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ORIGINAL RESEARCH

Prognostic Significance Of Platelet-To-Lymphocyte Ratio (PLR) And Mean Platelet Volume (MPV) During Etoposide-Based First-Line Treatment In Small Cell Lung Cancer Patients

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Background: Small cell lung cancer (SCLC) is a special type of lung cancer and it is responsive to chemotherapy. Blood parameters have been proved to be associated with survival for many types of malignancies. This study aimed to investigate the prognostic significance of platelet-to-lymphocyte ratio (PLR) and mean platelet volume (MPV) for SCLC patients with etoposide-based first-line treatment.

Methods: We retrospectively identified 138 patients diagnosed as SCLC who underwent etoposide-based first-line chemotherapy. The patients' baseline clinical characteristics and blood parameters were collected. Kaplan–Meier analysis and Cox regression methods were used to determine the factors associated with progression-free survival (PFS).

Results: The optimal cut-off value of diagnosis was depended on the ROC curve, the cut-off value of pretreatment PLR was 190 (sensitivity 39.0%, specificity 88.5%), and the cut-off value of pretreatment MPV was 10.0 (sensitivity 60.7%, specificity 61%). Kaplan–Meier analysis showed patients with high PLR levels in baseline had worse PFS than those with low PLR levels (P <0.001). Multivariate analysis revealed pretreatment MPV was an independent prognostic factor for PFS (HR: 0.815, 95% CI: 0.711–0.933, P =0.003). Further research suggested continuous high PLR indicated a poor therapy outcome (P =0.002).

Conclusion: Pretreatment MPV can be an independent predictor for first-line treatment outcome and a continuously high level of PLR suggested inferior PFS in etoposide-treated SCLC patients.

Keywords: small cell lung cancer, SCLC, first-line chemotherapy, mean platelet volume, MPV, platelet-to-lymphocyte ratio, PLR, prediction

Introduction

SCLC is a major type of lung cancer with neuroendocrine tumor characteristics. Compared with non-small cell lung cancer (NSCLC), SCLC has a high degree of malignancy, a rapid doubling time and a propensity for early metastasis.[1] SCLC is highly responsive to chemotherapy and radiotherapy, and it has a high remission rate during the initial treatment, but it is also easy to harbor drug resistance and relapse. Therefore, searching for clinically accessible indicators such as blood parameters to predict the therapeutic effect and to determine the prognosis of patients with SCLC is particularly significant for improving the life quality and prolonging the survival of patients, which is one of the most urgent clinical problems.

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Inflammation is an extremely considerable role in the development and progression of malignancies, and blood cells participate in various inflammatory processes by secreting diversified cytokines.[2,3] The sustained inflammatory response assists in the further evolvement of the tumor by attenuating the body's adaptive immune response.[4] Recently, several studies have suggested some indicators in blood were reflections of inflammatory changes in the tumor microenvironment.[5–7]

Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR) and systemic inflammation index (SII) reflected the level of systemic inflammation in the body.[8,9] Several studies had discovered the relationship between NLR, PLR, LMR, SII and NSCLC treatment outcomes in surgery, chemotherapy, radiotherapy, targeted therapy and even immunotherapy.[10–14] Recently, studies had attracted broad attention to the function of platelet activation to promote tumor angiogenesis, tumor cell proliferation and metastasis, thereby promoting drug resistance and disease progression, and more than that, platelet parameters could predict tumor treatment outcomes.[15,16] Mean platelet volume (MPV) was a new indicator of platelet size and activity, which had been proposed as a possible marker of platelet function and activation.[17] However, there was still a rare study about the relationship between platelet parameters and SCLC treatment. Thus, the purpose of this study was to explore PLR and MPV on the prognostic effect in first-line treatment for SCLC.

Materials And Methods

Patients

All patients diagnosed as SCLC without surgery were retrospectively reviewed, from September 2015 to December 2018 in Anhui Provincial Hospital. From the group of 454 patients, 138 cases meeting the requirements as follows were included in the study ultimately: patients were pathologically diagnosed as SCLC, without other types of lung cancer containing SCLC components or combining two or more types of tumors; patients received radiological examination to define specific tumor stages; patients received first-line chemotherapy regimen with etoposide combining platinum; patients took radiological examination to assess therapeutic effect every 2–3 months, which were evaluated according to the RECIST criteria, version 1.1; patients did not have hematological diseases, immune system diseases or hepatitis virus infections; patients did not receive long-term glucocorticoid therapy; patients had first-line treatment progression.

Clinical Data Collection

Clinical data were collected including age, gender, tumor stage, tumor metastasis condition, first-line chemotherapy regimen, first evaluation result and radiotherapy condition. Blood parameters were recorded before every cycle of chemotherapy, including total white blood cell count (WBC), absolute neutrophil count (NEUT), absolute lymphocyte count (LYMPH), absolute number of monocytes (MONO), total number of red blood cells (RBC), hemoglobin concentration (HGB), total platelet count (PLT), platelet volume distribution width (PDW), red blood cell volume distribution width (RDW), mean red blood cell volume (MCV), mean platelet volume (MPV), and then the quantitative values of NLR, PLR, LMR, SII (SII =PLT×NEUT/LYMPH), MCV/RBC ratio and PLT/MPV ratio were calculated. Progression-free survival (PFS) was defined as the time from the randomization to the progression or death of the disease. The incidence of marrow suppression and the cause of progression during the first-line treatment were also recorded.

Laboratory Testing

Patients were at a resting state during the early morning when blood samples were collected. The analytical instrument was a Sysmex XE-5000 automatic blood analyzer. EDTA-K2 (dipotassium ethylenediaminetetraacetate) vacuum anticoagulation tube was purchased from Shanghai Kehua Biotechnology Co., Ltd. The samples were tested by the instrument, and the instrument was in the best working condition according to the instrument operation rules, the blood test routine test of Standard Operating Procedure (SOP) file and the clinical test operation rules. All samples were tested within 2 hrs.

Statistical Analysis

All analyses and graphs were performed using SPSS 19.0 (IBM Corporation, Armonk, NY, USA) and Graphpad Prism 6.0 (GraphPad Software Inc., San Diego, CA, USA) statistical software. Receiver operating characteristic (ROC) curve was constructed from the pre-treatment blood indicators, the area under the curve (AUC) was used to assess their diagnostic value, Chi-square test was used for rates comparison, Student's *t*-test was used for normal distribution data comparison. Spearman test was used for correlation analysis. Potential factors were analyzed by the

Kaplan–Meier method for survival analysis, log rank test for statistical difference and Cox regression analysis for multivariate analysis. The difference was statistically significant at $P < 0.05$.

Ethical Approval And Informed Consent

This study was approved by the Ethics Committee of Anhui Provincial Hospital. All patients diagnosed with SCLC were from Anhui Provincial Hospital. The need for written informed consent was waived by the Ethics Committee because of the retrospective nature of this study. This study was conducted following the Declaration of Helsinki.

Results

Baseline Parameters

The data of 138 patients had been collected. The average age of these patients was 60.96 ±8.70 years old. There were 34 patients in the limited stage and 104 patients in the extensive stage. All patients had received etoposide-based chemotherapy for the first-line treatment. The clinical characteristics of the total patients are shown in Table 1.

According to mean PFS value (6.59 ±3.67 months), the ROC curve of the baseline blood parameter values was evaluated (State variable: PFS =7 months). NLR0, PLR0, LMR0, SII0, MCV0, MPV0, RDW0, PDW0, PLT0/MPV0 ratio, MCV0/RBC0 ratio, as the baseline data, showed their diagnostic values of indicators (Figure 1). Depending on the ROC curve results, NLR0, PLR0, LMR0, SII0, MPV0 showed favorable prognostic effects on PFS. As for the optimal cut-off point of diagnosis, PLR0 was at 190 (sensitivity =39.0%, specificity =88.5%), MPV0 was at 10.0 (sensitivity =60.7%, specificity =61%) (Table 2).

The Chi-square test demonstrated the difference between the baseline blood parameters and clinical characteristics. Gender, age, chemotherapy regimen and myelosuppression showed no difference in different blood parameter groups before the treatment. However, PFS (PFS ≥7 months vs. PFS <7 months) between all different blood parameter groups showed a significant difference. Moreover, stage and radiotherapy conditions differed in different pretreatment PLR groups, and there was still discrimination between the results of the first evaluation with different pre-treatment PLR and MPV groups (Table 3).

Kaplan–Meier analysis showed that PFS of the high PLR0 group was significantly shorter than the low PLR0 group in 138 patients ($P < 0.001$) (Figure 2B), while other blood parameter groups were not statistically significant (Figure 2A and C–F). Because stage conditions differed in pretreatment PLR groups, 138 patients were divided by stage condition into two groups as limited stage group (34 cases) and extensive stage group (104 cases) for further study. The outcome suggested that in patients with extensive stage, PFS of high PLR0 group was still shorter than the low PLR0 group (Figure 3B), as well as, the PFS of patients in low MPV0 group was shorter than high MPV0 group (Figure 3E). The other blood parameter groups were shown (Figure 3A and C–F).

Spearman test demonstrated the correlation between pre-treatment blood parameters and PFS. The results showed that there was a pleasurable correlation between MPV0 and PFS, and it was statistically significant (P

Table 1 The Clinical Characteristics Of 138 Patients With SCLC

Clinical Characteristics	Cases (n)	%
Gender		
Female	30	21.7
Male	108	78.3
Age (year)		
<65	85	61.6
≥65	53	38.4
x ±s	60.96 ±8.70	
Stage		
Limited stage (LS)	34	24.6
Extensive stage (ES)	104	75.4
First-line chemotherapeutic regimen		
Etoposide +Luoplatinum	83	60.1
Etoposide +Cisplatin or Carboplatin	55	49.9
Radiotherapy in first-line therapy		
Yes	58	42.0
No	80	58.0
First evaluation results		
CR	5	3.6
PR	84	60.9
SD	21	15.2
PD	28	20.3
Progress-Free Survival (months)		
<7.0	77	55.8
≥7.0	61	44.2
x ±s	6.59 ±3.67	
Reasons for the progress of first-line treatment		
Lesions increase	76	55.1
Distant metastasis	62	44.9

Abbreviations: CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.

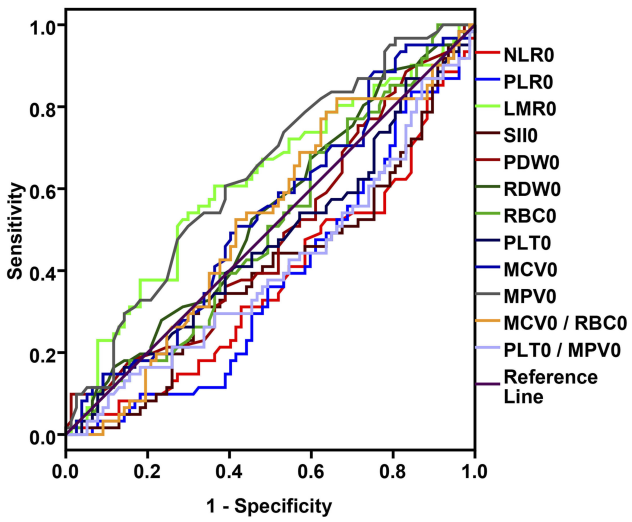

Figure 1 ROC curve based on pretreatment blood parameters.
Abbreviations: NLR, neutrophil-to-lymphocyte ratio (AUC =0.376, *P* =0.013); PLR, platelet-to-lymphocyte ratio (AUC =0.377, *P* =0.013); LMR, lymphocyte-to-monocyte ratio (AUC =0.617, *P* =0.019); SII, systemic inflammation index (AUC =0.402, *P* =0.049); MPV, mean platelet volume (AUC =0.637, *P* =0.006) and PLT/MPV ratio (AUC =0.410, *P* =0.068).

<0.05) (Figure 4E). The correlation between other blood parameters and PFS was shown (Figure 4A–F).

Afterward, Student's *t*-test revealed the differentiation of PFS between different clinical and blood parameter groups. PFS showed no statistical difference in gender, chemotherapy regimen (Figure 5A), NLR0, LMR0, SII0 and PLT0/MPV0 groups. But in low PLR0 group (7.24 ±3.80 months), PFS was longer than high PLR0 group (4.82 ±2.61 months) (*P* <0.001); meanwhile, in high MPV0 group (7.26 ±3.76 months), PFS was longer than low MPV0 group (5.96 ±3.50 months) (*P* =0.037) (Figure 5B).

The univariate analysis identified that gender, age, tumor stage, radiotherapy, results of the first evaluations and pretreatment PLR were significantly associated with PFS (Table 4). Multivariate analysis distinctly revealed that age (HR: 0.973, 95% CI: 0.954–0.992, *P* =0.006), stage (HR: 0.600, 95% CI: 0.385–0.937, *P* =0.025), radiotherapy (HR: 2.548, 95% CI: 1.721–3.772, *P* <0.0001), results of the first evaluations (HR: 2.155, 95% CI: 1.475–3.146, *P* =0.0001) and MPV0 (HR: 0.815, 95% CI: 0.711–0.933, *P* =0.003) were independent prognostic factors for PFS (Table 5).

Post-Chemotherapy Parameters

There were 4 patients having been received recombinant human granulocyte colony-stimulating factor (G-CSF) in hospitalization because of myelosuppression. In order to prevent these patients from interfering with the experiment result, the following analysis excluded them. In the remaining 134 patients, NLR1, PLR1, LMR1, SII1, as the post-chemotherapy data, were gathered for further research. The quartile of NLR1 was 2.155 (1.490–3.175), the quartile of PLR1 was 170.69 (122.77–232.13), the quartile of LMR1 was 2.425 (1.578–3.283), the quartile of SII1 was 467.55 (294.25–734.47). 134 patients were divided into three groups on the basis of pre-chemotherapy and post-chemotherapy data. We classified the patients into three subsets as follows: High NLR group (NLR0 >2.1 and NLR1 >2.1), Low NLR group (NLR0 ≤2.1 and NLR1 ≤2.1), Medium NLR group (NLR0 >2.1 and NLR1 ≤2.1 or NLR0 ≤2.1 and NLR1>2.1). Like NLR, patients were divided into three groups according to the changes of PLR, LMR and SII similarly.

Kaplan–Meier analysis demonstrated that PFS of the High PLR group was shorter than other groups (*P* =0.002) (Figure 6B), while the NLR change groups had a similar result (Figure 6A) but other blood parameter groups were not statistically significant (Figure 6C and D).

Discussion

There were some studies about the relationship between inflammatory indexes in hematology and SCLC.[18–21] However, most studies revealed a relationship between parameters and overall survival (OS),[21,22] the relationship between PFS of first-line treatment and blood parameters had not been fully uncovered.

Table 2 Cut-Off Values Of ROC Curve For Pretreatment Blood Parameters

Variable	NLR0	PLR0	LMR0	SII0	MPV0	PLT0/MPV0 Ratio
Cut-off value	2.1	190	3.1	465	10.0	21.0
Sensitivity	0.775	0.390	0.607	0.753	0.607	0.636
Specificity	0.468	0.885	0.636	0.475	0.61	0.557

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; SII, systemic inflammation index; MPV, mean platelet volume; PLT/MPV ratio, total platelet count/mean platelet volume.

Table 3 Correlation Between Hematological Parameters And Clinical Features Of 138 Patients With SCLC By Chi-Square Test

Clinical Features		NLR0			PLR0			LMR0			SII0			MPV0			PLT0/MPV0 Ratio		
		≤2.1	>2.1	P-Value	≤190	>190	P-Value	≤3.1	>3.1	P-Value	≤465	>465	P-value	≤10.0	>10.0	P-value	≤21.0	>21.0	P-value
Gender	Female	11	19	0.525	18	12	0.065	12	18	0.156	10	20	0.851	16	14	0.815	13	17	0.773
	Male	33	75		83	25		59	49		38	70		55	53		50	58	
Age (year)	<65	24	61	0.244	59	26	0.205	45	40	0.657	28	57	0.565	47	38	0.252	38	47	0.777
	≥65	20	33		42	11		26	27		20	33		24	29		25	28	
Stage	Limited stage	10	24	0.722	30	4	0.023	16	18	0.555	13	21	0.626	20	14	0.322	13	21	0.317
	Extensive stage	34	70		71	33		55	49		35	69		51	53		50	54	
Extensive stage	Single organ metastasis	51	26	<0.001	55	22	0.792	57	20	0.149	45	32	0.112	51	26	0.184	56	21	0.099
	Multiple organ metastasis	7	20		20	7		16	11		11	16		14	13		15	12	
Chemotherapeutic regimen	Etoposide + Cisplatin or Carboplatin	18	37	0.863	38	17	0.376	25	30	0.251	20	35	0.751	28	27	0.918	26	29	0.756
	Etoposide + Luoplatinum	26	57		63	20		46	37		28	55		43	40		37	46	
Radiotherapy	Yes	21	37	0.353	49	9	0.011	26	32	0.185	24	34	0.166	29	29	0.772	24	34	0.391
	No	23	57		52	28		45	35		24	56		42	38		39	41	
Results of the first evaluation	ORR (CR +PR)	33	56	0.078	72	17	0.006	41	48	0.088	36	53	0.060	40	49	0.039	50	39	<0.001
	SD+PD	11	38		29	20		30	19		12	37		31	18		13	36	
PFS (months)	<7	17	60	0.005	47	30	<0.001	47	30	0.011	19	58	0.005	47	30	0.011	29	48	0.034
	≥7	27	34		54	7		24	37		29	32		24	37		34	27	
Reasons for the progress	Lesions increase	24	52	0.932	54	22	0.531	41	35	0.516	20	56	0.021	43	33	0.182	33	43	0.560
	Distant metastasis	20	42		47	15		30	32		28	34		28	34		30	32	
Grade 3–4 myelosuppression	Yes	17	40	0.663	40	17	0.503	32	25	0.355	25	32	0.060	28	29	0.646	29	28	0.301
	No	27	54		61	20		39	42		23	58		43	38		34	47	

Abbreviations: ORR, objective response rate; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; SII, systemic inflammation index; MPV, mean platelet volume; PLT/MPV ratio, total platelet count/mean platelet volume.

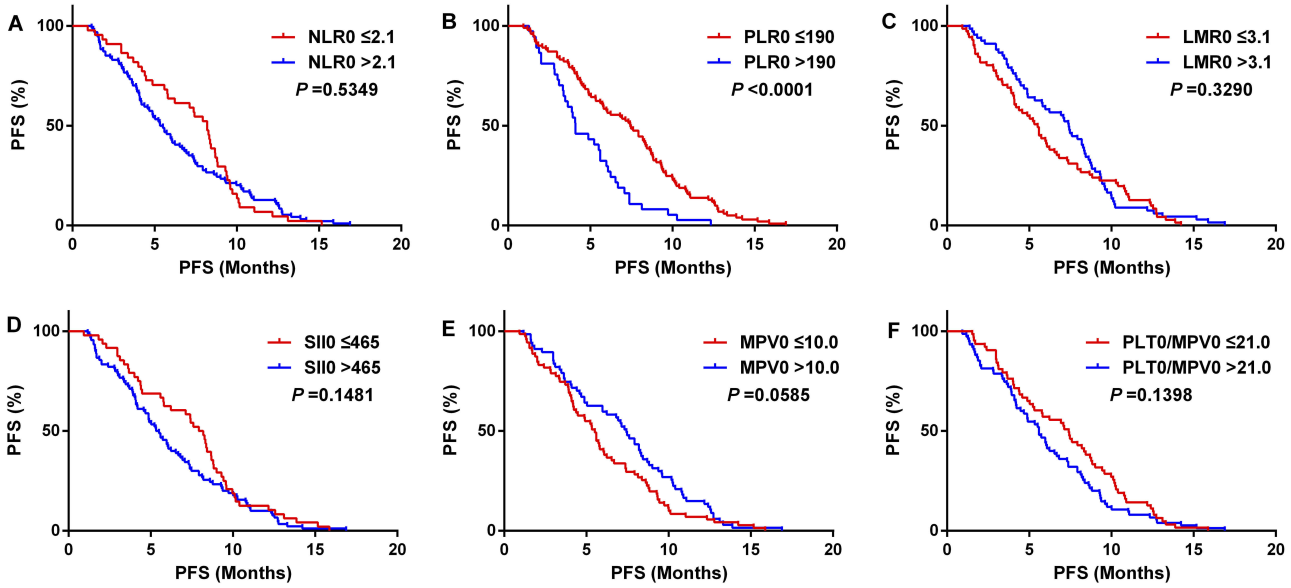

Figure 2 Kaplan–Meier analysis for progress-free survival (PFS) in all 138 patients with SCLC.
Notes: NLR, neutrophil-to-lymphocyte ratio (**A**); PLR, platelet-to-lymphocyte ratio (**B**); LMR, lymphocyte-to-monocyte ratio (**C**); SII, systemic inflammation index (**D**); MPV, mean platelet volume (**E**); PLT/MPV ratio, total platelet count/mean platelet volume (**F**).

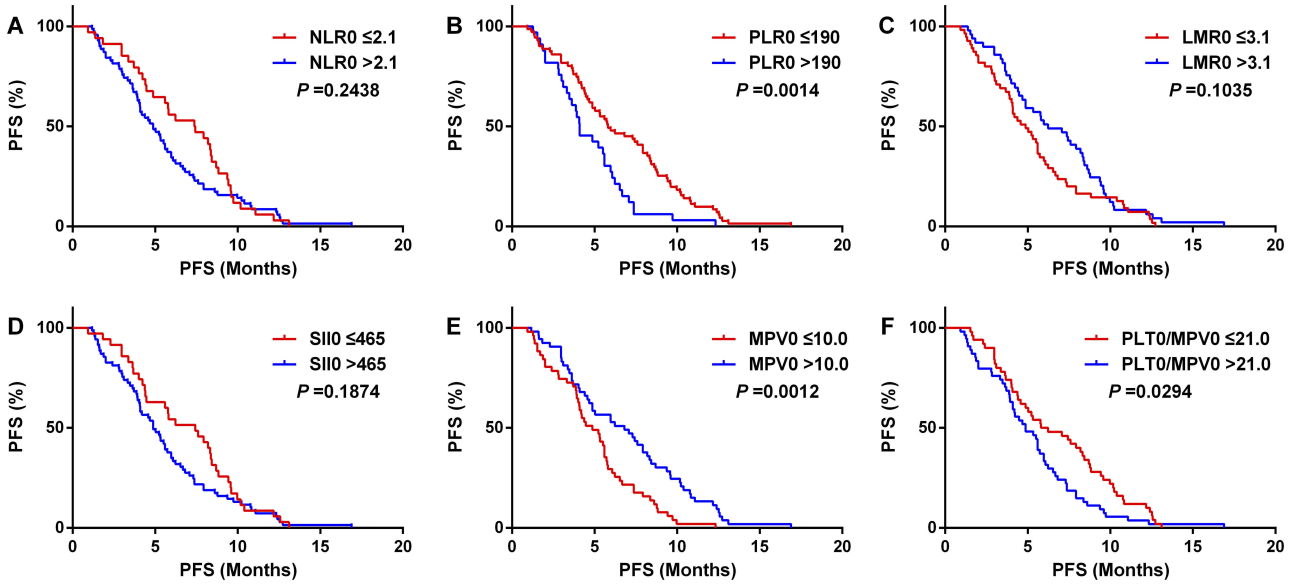

Figure 3 Kaplan–Meier analysis for progress-free survival (PFS) in 104 extensive stage SCLC patients.
Notes: NLR, neutrophil-to-lymphocyte ratio (**A**); PLR, platelet-to-lymphocyte ratio (**B**); LMR, lymphocyte-to-monocyte ratio (**C**); SII, systemic inflammation index (**D**); MPV, mean platelet volume (**E**); PLT/MPV ratio, total platelet count/mean platelet volume (**F**).

The study demonstrated that the baseline PLR had a preliminary prognostic value of PFS in the light of univariate analysis, and high PLR group (PLR0 >190) had an inferior PFS, the same results were obtained in all patients and extensive stage patients. However, multivariate analysis showed PLR was not the independent factor of PFS. Taking it into account that the Chi-square test suggested PLR0 was related to radiotherapy condition, more importantly, radiotherapy condition was an independent factor of PFS; therefore, it conjectured that radiotherapy condition had a deep influence on PLR to predict the PFS. A former study in 187 Korean patients had got a similar conclusion that baseline PLR was not associated with OS or PFS in patients treated with platinum-based chemotherapy.[23] So,

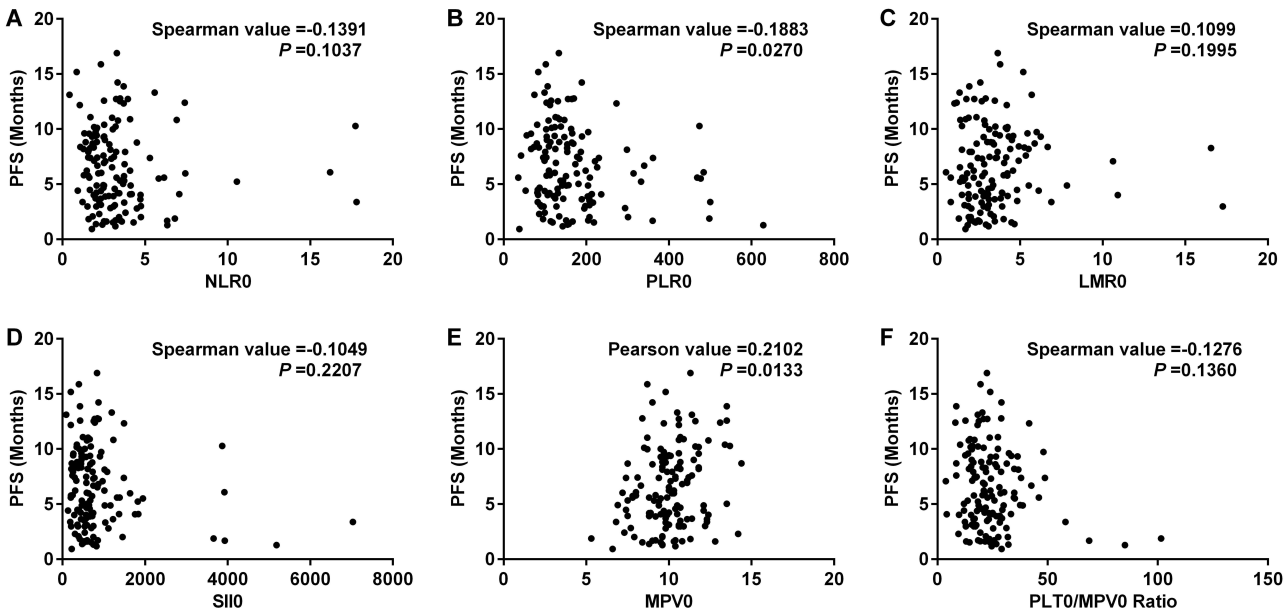

Figure 4 Correlation analysis between progress-free survival (PFS) and blood parameters in 138 patients with SCLC.
Notes: NLR, neutrophil-to-lymphocyte ratio (**A**); PLR, platelet-to-lymphocyte ratio (**B**); LMR, lymphocyte-to-monocyte ratio (**C**); SII, systemic inflammation index (**D**); MPV, mean platelet volume (**E**); PLT/MPV ratio, total platelet count/mean platelet volume (**F**).

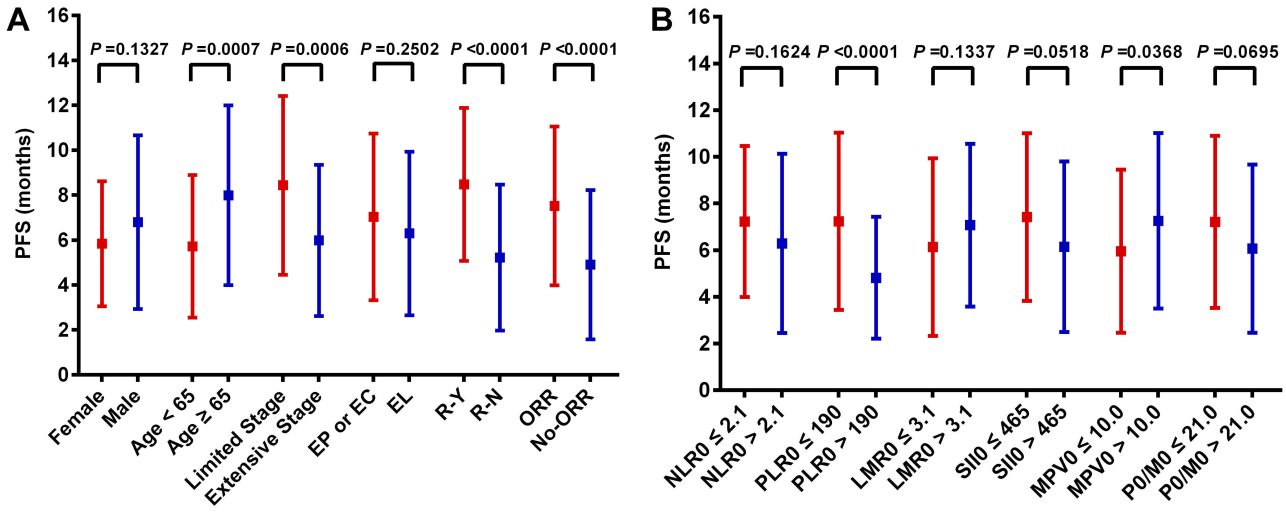

Figure 5 Student's *t*-test for progress-free survival (PFS) between different clinical features and blood parameters. (**A**) Comparison of mean progress-free survival (PFS) between the different clinical feature groups; (**B**) comparison of mean progress-free survival (PFS) between the different blood parameter groups.
Abbreviations: EP or EC group, chemotherapy regimen was etoposide + cisplatin or etoposide + cisplatin; RL group, chemotherapy regimen was etoposide + lobaplatin; RY group, patients received radiotherapy during first-line treatment; RN group, patients never received radiotherapy during first-line treatment; ORR group, the first-time evaluation results was CR or PR; No-ORR group, the first-time evaluation results was SD or PD; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; SII, systemic inflammation index; MPV, mean platelet volume, PLT/MPV ratio, total platelet count/mean platelet volume.

further research showed that continuous high PLR (high PLR0 and high PLR1) group patients had shorter PFS than the others. The combination of pretreatment and post-treatment PLR partly reduced the impact of radiotherapy factor, which made the results more reliable.

MPV was considered as a hallmark of platelet activation. Shi et al[24] retrospectively reviewed advanced NSCLC patients and the study showed MPV and plateletcrit (PCT) were negative predictors of drug resistance and both were independent factors associated with OS. Another study[25] in advanced NSCLC patients showed OS was significantly shorter in the group with a low MPV/PLT ratio than in the other group, and a low MPV/PLT ratio was an unfavorable independent prognostic factor for OS. In our study, the Chi-square test, Spearman

Table 4 Univariate Analysis Of PFS In 138 Patients With SCLC

Variable		Case (n)	HR (95% CI)	P-Value
Gender	Female Male	30 108	1.496 (1.025–2.568) 0.6686 (0.389–0.9754)	0.0439*
Age (year)	<65 ≥65	85 53	1.821 (1.358–2.651) 0.5493 (0.3772–0.7362)	0.0003*
Stage	Limited stage Extensive stage	34 104	0.5531 (0.3972–0.7924) 1.808 (1.262–2.518)	0.0016*
Chemotherapy regimen	Etoposide + Cisplatin or Carboplatin Etoposide + Luoplatinum	55 83	0.8491 (0.6057–1.187) 1.178 (0.8427–1.651)	0.3411
Radiotherapy	Yes No	58 80	0.4601 (0.2971–0.5891) 2.173 (1.697–3.366)	<0.0001*
Results of the first evaluation	ORR (CR + PR) SD + PD	89 49	0.5152 (0.2992–0.6687) 1.941 (1.495–3.342)	0.0001*
NLR0	≤2.1 >2.1	44 94	0.8949 (0.6282–1.269) 1.117 (0.7883–1.592)	0.5349
PLR0	≤190 >190	101 37	0.4679 (0.2207–0.5673) 2.137 (1.763–4.531)	<0.0001*
LMR0	≤3.1 >3.1	71 67	1.176 (0.8491–1.657) 0.8504 (0.6037–1.178)	0.329
SII0	≤465 >465	48 90	0.7752 (0.5525–1.090) 1.29 (0.9177–1.810)	0.1481
MPV0	≤10.0 >10.0	71 67	1.371 (0.9940–1.948) 0.7295 (0.513–1.006)	0.0585
PLT0/MPV0 ratio	≤21.0 >21.0	63 75	0.7804 (0.5547–1.082) 1.281 (0.9245–1.803)	0.1398

Note: *$P < 0.05$.
Abbreviations: CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; SII, systemic inflammation index; MPV, mean platelet volume; PLT/MPV ratio, total platelet count/mean platelet volume.

Table 5 Multivariate Analysis Of PFS In 138 Patients With SCLC

Variable	HR (95% CI)	P-value
Gender	1.407 (0.910–2.176)	0.125
Age (year)	0.973 (0.954–0.992)	0.006
Stage	0.600 (0.385–0.937)	0.025
Radiotherapy	2.548 (1.721–3.772)	<0.0001
Results of the first evaluation	2.155 (1.475–3.146)	<0.0001
PLR0	1.001 (0.999–1.003)	0.477
MPV0	0.815 (0.711–0.933)	0.003

Note: Univariate variables with P<0.1 were included in the multivariate analyses.
Abbreviations: PLR, platelet-to-lymphocyte ratio; MPV, mean platelet volume.

test and Student's *t*-test all revealed that MPV of baseline had a relationship with PFS, and Kaplan–Meier analysis showed PFS of patients in low MPV group was shorter than the other group in extensive stage patients. Strangely, MPV was not statistically significant in univariate analysis but multivariate analysis. It suggested MPV was an independent prognostic factor for PFS in SCLC patients. We considered univariate analysis had its shortness of test efficacy, and the result of multivariate analysis was more reliable. There had been no reports related to MPV and SCLC treatment so far. Only one study showed increased MPV was an important prognostic factor and an increased MPV level might be used as a prognostic biomarker to estimate for poor OS in patients with NSCLC.[26]

Notably, this study had not found the important significance of NLR in SCLC. Suzuki R et al[27] found the link between high NLR and inferior OS, but his conclusion was based on 122 patients with limited-stage SCLC without defined chemotherapy regimens. On the contrary, Bernhardt et al[18] did not find NLR was an independent

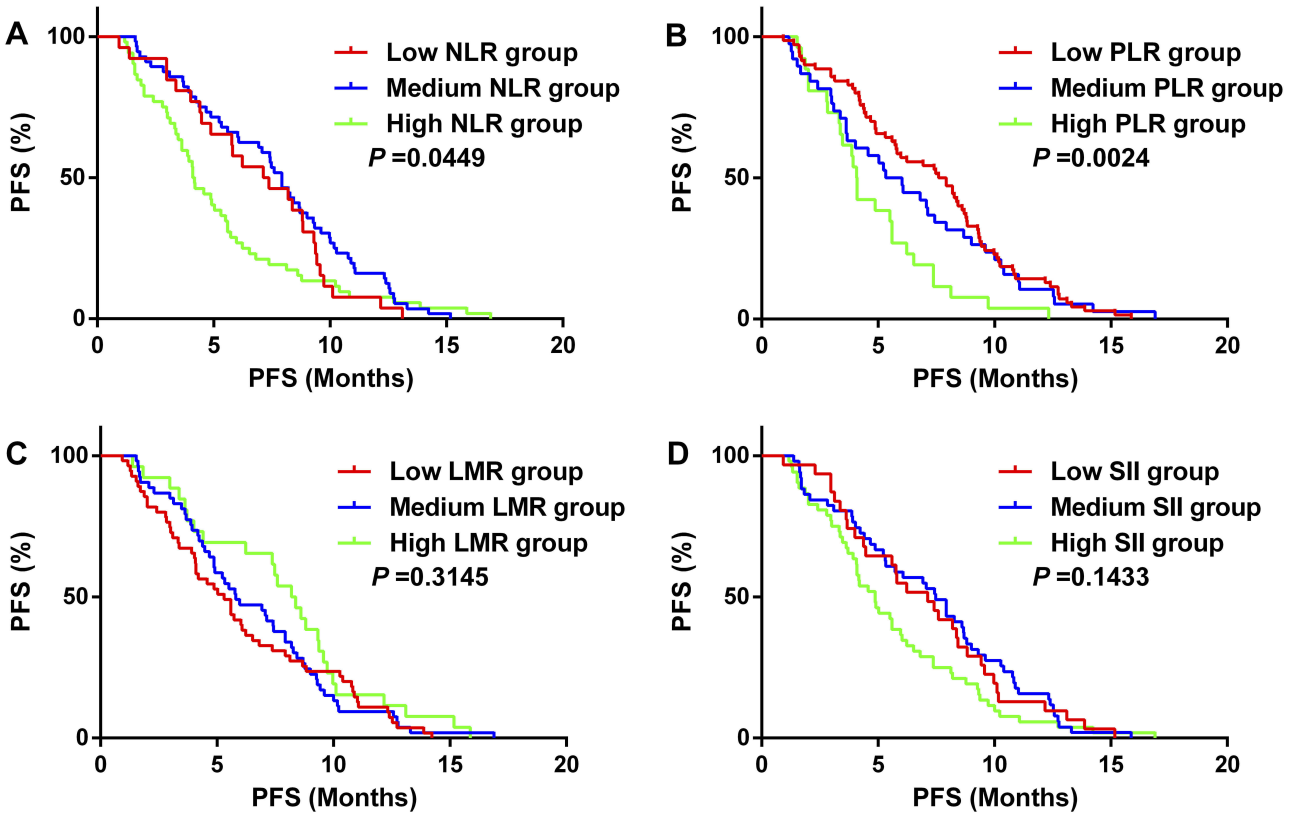

Figure 6 Kaplan–Meier analysis for progress-free survival (PFS) in 134 patients with SCLC. (**A**) High NLR group (NLR0 >2.1 and NLR1 >2.1), Low NLR group (NLR0 ≤2.1 and NLR1 ≤2.1), Medium NLR group (NLR0 >2.1 and NLR1 ≤2.1, or NLR0 ≤2.1 and NLR1 >2.1); (**B**) High PLR group (PLR0 >190 and PLR1 >190), Low PLR group (PLR0 ≤190 and NLR1 ≤190), Medium PLR group (PLR0 >190 and PLR1 ≤190, or PLR0 ≤190 and PLR1 >190); (**C**) High LMR group (LMR0 >3.1 and LMR1 >3.1), Low LMR group (LMR0 ≤3.1 and LMR1 ≤3.1), Medium LMR group (LMR0 >3.1 and LMR1 ≤3.1, or LMR0 ≤3.1 and LMR1 >3.1). (**D**) High SII group (SII0 >465 and SII1 >465), Low SII group (SII0 ≤465 and SII1 ≤465), Medium SII group (SII0 >465 and SII1 ≤465, or SII0 ≤465 and SII1 >465).
Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; SII, systemic inflammation index.

prognostic factor for OS in 350 SCLC in limited-stage. Suzuki R et al[20] found high NLR predicted inferior survival in extensive-stage SCLC patients received platinum-based chemotherapy. Liu et al[21] found NLR was an independent prognostic factor and could be used to predict the mortality risk of SCLC patients but they did not clearly describe the tumor stage or chemotherapy regimens. There still remained confusion about the role of NLR in SCLC. The cut-off value, therapeutic regimen and tumor stage of this study were partly different. Put it another way, patients with SCLC were prone to platelet-related complications such as superior vena cava obstruction; it hypothesized that platelet parameters had a better prognostic effect in SCLC than traditional white blood cell parameters; furthermore, platelet parameters were not easily affected by drugs like G-CSF.

There were still some limitations in this study. First, the cut-off value was individually determined by the ROC curve from the baseline blood parameters of 138 patients involved in this study. Second, as for the blood parameters of the first evaluation time, the impact from myelosuppression due to chemotherapy drugs could not be ignored; myelosuppression also was the reaction of the human body for treatment. Though 4 patients were excluded on account of having been received G-CSF in hospitalization, the situation of myelosuppression and support treatment in the discharge period were unknown, and the influence of G-CSF injection to NLR was unspecified. Lastly, the data of this study were from a single center and the research was a retrospective study. The outcomes still need larger and randomized clinical trials for validation.

In conclusion, baseline MPV was a significant predictor of outcome and a continuously high level of PLR suggested inferior PFS in etoposide-treated SCLC patients.

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Disclosure

The authors declare no conflicts of interest in this work.

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