที่ใหญ่ (major surgery) มากกว่า (50.7% vs. 18.3%, p<0.001) และระยะเวลานอนรักษาในโรงพยาบาลน้อยกว่าเมื่อเทียบกับกลุ่มที่มีภาวะตับแข็ง (10.8±8.9 วัน vs. 8.1±4.3 วัน, p = 0.006) ระยะเวลาในการผ่าตัด การเสียเลือดขณะผ่าตัดและอัตราการรับเลือดขณะผ่าตัดไม่แตกต่างกันในสองกลุ่ม ลักษณะพยาธิสภาพของโรคมะเร็ง HCC และพยาธิสภาพในเนื้อตับถูกนำมาเปรียบเทียบทั้งสองกลุ่ม พบว่าค่า DFS ในกลุ่มที่ไม่มีภาวะตับแข็งมีระยะเวลานานกว่ากลุ่มที่มีภาวะตับแข็ง (ค่ามัธยฐานของอัตราการรอดชีพโดยไม่มีโรคเท่ากับ 21 เดือน และ 11 เดือน ตามลำดับ) ปัจจัยที่มีผลต่อบ่งชี้ว่ามีค่า DFS ลดลงในกลุ่มที่ไม่มีภาวะตับแข็งคือ การมีต่อมน้ำเหลืองที่มีมะเร็งกระจาย (hazard ratio [HR] 4.598, 95% confident interval [CI] 1.1-19.212, p = 0.037) ในขณะที่กลุ่มที่มีภาวะตับแข็งมีปัจจัยที่มีผลคือ อายุมากกว่า 50 ปี (HR 2.998, 95% CI 1.298-6.925, p = 0.01) การมีมะเร็งหลายตำแหน่งในตับ (HR 5.835, 95% CI 1.122-30.342, p = 0.036) และการมีมะเร็งอยู่ในหลอดเลือด portal vein (HR 3.722, 95% CI 1.121-12.353, p = 0.032) การรักษาด้วยยาต้านไวรัสตับอักเสบ บี หลังการวินิจฉัยโรคมะเร็งตับ พบว่าเป็นปัจจัยที่สำคัญเช่นกัน แต่เป็นเพียง univariate analysis (p = 0.037)

สรุป: ลักษณะทางภาพรังสีและลักษณะทางพยาธิของมะเร็ง HCC ในกลุ่มผู้ป่วยที่มีและไม่มีภาวะตับแข็งในผู้ป่วยที่มีโรคไวรัสตับอักเสบ บี ไม่มีความแตกต่างกัน ยกเว้นกลุ่มที่ไม่มีภาวะตับแข็งมักมีขนาดของก้อนมะเร็งที่ใหญ่กว่า การมีมะเร็งกระจายเข้าต่อมน้ำเหลืองเป็นปัจจัยที่สำคัญที่บ่งถึงการเกิดมะเร็งตับกลับเป็นซ้ำในกลุ่มที่ไม่มีภาวะตับแข็ง ส่วนอายุที่เกิน 50 ปี การมีมะเร็งหลายตำแหน่งในตับ และการมีมะเร็งในหลอดเลือด portal vein เป็นปัจจัยที่บ่งชี้การเกิดมะเร็งกลับเป็นซ้ำในผู้ป่วยที่มีภาวะตับแข็ง ดังนั้นผู้ป่วยกลุ่มนี้ควรได้รับการตรวจมากขึ้น เพื่อดูการกลับเป็นซ้ำของมะเร็งหลังจากที่ได้รับการผ่าตัด การให้ยาต้านไวรัสตับอักเสบ บี อาจมีผลลดการเกิดมะเร็ง HCC เป็นซ้ำในผู้ป่วยกลุ่มที่มีภาวะตับแข็ง