Preoperative Platelet-Lymphocyte Ratio (PLR) as a prognostic inflammation biomarker in Asian HIV-infected patients with gastric cancer: a single-center study

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Abstract

Background The serum systemic inflammation biomarkers have been established as predictors of prognosis in gastric cancer (GC) patients, but their prognostic value in human immunodeficiency virus (HIV)-infected patients with GC has not been well studied. This retrospective study aimed to evaluate the prognostic value of preoperative systemic inflammation biomarkers in Asian HIV-infected patients with GC.

Methods We retrospectively analyzed 41 HIV-infected GC patients who underwent surgery between January 2015 and December 2021 at the Shanghai Public Health Clinical Center. Preoperative systemic inflammation biomarkers were measured and patients were divided into two groups based on the optimal cut-off value. Overall survival (OS) and progression-free survival (PFS) were measured using the Kaplan–Meier method and the log-rank test. Multivariate analysis of variables was performed using the Cox proportional regression model. As a comparison, 127 GC patients without HIV infection were also recruited.

Results The median age of the 41 patients included in the study was 59 years, with 39 males and two females. The follow-up period for OS and PFS ranged from 3 to 94 months. The cumulative three-year OS rate was 46.0%, and the cumulative three-year PFS rate was 44%. HIV-infected GC patients had worse clinical outcomes compared to the normal GC population. The optimal cut-off value for preoperative platelet to lymphocyte ratio (PLR) was 199 in HIV-infected GC patients. Multivariate Cox regression analysis revealed that a low PLR was an independent predictor of better OS and PFS (OS: HR = 0.038, 95% CI: 0.006–0.258, $P < 0.001$; PFS: HR = 0.027, 95% CI: 0.004–0.201, $P < 0.001$). Furthermore, higher preoperative PLR in HIV-infected GC was significantly associated with lower BMI, hemoglobin, albumin, CD4 + T, CD8 + T, and CD3 + T cell counts.

Conclusion The preoperative PLR is an easily measurable immune biomarker that may provide useful prognostic information in HIV-infected GC patients. Our findings suggest that PLR could be a valuable clinical tool for guiding treatment decisions in this population.

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Introduction

Gastric cancer (GC) remains a major cause of cancer-related mortality globally [1]. While D2 gastrectomy and chemotherapy are the standard treatment, the prognosis for advanced stages is still unsatisfactory [2, 3]. In recent years, there has been an increase in GC cases among patients infected with the human immunodeficiency virus (HIV) [4, 5]. *H.pylori* infection is a significant risk factor for GC, particularly in East-Asia, and HIV-induced immunodeficiency is thought to exacerbate this risk [4, 5]. Furthermore, HIV infection impairs the HIV-specific CD4 + T and CD8 + T lymphocytes, resulting in the inability of the host immune system to control HIV, which may lead to poorer outcomes of HIV-related cancers [6]. Early identification of the worse prognostic subgroup of HIV-infected GC is crucial for patients' survival [7].

Although molecular subtypes had the potential to identify GC patients with a worse prognosis, the results based on genomic data made them difficult to use in clinical practice. In addition to cancer-associated systemic inflammation, which is an important predictor of prognosis in GC patients, systemic inflammation biomarkers such as the neutrophil to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), platelet to lymphocyte ratio (PLR), prognostic nutritional index (PNI), systemic immune-inflammation index (SII), and systemic inflammation score (SIS) have been shown to be useful prognostic factors in numerous studies [8–11]. Building on previous research that suggests combination antiretroviral therapy (cART) can restore immune function in HIV-infected individuals [12] and that there may be no difference in tumor-infiltrating lymphocytes between HIV-positive and HIV-negative cancer [13], it may be feasible to evaluate systemic inflammatory biomarkers in HIV-infected GC patients. However, to our knowledge, no research has been conducted on the relationship between preoperative systemic inflammation biomarkers and HIV-infected GC. Early identification of these clinically feasible predictors could improve patients' chances of survival. Therefore, this study aims to evaluate the prognostic value of systemic inflammation biomarkers in HIV-related GC patients.

Methods

Patients

We conducted a retrospective study of 41 HIV-infected patients with preoperative pathologically diagnosed gastric adenocarcinoma who underwent gastrectomy (with or without standard lymphadenectomy) between January 2015 and December 2021 at Shanghai Public Health Clinical Center (SHPHC) in China. The study included characteristics such as gender, age, body mass index (BMI), disease history (hypertension, diabetes, tuberculosis infection, smoking, and alcohol abuse), duration of HIV infection and treatment (cART), preoperative tests (routine laboratory tests, tumor markers, and plasma lipids), tumor location, pathological stage (using the AJCC 8th edition), human epidermal growth factor receptor 2 (Her2) status (using immunohistochemical results of Her2 proteins), and surgical resection with or without tumor residuals. For comparison, we also retrospectively recruited 127 non-HIV infected patients diagnosed with gastric adenocarcinoma who underwent surgery treatment in our hospital during the same period. This study was conducted in accordance with the Declaration of Helsinki and approved by the Shanghai Public Health Clinical Center.

Follow-up

Regular follow-ups were conducted every three months during the first year after surgery and every six months for the following two years. Patients were admitted to the hospital for routine blood examination, enhanced chest and abdominal CT scans, and other necessary tests. After three years, the follow-up visits were scheduled annually. Progression was defined as the first detection of local recurrence, enlargement of unresected tumor lesions, and distant organ metastases. Death was confirmed through relevant information provided by the hospital or by notification from the patient's family during a telephone follow-up. The last censoring date for evaluating survival time was March 2022. Overall survival (OS) was defined as the time interval from surgery to death from any cause or the last censoring date. Progression-free survival (PFS) was defined as the time interval from surgery to progression or the last censoring date. Two of the 41 patients were lost to follow-up during the study period.

Definition of inflammation-based biomakers

The laboratory tests from each patient were obtained within 1-week before surgical resection of the primary tumour. In recent reports, neutrophil (N; ×10^9/L) to lymphocyte (L; ×10^9/L) ratio (NLR), lymphocyte (L; ×10^9/L) to monocyte (M; ×10^9/L) ratio (LMR) and platelet (P; ×10^9/L) to lymphocyte (L; ×10^9/L)

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ratio (PLR) had been evaluated as useful prognostic biomarkers of GC patients [14, 15]. The prognostic nutritional index (PNI) was calculated as serum albumin value $(g/L) + 5 \times$ lymphocyte $(L; \times 10^9/L)$ [16]. The systemic immune-inflammation index (SII) was calculated based on platelet $(P; \times 10^9/L)$, neutrophil $(N; \times 10^9/L)$, and lymphocyte $(L; \times 10^9/L)$ blood counts using the following formula: $SII = P \times N/L$ [17]. The systemic inflammation score (SIS) definition was based on the combination of the preoperative albumin level and LMR [9]. The SIS was defined as follows: patients with albumin level < 40 g/L and LMR < 4.44 were assigned a score of 2; patients with either albumin level ≥ 40 g/L or LMR ≥ 4.44 were assigned a score of 1; and patients with both albumin level ≥ 40 g/L and LMR ≥ 4.44 were assigned a score of 0.

Statistics

Categorical variables were reported as integers and proportions, and continuous variables were reported as medians, means (standard deviations), and maximum ranges. We used Wilcoxon rank-sum test for continuous variables and chi-square for classified variables. To analyze the survival differences, patients were categorized into two group based on the continuous variables best-cutoff using the "MaxStat" R package (maximally selected log-rank statistics) [18]. The Kaplan–Meier survival curves were constructed according to differences in group, which were analyzed using the log-rank test. Variables that significantly affected survival were estimated by univariate and multivariate analysis according to the Cox regression model. Stratified survival analysis results were discussed based on clinicopathological features. A two-tailed *P* < 0.05 was considered statistically significant. All statistical analyses were determined using R software (version 3.6.3, http://www.r-project.org).

Results

Patient characteristics

The clinicopathological characteristics of 41 HIV-infected patients with gastric cancer (GC) who underwent gastrectomy are summarized in Table S1. Of the 41 patients, 39 were male and two were female, with a median age of 59 years (range: 44–76 years) at the time of surgery. The median body mass index (BMI) was 21.1 (range: 15.1–26.6), and 22.0% of patients had a history of hypertension, 17.1% had diabetes, 4.9% had tuberculosis infection, and 17.1% had hyperlipidemia. Eight patients (19.5%) had a history of smoking, and five (12.2%) had a history of alcohol abuse. The median duration of HIV infection was one month, and most patients had not received anti-HIV

treatment. The preoperative test showed a mean CD4 + T lymphocyte count of 323.4 cell/μL and a CD8 + T lymphocyte count of 663.3 cell/μL. Based on postoperative pathology, 7 patients (17.1%) had an upper gastric tumor, 31 (75.6%) had a middle gastric tumor, and 3 (7.3%) had a tumor in the lower part of the stomach. According to the eighth edition of the AJCC TNM staging system, 9 (22.0%), 8 (19.5%), 19 (46.3%), and 5 (12.2%) of patients had stages I, II, III, and IV, respectively.

Survival outcomes

The follow-up time for overall survival (OS) and progression-free survival (PFS) ranged from 3 to 94 months. The cumulative three-year OS rate was 46.0%, and the cumulative three-year PFS rate was 44%. HIV-infected GC patients had significantly worse OS and PFS outcomes compared to non-HIV infected GC patients (Figure S1). Univariate analysis identified several inflammatory indicators associated with OS, including PLR, PNI, and Alb level (*P* < 0.05, Table 1). Variables such as BMI, history of signet ring cell, R0 resection, and TNM stage also significantly affected OS (*P* < 0.05, Table 1). In multivariate analyses, PLR ≤ 199.0 (HR: 0.038, 95% CI: 0.006–0.258), histology of signet ring cell (HR: 41.178, 95% CI: 6.287–269.722), and no R0 resection (HR: 277.461, 95% CI: 10.475–7349.318) were associated with OS (both *P* < 0.05, Table 1). Additionally, the prognostic effect of NLR, PLR, PNI, SII, BMI, histology of signet ring cell, R0 resection, TNM stage, and Alb level was significantly related to PFS in univariate analysis (Table 2). In multivariate analysis of PFS, PLR ≤ 199.0 (HR: 0.027, 95% CI: 0.004–0.201), histology of signet ring cell (HR: 42.638, 95% CI: 6.245–291.092), and no R0 resection (HR: 136.565, 95% CI: 8.048–2317.405) were independently associated with PFS outcomes (both *P* < 0.05, Table 2). In non-HIV infected GC patients, inflammatory indicators such as PLR were not associated with OS (Table S2) or PFS (Table S3) in univariate analysis. The Kaplan–Meier survival analysis and log-rank tests were conducted to investigate the association between PLR groups and postoperative survival time. Our results showed that PLR (> 199) was significantly associated with decreased OS and PFS (Fig. 1). We also evaluated the OS and PFS subgroups of HIV-infected GC patients. The Kaplan–Meier curves revealed that CD3 + count > 1022 cells/μL, both CD8 + groups, and CD4 + count > 323.4 cells/μL in the high PLR group (> 199) were closely associated with poor OS (Fig. 2). Additionally, CD3 + count > 998.8 cells/μL, both CD8 + groups, CD4 + count > 291.3 cells/μL, and CD4/CD8 > 0.6 in the high PLR group (> 199) were also associated with poor PFS rate (Fig. 3).

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Table 1 Univariate and multivariate analysis of clinicopathologic variables in relation to OS in patients living with HIV for GC

Clinicopathological features	Univariate analysis HR (95% CI)	P value	Multivariate analysis HR (95% CI)	P value
Gender				
Female	Reference			
Male	0(0-Inf)	0.998		
Age	0.973(0.915–1.033)	0.368		
BMI	0.763(0.634–0.918)	0.004	0.799(0.59–1.082)	0.147
Hypertension				
Yes	0.408(0.094–1.771)	0.231		
DM				
Yes	1.497(0.496–4.52)	0.474		
TB				
Yes	0.962(0.127–7.268)	0.97		
Smoking				
Yes	0.195(0.026–1.461)	0.112		
Alcohol abuse				
Yes	0.44(0.059–3.31)	0.425		
Hyperlipidemia				
Yes	0.763(0.222–2.622)	0.668		
Duration of HIV infection	1.001(0.988–1.014)	0.877		
Duration of HIV treatment	1.001(0.988–1.014)	0.882		
Tumor Location				
Upper	Reference			
Middle	0.892(0.256–3.111)	0.858		
Lower	1.609(0.267–9.696)	0.604		
Histology				
Signet ring cell	5.227(2.013–13.573)	< 0.001	41.178(6.287–269.722)	< 0.001
R0 rescetion				
No	5.204(1.678–16.141)	0.004	277.461(10.475–7349.318)	< 0.001
Her2 status				
0	Reference			
1+	0.728(0.273–1.941)	0.525		
2+	0.256(0.033–1.977)	0.192		
AJCC stage				
I-II	Reference		Reference	
III-IV	6.199(1.922–19.996)	0.002	0.314(0.034–2.867)	0.305
ALB (g/L)				
>38.1	Reference		Reference	
≤38.1	4.192(1.599–10.991)	0.004	10.715(0.632–181.541)	0.1
CD8 count (per ul)				
>661	Reference			
≤661	0.603(0.24–1.514)	0.281		
CD4 count (per ul)				
>348	Reference			
≤348	2.646(0.943–7.425)	0.065		
CD4/CD8				
>0.71	Reference			
≤0.71	2.062(0.738–5.762)	0.167		
NLR				
>3.9	Reference			

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Table 1 (continued)

Clinicopathological features	Univariate analysis HR (95% CI)	P value	Multivariate analysis HR (95% CI)	P value
≤3.9	0.416(0.157–1.102)	0.078		
LMR				
>6.5	Reference			
≤6.5	3.325(0.442–24.99)	0.243		
PLR				
>199.0	Reference		Reference	
≤199.0	0.365(0.147–0.903)	0.029	0.038(0.006–0.258)	<0.001
PNI				
>43.4	Reference		Reference	
≤43.4	3.05(1.216–7.653)	0.017	0.261(0.016–4.356)	0.349
SII				
>935	Reference			
≤935	0.356(0.126–1.006)	0.051		
SIS				
0	Reference			
1	0.704(0.198–2.502)	0.587		
2	1.854(0.566–6.074)	0.308		

DM diabetes mellitus, *TB* tuberculosis infection status, *Her2 status* immunohistochemical staining of Her-2, *ALB* serum albumin, *NLR* neutrophil–lymphocyte ratio, *LMR* lymphocyte-monocyte ratio, *PLR* platelet-lymphocyte ratio, *PNI* prognostic nutritional index, *SII* systemic immune-inflammation index, *SIS* systemic inflammation score

The relationship between PLR and clinical characteristics

The relationship between clinicopathological variables and PLR was summarized in Table 3. Higher PLR values were associated with lower BMI (19.7 vs 21.7, $P = 0.005$), a longer duration of HIV treatment (32.2 months vs 20.9 months, $P = 0.113$), and a higher tendency for advanced stages (III-IV: 76.9% vs 50.0%, $P = 0.173$). The comparison of PLR with preoperative laboratory tests was shown in Table 4. In addition to platelet and lymphocyte counts, mean values of hemoglobin (126.9 g/L vs 104.2 g/L, $P = 0.008$), albumin (39.7 g/L vs 36.5 g/L, $P = 0.041$), CD3 + cells count (1196.1 per uL vs 646.9 per uL), CD4 + cells count (373 per uL vs 216.5 per uL), and CD8 + cells counts (784.2 per uL vs 402.8 per uL) were significantly higher in the low PLR group than in the high PLR group. However, neutrophil counts were significantly higher in the high PLR group (4.7×10^3/uL) than in the low PLR group (3×10^3/uL).

Discussion

During the era of combination antiretroviral therapy (cART), the incidence of infection-related cancers increased in people living with HIV (PLWH) compared to the general population [4, 5, 19]. The longer life expectancy of PLWH exposed them to chronic infections such as herpes virus 8, human papillomavirus, hepatitis viruses, and *H. pylori*, leading to chronic inflammation and cancer development. However, common epithelial cancers without chronic pathogenic infections did not occur at higher rates, including colorectal, breast, and prostate cancers [4, 5, 20]. *H.pylori* infection was a major risk factor for gastric cancer in the general population, and due to dietary habits, its incidence may be increasing in PLWH in China. Reports suggested that PLWH with gastrointestinal cancer were less likely to receive cancer screening or regular treatment, leading to higher mortality than HIV-negative patients [7, 19]. Furthermore, few studies had examined the association of HIV status with gastric cancer treatment [21]. Our study found that HIV-infected gastric cancer patients had a three-year overall survival rate of only 46%, much lower than the average [3] and GC patients in the general population (Figure S1). Therefore, easily achievable prognostic predictors for patients with HIV-infected GC are needed, so that subgroups of patients with poorer prognoses can be identified earlier, and interventions and follow-up can be initiated. The preoperative systemic inflammation biomarker has proven reliable in various cancers, making it worthwhile to investigate in HIV-positive GC patients.

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Table 2 Univariate and multivariate analysis of clinicopathologic variables in relation to PFS in patients living with HIV for GC

Clinicopathological features	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Gender				
Female	Reference			
Male	0(0-Inf)	0.998		
Age	0.961(0.904–1.02)	0.192		
BMI	0.763(0.641–0.909)	0.002	0.884(0.684–1.142)	0.346
Hypertension				
Yes	0.363(0.084–1.572)	0.176		
DM				
Yes	1.282(0.428–3.839)	0.657		
TB				
Yes	0.824(0.109–6.21)	0.851		
Smoking				
Yes	0.177(0.024–1.325)	0.092		
Alcohol abuse				
Yes	0.399(0.053–2.991)	0.371		
Hyperlipidemia				
Yes	0.805(0.235–2.753)	0.729		
Duration of HIV infection	1.003(0.992–1.015)	0.586		
Duration of HIV treatment	1.003(0.991–1.016)	0.58		
Tumor Location				
Upper	Reference			
Middle	0.635(0.208–1.935)	0.424		
Lower	1.14(0.208–6.247)	0.88		
Histology				
Signet ring cell	3.939(1.578–9.836)	0.003	42.638(6.245–291.092)	< 0.001
R0 rescetion				
No	4.245(1.382–13.038)	0.012	136.565(8.048–2317.405)	< 0.001
Her2 status				
0	Reference			
1+	0.806(0.302–2.149)	0.667		
2+	0.563(0.126–2.521)	0.453		
AJCC stage				
I-II	Reference		Reference	
III-IV	6.297(1.96–20.228)	0.002	0.766(0.135–4.341)	0.764
ALB (g/L)				
> 38.1	Reference		Reference	
≤ 38.1	4.041(1.553–10.515)	0.004	3.73(0.309–45.103)	0.301
CD8 count (per ul)				
> 661	Reference			
≤ 661	0.741(0.302–1.822)	0.514		
CD4 count (per ul)				
> 348	Reference			
≤ 348	2.667(0.957–7.436)	0.061		
CD4/CD8				
> 0.71	Reference			
≤ 0.71	1.52(0.581–3.978)	0.394		
NLR				
> 3.9	Reference		Reference	

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Table 2 (continued)

Clinicopathological features	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
≤ 3.9	0.346(0.137–0.873)	0.025	0.109(0.008–1.56)	0.103
LMR				
> 6.5	Reference			
≤ 6.5	3.538(0.472–26.497)	0.219		
PLR				
> 199.0	Reference		Reference	
≤ 199.0	0.298(0.123–0.723)	0.007	0.027(0.004–0.201)	< 0.001
PNI				
> 43.4	Reference		Reference	
≤ 43.4	3.129(1.265–7.737)	0.014	0.756(0.057–10.062)	0.832
SII				
> 935	Reference		Reference	
≤ 935	0.275(0.104–0.729)	0.009	14.322(0.783–261.811)	0.073
SIS				
0	Reference			
1	0.555(0.156–1.978)	0.364		
2	1.667(0.515–5.393)	0.393		

DM diabetes mellitus, *TB* tuberculosis infection status, *Her2 status* immunohistochemical staining of Her-2, *ALB* serum albumin, *NLR* neutrophil–lymphocyte ratio, *LMR* lymphocyte-monocyte ratio, *PLR* platelet-lymphocyte ratio, *PNI* prognostic nutritional index, *SII* systemic immune-inflammation index, *SIS* systemic inflammation score
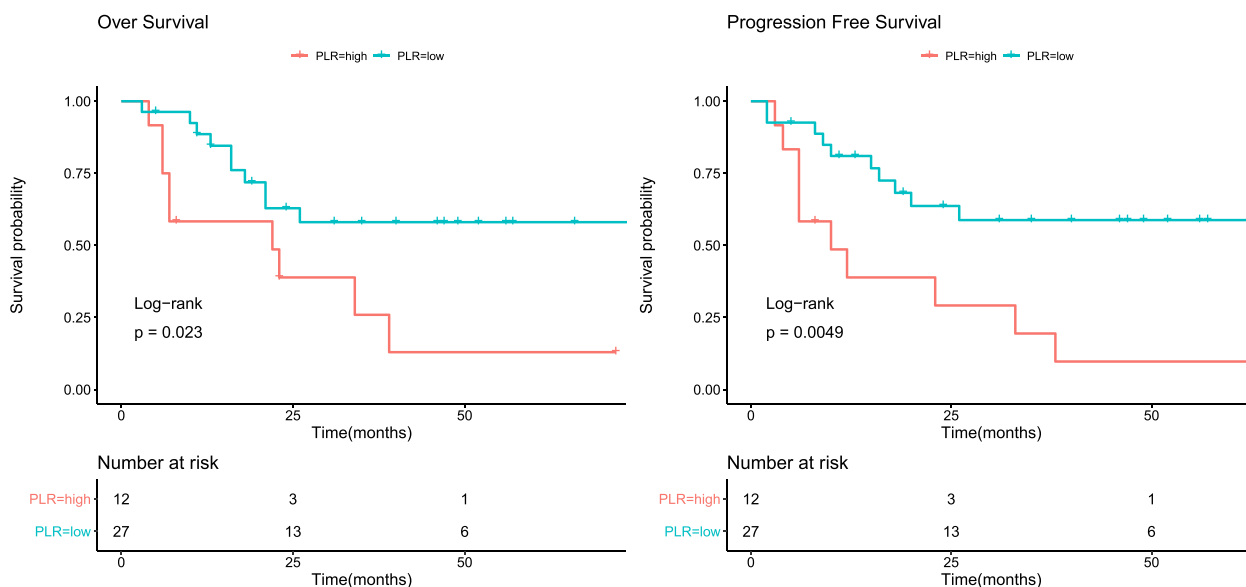

Fig. 1 The Kaplan–Meier survival analysis of overall survival and progression free survival according to PLR in HIV-related GC

This study investigated the prognostic value of six systemic inflammation biomarkers (NLR, LMR, PLR, PNI, SII, and SIS) in HIV-infected gastric cancer (GC) patients and compared their prognostic value with non-HIV-infected GC patients at the same center (Table S2 and 3). Previous studies have shown that systemic inflammation biomarkers are useful prognostic factors of gastrointestinal carcinomas [10, 15, 22, 23]. Our results revealed that among surgically treated HIV-infected GC patients, those with high platelet to lymphocyte ratio
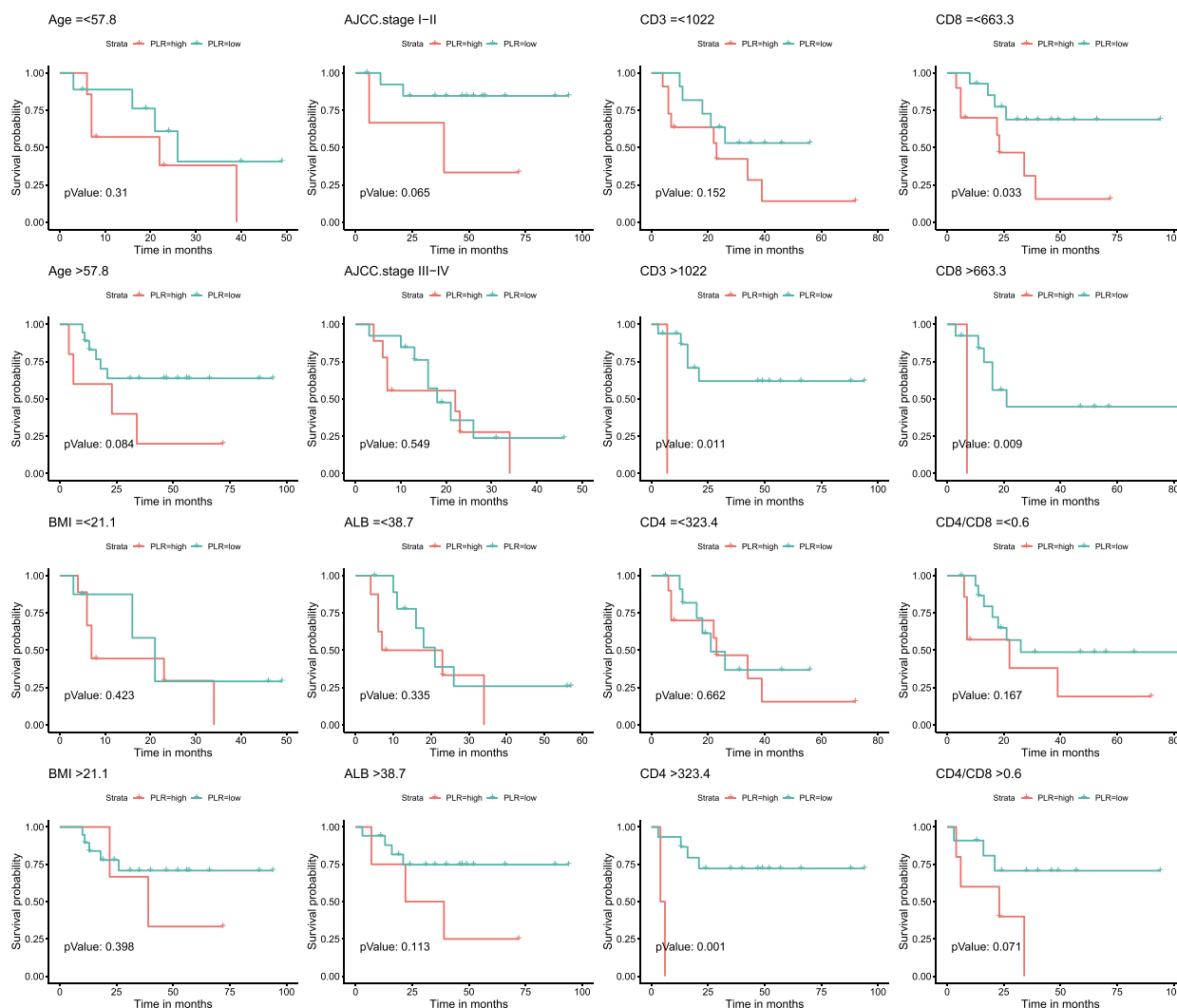
Fig. 2 Subgroup analysis of OS based on age, BMI, AJCC stage, albumin level, CD3 cell counts, CD4 cell counts, CD8 cell counts and CD4/CD8 ratio

(PLR) had significantly shorter overall survival (OS) and progression-free survival (PFS) than those with low PLR. Furthermore, multivariate analysis demonstrated that PLR was an independent factor influencing survival outcomes. The findings emphasize the importance of considering systemic inflammation biomarkers, particularly PLR, as prognostic predictors in HIV-infected GC patients.

Lymphocytes play a crucial role in the peritumoral inflammatory response, which reflects the cancer immunosurveillance in the host [24]. Low serum lymphocyte counts have been linked to poor outcomes in patients with gastric cancer (GC) [25]. Platelets, the typical blood cell component responsible for the inflammatory response, are often increased in patients with solid tumors associated with chronic inflammation [26]. In the tumor microenvironment, platelets can interact directly with cancer cells and promote tumorigenesis by releasing pro-angiogenic proteins such as vascular epidermal growth factor and transforming growth factor β [27]. They can also protect circulating tumor cells from host immune surveillance by creating a defense barrier around them [17]. Thus, a higher platelet to lymphocyte ratio (PLR) indicates a greater susceptibility of tumors to immune escape and progression. The PLR has been found to be negatively correlated with patients' survival outcomes in gastric [28], lung [29], urological [30], colorectal [31] and breast cancer [32]. Currently, PLR has significant references for the surgical selection and prognosis of HIV-infected GC patients.
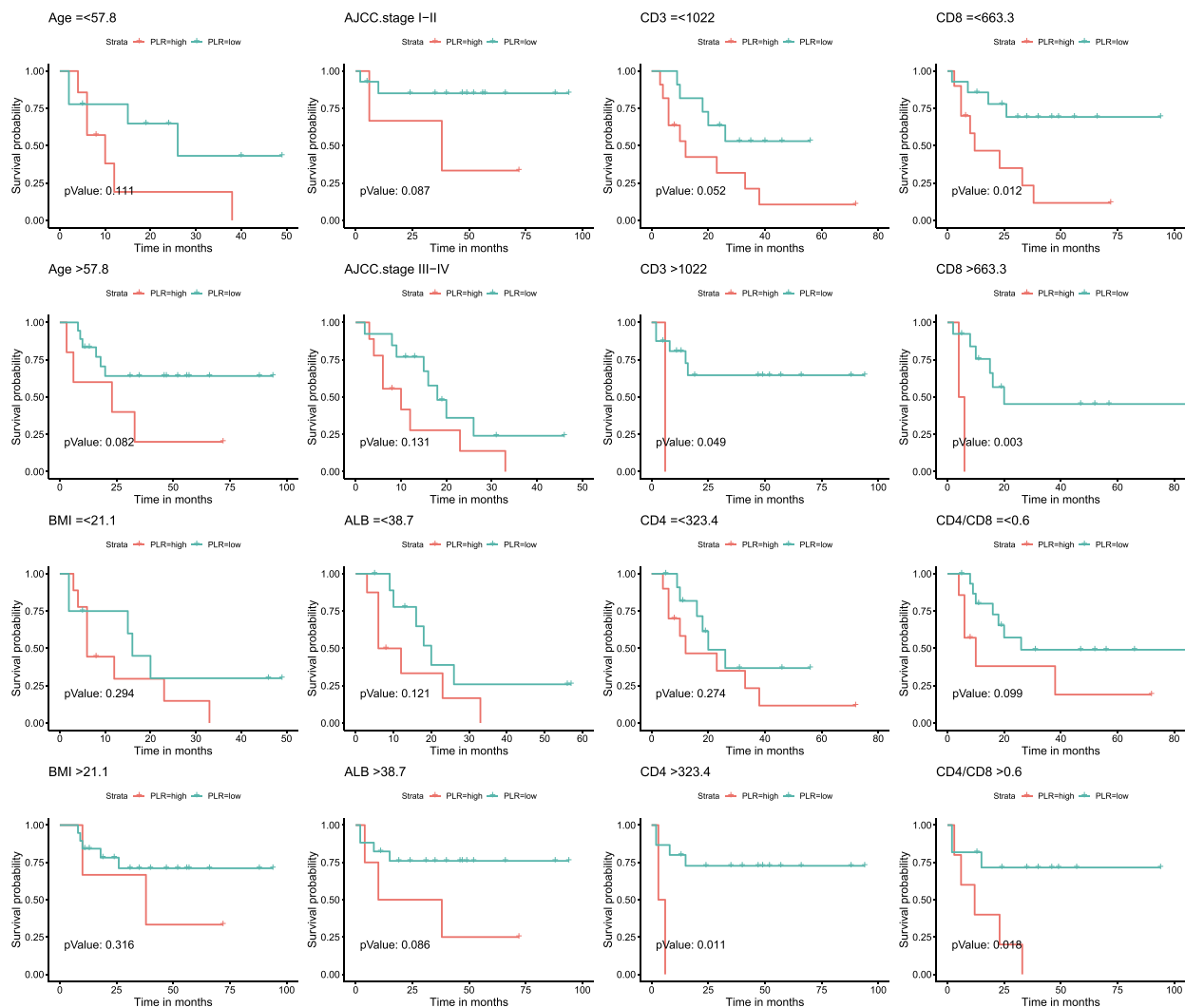
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Fig. 3 Subgroup analysis of PFS based on age, BMI, AJCC stage, albumin level, CD3 cell counts, CD4 cell counts, CD8 cell counts and CD4/CD8 ratio

To investigate the correlation between PLR and clinicopathological features, we divided all HIV-infected GC patients into high and low PLR groups according to the cut-off values. The results showed that higher PLR was significantly associated with lower BMI, hemoglobin, and albumin levels (Tables 3 and 4), indicating preoperative malnutrition. This may be one of the reasons explaining the poorer prognosis in the high PLR group. In addition, the high PLR subgroup had a high percentage of postoperative stage III-IV (76.9% vs 50.0%), suggesting a negative correlation between preoperative result of PLR and postoperative disease severity in HIV-infected GC patients (Table 3). Circulating lymphocytes, which are recruited from the bone marrow and differentiate into various types, play a crucial role in accomplishing an antitumor response in the tumor microenvironment [33]. In our study, lower PLR was associated with higher peripheral CD4+and CD8+T cell counts (Table 4). Moreover, PLR had better predictive value in subgroups with high CD3+, CD4+, and CD8+T cell counts (Figs. 2 and 3). We hypothesized that serum PLR levels may reflect the recovered status of tumor-specific lymphocytes in HIV-infected GC patients, but this needs further research. Furthermore, the high PLR subgroup showed increased neutrophil counts. Neutrophil counts in the circulation were observed to increase during tumor progression [34], but the relationship between neutrophils and PLR in HIV-related GC patients remains unclear.

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Table 3 Relationship between PLR and clinicopathological features in GC patients living with HIV

	low PLR group (*n* = 28)	high PLR group (*n* = 13)	*P*value
Gender			1
Male	26 (92.9%)	13 (100.0%)	
Female	2 (7.1%)	0 (0.0%)	
Age			0.408
Mean (SD)	58.2 (7)	56.8 (9.8)	
Median [MIN, MAX]	60 [44,70]	56 [44,76]	
BMI			0.005
Mean (SD)	21.7 (2.7)	19.7 (1.4)	
Median [MIN, MAX]	21.1 [15.1,26.6]	20.2 [17.3,21.7]	
Hypertension			0.692
No	21 (75.0%)	11 (84.6%)	
Yes	7 (25.0%)	2 (15.4%)	
DM			0.399
No	22 (78.6%)	12 (92.3%)	
Yes	6 (21.4%)	1 (7.7%)	
TB			1
No	26 (92.9%)	13 (100.0%)	
Yes	2 (7.1%)	0 (0.0%)	
Smoking			0.398
No	21 (75.0%)	12 (92.3%)	
Yes	7 (25.0%)	1 (7.7%)	
Alcohol abuse			1
No	24 (85.7%)	12 (92.3%)	
Yes	4 (14.3%)	1 (7.7%)	
Hyperlipidemia			1
No	23 (82.1%)	11 (84.6%)	
Yes	5 (17.9%)	2 (15.4%)	
Duration of HIV infection			0.377
Mean (SD)	22.7 (40.8)	32.5 (37.6)	
Median [MIN, MAX]	1 [0,132]	24 [0,108]	
Duration of HIV treatment			0.113
Mean (SD)	20.9 (37.2)	32.2 (37.2)	
Median [MIN, MAX]	0 [0,110]	24 [0,108]	
Tumor Location			1
Upper	5 (17.9%)	2 (15.4%)	
Middle	21 (75.0%)	10 (76.9%)	
Lower	2 (7.1%)	1 (7.7%)	
Histology			0.719
Signet ring cell	9 (32.1%)	3 (23.1%)	
Her2 status			0.66
0	13 (46.4%)	8 (61.5%)	
1+	11 (39.3%)	3 (23.1%)	
2+	4 (14.3%)	2 (15.4%)	
SBR			0.694
1	3 (10.7%)	2 (15.4%)	
2	8 (28.6%)	2 (15.4%)	

Table 3 (continued)

	low PLR group (*n* = 28)	high PLR group (*n* = 13)	*P*value
3	17 (60.7%)	9 (69.2%)	
R0			1
Yes	25 (89.3%)	12 (92.3%)	
No	3 (10.7%)	1 (7.7%)	
T stage			0.657
I	7 (25.0%)	2 (15.4%)	
II	1 (3.6%)	1 (7.7%)	
III	11 (39.3%)	4 (30.8%)	
IV	9 (32.1%)	6 (46.2%)	
N stage			0.719
Non-metastasis	9(32.1%)	3(23.1%)	
Metastasis	19(67.9%)	10(76.9%)	
M stage			0.645
Non-metastasis	25 (89.3%)	11 (84.6%)	
Metastasis	3 (10.7%)	2 (15.4%)	
AJCC stage			0.173
I-II	14(50.0%)	3(23.1%)	
III-IV	14(50.0%)	10(76.9%)	

DM diabetes mellitus, *TB* tuberculosis infection status, *Her2 status* immunohistochemical staining of Her-2, *R0* radical resection, *SBR* Scarff-Bloom-Richardson score, *PLR* platelet-lymphocyte ratio

While this study provides the insights into the prognostic value of PLR in HIV-infected GC patients, there are some limitations that should be considered. Firstly, the relatively small sample size and lack of validation using an independent cohort may have potential for selection bias. It is challenging to collect sufficient number of HIV-related GC cohorts due to the rarity, inadequate knowledge and discriminatory attitudes of this disease. Therefore, collaboration with other HIV treatment centers is crucial to validate the broader applicability of PLR in the future. Secondly, the absence of preoperative C-reactive protein (CRP) data prevented the analysis of CRP-related markers, which may have provided additional prognostic information. Moreover, the lack of data on *H.pylori* infection history limited the exploration of the relationship between inflammation biomarkers and GC exposure factors. Therefore, future studies with larger sample sizes, multi-center, and a more comprehensive analysis of exposure factors are necessary to further elucidate the differences in the prognostic value of inflammation biomarkers in HIV-infected GC patients.

Conclusion

With the availability of combination antiretroviral therapy (cART), the incidence of gastric cancer (GC) is increasing in individuals infected with human

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Table 4 Relationship between PLR and preoperative laboratory tests in GC patients living with HIV

	Low PLR group (n = 28)	High PLR group (n = 13)	Pvalue
CA125 (0-35U/ml)			0.232
Normal	27 (96.4%)	11 (84.6%)	
Increased	1 (3.6%)	2 (15.4%)	
CA153 (0–32.3U/ml)			0.317
Normal	28 (100.0%)	12 (92.3%)	
Increased	0 (0.0%)	1 (7.7%)	
CA199 (0-37U/ml)			0.228
Normal	20 (71.4%)	12 (92.3%)	
Increased	8 (28.6%)	1 (7.7%)	
AFP (0.89–8.78 ng/ml)			0.539
Normal	25 (89.3%)	13 (100.0%)	
Increased	3 (10.7%)	0 (0.0%)	
CEA (0-5 ng/ml)			0.659
Normal	24 (85.7%)	10 (76.9%)	
Increased	4 (14.3%)	3 (23.1%)	
HGB (g/L)			0.008
Mean (SD)	126.9 (23.1)	104.2 (22.6)	
Median [MIN, MAX]	133 [75,159]	104 [66,134]	
PLT count (*1000 per uL)			0.007
Mean (SD)	184.2 (45.4)	255.4 (106.7)	
Median [MIN, MAX]	182 [101,264]	243 [65,470]	
NEUT count (*1000 per uL)			0.048
Mean (SD)	3 (1.4)	4.7 (3.1)	
Median [MIN, MAX]	2.6 [1.4,8.3]	3.9 [1,12.7]	
LYMPH count (*1000 per uL)			< 0.001
Mean (SD)	1.7 (0.6)	0.9 (0.3)	
Median [MIN, MAX]	1.7 [0.8,3]	1 [0.3,1.5]	
MONO count (*1000 per uL)			0.274
Mean (SD)	0.4 (0.2)	0.6 (0.4)	
Median [MIN, MAX]	0.4 [0.2,0.9]	0.4 [0.2,1.8]	
ALB (g/L)			0.041
Mean (SD)	39.7 (5)	36.5 (4.5)	
Median [MIN, MAX]	40 [25,47.9]	34.9 [29.5,43.9]	
CD3 count (per ul)			< 0.001
Mean (SD)	1196.1 (390.2)	646.9 (277.5)	
Median [MIN, MAX]	1167 [428,1844]	606 [159,1039]	
CD8 count (per ul)			0.001
Mean (SD)	784.2 (353.9)	402.8 (211.6)	
Median [MIN, MAX]	689 [157,1493]	377 [117,769]	
CD4 count (per ul)			0.018
Mean (SD)	373 (221.2)	216.5 (122.9)	
Median [MIN, MAX]	353.5 [21,944]	201 [31,476]	
CD4/CD8			0.501
Mean (SD)	0.6 (0.7)	0.7 (0.4)	
Median [MIN, MAX]	0.5 [0.1,3.2]	0.5 [0.1,1.6]	

AFP alpha fetoprotein, *CEA* carcinoembryonic antigen, *HGB* hemoglobin, *PLT* platelet, *NEUT* neutrophil, *LYMPH* lymphocyte, *MONO* monocyte, *ALB* albumin

immunodeficiency virus (HIV). Our study demonstrates that preoperative platelet-to-lymphocyte ratio (PLR) can serve as an independent biomarker of overall survival (OS) and progression-free survival (PFS) in HIV-infected GC patients, reflecting their immune status. This simple prognostic biomarker could potentially be used to stratify patients' preoperative risks, which enables personalized treatment for patients with HIV and gastric cancer.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-023-02828-x.

Additional file 1: Table S1. Baseline clinicopathologic features and preoperative laboratory tests of GC patients living with HIV. **Table S2.** Univariate and multivariate analysis of clinicopathologic variables in relation to OS in GC patients without HIV infection. **Table S3.** Univariate and multivariate analysis of clinicopathologic variables in relation to PFS in GC patients without HIV infection. **Figure S1.** The Kaplan-Meier survival analysis of Overall Survival and Progression Free Survival between HIV-related and non-HIV related GC patients.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Shanghai Public Health Clinical Center (Grant No. 2022-S022-01). The consent to participate was waived by the Ethics Committee of Shanghai Public Health Clinical Center as this study was a retrospective analysis that presents no risk, does not adversely affect the rights of the subjects. All methods were performed in accordance with the guidelines of the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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