Retrospective analysis of the association between monocyte percentage and outcomes in newly diagnosed diffuse large B-cell lymphoma

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Abstract. The aim of the present study was to analyze the prognostic value of monocyte percentage (MP) at diagnosis in patients with diffuse large B-cell lymphoma (DLBCL). Overall, 169 patients with newly diagnosed DLBCL who were treated with rituximab-based therapy at the Department of Hematology, Ganzhou People's Hospital (Ganzhou, China) between January 2015 and December 2023 were retrospectively analyzed. Univariate and multivariate analyses were used to assess the impact of MP and clinical characteristics on prognosis. Kaplan-Meier curves and log-rank tests were used to analyze progression-free survival (PFS) and overall survival (OS). The prediction performance for OS was assessed using receiver operating characteristic (ROC) analysis. A total of 16 patients passed away during the follow-up, whereas 53 patients experienced disease progression/relapse. Patients were divided into groups with low (≤10%) and high (>10%) MPs, with 10% serving as the cutoff. A high MP was independently associated with worse PFS (hazard ratio, 2.54; 95% confidence interval, 1.08-5.99; P=0.033) and OS (P<0.05). When MP was combined with International Prognostic Index (IPI) scores, predictive accuracy was significantly higher than upon using IPI alone (area under the ROC curve, 0.907 vs. 0.792, respectively; P=0.043). In conclusion, in patients with DLBCL, a high MP at diagnosis is significantly associated with poor survival outcomes. Combining MP with IPI score improves prognostic stratification.

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most prevalent subtype of non-Hodgkin lymphoma (NHL), characterized by aggressive mature B-cell tumors with heterogeneous clinical features and varying responses to treatment (1-3). Only 60% of patients achieve long-term remission, and approximately one-third experience treatment resistance or relapse, despite conventional immunochemotherapy with a rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) regimen (4).

The International Prognostic Index (IPI) (5) is the leading prognostic tool for clinical decision-making, and incorporates age, stage, lactate dehydrogenase (LDH) level, performance status and extranodal involvement. Although gene expression profiling and molecular markers (including MYD88, TP53 and KMT2D) provide useful prognostic information (6,7), their high expense, technical requirements and time-consuming procedures prevent widespread clinical use. Therefore, there is an urgent need for accessible and cost-effective prognostic biomarkers.

By inhibiting antitumor immunity, promoting angiogenesis and providing trophic factors for malignant lymphocyte survival, monocytes and tumor-associated macrophages play important roles in the pathophysiology of lymphomas (8,9). Absolute monocyte counts (AMCs) have demonstrated prognostic value in lymphoma (10,11), but have important clinical limitations. Patients with DLBCL frequently present with significant hematological variations, including treatment-induced leukopenia or leukocytosis, bone marrow involvement, infection-related white blood cell (WBC) fluctuations (12) and corticosteroid effects (13). These factors can substantially alter absolute counts while potentially masking the underlying immune composition.

By contrast, monocyte percentage (MP) offers several distinct advantages: First, MP reflects the relative immune cell composition and the proportional balance between immunosuppressive monocytes and other immune populations, which may more accurately represent tumor-immune microenvironment dynamics given that monocytes play pivotal roles in shaping immunosuppressive environments through various mechanisms (14). Second, MP is less susceptible to the confounding effects of total WBC variations, providing a more stable measure across different clinical scenarios (15). Third, MP may eliminate variability from laboratory-specific reference ranges, enhancing standardization and applicability across diverse healthcare settings. Despite these theoretical advantages and the established role of monocytes in lymphoma pathogenesis, MP has been underexplored as an independent prognostic marker in DLBCL.

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Therefore, the present retrospective cohort study was conducted to evaluate the prognostic value of MP in patients with newly diagnosed DLBCL treated with R-CHOP, and to assess its independent prognostic significance beyond established markers, including analysis of IPI and AMC.

Patients and methods

Study design and participants. The present study included patients with newly diagnosed DLBCL who received R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, tumor protein, and prednisone) treatment and evaluation at Ganzhou People's Hospital (Ganzhou, China) between January 2015 and December 2023. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ganzhou People's Hospital Ethics Committee (Ganzhou, China; approval no. PJB2025-210-01). The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study and the use of fully anonymized clinical data. Exclusion criteria included autoimmune diseases, a human immunodeficiency virus-positive status, inflammatory conditions, other lymphomas (such as follicular lymphoma, mantle cell lymphoma) or leukemias and previous chemoradiotherapy. The following clinical baseline data were retrieved from medical records during diagnosis: Sex, age, Eastern Cooperative Oncology Group Score (16), Ann Arbor tumor stage (17), molecular sub-type, extranodal infiltration number, lactate dehydrogenase level, IPI score, bone marrow involvement and pathology results, WBC count, MP, AMC, absolute lymphocyte count, red blood cell (RBC) count, blood platelet (PLT) count, hemoglobin level, fibrinogen level, LDH, albumin level and immunophenotype. Clinicopathological criteria from either an initial lymph node biopsy or an external biopsy of the primary nodes were used to confirm the DLBCL diagnosis. The molecular subtype of DLBCL was classified into germinal center B-cell-like (GCB) and non-GCB subtypes using the Hans algorithm, which is based on immunohistochemical staining for CD10, BCL6 and MUM1 (6) When diagnosing DLBCL, an automated complete blood count (CBC) is frequently used to measure the MP in peripheral WBCs.

Grouping strategy. Patients were divided into two groups based on MP, with the clinical laboratory standard upper limit threshold of 10% used as the primary cutoff; however, receiver operating characteristic (ROC) analysis using the Youden Index suggested using an optimal threshold of 8.7%. The 10% threshold represents the established upper limit for normal MP and defines monocytosis in standard clinical practice. To evaluate how cutoff selection affected prognostic performance, a sensitivity analysis was conducted comparing the two thresholds. Participants were classified based on a cut-off value of MP (≤10 and >10%) for the primary analysis.

Follow-up and outcome definitions. Follow-up was conducted by reviewing medical histories or through telephone conversations. Progression-free survival (PFS) time was defined as the interval between the date of diagnosis and disease progression, recurrence, death or the end of follow-up. Overall survival (OS) time was defined as the interval between diagnosis and death or the end of follow-up.

Statistical analysis. Categorical variables are presented as n (%), and continuous variables that are normally distributed are presented as mean ± standard deviation. Continuous variables with skewed distribution are presented as median (interquartile range). All comparisons were performed with appropriate statistical tests (χ^2/Fisher's exact test for categorical variables and unpaired t-test/Mann-Whitney U-test for continuous variables) with P-values reported.

A multivariate Cox proportional hazard regression model was used to adjust for potential confounders to estimate the association of MP with OS and PFS in newly diagnosed DLBCL. The lower group (≤10%) was the reference group. Model 1 had no adjustments, whereas model 2 was adjusted for age and sex. Model 3 was further adjusted for Ann Arbor tumor stage, molecular subtype, double expression, extranodal infiltration number, IPI score, bone marrow involvement, Epstein-Barr virus infection, WBC count, RBC count, PLT count, hemoglobin level, fibrinogen level and albumin level. To determine the association of MP with OS and PFS, the cumulative Kaplan-Meier curve was plotted. Eventually, by calculating the area under the ROC curve (AUC) and 95% confidence intervals (CIs) for outcomes, the predictive power of IPI scores and their combination with the MP was evaluated. P<0.05 was used to indicate a statistically significant difference.

All statistical analyses were conducted using the software package R (http://www.R-project.org) and Empower Stats (http://www.empowerstats.com; X&Y Solutions, Inc.).

Results

Patient characteristics. A total of 169 newly diagnosed DLBCL patients were included in the present study, with a median age of 59.0±13.0 years (median, 61.0 years; IQR 53.0-68.0) and 53.8% male predominance. Based on the optimal cutoff of 10% MP, 117 patients (69.2%) were classified in the low MP group and 52 (30.8%) in the high MP group (Table I).

Baseline characteristics were generally balanced between groups regarding age, sex, double expression, IPI score, extranodal involvement, bone marrow infiltration, concurrent malignancy, EBV DNA levels and fibrinogen levels (all P>0.05). However, significant differences emerged in several key features. Patients with high MP more frequently presented with advanced stage III-IV disease (94.2 vs. 76.1%; P=0.016) and GCB subtype (80.8 vs. 59.8%; P=0.008). Laboratory analyses revealed that high MP was associated with elevated LDH (median, 344.5 vs. 208.0 U/l; P=0.001), with 63.5% exceeding the upper limit of normal LDH level compared with 30.8% in the low MP group (P<0.001). Despite lower total WBC counts ($5.1x10^9$/l vs. $6.9x10^9$/l; P<0.001), the high MP group had a higher AMC ($0.7x10^9$/l vs. $0.4x10^9$/l; P<0.001) but lower ALC ($0.9x10^9$/l vs. $1.4x10^9$/l; P<0.001), indicating a shift in immune cell composition. Additionally, high MP was associated with lower hemoglobin (112.3 vs. 127.5 g/l; P<0.001), PLTs ($172.5x10^9$/l vs. $234.0x10^9$/l; P<0.001) and albumin (38.6 vs. 41.6 g/l; P=0.001) levels, and a higher ferritin level (317.0 vs. 244.7 ng/ml; P=0.045), suggesting greater disease burden.

Univariate analysis. Using univariate Cox regression analysis, various prognostic factors that affect PFS and OS were analyzed (Table II). PFS was strongly correlated with Ann Arbor stages III

Table I. Association between MP and clinical characteristics in patients with newly diagnosed diffuse large B-cell lymphoma.

Variables	Total (n=169)	MP ≤10% (n=117)	MP >10% (n=52)	P-value
Sex, n (%)				0.738
Female	78 (46.2)	53 (45.3)	25 (48.1)	
Male	91 (53.8)	64 (54.7)	27 (51.9)	
Age, years				0.757
≤60	75 (44.4)	51 (43.6)	24 (46.2)	
>60	94 (55.6)	66 (56.4)	28 (53.8)	
Mean ± SD	59.0±13.0	59.0±13.2	59.2±12.7	0.893
Median (IQR)	61.0 (53.0, 68.0)	61.0 (53.0, 68.0)	61.0 (53.0, 69.0)	0.969
Hans algorithm, n (%)				
GCB	112 (66.3)	70 (59.8)	42 (80.8)	
Non-GCB	57 (33.7)	47 (40.2)	10 (19.2)	
Double expression, n (%)				0.149
No	126 (74.6)	91 (77.8)	35 (67.3)	
Yes	43 (25.4)	26 (22.2)	17 (32.7)	
Ann Arbor clinical stage, n (%)				0.016
I-II	27 (16.0)	24 (20.5)	3 (5.8)	
III-IV	138 (81.7)	89 (76.1)	49 (94.2)	
NA	4 (2.4)	4 (3.4)	0 (0.0)	
IPI score, n (%)				0.278
0	12 (7.1)	10 (8.5)	2 (3.8)	
1	34 (20.1)	26 (22.2)	8 (15.4)	
2	41 (24.3)	27 (23.1)	14 (26.9)	
3	43 (25.4)	32 (27.4)	11 (21.2)	
4	27 (16.0)	14 (12.0)	13 (25.0)	
5	12 (7.1)	8 (6.8)	4 (7.7)	
Extranodal involvement, n (%)				0.062
<2	73 (43.2)	45 (38.5)	28 (53.8)	
≥2	96 (56.8)	72 (61.5)	24 (46.2)	
Bone marrow infiltration, n (%)				0.769
No	145 (85.8)	101 (86.3)	44 (84.6)	
Yes	24 (14.2)	16 (13.7)	8 (15.4)	
Combined with cancer, n (%)				0.703
No	161 (95.3)	112 (95.7)	49 (94.2)	
Yes	8 (4.7)	5 (4.3)	3 (5.8)	
EBV DNA >500 copies/ml, n (%)				0.253
No	136 (80.5)	98 (83.8)	38 (73.1)	
Yes	24 (14.2)	14 (12.0)	10 (19.2)	
NA	9 (5.3)	5 (4.3)	4 (7.7)	
Mean WBC ± SD, $x10^9$/l	6.4±3.1	6.9±3.3	5.1±2.4	<0.001
AMC, $x10^9$/l[a]	0.5 (0.3-0.7)	0.4 (0.3-0.6)	0.7 (0.5-1.0)	<0.001
ALC, $x10^9$/l[a]	1.3 (0.9-1.7)	1.4 (1.0-1.8)	0.9 (0.5-1.4)	<0.001
Mean RBC ± SD, $x10^{12}$/l	4.2±0.8	4.3±0.7	3.8±0.9	<0.001
Mean Hb ± SD, g/l	122.9±25.5	127.5±23.2	112.3±27.3	<0.001
PLT, $x10^9$/l[a]	219.0 (159.0-284.0)	234.0 (188.0-308.0)	172.5 (122.2-246.2)	<0.001
Mean Fbg ± SD, g/l	3.8±1.3	3.8±1.2	3.8±1.4	0.980

Table I. Continued.

Variables	Total (n=169)	MP ≤10% (n=117)	MP >10% (n=52)	P-value
Mean Alb ± SD, g/l	40.7±5.7	41.6±5.4	38.6±6.0	0.001
Ferritin, ng/ml[a]	261.2 (148.9-464.9)	244.7 (144.1-440.6)	317.0 (168.2-748.0)	0.045
LDH, U/l[a]	233.0 (182.5-448.5)	208.0 (172.0-327.0)	344.5 (209.2-550.8)	0.001
LDH >ULN, n (%)	69 (40.8)	36 (30.8)	33 (63.5)	<0.001

[a]Median (IQR). χ^2/Fisher's exact test were used for categorical variables, and unpaired t-test/Mann-Whitney U-test for continuous variables. IQR, interquartile range; SD, standard deviation; MP, monocyte percentage; IPI, International Prognostic Index; EBV, Epstein-Barr virus; GCB, germinal center B-cell-like lymphoma; WBC, white blood cell count; AMC, absolute monocyte count; ALC, absolute lymphocyte count; RBC, red blood cell count; PLT, platelet; Fbg, fibrinogen; Alb, albumin; LDH, lactic dehydrogenase; ULN, upper limit of reference value; NA, not available.

Table II. Univariate analysis of clinicopathological parameters for OS and PFS time in patients with newly diagnosed diffuse large B-cell lymphoma.

	PFS		OS	
Factors	HR (95% CI)	P-value	HR (95% CI)	P-value
Female	1.28 (0.74-2.21)	0.383	1.12 (0.40-3.14)	0.831
Age >60 years	1.31 (0.76-2.26)	0.335	1.00 (0.96-1.04)	0.840
Ann Arbor stage III-IV	8.30 (1.14-60.23)	0.036	7.45 (1.24-54.68)	0.002
Hans type	1.54 (0.87-2.72)	0.137	1.08 (0.27-4.26)	0.917
IPI scores	4.64 (2.68-8.02)	<0.001	5.12 (1.62-16.18)	0.005
Extranodal sites ≥2	1.20 (0.69-2.10)	0.516	0.20 (0.41-3.54)	0.744
Bone marrow involvement	3.05 (1.64-5.68)	<0.001	1.96 (0.61-6.29)	0.260
EBV DNA >500 copies	1.17 (0.46-3.00)	0.736	2.10 (0.25-17.61)	0.493
Combined with tumor	2.26 (0.81-6.32)	0.119	1.81 (0.40-8.29)	0.442
WBC	0.92 (0.82-1.02)	0.120	0.75 (0.58-0.97)	0.028
RBC	0.59 (0.42-0.83)	0.002	0.63 (0.35-1.15)	0.133
Hb	0.99 (0.98-1.00)	0.016	0.98 (0.97-1.00)	0.072
PLT	1.00 (0.99-1.00)	0.023	1.00 (0.99-1.00)	0.383
Fbg	1.02 (0.81-1.29)	0.843	0.64 (0.37-1.10)	0.106
Alb	0.95 (0.91-1.00)	0.048	0.92 (0.84-1.00)	0.064
Ferritins	1.00 (1.00-1.00)	0.337	1.00 (1.00-1.00)	0.492

PFS, progression-free survival; OS, overall survival; IPI, International Prognostic Index; EBV, Epstein-Barr virus; WBC, white blood cell count; RBC, red blood cell count; Hb, hemoglobin; PLT, platelet; Fbg, fibrinogen; Alb, albumin; HR, hazard ratio; CI, confidence interval.

to IV (HR=8.30, 95% CI: 1.14-60.23; P=0.036), bone marrow involvement (HR=3.05, 95% CI: 1.64-5.68; P<0.001), IPI scores >3 (HR=4.64, 95% CI: 2.68-8.02; P<0.001), RBC (HR=0.59, 95% CI: 0.42-0.83; P=0.002), hemoglobin (HR=0.99, 95% CI: 0.98-1.00; P=0.016), PLT count (HR=1.00, 95% CI: 0.99-1.00; P=0.023) and albumin level (HR=0.95, 95% CI: 0.91-1.00; P=0.048). Similarly, OS was strongly associated with Ann Arbor stages III to IV (HR=7.45, 95% CI: 1.24-54.68; P=0.002), IPI scores >3 (HR=5.12, 95% CI: 1.62-16.18; P=0.005) and WBC count (HR=0.75, 95% CI: 0.58-0.97; P=0.028).

Cutoff value determination. The following performance metrics were observed by comparing the ROC-optimal (8.7%) and clinical (10%) cutoffs: The 8.7% cutoff demonstrated higher sensitivity (62.3 vs. 45.3%), Youden Index (0.286 vs. 0.194) and negative predictive value (NPV) (79.4 vs. 74.8%), whereas the 10% cutoff showed superior specificity (74.1 vs. 66.4%). Between the 8.7 and 10% cutoffs, positive predictive values were comparable (45.8 vs. 44.4%; difference 1.4%). The 10% threshold was selected for its clinical practicality as a round number and higher specificity, which minimizes false-positive risk stratification despite slightly lower sensitivity and NPV. Table SI summarizes the performance comparison.

In order to ascertain the predictive value of the MP in peripheral blood, MP was measured from peripheral blood samples collected at initial diagnosis. In the multivariate Cox

Table III. Multivariate Cox proportional analysis of MP for the prediction of OS and PFS in patients with DLBCL.

A, Model 1

	Multivariate analysis PFS		Multivariate analysis OS	
Parameter	HR (95% CI)	P-value	HR (95% CI)	P-value
MP (per 1% increase)	1.10 (1.05-1.15)	<0.001	1.13 (1.04-1.22)	0.003
MP (>10 vs. ≤10%)	1.94 (1.12-3.37)	0.018	3.73 (1.01-13.77)	0.049

B, Model 2

	Multivariate analysis PFS		Multivariate analysis OS	
Parameter	HR (95% CI)	P-value	HR (95% CI)	P-value
MP (per 1% increase)	1.09 (1.03-1.15)	0.001	1.14 (1.05-1.24)	0.002
MP (>10 vs. ≤10%)	1.79 (1.02-3.13)	0.042	3.92 (1.05-14.72)	0.043

C, Model 3

	Multivariate analysis PFS		Multivariate analysis OS	
Parameter	HR (95% CI)	P-value	HR (95% CI)	P-value
MP (per 1% increase)	1.14 (1.05-1.25)	0.002	2.15 (1.14-4.03)	0.017
MP (>10 vs. ≤10%)	2.54 (1.08-5.99)	0.033	5.34 (0.57-50.14)	0.143

MP, monocyte percentage; PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval.

regression analysis, MP was analyzed both as a continuous variable and as a dichotomized variable using a 10% cutoff.

Multivariate analysis. When MP was analyzed as a continuous variable, it demonstrated consistent prognostic significance across all three models. In model 1, each 1% increase in MP was associated with worse PFS (HR, 1.10; 95% CI, 1.05-1.15; P<0.001) and OS (HR, 1.13; 95% CI, 1.04-1.22; P=0.003) (Table III). In model 2, MP remained significantly associated with PFS (HR, 1.09; 95% CI, 1.03-1.15; P=0.001) and OS (HR, 1.14; 95% CI, 1.05-1.24; P=0.002). In model 3, MP continued to be an independent prognostic factor for both PFS (HR, 1.14; 95% CI, 1.05-1.25; P=0.002) and OS (HR, 2.15; 95% CI, 1.15-4.03; P=0.017) (Table III).

When MP was analyzed as a dichotomized variable with 10% as the cutoff, patients with MP >10% showed significantly worse outcomes compared with those with MP ≤10% (reference group). In model 1, elevated MP (>10%) was associated with worse PFS (HR, 1.94; 95% CI, 1.12-3.37; P=0.018) and OS (HR, 3.73; 95% CI, 1.01-13.77; P=0.049). In model 2, the associations remained significant for both PFS (HR, 1.79; 95% CI, 1.02-3.13; P=0.042) and OS (HR, 3.92; 95% CI, 1.05-14.72; P=0.043). In model 3, MP remained an independent predictor of PFS, compared with the reference group (HR, 2.54; 95% CI, 1.08-5.99; P=0.033). By contrast, no significant difference was observed when comparing OS to the reference group (HR, 5.34; 95% CI, 0.57-50.14; P=0.143) (Table III).

Survival analysis. Kaplan-Meier survival curves were used to compare the two groups (≤10 and >10%). Both PFS (P=0.017) and OS (P=0.037) were poor in the high MP group compared with those in the low MP group (Fig. 1A and B).

To evaluate the predictive value of MP and assess the impact of identifying multiple biomarkers on OS prediction, ROC curves were plotted for patients with OS outcomes. Compared with the international IPI score for assessing risk factors, incorporating the MP increased the AUC (0.792 vs. 0.907; P=0.043) (Fig. 1C).

Discussion

The results of the present study suggest that MP at diagnosis may be utilized as a biomarker to predict survival in patients with newly diagnosed DLBCL treated with R-CHOP. A high MP was associated with poor PFS and OS. Additionally, MP provided prognostic information independent of IPI score, and it may increase the predictive effectiveness of outcomes when combined with IPI score. Although the prognostic value of AMC in DLBCL has been reported (10,11), the precise function of MP as a readily available biomarker remains unknown. To the best of our knowledge, the present study is the first to systematically evaluate the value of MP as an independent prognostic indicator. Compared with AMC, MP provides a standardized assessment method that is unaffected by factors such as hemodilution or hemoconcentration, offering better clinical applicability.

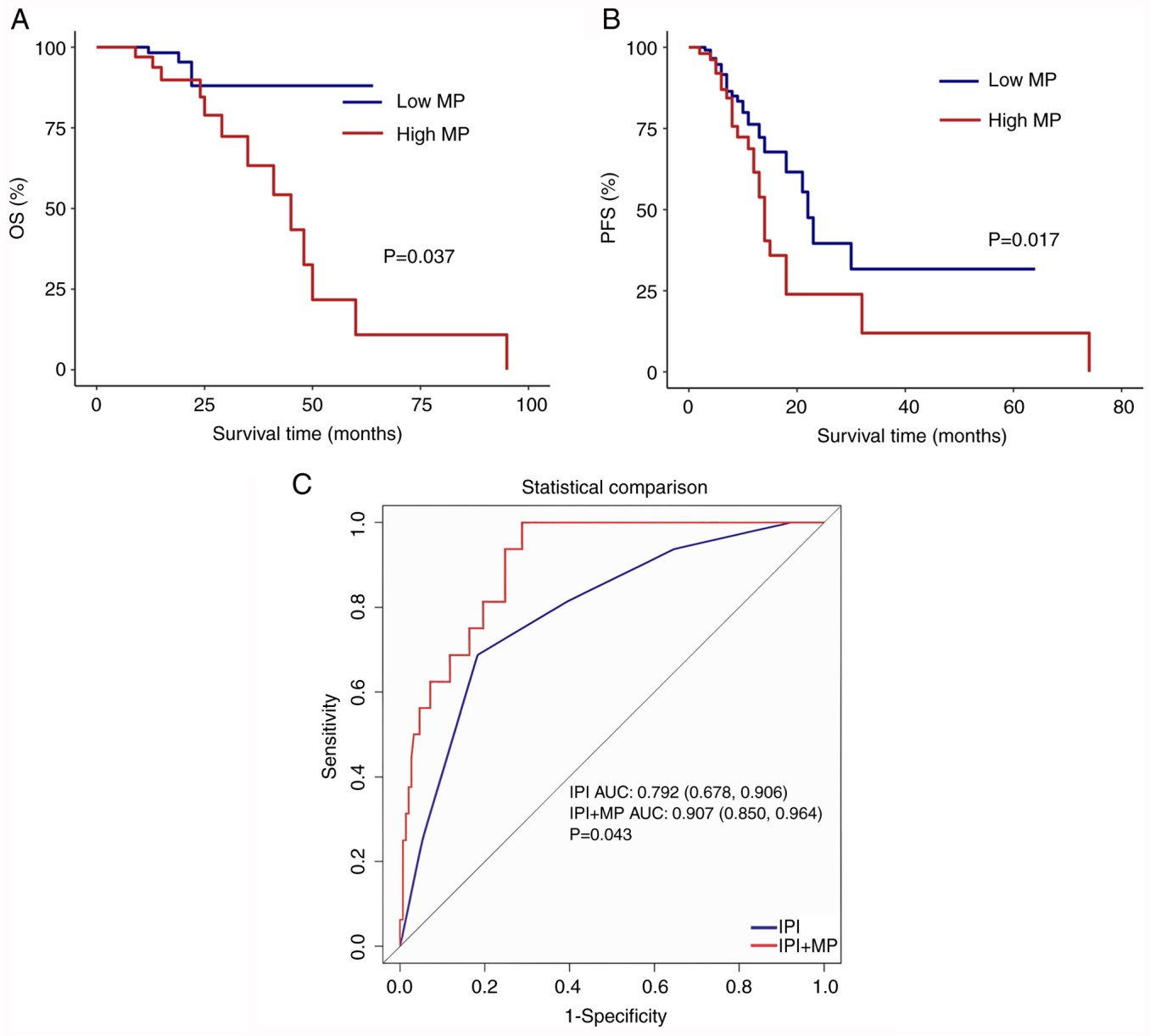

Figure 1. Kaplan-Meier curves for (A) PFS and (B) OS probability comparing low (≤10%) and high (>10%) MP. (C) Receiver operating characteristic curve analysis for the prediction of OS in patients with diffuse large B-cell lymphoma. Model 1 (blue) represents IPI scores, model 2 (red) includes IPI scores and MP. MP, monocyte percentage; IPI, International Prognostic Index; PFS, progression-free survival; OS, overall survival; AUC, area under the receiver operating characteristic curve.

The tumor microenvironment and host immunity are crucial factors in DLBCL outcomes (18,19). Monocytes and monocytic myeloid-derived suppressor cells may suppress host antitumor immunity through several mechanisms, including secretion of immunosuppressive cytokines (e.g., IL-10, TGF-β), depletion of amino acids via arginase-1 and inducible nitric oxide synthase, production of reactive oxygen species, and expression of immune checkpoint molecules such as PD-L1 (20). Additionally, myeloid cells have been implicated in fostering tumor angiogenesis within the tumor microenvironment (21). Furthermore, immune-derived myeloid cells produced by tumors directly promote tumor growth and vascularization by their differentiation into endothelial cells (22). In human umbilical vein endothelial cell cultures, monocytes actively promote endothelial cell proliferation through C-X3-C motif chemokine receptor 1/fractalkine interaction (23).

Beyond promoting tumor cell angiogenesis, monocytes can suppress the host's antitumor immune response. T-cell co-inhibitory ligand B7-homolog 1 (also known as programmed death-ligand 1) is expressed in the tumor microenvironment by peripheral blood monocytes and their progeny (24). Moreover, lymphoma B cells can recruit monocytes via chemokine C-C motif ligand 5, which enhances the survival and proliferation of neoplastic B lymphocytes while suppressing the proliferation of healthy T cells (25). Finally, monocytes are an essential source of soluble mediators, such as B lymphocyte stimulator, that promote the growth and survival of healthy and malignant B cells (26,27). It follows that monocytes promote the growth of malignant lymphocytes in both T-cell and B-cell NHL (8,28). The mechanism underlying the association between monocytes and rituximab-mediated B-cell lymphoma outcomes was elucidated by these cited earlier investigations.

Different molecular subtypes and clinical features may affect the association between MP and DLBCL outcomes. Germinal center B-cell-like (GCB) and non-GCB DLBCL subtypes exhibit fundamentally different tumor microenvironments and inflammatory profiles. In contrast to GCB subtypes, non-GCB subtypes may promote more monocyte recruitment and activation owing to their constitutive NF-κB activation and elevated inflammatory signaling (29,30). By promoting angiogenesis and suppressing the immune system, these activated monocytes can differentiate into tumor-associated macrophages, which aid in tumor growth (31).

Double expressor lymphomas ($MYC^+/BCL2^+$) are a physiologically aggressive subtype with distinct immune characteristics. MYC overexpression has been associated with changes in immune cell recruitment and function, which may affect the differentiation state of circulating monocytes (32,33). By altering apoptotic pathways in both tumor cells and immune effector cells, the concomitant upregulation of BCL2 may further modulate the tumor-immune interface (34). Similarly, more aggressive disease biology and systemic inflammatory responses that may influence MP and function are frequently reflected in extranodal involvement.

Importantly, the multivariate analysis in the present study demonstrated that MP maintained independent prognostic value even after adjusting for the established molecular markers (GCB subtype and double expressor status) and clinical variables (extranodal involvement). The novelty of this study lies in, to the best of our knowledge, the first demonstration that MP retains independent prognostic value after adjusting for molecular markers (GCB subtype and double expressor status) and clinical variables. This suggests that MP may capture biological information not reflected by existing molecular and clinical stratification methods. Thus, MP may reflect the complex interplay between systemic immune status and local tumor microenvironment dynamics, capturing further biological information beyond the current molecular and clinical stratification approaches.

In the present study, patients with DLBCL who had a high MP at diagnosis tended to have poor PFS and OS. After controlling for other key negative prognostic variables, multivariate analysis retained the predictive value of MP. These results support the adverse prognostic impact of elevated MP on B-cell NHL and are in line with earlier research (19,35,36). The majority of studies have suggested that the AMC may be considered a prognostic indicator for DLBCL. However, the precise association between a high MP acquired from a CBC and a poor prognosis remains debatable. Notably, monocytes may contribute to tumor immunity and the tumor microenvironment as vital components of the immune system. Hemoglobin levels and PLT counts are independent predictors of poor 5-year OS and disease-free survival rates in patients with DLBCL (37). Similarly, Li *et al* (38) reported that decreased peripheral blood PLT count may be a factor associated with a poor prognosis in newly diagnosed DLBCL. The present results, which suggested that the PLT count was a protective factor for PFS, are in line with this previous research. Using univariate Cox regression analysis, the present study demonstrated positive associations between hemoglobin levels and PFS. However, the hemoglobin level did not affect OS. Unlike gene expression profiling or immunohistochemistry, which require complex testing, MP is a simple indicator readily obtainable from a routine CBC, yet its prognostic value has been underrecognized. To the best of our knowledge, the present study is the first to validate MP as an independent prognostic biomarker and demonstrate its ability to enhance the predictive power of the National Comprehensive Cancer Network (NCCN)-IPI.

Despite increasing evidence emphasizing the association between the tumor microenvironment and lymphoma, it is challenging to incorporate tumor microenvironment-related prognostic variables into standard clinical practice. This is because gene expression profiles or immunohistochemical data often form the basis for most research estimating such associations. By contrast, the MP data achieved from a CBC may be widely used and easily incorporated into clinical practice. The important contribution of the present study is identifying MP as a unique prognostic indicator from among numerous hematological parameters. While previous studies have focused on AMC, MP as a relative proportion indicator offers several advantages: i) It is unaffected by individual blood volume variations; ii) it reflects the relative balance of immune cell composition; and iii) it may more accurately reflect tumor-associated systemic immune status changes. Furthermore, MP, a novel prognostic metric derived from CBC that is easily accessible in clinical data, presents information independent of NCCN-IPI. Additionally, it may provide further predictive value when combined with NCCN-IPI.

The present study has several limitations. First, the limited number of OS events (n=16; 9.5%) resulted in large confidence intervals and low statistical power for multivariate analysis. Post-hoc power analysis suggested that ~50 OS events would be required to detect the observed effect size with 80% power. This explains why the hazard ratio remained high (HR, 5.34) but had wide confidence intervals (95% CI, 0.57-50.14) in the non-significant multivariate Cox model (P=0.143), compared with the significant univariate Kaplan-Meier analysis (P=0.037). Second, although the association between MP and DLBCL prognosis was assessed using multivariate Cox regression analysis, the influence of unaccounted-for confounding factors could not be excluded entirely. Third, although the 10% MP cutoff was based on laboratory reference ranges, it may not be optimal for prognostic stratification and warrants further investigation in larger cohorts using ROC-derived thresholds. Therefore, larger prospective multi-center studies with longer follow-up periods are warranted to confirm the predictive efficacy of MP, an easily available and affordable parameter for determining patient prognosis in those with DLBCL.

In conclusion, the present cohort study demonstrated a significant association between elevated MP and poor survival outcomes. Furthermore, combining MP with IPI may improve the predictive efficiency of these results.

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Availability of data and materials

The data supporting this study's findings are available online at DOI 10.6084/m9.figshare.25151393.

Authors' contributions

XX and CZ contributed to the study design and data collection. XX performed the statistical analysis and data analysis. CZ was involved in the writing and revision of the manuscript. XX and CZ confirm the authenticity of all the raw data. Both authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Ganzhou People's Hospital Ethics Committee (Ganzhou, China; approval no. PJB2025-210-01). The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study and the use of fully anonymized clinical data.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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