RESEARCH ARTICLE

After neoadjuvant chemotherapy platelet/lymphocyte ratios negatively correlate with prognosis in gastric cancer patients

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Introduction: Circulating predictors prognostic factors of neoadjuvant chemotherapy, which identify the patients who are potential possibly to benefit from it are limited at present. In this research, we aimed to compare the prognostic significance of neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) in patients with locally advanced gastric carcinoma who were treated with neoadjuvant chemotherapy (NAC) followed by D2 gastrectomy.

Materials and methods: From 2007 to 2015, 91 patients with locally advanced gastric cancer treated with NAC followed by D2 gastrectomy included in this retrospective cohort study. The correlation of clinical data, including tumor regression, response evaluation, tumor location, pathological type, systemic therapy, tumor size (cm), neural invasion, lymphatic-vascular invasion, ypTNM stage, and survival prognosis were analyzed.

Results: Platelet/lymphocyte ratio and neutrophil/lymphocyte ratio in gastric cancer patients were higher than in matched normal volunteers. PLR levels higher after neoadjuvant chemotherapy are associated with worse OS. Multivariate Cox proportional analysis showed that pre-neoadjuvant chemotherapy PLR was an independent prognostic factor.

Conclusions: Pre-neoadjuvant chemotherapy PLR may be a feasible biomarker for survival prognosis in patients with locally advanced gastric cancer. PLR and NLR were reduced after neoadjuvant chemotherapy. After neoadjuvant chemotherapy, PLR level was negatively correlated with survival prognosis.

KEYWORDS

D2 gastrectomy, Gastric cancer, neoadjuvant chemotherapy, platelet/lymphocyte ratios, prognosis

1 | INTRODUCTION

Gastric cancer (GC) as the second most normally diagnosed cancer is rampant in China. Approximately 679 100 new patients of gastric cancer will be diagnosed per year, and about 498 000 people will eventually die from this disease.¹ More than 80% of cases are diagnosed at an locally advanced stage. 5-fluorouracil (5-FU) is still the main drug for management of gastric cancer, and higher remission rates were observed in patients who were treated with combination chemotherapy

with 5-FU.² Gastrectomy combined with D2 lymph node dissection is the golden standard for curable gastric cancer in Eastern Asia. Adjuvant chemoradiation, neoadjuvant chemotherapy, and postoperative chemotherapy for locally advanced gastric cancer have drawn more attention to the management of gastric cancer in the multidisciplinary treatment model at present.

Neoadjuvant chemotherapy as a recommended treatment for locally advanced gastric cancer can improve R0 resection rate and down the tumor stage.³⁻⁵ Although diverse clinical and molecular predictors

for preoperative chemotherapy have been found to be related to poor prognosis in gastric cancer people, CT scan is an important method for preoperative evaluation. But the overall accuracy is from 43% to 82%,⁶ and to find predictors of curative effect for neoadjuvant chemotherapy for T staging is necessary.

Immune cells are closely associated with tumorigenesis. They play a critical role in almost every stage of cancer development.⁷ Several reports have suggested that elevated inflammatory markers such as platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR), in patients with different types of malignancies, were associated with a poor prognosis.⁸⁻¹² Evidence for these biomarkers as direct predictors of result in advanced gastric cancer patients who received neoadjuvant chemotherapy is limited. Therefore, we conducted this research to evaluate the association NLR and PLR levels with the clinical outcome of neoadjuvant chemotherapy in patients with locally advanced gastric cancer. Furthermore, the changes in these biomarkers after NAC were also assessed to discuss their value as potentially useful predictors.

2 | MATERIALS AND METHODS

2.1 | Patients

A total of 111 gastric cancer patients (stage T3 or T4 and node-positive) who received preoperative NAC followed by D2 gastrectomy in the Shandong cancer hospital affiliated to Shandong University between 2007 and 2015 were evaluated retrospectively.

Before preoperative NAC, gastric adenocarcinoma was histologically confirmed in all patients. The exclusive criteria were as follows: (i) The patients died of other diseases; (ii) the patients had autoimmune diseases; (iii) the patients were found to have other tumors; (iv) the patients with distant metastases did not do R0 resection; a total of 91 normal volunteers (NVs) were also recruited in this research. Written informed consent was obtained from all people. All NVs underwent a physical examination at Shandong cancer hospital affiliated to Shandong University between 2007 and 2015 for inclusion. The excluding criteria were as follows: (i) tumor patients; (ii) recent steroid therapy; (iii) evidence of a severe inflammatory condition; and (iv) autoimmune disorders.

2.2 | Chemotherapy regimen

Gastric cancer patients were treated with NAC every 2 weeks, and the regimens were as follows: DOF scheme (docetaxel 50 mg/m², oxaliplatin 85 mg/m², 5-FU 400 mg/m², 5-FU 2400 mg/m²), DF scheme (docetaxel 85 mg/m², 5-FU 400 mg/m², 5-FU 2400 mg/m²), and FOLFOX scheme (Oxaliplatin 100 mg/m², 5-FU 400 mg/m², 5-FU 2400 mg/m²). All patients were routinely examined by CT during the period of NAC, and NAC efficacy was evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST) guideline version 1.1.¹³ Based on the clinical reaction, the patients were separated into non-responder group (PD) and responder group (CR, PR, and SD). Patients were followed up until death or until the cutoff date of

FIGURE 1 Blood cell counts from normal volunteers and patients with GC. There was no significant difference in age and gender between NVs and patients with GC, and overall survival of patients treated with different neoadjuvant chemotherapy regimens. (all $P > .05$)

May 2016. The median follow-up interval was 22 months (from 8 to 67 months). Finally, a total of 91 patients were eligible in this research. 91 patients were divided into patients who received DOF regimens ("Docetaxel, oxaliplatin and fluo" group) and patients who received FOLFOX or DF regimens ("Other, fluorouracil" group). There was no statistically significant difference between the two groups regarding either median OS (25 vs 27 months; $P = .275$; Figure 1C).

2.3 | Blood sample analysis

Blood samples were obtained within 7 days before NAC. WBC, neutrophil, lymphocyte, and platelet counts were recorded. After NAC

blood samples were obtained from laboratory results approximately 3 weeks after neoadjuvant chemotherapy before surgery, pre-NAC NLR, pre-NAC PLR, aft-NAC NLR, and aft-NAC PLR were calculated from external blood cell count, and their optimal cutoff levels were determined by receiver-operating characteristic curves.

2.4 | The best threshold values for sensitivity and specificity were determined by receiver-operating characteristic (ROC) curves

The cutoff values of PLR and NLR were determined by the ROC curves. The cutoff value of pre-NAC NLR was 1.44, sensitivity of 0.738 and specificity of 0.577; pre-NAC PLR was 161, sensitivity of 0.262 and specificity of 0.115; aft-NAC NLR was 1.05, sensitivity of 0.662 and specificity of 0.538; and aft-NAC NAC PLR was 108, sensitivity of 0.338 and specificity of 0.077. Based on the selected values of pre-NAC NLR, pre-NAC PLR, aft-NAC NLR, and aft-NAC PLR, the patients were separated into the pre-NAC NLR^{hi} group (NLR > 1.44), the pre-NAC NLR^{low} group (NLR ≤ 1.44), the pre-NAC PLR^{hi} group (PLR > 161), the pre-NAC PLR^{low} group (PLR ≤ 161), and the aft-NLR^{hi} group (NLR > 1.05), the aft-NAC NLR^{low} group (NLR ≤ 1.05), the aft-NAC PLR^{hi} group (PLR > 108), and the aft-PLR^{low} group (PLR ≤ 108), respectively.

Clinical characteristics of patients, including age, gender, response evaluation, tumor location, pathological type, pathological type, systemic therapy, tumor size, tumor regression score, primary tumor (T), regional lymph nodes (N), neural invasion, lymphatic-vascular invasion, tumor stage, were collected and exhibited in Table 1. Data were obtained from medical records room.

2.5 | Tumor regression score

The degree of tumor regression was recorded based on NCCN guidelines version 2.2016 gastric cancer.¹⁴

2.6 | Statistical analysis

The SPSS 22.0 software (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. A value of $P < .05$ was regarded as significantly different. Count data were analyzed by chi-square test. Measurement data were expressed as the mean ± standard deviation (SD) and analyzed by t test. The Kaplan–Meier method was used to analyze the five-year survival rate. The log-rank was employed in univariate survival analysis.

3 | RESULTS

3.1 | Patient characteristics

In total, 91 normal volunteers (NVs) were recruited, with the GC group presenting similar gender and age proportion as the NV group (both $P > .05$, Figure 1A and B). Compared with GC patients, PLR and NLR were significantly lower in NVs ($P < .05$, Figure 2). The characteristics of the 91 GC patients are shown in Table 1: 22 patients were female

TABLE 1 Demographic and clinicopathological characteristics of 91 patients with gastric cancer

Parameters (pre-NAC)	Number	%
Age (y)		
≤60	65	71.4
>60	26	28.6
Gender		
Male	69	75.8
Female	22	24.2
Response evaluation		
CR	0	0.0
PR	44	48.4
SD	34	37.4
PD	13	13.0
Tumor location		
Upper third	23	25.3
Middle third	29	31.9
Lower third	33	36.3
Entire	6	6.6
Pathological type		
Well differentiated	2	2.2
Moderately differentiated	32	35.2
Poorly differentiated	50	54.9
Signet ring cell or Mucinous	7	7.7
Tumor regression score		
0 (Complete response)	3	3.3
1 (Moderate response)	10	11.0
2 (Minimal response)	39	42.9
3 (Poor response)	39	42.9
Tumor size (cm)		
5	53	58.2
>5	38	41.8
Neural invasion		
Yes	8	8.8
No	83	91.2
Lymphatic-vascular invasion		
Yes	16	17.6
No	75	82.4
Pathological TNM classification		
yT stage		
T0	2	2.2
T1	3	3.3
T2	4	4.4
T3	15	16.5
T4	67	73.6
yN stage		
N0	10	11.0
N1	29	31.9

(Continues)

TABLE 1 (Continued)

Parameters (pre-NAC)	Number	%
N2	20	22.0
N3	32	35.2
yTNM stage		
Tis	1	1.1
I	3	3.3
II	22	24.2
III	65	71.4
Chemotherapy regimen		
DOF	49	53.8
DF or FOLFOX	42	45.2
Types of surgery		
Total	52	57.1
Subtotal	39	42.9

FIGURE 2 The blood PLR and NLR in patients with GC were significantly higher than those in NVs (127.8 ± 63.5 vs 110.9 ± 23.5 ; 1.85 ± 0.08 , 1.62 ± 0.06 ; $P < .05$)

and 69 were male, with a median age of 55 years (range 26–70 years). Of the 91 patients, 49 were treated with a DOF regimen and 42 patients received a FOLFOX or DF regimen. All 91 patients underwent D2 gastrectomy; 39 (42.9%) subtotal gastrectomy and 52 (57.1%) total gastrectomy, and clinical and pathological characteristics classified based on the 7th AJCC staging were as follows: pathological ypTNM classification based on after resection of the primary cancer specimens showed that one patient had stage Tis disease, three patients had stage I disease, 22 patients had stage II disease, and 65 had stage III disease (Table 1).

3.2 | Clinical-pathological characteristics of patients with GC in the NLR and PLR before and after NAC

The PLR and NLR were reduced after NAC. (127.81 ± 63.46 vs 93.19 ± 37.04 , $P < .001$) (1.89 ± 0.91 vs 1.35 ± 0.99 , $P < .001$; (Figure 3).

The results demonstrated that pre-NAC NLR and pre-NAC PLR did not show any significant difference in age, gender, response

FIGURE 3 The blood PLR and NLR were lower post-NAT in patients with GC. (127.81 ± 63.46 vs 93.19 ± 37.04 ; 1.89 ± 0.91 vs 1.35 ± 0.99 , $P < .05$)

TABLE 2 Clinical-pathological factors of patients with GC in the pre-NAC NLR and pre-NAC PLR groups

Parameters (pre-NAC)	Number			Number		
	NLR (n = 91)		P value	PLR (n = 91)		P value
	Low (n = 29)	High (n = 62)		Low (n = 71)	High (n = 20)	
Age (y)						
≤60	23	42	.225	50	15	.689
>60	6	20		21	5	
Gender						
Male	24	45	.291	57	12	.115
Female	5	17		14	8	
Response evaluation						
PR	12	21	.522	28	5	.292
SD+PD	17	40		43	14	
Tumor location						
Upper third	5	18	.475	19	4	.794
Middle third	12	23		26	9	
Lower third	12	21		26	7	
Pathological type						
Well moderately differentiated	14	20	.141	28	6	.441
Poorly differentiated Signet ring cell or Mucinous	15	42		43	14	
Systemic therapy						
Docetaxel, oxaliplatin and fluorouracil	36	13	.257	36	13	.257
Other, fluorouracil	35	7		35	7	
Tumor regression score						
0-2	18	34	.516	41	11	.826
3	11	28		30	9	
Tumor size (cm)						
≤5	18	35	.613	42	11	.739
>5	11	27		29	9	
Primary tumor (T)						
T0-T3	9	15	.490	18	6	.677
T4	20	47		53	14	
Regional lymph nodes (N)						
N0-N2	18	41	.705	44	15	.281
N3	11	21	.942	27	5	
Neural invasion						
Yes	2	6	.969	6	2	.829
No	27	56		65	18	
Lymphatic-vascular invasion						
Yes	17	32	.532	13	3	.991
No	12	30		58	17	
Tumor stage						
Tis-II	9	17	.722	20	6	.873
III	20	45		51	14	

TABLE 3 Clinical-pathological factors of patients with GC in the aft-NAC NLR and aft-NAC PLR groups

Parameters (aft-NAC)	Number		P value	Number		P value
	NLR (n = 91)			PLR (n = 91)		
	Low (n = 34)	High (n = 57)		Low (n = 67)	High (n = 24)	
Age (y)						
≤60	21	44	.115	49	16	.547
>60	13	13		18	8	
Gender						
Male	26	43	.911	53	16	.222
Female	8	14		14	8	
Response evaluation						
PR	14	20	.561	25	9	.987
SD+PD	20	37		42	15	
Tumor location						
Upper third	7	16	.626	17	6	.989
Middle third	15	20		26	9	
Lower third	12	21		24	9	
Pathological type						
Well Moderately differentiated	14	20	.561	24	10	.611
Poorly differentiated Signet ring cell or Mucinous	20	37		43	14	
Systemic therapy						
Docetaxel, oxaliplatin and fluorouracil	21	28	.242	36	13	.971
Other, fluorouracil	13	29		31	11	
Tumor regression score						
0-2	25	27	.015	42	10	.074
3	9	30		25	14	
Tumor size (cm)						
5	23	30	.16	40	13	.637
>5	11	27		27	11	
Primary tumor (T)						
T0-T3	10	14	.611	18	6	.859
T4	24	43		49	18	
Regional lymph nodes (N)						
N0-N2	24	35	.375	40	19	.087
N3	10	22		27	5	
Neural invasion						
Yes	2	6	.708	6	2	.926
No	32	51		61	22	
Lymphatic-vascular invasion						
Yes	3	13	.09	9	7	.154
No	31	44		58	17	
Tumor stage						
Tis-II	12	14	.273	20	6	.652
III	22	43		47	18	

TABLE 4 Univariate analysis of clinicopathological variables in relation to OS in patients with GC after NAC undergoing radical resection

	Wald	HR	95.0% CI for HR		P
			Lower	Upper	
Gender	1.379	0.657	0.326	1.325	.240
Neural invasion	0.382	1.481	0.426	5.145	.536
Lymphatic-vascular invasion	0.727	1.459	0.612	3.477	.394
Age	0.018	0.956	0.496	1.842	.893
Primary tumor (T)	0.847	0.652	0.262	1.621	.357
Regional lymph nodes (N)	1.206	1.430	0.755	2.708	.272
Tumor Regression Score	2.635	1.886	0.877	4.056	.105
ypTNM	0.073	1.148	0.421	3.134	.787
Response evaluation	0.989	0.750	0.426	1.322	.320
Pathological type	0.334	1.193	0.656	2.170	.563
Tumor location	0.204	0.917	0.628	1.337	.651
pre-NTC PLR	6.965	2.721	1.294	5.724	.008
pre-NTC NLR	1.534	1.548	0.775	3.091	.216
aft-NTC PLR	0.727	1.358	0.672	2.743	.394
aft-NTC NLR	0.121	0.887	0.453	1.740	.728
Tumor size (cm)	0.126	0.880	0.436	1.779	.722

evaluation, tumor location, pathological type, pathological type, systemic therapy, tumor size, tumor regression score, primary tumor (T), regional lymph nodes (N), neural invasion, lymphatic-vascular invasion, tumor stage (Table 2).

The results demonstrated that aft-NAC NLR and aft-NAC PLR did not show any significant difference in age, gender, response evaluation, tumor location, pathological type, pathological type, primary tumor (T), regional lymph nodes (N), neural invasion, lymphatic-vascular invasion, tumor stage. Moreover, we found that the low aft-NAC NLR patients had the higher rate of tumor regression than the patients with high aft-NAC NLR ($P = .015$) after neoadjuvant chemotherapy but before surgery (Table 3). The univariate analyses showed that pre-NAC PLR^{low} patients had better OS ($P < .05$; Table 4). Worse OS was seen in high pre-NAC PLR patients than those with low pre-NAC PLR. (median OS 15 months vs 33 months; $P < .05$). The multivariate Cox proportional hazard regression analysis indicated that pre-PLR was an independent prognostic factor (HR = 0.353, 95% CI: 0.162-0.769, $P < 0.05$) (Table 5).

3.3 | PLR variation correlation with OS

Of the 91 patients, 22 patients with pre-NAC NLR^{low}→aft-NAC NLR^{low} had better mean OS than the 38 patients with pre-NAC

TABLE 5 Multivariate analysis (Cox proportional hazard model) of overall survival for patients with gastric cancer after NAC undergoing radical resection

	Wald	HR	95.0% CI for HR		P
			Lower	Upper	
Gender	1.297	1.504	0.745	3.034	.255
Neural invasion	0.442	0.652	0.185	2.300	.506
Lymphatic-vascular invasion	0.712	0.688	0.288	1.641	.399
Age	0.010	1.035	0.536	1.997	.919
Primary tumor (T)	0.624	1.466	0.567	3.788	.430
Regional lymph nodes (N)	1.180	0.702	0.371	1.329	.277
Tumor Regression Score	2.699	0.526	0.245	1.132	.100
ypTNM	0.033	0.908	0.322	2.560	.856
Response evaluation	1.088	1.358	0.764	2.413	.297
Pathological type	0.399	0.821	0.446	1.513	.528
Tumor location	0.327				.849
Middle third	0.266	1.223	0.569	2.625	.606
Lower third	0.001	0.991	0.510	1.925	.978
pre-NTC PLR	6.859	0.353	0.162	0.769	.009
pre-NTC NLR	1.437	0.654	0.326	1.310	.231
aft-NTC PLR	0.550	0.760	0.369	1.568	.458
aft-NTC NLR	0.120	1.126	0.575	2.203	.729
Tumor size (cm)	0.065	1.099	0.532	2.272	.799

NLR^{hi}→aft-NAC NLR^{low} (40.0 vs 28.9 months; $P = .048$), and similar mean OS as the 24 patients with pre-NAC NLR^{hi}→aft-NAC NLR^{hi} (40.0 vs 27.7 months; $P = .013$). Forty-two patients with pre-NAC PLR^{low}→aft-NAC PLR^{low} had better mean OS than the eight patients with pre-NAC PLR^{low}→aft-NAC PLR^{hi} (33.5 vs 19.5 months; $P = .032$), and mean OS as the 25 patients with pre-NAC PLR^{hi}→aft-NAC PLR^{low} (19.5 vs 35.3 months; $P = .009$). Twenty-five patients with pre-NAC PLR^{hi}→aft-NAC PLR^{low} had better mean OS than the 16 patients with pre-NAC PLR^{hi}→aft-NAC PLR^{hi} (35.3 vs 22.6 months; $P = .026$) before both chemotherapy and surgery. Aft-NAC PLR levels lower are associated with better OS. Aft-NAC PLR levels higher are associated with worse OS (Table 6, Figure 4).

4 | DISCUSSION

Gastric cancer is usually diagnosed at a locally advanced stage. Multimodal therapy, including perioperative chemotherapy, targeted therapy, and radiotherapy, has greatly improved the survival of

TABLE 6 Survival of patients according to NLR and PLR before both neoadjuvant chemotherapy and surgery

Changed by chemotherapy ^a	Number of patient	OS mean	Changed by chemotherapy	Number of patient	OS mean	P value
pre-NAC NLR ^{low} → aft-NAC NLR ^{low}	22	40	pre-NAC NLR ^{low} → aft-NAC NLR ^{hi}	7	30.1	.198
			pre-NAC NLR ^{hi} → aft-NAC NLR ^{low}	38	28.9	.048
			pre-NAC NLR ^{hi} → aft-NAC NLR ^{hi}	24	27.7	.013
pre-NAC NLR ^{low} → aft-NAC NLR ^{hi}	7	30.1	pre-NAC NLR ^{hi} → aft-NAC NLR ^{low}	38	28.9	.763
			pre-NAC NLR ^{hi} → aft-NAC NLR ^{hi}	24	27.7	.532
pre-NAC NLR ^{hi} → aft-NAC NLR ^{low}	38	28.9	pre-NAC NLR ^{hi} → aft-NAC NLR ^{hi}			.96
pre-NAC PLR ^{low} → aft-NAC PLR ^{low}	42	33.5	pre-NAC PLR ^{low} → aft-NAC PLR ^{hi}	8	19.5	.032
			pre-NAC PLR ^{hi} → aft-NAC PLR ^{low}	25	35.3	.839
			pre-NAC PLR ^{hi} → aft-NAC PLR ^{hi}	16	22.6	.066
pre-NAC PLR ^{low} → aft-NAC PLR ^{hi}	8	19.5	pre-NAC PLR ^{hi} → aft-NAC PLR ^{low}	25	35.3	.009
			pre-NAC PLR ^{hi} → aft-NAC PLR ^{hi}	16	22.6	.602
pre-NAC PLR ^{hi} → aft-NAC PLR ^{low}	25	35.3	pre-NAC PLR ^{hi} → aft-NAC PLR ^{hi}			.026

^aChange between pre-NAC and aft-NAC NLR, PLR.

advanced gastric cancer patients. Two studies demonstrated that neoadjuvant chemotherapy greatly improved PFS and OS, and the five-year survival rates in those who received perioperative chemotherapy and the surgery group were significantly different.^{15,16} Neoadjuvant chemotherapy improved the curative resection rate.¹⁶ These results established neoadjuvant chemotherapy as new alternative treatment for patients with locally advanced gastric cancer. How can we find those patients mostly getting benefit from NAC treatment?

In the last decade, more and more studies have reported that the systemic inflammatory response is closely related to a poor outcome in many types of tumor.¹⁷⁻²² The accumulating increase in NLR and PLR may be caused by peritumoral inflammation produced by a huge amount of cancer cells in patients with advanced cancer. Many studies demonstrate that PLR and NLR are useful biomarkers to predict prognostic outcome in unresectable gastric cancer, resectable gastric cancer, or gastric cancer patients who received chemotherapy.²³⁻²⁵ However, whether they were associated with locally advanced gastric cancer patients treated with NAC followed by radical gastrectomy is rarely reported.

Our study showed that high pre-NAC PLR was significantly worse for OS than that in the low group in locally advanced gastric cancer patients who received NAC followed by gastrectomy ($P < .05$). Kishietal²⁶ reported that normalization of high NLR by chemotherapy could improve survival. In this study, we found that high NLR values were normalized after NAC in 38 patients. But the normalization of high NLR did not improve OS. However, high PLR values were normalized after NAC in 25 patients, and that normalization of high PLR observed improved OS, with patients in whom it occurred having similar survival to those with low PLR before and after NAC. Low PLR values were elevated after NAC in eight patients, and that the elevation of low PLR indicated worse OS, with patients in whom it occurred having similar survival to those with high PLR before and after NAC.

A meta-analysis²⁷ that includes 12 studies showed that preoperative NLR is an independent predictor of survival of epithelial ovarian cancer. Low NLR had better OS in ovarian cancer patients

compared with high NLR (summarized HR = 1.72; 95% CI = 1.18-2.51). Studies demonstrated that high prechemotherapy NLR and high pre-chemotherapy PLR independently predicted worse prognostic factor for OS in gastric cancer patients who received neoadjuvant chemotherapy.^{11,28} Our findings pre-NAC PLR independently predicted worse prognostic factor for OS in gastric cancer patients with NAC. Furthermore, we also found that PLR level variation after NAC predicted OS. But pre-NAC NLR, aft-NAC PLR, and aft-NAC NLR lost its meaning as a independently prognostic factor.

5 | CONCLUSIONS

Pre-NAC PLR could be an easily measured, convenient prognostic indicator for locally advanced gastric cancer patients treated with NAC. Patients with high pre-NAC PLR values need multimodal therapy. Aft-NAC PLR level was negatively correlated with survival prognosis. Aft-NAC NLR level may help clinicians to find those patients with gastric cancer who will benefit from NAC, and aft-NAC PLR level variation may represent prognostic indicator.

The major limitations of our research were a retrospective study and insufficient number of patients. However, we found that measurement of pre-NAC PLR using a quick, low-cost, and easy test based on peripheral blood count can be used as a clinical marker and predict prognosis in gastric cancer patients. Aft-NAC PLR level variation may represent prognostic indicator in patients with NAC gastric cancer. (The literature available data in this field is limited). But our findings will need to be confirmed with randomized, prospective, larger studies.

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FIGURE 4 Overall survival of patients based on changes in PLR and NLR after neoadjuvant chemotherapy

AVAILABILITY OF DATA AND MATERIALS

The work is original research that has not been published previously and not under consideration for publication elsewhere, in whole or in part. Data are shared during the current study.

AUTHORS' CONTRIBUTIONS

XQ supervised this study and revised the article. WPG interpreted data and statistical analyses and drafted the article. LZ, ZGD, YD, YGL, and CM were responsible for collecting relevant clinicopathological data and statistical analyses. All authors read and approved the final work.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Shandong cancer hospital affiliated to Shandong University ethics committee approved this article.

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