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A potential novel inflammation biomarker for predicting the prognosis of decompensated liver cirrhosis

Yanan Xie, Chiyi He and Wei Wang

Department of Gastroenterology, Yijishan Hospital of Wannan Medical College, Wuhu, PR China

ABSTRACT

Objective: This study aimed to explore the prognostic value of the lymphocyte (LYM)-to-white blood cell (WBC) ratio (LWR) in patients with decompensated liver cirrhosis (DLC).

Methods: This study was conducted by recruiting 214 patients with DLC with different aetiologies (development cohort). Receiver operating characteristic (ROC) curve analyses were used to assess the predictive accuracy of the LWR, and Youden's index was used to determine the optimal cut-off values of the LWR based on the ROC curve. Next, patients were divided into high- and low-LWR groups according to the cut-off values. Multivariate logistic analyses were performed to determine the independent predictors for the 1-, 3- and 6-month mortality. Restricted cubic spline (RCS) was used to determine and visualize the association between LWR and the risk of death. We verified the predictive ability of LWR in the validation cohort of 139 patients.

Results: In the development cohort, there were 16 (7.5%), 22 (10.3%) and 30 patients (14.0%) who died at 1, 3 and 6 months, respectively. The LWR was significantly lower in non-survivors than in survivors and was an independent predictor of poor outcomes. The ROC analyses with the Delong test showed that the LWR had comparable predictive power with the Model for End-Stage Liver Disease (MELD) score, neutrophil-to-LYM ratio (NLR) and Chronic Liver Failure consortium score for acute decompensated (CLIF-C ADs). RCS showed a non-linear relationship between the LWR and the risk of death at 1 and 3 months, whereas a linear relationship was observed between the LWR and the risk of death at 6 months. We verified that the decreased LWR was an independent predictor of adverse outcomes at 3-, and 6-month follow-up endpoints in the validation cohort.

Conclusions: Our findings indicate that a lower LWR is an independent factor for unfavourable outcomes and may serve as a potential novel prognostic predictor in patients with DLC.

KEY MESSAGES

- This study is the first report on the prognostic value of the lymphocyte (LYM)-to-white blood cell (WBC) ratio (LWR) in patients with decompensated liver cirrhosis (DLC).
- Decreased LWR is an independent factor for adverse outcomes in patients with DLC.

Introduction

Liver cirrhosis is prevalent worldwide and associated with high morbidity and mortality [1]. In China, the annual progression rate from compensated liver cirrhosis to decompensated liver cirrhosis (DLC) is approximately 3% [2,3], and a 5-year mortality rate of 85% is estimated in patients with DLC [4–6]. Although liver transplantation can significantly improve the survival rates, it is not widely used owing to insufficient sources of donor livers, high costs and serious post-transplantation complications [7]. This necessitates the

accurate and early detection of high-risk patients, which will aid the timely decision of a treatment strategy to ameliorate the prognosis of patients with DLC.

A growing body of evidence has shown that haematological inflammation indicators, such as the neutrophil-to-lymphocyte (LYM) ratio (NLR), platelet-to-white blood cell (WBC) ratio, monocyte-to-LYM ratio and C-reactive protein-to-albumin ratio are reliable prognostic indicators in various diseases, such as cerebral haemorrhage, ischemic stroke, major cardiac events, renal failure, acute respiratory distress syndrome, cancer, acute-on-chronic liver failure and infectious

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pathologies [8–18]. In recent years, inflammation-based markers have received increasing attention in clinical practice and are used in the prognosis of liver cirrhosis [19–24]. Moreover, it has been reported that the LYM-to-WBC ratio (LWR) is a predictor of prognosis in patients suffering from cancer, COVID-19, acute heart failure and infective endocarditis [25–30]. However, the role of LWR in the prognosis of patients with DLC remains unclear. Therefore, the present investigation aims to explore the prognostic value of the LWR in patients with DLC.

Materials and methods

Patients

Patients with DLC referred to the Department of Gastroenterology, Yijishan Hospital of Wannan Medical College between January 2018 and March 2021 were included in this study as the development cohort (cohort I). We recruited patients with DLC as the validation cohort (cohort II) in the Yijishan Hospital of Wannan Medical College between April 2021 and February 2022. Liver decompensation was defined by the clinical, laboratory and imaging data and endoscopic and histological findings [31]. The exclusion criteria were as follows: (1) non-first admission, (2) malignant diseases, (3) autoimmune diseases, (4) primary kidney disease, (5) cardio-cerebrovascular diseases, (6) hyperpyrexia, (8) loss to follow-up and (9) incomplete data. Survival was assessed at 1, 3 and 6 months based on medical records and/or by direct telephonic conversations with patients or patient families. Since the study was retrospective in nature, the requirement for informed consent from the patients was waived. The study was approved by the Institutional Review Board of the Yijishan Hospital of Wannan Medical College (2022–26).

Data collection

Demographic data, laboratory variables and clinical information of the patients, including gender, age, routine blood test reports, hepatic function test reports, coagulation parameters, creatinine (Cr), cause of liver cirrhosis and modes of decompensation, were comprehensively collected on admission. The LWR was calculated as the LYM count ($\times 10^9$/L) divided by the WBC count ($\times 10^9$/L) [25]. In addition, the NLR, Model for End-Stage Liver Disease (MELD) score, and Chronic Liver Failure consortium score for acute decompensated (CLIF-C ADs) were calculated as previously described [13,32,33].

Statistical analysis

Continuous variables were presented as the means ± standard deviation or medians (25th–75th percentiles). Categorical variables were expressed as a frequency. Continuous variables were compared using an independent sample t-test or the Mann–Whitney U test, whereas categorical variables were compared using the chi-square test or Fisher's exact test [34]. To evaluate the correlation between the LWR and MELD scores, Spearman's correlation test was used [35]. The predictive accuracy of the LWR was evaluated by analysing the area under the receiver operating characteristic (ROC) curve, whereas Youden's index was used to determine the optimal cut-off values of the LWR based on the ROC curve [36]. The Delong test was used to compare the value of the area under the ROC curve [37]. Patients with DLC were categorized into high- and low-LWR groups according to the cut-off values. Multivariate logistic regression analysis was used to identify the independent predictors for mortality. Besides, restricted cubic spline (RCS) was used to evaluate the non-linear relationship between the LWR and risk of death based on multivariate analysis [38]. To achieve an optimum fit and avoid overfitting in the main splines, the number of knots between three and five was selected according to the minimum value for the Akaike information criterion [39]. The statistical analyses were performed using R version 4.0.2 (The R Foundation for Statistical Computing, Vienna, Austria), SPSS version 25.0 (SPSS Inc., Chicago, IL) and Medcalc version 15.2 (MedCalc Inc., Ostend, Belgium). All statistical tests were two-sided, and p values < 0.05 were considered to be statistically significant.

Results

Baseline characteristics

In this study, 353 eligible patients with DLC were recruited (Figure 1). In the cohort I, the average age of patients was 61.4 ± 12.9 years, and approximately 60% of the patients were male. The main aetiology of liver cirrhosis was chronic infection with hepatitis B virus. The causes of decompensation events included ascites (84.6%), variceal bleeding (32.2%), hepatic encephalopathy (4.2%) and hepatorenal syndrome (2.3%). The mortality rates of all patients at 1, 3 and 6 months were 7.5%, 10.3% and 14.0%, respectively. In addition, the baseline characteristics of patients in the cohort II are shown in Supplementary Table 1.
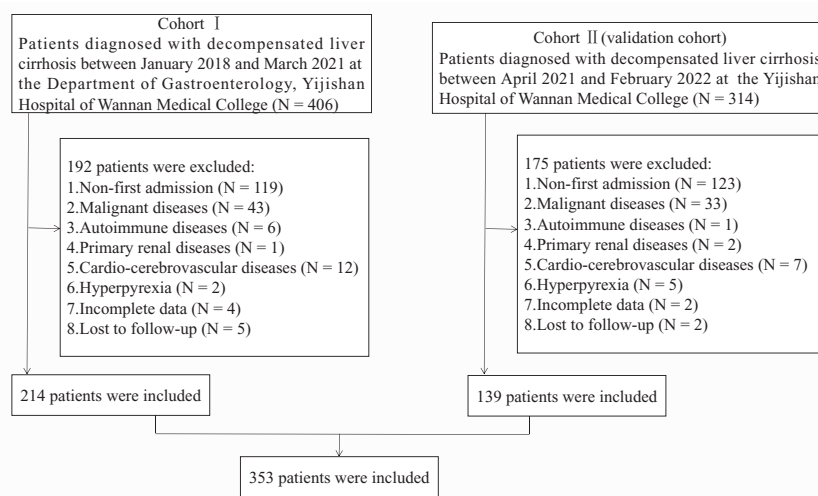
Figure 1. Flow chart of the patient selection process.

Baseline characteristics of patients between the survival and the Non-Survival groups

The clinical-laboratory characteristics of the patients with DLC in the cohort I are shown in Table 1. The patients with DLC were divided into survival and non-survival groups according to their outcomes at 1, 3 and 6 months. During the stages of follow-up, the WBC, platelet, NLR, CLIF-C ADs and MELD score of the non-survivor were significantly higher than the survivor ($p < 0.05$). However, the LWR and albumin (ALB) of the non-survivor were significantly lower than the survivor ($p < .05$). Besides, the prothrombin time (PT) of the non-survivor was significantly higher than the survivor at 1 month ($p < 0.05$), but no significant differences were observed at 3 or 6 months ($p > 0.05$). Similarly, no significant differences in gender, age, LYM, total bilirubin, alanine aminotransferase, aspartate aminotransferase, γ-glutamyl transpeptidase (GGT) or Cr were observed at any time point during the follow-up ($p > 0.05$). In addition, the clinical-laboratory characteristics of the patients between the survival and the non-survival groups in the cohort II are listed in Supplementary Table 1.

Baseline characteristics of patients with different LWR levels

The LWR cut-off values for 1, 3 and 6 months are 0.163, 0.163 and 0.264, respectively. The clinical-laboratory characteristics of the patients with DLC in the high- and low-LWR groups in the cohort I are listed in Table 2. A decreased LWR was associated with higher WBC, higher PT, higher MELD score, higher NLR, higher CLIF-C ADs, lower LYM, lower ALB, lower GGT and higher mortality. Moreover, Spearman's

correlation test showed a significant negative correlation between the LWR and the MELD score ($r = -0.26$, $p < 0.001$) (Figure 2). In addition, the baseline characteristics of patients in the high- and low-LWR groups in the cohort II are shown in Supplementary Table 2.

Low LWR as an independent risk factor for death in patients with DLC

We demonstrated that decreased LWR was an independent factor of unfavourable outcomes in patients with DLC in the cohort I after adjusting the effects of covariates on 1-, 3- and 6- months mortality, respectively (Table 3). As shown in Figure 3, the LWR had comparable predictive power with the NLR, MELD score and CLIF-C ADs (all Delong test p value > 0.05).

Nonlinear relationship between the LWR and risk of death

RCS was used to flexibly model and visualize the relationship between the LWR and the risk of death in patients with DLC based on multivariate analysis. The odds ratio (OR) curves showed an overall declining tendency with an increase in LWR at the 1- and 3-month follow-up endpoints (Figure 4). A nonlinear relationship was observed between the LWR and the risk of death 1 and 3 months (p for non-linearity < 0.05), Moreover, the risk of death decreased with an increase in LWR and was relatively flat when the LWR approached 0.23. However, a linear correlation was observed between the LWR and the 6-month risk of death (p for non-linearity > 0.05), indicating that the risk of death decreased with an increase in LWR.

Table 1. Clinical and laboratory characteristics of the decompensated liver cirrhosis patients in cohort I at the 1-, 3- and 6-month follow-ups.

| Variables	All patients (n = 214)	1 month			3 months			6 months		
		Survivors (n = 198)	Non-survivors (n = 16)	p Value	Survivors (n = 192)	Non-survivors (n = 22)	p Value	Survivors (n = 184)	Non-survivors (n = 30)	p Value
Gender (n, %)				0.429			0.161			0.054
Male	127 (59.3%)	119 (60.1%)	8 (50.0%)		117 (60.9%)	10 (45.5%)		114 (62.0%)	13 (43.3%)	
Female	87 (40.7%)	79 (39.9%)	8 (50.0%)		75 (39.1%)	12 (54.5%)		70 (38.0%)	17 (56.7%)	
Age (years)	61.4 ± 12.9	61.4 ± 13.0	61.8 ± 11.5	0.906	61.1 ± 13.0	64.6 ± 11.7	0.228	60.8 ± 12.7	65.1 ± 13.7	0.094
WBC (10^9/L)	3.80 (2.60–5.40)	3.60 (2.50–5.10)	5.65 (4.33–8.13)	<0.001	3.60 (2.50–5.10)	5.05 (3.85–6.40)	0.004	3.60 (2.50–5.10)	4.45 (3.55–6.63)	0.005
LYM (10^9/L)	0.80 (0.60–1.20)	0.80 (0.60–1.20)	0.85 (0.50–1.30)	0.965	0.80(0.60–1.20)	0.85 (0.50–1.23)	0.893	0.80 (0.60–1.20)	0.80 (0.50–1.23)	0.940
HGB (g/L)	96.29 ± 25.35	96.42 ± 24.54	94.81 ± 34.78	0.858	96.35 ± 24.70	95.86 ± 31.12	0.932	96.25 ± 25.09	96.60 ± 27.32	0.944
PLT (10^9/L)	61.50 (44.00–98.50)	58.50 (43.75–95.00)	94.50 (63.00–124.50)	0.013	58.00 (43.25–94.00)	92.50 (62.75–152.25)	0.007	57.50 (43.25–90.75)	98.50 (62.75–130.75)	0.004
ALB (g/L)	29.61 ± 6.17	29.92 ± 6.14	25.76 ± 5.39	0.009	30.02 ± 6.18	26.04 ± 4.89	0.004	30.23 ± 6.13	25.81 ± 5.02	<0.001
TBIL (umol/L)	24.78 (16.64–37.51)	24.40 (16.62–36.28)	38.90 (21.23–83.36)	0.050	24.43 (16.81–36.59)	34.07 (16.50–56.15)	0.170	24.47 (17.35–36.75)	27.06 (15.27–51.50)	0.669
ALT (U/L)	25.00 (16.00–41.00)	24.43 (16.62–36.28)	21.50 (11.00–44.50)	0.477	25.00 (17.00–41.00)	23.50 (13.25–41.50)	0.465	25.00 (17.00–41.75)	23.00 (14.75–34.25)	0.241
AST (U/L)	34.00 (23.00–58.00)	25.00 (17.00–41.00)	47.00 (22.25–62.25)	0.620	33.00 (22.25–58.00)	43.00 (26.75–59.75)	0.422	34.00 (22.25–58.00)	32.50 (26.00–55.00)	0.994
GGT (U/L)	54.50 (23.00–145.25)	33.00 (23.00–58.00)	46.50 (18.25–208.75)	0.906	55.50 (23.50–136.25)	46.50 (18.75–200.25)	0.815	55.50 (25.00–132.50)	47.00 (18.75–214.75)	0.757
Cr (umol/L)	67.25 (55.98–85.30)	55.50 (24.50–138.50)	65.95 (43.10–93.93)	0.510	67.25 (55.93–84.35)	69.65 (54.20–120.35)	0.383	67.25 (56.05–84.35)	68.10 (54.38–104.65)	0.532
PT (S)	14.55 (13.30–16.23)	14.40 (13.28–16.13)	16.10 (14.93–19.45)	0.022	14.40 (13.23–16.18)	15.65 (14.35–17.20)	0.050	14.40 (13.30–16.10)	15.65 (13.08–19.15)	0.080
LWR	0.23 (0.17–0.31)	0.25 (0.18–0.32)	0.14 (0.10–0.22)	0.001	0.25 (0.18–0.32)	0.15 (0.12–0.23)	0.002	0.25 (0.18–0.32)	0.17 (0.13–0.23)	0.001
NLR	2.72 (1.78–4.21)	2.56 (1.73–4.00)	5.27 (2.93–8.26)	0.001	2.55 (1.72–4.00)	4.90 (2.83–6.63)	0.002	2.50 (1.71–4.00)	4.17 (2.72–6.24)	0.002
CLIF-C ADS	41.72 (37.11–48.06)	41.28 (36.77–47.25)	51.34 (45.50–54.61)	<0.001	41.24 (36.77–46.32)	51.09 (45.06–55.24)	<0.001	41.20 (36.71–46.65)	49.73 (43.98–54.51)	<0.001
MELD score	11.22 (9.14–13.62)	11.17 (9.05–13.21)	14.08 (10.10–18.81)	0.031	11.16 (9.02–13.21)	14.08 (10.61–17.88)	0.005	11.16 (9.03–12.95)	13.59 (9.99-17.31)	0.017
Aetiology (n, %)										
HBV	134 (62.6%)	123 (62.1%)	11 (68.8%)		119 (62.0%)	15 (68.2%)		112 (60.9%)	22 (73.3%)	
HCV	7 (3.3%)	7 (3.5%)	0		7 (3.6%)	0		7 (3.8%)	0	
Alcoholism	5 (2.3%)	5 (2.5%)	0		5 (2.6%)	0		5 (2.7%)	0	
Others	68 (31.8%)	63 (31.8%)	5 (31.3%)		61 (31.8%)	7 (31.8%)		60 (32.6%)	8 (26.7%)	
Modes of decompensation (n, %)										
Ascites	181 (84.6%)	168(84.8%)	13 (81.3%)		162 (84.4%)	19 (86.4%)		155 (84.2%)	26 (86.7%)	
Variceal bleeding	69 (32.2%)	64 (32.3%)	5(31.3%)		64 (33.3%)	5 (22.7%)		63 (34.2%)	6 (20.0%)	
HE	9 (4.2%)	5 (2.5%)	4 (25.0%)		5 (2.6%)	4 (18.2%)		5 (2.7%)	4 (13.3%)	
HRS	5 (2.3%)	3 (1.5%)	2 (12.5%)		1 (0.5%)	4 (18.2%)		0	5 (16.7%)	

Data are expressed as number, mean ± standard deviation, median (25th– 75th percentiles), or frequency (percentage (%)).
WBC: white blood cell; LYM: lymphocyte; HGB: haemoglobin; PLT: platelet; ALB: albumin; TBIL: total bilirubin; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: γ-glutamyl transpeptidase; PT: prothrombin time; Cr: creatinine; LWR: lymphocyte-to-white blood cell ratio; NLR: neutrophil-to-lymphocyte ratio; CLIF-C ADs: Chronic Liver Failure-consortium score for acute decompensated; MELD: Model for End-Stage Liver Disease; HBV: hepatitis B virus; HCV: hepatitis C virus; HE: hepatic encephalopathy; HRS: hepatorenal syndrome.

Table 2. Comparison of Clinical and laboratory characteristics between low and high LWR groups in patients with decompensated liver cirrhosis in cohort I.

	1 month			3 months			6 months		
Variables	LWR < 0.163 (n = 49)	LWR > 0.163 (n = 165)	p Value	LWR < 0.163 (n = 49)	LWR > 0.163 (n = 165)	p Value	LWR < 0.264 (n = 124)	LWR > 0.264 (n = 90)	p Value
Gender (n, %)			0.194			0.194			0.127
Male	33 (67.3%)	94 (57.0%)		33 (67.3%)	94 (57.0%)		79 (63.7%)	48 (53.3%)	
Female	16 (32.7%)	71 (43.0%)		16 (32.7%)	71 (43.0%)		45 (36.3%)	42 (46.7%)	
Age (years)	59.2 ± 12.5	62.1 ± 13.0	0.153	59.2 ± 12.5	62.1 ± 13.0	0.153	61.1 ± 13.4	62.0 ± 12.3	0.615
WBC (10^9/L)	5.30 (3.50–7.15)	3.50 (2.45–4.70)	<0.001	5.30 (3.50–7.15)	3.50 (2.45–4.70)	<0.001	4.25 (2.90–6.08)	3.20 (2.20–4.43)	<0.001
LYM (10^9/L)	0.50 (0.40–0.80)	0.90 (0.70–1.40)	<0.001	0.50 (0.40–0.80)	0.90 (0.70–1.40)	<0.001	0.70 (0.43–1.00)	1.05 (0.80–1.50)	<0.001
HGB (g/L)	94.80 ± 27.37	96.75 ± 24.79	0.637	94.80 ± 27.37	96.75 ± 24.79	0.637	93.36 ± 26.51	100.35 ± 23.20	0.046
PLT (10^9/L)	59.00 (31.50–97.00)	62.00 (46.50–101.00)	0.300	59.00 (31.50–97.00)	62.00 (46.50–101.00)	0.300	61.50 (41.00–104.75)	61.00 (48.00–90.00)	0.793
ALB (g/L)	28.28 ± 5.73	30.00 ± 6.26	0.086	28.28 ± 5.73	30.00 ± 6.26	0.086	28.90 ± 6.17	30.58 ± 6.07	0.048
TBIL (umol/L)	30.92 (15.65–51.28)	23.76 (16.97–36.75)	0.241	30.92 (15.65–51.28)	23.76 (16.97–36.75)	0.241	25.99 (16.50–40.95)	23.67 (17.53–36.08)	0.490
ALT (U/L)	24.00 (15.00–36.50)	25.00 (17.00–41.50)	0.504	24.00 (15.00–36.50)	25.00 (17.00–41.50)	0.504	24.00 (14.00–39.75)	25.50 (20.00–46.25)	0.144
AST (U/L)	29.00 (21.50–51.00)	36.00 (23.50–59.00)	0.077	29.00 (21.50–51.00)	36.00 (23.50–59.00)	0.077	30.00 (22.00–54.00)	39.50 (26.50–67.25)	0.015
GGT (U/L)	31.00 (18.00–76.50)	64.00 (27.00–155.50)	0.003	31.00 (18.00–76.50)	64.00 (27.00–155.50)	0.003	37.00 (18.00–131.50)	78.50 (37.75–156.75)	0.001
Cr (umol/L)	67.30 (60.20–91.85)	67.20 (54.45–84.80)	0.281	67.30 (60.20–91.85)	67.20 (54.45–84.80)	0.281	70.00 (58.63–92.28)	63.50 (52.68–79.38)	0.011
PT (s)	15.70 (14.35–16.95)	14.20 (13.10–16.10)	0.003	15.70 (14.35–16.95)	14.20 (13.10–16.10)	0.003	15.00 (13.43–16.58)	14.20 (12.98–16.03)	0.021
LWR	0.13 (0.08–0.14)	0.27 (0.22–0.33)	<0.001	0.13 (0.08–0.14)	0.27 (0.22–0.33)	<0.001	0.18 (0.13–0.22)	0.33 (0.29–0.38)	<0.001
NLR	6.33 (5.23–10.44)	2.20 (1.63–3.15)	<0.001	6.33 (5.23–10.44)	2.20 (1.63–3.15)	<0.001	4.00 (3.08–6.00)	1.70 (1.33–2.00)	<0.001
CLIF-C ADs	45.26 (40.34–54.12)	41.05 (36.56–46.14)	<0.001	45.26 (40.34–54.12)	41.05 (36.56–46.14)	<0.001	44.02 (38.76–50.75)	39.57 (33.92–42.68)	<0.001
MELD score	12.39 (10.40–16.51)	10.78 (8.79–12.88)	0.001	12.39 (10.40–16.51)	10.78 (8.79–12.88)	0.001	11.61 (9.74–15.52)	9.84 (8.29–12.48)	0.001
Mortality (n, %)	11 (22.4%)	5 (3.0%)	<0.001	13 (26.5%)	9 (5.5%)	<0.001	26 (21.0%)	4 (4.4%)	0.001

Data are expressed as number, mean ± standard deviation, median (25th–75th percentiles), or frequency (percentage (%)).
WBC: white blood cell; LYM: lymphocyte; HGB: haemoglobin; PLT: platelet; ALB: albumin; TBIL: total bilirubin; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: γ-glutamyl transpeptidase; PT: prothrombin time; Cr: creatinine; LWR: lymphocyte-to-white blood cell ratio; NLR: neutrophil-to-lymphocyte ratio; CLIF-C ADs: Chronic Liver Failure-consortium score for acute decompensated; MELD: Model for End-stage Liver Disease
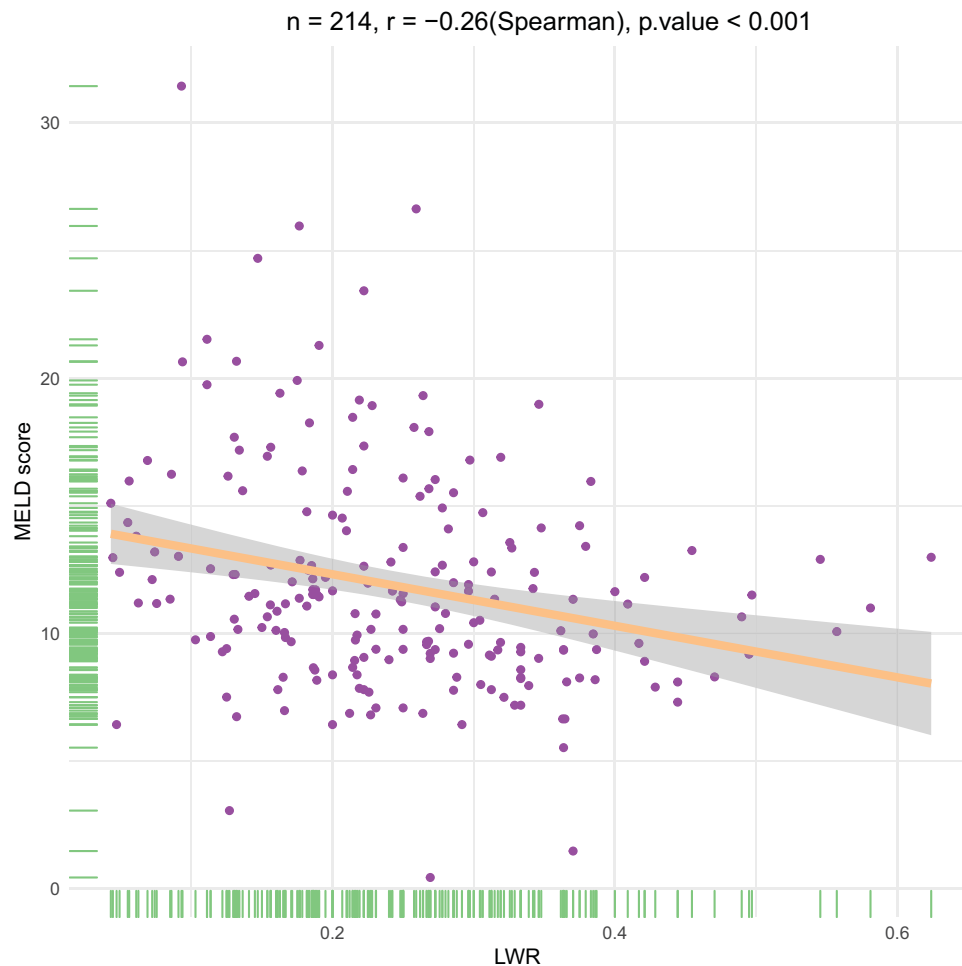
Figure 2. Scatter plot illustrating the correlation between the LWR and the MELD score in the development cohort.

Validation of the predictive accuracy of the LWR

In the cohort II, we demonstrated that the LWR was an independent predictor of 3- and 6-month mortality in patients with DLC; but not for 1-month follow-up endpoint (OR, 0.245; 95% CI, 0.047–1.276) (Table 3). Furthermore, the ROC analysis showed that the LWR had comparable predictive ability with the NLR, MELD score and CLIF-C ADs, no matter in the cohort II or all patients (All Delong test p value > 0.05) (Supplementary Figure 1). The exact p values for Delong test for the comparisons of the area under the ROC curve of these biomarkers are listed in Supplementary Table 3.

Discussion

In this research, we investigated the prognostic value of the LWR in patients with DLC. Our results indicated that the reduction in LWR was an independent predictor of adverse outcomes at 3- and 6-month follow-up endpoints.

The MELD score has been extensively used to predict the prognosis of liver disease patients. The MELD score helps to prioritize patients for liver transplants and is determined by three complex parameters (Cr, total bilirubin and international normalized ratio) that are not convenient for use in clinical application [40]. Conversely, LWR uses two routine indicators of blood, which make it more convenient and easier to calculate than the MELD score. Moreover, the LWR is a ratio and is not influenced by the test location or method, which makes it an objective predictive indicator with no additional cost or resource requirement [41]. Our results showed a significant negative correlation between the LWR and MELD scores, and the LWR has comparable predictive ability with the MELD score in patients with DLC.

Systemic inflammation is a well-recognized feature of DLC, and several studies have shown the important role of the inflammatory response in the pathogenesis of advanced cirrhosis and their correlation with unfavourable outcomes [42–45]. Zhang et al. reported that elevated WBC reflected the severity of systemic

Table 3. Indicators associated with 1-month, 3-month, and 6-month mortality in multivariate analyses in patients with decompensated liver cirrhosis in cohort I& II.

|	Cohort I						Cohort II (validation cohort)					
Variables	1 month OR (95% CI)	p	3 months OR (95% CI)	p	6 months OR (95% CI)	p	1 month OR (95% CI)	p	3 months OR (95% CI)	p	6 months OR (95% CI)	p
PLT (10⁹/L)	1.008 (1.003–1.014)	0.004	1.006 (1.001–1.012)	0.013	1.005 (1.000–1.010)	0.026	1.009 (0.995–1.023)	0.197	1.006 (0.995–1.018)	0.285	1.003 (0.992–1.014)	0.595
ALB (g/L)	0.959 (0.844–1.082)	0.504	0.943 (0.850–1.040)	0.251	0.913 (0.836–0.992)	0.037	0.851 (0.688–1.053)	0.137	0.901 (0.774–1.049)	0.179	0.877 (0.776–0.991)	0.036
TBIL (umol/L)	0.997 (0.977–1.015)	0.766					0.998 (0.972–1.024)	0.866				
AST (U/L)	1.001 (0.997–1.006)	0.531	1.002 (0.998–1.006)	0.395			0.943 (0.888–1.001)	0.054	0.988 (0.972–1.005)	0.165		
PT (s)	1.161 (0.900–1.507)	0.251	0.999 (0.795–1.249)	0.996	1.032 (0.853–1.249)	0.743	0.970 (0.782–1.203)	0.782	0.942 (0.771–1.150)	0.554	1.148 (0.924–1.425)	0.213
MELD score	1.087 (0.887–1.307)	0.395	1.125 (0.970–1.300)	0.114	1.070 (0.942–1.212)	0.284	1.297 (1.002–1.680)	0.049	1.238 (1.032–1.487)	0.022	1.05 (0.918–1.214)	0.445
LWR		0.002		0.002		0.014		0.095		0.007		0.026
Low	Ref		Ref		Ref		Ref		Ref		Ref	
High	0.139 (0.037–0.456)		0.211 (0.075–0.574)		0.234 (0.064–0.679)		0.245 (0.047–1.276)		0.169 (0.047–0.613)		0.271 (0.085–0.858)	

PLT: platelet; ALB: albumin; TBIL: total bilirubin; AST: aspartate aminotransferase; PT: prothrombin time; MELD: Model for End-stage Liver Disease; LWR: lymphocyte-to-white blood cell ratio; OR: odds ratio; CI: confidence interval.

Age, sex, haemoglobin, PLT, ALB, TBIL, AST, PT, LWR, MELD score, alanine aminotransferase, γ-glutamyl transpeptidase and creatinine were included in the univariate logistic regression analysis. Variables that did not have a significant effect on mortality in the univariate logistic regression analysis were not included in the multivariate logistic regression analysis.

inflammation following liver injury, which may affect the prognosis of patients with DLC [24]. It has also been reported that LYMs play a critical role in the body's immune response, immune surveillance and immune defence functions [25]. Lower LYM counts may be associated with a poor nutritional status and impaired immune response in patients with liver disease and are a predictor of prognosis on the liver transplant waiting list [46,47]. Besides, LWR can be regarded as a combined marker of immune status and inflammatory. Decreased levels of LWR may reflect a suppressed immune response and/or an enhanced inflammatory response. Several studies have evaluated the association between the LWR and the prognosis of various diseases [25–30]. Zhang et al. reported that a lower LWR is an independent risk factor for mortality in patients with infective endocarditis [29]. Further, Ding et al. reported that a decreased LWR was associated with poor overall survival, disease-free survival, and metastasis-free survival and was also an independent factor of decreased metastasis-free survival in patients with oral squamous cell carcinoma [30]. Pitre et al. reported that a lower LWR was correlated with a poor prognosis for patients with COVID-19 [25]. Similar to these findings, our findings indicated that the LWR can be serving as an independent indicator for predicting the prognosis of patients with DLC.

Several predictive scoring systems have been developed to assess the prognosis of patients with advanced liver disease, such as the MELD score, sequential organ failure assessment and CLIF-C ADs [32,33,48–50]. However, most predictive scoring systems do not consider the systemic inflammatory response, which is significantly associated with the progression of cirrhosis and related complications, except CLIF-C ADs [42–45]. In previous studies, CLIF-C ADs have been shown to be an independent predictor of mortality in patients with DLC [33,51,52]. Based on the results of our study, we found that LWR had comparable predictive power to CLIF-C ADs at all follow-up endpoints, while CLIF-C ADs had better predictive power than the MELD score in the development cohort and all patients at 6-month follow-up endpoints (Supplementary Table 3). The results were similar to the findings of the above studies. Previous studies have identified various inflammatory indicators associated with prognosis in patients with liver cirrhosis, such as neutrophil- LYM ratio, monocyte-LYM ratio and platelet-WBC ratio [19–24], and these indicators may be complementary to the widely used prognostic scoring systems, as discussed earlier. Our results
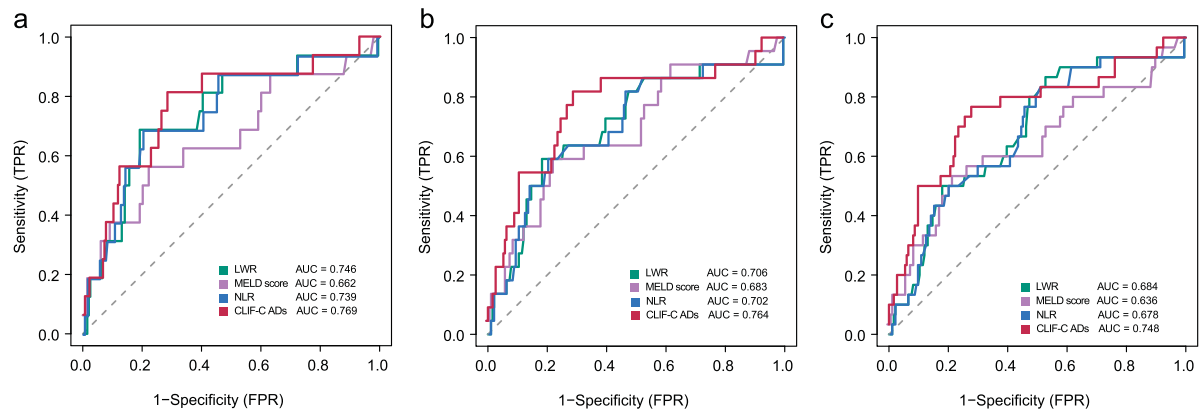
Figure 3. Receiver operating curves of the NLR, MELD score, CLIF-C ADs and the LWR for prediction of mortality at (a) 1, (b) 3 and (c) 6 months in patients with decompensated liver cirrhosis in the development cohort.
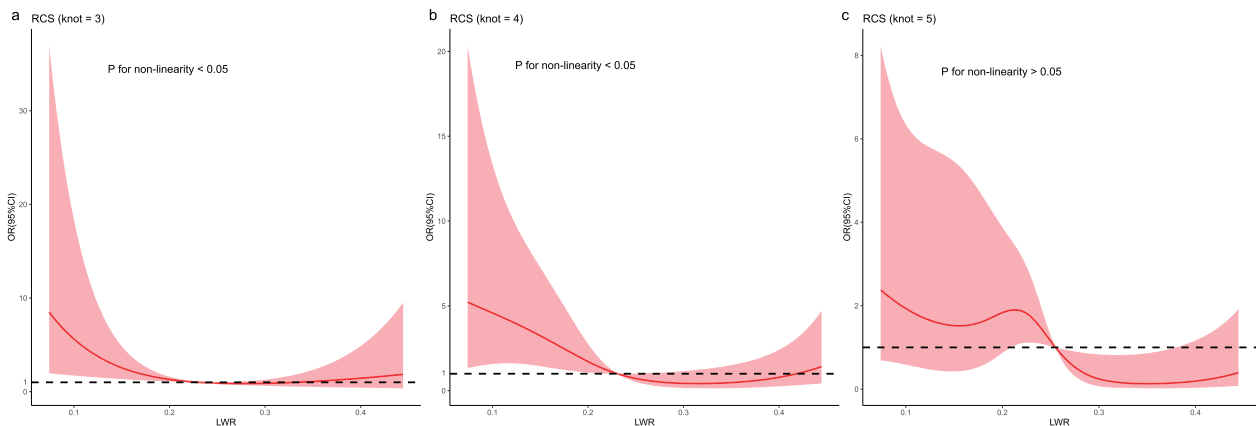
Figure 4. Associations of the LWR with the risk of death at (a) 1, (b) 3 and (c) 6 months in patients with decompensated liver cirrhosis using restricted cubic spline in the development cohort.

showed that the LWR may be used as a potential indicator to predict prognosis in patients with DLC.

There are several limitations to our study. First, it is a retrospective and single-centre study, and thus, selection biases were inevitable. Second, the study did not evaluate pro-inflammatory cytokines, such as TNF-α and IL-6, which may help in understanding the mechanism. Therefore, further prospective studies at multiple centres are required to validate the predictive value of the LWR for patients with DLC.

Conclusions

In summary, the LWR can serve as a potential prognostic indicator in the early identification of high-risk patients with DLC. The index can be conveniently calculated, is easily accessible, and has comparable predictive ability with the MELD score. Thus, our findings may help clinicians improve the disease predictability as well as prevent and manage the condition.

Author contributions

Wei Wang designed the research. Yanan Xie, Chiyi He and Wei Wang analysed the data. Yanan Xie drafted the paper and interpreted the data. Wei Wang revised the paper critically for intellectual content. All authors read and approved the final manuscript to be published. All authors agree to be accountable for all aspects of the work.

Disclosure statement

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Data availability statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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