Prognostic value of neutrophil/lymphocyte ratio, lymphocyte/monocyte ratio, lactate dehydrogenase, and mean platelet volume in the diagnosis of patients with diffuse large B-cell lymphoma

Mehmet Bakırtaş, Semih Başcı, Burcu Aslan Candır, BaharUncu Ulu, Samet Yaman, Tuğçe Nur Yiğenoğlu, Mehmet Sinan Dal, MerihKızıl Çakar, Fevzi Altuntaş

Background Diffuse large B-cell lymphoma (DLBCL), a heterogeneous type of lymphoma, encompasses various biologic abnormalities and numerous morphologic variants, showing several clinical findings and responses to treatments. Lactate dehydrogenase (LDH) is a well-established diagnostic and prognostic marker for DLBCL, and neutrophil/lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and mean platelet volume (MPV) have been shown to have prognostic values in several malignancies.

Objectives In the study, we examined the prognostic value of LMR, NLR, LDH, and MPV in the stage and prognosis of DLBCL by analyzing the data of patients treated with rituximab-based chemotherapies.

Patients and methods A total of 188 patients diagnosed as having DLBCL between January 2012 and January 2020 were selected. DLBCL stages were categorized as early and late, international prognostic index was categorized as below and above 4, and the treatment response was categorized as responders and nonresponders. NLR, LMR, LDH, MPV, and other factors predicting these outcomes were analyzed.

Results Logistic regression analysis showed that the factors influencing stage of DLBCL were NLR [*P*=0.009, odds ratio (OR)=1.220, 95% confidence interval (CI): 1.050–1.417] and LDH (*P*=0.001, OR=0.286, 95% CI: 0.146–0.561). The factor influencing international prognostic index score was LMR (*P*=0.001, OR=6.226, 95% CI: 2.092–18.533). Factors influencing response were R-CHOP treatment (*P*=0.001, OR=0.181, 95% CI: 0.068–0.478) and stage (*P*=0.005, OR=18.306, 95% CI: 2.383–140.607).

Conclusion The pretreatment LMR, NLR, LDH, and MPV values may affect the stage and prognosis of DLBCL, which showed influences on the treatment response.

Egypt J Haematol 2023 47:233–238

Egyptian Journal of Haematology 2023 47:233–238

Keywords: diffuse large B-cell lymphoma, lactate dehydrogenase, lymphocyte–monocyte ratio, mean platelet volume, neutrophil/lymphocyte ratio

Department of Hematology and Bone Marrow Transplantation Center, Ankara Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital, University of Health Sciences, Ankara, Turkey

Correspondence to Semih Başcı, MD, Department of Hematology and Bone Marrow Transplantation Center, Ankara Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital, University of Health Sciences, Ankara 06200, Turkey.
Gsm: +90 506 292 98 90; tel: +90 312 3360909-7215;
e-mail: dr.semihbasci@gmail.com

Received: 30 March 2022 **Revised:** 03 April 2022
Accepted: 04 April 2022 **Published:** 09 March 2023

Background

Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous type of lymphoma, comprising 25% of all non-Hodgkin's lymphomas [1]. As the most common entity, DLBCL encompasses various biologic abnormalities and numerous morphologic variants, showing several clinical outcomes and responses to the treatments [2]. The regular first-line therapy of DLBCL is immunotherapy with rituximab combined with an anthracycline-based chemotherapy, for example, doxorubicin, cyclophosphamide, prednisone, and vincristine [3]. Although a number of patients who receive this first-line treatment have been cured and achieved long-term disease-free intervals, 30–40% of patients have experienced a relapse or cannot respond to first-line therapy [4].

To stratify risk and define four different risk categories for patients with DLBCL, five clinical factors involving age, extranodal site number, lactate dehydrogenase (LDH), Ann Arbor stage, and Eastern Cooperative Oncology Group (ECOG) score were used. The high-risk category (4 or 5 risk factors) was related with 26% 5-year overall survival (OS). The introduction of rituximab (R) to traditional CHOP or CHOP-like regimens for DLBCL has contributed to a substantial increase in survival among all risk groups since the last two decades [5].

The inflammatory biomarkers have been found during the systemic inflammation to be associated with the progression and prognosis of many types of tumor [6]. One of these biomarkers, the neutrophil-to-lymphocyte ratio (NLR), is estimated as the absolute neutrophil

 DOI: 10.4103/ejh.ejh_14_22

count divided by the absolute lymphocyte count (ALC) calculated in the peripheral blood [7]. Recently, NLR has been determined as a prognostic factor for several solid and hematologic malignancies including DLBCL [8,9]. A meta-analysis demonstrated that the patients with DLBCL who have greater NLR are prone to show worse prognosis than those having lower NLR [10].

As the main part of immune cells, lymphocytes reflect the immune condition of the host and the extent of tumor progression. The monocytes represent the tumor microenvironment; hence, the lymphocyte-to-monocyte ratio (LMR) in the peripheral blood at diagnosis of lymphomas may reveal the relation between these two entities. Current studies have demonstrated that LMR at diagnosis may predict the long-term outcomes and is related with OS in hematological malignancies, including DLBCL [11]. Moreover, LMR at diagnosis is suggested to be an independent prognostic factor of clinical findings in DLBCL [6].

Mean platelet volume (MPV) is analyzed routinely as part of the complete blood count, reflecting the platelet activity. MPV was found to be associated with platelet aggregation, thromboxane B2 release, and increased expression of the platelet adhesion molecule glycoprotein IIb–IIIa [12]. Elevated MPV values were associated with an improved survival of patients with cancer [13,14]. The baseline low MPV was associated with decreased overall and progression-free survival in patients with DLBCL [15,16].

Objectives

In this study, we aimed to determine whether the pretreatment levels of LMR, NLR, LDH, and MPV were the influential factors in the stage and prognosis of DLBCL in the patients treated with either standard R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy or other treatments such as R-steroid, R-mini-CHOP, and R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin).

Patients and methods

Patients

We carried out a retrospective study with a total of 188 patients diagnosed with DLBCL and treated accordingly at Hospital, Department of Hematology and Bone Marrow Transplantation Center between January 2012 and January 2020. The ethical approval was received from local ethical committee. The patient consent was waived since it is a retrospective study. A total of 188 patients having all laboratory data and who met the following criterion were enrolled in the study: no history of former treatment, any malignancy, chronic hepatitis B or C, rheumatological disease, or immunosuppression. Patients with any acute or chronic infection at diagnosis, any hematological disease known other than lymphoma, any infectious disease-causing lymphocytosis-monocytosis, any known inflammatory disease, vasculitis, or sarcoidosis-lipid storage disease were excluded from the study. Patients were treated with standard R-CHOP chemotherapy and other treatments such as R-steroid, R-mini-CHOP, and R-EPOCH.

The study was conducted according to the principles outlined in the Declaration of Helsinki. The local ethical approval was obtained.

Data

The demographics and clinical parameters included patient age and sex; the stage of DLBCL according to Ann Arbor; pathological subtypes including germinal center B-cell (GCB) and non-GCB; ECOG status; lymphoma international prognostic index (IPI) score; systemic B symptoms; involvement of other organs; laboratory data at diagnosis, including total blood counts, MPV, and serum LDH; information about the therapies; and the treatment outcomes.

Treatments

Most of the patients were treated with R-CHOP, and radiotherapy at the extranodal site was given by physician's choice. Early-stage (I–II) patients were given 3–4 R-CHOP and patients in complete remission were given RT as consolidation. Late-stage (III–IV) patients and also early-stage patients with PR response were given six to eight cycles of R-CHOP treatment. For residual lesions after chemotherapy, RT was applied as consolidation.

Statistical analysis

IBM SPSS software (version 26, IBM Inc., Armonk, NY, USA) was used for statistical analyses. To summarize data descriptive statistics applied, the categorical data were presented as percentage and the numerical data were presented as median (minimum–maximum). The disease stages were categorized as early and late, IPI score was categorized as IPI less than 4 and IPI more than or equal to 4, and the treatment response was categorized as responders and nonresponders. Logistic regression analysis was used to assess the predictors of stage, IPI, and

treatment response. Variables with *P* value less than 0.1 were involved in the multivariate analysis. *P* values less than or equal to 0.05 were considered statistically significant.

Results

The median age of 188 patients was 62 years (range, 21–86 years). A total of 98 (52.1%) patients were male and monocities 90 (47.9%) patients were female. The median follow-up time was 11 months (range, 1–80 months). The features of the patients are represented in Table 1.

Table 1 Patient characteristics

Factors	*N*=188 [*n* (%)]
Age [median (range)]	62 (21–86)
Sex (M/F)	98/90
ECOG status (2–4)	50 (26.5)
Stages (III–IV)	124 (65.9)
IPI score (≥4)	34 (18.1)
B symptom	94 (50)
Extranodal involvement	73 (38.8)
Bone marrow involvement	11 (5.9)
Liver involvement	12 (6.4)
Spleen involvement	20 (10.6)
Pathological subtype	
GCB	61 (32.4)
Non-GCB	127 (67.6)
LDH (high)	109 (58)

ECOG, Eastern Cooperative Oncology Group; GCB, germinal center B-Cell like; IPI, lymphoma international prognostic index; LDH, lactate dehydrogenase.

Table 2 Complete blood counts

Parameters	Median (minimum–maximum)
White blood count (10^3/l)	7300 (500–20 280)
Absolute neutrophil (10^3/l)	4830 (20–16 880)
Lymphocyte (10^3/l)	1400 (220–4620)
Monocyte (10^3/l)	515 (40–4200)
MPV (fl)	8.1 (5.7–13.2)
NLR ratio	3.44 (0.06–30.57)
LMR ratio	0.35 (0.04–3.57)

LMR, Lymphocyte/monocyte ratio; MPV, Mean platelet volume; NLR, Neutrophil/lymphocyte ratio.

When the pathological subtypes were evaluated by immunochemical staining, 61 (32.4%) patients were classified as GCB subtype and 127 (67.6%) as non-GCB. Ann Arbor stage III–IV cases were found in most patients (65.9%).

Although most patients [158 (84%)] received R-CHOP-based treatments, 30 (16%) patients received other treatments such as R-steroid, R-mini-CHOP, and R-EPOCH. After the initial treatment, overall response rate was obtained in 136 (72.3.9%) patients. Blood counts at diagnosis are displayed in Table 2.

Factors influencing the stage of DLBCL were investigated by univariate and multivariate analyses (Table 3). NLR [*P*=0.009, odds ratio (OR)=1.220, 95% confidence interval (CI): 1.050–1.417] and LDH (*P*=0.001, OR=0.286, 95% CI: 0.146–0.561) were observed to be statistically significant in both analyses (Table 3).

Factors influencing the IPI score were investigated by univariate and multivariate analyses (Table 4). LMR (*P*=0.001, OR=6.226, 95% CI: 2.092–18.533) was the only factor to be found statistically significant by the multivariate analysis. Additionally, the pathological type of DLBCL almost reached a statistically significant level represented by the multivariate analysis (*P*=0.056, OR=0.365, 95% CI: 0.129–1.027).

Factors influencing the treatment response were investigated by univariate and multivariate analyses (Table 5). R-CHOP treatment (*P*=0.001, OR=0.181, 95% CI: 0.068–0.478) and the stage of DLBCL

Table 3 Influence of factors on the disease stage (early vs. late)

Factors	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Age	1.019 (0.995–1.043)	0.113		
Sex (based male)	0.741 (0.358–1.535)	0.420		
MPV	0.968 (0.735–1.276)	0.818		
NLR	1.211 (1.005–1.458)	0.044*	1.220 (1.050–1.417)	0.009*
LMR	1.317 (0.332–5.222)	0.696		
Pathological type (based GCB)	0.734 (0.360–1.495)	0.394		
LDH (based normal)	0.334 (0.165–0.675)	0.002*	0.286 (0.146–0.561)	0.000*
Constant	0.768	0.860	1.564	0.238

CI, confidence interval; GCB, germinal center B-cell like; LDH, lactate dehydrogenase; LMR, lymphocyte/monocyte ratio; MPV, mean platelet volume; NLR, neutrophil/lymphocyte ratio.
Estimated by logistic regression, Nagelkerke R^2=0.249, *P* value less than or equal to 0.05 was considered statistically significant. Variables with *P* value less than 0.1 were included for multivariate analysis; *statistically significance $P < 0.05$.

Table 4 Influence of factors on lymphoma international prognostic index score (international prognostic index < 4 vs. international prognostic index ≥4)

Factors	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Sex (based male)	0.540 (0.229–1.277)	0.161		
MPV	0.760 (0.550–1.050)	0.096	0.779 (0.569–1.067)	0.120
NLR	1.092 (0.960–1.241)	0.181		
LMR	3.209 (0.874–11.785)	0.079	6.226 (2.092–18.533)	0.001*
Pathological type	0.408 (0.142–1.168)	0.095	0.365 (0.129–1.027)	0.056
Constant	1.210	0.888	0.846	0.895

CI, confidence interval; GCB, germinal center B-cell like; LMR, lymphocyte/monocyte ratio; MPV, mean platelet volume; NLR, neutrophil/lymphocyte ratio.
Estimated by logistic regression, Nagelkerke R^2=0.242, *P* value less than or equal to 0.05 was considered statistically significant. Variables with *P* value less than 0.1 were included for multivariate analysis; *statistically significance $P < 0.05$.

Table 5 Influence of factors on treatment response (responders vs. nonresponders)

Factors	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Age	1.025 (0.989–1.062)	0.182		
Sex (based male)	0.682 (0.241–1.930)	0.471		
MPV	1.145 (0.789–1.661)	0.476		
NLR	1.043 (0.882–1.232)	0.624		
LMR	1.323 (0.179–9.761)	0.784		
Pathological type	1.190 (0.396–3.577)	0.757		
LDH (based normal)	2.629 (0.762–9.068)	0.126		
R-CHOP (based non-R-CHOP)	0.124 (0.034–0.455)	0.002*	0.181 (0.068–0.478)	0.001*
IPI score≥4	2.640 (0.803–8.687)	0.110		
Stage (based on early)	10.995 (1.342–90.051)	0.025*	18.306 (2.383–140.607)	0.005*
Constant	0.119	0.345		

CI, confidence interval; GCB, germinal center B-cell like; IPI, lymphoma international prognostic index; LDH, lactate dehydrogenase; LMR, lymphocyte/monocyte ratio; MPV, mean platelet volume; NLR, neutrophil/lymphocyte ratio.
Estimated by logistic regression, Nagelkerke R^2=0.352, *P* value less than or equal to 0.05 was considered statistically significant. Variables with *P* value less than 0.1 were included for multivariate analysis; *statistically significance $P < 0.05$.

categorized as early and late (*P*=0.005, OR=18.306, 95% CI: 2.383–140.607) were statistically significant represented by the multivariate analysis (Table 5).

MPV was not an influencing factor for all outcomes, that is, for the stage of DLBCL (*P*=0.818, OR=0.968, 95% CI: 0.735–1.276), for the IPI score (*P*=0.096, OR=0.760, 95% CI: 0.550–1050), and for the treatment response (*P*=0.476, OR=1.145, 95% CI: 0.789–1.661).

Discussion

The measurements of LMR, NLR, LDH, and MPV are easily performed in the clinics and are inexpensive biomarkers that can be determined in blood using widely available standard techniques. The ratios of cell counts can be a simple component that provides extra information in the prognosis and progression of cancers and posttreatment responses especially in aggressive one. The combination of different prognostic factors may help to distinguish the posttreatment responses better among various cancer therapies [17]. However, there is a lack of information about the clinical value of LMR, NLR, LDH, and MPV to implement in predicting the prognosis of DLBCL. Therefore, in the present study, we state that the pretreatment values of LMR, NLR, LDH, and MPV were effective factors in the stage and prognosis of DLBCL in the patients treated with either a standard R-CHOP chemotherapy or other treatments including R-steroid, R-mini-CHOP, and R-EPOCH.

There are several biomarkers including LDH that appear to show a prognostic effect on the lymphoma at both diagnosis and relapse; however, none of them are currently ideal markers to be useful in the prognosis of disease. Reports have examined the dominance of these markers in diagnosis and prognosis of disease in various cohorts of patients [18–20]. One of these studies showed that elevated LDH in patients with DLBCL is one of the independent predictors of OS [20]. They also reported that the patients with higher NLR had an advanced disease stage, with B symptoms, and had significantly poorer ECOG status, higher LDH, greater IPI, and more extranodal sites of disease at diagnosis. In a multivariate analysis, higher LDH

was determined as an independent predictor of the outcome of standard therapy and probably relative contraindications with salvage therapy of patients with DLBCL [21]. In the present study, LDH with NLR were found as the factors influencing the stage of DLBCL.

NLR is an easily measurable index, but it has not been well known what is the underlying mechanism of the poor prognosis of patients with cancer who have higher NLRs. NLR might be a good index that indicates the balance between immunoreaction and inflammation in cancer. NLR has been determined to be a prognostic tool in patients with DLBCL, associated with worse survival [8,9,20]. A meta-analysis including the outcomes of Asian countries demonstrated that NLR was associated with a poor OS and also a worse progression-free survival [9]. Another study by Azuma *et al.* [7] showed that patients with an NLR of less than or equal to 5.2 were prone to have a better prognosis for both OS and progression-free survival. However, their study could not define the predictive value of NLR. In the present study, NLR with LDH may be factors influencing the stage of DLBCL but not the prognosis indicated by IPS score, suggesting that NLR may be challenging to reflect the prognosis of DLBCL as the innate immunity of host has been damaged and the number tumor-infiltrating lymphocytes may be reduced in these patients.

LMR can indicate the balance between the host immunity and tumor microenvironment. Low LMR at diagnosis is suggested to be correlated with a more advanced nature of disease or with a poorer tolerance to the cancer treatment. LMR has been determined as an effective prognostic factor of the clinical findings of patients with DLBCL [6]. Recently, Lee *et al.* [17] reported a strong correlation between the baseline LMR and survival outcomes and suggested LMR to be a better prognostic biomarker in Hodgkin lymphoma. On the contrary, the ratio of absolute lymphocyte/absolute monocyte count (ALC/AMC ratio) in the peripheral blood at diagnosis was reported as an independent prognostic factor in DLBCL [22], and the cutoff values of ALC/AMC were calculated between 1.1 and 3.8 [6,23,24]. We found LMR is the only factor influencing the IPI score, suggesting it to be effective in the prognosis of DLBCL. The absolute monocyte and lymphocyte levels may differ between populations, even in the same patient before and after treatment. Therefore, the combined standard value of LMR for the prognosis of patients with DLBCL may need further assessment in an independent cohort including many samples in advance trials.

MPV is a commonly used laboratory tool that is associated with platelet function including the platelet reactivity [25]. The platelets have been revealed to affect the metastasis and progression of several cancers [26,27]. There are contradictory data about the predictive values of MPV in prognosis and progression of different cancers [15,28,29]. Zhou *et al.* [15] retrospectively analyzed 161 patients with DLBCL who were treated with R-CHOP or R-CHOP-like chemotherapy and found that the patients with MPV less than or equal to 9.1 fl experienced a shorter progression-free and OS, compared with those with MPV more than 9.1 fl. They also reported that MPV less than or equal to 9.1 fl was an independent prognostic factor of overall and progression-free survival in DLBCL. The present study implied no effect of MPV on the stage, prognosis, and treatment response of patients with DLBCL, which oppose the findings of previous studies [15,16].

The limitations of retrospective analysis in the present study are the recruitment of data from a single institution, which might have presented another limitation on the primary and secondary outcomes resulting in a possibly limited external validity. Another limiting factor of the present study is the relatively small sample size, which may limit the power of final outcomes. Another limitation of the study is the lack of a receiver operating characteristic analysis to show the predictive value of NLR, LMR, and MPV.

Conclusion

We found that the pretreatment values of NLR, LDH, and LMR may affect the stage and prognosis of DLBCL, which showed influences on the treatment response, but we were not able to demonstrate any effect of MPV on these outcomes. As available parameters that are easily determined in routine blood analysis, the prognostic values of NLR, LDH, and LMR in the stage and prognosis of disease may be considered during the treatment of DLBCL. However, the underlying mechanisms about the exact role of LDH, lymphocytes, and monocytes on the posttreatment response in patients with DLBCL are not well known yet. This needs further studies to explain the exact underlying mechanisms through which the immune and inflammatory cells affect the prognosis of patients with DLBCL.

Financial support and sponsorship

Nil.

Conflicts of interest

We have no conflict of interest.

References

1 Sabattini E, Bacci F, Sagramoso C, Pileri SA. WHO classification of tumours of haematopoietic and lymphoid tissues in 2008: an overview. *Pathologica* 2010; **102**:83–87.

2 Habermann TM. New developments in the management of diffuse large B-cell lymphoma. *Hematology* 2012; **17**(Suppl 1):S93–S97.

3 Pfreundschuh M, Trümper L, Osterborg A, Pettengell R, Trneny M, Imrie K, *et al*. MabThera International Trial Group. CHOP-like chemotherapy plus rituximab versus CHOP-like chemotherapy alone in young patients with good-prognosis diffuse large-B-cell lymphoma: a randomised controlled trial by the MabThera International Trial (MInT) Group. *Lancet Oncol* 2006; **7**:379–391.

4 González-Barca E, Boumendil A, Blaise D, Trněný M, Masszi T, Finel H, *et al*. Outcome in patients with diffuse large B-cell lymphoma who relapse after autologous stem cell transplantation and receive active therapy. A retrospective analysis of the Lymphoma Working Party of the European Society for Blood and Marrow Transplantation (EBMT). *Bone Marrow Transplant* 2020; **55**:393–399.

5 Zhou Z, Sehn LH, Rademaker AW, Gordon LI, Lacasce AS, Crosby-Thompson A, *et al*. An enhanced International Prognostic Index (NCCN-IPI) for patients with diffuse large B-cell lymphoma treated in the rituximab era. *Blood* 2014; **123**:837–842.

6 Zhao P, Zang L, Zhang X, Chen Y, Yang H, Zhao H, *et al*. The lymphocyte-monocyte ratio and the platelet-lymphocyte ratio at diagnosis as independent prognostic factors in primary gastrointestinal diffuse large B Cell lymphoma. *Indian J Hematol Blood Transfus* 2017; **33**:333–341.

7 Azuma Y, Nakaya A, Fujita S, Satake A, Nakanishi T, Tsubokura Y, *et al*. Neutrophil-to-lymphocyte ratio (NLR) fails to predict outcome of diffuse large B cell lymphoma. *Leuk Res Rep* 2019; **12**:100173.

8 Ni J, Wang YQ, Zhang YP, Wu W, Zeng QS, Yang MZ, *et al*. Value of neutrophil/lymphocyte ratio and platelet/lymphocyte ratio for prognostic evaluation of diffuse large B-cell lymphoma. *Zhongguo Shi Yan Xue Ye Xue Za Zhi* 2016; **24**:427–432.

9 Wang J, Zhou X, Liu Y, Li Z, Li X. Prognostic significance of neutrophil-to-lymphocyte ratio in diffuse large B-cell lymphoma: a meta-analysis. *PLoS ONE* 2017; **12**:e0176008.

10 Mu S, Ai L, Fan F, Qin Y, Sun C, Hu Y. Prognostic role of neutrophil-to-lymphocyte ratio in diffuse large B cell lymphoma patients: an updated dose-response meta-analysis. *Cancer Cell Int* 2018; **18**:119.

11 Markovic O, Popovic L, Marisavljevic D, Jovanovic D, Filipovic B, Stanisavljevic D, *et al*. Comparison of prognostic impact of absolute lymphocyte count, absolute monocyte count, absolute lymphocyte count/absolute monocyte count prognostic score and ratio in patients with diffuse large B cell lymphoma. *Eur J Intern Med* 2014; **25**:296–302.

12 Giles H, Smith RE, Martin JF. Platelet glycoprotein IIb-IIIa and size are increased in acute myocardial infarction. *Eur J Clin Invest* 1994; **24**: 69–72.

13 Riedl J, Kaider A, Reitter EM, Marosi C, Jäger U, Schwarzinger I, *et al*. Association of mean platelet volume with risk of venous thromboembolism and mortality in patients with cancer. Results from the Vienna Cancer and Thrombosis Study (CATS). *Thromb Haemost* 2014; **111**:670–678.

14 Zhuang Q, Xiang L, Xu H, Fang F, Xing C, Liang B, *et al*. The independent association of mean platelet volume with overall survival in multiple myeloma. *Oncotarget* 2016; **7**:62640–62646.

15 Zhou S, Ma Y, Shi Y, Tang L, Zheng Z, Fang F, *et al*.. Mean platelet volume predicts prognosis in patients with diffuse large B-cell lymphoma. *Hematol Oncol* 2018; **36**:104–109.

16 Rupa-Matysek J, Gil L, Kroll-Balcerzak R, Barańska M, Komarnicki M. Mean platelet volume as a predictive marker for venous thromboembolism and mortality in patients treated for diffuse large B-cell lymphoma. *Hematol Oncol* 2017; **35**:456–464.

17 Lee SF, Ng TY, Spika D. Prognostic value of lymphocyte-monocyte ratio at diagnosis in Hodgkin lymphoma: a meta-analysis. *BMC Cancer* 2019; **19**:338.

18 El-Sharkawi D, Basu S, Ocampo C, Qian W, D'Sa S, Hoskin PJ, *et al*. Elevated lactate dehydrogenase levels detected during routine follow-up do not predict relapse in patients with diffuse large B-cell lymphoma who achieve complete remission after primary treatment with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone-like immunochemotherapy. *Leuk Lymphoma* 2012; **53**:1949–1952.

19 Wakao D, Murohashi I, Tominaga K, Yoshida K, Kishimoto K, Yagasaki F, *et al*. Serum thymidine kinase and soluble interleukin-2 receptor predict recurrence of malignant lymphoma. *Ann Hematol* 2002; **81**:140–146.

20 Wang S, Ma Y, Sun L, Shi Y, Jiang S, Yu K, *et al*. Prognostic significance of pretreatment neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in patients with diffuse large B-Cell lymphoma. *Biomed Res Int* 2018; **2018**:9651254.

21 Lekakis LJ, Moskowitz CH. The role of autologous stem cell transplantation in the treatment of diffuse large b-cell lymphoma in the era of CAR-T cell therapy. *Hemasphere* 2019; **3**:e295.

22 Li ZM, Huang JJ, Xia Y, Sun J, Huang Y, Wang Y, Zhu YJ, *et al*. Blood lymphocyte-to-monocyte ratio identifies high-risk patients in diffuse large B-cell lymphoma treated with R-CHOP. *PLoS ONE* 2012; **7**:e41658.

23 Porrata LF, Ristow K, Colgan JP, Habermann TM, Witzig TE, Inwards DJ, *et al*. Peripheral blood lymphocyte/monocyte ratio at diagnosis and survival in classical Hodgkin's lymphoma. *Haematologica* 2012; **97**: 262–269.

24 Li YL, Pan YY, Jiao Y, Ning J, Fan YG, Zhai ZM. Peripheral blood lymphocyte/monocyte ratio predicts outcome for patients with diffuse large B cell lymphoma after standard first-line regimens. *Ann Hematol* 2014; **93**:617–626.

25 Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Des* 2011; **17**:47–58.

26 Lian L, Xia YY, Zhou C, Shen XM, Li XL, Han SG, *et al*. Mean platelet volume predicts chemotherapy response and prognosis in patients with unresectable gastric cancer. *Oncol Lett* 2015; **10**:3419–3424.

27 Nash GF, Turner LF, Scully MF, Kakkar AK. Platelets and cancer. *Lancet Oncol* 2002; **3**:425–430.

28 Zhang W, Dang S, Hong T, Tang J, Fan J, Bu D, *et al*. A humanized single-chain antibody against beta 3 integrin inhibits pulmonary metastasis by preferentially fragmenting activated platelets in the tumor microenvironment. *Blood* 2012; **120**:2889–2898.

29 Mutlu H, Artis TA, Erden A, Akca Z. Alteration in mean platelet volume and platicrit values in patients with cancer that developed thrombosis. *Clin Appl Thromb Hemost* 2013; **19**:331–333.