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Neutrophil-to-lymphocyte ratio and short-term mortality in patients having anti-MDA5-positive dermatomyositis with interstitial lung disease: a retrospective study

Hongxia Xin[1,2†], Ping He[3†], Bin Xi[4†], Zhaojun Wang[5], Han Wang[6], Faxuan Wang[7], Zhanbing Ma[8], Jing Xue[9], Yuanyuan Jia[9], Hourong Cai[10*†], Bi Chen[11*†] and Juan Chen[1*†]

Abstract

Background In this study, we aimed to explore the association between baseline and early changes in the neutrophil-to-lymphocyte ratio (NLR) and the 30-day mortality rate in patients having anti-melanoma differentiation-associated gene 5 (MDA5)-positive dermatomyositis with interstitial lung disease (DM-ILD).

Methods Overall, 263 patients with anti-MDA5 DM-ILD from four centers in China were analyzed. Multivariate logistic regression analysis was used to evaluate the impact of baseline NLR on the 30-day mortality rate in patients with anti-MDA5-positive DM-ILD. Furthermore, a generalized additive mixed model (GAMM) was applied to compare the NLR variations over time between 30-day survival group and non-survival group.

Results Two hundred sixty-three patients with anti-MDA5-positive DM-ILD were divided into different groups based on their NLR and whether they survived or not within 30 days. The multivariate logistic regression analysis, accounting for confounding factors, identified an elevated baseline NLR as a prognostic indicator for 30-day mortality in patients with anti-MDA5-positive DM-ILD (hazard ratio 2.68, 95% confidence interval [CI] 1.18,6.00, $P=0.019$). Furthermore, the GAMM results indicated that the NLR gradually increased more in the non-survival group compared with the survival group within 14 days of admission, with a daily average increase of 1.03 ($\beta=1.03$; 95% CI, 0.75–1.31; $P<0.001$).

Conclusions We found that an elevated baseline NLR and its progressive increase are associated with 30-day mortality in patients with anti-MDA5-positive DM-ILD.

Keywords Anti-MDA5, Dermatomyositis, Interstitial lung disease, Neutrophil-to-lymphocyte ratio

†Hongxia Xin, Ping He and Bin Xi contributed equally to this work.

†Hourong Cai, Bi Chen and Juan Chen contributed equally to this work.

*Correspondence:
Hourong Cai
caihourong2013@163.com
Bi Chen
chenbi207@126.com
Juan Chen
chenjuan7419@163.com
Full list of author information is available at the end of the article

Background

Idiopathic inflammatory myopathies include diverse auto-immune diseases [1] characterized by muscular and extra-muscular manifestations. Pulmonary involvement is a common and challenging phenomenon [2, 3], and rapidly progressive interstitial lung disease (RPILD) is the primary cause of mortality. Anti-melanoma differentiation-associated gene 5 (MDA5) antibody is a myositis-specific antibody (MSA) [4]. Previous studies have shown that patients with dermatomyositis (DM) who are positive for the anti-MDA5 antibody are more vulnerable to developing interstitial lung disease (ILD), particularly RPILD, compared to those positive for other MSAs [5]. Despite aggressive immunosuppressive and corticosteroid treatments, the 6-month mortality rate in patients with anti-MDA5-positive DM-with RPILD is 50–70% [6].

The inflammatory response plays a critical role in the onset and progression of dermatomyositis (DM) in patients with anti-MDA5 antibodies and has a significant impact on their prognosis. Previous studies have shown that the levels of the inflammatory markers lactate dehydrogenase (LDH) [7] and ferritin [8] are reliable prognostic indicators that reflect disease severity and predict survival. Patients with vasculitis activation are more prone to develop RPILD, with peripheral blood neutrophils and lymphocytes implicated in ILD pathogenesis [9]. The neutrophil-to-lymphocyte ratio (NLR) serves as an indicator of systemic inflammation because it reflects the balance between neutrophils and lymphocytes, which are two key components of the immune response [10]. Neutrophils are typically elevated in response to acute inflammation, infection, or tissue damage [11], while lymphocytes are involved in regulating the immune response and controlling inflammation [12]. The mechanisms underlying the association between NLR and systemic inflammation may be due to neutrophil activation [11] or lymphocyte modulation [13]. Additionally, the NLR is more accessible compared to other inflammatory markers like LDH or ferritin. However, the predictive value of dynamic changes in the NLR in determining the outcome of anti-MDA5-positive DM-ILD remains unclear. Therefore, in this study, we aimed to investigate whether elevated baseline NLR and its dynamic changes could predict the 30-day mortality in patients with anti-MDA5 positive DM-ILD.

Methods

Study population

Patients with anti-MDA5-positive DM-ILD were retrospectively recruited from four centers across different regions of China, including the Nanjing Drum Tower Hospital, General Hospital of Ningxia Medical University, Xuzhou Medical University Affiliated Hospital, and Third People's Hospital of Chengdu, between January 2017 and November 2021. The patient data were de-identified, and the requirement for informed consent was waived. The diagnosis of anti-MDA5-positive DM was made following the Bohan and Peter criteria and the 239th European Neuromuscular Centre guidelines [14]. The exclusion criteria were as follows, (1) concurrent diagnosis of other connective tissue diseases, (2) a prior diagnosis of a tumor, (3) incomplete clinical or laboratory data within three days of admission, and (4) age under 18 years of age. Ethical approval was obtained by each hospital's ethics committee (reference numbers: 2020–050-01, XYFY2022-KL427-02, KYLL-2023–0512, and [2023] S-139, respectively). This study was conducted in accordance with the Declaration of Helsinki.

Group and variable definitions

Patients who did not die within 30 days after the initial hospitalization were defined as the survival group, and those who died within 30 days were defined as the non-survival group. Based on NLR baseline values, they were divided into three groups: the lowest tertile assigned a value of 2.8 ($n=88$), $1.00 \leq \text{NLR} \leq 4.20$ was defined as Tertile1_2.80; the median tertile assigned a value of 5.93 ($n=87$), $4.30 \leq \text{NLR} \leq 8.60$ was defined as Tertile2_5.93; and the highest tertile assigned a value of 12.45 ($n=88$), $8.70 \leq \text{NLR}$ 37.00 was defined as Tertile3_12.45. From days 1 to 14 after admission, adjacent days were combined into one group. For example, days 1 and 2 were combined into one group and named D1-2 (Table Additional File 2). RP-ILD is defined as radiographic progression within 3 months accompanied by dyspnea and hypoxemia. Variables in the study included age, gender, smoking, mechanic's hands, heliotrope rash, Gottron's sign, shawl sign, periungual erythema, raynaud phenomenon, skin ulcers, muscle weakness, arthritis, RP-ILD, V-sign, antinuclear antibody (ANA), rheumatoid factor (RF), Ro52, fever, lymphocyte category, lymphocyte count, duration, albumin (ALB), alanine transaminase (ALT), aspartate transaminase (AST), creatine kinase (CK), lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin, erythrocyte sedimentation rate (ESR), neutrophil-to-lymphocyte ratio (NLR), white blood cell count (WBC), treatment regimens.

Statistical analysis

Demographic and clinical variables were analyzed using descriptive statistics. Continuous variables are expressed as means (standard deviations), whereas categorical variables are presented as percentages. Statistical comparisons were made using Student's t-test for means, Mann–Whitney U test for medians, and Fisher's exact test for frequencies. Statistical significance was set at

$P < 0.05$. Statistical analyses were performed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA), R (version 4.1.3; R Foundation for Statistical Computing, Vienna, Austria), and Python (version 3.4.3; Python Software Foundation, Wilmington DE, USA).

We investigated the correlation between the baseline NLR and short-term clinical outcomes in patients with anti-MDA5-positive DM. Patients were categorized into three groups based on the tertiles of baseline NLR values. Cox regression analysis and smooth curve fitting were used to evaluate the independent influence of baseline NLR on 30-day mortality rates in the crude and full models. Adjusted variables in the analysis included sex, smoking status, mechanic's hand, Gottron's sign/papules, heliotrope rash, age, disease duration, V sign, shawl sign, periungual erythema, Raynaud phenomenon, skin ulcer, muscle weakness, arthralgia, presence of Ro52, fever, ANA, rheumatoid arthritis, ferritin, ALB, ALT, AST, CK, LDH, ESR, and CRP, treatment regimens.

In addition to investigating the correlation between early NLR changes (1–14 days) and 30-day mortality rates, we assessed the disparities in NLR between survivors and non-survivors during the 14 days preceding admission. Generalized Additive Mixed Models (GAMMs) are used to analyze nonlinear relationships and data with complex structures [15]. GAMMs were employed to scrutinize the temporal fluctuations in early NLR alterations among survivors and non-survivors, encompassing the unadjusted and adjusted models.

Results

Patient characteristics

This study included 263 patients with anti-MDA5 antibodies. Among them, 185 were in the 30-day survival group, and 78 were in the non-survival group. As presented in our published data [16] Table 1 lists the characteristics of the participants, while in our study Table 1 provides some additional baseline information not included in the published article. The median age of the patients was 53 years (interquartile range 48.0,62.00); 33.08% were female, and the majority (85.55%) had never smoked. The median baseline NLR for all patients was 5.9 (3.5,10.0), with the 30-day survival group and non-survival group having NLRs of 5.0 (3.2,8.7) and 8.7 (5.4,13.3), respectively. Additionally, age, fever, arthritis, muscle weakness, albumin (ALB), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood cell count (WBC), ferritin, and the use of steroid and immunosuppressants were all higher in the non-survival group compared to the survival group ($P < 0.05$). In contrast, there were no statistically significant differences between the two groups in terms of dermatomyositis-related skin vascular lesions such as mechanic's hands, heliotrope rash, Gottron's sign, shawl sign, periungual erythema, Raynaud phenomenon, skin ulcers, V-sign, and antibodies such as ANA, RF, and Ro52.

The R statistical analysis identified the optimal cut-off value of NLR affecting prognosis as 6.5. The Youden index was calculated to be 0.35, with a sensitivity of 0.71 and a specificity of 0.65(Additional_File_1). Kaplan–Meier curves showed that patients with a baseline NLR of < 6.5 had higher 1-month survival rates compared with those with a baseline NLR of ≥ 6.5 ($P < 0.001$; Fig. 1).

Association between the baseline NLR and mortality

Our study showed a positive correlation between the elevated baseline NLR and short-term mortality in patients

Table 1 Supplementary baseline data

Variables	Total ($n = 263$)	Survival group ($n = 185$)	Non-survival group ($n = 78$)	*P*-value
Age, median, years	53.0 [48.0,62.0]	51.0[46.0,58.0]	57.0[51.0,63.0]	< 0.001
Sex (female, n%)	87.0 (33.1)	58.0 (31.4)	29.0 (37.2)	0.359
Smoke, n (%)	38.0 (14.4)	21.0 (11.4)	17.0(21.8)	0.0282
Duration, median, month	2.0[1.0,3.0]	2.0[1.0,4.0]	1.0[0.7,2.0]	< 0.001
Ferritin, median, ug/L	865.0[366.5,1570.0]	548.2[270.0,1275.8]	1349.0[795.5,2620.4]	< 0.001
Treatment after admission				
Steroid used, n (%)	56 (21.3%)	10 (5.4%)	46 (59.0%)	< 0.001
Immunosuppressant used				
CTX, n (%)	64 (24.3%)	20 (10.8%)	24 (30.8%)	< 0.001
CsA, n (%)	47 (17.9%)	13 (7.0%)	24 (30.8%)	< 0.001
Tac, n (%)	36 (13.7%)	7 (3.8%)	29 (37.2%)	< 0.001
Tofacitinib, n (%)	56 (21.3%)	19 (10.3%)	37 (47.4%)	< 0.001
IVIG, n (%)	57 (21.7%)	34 (18.4%)	23 (29.5%)	< 0.001

Abbreviations: CTX cyclophosphamide, *CsA* cyclosporin A, *Tac* tacrolimus, *IVIG* intravenous immune globulin

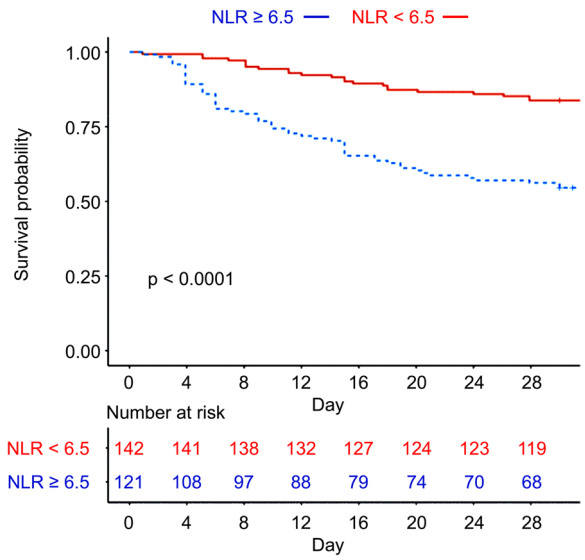

Fig. 1 Kaplan–Meier survival curves in anti-MDA5-positive DM-ILD based on the initial NLR. Abbreviation: DM-ILD, dermatomyositis with interstitial lung disease; MDA-5, melanoma differentiation-associated gene 5; NLR, neutrophil-to-lymphocyte ratio

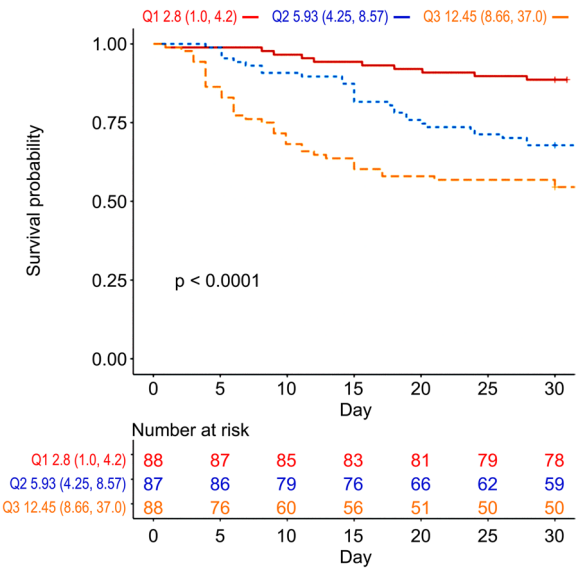

Fig. 2 Kaplan–Meier survival curves for the association between the initial NLR tertiles and 30-day mortality. Abbreviation: NLR, neutrophil-to-lymphocyte ratio

with anti-MDA5-positive DM. Participants were divided into three groups based on the tertiles of baseline NLR values. We observed that a higher NLR was associated with increased 30-day mortality rates. Additionally, Kaplan–Meier curves demonstrated significant differences in 30-day mortality among the different baseline NLR groups (Fig. 2). Importantly, the random forest model identified the baseline NLR as the second most crucial predictor of mortality (Fig. 3).

We conducted a multivariate Cox regression analysis (Table 2) to further validate our findings. After adjusting for clinical confounders, we found that patients with a high NLR (≥12.45) had a significantly higher risk of 30-day mortality compared to those with a low baseline NLR (<5.93) (hazard ratio, 2.68; 95% confidence interval [CI], 1.18,6.00; $P=0.019$) in the adjusted model.

Relationship between short-term changes in NLR and mortality

Smooth curve fitting reveals that a gradual increase in NLR values correlates with 30-day mortality (Fig. 4). Over a 14-day period, the trend in NLR changes shows that the NLR in the non-survival group steadily rises compared to the survival group. Moreover, the difference in NLR between the two groups becomes increasingly pronounced over time (Additional_File_2 and Additional_File_3). We further developed a Generalized Additive Mixed Model (GAMM) to analyse the dynamic changes in NLR from day 1 to day 14. The results shown that the NLR in the non-survival group was consistently higher than in the survival group, with the difference showing an increasing trend and an average daily increase of 1.01. Notably, after adjusting for confounders, model 3 demonstrated robustness (β = 1.03, 95% CI

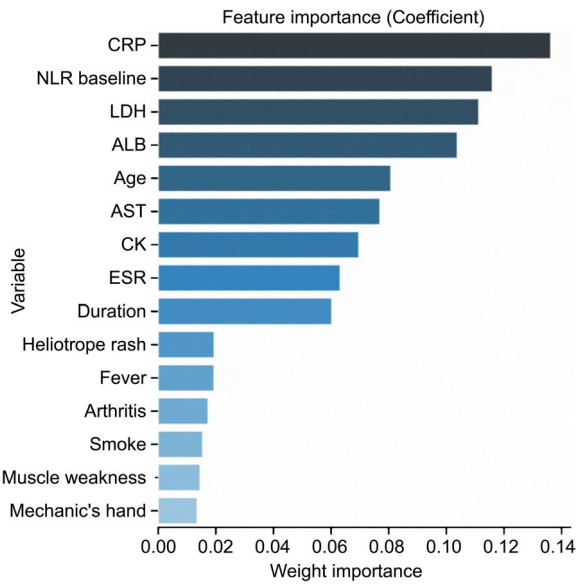

Fig. 3 Random forest feature importance with 30-day mortality. Abbreviations: ALB, albumin; AST: aspartate aminotransferase; CK, creatine kinase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio

Table 2 Association between baseline NLR and the likelihood of 30-day mortality

Tertile of NLR	N	Non-adjusted			Adjusted		
		HR	95% CI	*P*-value	HR	95% CI	*P*-value
Tertile1_2.80	88	1.00	(Reference)		1.00	(Reference)	
Tertile2_5.93	87	3.06	[1.50,6.35]	0.002	2.05	[0.90,4.63]	0.086
Tertile3_12.45	88	5.35	[2.67,10.70]	0.000	2.68	[1.18,6.00]	0.019
P for trend	263	1.15	[1.09,1.21]	0.000	1.07	[1.01,1.15]	0.034

T1 means the median NLR 2.80 (1.00,4.20); T2 is the median NLR 5.93 (4.25,8.57]); and T3 is the median NLR 12.45 (8.66,37.00]). Adjustment factors included sex, smoking, mechanic's hand, Gottron's sign/papules, heliotrope rash, age, duration, V sign, Shawl sign, periungual erythema, Raynaud phenomenon, skin ulcer, muscle weakness, arthritis, Ro52, fever, ANA, RA, ALB, ALT, AST, CK, LDH, ESR, and CRP

Abbreviations: *ALB* albumin, *ALT* alanine aminotransferase, *ANA* antinuclear antibody, *AST* aspartate aminotransferase, *CI* confidence interval, *CK* creatine kinase, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *HR* hazard ratio, *LDH* lactate dehydrogenase, *NLT* neutrophil-to-lymphocyte ratio, *RA* rheumatoid arthritis, *WBC* white blood cell count

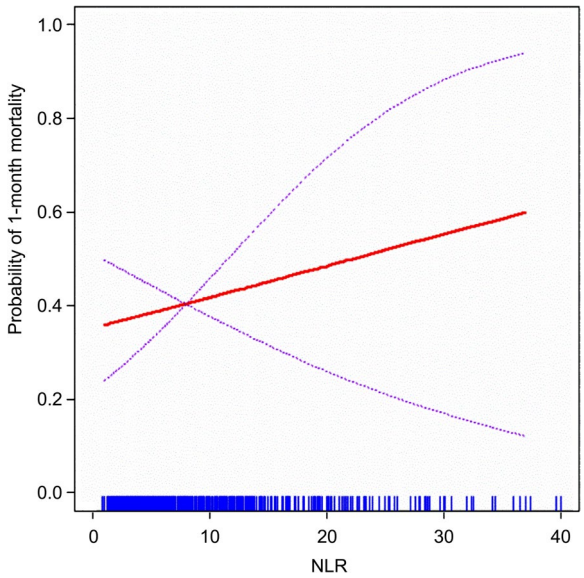

Fig. 4 Smooth-fitted curve illustrating the association between the initial NLR and short-term mortality. Abbreviation: NLR, neutrophil-to-lymphocyte ratio

0.75–1.31, $P<0.0001$) (Table 3). These findings suggest that early dynamic changes in NLR are associated with the 30-day mortality rate in patients with anti-MDA5 antibodies.

Discussion

Anti-MDA5-positive DM represents a subtype of DM characterized by distinct extra-muscular symptoms, notably, there is an increased mortality risk associated with lung complications, and myositis symptoms may be mild or even absent. The clinical presentation of anti-MDA5-positive DM differs from that of typical cutaneous DM, which may sometimes result in delays in diagnosis [17]. However, the exact pathophysiology of anti-MDA5-positive DM remains unclear [18]. Increasing evidence suggests that viral infections may serve as potential triggers for MDA5-DM. Various factors, including T cells, B cells, neutrophils, and macrophages, play critical roles in the pathophysiology of MDA5-DM [19]. Neutrophils and lymphocytes produce various cytokines involved in the occurrence and development of DM in

Table 3 Association between NLR changes (0–14 days) and short-term mortality in patients with anti-MDA5 positive DM-ILD using a GAMM

	Model 1		Model 2		Model 3	
30-day mortality	β (95% CI)	*P*-value	β (95% CI)	*P*-value	β (95% CI)	*P*-value
Day	0.03 (−1.06,0.23)	0.770	0.03 (0.16,0.22)	0.780	0.03 (−0.17,0.23)	0.800
Death	4.02 (1.40,6.63)	0.003	3.88 (1.17,6.59)	0.005	4.59 (1.61,7.58)	0.003
Day × death	1.01 (0.73,1.29)	< 0.001	1.01 (0.73,1.29)	< 0.001	1.03 (0.75,1.31)	< 0.001

Time, the mean daily increase in NLR over time (1–14 days) in the survival group; death, the mean difference in NLR between the survivor and non-survivor groups at admission; death × day, daily rise in NLR, specifically within the non-survivor group compared with the survivor group

Model 1, not adjusted for any variables. Model 2, adjusted for age and sex. Model 3, adjusted for age, sex, duration, smoking, mechanic's hand, heliotrope rash, Gottron's sign/papules, V sign, Shawl sign, periungual erythema, Raynaud phenomenon, skin ulcer, muscle weakness, arthritis, Ro52, fever, ANA, RA, ALB, ALT, AST, CK, LDH, CRP, ESR, and WBC count

Abbreviations: ALB albumin, *ALT* alanine aminotransferase, *ANA* antinuclear antibody, *AST* aspartate aminotransferase, *CI* confidence interval, *CK* creatine kinase, *CRP* C-reactive protein, *DM-ILD* dermatomyositis with interstitial lung disease, *ESR* erythrocyte sedimentation rate, *GAMM* Generalized Additive Mixed Model, *HR* hazard ratio, *LDH* lactate dehydrogenase, *NLR* neutrophil-to-lymphocyte ratio, *RA* rheumatoid arthritis, *WBC* white blood cell count

patients with anti-MDA5-positive DM [20]. As part of a routine blood test, the NLR has recently gained increasing attention owing to its application in inflammation and autoimmune diseases. Some studies suggest that the NLR may provide enhanced diagnostic and prognostic value for these conditions compared to individual neutrophil or lymphocyte counts [21]. During the inflammatory process, cytokines and growth factors are released, which activate and extend the lifespan of neutrophils. This results in neutrophil activation at the inflammation site [22, 23]. Neutrophil-produced cytokines stimulate neutrophil activation, and systemic inflammation can induce lymphocyte apoptosis, consequently elevating the NLR in patients with DM [24–26].

Previous research has shown a connection between increased NLR and unfavorable short-term outcomes in patients with cancer, cardiovascular diseases, and inflammatory conditions [27–30]. Patients with systemic lupus erythematosus exhibit a significantly elevated NLR compared with healthy individuals, indicating a more precise diagnostic evaluation [27]. Moreover, a notable increase in the NLR has been observed in individuals with active Behçet's disease [31]. In a study conducted on individuals with esophageal squamous cell carcinoma, Feng et al. established a robust link between elevated preoperative NLR levels and a higher mortality rate, identifying NLR as a prognostic factor for survival [32]. Lee et al. suggested that the NLR serves as an independent prognostic indicator of survival in patients with gastric cancer [33]. In chronic diseases like ILD, an increased NLR may correlate with more severe disease progression, as it signals an ongoing inflammatory process with the potential for tissue damage and fibrosis [34]. The inflammatory response is crucial in the onset and advancement of anti-MDA5-positive DM-ILD. Multiple indicators, such as anti-MDA5 antibody titres [35], ferritin levels [36], Krebs von den Lungen-6 (KL-6) levels [37], and CD4 + CXCR4 + T cell ratio [38], have been associated with the prognosis of anti-MDA5-positive DM. In clinical practice, obtaining immediate test results for serum KL-6 levels and the ratio of CD4 + CXCR4 + T cells is often challenging, and the standardization of anti-MDA5 antibody titres may vary across different detection methods. In contrast, NLR is easy to access and standardize. Our data demonstrated an association between elevated baseline NLR and 30-day mortality in patients with anti-MDA5-positive dermatomyositis, which is consistent with previous studies [20]. Liu et al. [20] reported data from Signal Central indicating that the NLR is an independent predictor of mortality in anti-MDA5-positive DM-ILD. They found that an NLR greater than 4.8 may serve as a significant prognostic marker for mortality. In our study, we observed that a NLR greater than 6.5 was associated with mortality in patients with anti-MDA5-positive DM-ILD. This variation may be attributed to differences in sample size and the analytical methodologies employed. Previous study had shown that the mortality rate among patients with MDA5 + DM-ILD is particularly high within the first 90 days following diagnosis. After this initial period, the overall survival rate tends to stabilize [39]. Currently, there is a lack of data on the relationship between baseline NLR and its short-term changes with 30-day mortality in patients with anti-MDA5 positive DM-ILD. Our research found that a higher baseline NLR is associated with an increased risk of death within 30 days in patients with anti-MDA5-positive DM-ILD. Furthermore, during the first two weeks of hospitalization, NLR dynamics in the non-survival group showed a gradual increase compared to the survival group, the short-term changes in NLR appear to be a crucial prognostic indicator for patients with anti-MDA5 positive dermatomyositis.

This study has several limitations that should be acknowledged. First, its retrospective design may introduce selection bias, as the cohort may not fully represent all anti-MDA5 positive DM-ILD patients. This design also limits our ability to establish causal relationships between treatments and outcomes. Variations in treatment regimens, such as the use of multiple immunosuppressants and corticosteroids, may reflect differences in disease severity rather than directly causing the observed outcomes. It's important to consider the effects of corticosteroids on immune cell counts and NLR when interpreting results. Future prospective studies with controlled treatment protocols are needed to better understand the impact of specific treatments on NLR and mortality in these patients. Secondly, the study focuses on hospitalized patients, potentially skewing findings towards more severe cases and affecting generalizability. While we found an association between elevated NLR and poor outcomes, the causal link between elevated NLR, early changes, and mortality is unclear, which may limit NLR's utility as a prognostic marker. Although NLR is a useful indicator of disease activity and severity, the mechanisms underlying its role require further investigation.

Conclusions

The higher baseline NLR and its progressive increase are associated with 30-day mortality in patients with anti-MDA5-positive DM-ILD.

Abbreviations

ALB	Albumin
ALT	Alanine aminotransferase
ANA	Antinuclear antibody
AST	Aspartate aminotransferase
CI	Confidence interval
CK	Creatine kinase

CRP	C-reactive protein
DM	Dermatomyositis
ESR	Erythrocyte sedimentation rate
GAMM	Generalized Additive Mixed Model
ILD	Interstitial lung disease
KL-6	Krebs von den Lungen-6
LDH	Lactate dehydrogenase
MDA5	Melanoma differentiation-associated gene 5
MSA	Myositis-specific antibody
NLR	Neutrophil-to-lymphocyte ratio
RPILD	Rapidly progressive interstitial lung disease
WBC	White blood cell count
CTX	Cyclophosphamide
CsA	Cyclosporin A
Tac	Tacrolimus
IVIG	Intravenous immune globulin

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03512-4.

Additional file 1: Supplementary Figure S1. ROC curves of NLR as a prognostic biomarker. Abbreviations: ALB, albumin; AST: aspartate aminotransferase; CK, creatine kinase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio.

Additional file 2: Supplementary Table S1. The evolution of NLR between the survivor and non-survivor groups. Abbreviations: IQR, interquartile range; NLR, neutrophil-to-lymphocyte ratio.

Additional file 3: Supplementary Figure S2. Association between changes in the NLR and 30-day mortality. Abbreviation: NLR, neutrophil-to-lymphocyte ratio.

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Authors' contributions
HX: Writing – original draft, Data curation, Conceptualization; PH: Data curation, Conceptualization, Investigation; BX: Conceptualization, Data curation, Investigation; ZW: Data curation; HW: Methodology; FW: Methodology; ZM: Formal analysis; JX: Supervision; YJ: Supervision; Hourong Cai: Formal analysis, Methodology, Software; BC: Data curation, Conceptualization; JC: Writing – review & editing, Project administration, Resources.

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Data availability
The data used in this study has been fully described in this article and can be obtained through the following means: All data will be stored in our data storage system and can be obtained by contacting the corresponding author.

Declarations

Ethics approval and consent to participate
Ethical approval was granted by the ethics committees of Nanjing Drum Tower Hospital, General Hospital of Ningxia Medical University, Xuzhou Medical University Affiliated Hospital, and Third People's Hospital of Chengdu, between January 2017 and November 2021 (reference numbers: 2020–050-01; XYFY2022-KL427-02; KYLL-2023–0512; and [2023] S-139; respectively). Patient data were de-identified and the requirement for informed consent was waived.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Key Laboratory of Ningxia Stem Cell and Regenerative Medicine, Institute of Medical Sciences, Department of Pulmonary and Critical Care Medicine, General Hospital of Ningxia Medical University, Yinchuan, Ningxia 750004, China. [2]Department of Geriatrics, People's Hospital of Ningxia Hui Autonomous Region, Yinchuan 750000, China. [3]Department of Respiratory and Critical Care Medicine, the Third People's Hospital of Chengdu, Chengdu 610014, China. [4]Department of Respiratory and Critical Care Medicine, Affiliated Hospital of Xuzhou Medical University, Xuzhou 221004, China. [5]Department of Intensive Care Unit, General Hospital of Ningxia Medical University, Yinchuan, Ningxia 750004, China. [6]School of Information Science and Technology, Institute of Computational Biology, Northeast Normal University, Changchun 130024, China. [7]School of Public Health, Ningxia Medical University, Yinchuan 750004, People's Republic of China. [8]Department of Medical Genetics and Cell Biology, College of Basic Medicine, Ningxia Medical University, Yinchuan 750004, China. [9]Department of Key Laboratory of Ningxia Stem Cell and Regenerative Medicine, Institute of Medical Sciences, General Hospital of Ningxia Medical University, Yinchuan 750004, China. [10]Department of Respiratory Medicine, Nanjing Drum Tower Hospital, Nanjing 210008, China. [11]Department of Respiratory and Critical Care Medicine, Affiliated Hospital of Xuzhou Medical University, 99 West Huaihai Road, Xuzhou, Jiangsu 221000, China.

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