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Determinants of outcomes in patients with hepatitis B virus-decompensated cirrhosis

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The role of pre-treatment HBV DNA levels on the prognosis of hepatitis B virus-related decompensated cirrhosis is unclear. This study investigated the effects of pre-treatment HBV DNA and other determinants on short-term and long-term survival of chronic hepatitis B (CHB) patients with decompensated cirrhosis. A total of 278 cirrhotic decompensated CHB patients treated with entecavir or tenofovir disoproxil fumarate were retrospectively enrolled. Cox regression models were used to analyze factors associated with all-cause mortality. The median follow-up time was 17 months (IQR2.17–58.94), during which 132 patients (47.4%) either died or underwent liver transplantation. The cumulative incidence of all-cause mortality was 16%, 29%, 34%, 39%, and 51% at the 1-month, 3-month, 6-month, 1-year, and 5-year follow-ups, respectively. Risk factors associated with 3-month all-cause mortality were age, presence of ascites and hepatic encephalopathy, baseline hepatitis flares, pre-treatment HBV DNA levels, and MELD scores. In the subgroup analysis, for 3-month all-cause mortality, significant associations of age, baseline hepatitis flares, and MELD scores with pre-treatment HBV DNA levels were observed (*p* for interaction were 0.005, 0.032, and 0.030, respectively). Risk factors associated with 5-year all-cause mortality were age, the presence of ascites and hepatic encephalopathy, and MELD scores. Liver functional reserve and age played a critical role in the prognosis of CHB patients with decompensated cirrhosis. Pre-treatment HBV DNA levels had an impact on short-term all-cause mortality, but not on long-term all-cause mortality.

Keywords Chronic hepatitis B, Decompensated cirrhosis, HBV DNA

Hepatitis B virus ((HBV) infection poses a major public health problem, with an estimated approximately 296 million infected individuals worldwide[1]. HBV-related hepatic complications, including hepatic decompensation, liver cirrhosis (LC), and hepatocellular carcinoma (HCC) occurred in 15%-40% of chronic hepatitis B (CHB) patients[2,3]. An estimated 820,000 people died from HBV-related disease in 2019, with deaths related to HBV-related LC and HCC contributing to 52% and 38%, respectively[1,4].

There are two natural progressions of hepatic decompensated cirrhosis from compensated cirrhosis. One is an acute episode of preceding hepatitis B flares, while the other follows a gradual deterioration pattern leading to end-stage liver conditions[5,6]. Patients with decompensated cirrhosis generally have a worse prognosis compared to those with compensated cirrhosis. The 1-year, 2-year, and 3-year cumulative survival rates were 100% and 81.2% , 98.5% and 75.6%, and 98.5% and 69.5% in patients with compensated cirrhosis and decompensated cirrhosis, respectively[7]. The 5-year survival rate without liver transplantation drops to 14% -35% in decompensated cirrhotic CHB patients[6]. Patients with decompensated cirrhosis have a higher risk of disease progression to acute on-chronic liver failure (ACLF), which is characterized by hepatic and extrahepatic organ failure(s)[8,9]. The 28-day transplant-free mortality rates in HBV-related decompensated cirrhotic patients and

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cirrhotic HBV-ACLF patients were 4.5% and 52.1%, respectively, with corresponding 90-day mortality rates of 7.1% and 69.7%[10].

Thus, international hepatitis B virus associations recommend immediate treatment with antiviral agents for CHB patients with decompensated cirrhosis to prevent deterioration of hepatic decompensation[11–13]. The role of pre-treatment HBV DNA levels in the prognosis of HBV-related decompensated cirrhosis remain unclear. This study aimed to investigate the impact of pre-treatment HBV DNA levels and identify factors during hepatic decompensation that could determine clinical outcomes in decompensated cirrhotic CHB patients treated with entecavir (ETV) or tenofovir (TDF).

Materials and methods

Patients and study design

This study population consisted of patients from an observational retrospective cohort of decompensated cirrhotic CHB patients treated with ETV or TDF between June 2009 and October 2022 in Taichung Veterans General Hospital. Hepatic decompensation was defined as an increase in serum total bilirubin (T-Bil) level greater than 2 mg/dL, prolongation of prothrombin time (PT) ≥ 3 s, or an international normalized ratio (INR) > 1.5 with or without the presence of ascites and /or hepatic encephalopathy[14]. The definition of CHB was hepatitis B surface antigen seropositivity for 6 months. The diagnosis of cirrhosis was based on the characteristic findings from radiological tests (such as a shrunken liver, surface nodular pattern or splenomegaly) of ultrasonography, computed tomography or magnetic resonance imaging. We excluded patients aged younger than 18 years old, those with current coinfection with the hepatitis C virus, or human immunodeficiency virus, or a history of hepatic tumor or non-hepatic tumor.

Ethical declaration

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board and Ethics Committee of Taichung Veterans General Hospital (IRB: CE-18232A) and the Ethics Committee waived informed consent.

Assessment and follow-up evaluation

The baseline date was defined as the date when decompensated status was noted. Prescription of TDF or ETV was initiated upon recognition of the decompensated status. Patients' baseline characteristics were assessed and laboratory tests were conducted, including age, sex, liver biochemical test, creatinine, serum HBV DNA, hepatitis B e antigen (HBeAg), and model for end-stage liver disease (MELD) scores. MELD scores were calculated at baseline according to the following equations: (0.378 * loge(bilirubin)) + (1.120*loge(INR)) + (0.957*loge(creatinine)) + 0.643) * 10 (if hemodialysis, value for creatinine is automatically set to 4.0)[15]. ALT normalization was defined as values within the upper limit of normal (ULN) and was set at 50 U/L for men and 35U/L for women according to the local laboratory reference. The definition of hepatitis flares was a rise of ALT levels to > 5 times ULN.

Patients with hepatic decompensation were followed-up closely every 1–2 weeks during the first 3 months and then every 3 months. The primary end-point was 3-month all-cause mortality and the secondary end-point was 5-year all-cause mortality. Patients who died or underwent liver transplantation were included in all-cause mortality categories during the period of follow-up.

Laboratory methods

HBV DNA levels were measured using a real-time PCR assay and Roche CobasTaqMan HBV Test, with a lower limit of quantification of 20 IU/mL (Roche Diagnostics, Branchburg, USA). The status of HBsAg was determined using a qualitative Architect assay (Abbott Laboratories, Chicago, Illinois, USA). Qualitative HBeAg was determined by commercial enzyme immunoassays (Roche Diagnostics, Mannheim, Germany).

Statistical analysis

Categorical variables were expressed as number of cases and compared by the Chi-squared test or Fisher's exact test. Continuous variables were expressed as median ± interquartile range (IQR) and compared by the Mann–Whitney U test. The cumulative incidence of 3-month and 5-year all-cause mortality were calculated using the Kaplan–Meier method and compared using the log-rank test. Cox proportional hazards models were employed to assess factors associated with 3-month and 5-year all-cause mortality, adjusting for all independent variables with a p value < 0.05, which was considered statistically significant in the univariate analyses. Sensitivity analyses were conducted to explore the associations of pretreatment HBV DNA levels with 3-month and 5-year all-cause mortality. Statistical tests were performed using SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Patients' characteristics

Figure 1 shows that a total of 278 decompensated cirrhotic CHB patients treated with ETV or TDF were included in this study. The median follow-up duration was 17 months (IQR2.17–58.94). Of these patients, with median age of 56.22 years (IQR 47.39–64.62), 223 (80.20%) were male and 37 (13.30%) were HBeAg-positive. Specifically, 230 patients (82.70%) received ETV, while 48 (17.30%) were treated with TDF (Table 1). Patients who died or underwent liver transplant had a higher percentage of the presence of ascites and hepatic encephalopathy (75.80% vs. 43.20%, $p < 0.001$; 22.70% vs. 3.40%, $p < 0.001$), lower albumin levels (2.8 g/dL vs. 3.1 g/dL, $p < 0.001$), higher bilirubin levels (7.85 mg/dl vs. 3.20 mg/dl, $p < 0.001$), prolonged prothrombin time (17.35 s vs. 13.7 s, $p < 0.001$), and high MELD scores (22.58 vs. 14.92, $p < 0.001$) compared to those who survived.

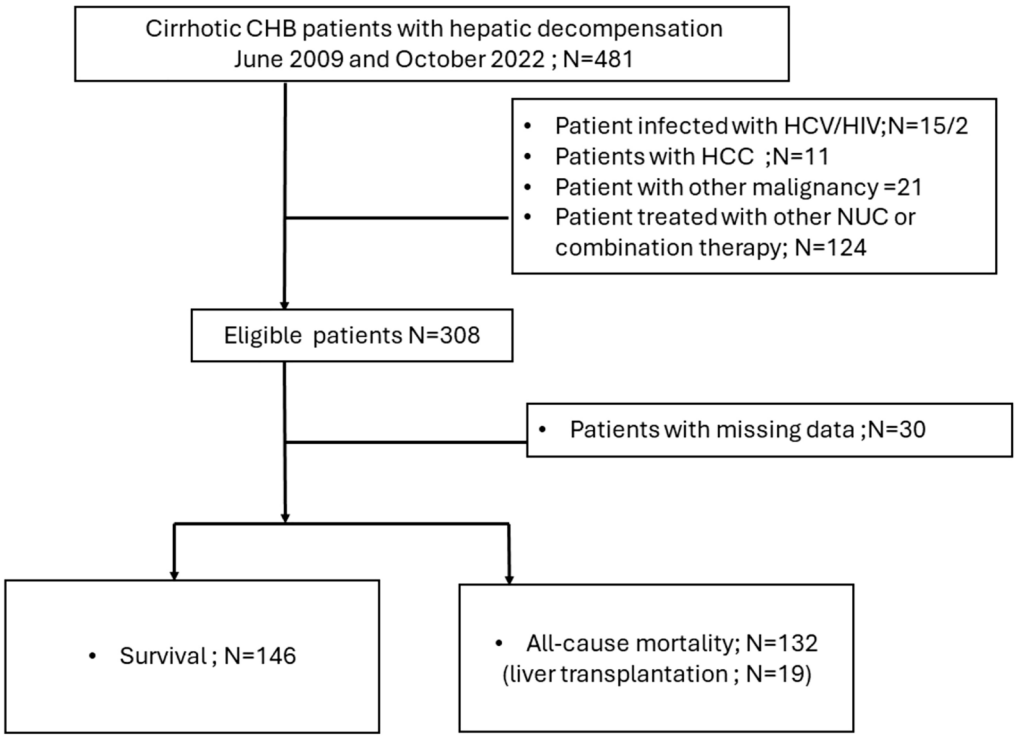

Fig. 1. Flow chart of the enrolled patients. CHB, chronic hepatitis B; HCV, hepatitis C virus; HIV, human immunodeficiency; HCC, hepatocellular carcinoma; NUC, nucleoside/nucleotide analogs.

Factors associated with 3-month all-cause mortality

In total, 80 patients (28.80%) died or underwent liver transplantation, including 15 treated with TDF and 65 with ETV during the first 3 months. The cumulative incidence of all-cause mortality was 16%, 29%, 34%, 39% and 51% at the 1-month, 3-month, 6-month, 1-year, and 5-year follow-ups, respectively (Fig. 2A and 2B).

Factors associated with all-cause mortality within 3 months were analyzed by Cox regression analysis, and the choice of ETV or TDF was not found to be associated with 3-month all-cause mortality. In the multivariate Cox regression analysis, significant risk factors for all-cause mortality within 3 months included older age (hazard ratio [HR] = 1.037, 95%CI:1.014–1.061, $p = 0.001$), presence of ascites and hepatic encephalopathy (HR = 2.972, 95%CI:1.541–5.731, $p = 0.001$; and HR = 3.307, 95%CI:1.767–6.188, $p < 0.001$), ALT≧5 × ULN (HR = 2.094, 95%CI:1.088–4.030, $p = 0.027$), MELD scores (HR = 1.101, 95%CI: 1.058–1.146, $p < 0.001$), and pre-treatment HBV DNA levels (HR = 1.147, 95%CI: 1.004–1.312, $p = 0.044$) (Table 2).

In this study, 189 enrolled patients met APASL ACLF criteria[9]. Significant risk factors for 3-month all-cause mortality in patients who fulfilled the APASL ACLF criteria are detailed in Supplementary Table 1 (Table S1).

Hazard ratios for all-cause mortality within 3 months for patients across different patient subgroups based on levels of pre-treatment HBV DNA are shown in Fig. 3. The risk of 3-month all-cause mortality was significantly higher in patients with pre-treatment HBV DNA levels ≧ 4 Log_{10} IU/mL compared to those with pre-treatment HBV DNA levels < 4 Log_{10} IU/mL (HR = 2.354; 95%CI: 1.322–4.192; $p = 0.004$). Moreover, we observed significant interactions between pre-treatment HBV DNA levels with age, baseline hepatitis flares, and MELD score (p for interaction = 0.005, 0.032, and 0.030, respectively). The effect of pre-treatment HBV DNA levels ≧ 4 Log_{10} IU/mL was more pronounced in patients under 60 years of age, without baseline hepatitis flares, and those with MELD score ≧20 compared to their counterparts.

Figure 4 illustrates the combined effect of HBV DNA ≧4 Log_{10} IU/mL and MELD scores ≧ 20 on 3-month all-cause mortality, showing an adjusted HR of 2.795 (95% CI: 1.094–7.140, $p = 0.032$).

Factors associated with 5-year all-cause mortality

A total of 132 patients (47.5%) either died or underwent liver transplantation, including 20 treated with TDF and 112 with ETV over a period of 5 years. Among the 278 enrolled patients, 143 of them regained liver compensation, defined as having serum bilirubin levels < 2 mg/dL and an INR prolongation of < 3 s. Factors associated with 5-year all-cause mortality were analyzed using Cox regression analysis, and the choice of ETV or TDF was not associated with 5-year all-cause mortality. In the multivariate Cox regression analysis, significant risk factors for 5-year all-cause mortality were older age (HR = 1.021, 95% CI: 1.004–1.039, $p = 0.017$), presence of ascites and hepatic encephalopathy (HR = 2.519, 95% CI: 1.538–4.125, $p < 0.001$; and HR = 3.634, 95% CI: 2.167–6.094, $p < 0.001$), and MELD scores (HR = 1.071, 95% CI: 1.041–1.102, $p < 0.001$) (Table 3).

Variables	Total (n = 278)		Survival n = 146		Mortality n = 132		*p* value
Age, years	**56.22**	**(47.39–64.62)**	**55.21**	**(45.43–63.37)**	**57.24**	**(48.98–65.49)**	**0.12**
Follow-up time (months)	17.00	(2.17–58.94)	54.95	(28.62–91.14)	1.93	(0.73–8.21)	<0.001
Male sex, n (%)	223	80.20%	120	83.60%	103	78.00%	0.384
Naïve, n(%)	239	86%	125	85.60%	144	86.4%	0.858
NUC							0.375
TDF	48	17.30%	28	19.20%	20	15.20%	
ETV	230	82.70%	118	80.80%	112	84.80%	
HBV DNA (log_{10} IU/ml)	5.52	(2.99–6.91)	5.20	(2.67–6.72)	5.66	(3.48–7.16)	0.153
HBeAg-positivity, n (%)	37	13.30%	23	15.80%	14	10.60%	0.207
Ascites, n(%)	163	58.60%	63	43.20%	100	75.80%	<0.001
Hepatic encephalopathy, n (%)	35	12.60%	5	3.40%	30	22.70%	<0.001
Platelet, 10^3/μL	89	(61–124.5)	87.00	(61–121.25)	99	(61–131)	0.969
APF, ng/mL	10.35	(5.34–39.90)	10.91	(5.57–41.40)	10.32	(4.93–32.68)	0.625
ALT, U/L	95	(43–397.75)	84.5	(47–290.75)	134	(40.25–794.5)	0.195
Albumin, g/dL	3	(2.6–3.4)	3.1	(2.7–3.6)	2.8	(2.4–3.2)	<0.001
Total bilirubin, mg/dL	4.6	(2.6–10.9)	3.2	(2.4–5.925)	7.85	(2.95–16.17)	<0.001
Prothrombin time, s	15.1	(13.2–18.025)	13.7	(12.6–15.93)	17.35	(14.25–21.5)	<0.001
Creatinine, mg/dL	0.86	(0.69–1.1)	0.84	(0.66–1)	0.9	(0.7–1.26)	0.102
MELD score	17.51	(13.69–24.01)	14.92	(12.34–19.20)	22.58	(17.08–27.06)	<0.001

Table1. Baseline characteristics. Mann–Whitney U test. Chi-Square test. Fisher's exact test. The quantitative variables are expressed as the median (75th (Q3) –25th (Q1) percentiles of the data: interquartile range. NUC, Nucleoside/nucleotide analogs; TDF, Tenofovir disoproxil fumarate; ETV, entecavir; AFP, alpha-fetoprotein; ALT, alanine aminotransferase; MELD, Model for End-Stage Liver Disease.

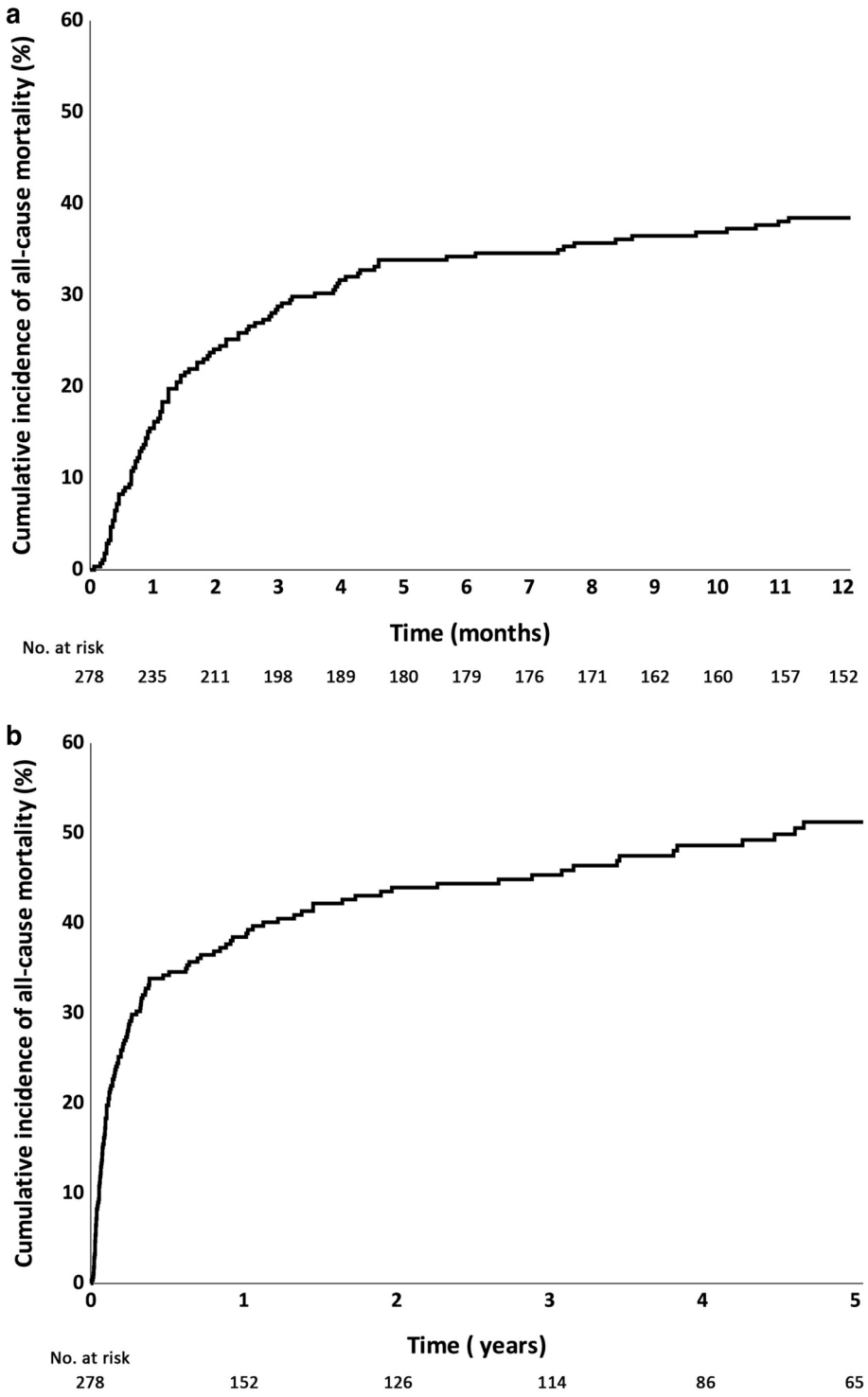

Fig. 2. The cumulative incidences of all-cause mortality; (**A**) one-year cumulative incidence, (**B**) 5-year cumulative incidence.

There were no significant differences or interactions in hazard ratios for 5-year all-cause mortality among patients with varying levels of pre-treatment HBV DNA across different subgroups. Additional details can be found in Supplementary Fig. 1.

Discussion

The cumulative incidence of all-cause mortality was 16%, 19%, 34%, 39%, and 51% at the 1-month, 3-month, 6-month, 1-year, and 5-year follow-ups, respectively. ETV or TDF was not an independent factor of the prognosis in CHB patients with decompensated cirrhosis regardless of whether assessing 3-month or 5-year all-

	Univariate model				Multivariate model			
	HR	(95%CI)		p value	HR	(95%CI)		*p* value
Age, year	**1.031**	**1.012**	**1.050**	**0.001**	**1.037**	**1.014**	**1.061**	**0.001**
Male sex	0.924	0.541	1.579	0.773	0.832	0.431	1.605	0.583
HBeAg-positivity	0.918	0.473	1.780	0.799				
Ascites	3.311	1.914	5.729	<0.001	2.972	1.541	5.731	0.001
Hepatic encephalopathy	5.617	3.505	9.004	<0.001	3.307	1.767	6.188	<0.001
APF (ng/ml)	1.001	0.999	1.002	0.442				
Platelet (10^3/μL)	1.006	1.002	1.010	0.004	0.999	0.994	1.005	0.810
ALT ≧ 5×ULN	4.040	2.565	6.365	<0.001	2.094	1.088	4.030	0.027
Albumin (g/dL)	0.586	0.385	0.894	0.013	1.219	0.658	2.259	0.530
Total bilirubin (mg/dL)	1.096	1.071	1.122	<0.001				
Prothrombin time (s)	1.070	1.053	1.088	<0.001				
Creatinine (mg/dL)	1.102	0.989	1.227	0.077				
MELD score	1.134	1.105	1.164	<0.001	1.101	1.058	1.146	<0.001
HBV DNA (Log_{10} IU/ml)	1.239	1.064	1.442	0.006	1.147	1.004	1.312	0.044
ETV	0.881	0.503	1.545	0.659				

Table 2. Factors associated with 3-month all-cause mortality. Cox proportional hazards models. HBeAg, hepatitis B e antigen ; AFP, alpha-fetoprotein; ALT, alanine aminotransferase; ULN, upper limited normal; MELD, Model for End-Stage Liver Disease. ETV, entecavir.

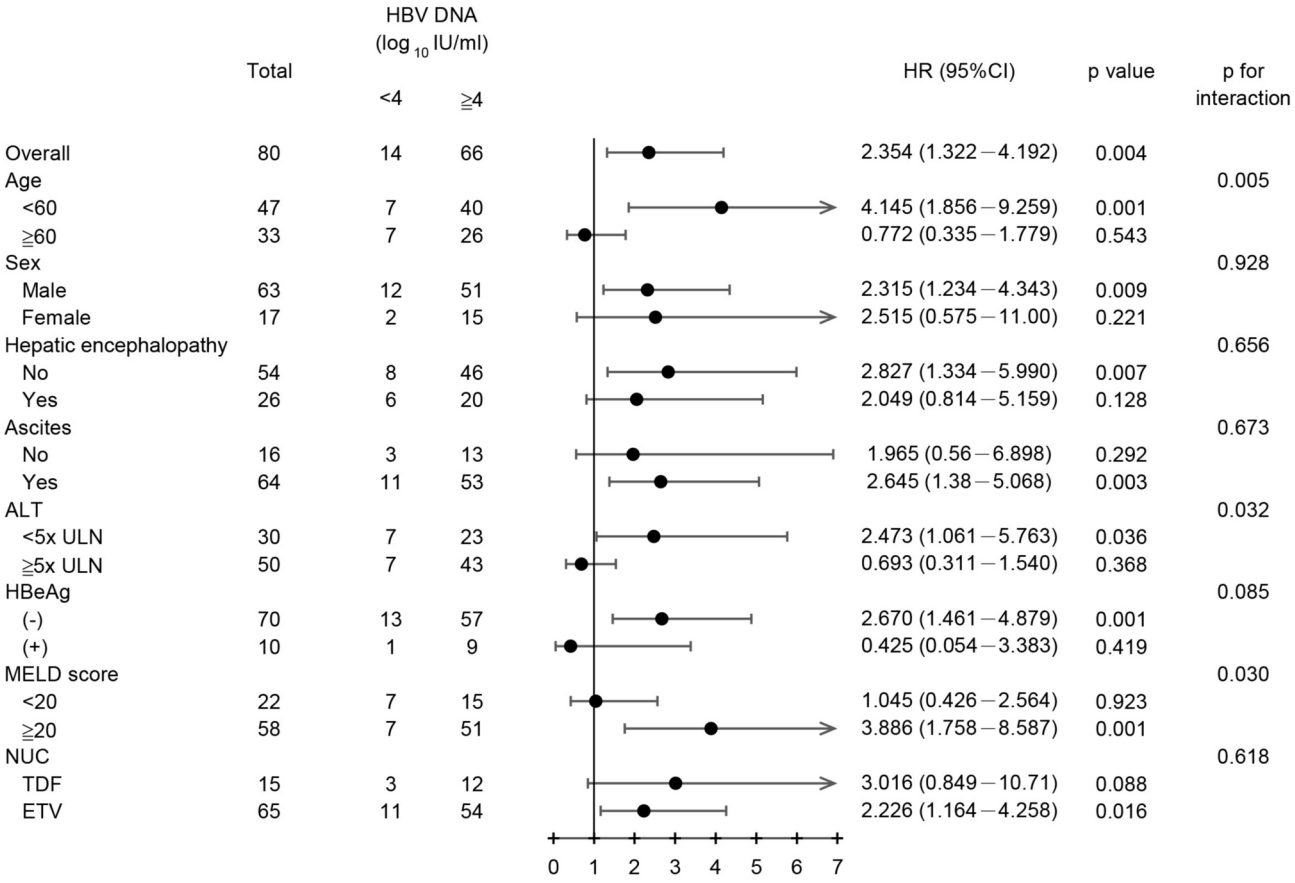

Fig. 3. Sensitivity analyses for 3-months all-cause mortality for HBV-related decompensated cirrhotic patients with pre-treatment HBV DNA < 4 and ≧ 4 $\log_{10}$ IU/mL. HBeAg, hepatitis B e antigen ; ALT, alanine aminotransferase; MELD, Model for End-Stage Liver Disease; NUC, Nucleoside/nucleotide analogs; TDF, Tenofovir disoproxil fumarate; ETV, entecavir.

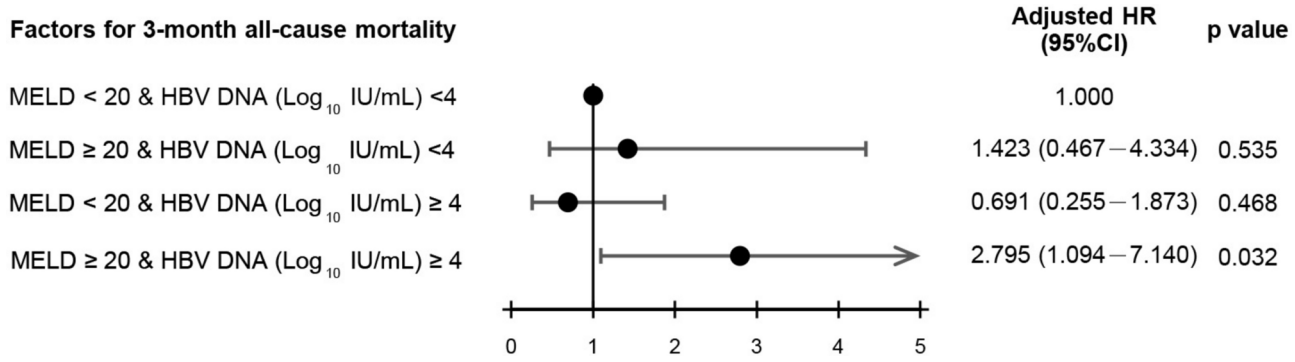

Fig. 4. Covariate-adjusted hazard ratio in relation to combined independent factors. MELD, model for end-stage liver disease; HR, hazard ratio.

cause mortality. Age, presence of ascites and hepatic encephalopathy, and higher MELD scores were predictors of both 3-month and 5-year all-cause mortality. Higher levels of HBV DNA and hepatitis flares at baseline were also independent predictors of 3-month all-cause mortality, but not 5-year all-cause mortality.

In concordance with findings from other studies, our study demonstrated that the choice of antiviral therapy was not an independent factor of all-cause mortality in CHB -patients with decompensated cirrhosis[14,16]. The severity and prognosis of decompensated cirrhosis has been associated with pre-existing liver disease and baseline liver function reserve. TCF-Yip et al. reported younger age, as well as lower baseline MELD scores and ALT levels were predictors of 6-month transplantation-free survival in CHB cirrhotic patients with baseline MELD scores≧15[17]. In a Taiwan 8-year cohort study, the presence of hepatic encephalopathy and baseline

	Univariate model				Multivariate model			
	HR	(95%CI)		p value	HR	(95%CI)		*p* value
Age, year	**1.015**	**1.001**	**1.030**	**0.044**	**1.021**	**1.004**	**1.039**	**0.017**
Male sex	0.863	0.571	1.303	0.483	0.960	0.577	1.597	0.875
HBeAg-positivity	0.758	0.436	1.320	0.328				
Ascites	3.084	2.064	4.601	<0.001	2.519	1.538	4.125	<0.001
Hepatic encephalopathy	4.828	3.173	7.347	<0.001	3.634	2.167	6.094	<0.001
APF (ng/ml)	1.000	0.999	1.001	0.937				
Platelet (10^3 /μL)	1.004	1.001	1.007	0.021	1.000	0.996	1.004	0.958
ALT ≧ 5×ULN	1.925	1.361	2.722	<0.001	1.613	0.977	2.664	0.062
Albumin (g/dL)	0.438	0.312	0.613	<0.001	0.734	0.459	1.173	0.196
Total bilirubin (mg/dL)	1.074	1.054	1.094	<0.001				
Prothrombin time (s)	1.061	1.046	1.077	<0.001				
Creatinine (mg/dL)	1.071	0.976	1.176	0.150				
MELD score	1.103	1.081	1.126	<0.001	1.071	1.041	1.102	<0.001
HBV DNA (Log_{10} IU/ml)	1.085	1.002	1.174	0.044	1.081	0.980	1.192	0.121
ETV	1.092	0.678	1.757	0.718				

Table 3. Factors associated with 5-year all-cause mortality. Cox proportional hazards models. HBeAg, hepatitis B e antigen. AFP, alpha-fetoprotein; ALT, alanine aminotransferase; ULN, upper limited normal; MELD, Model for End-Stage Liver Disease. ETV, entecavir.

MELD score were independent predictors of both 3-month and 8-year liver-related morality in decompensated CHB patients[14]. In our study, older age, the presence of ascites and hepatic encephalopathy, and higher baseline MELD scores were predictors of both 3-month and 5-year all-cause mortality.

The key finding in the present study is that higher levels of HBV DNA and hepatitis flares at baseline were also predictors of 3-month all-cause mortality, but not 5-year all-cause mortality. Ying Zhu report that HBV reactivation exhibited a higher risk of 90-day mortality in cirrhotic patients compared to those without cirrhosis[18]. This could be explained by the fact that HBV-triggered flares could cause hepatocytes damage induced by interactions between a vigorous host immune response and a high viral load. Such conditions increase the risk of developing liver failure, leading to a higher short-term mortality rate in cirrhotic CHB patients[19]. In sensitivity analyses, the effects of pre-treatment HBV DNA $\geqq 4$ Log_{10} IU/mL and 3-month all-cause mortality were more pronounced in patients under 60 years of age and in those without baseline hepatitis flares compared to their counterparts. A possible explanation for these findings is the prolonged presence of high HBV DNA levels in serum, which can cause more severe liver fibrosis and accelerate the progressive deterioration of cirrhosis in younger cirrhotic decompensated CHB patients without high levels of ALT[20,21]. Furthermore, ETV and TDF, the first-line treatment options for CHB, achieved undetectable HBV DNA in 82.9% and 71.4% of treatment-naïve CHB patients, respectively, after one year of antiviral therapy[22,23]. This implies that due to their high potency and low resistance of TDF and ETV against HBV replication, long-term antiviral therapy could lead to sustained viral suppression, stabilizing liver function over time and improving long-term survival[12,16]. These factors help explain why baseline HBV DNA had less impact on 5-year all-cause mortality.

Our findings have clinical implications as we identified risk factors associated with all-cause mortality in patients with hepatitis B virus-related decompensated cirrhosis. The initial 3–6 months following the diagnosis of decompensation status appear to be crucial for determining whether liver reserve can recover or stabilize for patients with hepatitis B virus-related decompensated cirrhosis[5]. Our study observed a sharp rapid increase in all-cause mortality within the first 3-months, with independent factors, including age, baseline HBV DNA levels, ALT levels, MELD scores, the presence of ascites and hepatic encephalopathy, contributing to 3-month all-cause mortality. Interestingly, baseline HBV DNA levels were found to be associated with short-term all-cause mortality, but not long-term all-cause mortality, suggesting a critical role in initial disease progression. The MELD score, validated as one of the criteria for allocation of liver transplantation in patients with end-stage liver disease[24], also demonstrated that the combination of MELD score $\geqq 20$ and HBV DNA $\geqq 4$ log_{10} IU/mL contributed to a joint effect in the 3-month all-cause mortality. This underscores the heightened risk of short-term all-cause mortality for HBV-mediated liver decompensation and liver failure in patients with poor liver reserve at baseline. Additionally, our findings indicate that aggressive treatment with antiviral therapy to suppress HBV viral replication in CHB patients with cirrhosis is crucial to reduce the HBV-triggered persistent damage in liver reserve. Antiviral therapy to achieve HBV suppression is essential to improve long-term survival if patients can recover from the crisis of acute liver decompensation or liver failure[16]. Clinicians can potentially use these insights to predict unfavorable outcomes and determine the likelihood of the need for liver transplantation, as the process of hepatic decompensation could be irreversible despite antiviral therapy for suppressing HBV viral load.

There were several limitations in this study. First, this was a retrospective study with an insufficient number to perform propensity score matching, which could reduce baseline confounding variables between patients treated with ETV and TDF. Second, data on HBV genotype were unavailable, and different HBV genotypes (such as genotype B and C, which are strongly associated with development of cirrhosis and HCC[25]) could influence disease progression differently. Therefore, we did not adequately elucidate the impact of HBV genotype on the outcomes in decompensated cirrhotic CHB patients. Third, a liver biopsy was not performed for all enrolled patients due to coagulopathy to confirm the severity of cirrhotic status. Fibroscan and elastography were also not available before decompensated status and during the period of follow-up. Baseline non-invasive laboratory-based tests (e.g., Fibrosis-4 Index, aspartate aminotransferase-to-platelet ratio index) might be affected in the setting of acute decompensated status initially. The diagnosis of cirrhosis was based on the discretion of gastroenterologists interpreting radiological findings, which may not always be sufficient for an accurate diagnosis. Additionally, it is challenging to confirm the presence of hepatic steatosis without liver biopsies in our study. Forth, data on Serum GGT were not available for all patients. Therefore, we did not adequately elucidate the impact of GGT on the outcomes in decompensated cirrhotic CHB patients. Fifth, details regarding daily alcohol consumption were not always documented in our retrospective study, so we were unable to confirm whether patients consumed alcohol (> 20 g/day) or not. Finally, in analyzing risk factors for mortality among our participants, we did not account for non-liver related mortality as a competing risk in assessing the association of liver-related mortality and independent variables. Instead, we used all-cause mortality as the study endpoint because the number of cases of non-liver related mortality was small.

In conclusion, hepatic reserve and age were associated with both 3-month and 5-year all-cause mortality in decompensated cirrhotic CHB patients. Additionally, higher levels of baseline HBV DNA and hepatitis flares were predictors of 3-month, but not 5-year all-cause mortality, suggesting that flares mediated by high HBV viral load play a crucial role in the short-term survival of CHB patients with decompensated cirrhosis.

Data availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

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Author contributions

Conceptualization: Y.-J.H. and T.-C.L.; methodology: Y.-J.H., T.-C.L. and C.-H.C. (Cheng-Hsu Chen); formal analysis: Y.-J.H. and T.-C.L.; resources: Y.-J.H., C.-H.C. (Chung-Hsin Chang), S.-C.L., Y.-C.P., S.-W.L. and T.-Y.L.; investigation: Y.-J.H. and T.-C.L.; writing—original draft: Y.-J.H., T.-C.L.; writing—review and editing: C.-H.C. (Cheng-Hsu Chen), C.-H.C. (Chung-Hsin Chang), S.-C.L., Y.-C.P., S.-W.L., T.-Y.L., J.-S.W., T.-C.L.; supervision: T.-C.L. All authors have read and agreed to the published version of the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board and Ethics Committee of Taichung Veterans General Hospital (IRB: CE-18232A) and the Ethics Committee waived informed consent.

Additional information

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