The Lymphocyte–Monocyte Ratio and the Platelet–Lymphocyte Ratio at Diagnosis as Independent Prognostic Factors in Primary Gastrointestinal Diffuse Large B Cell Lymphoma

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Abstract To study the role of the absolute lymphocyte count (ALC), absolute monocyte count (AMC), platelet count (PLT), lymphocyte–monocyte ratio (LMR) and the platelet–lymphocyte ratio (PLR) in the prognosis of primary gastrointestinal diffuse large B cell lymphoma (PGI-DLBCL). We retrospectively analyzed the prognostic value of the ALC, AMC, PLT, LMR, PLR at diagnosis in 173 PGI-DLBCL patients through histopathological examination from March 2009 to February 2015. In total, 173 patients with histopathological diagnosis of PGI-DLBCL in this study, the median age was 51 years (range 12–90 years), median follow-up time was 44 months (range 7–89 months). In univariate analysis, age <60 years, B symptoms, Lugano stage I–II, low international prognostic index (IPI) or low age-adjusted international prognostic index (aaIPI), normal lactate dehydrogenase (LDH), normal β 2-microglobulin (β 2m), $Hb \geq 11$ g/dL, $ALC \geq 1.5 \times 10^9/L$, $AMC \leq 0.50 \times 10^9/L$, $LMR \geq 2.5$, $PLR \leq 170$ were related with superior overall survival (OS) and progression-free survival (PFS) ($p \leq 0.05$). Multivariate analysis suggested that ALC, LMR, LDH were related with PFS ($p \leq 0.05$). Similarly, age and LMR were related with OS ($p \leq 0.05$). The parameters (ALC, AMC, LMR, PLR) may be valuable prognostic factors in PGI-DLBCL patients. LMR, PLR at diagnosis are expected to be independent prognostic factors for PGI-DLBCL patients.

Keywords Primary gastrointestinal diffuse large B-cell lymphoma · The lymphocyte–monocyte ratio · The platelet–lymphocyte ratio · Inflammatory · Prognosis

Introduction

Primary gastrointestinal non Hodgkin's lymphoma (PGI-NHL) represents the most common types of extranodal lymphoma and DLBCL is the most frequent histologic type. PGI-DLBCL is a relatively rare disease, accounting for only 1–4 % of those with gastrointestinal malignancies. The most frequent site is stomach followed by small intestine and ileocecal region [1–3]. Endoscopic examination combined with pathological biopsy is still the most important and reliable method for detection of PGI-DLBCL. Nowadays, there is still no consensus on its treatment, the majority of patients were treated with combined therapy (chemotherapy and radiotherapy, surgery plus chemotherapy, surgery plus chemotherapy, and radiotherapy). The majority of chemotherapeutic protocols was CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone)-like regimens and/without rituximab [4–6]. Immunodeficiency is considered to be one of the most dangerous factors in NHL, with a greater risk of developing lymphoma with congenital or acquired immunodeficiency. Gene expression profiling (GEP) have provided crucial information as to the intrinsic heterogeneity of lymphoma cells and the role of the tumor microenvironment. The prognostic model based on gene expression in DLBCL indicates that the prognosis of patients not only dependent on the clinical parameters, but also on the gene regulation of tumor microenvironment [7, 8]. However, many of these risk factors are costly, difficult to perform and not easily interpreted. Therefore, prognostic models for PGI-DLBCL

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that are inexpensive, widely available and easily interpreted by clinicians are needed [9]. Lymphocyte is the main component of immune cells, which has important anti-tumor effect. It reflects both the immune status of the host and the degree of tumor progression. The systemic inflammation has been recognized as correlating with tumor progression and inflammatory markers have been reported to be useful for predicting the tumor prognosis. The monocytes and platelet are inflammatory markers [4, 10, 11]. Previous studies [7–11] showed that ALC, AMC, PLT, LMR and PLR were prognostic factors for many malignancies. In another study, we found that the LMR could be an efficient prognostic factor for these newly-diagnosed MM patients with extramedullary invasion. However, there are limited data by now to demonstrate their usefulness for PGI-DLBCL. The aim of this study was to determine whether ALC, AMC, PLT, LMR and PLR were prognostic factors for PGI-DLBCL.

Patients and Methods

Patients

We carried out a retrospective study of 173 patients with PGI-DCBCL diagnosed at Tianjin Medical University Cancer Institute and Hospital in March 2009–February 2015. All patients met the following criteria: no previous treatment, no previous history of malignancy, or immunosuppression. There were 111 males and 62 females. The median age was 51 years (range 12–90 years), median follow-up time was 44 months (range 7–89 months). Clinical parameters included patient age, gender, primary site, GCB or nGCB, systemic B symptoms, Lugano stage, IPI, Hb, ALC, AMC, PLT, LDH, β 2m, surgery or not. Definitions of response criteria, overall survival, progression-free survival, and time to progression were based on the guidelines from the International Harmonization Project on Lymphoma. OS was defined as the time from diagnosis of PGI-DLBCL to death from any cause. PFS was defined as time from diagnosis to lymphoma relapse, progression or death of any cause.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows (Version 17.0). The time-dependent receiver operating characteristic (ROC) curve analysis was used to determine the best cut-off value of preoperative ALC, AMC, LMR, PLR. Survival was analyzed by the Kaplan–Meier and compared by different groups using the log-rank test and the Cox proportional hazards model. $p < 0.05$ was considered statistically significant.

Results

Selection of the Best Cut-Off Value of ALC, AMC, LMR, PLR for PGI-DCBCL Patients

The cutoff points of ALC, AMC, LMR and PLR were selected by the receiver operating characteristics curves analysis. The best cutoff value of ALC was $1.5 \times 10^9/L$, with an area under the curve (AUC) value of 0.663 (95 % CI 0.578–0.748, $p < 0.001$) (Fig. 1a). The most discriminative cutoff value of AMC was $0.5 \times 10^9/L$, with an AUC value of 0.629 (95 % CI 0.543–0.715, $p = 0.004$) (Fig. 1b). ROC curve analysis in 173 patients established 2.5 as the cutoff point of LMR with an AUC of 0.718 (95 % CI 0.638–0.799, $p < 0.001$) (Fig. 1c) and established 170 as the cutoff point of PLR with an AUC of 0.590 (95 % CI 0.500–0.679, $p = 0.004$) (Fig. 1d).

In Univariate Analysis: Prognostic Significance of Clinical Parameters

We retrospectively analyzed the prognostic significance of all parameters in 173 patients. We found that patients with an

Fig. 1 Receiver operating characteristic curve (ROC) and area under the curve (AUC) for the ALC (a), AMC (b), LMR (c) and PLR (d) at diagnosis. Abbreviations: ALC absolute lymphocyte count, AMC absolute monocyte count, LMR absolute lymphocyte count/absolute monocyte count ratio, PLR platelet count/lymphocyte count ratio, CI confidence interval

Fig. 2 Kaplan-Meier curve of overall survival and PFS according to: **a, b** ALC; **c, d** AMC; **e, f** LMR; **g, h** PLR

Table 1 In univariate analysis: Prognostic Significance of clinical parameters

Characteristics	Classification	N = 173	5OS (%)	<i>p</i> value	5PFS (%)	<i>p</i> value
Sex	Male	111	56.8	0.128	51.4	0.300
	Female	62	66.1		58.1	
Age	<60 years	105	68.9	<0.001	60.0	0.005
	≥60 years	68	47.1		44.1	
Primary site	Stomach	101	64.4	0.437	58.4	0.351
	Ileocecal	16	62.5		56.3	
	Small intestine	33	57.6		48.5	
	Colorectal	23	43.5		9.1	
B symptoms	No	103	65.0	0.040	60.2	0.011
	Yes	70	52.9		44.3	
Lugano stage	I–II stage	110	71.8	<0.001	64.5	<0.001
	III–IV stage	63	39.7		34.9	
Immune subtype	GCB	64	65.6	0.452	62.5	0.107
	nGCB	109	56.9		48.6	
IPI	≤2 score	124	73.4	<0.001	66.9	<0.001
	>2 score	49	26.5		20.4	
Hb	>11 g/dL	118	66.9	0.009	61.0	0.004
	≤11 g/dL	55	45.5		38.2	
ALC	≥ $1.5 \times 10^9/L$	87	73.6	<0.001	67.8	<0.001
	< $1.5 \times 10^9/L$	86	46.5		39.5	
AMC	≤ $0.5 \times 10^9/L$	93	69.9	0.013	63.4	0.011
	> $0.5 \times 10^9/L$	80	48.8		42.5	
PLT	≤ $250 \times 10^9/L$	71	56.3	0.323	50.7	0.353
	> $250 \times 10^9/L$	102	62.7		55.9	
LMR	≥2.5	115	73.0	<0.001	67.8	<0.001
	<2.5	58	34.5		25.9	
PLR	≤170	80	68.8	0.011	68.4	0.008
	>170	93	52.7		43.2	
LDH	≤240	107	72.0	<0.001	68.2	<0.001
	>240	66	40.9		30.3	
β2m	≤2.6	97	77.3	<0.001	71.1	<0.001
	>2.6	76	38.2		31.6	
Surgery	No	58	51.7	0.012	44.8	0.008
	Yes	115	64.3		58.3	

IPI international prognostic index, *Hb* hemoglobin, *ALC* the absolute lymphocyte count, *AMC* absolute monocyte count, *PLT* platelet count, *LMR* lymphocyte–monocyte ratio, *PLR* platelet–lymphocyte ratio, *LDH* lactate dehydrogenase, *β2m* β 2-microglobulin, *OS* overall survival, *PFS* progression-free survival

ALC < $1.5 \times 10^9/L$ had a significantly lower 5-year OS (46.5 vs 73.5 %, $p < 0.001$) (Fig. 2a) and PFS (39.5 vs 67.8 %, $p < 0.001$) (Fig. 2b). Patients with an AMC > $0.5 \times 10^9/L$ had a significantly lower 5-year OS (48.8 vs 69.9 %, $p = 0.013$) (Fig. 2c) and PFS (42.5 vs 63.4 %, $p = 0.011$) (Fig. 2d). The estimated 5-year OS and PFS in the patients with LMR < 2.5 and LMR ≥ 2.5 were 34.5 versus 73.0 % ($p < 0.001$) (Fig. 2e) and 25.9 versus 67.8 % ($p < 0.001$) (Fig. 2f). The estimated 5-year OS and PFS in the patients with PLR > 170 and PLR ≤ 170 were 52.7 versus 68.8 % ($p = 0.012$) (Fig. 2g) and 45.7 versus 63.3 % ($p = 0.005$) (Fig. 2h). On univariate analysis, both

the OS and PFS outcomes were associated with age >60 years, systemic B symptoms, stage III–IV, Hb ≤ 11 g/dL, IPI > 2 score, high LDH, high β2m, no surgery. However, gender, primary site, PLT and immune subtype are in no way associated with the OS and PFS outcome (Table 1).

Relationship Between ALC, AMC, LMR, PLR and Other Prognostic Factors

The clinical features of the patients with an ALC ≥ $1.5 \times 10^9/L$ and those with an ALC < $1.5 \times 10^9/L$ are summarized in Table 2. Eighty-seven patients (50.3 %) were

Table 2 Patient characteristics according to the ALC $\geq 1.5 \times 10^9/L$ versus $<1.5 \times 10^9/L$

Characteristics	Classification	ALC $\geq 1.5 \times 10^9/L$	ALC $< 1.5 \times 10^9/L$	<i>p</i> value
Sex	Male	51 (58.6 %)	60 (69.8 %)	0.154
	Female	36 (41.4 %)	26 (30.2 %)	
Age	<60 years	55 (63.2 %)	50 (58.1 %)	0.535
	≥ 60 years	32 (36.8 %)	36 (41.9 %)	
Primary	Stomach	55 (63.2 %)	46 (53.5 %)	0.405
	Ileoceca	6 (6.9 %)	10 (11.6 %)	
	Small intestine	17 (19.5 %)	16 (18.6 %)	
	Colorectal	9 (10.3 %)	14 (16.3 %)	
B symptoms	No	60 (69.0 %)	43 (50.0 %)	0.013
	Yes	27 (31.0 %)	43 (50.0 %)	
Lugano stage	I–II stage	59 (67.8 %)	51 (59.3 %)	0.271
	III–IV stage	28 (32.2 %)	35 (40.7 %)	
IPI	≤ 2 score	69 (79.3 %)	55 (64.0 %)	0.029
	> 2 score	18 (20.7 %)	31 (36.0 %)	
Immune subtype	GCB	32 (36.8 %)	32 (37.2 %)	1.000
	nGCB	55 (63.2 %)	54 (62.8 %)	
Hb	> 11 g/dL	69 (79.3 %)	49 (57.0 %)	0.002
	≤ 11 g/dL	18 (20.7 %)	37 (43.0 %)	
LDH	≤ 240	64 (73.6 %)	43 (50.0 %)	0.002
	> 240	23 (26.4 %)	43 (50.0 %)	
$\beta 2m$	≤ 2.6	55 (63.2 %)	42 (48.8 %)	0.067
	> 2.6	32 (36.8 %)	44 (51.2 %)	
Surgery	No	28 (32.2 %)	30 (34.9 %)	0.749
	Yes	59 (67.8 %)	56 (65.1 %)	

IPI international prognostic index, *Hb* hemoglobin, *ALC* the absolute lymphocyte count, *LDH* lactate dehydrogenase, $\beta 2m$ β 2-microglobulin

had an ALC $\geq 1.5 \times 10^9/L$ and 86 patients (49.7 %) had an ALC $< 1.5 \times 10^9/L$. ALC was significantly correlated with the presence of B symptoms, IPI > 2 , Hb ≤ 11 g/dL, a higher LDH ($p < 0.05$). But not significantly associated with age, primary site, sex, Lugano stage, immune subtype, $\beta 2m$, surgery ($p > 0.05$). Ninety-three patients (53.76 %) had an AMC $\leq 0.5 \times 10^9/L$ and 80 patients (46.24 %) had an AMC $> 0.5 \times 10^9/L$. We found a significantly difference between the patients with AMC $\leq 0.5 \times 10^9/L$ and $> 0.5 \times 10^9/L$ regarding male, IPI, $\beta 2m$ ($p < 0.05$), but not regarding age, primary site, sex, B symptoms, Lugano stage, immune subtype, LDH, Hb, surgery ($p > 0.05$). The clinical features of the patients with an LMR ≥ 2.5 and those with an LMR < 2.5 are summarized in Table 3. One hundred and fifteen patients (66.7 %) had an LMR ≥ 2.5 and 58 patients (33.53 %) had an LMR < 2.5 . LMR was significantly correlated with the presence of B symptoms, a higher $\beta 2m$, a higher LDH ($p < 0.05$). But not significantly associated with age, primary site, sex, Lugano stage, immune subtype, Hb, $\beta 2m$, surgery ($p > 0.05$). The clinical features of the patients with an PLR ≤ 170 and those with an PLR > 170 are summarized in Table 4. Seventy-nine patients (45.7 %) had an PLR ≤ 170 and 94 patients (54.3 %) had an PLR > 170 .

We found a significantly difference between the patients with PLR ≤ 170 and > 170 regarding the presence of B symptoms, IPI, Lugano stage, Hb ≤ 11 g/dL, $\beta 2m$, LDH ($p < 0.05$), but not significantly related with age, primary site, sex, immune subtype, surgery ($p > 0.05$).

Multivariate Analysis for OS and PFS Outcomes

We used Cox Regression analysis to evaluate the prognostic impact of LMR at diagnosis on the survival of PGI-DLBCL patients. Parameters included in the multivariate survival analysis are shown in Table 5. This study showed that LMR was identified as an independent prognostic factor for OS and PFS. Age was shown to be independent prognostic factors for OS, while LDH, ALC were independent risk factors for PFS.

Discussion

Primary gastrointestinal diffuse large B-cell lymphoma is the most common extranodal site involved by diffuse large B-cell lymphoma [12]. The international prognostic index

Table 3 Patient characteristics according to the LMR ≥ 2.5 versus <2.5

Characteristics	Classification	LMR ≥ 2.5	LMR < 2.5	<i>p</i> value
Sex	Male	67 (58.3 %)	44 (75.9 %)	0.065
	Female	48 (41.7 %)	14 (24.1 %)	
Age	<60 years	69 (60.0 %)	36 (62.1 %)	0.711
	≥ 60 years	46 (40.0 %)	22 (37.9 %)	
Primary site	Stomach	77 (67.0 %)	24 (41.4 %)	0.064
	Ileocecal	8 (7.0 %)	8 (13.8 %)	
	Small intestine	18 (15.7 %)	15 (25.9 %)	
	Colorectal	12 (10.4 %)	11 (18.9 %)	
B symptoms	No	78 (67.8 %)	25 (43.1 %)	0.005
	Yes	37 (32.2 %)	33 (56.9 %)	
Lugano stage	I–II stage	78 (67.8 %)	32 (55.2 %)	0.135
	III–IV stage	37 (32.2 %)	26 (44.8 %)	
IPI	≤ 2 score	88 (76.5 %)	36 (62.1 %)	0.052
	> 2 score	27 (23.5 %)	22 (37.9 %)	
Immune subtype	GCB	43 (37.4 %)	21 (36.2 %)	0.742
	nGCB	72 (62.6 %)	37 (63.8 %)	
Hb	> 11 g/dL	83 (72.2 %)	35 (63.8 %)	0.199
	≤ 11 g/dL	32 (27.8 %)	23 (39.7 %)	
LDH	≤ 240	81 (70.4 %)	26 (44.8 %)	0.003
	> 240	34 (29.6 %)	32 (55.2 %)	
$\beta 2m$	≤ 2.6	78 (67.8 %)	19 (32.8 %)	< 0.001
	> 2.6	37 (32.2 %)	39 (67.2 %)	
Surgery	No	34 (29.6 %)	24 (41.4 %)	0.202
	Yes	81 (70.4 %)	34 (58.6 %)	

IPI international prognostic index, *Hb* hemoglobin, *LMR* lymphocyte–monocyte ratio, *LDH* lactate dehydrogenase, $\beta 2m$ β 2-microglobulin

(IPI) developed for DLBCL is, at present, the most valuable and widely used for the stratification of almost all subtypes of NHL. Because of ignoring the host adaptive immunity and tumor microenvironment which play an important role in the pathogenesis of lymphoma, the guidance mode cannot really distinguish high-risk populations with the use of rituximab. Gene expression profiling studies in NHL, shows that gene expression by tumor-infiltrating lymphocytes and myeloid-derived cells can predict clinical outcomes [9, 13, 14]. Therefore, these findings give us evidence that peripheral lymphocyte counts and monocyte counts, which were biomarkers of host immunity and the tumor microenvironment, can predict the prognosis of patients. Our study showed that the correlations of ALC, AMC, LMR and PLR levels with the prognosis of PGI-DLBCL.

A total of 173 patients in this study, We found that lower ALC and LMR, higher AMC and PLR were indicators of poor prognosis.

Lymphocytes act as basic components of the immune system. Reducing lymphocytes in the blood and in the tumor stroma lead to a down regulation of the immune

response against the tumor. Lymphopenia before initiation of systemic treatment was noted to be a negative of clinical outcome in solid malignancies as well as in hematological malignancies [7, 15]. The important contribution of T and NK cells in immune surveillance, illustrated by occurrence of post-transplant lymphoproliferative disease and HIV-associated lymphomas. Lymphocytopenia was found to be a strong negative prognostic marker which correlated strongly with the disease burden, patients' fitness and overall outcome. Thus, lymphopenia is considered as a sign of the host immune deficiency [16]. In our study, the univariate analysis of prognostic parameters showed that ALC was significantly associated with OS and PFS. In multivariate analysis, ALC was related with PFS, but not associated with the OS.

Monocyte, which is an important source of soluble mediators, plays an important role in suppress adaptive immunity and promotes angiogenesis, invasion, migration, and tumor growth [17, 18]. In addition, monocyte-derived cells may also provide nutrition factors that directly promote the growth and survival of malignant lymphocytes. Peripheral blood monocytes and their progeny within the

Table 4 Patient characteristics according to the PLR $\leq$ 170 versus >170

Characteristics	Classification	PLR $\leq$ 170	PLR $>$ 170	<i>p</i> value
Sex	Male	45 (57.0 %)	66 (70.2 %)	0.081
	Female	34 (43.0 %)	28 (29.8 %)	
Age	<60 years	44 (55.7 %)	61 (64.9 %)	0.274
	≥ 60 years	35 (44.3 %)	33 (35.1 %)	
Primary site	Stomach	44 (67.1 %)	48 (51.1 %)	0.189
	Ileocecal	5 (6.3 %)	11 (11.7 %)	
	Small intestine	12 (15.2 %)	21 (22.3 %)	
B symptoms	Colorectal	9 (11.4 %)	14 (14.9 %)	0.019
	No	55 (69.6 %)	48 (51.1 %)	
	Yes	24 (30.4 %)	46 (48.9 %)	
Lugano stage	I–II stage	56 (70.9 %)	54 (57.4 %)	0.081
	III–IV stage	23 (29.1 %)	40 (42.6 %)	
IPI	≤ 2 score	64 (81.0 %)	60 (63.8 %)	0.017
	>2 score	15 (19.0 %)	34 (36.2 %)	
Immune subtype	GCB	27 (34.2 %)	37 (39.4 %)	0.529
	nGCB	52 (65.8 %)	57 (60.6 %)	
Hb	>11 g/dL	65 (82.3 %)	53 (56.4 %)	<0.001
	≤ 11 g/dL	14 (17.7 %)	41 (43.6 %)	
LDH	≤ 240	56 (70.9 %)	51 (54.3 %)	0.028
	>240	23 (29.1 %)	43 (45.7 %)	
$\beta 2m$	≤ 2.6	52 (65.8 %)	45 (47.9 %)	0.021
	>2.6	27 (34.2 %)	49 (52.1 %)	
Surgery	No	26 (32.9 %)	32 (34.0 %)	1.000
	Yes	53 (67.1 %)	62 (66.0 %)	

IPI international prognostic index, *Hb* hemoglobin, *PLR* platelet–lymphocyte ratio, *LDH* lactate dehydrogenase, $\beta 2m$ β 2-microglobulin

Table 5 Multivariate analysis of prognostic factors for survival in testing set

Characteristics	<i>p</i> value (OS)	HR (95 % CI)	<i>p</i> value (PFS)	HR (95 % CI)
Age	0.014	2.011 (1.154–3.513)	0.162	1.446 (0.861–2.436)
B symptoms	0.856	1.047 (0.633–1.735)	0.404	1.211 (0.771–1.905)
Lugano stage	0.287	1.461 (0.727–2.937)	0.344	1.352 (0.723–2.532)
IPI	0.085	2.027 (0.908–4.521)	0.134	1.764 (0.840–3.702)
Hb	0.800	1.075 (0.616–1.876)	0.414	1.243 (0.739–2.088)
ALC	0.079	1.869 (0.930–3.748)	0.024	2.145 (1.107–4.135)
AMC	0.529	1.207 (0.673–2.163)	0.310	1.329 (0.769–2.288)
LMR	0.043	1.636 (0.244–0.976)	0.009	2.014 (0.226–0.813)
PLR	0.461	0.763 (0.376–1.557)	0.150	0.590 (0.292–1.207)
LDH	0.109	0.488 (0.896–2.992)	0.011	0.428 (1.172–3.471)
$\beta 2m$	0.075	1.694 (0.949–3.026)	0.170	1.464 (0.849–2.527)
Surgery	0.613	0.870 (0.508–1.491)	0.440	0.820 (0.497–1.355)

IPI international prognostic index, *Hb* hemoglobin, *ALC* the absolute lymphocyte count, *AMC* absolute monocyte count, *LMR* lymphocyte–monocyte ratio, *PLR* platelet–lymphocyte ratio, *LDH* lactate dehydrogenase, $\beta 2m$ β 2-microglobulin, *OS* overall survival, *PFS* progression-free survival, *HR* hazard ratio

tumor microenvironment express the T-cell co-inhibitory ligand B7-H1 (PD-L1), which stimulates the expansion of suppressive regulatory T cells. Therefore it is not surprising

that peripheral blood monocytois is adverse prognostic factor in various tumors [15–17]. Platelets, an important factor in thrombosis, has been known as mediate cancer

cell growth, dissemination and angiogenesis. Activated platelets are able to interact with tumor cells through paracrine signaling or direct contact, thus promoting cancer cell growth and survival. Clinical data also suggested that elevated platelet number was related with poor prognosis in many types of tumors [4, 18–22]. We retrospectively analyzed all parameters in 173 patients and found that the univariate analysis of prognostic parameters showed that AMC was significantly associated with OS and PFS. However, in multivariate analysis, AMC has less significance of OS and PFS.

The LMR as a surrogate marker of host immunity (ALC) and tumor-microenvironment (AMC) has been reported as prognostic factor of clinical outcomes in DLBCL. Our study showed that LMR is also an effective prognostic factor in PGI- DLBCL patients. Besides, we found PLR's significant role in the diagnosis of all kinds of tumors [18–22], PLR was generally high in tumor patients and patients with higher value of PLR had lower survival. Our findings suggested that patients with an PLR > 170 in PGI-DLBCL might be lower OS and PFS.

The gene expression profiling (GEP) of lymphoma cells is another Important factor that influences the prognosis of PGI-DLBCL patients. According to GEP, three gene-expression subgroups—germinal-center B-cell-like (GCB), activated B-cell-like (ABC), and type 3 diffuse large-B-cell lymphoma—were demonstrated [23]. Although a quite powerful tool that reveals wide-ranging biological information about tumor biology, gene expression profiling is not easily available in most laboratories. Immunohistochemistry stain is readily available and routinely performed. It is used to divided DLBCL into GCB and non-GCB groups [24]. Studies have reported that GCB phenotype has a significantly better prognosis compared to patients with the non-GCB phenotype [25]. In our study, both PFS and OS data were not significantly different between the two groups.

Conclusion

In summary, although the means of evaluating PGI-DLBCL prognosis are varied, but these tools have some flaws. IPI totally overlooked the host immunity and tumor microenvironment which are important to the pathogenesis of lymphoma. The price of immunohistochemical stain is very high and sampling method is difficultly. Positron Emission Tomography/Computed Tomography (PET/CT) is not only expensive but also increases the number of false positive. The Peripheral blood cell count, readily available, inexpensive, objective data, is expected to become a means to evaluate the prognosis of PGI-DLBCL patients.

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Compliance with Ethical Standards

Conflict of interest The authors have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

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