Journal of Hepatocellular Carcinoma

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Outcomes and Prognostic Factors in Cirrhotic Patients with Acute Variceal Bleeding and Hepatocellular Carcinoma: A Nested Case–Control Study

Guofeng Liu*, Songchi Xiao*, Tong Xiang, Xiaoze Wang, Yi Shen, Li Yang, Xuefeng Luo

Department of Gastroenterology and Hepatology, Sichuan University-University of Oxford Huaxi Joint Centre for Gastrointestinal Cancer, West China Hospital, Sichuan University, Chengdu, Sichuan, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xuefeng Luo; Li Yang, Department of Gastroenterology and Hepatology, Sichuan University-University of Oxford Huaxi Joint Centre for Gastrointestinal Cancer, West China Hospital, Sichuan University 37 Guoxue Lane, Chengdu, Sichuan, 610041, People's Republic of China, Email luo_xuefeng@wchscu.cn; yangli_hx@scu.edu.cn

Purpose: The treatment outcomes and risk factors for the prognosis of acute variceal bleeding (AVB) in hepatocellular carcinoma (HCC) patients remain unclear. Hence, we assessed the clinical outcomes and prognostic factors of these patients.

Methods: This study retrospectively enrolled 1532 AVB patients with cirrhosis from January 2016 to December 2022. Of these patients, 310 had HCC, and after 1:1 individual matching, 306 of them were matched with 306 patients without HCC. Six-week mortality, one-year mortality, and five-day treatment failure were recorded.

Results: In the matched-pair analysis, patients with HCC had a higher rate of 6-week and 1-year mortality than those without HCC (6-week: 24.5% vs 7.8%, $P < 0.001$; 1-year: 45.9% vs 16.2%, $P < 0.001$). The rate of 5-day treatment failure was similar between the two groups (21.1% vs 16.7%, $P = 0.213$). Among AVB patients with HCC, the multivariate analysis revealed that the Child-Pugh score (HR, 1.239, 95% CI, 1.121–1.370; $P < 0.001$) and Barcelona Clinic Liver Cancer (BCLC) stage (C-D vs 0-B) (HR, 14.409; 95% CI, 5.758–36.055; $P < 0.001$) were independently associated with 6-week mortality. Moreover, the rate of 6-week mortality was 60.2% in patients who had a high Child-Pugh score (≥9) and advanced BCLC stage (C–D), much higher than in those with low Child-Pugh score (<9) and earlier BCLC stage (0-B) ($P < 0.001$).

Conclusion: Among patients with cirrhosis and AVB, patients with HCC had significantly worse outcomes than those without. The severity of liver disease and the stage of HCC are the main determinants of mortality in HCC patients.

Keywords: acute variceal bleeding, hepatocellular carcinoma, cirrhosis, portal hypertension

Introduction

Acute variceal bleeding (AVB) is the most life-threatening complication of cirrhosis, with high morbidity and mortality.[1,2] Although the management of AVB has improved in the past decades, including restrictive volume restitution, vasoactive agents, timely endoscopy, prophylactic antibiotics, and interventional treatments, the 6-week mortality is as high as 20%.[3,4]

Around 90% of hepatocellular carcinoma (HCC) cases develop in patients with cirrhosis.[5] Variceal hemorrhage is one of the leading causes of noncancer-related deaths in cirrhotic patients with HCC.[5–7] Several risk factors have been identified to be associated with mortality of AVB, including a high model of end-stage liver disease (MELD) score or Child-Pugh score, hypovolemic shock, active bleeding on endoscopy, and higher hepatic venous pressure gradient.[8–11]

The presence of HCC has been consistently associated with poorer clinical outcomes in patients with cirrhosis, including those experiencing AVB.[11–13] In addition to tumor burden, liver function impairment and portal hypertension,

Received: 8 November 2024
Accepted: 8 February 2025
Published: 19 February 2025

especially in patients with portal vein tumor thrombosis (PVTT), are the critical determinants for prognosis of this subgroup of patients. However, the management of AVB in patients with HCC is not standardized and varies across disciplines. Moreover, previous studies have been limited by relatively small sample sizes. Given the high mortality rate in this patient population, more data are needed to elucidate their clinical characteristics and outcomes and provide robust evidence to support clinical decision-making.

The aim of our study is to assess the outcomes of AVB in cirrhotic patients with HCC, compared to a matched cohort of cirrhotic patients without HCC. Furthermore, we seek to investigate potential risk factors associated with 6-week mortality in these patients, based on data from a single high-volume referral center.

Materials and Methods

Study Population

This retrospective analysis included data of consecutive AVB patients with cirrhosis treated at West China Hospital from January 2016 to December 2022. Patients who met the following inclusion criteria were considered to be included: (1) liver cirrhosis as diagnosed based on clinical symptoms, and imaging tests or liver biopsy; (2) endoscopy-proven AVB between January 2016 and December 2022; (3) established diagnosis of HCC before or at the time of the bleeding episode. Exclusion criteria were incompletion of at least six weeks of follow-up or insufficient documentation. The study cohort was identified through the review of the hospital's electronic medical records, selecting patients diagnosed with liver cirrhosis and AVB in our hospital. A propensity-matched cohort of AVB patients without HCC was selected, matched based on age, sex, etiology, bleeding history, hemoglobin levels, and Child-Pugh classification, to facilitate a comparison of outcomes.

Management of Variceal Bleeding

Patients with hemodynamic instability were given packed red blood cell (PRBC) transfusions to a hemoglobin of 7~8 g/dl. Vasoactive drugs (octreotide, terlipressin, or somatostatin) and endoscopy were given to all patients as soon as possible. The performance of endoscopic treatment for AVB was recorded. Esophageal variceal band ligation (EVL) and endoscopic gastric variceal obturation (EVO) were performed as the main treatments for esophageal or gastric variceal bleeding, respectively. Balloon tamponade was used as a bridge to endoscopy or to transjugular intrahepatic portosystemic shunt (TIPS) when necessary.

Data Collection

Data regarding demographic, clinical, laboratory, endoscopic, blood transfusion, and treatments were collected from our hospital's electronic medical records. The baseline liver disease-specific scores such as Child–Pugh–Turcotte (CTP) and model for end-stage liver disease (MELD) scores were calculated.

In patients with HCC, information regarding tumors and anti-HCC treatment was also recorded. The Barcelona Clinic Liver Cancer (BCLC) classification was used to stage HCC.[14] The day of onset of variceal bleeding was defined as day 0. All patients were followed until death, liver transplantation, the date of last follow-up, or loss of follow-up.

Endpoints

The primary endpoint was 6-week mortality. The secondary endpoints were 5-day treatment failure and 1-year mortality. Five-day treatment failure was defined either by the absence of control of bleeding or by rebleeding within the first five days, according to Baveno VII.[15]

Statistical Analysis

To minimize baseline differences and equalize background risks between the two study groups, we performed 1:1 propensity score matching (PSM) with a caliper width of 0.02. Key variables included in the matching process were age, sex, etiology, history of variceal bleeding, hemoglobin levels, Child–Pugh classification, and presence of infection by SPSS version 25.0. The means ± standard deviation and medians (interquartile range; IQR) of parametric and

nonparametric variables were calculated, respectively. Variables with categorical characteristics were defined using proportions. The Student's t, the Chi-square, and Mann–Whitney *U*-tests were used based on the characteristics of the variables. As appropriate, Kaplan–Meier analysis was used to compare the probability of survival with the Log rank test. The independent risk factors on survival were identified and the hazard ratio (HR) and 95% confidence interval (CI) were also determined by univariate and multivariate Cox regression analyses. Variables that were required for calculating the MELD score or Child-Pugh score were eliminated from the multivariate analysis due to the presence of collinearity. The collinearity assessment between BCLC stage and Child-Pugh score was performed. The receiver operating characteristic analysis was used to calculate the optimal cut-off value by maximizing the sum of the sensitivity and specificity. All data were analyzed using SPSS 25.0 (PASW Inc., Chicago, IL, USA) and a 2-side p-value < 0.05 was considered to be statistically significant.

Result

Baseline Characteristics

A detailed flowchart illustrating the patient selection process was presented in Figure S1. A total of 310 patients with cirrhosis and HCC presenting with AVB were included in our study. The baseline characteristics of patients with and without HCC are detailed in Table S1. After propensity score matching, 306 patients with HCC were matched with 306 patients without HCC. Table 1 summarizes the baseline characteristics of the patients in the matched cohort. The whole population of matched cohort had a median age of 53 years (IQR, 47–63) and was predominantly male (n = 533, 87.1%). Viral hepatitis (n = 478, 78.1%) was the leading cause of cirrhosis, followed by alcohol (n = 53, 8.7%). The median

Table 1 Baseline Characteristics in Matched Cohort

	All (n=612)	HCC (n=306)	Non-HCC (n=306)	P value
Age (years)	53 (47–63)	54 (46–63)	53 (47–63)	0.335
Sex, male	533 (87.1)	266 (86.9)	267 (87.3)	0.904
Etiology				0.440
Viral	478 (78.1)	243 (79.4)	235 (76.8)	
Alcohol	53 (8.7)	22 (7.2)	31 (10.1)	
Viral + Alcohol	37 (6.0)	21 (6.9)	16 (5.2)	
Others	44 (7.2)	20 (6.5)	24 (7.8)	
Previous VB	235 (38.4)	109 (35.6)	126 (41.2)	0.158
PVT	251 (41.0)	173 (56.5)	78 (25.5)	<0.001
Child-Pugh score	8 (7–9)	8 (7–9)	8 (7–9)	1.000
Child-Pugh class				0.841
A	89 (14.5)	42 (13.7)	47 (15.4)	
B	383 (62.6)	194 (63.4)	189 (61.8)	
C	140 (22.9)	70 (22.9)	70 (22.9)	
MELD score	12 (9–15)	12 (9–15)	11 (9–15)	0.784
Infection	283 (46.2)	127 (41.5)	156 (51.0)	0.019
HE	86 (14.1)	37 (12.1)	49 (16.0)	0.163

(*Continued*)

Table 1 (Continued).

	All (n=612)	HCC (n=306)	Non-HCC (n=306)	P value
Ascites				0.150
None	127 (20.8)	58 (19.0)	69 (22.5)	
Mild	189 (30.9)	88 (28.8)	101 (33.0)	
Severe	296 (48.4)	160 (52.3)	136 (44.4)	
Hematemesis at the initial presentation	437 (71.4)	223 (72.9)	214 (69.9)	0.421
Heart rate	91 (78–104)	94 (80–107)	88 (76–101)	<0.001
Initial systolic blood pressure	112 (100–124)	112 (100–124)	112 (101–124)	0.582
Source of bleeding				0.805
EV	367 (60.0)	182 (59.5)	185 (60.5)	
GV	245 (40.0)	124 (40.5)	121 (39.5)	
BCLC 0/A/B/C/D (%)		21/65/67/106/47 (6.9/21.3/21.9/34.6/15.3)		
Laboratory variables				
Hemoglobin (g/L)	76 (64–93)	77 (65–92)	75 (64–95)	0.963
Platelet count ($\times 10^9$/L)	71 (46–108)	89 (59–132)	59 (39–83)	<0.001
WBC count ($\times 10^9$/L)	5.57 (3.63–8.62)	6.14 (4.15–9.36)	5.01 (3.16–7.85)	<0.001
Total bilirubin (umol/L)	23.6 (16.3–39.4)	23.5 (16.5–40.9)	23.7 (15.8–38.3)	0.736
Albumin (g/L)	30.3 (27.2–33.9)	30.4 (26.9–34.1)	30.2 (27.6–33.5)	0.679
INR	1.32 (1.20–1.50)	1.31 (1.20–1.50)	1.32 (1.20–1.50)	0.830
Cr (umol/L)	74 (61–88)	74 (60–90)	74 (62–88)	0.390

Note: Data are presented as median (interquartile range) or number (%).
Abbreviations: BCLC, Barcelona Clinic Liver Cancer; Cr, creatinine; EV, esophageal varices; GV, gastric varices; HCC, hepatocellular carcinoma; HE, hepatic encephalopathy; INR, international normalized ratio; MELD, the model for end-stage liver disease; PVT, portal vein thrombosis; VB, variceal bleeding; WBC, white blood cells.

Child-Pugh score was 8 points; most patients were Child-Pugh class B (n = 383, 62.6%). A total of 235 patients (38.4%) had a previous history of AVB. The hemorrhage was from esophageal varices in 367 patients (60.0%) and from gastric varices in 245 patients (40.0%), respectively. Patients with HCC had a higher proportion of portal vein thrombosis (PVT) than those without (56.5% vs 25.5, P < 0.001). The median MELD score (P = 0.784) and Child-Pugh score (P = 1.000) were similar between the two groups.

Among HCC patients in matched cohort, BCLC stages were as follows: 21 (6.9%) with BCLC 0, 65 (21.3%) with BCLC A, 67 (21.9%) with BCLC B, 106 (34.6%) with BCLC C, 47 (15.3%) with BCLC D. The portal vein tumor thrombosis (PVTT) was determined in 110 patients (35.9%) via enhanced computed tomography or magnetic resonance imaging.

Treatment Outcomes of AVB in the Matched Cohorts

No differences were observed regarding initial pharmacological and endoscopic treatment between the two groups (Table 2). The proportion of patients receiving blood transfusion treatment (55.6% vs 56.5%, P = 0.807), balloon tamponade (15.7% vs 11.4%, P = 0.125), and salvage TIPS (4.9% vs 5.9%, P = 0.591) were similar.

Five-day treatment failure was not significantly different between the two groups (21.1% vs 16.7%, P = 0.213). A total of 99 patients (16.2%) died within 6 weeks. Gastrointestinal hemorrhage (n = 67, 67.7%) was the leading cause of

Table 2 Treatments of Variceal Bleeding

	All (n=612)	HCC (n=306)	Non-HCC (n=306)	P value
Antibiotic prophylaxis	426 (69.6)	203 (66.3)	223 (72.9)	0.079
Blood transfusion	343 (56.0)	170 (55.6)	173 (56.5)	0.807
PRBC transfusion (U)	4 (2–7)	4 (2–6)	4 (2–7)	0.314
Use of balloon tamponade (%)	83 (13.6)	48 (15.7)	35 (11.4)	0.125
Endoscopic treatment (%)	520 (85.0)	257 (84.0)	263 (85.9)	0.497
Intubation	19 (3.1)	10 (3.3)	9 (2.9)	0.816
Salvage TIPS	33 (5.4)	15 (4.9)	18 (5.9)	0.591
Hospital stay (days)	10 (7–14)	11 (8–15)	9 (7–13)	0.742

Note: Data are presented as number (%) or median (interquartile range).
Abbreviations: HCC, hepatocellular carcinoma; PRBC, packed red blood cell; TIPS, transjugular intrahepatic portosystemic shunt.

death, followed by liver failure (n = 22, 22.2%). The 6-week and 1-year mortality were 24.5% and 45.9% in patients with HCC and 7.8% and 16.2% in patients without HCC, respectively.

Impact of HCC on 6-Week Mortality in AVB Patients

Patients with HCC presenting with AVB had a significantly higher 6-week (Figure 1, Log rank test P < 0.001) and 1-year (Figure S2, Log rank test P < 0.001) mortality than patients without. As presented in Table 3, the multivariate analysis revealed the presence of HCC (HR, 3.296; 95% CI, 2.043–5.316, P < 0.001), PVT (HR, 1.561; 95% CI, 1.031–2.364; P =

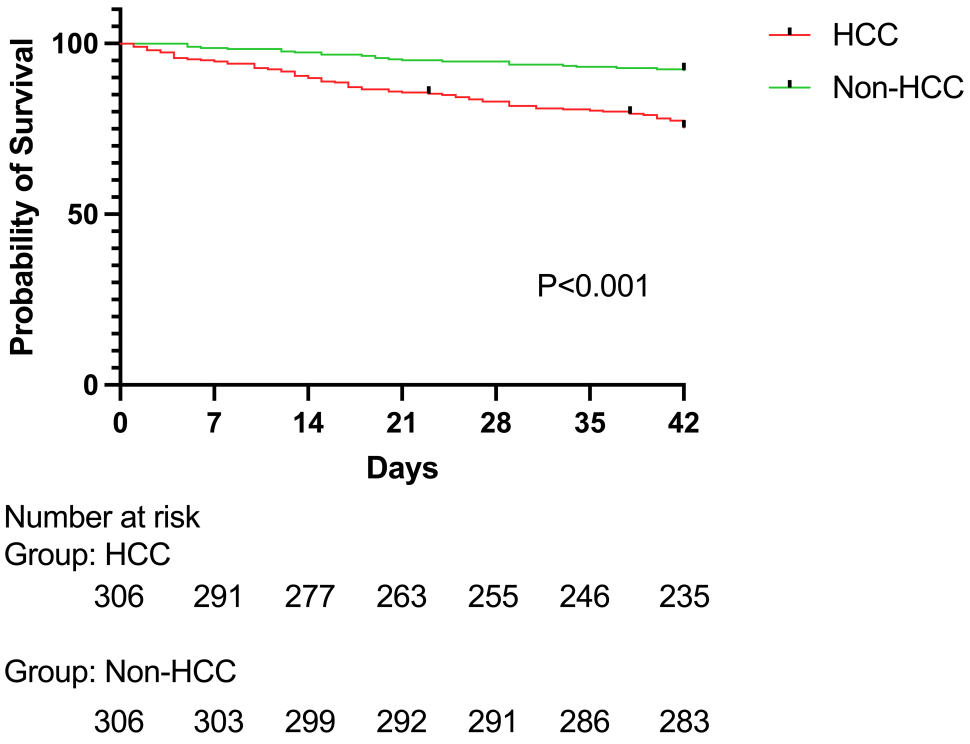

Figure 1 Cumulative survival rates at 6 weeks according to the presence of HCC. AVB patients with HCC had higher 6-week mortality than patients without.
Abbreviations: AVB, acute variceal bleeding; HCC, hepatocellular carcinoma.

https://doi.org/10.2147/JHC.S502658

Table 3 Independent Risk Factors for 6-Week Mortality in Patients with AVB

Variable	Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value
HCC	3.002 (1.933–4.660)	<0.001	2.591 (1.626–4.129)	<0.001
PVT	2.566 (1.727–3.812)	<0.001	1.967 (1.294–2.991)	0.002
Child-Pugh score	1.366 (1.260–1.480)	<0.001	1.406 (1.292–1.530)	<0.001
MELD score	1.077 (1.039–1.116)	<0.001		
Infection	1.896 (1.282–2.803)	<0.001		

Note: Variables included in MELD score were not included in the multivariate analysis to avoid colinearity.
Abbreviations: AVB, acute variceal bleeding; HCC, hepatocellular carcinoma; PVT, portal vein thrombosis; MELD, the model for end-stage liver disease.

0.035), and Child-Pugh score (HR, 1.361; 95% CI, 1.249–1.483, P < 0.001) were identified as independent factors for death at 6 weeks in AVB patients.

Risk Factors of Death at 6 weeks in AVB Patients with HCC

Variables associated with 6-week mortality in patients with HCC were identified via univariate Cox regression analysis and are depicted in Table 4. PVT, Child-Pugh score, MELD score, infection, and BCLC stage were associated with mortality at 6 weeks in univariate analysis. Even when considering the other variables in multivariate analysis, BCLC stage (C-D vs 0-B) (HR, 14.409; 95% CI, 5.758–36.055; P < 0.001) and Child-Pugh score (HR, 1.239, 95% CI, 1.121–1.370; P < 0.001) were independently associated with death at 6 weeks in patients with HCC group.

As illustrated in Figure 2, the Child-Pugh score was a strong predictor for 6-week mortality, with a high area under the receiver operating characteristic (AUROC = 0.748, P < 0.001). The cut-off value of the Child-Pugh score for 6-week mortality was 9. The risk stratification of these patients was conducted based on the Child-Pugh score and BCLC classification. In patients with a Child-Pugh score ≥9 and advanced HCC (BCLC C–D), the rate of 6-week mortality was determined as high as 60.2%, significantly higher than in those who had a lower Child-Pugh score and earlier BCLC stage (Figure 3, Log rank test P < 0.001).

Independent Factors of 5-Day Treatment Failure and Death at 1 Year in AVB Patients with HCC

As presented in Table S2 and S3. Shock index (HR, 20.598; 95% CI, 6.092–69.653; P < 0.001) and Child-Pugh score (HR, 1.229; 95% CI, 1.055–1.433; P = 0.008) were significantly associated with the 5-day treatment failure in

Table 4 Independent Risk Factors for 6-Week Mortality in HCC Patients with AVB

Variable	Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value
BCLC class (C-D vs 0-B)	18.092 (7.297–44.855)	<0.001	14.409 (5.758–36.055)	<0.001
PVT	2.326 (1.394–3.881)	0.001		
Child-Pugh score	1.389 (1.259–1.533)	<0.001	1.239 (1.121–1.370)	<0.001
MELD score	1.090 (1.040–1.142)	<0.001		
Infection	1.744 (1.108–2.746)	0.016		

Note: Variables included in MELD score were not included in the multivariate analysis to avoid colinearity.
Abbreviations: AVB, acute variceal bleeding; BCLC, Barcelona Clinic Liver Cancer; HCC, hepatocellular carcinoma; PVT, portal vein thrombosis; MELD, the model for end-stage liver disease.

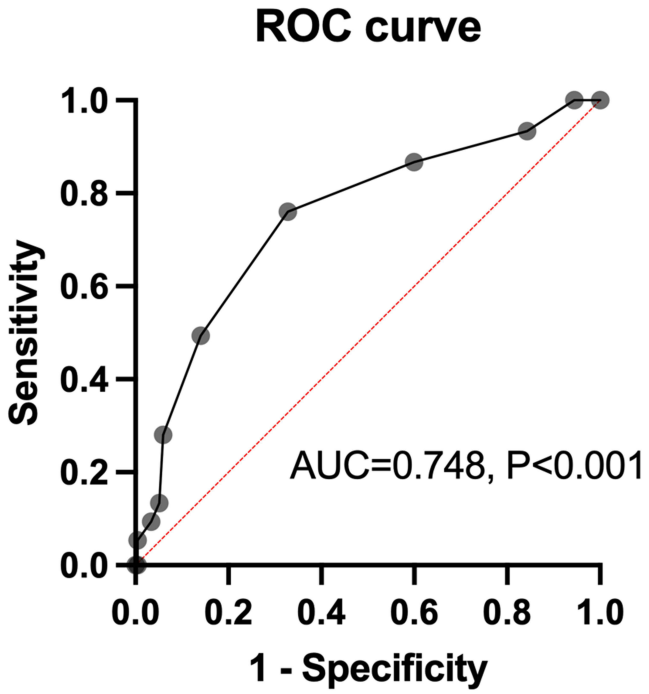

Figure 2 Receiver operating characteristic analyses demonstrated the strong predictive value of the Child-Pugh score for 6-week mortality.

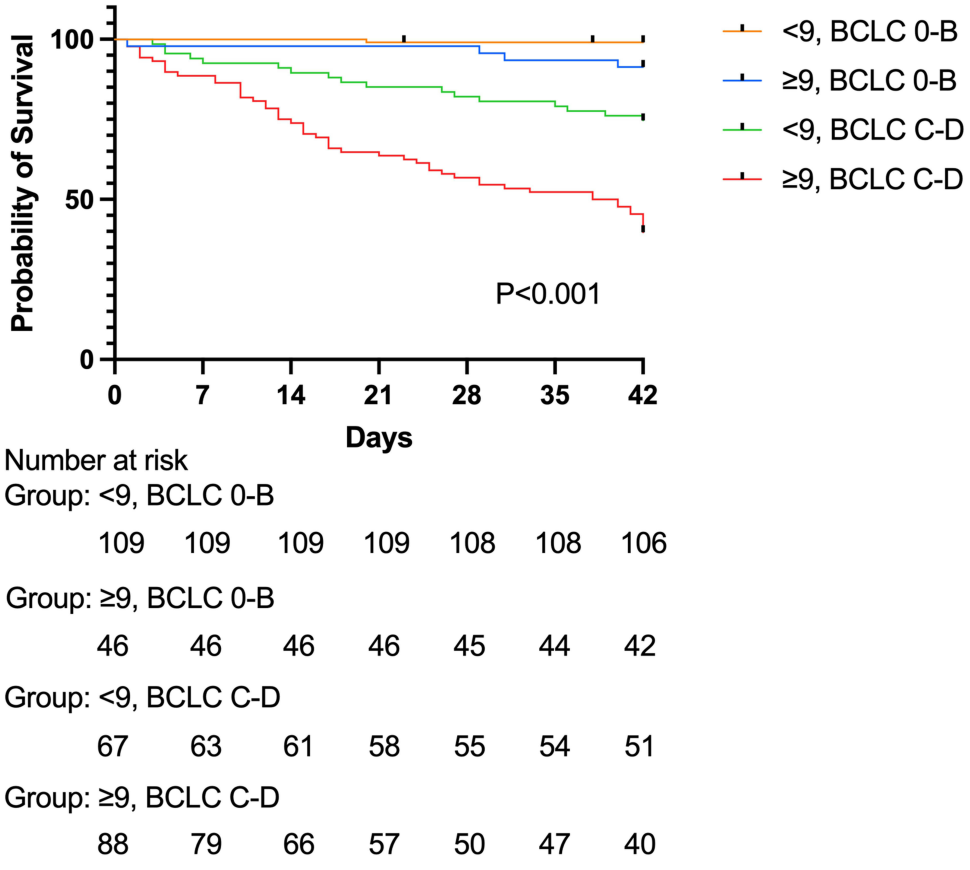

Figure 3 Cumulative survival rates at 6 weeks based on Child-Pugh score and BCLC stage. The risk of 6-week mortality was significantly higher among patients with a Child-Pugh score ≥ 9 and BCLC stage C–D than among patients with a lower Child-Pugh score and earlier BCLC stage (Log rank test $p < 0.001$).
Abbreviation: BCLC, Barcelona Clinic Liver Cancer.

https://doi.org/10.2147/JHC.S502658

multivariate analysis. Additionally, advanced BCLC stage (HR, 5.192; 95% CI, 3.293–8.184; P < 0.001) and higher Child-Pugh score (HR, 1.219, 95% CI, 1.125–1.321; P < 0.001) remained independent risk factors of death at 1 year.

Discussion

In this matched study of AVB patients with cirrhosis, we compared the mortality between patients with HCC and those without and explored the potential risk factors for death in AVB patients with HCC. We found that patients with HCC had higher mortality at 6 weeks and 1 year than those without. Child-Pugh score and BCLC stage were identified as the independent risk factors of death at 6 weeks in HCC patients, and significantly higher mortality was observed in those who had a higher Child-Pugh score and advanced BCLC stage.

Previous research has focused on predicting the prognosis of HCC patients using clinical characteristics, tumor staging systems, and molecular biomarker-based models.[16–18] The majority of these studies primarily included patients without cirrhosis or with compensated cirrhosis. However, portal hypertension and HCC can coexist in the same patient and impact the prognosis, especially in patients with acute variceal bleeding. A few studies demonstrated that the presence of HCC was strongly related to poor outcomes in patients with AVB.[11,13] However, the difference in the severity of liver disease between patients with the HCC group and those with non-HCC might affect the prognosis in the previous study.[13] Hence, to eliminate the potential influence, patients without HCC were matched based on propensity score in our study. Mortality at 6 weeks was much higher in patients with HCC than in those without (24.5% vs 7.8%). Similar to previous studies,[13,19] the BCLC classification was an independent factor of death in our study. Patients with advanced BCLC stage (C-D) had worse outcomes in comparison to patients with earlier BCLC stage (0-B), suggesting the poor outcomes of patients with HCC were mainly influenced by the disease stage.

The majority of AVB patients died from gastrointestinal bleeding within 6 weeks. No difference in pharmacological and endoscopic treatment in the AVB period between the two groups, while the number of deaths from gastrointestinal bleeding in patients with HCC was almost twice as much as in those without, which might be explained partly by the proportion of the TIPS administration in two groups.

Previous studies have shown that the use of secondary prophylaxis has survival benefits, and TIPS implantation is superior to endoscopic + β-blocker therapy for preventing rebleeding and prolonging survival in patients with HCC.[19,20] In our study, the proportion of receiving secondary prophylaxis between the two groups did not differ (83.7% vs 85.2%, P = 0.427), but only 26 patients in HCC group underwent TIPS for preventing variceal rebleeding, in comparison to 71 patients in non-HCC group. HCC has traditionally been regarded as a contraindication to TIPS, mainly due to concerns about the risk of causing metastasis and the potential short-life expectancy, especially in patients with PVTT and in those in whom the shunt traversed the tumor.[21] In fact, only the condition that tumors in the liver parenchyma preclude TIPS creation was considered as the absolute contraindications to TIPS.[22] However, recent studies have shown TIPS was safe and effective for preventing variceal rebleeding in HCC patients.[23,24] Whether HCC patients with variceal rebleeding can benefit from TIPS remains to be studied in the future.

As the most utilized severity scoring system, the Child-Pugh score was significantly related to the mortality at 6 weeks in AVB patients.[25] In our study, the Child-Pugh score remained a strong predictor for death at 6 weeks in AVB patients with HCC. Accordingly, we stratify HCC patients into four groups based on the Child-Pugh score and BCLC stage. We found that patients with higher Child-Pugh score (≥9) and advanced BCLC stage (C-D) had an increased risk of death at 6 weeks, reaching 60.2%. Of note, the majority (60/88) of these high-risk patients experienced the first episode of variceal bleeding in our study. Considering the much higher mortality after the episode of AVB in these patients, in addition to offering adequate treatment for HCC, the management of portal hypertension, including primary prophylaxis for variceal bleeding, is a major issue.[26]

There were a few limitations in the study. First, this was a single-center retrospective analysis with data collection and analysis restricted to patients presenting with AVB. Second, worsening of liver function and the history of variceal bleeding limit the systemic treatment for HCC. We cannot assess the effect of systemic treatment on outcomes in our study. Third, due to a lack of information regarding primary prophylaxis, whether the administration of primary prophylaxis improves outcomes in these patients needs to be illustrated in the future.

Conclusion

Our study found patients with HCC had significantly worse outcomes than those without in this matched study. The severity of liver disease and the stage of HCC are the main determinants of mortality in HCC patients. Overall management strategy for patients with symptomatic portal hypertension and HCC needs further optimization.

Data Sharing Statement

The data and materials of this article could be available by contacting the corresponding author.

Ethics Approval and Informed Consent

All patient data were anonymized to ensure confidentiality and the study followed the principles outlined in the Declaration of Helsinki and was approved by the Biomedical Research Ethics Committee of West China Hospital, Sichuan University [IRB No. 2022(339)]. Written informed consent was waived because of the retrospective nature of this study.

Acknowledgments

The authors thank all the colleagues who contributed to this work.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the Project for Science & Technology Department of Sichuan Province (No. 2020YFH0089).

Disclosure

The authors declare no conflicts of interest. The abstract of this paper was presented at Digestive Disease Week 2023 as a poster presentation talk with interim findings. The poster's abstract was published in "Poster Abstracts" in Gastroenterology: http://dx.doi.org/10.1016/s0016-5085(23)04136-7.

References

1. Graham DY, Smith JL. The course of patients after variceal hemorrhage. *Gastroenterology*. 1981;80(4):800–809. doi:10.1016/0016-5085(81)90144-X
2. Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. *N Engl J Med*. 2010;362(9):823–832. doi:10.1056/NEJMra0901512
3. Carbonell N, Pauwels A, Serfaty L, Fourdan O, Lévy VG, Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. *Hepatology*. 2004;40(3):652–659. doi:10.1002/hep.20339
4. Chalasani N, Kahi C, Francois F, et al. Improved patient survival after acute variceal bleeding: a multicenter, cohort study. *Am J Gastroenterol*. 2003;98(3):653–659. doi:10.1111/j.1572-0241.2003.07294.x
5. Garrido A, Djouder N. Cirrhosis: a Questioned Risk Factor for Hepatocellular Carcinoma. *Trends Cancer*. 2021;7(1):29–36.
6. Akinyemiju T, Abera S, Ahmed M, et al. The Burden of Primary Liver Cancer and Underlying Etiologies From 1990 to 2015 at the Global, Regional, and National Level: results From the Global Burden of Disease Study 2015. *JAMA Oncol*. 2017;3(12):1683–1691.
7. Couto OF, Dvorchik I, Carr BI. Causes of death in patients with unresectable hepatocellular carcinoma. *Dig Dis Sci*. 2007;52(11):3285–3289. doi:10.1007/s10620-007-9750-3
8. Bambha K, Kim WR, Pedersen R, Bida JP, Kremers WK, Kamath PS. Predictors of early re-bleeding and mortality after acute variceal haemorrhage in patients with cirrhosis. *Gut*. 2008;57(6):814–820. doi:10.1136/gut.2007.137489
9. Augustin S, Muntaner L, Altamirano JT, et al. Predicting early mortality after acute variceal hemorrhage based on classification and regression tree analysis. *Clin Gastroenterol Hepatol*. 2009;7(12):1347–1354. doi:10.1016/j.cgh.2009.08.011
10. Abraldes JG, Villanueva C, Bañares R, et al. Hepatic venous pressure gradient and prognosis in patients with acute variceal bleeding treated with pharmacologic and endoscopic therapy. *J Hepatol*. 2008;48(2):229–236. doi:10.1016/j.jhep.2007.10.008

11. Amitrano L, Guardascione MA, Bennato R, Manguso F, Balzano A. MELD score and hepatocellular carcinoma identify patients at different risk of short-term mortality among cirrhotics bleeding from esophageal varices. *J Hepatol*. 2005;42(6):820–825. doi:10.1016/j.jhep.2005.01.021
12. D'Amico G, De Franchis R. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. *Hepatology*. 2003;38 (3):599–612. doi:10.1053/jhep.2003.50385
13. Lee YR, Park SY, Tak WY. Treatment outcomes and prognostic factors of acute variceal bleeding in patients with hepatocellular carcinoma. *Gut Liver*. 2020;14(4):500–508. doi:10.5009/gnl19155
14. Reig M, Forner A, Rimola J, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. *J Hepatol*. 2022;76 (3):681–693. doi:10.1016/j.jhep.2021.11.018
15. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C, Baveno VII. Renewing consensus in portal hypertension. *J Hepatol*. 2022;76 (4):959–974. doi:10.1016/j.jhep.2021.12.022
16. Huo TI, Ho SY, Liao JI. Improving the accuracy of outcome prediction for hepatocellular carcinoma: Asia strategies. *Liver Int*. 2022;42 (3):714–715. doi:10.1111/liv.15167
17. Huang XT, Chen LH, Huang CS, et al. Establishment of a nomogram by integrating molecular markers and tumor-node-metastasis staging system for predicting the prognosis of hepatocellular carcinoma. *Dig Surg*. 2019;36(5):426–432. doi:10.1159/000494219
18. Li YK, Wu S, Wu YS, et al. Portal venous and hepatic arterial coefficients predict post-hepatectomy overall and recurrence-free survival in patients with hepatocellular carcinoma: a retrospective study. *J Hepatocell Carcinoma*. 2024;11:1389–1402. doi:10.2147/JHC.S462168
19. Ripoll C, Genescà J, Araujo IK, et al. Rebleeding prophylaxis improves outcomes in patients with hepatocellular carcinoma. A multicenter case-control study. *Hepatology*. 2013;58(6):2079–2088. doi:10.1002/hep.26629
20. Chen Y, Ma X, Zhang X, et al. Prevention of variceal rebleeding in cirrhotic patients with advanced hepatocellular carcinoma receiving molecularly targeted therapy: a randomized pilot study of transjugular intrahepatic portosystemic shunt versus endoscopic plus β-blocker. *Hepatol Int*. 2022;16 (6):1379–1389. doi:10.1007/s12072-022-10388-7
21. Dariushnia SR, Haskal ZJ, Midia M, et al. Quality improvement guidelines for transjugular intrahepatic portosystemic shunts. *J Vasc Interv Radiol*. 2016;27(1):1–7. doi:10.1016/j.jvir.2015.09.018
22. Boike JR, Thornburg BG, Asrani SK, et al. North American practice-based recommendations for transjugular intrahepatic portosystemic shunts in portal hypertension. *Clin Gastroenterol Hepatol*. 2022;20(8):1636–1662.e1636.
23. Luo J, Li M, Wu C, et al. Transjugular intrahepatic portosystemic shunt versus endoscopic therapy for prevention of variceal rebleeding in patients with hepatocellular carcinoma meeting the Milan criteria. *Eur J Gastroenterol Hepatol*. 2021;33(3):436–442.
24. Tsauo J, Tie J, Xue H, et al. Transjugular intrahepatic portosystemic shunt creation for the prevention of gastric variceal rebleeding in patients with hepatocellular carcinoma: a multicenter retrospective study. *J Vasc Interv Radiol*. 2021;32(7):963–969. doi:10.1016/j.jvir.2021.04.005
25. Conejo I, Guardascione MA, Tandon P, et al. Multicenter external validation of risk stratification criteria for patients with variceal bleeding. *Clin Gastroenterol Hepatol*. 2018;16(1):132–139.e138. doi:10.1016/j.cgh.2017.04.042
26. Allaire M, Thabut D. Portal hypertension and variceal bleeding in patients with liver cancer: evidence gaps for prevention and management. *Hepatology*. 2023;71: 213–23.