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Neutrophil-derived ratios as predictors of short-term mortality in HBV-associated decompensated cirrhosis

Yang Xiang[1] and WeiLin Mao[2*]

Abstract

Background Hepatitis B virus-associated decompensated cirrhosis (HBV-DC) is recognized as a critical illness with an increased risk of short-term mortality. Neutrophil-derived ratios, including neutrophil-to-lymphocyte ratio (NLR), neutrophil-to-albumin ratio, neutrophil-to-high-density lipoprotein-cholesterol ratio, neutrophil-to-hemoglobin ratio, and neutrophil-to-platelet ratio, have emerged as potential prognostic markers in various liver diseases. The present study aimed to determine the effectiveness of these neutrophil-derived ratios for prediction of mortality in patients with HBV-DC.

Methods We conducted a retrospective analysis of HBV-DC patients at our hospital between April 2022 and April 2024. The study endpoint was the 30-day mortality rate. These neutrophil-derived ratios were calculated from data obtained during routine laboratory tests on admission. Disease severity was assessed using the Model for End-Stage Liver Disease (MELD) score. Multivariate regression analyses and receiver operating characteristic (ROC) curve analyses were conducted.

Results The study investigated 160 HBV-DC patients, of whom 23 (14.4%) experienced mortality within 30 days. Non-survivors exhibited markedly higher values for neutrophil-derived ratios than survivors. All neutrophil-derived ratios were associated with mortality in univariate analyses, but only NLR and MELD score remained as independent predictors of mortality in multivariate analyses. In the ROC analyses, NLR showed a similar prognostic value to MELD score. Moreover, both NLR and MELD score had high specificity for prediction of mortality in HBV-DC patients.

Conclusions Among neutrophil-derived ratios, NLR stands out as a simple and reliable predictor of mortality in HBV-DC patients.

Keywords Neutrophil-derived ratios, Decompensated cirrhosis, Hepatitis B virus, Predictor, Mortality

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Introduction

Cirrhosis is a major cause of death worldwide. Hepatitis B virus (HBV) infection is the predominant cause of cirrhosis in Asian-Pacific countries [1]. Cirrhosis is typically classified into compensated or decompensated stages, with the transition from compensated to decompensated occurring at an annual rate of 3% [2]. In patients with decompensated cirrhosis (DC), the survival rates drop to 14–35% at the 5-year mark [3]. HBV-associated decompensated cirrhosis (HBV-DC) is accompanied by various complications that are closely associated with the patient prognosis [2, 3]. Currently, liver transplantation remains a potential life-saving measure for these patients. However, the scarcity of available donors restricts its widespread application. Consequently, there is a growing focus on the identification of dependable and precise indicators for the clinical prognosis of HBV-DC patients, with the goal of facilitating timely interventions and thereby reducing mortality rates.

Inflammation plays a crucial role in the progression of end-stage liver disease, and systemic inflammation is associated with alterations in peripheral blood leukocytes, including neutrophils, lymphocytes, and platelets. As a result, combinations of these variables may serve as prognostic markers for liver diseases. Neutrophils comprise the largest population of circulating leukocytes and act as the primary defense against pathogens [4]. These cells release antimicrobial substances and signals for other immune cells to combat invaders [5, 6]. Thus, neutrophils are central to the systemic inflammatory response to infection and function as essential components of the immune system [7–9]. In recent years, laboratory-based biomarkers have become a major focus in studies on risk factors for clinical diseases. Among these, various neutrophil-derived ratios, including neutrophil-to-lymphocyte ratio (NLR), neutrophil-to-albumin ratio (NAR), neutrophil-to-high-density lipoprotein-cholesterol ratio (NHR), neutrophil-to-hemoglobin ratio (NHBR), and neutrophil-to-platelet ratio (NPR), have emerged as potential diagnostic or prognostic biomarkers, particularly in liver diseases [10–13]. However, no studies have compared these neutrophil-derived ratios (NLR, NAR, NHR, NHBR, and NPR) for prognostic purposes in HBV-DC patients. To address this gap in knowledge, we conducted a retrospective study to ascertain and compare the predictive performance of these ratios with 30-day outcomes in HBV-DC patients.

Materials and methods

Patient enrollment

This retrospective study recruited 211 HBV-DC patients admitted to the Division of Infectious Diseases at our hospital between April 2022 and April 2024. Decompensation was characterized by onset of ascites, variceal bleeding, hepatic encephalopathy, and/or hepatorenal syndrome [14]. The exclusion criteria were: (1) hepatocellular carcinoma; (2) underlying liver diseases (e.g., other viral hepatitis diseases, alcoholic liver diseases, or drug-induced liver diseases); (3) hematological diseases; (4) liver transplantation; and 5) incomplete clinical data. Patients using steroid or immunosuppressants were also excluded. Finally, 160 patients were enrolled (Fig. 1). All participants received standardized management in accordance with current guidelines, including antiviral therapy, antibiotics, and evidence-based supportive care. The endpoint was 30-day mortality. Comprehensive follow-up was conducted using inpatient medical records and telephone interviews for discharged patients. No patients were lost to follow-up or underwent liver transplantation during the 30-day observation period.

Data collection

Demographic information, such as age and gender, as well as routine laboratory test data on admission, such as blood counts (neutrophils, lymphocytes, platelets, hemoglobin), liver function parameters (total bilirubin, alanine transaminase, aspartate transaminase, total protein, albumin), coagulation parameters (international normalized ratio [INR]), kidney function parameters (serum creatinine), and serum HDL-C levels, were extracted from the electronic medical records. The Model for End-Stage Liver Disease (MELD) score was calculated as described previously [15].

Prognostic scores

The prognostic scores were calculated using the following equations (all scores and ratios are unitless):

MELD score = 3.8 ln (total bilirubin, mg/dL) + 11.2 ln (INR) + 9.6 ln (creatinine, mg/dL) + 6.4.

NLR = neutrophil count ($\times 10^9$/L) / lymphocyte count ($\times 10^9$/L).

NAR = neutrophil count ($\times 10^9$/L) / albumin (g/dL).

NHR = neutrophil count ($\times 10^9$/L) / HDL-C (mmol/L).

NHBR = neutrophil count (×109/L) / hemoglobin (g/dL).

NPR = neutrophil count ($\times 10^9$/L) / platelet count ($\times 10^4$/L).

Statistical analysis

Data analyses were undertaken using SPSS ver. 25 and MedCalc ver. 14.8.1, with the level of accepted statistical significance set at $p < 0.05$. Variables were presented as median (range) and number. Comparisons between groups were conducted using the chi-square test or Mann–Whitney test. Spearman's rank correlation was utilized to assess the associations of MELD score with NLR, NAR, NHR, NHBR, and NPR. Univariate and multivariate analyses were performed to explore the risk

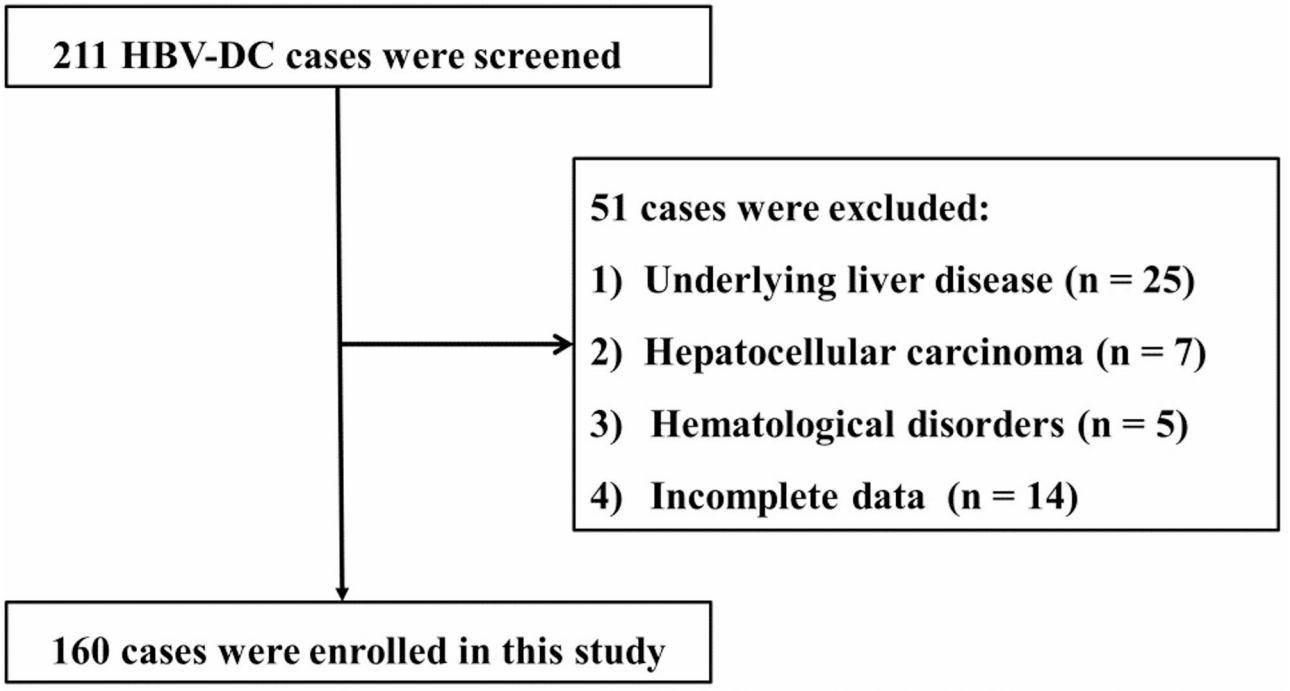

Fig. 1 Flowchart of the participant selection

factors associated with mortality in HBV-DC patients. Receiver operating characteristic (ROC) curve analyses were performed to assess the predictive accuracy for mortality. The discriminatory ability was estimated using the area under the ROC curve (AUC) values. By employing the Youden Index values based on the AUC values, cut-off values were determined for the neutrophil-derived ratios, and their sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were computed. To ensure model robustness, we assessed the events-per-variable (EPV) ratio and performed multicollinearity diagnostics (using variance inflation factors, VIF) to validate the reliability of the regression models.

Results

Patient characteristics

The study included 160 patients with HBV-DC, comprising 130 men and 30 women with a median age of 53 years. Clinical decompensation at admission included ascites (76.3%, 122/160), variceal bleeding (20.0%, 32/160), hepatorenal syndrome (15.0%, 24/160), and hepatic encephalopathy (6.3%, 10/160). Notably, 40 patients (25.0%) presented with more than one decompensation feature. The median values of neutrophil-derived ratios were as follows: NLR, 2.31 (range 1.40–3.78); NAR, 0.70 (range 0.48–1.15); NHR, 3.15 (range, 1.51–7.28), indicating a neutrophil count ($\times 10^9$/L) approximately 3 times the HDL-C concentration (mmol/L); NHBR, 0.22 (range 0.13–0.33); NPR, 0.29 (range 0.19–0.50). Correlation analyses demonstrated varying associations with MELD scores: NLR ($r = 0.215$, $p = 0.006$) and NHBR ($r = 0.201$, $p = 0.011$) showed weak positive correlations, while NAR ($r = 0.302$, $p < 0.001$), NHR ($r = 0.460$, $p < 0.001$) and NPR ($r = 0.420$, $p < 0.001$) exhibited moderate correlations (Fig. 2A–E).

HBV-DC patients were stratified by 30-day post-admission mortality into non-survivors ($n = 23$, 14.4%) and survivors ($n = 137$, 85.6%). The causes of death were hepatic failure ($n = 6$), gastrointestinal bleeding ($n = 3$), hepatic encephalopathy ($n = 7$), and hepatorenal syndrome ($n = 7$). Comparative analysis revealed that non-survivors had significantly elevated levels of neutrophils, all neutrophil-derived ratios, total bilirubin, creatinine, and INR, along with higher MELD scores, but lower HDL-C concentrations (each $p < 0.05$). In contrast, baseline demographic characteristics (age and gender) and routine laboratory parameters including alanine aminotransferase, aspartate aminotransferase, albumin, total protein, hemoglobin, lymphocyte count, and platelet count showed no statistically significant intergroup differences (each $p > 0.05$; Table 1).

Logistic regression analysis

In univariate analysis, all neutrophil-derived ratios and MELD scores showed significant associations with 30-day mortality (each $p < 0.05$). Multivariate analysis identified NLR (adjusted odds ratio [OR]: 1.356, 95% confidence interval [95% CI]: 1.135–1.619; $p = 0.001$) and MELD score (adjusted OR: 1.223, 95% CI: 1.105–1.355;

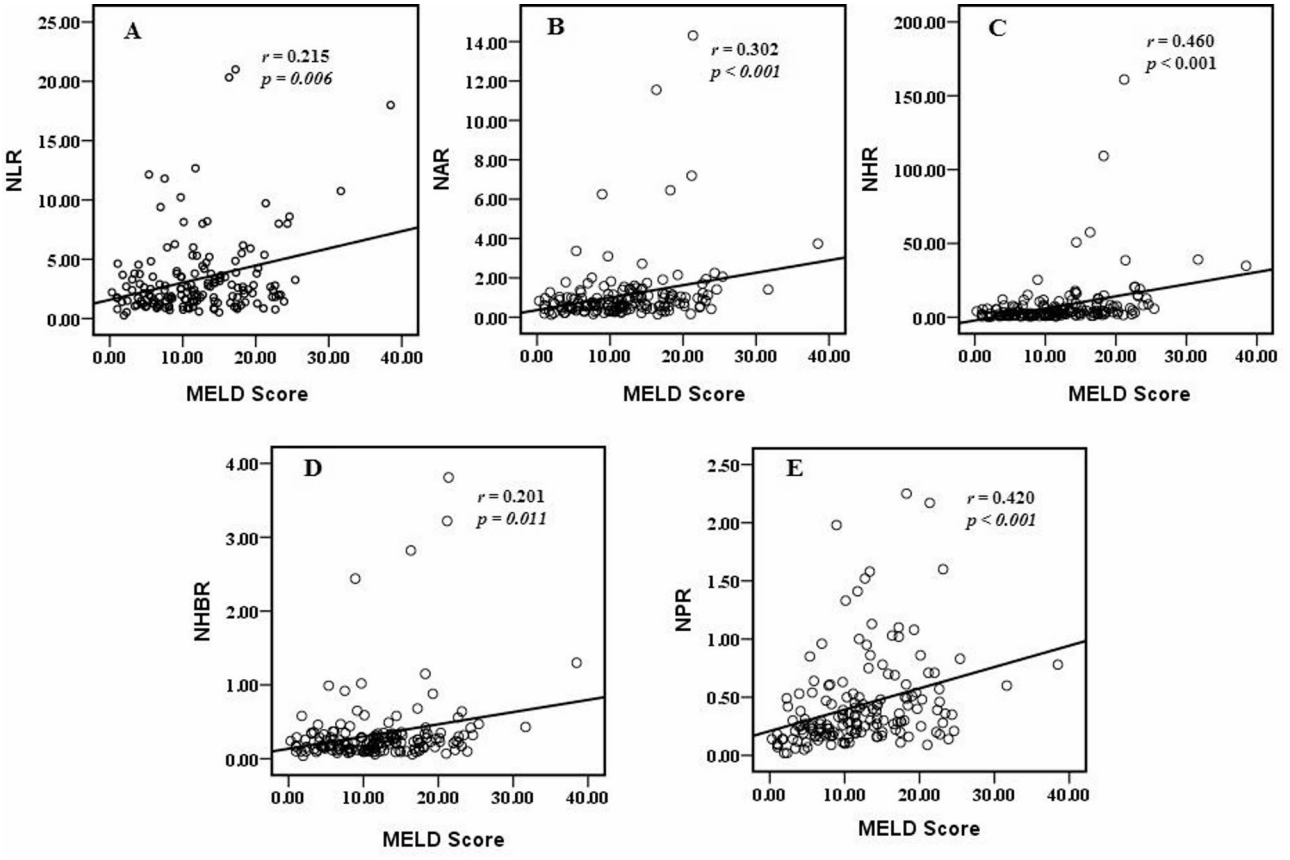

Fig. 2 Scatter plots of the relationships between MELD score and neutrophil-derived ratios. The correlations with MELD score in HBV-DC patients were: (**A**) NLR ($r = 0.215$, $p = 0.006$); (**B**) NAR ($r = 0.302$, $p < 0.001$); (**C**) NHR ($r = 0.460$, $p < 0.001$); (**D**) NHBR ($r = 0.201$, $p = 0.011$) and (**E**) NPR ($r = 0.420$, $p < 0.001$)

$p < 0.001$) as independent predictors of 30-day mortality (Table 2).

Events-per-variable ratio and multicollinearity assessment

The initial multivariate model included six predictors with 23 events, yielding an events-per-variable (EPV) ratio of 3.8—below the conventional threshold of EPV ≥ 10. To assess potential overfitting, we conducted collinearity diagnostics. Variance inflation factor (VIF) analysis revealed severe multicollinearity between the MELD score and two predictors: NAR (VIF = 11.990) and NHBR (VIF = 12.310), both exceeding the critical cutoff (VIF > 10). In contrast, the remaining predictors demonstrated acceptable independence from the MELD score: NLR (VIF = 1.735), NPR (VIF = 1.883), and NHR (VIF = 2.028).

Tiered sensitivity analyses

To evaluate model robustness, we conducted a sequential sensitivity analysis using progressively adjusted models (Supplementary Table 1):

Model 1 (Baseline): MELD score alone.

Model 2: MELD score + non-collinear ratios (NLR, NPR, NHR).

Model 3: Model 2 + individually added collinear ratios (NAR).

Model 4: Model 2 + individually added collinear ratios (NHBR).

The results showed concordance with the findings presented in Table 2. Both MELD score and NLR maintained statistical significance ($p < 0.05$) across all model specifications, with coefficient variations remaining below 15%. Importantly, the collinear indices (NAR and NHBR) became non-significant when introduced to models that already included both MELD score and NLR. Moreover, their inclusion did not significantly alter the effect estimates of the primary predictors.

ROC analysis for prognostic performance

To evaluate the prognostic value of these factors, ROC analyses were performed. Key performance metrics - including AUC (with 95% CIs), sensitivity, specificity, positive and negative predictive values (PPVs/NPVs), and Youden's index-determined optimal cutoff points - are presented in Fig. 3 (ROC curves) and Table 3 (detailed numerical results).

The predictive accuracy assessment yielded the following AUC values (95% CIs): MELD score 0.818

Table 1 Comparisons of baseline clinical and laboratory parameters between the survivors and non-survivors in HBV-DC patients

	All patients (*n* = 160)	**non-survivors (*n* = 23)**	**survivors (*n* = 137)**	***P***
Gender (female/male)	30/130	5/18	25/112	0.914
Age (years)	53 (46–62)	55(45–63)	53 (46–62)	0.846
Total protein (g/dL)	6.14 (5.64–6.69)	5.94 (5.17–6.75)	6.15 (5.76–6.68)	0.136
Albumin (g/dL)	3.11 (2.64–3.48)	2.89 (2.56–3.11)	3.13 (2.70–3.51)	0.077
Alanine aminotransferase (U/L)	29.0 (16.0-47.8)	30.0 (17.0-53.3)	29.0 (16.0–43.0)	0.467
Aspartate aminotransferase (U/L)	44.0 (28.0–72.0)	49.0 (30.0-73.3)	43.0 (27.3–71.8)	0.523
Serum creatinine (μmol/L)	74.0 (61.0–87.0)	100.0 (63.3-128.5)	73.0 (60.8–84.0)	0.007
Total bilirubin (μmol/L)	37.5 (17.5–93.0)	90.0 (52.8-208.8)	34.0 (16.8–80.0)	0.001
INR	1.34 (1.18–1.60)	1.66 (1.35–1.92)	1.30 (1.16–1.56)	0.001
HDL-C (mmol/L)	0.72 (0.44–1.05)	0.50 (0.33–0.77)	0.76 (0.45–1.07)	0.011
Neutrophil ($\times 10^9$/L)	2.30 (1.40–3.40)	3.70 (2.48–6.53)	2.00 (1.40–3.10)	0.001
Lymphocytes ($\times 10^9$/L)	1.00 (0.65–1.40)	0.80 (0.53–1.45)	1.00 (0.70–1.40)	0.315
Platelet ($\times 10^4$/μL)	7.0 (4.3–12.1)	7.2 (6.1–17.4)	6.6 (4.1–11.2)	0.195
Hemoglobin (g/dL)	10.3 (8.5–12.0)	9.6 (8.8–11.3)	10.4 (8.5–12.0)	0.245
NLR	2.31 (1.40–3.78)	4.63 (2.16–10.10)	2.00 (1.32–3.43)	< 0.001
NAR	0.70 (0.48–1.15)	1.23 (0.78–2.53)	0.64 (0.44–1.02)	0.001
NHR	3.15 (1.51–7.28)	7.05 (3.24–31.3)	2.67 (1.40–6.03)	0.001
NHBR	0.22 (0.13–0.33)	0.32 (0.28–0.67)	0.21 (0.13–0.29)	0.001
NPR	0.29 (0.19–0.50)	0.43 (0.20–0.98)	0.28 (0.19–0.49)	0.036
MELD score	11.4 (6.8–16.9)	19.7 (14.9–22.3)	10.5 (6.1–14.4)	< 0.001

Notes: Data are expressed as number or median (range)

Abbreviations: HBV-DC, Hepatitis B virus-associated decompensated cirrhosis; INR, international normalized ratio; HDL-C, high-density lipoprotein-cholesterol; NLR, neutrophil-to-lymphocyte ratio; NAR, neutrophil-to-albumin ratio; NHR, neutrophil-to-HDL-C ratio; NHBR, neutrophil-to-hemoglobin ratio; NPR, neutrophil-to-platelet ratio; MELD score, Model for End-Stage Liver Disease score

Table 2 Results of univariable and multivariable analyses for prediction of mortality in HBV-DC patients

	Univariable			**Multivariable**		
	Odds ratio	**95% CI**	***P***	**Odds ratio**	**95% CI**	***P***
MELD score	1.223	1.120–1.335	< 0.001	1.223	1.105–1.355	< 0.001
NLR	1.363	1.177–1.578	< 0.001	1.356	1.135–1.619	0.001
NAR	1.647	1.168–2.323	0.004			
NHR	1.035	1.005–1.067	0.024			
NHBR	3.264	1.405–7.581	0.006			
NPR	4.278	1.665–10.993	0.003			

Abbreviations: HBV-DC, Hepatitis B virus-associated decompensated cirrhosis; CI, Confidence interval; MELD score, Model for End-Stage Liver Disease score; NLR, neutrophil-to-lymphocyte ratio; NAR, neutrophil-to-albumin ratio; NHR, neutrophil-to-HDL-C ratio; NHBR, neutrophil-to-hemoglobin ratio; NPR, neutrophil-to-platelet ratio

(0.749–0.874), NLR 0.758 (0.684–0.822), NAR 0.736 (0.670–0.802), NHR 0.748 (0.674–0.813), and NHBR 0.768 (0.695–0.831), with all values being significantly greater than the null AUC of 0.5 (each $p < 0.01$ by DeLong's test). While comparative analysis revealed no statistically significant difference between MELD score and NLR predictive performance ($Z = 0.704$, $p = 0.481$), NPR showed limited discriminative power for mortality (AUC = 0.636, 95% CI 0.558–0.714; $p = 0.055$ versus null AUC = 0.5). The combined MELD-NLR model showed improved predictive performance (AUC = 0.869); however, this enhancement over individual markers was modest and not statistically significant (each $p > 0.05$ by DeLong's test).

Regarding test characteristics, NLR and MELD score exhibited the highest prognostic specificities (81.8% and 89.8%, respectively), NAR and NHR had the next highest specificities (73.7% and 78.8%, respectively), and NPR and NHBR with the lowest specificities (66.4% and 68.6%, respectively). NHBR showed the highest prognostic sensitivity (82.6%), while MELD score, NLR, NPR, and NAR had the next highest sensitivities (65.2%, 60.9%, 65.2%, and 69.6%, respectively), and NHR exhibited the lowest sensitivity (56.5%). All biomarkers exhibited NPVs exceeding 90%, indicating their clinical utility for ruling out mortality risk when test results were negative. Notably, only MELD score and NLR demonstrated PPVs above 35%. While these PPVs may appear modest in absolute terms, they represent a clinically significant 2.5-fold

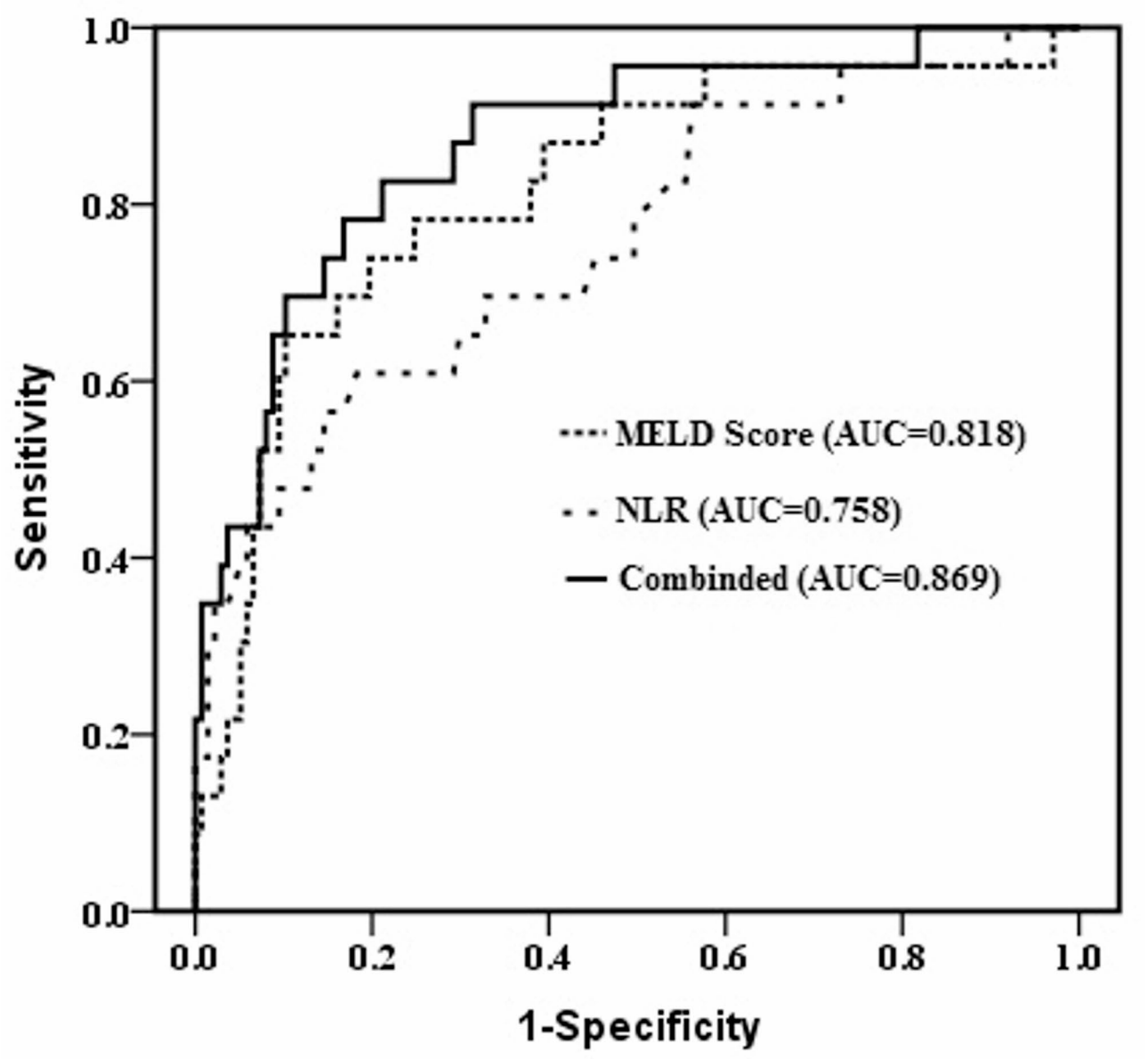

Fig. 3 ROC curve analysis of the MELD score, NLR, and the combination of MELD score and NLR for predicting mortality in HBV-DC patients

Table 3 Prognostic accuracy of neutrophil-derived ratios and MELD score in HBV-DC mortality

	AUC	95% CIs	*P*	Cut-off value	Sensitivity	Specificity	NPV	PPV Youden Index
MELD score	0.818	0.749–0.874	< 0.001	18.2	65.2	89.8	93.9	51.8 0.550
NLR	0.758	0.684–0.822	< 0.001	3.78	60.9	81.8	92.6	36.0 0.426
NAR	0.736	0.670–0.802	0.001	0.99	69.6	73.7	93.5	30.8 0.433
NHR	0.748	0.674–0.813	< 0.001	6.90	56.5	78.8	91.5	31.0 0.354
NHBR	0.768	0.695–0.831	< 0.001	0.26	82.6	68.6	95.9	30.7 0.512
NPR	0.636	0.558–0.714	0.055	3.85	65.2	66.4	91.9	24.6 0.316

Abbreviations: HBV-DC, Hepatitis B virus-associated decompensated cirrhosis; AUC, Areas under the curve; CIs, Confidence intervals; NPV, Negative predictive value; PPV, Positive predictive value; MELD score, Model for End-Stage Liver Disease score; NLR, neutrophil-to-lymphocyte ratio; NAR, neutrophil-to-albumin ratio; NHR, neutrophil-to-HDL-C ratio; NHBR, neutrophil-to-hemoglobin ratio; NPR, neutrophil-to-platelet ratio

increase compared to the baseline mortality probability of 14.4%.

Discussion

Accurate evaluation of disease severity and prognosis plays a critical role in determining suitable treatment strategies for HBV-DC patients. The MELD scoring system is a conventional tool that is currently used widely in clinical settings to assess liver disease severity and predict prognosis in cirrhotic patients. In this system, higher scores indicate worse liver function and poorer prognosis. However, some clinicians contend that MELD falls short in prognostication because it fails to account for important factors such as nutrition, inflammation, specific complications, and overall physical condition. These factors can significantly impact outcomes. In this study, we focused on neutrophil-derived ratios (NLR, NAR, NHR, NHBR, and NPR) that are easily obtainable using blood parameter data. The objective was to ascertain and compare the predictive efficacies of these ratios in HBV-DC patients. The results showed that neutrophil counts and neutrophil-derived ratios were significantly higher in non-survivors compared with survivors. Furthermore, all neutrophil-derived ratios had positive correlations with MELD score, suggesting that these ratios and MELD score may have similar efficacies for assessing liver injury and predicting prognosis in HBV-DC patients. In addition, all these ratios and MELD score had excellent NPVs, indicating their efficacies for ruling out mortality. However, the prognostic significance of these ratios varied, with only NLR providing valuable prognostic insights for 30-day outcomes in HBV-DC patients. Several observations from the present study warrant further investigation and discussion.

First, platelet counts and hemoglobin levels are easily measured laboratory parameters in complete blood counts. Thrombocytopenia and anemia are frequent and severe complications that can indicate a poor prognosis in cirrhotic patients. Thrombocytopenia can arise through several factors, including hypersplenism, increased platelet destruction, reduced platelet production, and antiplatelet antibodies, in chronic liver disease [16–18]. Similarly, decreased hemoglobin levels may suggest variceal bleeding or hypersplenism, both representing significant complications in DC that can lead to unfavorable outcomes. Platelet counts and hemoglobin levels were comparable between non-survivors and survivors. However, NHBR and NPR exhibited significantly different predictive performance (AUC: 0.768 for NHBR vs. 0.636 for NPR, $p < 0.05$), with NHBR showing better prognostic value. In a previous study, Qamar et al. [19] noted that thrombocytopenia is the earliest hematological abnormality to appear in cirrhotic patients, followed by anemia. This sequence may indicate a more advanced disease state in patients who develop anemia. Therefore, NHBR may offer superior predictive value compared with NPR, although neither emerged as an independent mortality predictor in multivariate analysis.

Second, the liver is essential for the regulation of metabolic processes in the body, and cirrhosis significantly impairs its function, leading to systemic metabolic disruptions and varying degrees of malnutrition. Serum HDL-C and albumin levels are commonly used indicators for nutritional status, and play crucial roles for assessment of liver function and prediction of outcomes in liver disease patients. Studies have consistently emphasized the significance of these biomarkers. For example, reduced albumin levels are frequently observed in cirrhotic patients, and are often associated with complications such as ascites, hepatic encephalopathy, and heightened susceptibility to spontaneous bacterial peritonitis, all of which adversely impact prognosis [20, 21]. Similarly, HDL-C has been identified as a prognostic indicator correlated with disease severity in end-stage liver disease [22–25]. Moreover, studies have indicated that HDL-C typically functions as an anti-inflammatory lipoprotein [26–28], while albumin produced by the liver generally acts as an acute-phase protein, decreasing in response to inflammation and thus serving as a classic inflammatory indicator. Thus, serum albumin and HDL-C have been proposed as biomarkers for the so-called 'malnutrition-inflammatory syndrome'—a combined state of chronic malnutrition and systemic inflammation characterized by low albumin and HDL-C levels [26–28]. Our data revealed significantly higher HDL-C levels in survivors compared to non-survivors. In contrast, serum albumin levels were only slightly higher in survivors. This observation may be explained by two factors: first, the relatively small sample size may have limited the statistical power to detect a significant difference; second, serum albumin levels can be influenced by various confounders, such as nutritional intake and hydration status, potentially reducing the prognostic reliability of a single measurement. Our findings demonstrated that both NAR and NHR exhibited comparable predictive value for mortality risk in HBV-DC patients (AUC: 0.736 vs. 0.748, $p > 0.05$). However, similar to NHBR and NPR, neither ratio was identified as an independent predictor of mortality in multivariate analyses.

Third, lymphocytes are important for cell-mediated immunity, and a decreased lymphocyte count suggests compromised immune function, potentially weakening the antiviral response [29, 30]. Recent research has suggested that progression of advanced cirrhosis may lead to a gradual decline in lymphocyte counts, potentially resulting in unfavorable outcomes [31]. Moreover, lymphopenia before liver transplantation was found to be associated with a poor prognosis in recipients [32,

33]. However, in our data obtained on hospital admission, there was no significant difference in the lymphocyte counts between survivors and non-survivors. These findings were consistent with those of Mao et al. [34], who reported slightly lower lymphocyte counts in non-survivors. Among neutrophil-derived ratios, NLR emerged as the most promising biomarker for mortality prediction in HBV-DC patients, showing prognostic value comparable to the MELD score. These findings align with those reported by Li et al. [35], who also found NLR have superior predictive performance compared to other hematologic indices (including lymphocyte-to-monocyte ratio and red cell distribution width) in patients with HBV-related cirrhosis. Our analysis demonstrated that both MELD score and NLR showed the highest positive predictive values (PPVs > 35%), indicating their potential clinical utility for identifying high-risk patients. In cirrhosis patients, inflammation and immune deficiency contribute to 30% of deaths [36]. As NLR reflects the balance between inflammation (neutrophil count) and immune response (lymphocyte count), it may provide more insightful prognostic information for HBV-DC patients compared to other neutrophil-derived ratios (NAR, NHR, NHBR, and NPR). Our findings further demonstrate that both MELD score and NLR remain stable and significant predictors across different models, even when considering the limited EPV ratio and the presence of multicollinearity. The minimal coefficient variation (< 15%) and unaffected effect estimates confirm their robustness as independent prognostic markers in HBV-DC. Recent studies have demonstrated the prognostic value of NLR in liver diseases. Moreau et al. [37] reported that an NLR > 6.5 within 24 h was associated with increased 90-day mortality in liver failure patients. Similarly, Leithead et al. [38] identified NLR > 5 as an independent predictor of mortality in transplant-listed liver failure patients, while Biyik et al. [39] established NLR cut-off values of 4.22, 3.07, and 2.96 for predicting 12-, 24-, and 36-month mortality in cirrhosis patients, respectively. In our HBV-DC cohort, NLR ≥ 3.78 independently predicted short-term mortality. The variation in cutoffs likely reflects differences in disease severity, sample sizes, and follow-up periods.

Our study has several important limitations that warrant consideration: First, as a retrospective single-center investigation with a relatively small sample size ($n = 160$), the findings may be susceptible to selection bias. Second, the unavailability of certain clinically relevant confounders means the prognostic value of these neutrophil-derived ratios may partially reflect unmeasured infectious or inflammatory processes rather than representing truly independent prognostic markers. Third, the absence of other inflammatory markers (e.g., CRP, procalcitonin) restricts our ability to explore underlying mechanisms. Fourth, reliance on single baseline measurements without serial assessment of dynamic changes may affect the precision of our prognostic estimates. Fifth, while our findings demonstrate prognostic utility in HBV-DC, validation in other liver disease etiologies remains necessary. Sixth, the lack of an external validation cohort underscores the need for confirmation in independent populations. Seventh, while the 30-day follow-up period effectively captures acute mortality risk, it limits the assessment of long-term outcomes. Future studies with extended follow-up durations are needed to evaluate the sustained predictive value of these neutrophil-derived ratios. Finally, while we employed standard methodology (Youden Index) to determine optimal cutoffs (e.g., NLR ≥ 3.78), these data-derived thresholds require prospective validation before clinical implementation.

Conclusions

In summary, our study compared the prognostic significance of neutrophil-derived ratios (NLR, NAR, NHR, NHBR, and NPR) in HBV-DC patients. The findings revealed that the prognostic roles of these ratios were different. NLR exhibited the highest specificity, and a multivariate analysis identified NLR as the only factor independently associated with poor outcomes among these ratios. Importantly, NLR showed similar prognostic value to MELD score. These findings suggest NLR may serve as a practical tool for early risk stratification in HBV-DC. Further multicenter validation studies with larger cohorts are warranted to confirm these observations.

Abbreviations

AUCs	Areas under the curve
CI	Confidence interval
DC	Decompensated cirrhosis
EPV	Events-per-variable
HBV	Hepatitis B virus
INR	International normalized ratio
MELD	Score, Model for end stage liver disease score
NLR	Neutrophil-to-lymphocyte
NAR	Neutrophil-to-albumin ratio
NHBR	Neutrophil-to-hemoglobin ratio
NHR	Neutrophil-to-high-density lipoprotein cholesterol ratio
NPR	Neutrophil-to-platelet counts ratio
NPV	Negative predictive value
PPV	Positive predictive value
ROC	Receiver operating characteristic
VIF	Variance inflation factor

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-03991-z.

Supplementary Material 1

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None.

Author contributions
WeiLin Mao designed the study and wrote the manuscript; Yang Xiang enrolled the patients, collected clinical data and analyzed the data. All authors have read and approved the final manuscript.

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No.

Data availability
The data are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was performed according to the Declaration of Helsinki, and the procedures were approved by the Ethics Committee of The First Affiliated Hospital of the Medical College at Zhejiang University in China (No. 2021-22). Due to the retrospective design of this study, the need for written informed consent was waived by the ethics committee.

Competing interests
The authors declare no competing interests.

Consent for publication
Not applicable.

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