2023 APPLE
The 13th Asia-Pacific Primary Liver Cancer Expert Meeting
Novel Insights into the Evolution of Liver Cancer Management
July 6-8, 2023 | Grand InterContinental Seoul Parnas, Seoul, Korea

Development of a prognostic scoring system for h epatocellular carcinoma with hepatic vena cava B udd–Chiari syndrome

Xiaowei Dang, Shengan Liu, Luhao Li, Zhaochen Liu, Suxin Li

Department of Hepatopancreatobiliary Surgery, the First Affiliated Hospital of Zhengzhou University, Zhengzhou, China

Background and Aim

Hepatic vena cava Budd–Chiari syndrome (HVC-BCS) is a rare, heterogeneous disease cau sed by an obstruction of the inferior vena cava (IVC) above the hepatic vein opening, with o r without hepatic vein involvement, which can lead to portal vein and IVC hypertension syn drome.

HVC-BCS is characterized by a long-term latent chronic course. The liver remains in a state of congestion and hypoxia for a long period of time, which can lead to liver fibrosis and cirr hosis. Compared with classic BCS characterized by acute hepatic vein thrombosis, HVC-B CS is more likely to be complicated by hepatocellular carcinoma (HCC), which significantl y reduces the quality of life and shortens the survival time of patients. However, there are fe w reports on the prognostic factors of HCC in patients with HVC-BCS.

This study aims to explore the prognostic factors of patients with HCC with HVC-BCS and to establish a simple prognostic scoring system to help clinicians evaluate the prognosis of s uch patients.

Methods

The clinical and follow-up data of 64 HVC-BCS patients with HCC who received invasive t reatment at the First Affiliated Hospital of Zhengzhou University between January 2015 and December 2019 were retrospectively analyzed. Kaplan-Meier curves and log-rank tests wer e used to analyze the survival curve of patients and the difference in prognoses between the groups. Univariate and multivariate Cox regression analyses were performed to analyze the influence of biochemical, tumor, and etiological characteristics on the total survival time of patients, and a new prognostic scoring system was developed according to the regression co efficients of the independent predictors in the statistical model. The prediction efficiency wa s evaluated using the time-dependent receiver operating characteristics curve.

Results

The analyses of the 64 patients, showed that serum albumin level < 34 g/L, maximum tumor diameter (MTD) > 7 cm, and IVC stenosis (IVC stenosis was defined as a reduction of > 50 % in the lumen diameter) were independent predictors of survival. Ultimately, 2 points were given for maximum tumor diameter > 7 cm, 1 point was given for serum albumin level < 34 g/L and inferior vena cava stenosis. The new prognostic scoring system was defined as the s um of three scores, and patients were classified as grades A, B, C and D with sum scores of 0, 1, 2, or > 2 points, respectively. Significant differences in survival were found among diff erent groups. The time-ROC curve showed that the new prognostic scoring system had good prediction efficiency at different follow-up time points, the corresponding area under the cur ve values were all > 0.7 and higher than commonly used tumor staging.

Table 1
Baseline characteristics of HVC-BCS patients with HCC.

Characteristics	All patients (n = 64)	Stenosis present (n = 29)	Stenosis absent (n = 35)	P value
Age (yr)	51.02 ± 8.88	51.31 ± 8.82	50.77 ± 9.06	0.811
Sex				0.572
Male	29 (45.3%)	13 (44.8%)	16 (45.7%)	
Female	35 (54.7%)	16 (55.2%)	19 (54.3%)	
Child-Turcotte-Pugh class				0.285
A	43 (67.2%)	17 (58.6%)	26 (74.3%)	
B	21 (32.8%)	12 (41.4%)	9 (25.7%)	
MELD	4.80 ± 3.84	4.64 ± 3.96	4.94 ± 3.78	0.310
BCLC stage				0.171
A	41 (64.1%)	15 (51.7%)	26 (74.3%)	
B	14 (21.9%)	8 (27.6%)	6 (17.1%)	
C	9 (14.1%)	6 (20.7%)	3 (8.6%)	
CLIP				0.237
0	20 (31.3%)	5 (17.2%)	15 (42.9%)	
1	20 (31.3%)	11 (37.9%)	9 (25.7%)	
2	12 (18.8%)	5 (17.2%)	7 (20.0%)	
3	5 (7.8%)	3 (10.3%)	2 (5.7%)	
4	3 (4.7%)	2 (6.9%)	1 (2.9%)	
5	4 (6.3%)	3 (10.3%)	1 (2.9%)	
Okuda				**0.037**
I	26 (40.6%)	7 (24.1%)	19 (54.3%)	
II	34 (53.1%)	20 (69.0%)	14 (40.0%)	
III	4 (6.3%)	2 (6.9%)	2 (5.7%)	
TNM				0.229
I	36 (56.3%)	13 (44.8%)	23 (65.7%)	
II	10 (15.6%)	5 (17.2%)	5 (14.3%)	
III	18 (28.1%)	11 (37.9%)	7 (20.0%)	
Maximum tumor diameter				0.501
≤ 3 cm	16 (25.0%)	6 (20.7%)	10 (28.6%)	
3.1-5.0 cm	19 (29.7%)	9 (31.0%)	10 (28.6%)	
5.1-7.0 cm	10 (15.6%)	3 (10.3%)	7 (20.0%)	
> 7 cm	19 (29.7%)	11 (37.9%)	8 (22.9%)	
Tumor number				0.128
1	38 (59.4%)	14 (48.3%)	24 (68.6%)	
≥ 2	26 (40.6%)	15 (51.7%)	11 (31.4%)	
Portal vein tumor thrombus	9 (14.1%)	6 (20.7%)	3 (8.6%)	0.279
Alpha-fetoprotein				0.204
≤ 400 ng/mL	39 (60.9%)	15 (51.7%)	24 (68.6%)	
> 400 ng/mL	25 (39.1%)	14 (48.3%)	11 (31.4%)	
Platelet (× 10^9/L)	95.0 (71.3-125.3)	96.0 (73.5-128.5)	90.0 (65.0-126.0)	0.613
Total bilirubin (μmol/L)	19.6 (14.2-30.2)	19.4 (14.6-34.9)	19.7 (14.0-28.1)	0.466
Albumin (g/L)	38.55 ± 5.43	38.56 ± 6.02	38.46 ± 4.97	0.991
Creatinine (μmol/L)	58.48 ± 13.70	57.08 ± 15.28	59.65 ± 12.33	0.459
Prothrombin time (INR)	1.12 (1.07-1.19)	1.12 (1.07-1.19)	1.11 (1.04-1.22)	0.962
Ascites	30 (46.9%)	19 (65.5%)	11 (31.4%)	**0.011**
Initial treatment				0.488
Resection	14 (21.9%)	5 (17.2%)	9 (25.7%)	
TACE	39 (60.9%)	20 (69.0%)	19 (54.3%)	
RFA	11 (17.2%)	4 (13.8%)	7 (20.0%)	

MELD: model for end-stage liver disease; BCLC: Barcelona Clinic Liver Cancer; CLIP: Cancer of the Liver Italian Program; TNM: tumor node metastasis classification; INR: international normalized ratio; IVC: inferior vena cava; TACE: transarterial chemoembolization; RFA: radiofrequency ablation.

Table 2
Univariate Cox regression analysis of potential predictors for overall survival and characteristics of survivors and non-survivors.

Variables	Survivors (n = 33)	Non-survivors (n = 31)	HR (95% CI)	P value
Age (yr)	50.94 ± 9.31	51.10 ± 8.56	1.010 (0.970-1.051)	0.624
Female	20 (60.6%)	15 (48.4%)	0.678 (0.335-1.374)	0.281
Platelet (× 10^9/L)	99 (72-134)	84 (62-115)	0.999 (0.991-1.007)	0.861
Prothrombin time (INR)	1.10 (1.04-1.17)	1.14 (1.08-1.36)	1.252 (0.498-3.152)	0.633
Total bilirubin (μmol/L)	19.70 (15.55-30.84)	18.67 (13.10-30.20)	1.007 (0.993-1.021)	0.347
Creatinine (μmol/L)	57.21 ± 13.46	59.70 ± 14.07	1.003 (0.975-1.032)	0.826
Portal vein tumor thrombus	0	9 (29.0%)	9.016 (3.797-21.412)	**< 0.001**
Alpha-fetoprotein > 400 ng/mL	7 (21.2%)	18 (58.1%)	3.707 (1.777-7.735)	**< 0.001**
Albumin < 34 g/L	1 (3.0%)	12 (38.7%)	4.461 (2.131-9.338)	**< 0.001**
Tumor number ≥ 2	7 (21.2%)	19 (61.3%)	3.354 (1.620-6.944)	**0.001**
MTD > 7 cm	2 (6.1%)	17 (54.8%)	8.910 (4.070-19.504)	**< 0.001**
Ascites	11 (33.3%)	19 (61.3%)	2.335 (1.130-4.823)	**0.022**
IVC stenosis	10 (30.3%)	19 (61.3%)	3.074 (1.459-6.473)	**0.002**

HR: hazard ratio; CI: confidence interval; INR: international normalized ratio; MTD: maximum tumor diameter; IVC: inferior vena cava.

Table 3
Multivariate Cox regression analysis for overall survival using stepwise forward selection of variables.

Variables	β	HR (95% CI)	P value
Albumin < 34 g/L	1.393	4.027 (1.816-8.932)	**0.001**
IVC stenosis	1.284	3.612 (1.646-7.928)	**0.001**
MTD > 7 cm	2.154	8.623 (3.771-19.715)	**< 0.001**

IVC: inferior vena cava; MTD: maximum tumor diameter; HR: hazard ratio; CI: confidence interval.

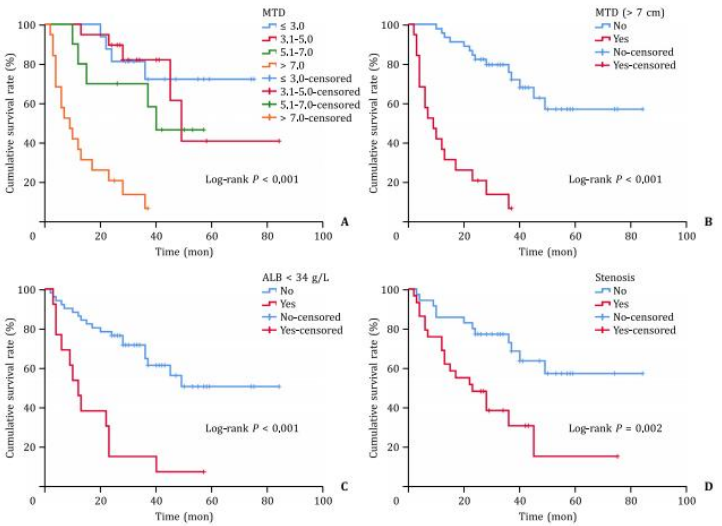

Fig. 1. A: Kaplan-Meier curves depict survival according to the different tumor diameters, and there was no difference in survival outcomes when the MTD ≤ 7 cm; **B-D:** Kaplan-Meier curves depict survival according to the MTD (**B**), ALB (**C**) and IVC stenosis (**D**). MTD: maximum tumor diameter; ALB: albumin; IVC: inferior vena cava.

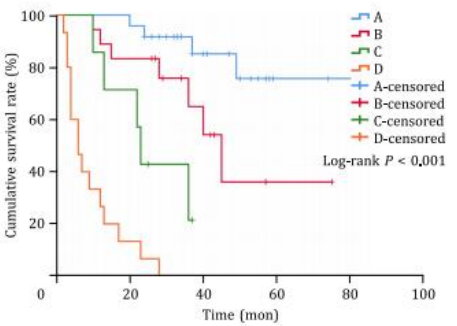

Fig. 2. Kaplan–Meier survival curves according to new prognostic scoring system. The new prognostic scoring system showed statistical evidence for a reduction in OS when moving from A to D (Log-rank P < 0.05).

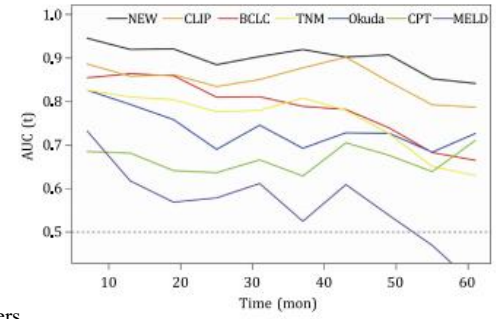

Fig. 3. Time-ROC curve analysis to compare the ability of TNM, Okuda, CLIP, BCLC, CTP, MELD and new prognostic scoring system in predicting the survival.

Conclusions

This study successfully developed a prognostic scoring system for HVC-BCS patients with HCC, which is helpful for clinical evaluation of patient prognosis.