RESEARCH ARTICLE

Clinical implications of pretreatment inflammatory biomarkers as independent prognostic indicators in prostate cancer

Zhaohui Sun¹ | Ying Ju² | Fuyan Han² | Xiya Sun³ | Fang Wang¹

¹Department of Clinical Laboratory, The Second Hospital of Shandong University, Jinan, Shandong, China

²Department of Clinical Laboratory, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, Shandong, China

³School of Basic Medical Sciences of Lanzhou University, Lanzhou, Gansu, China

Correspondence

Zhaohui Sun, Department of Clinical Laboratory, The Second Hospital of Shandong University, Jinan, Shandong, China.
Email: sun_zhsdey@126.com

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Objectives: Research on the relationship between inflammatory biomarkers and malignant tumors has become a hotspot. Many studies have demonstrated that neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and red blood cell distribution width (RDW) could act as independent prognostic indicators for several solid tumors. This study aimed to evaluate the clinical implications of pretreatment inflammatory biomarkers, including NLR, PLR, and RDW as independent prognostic indicators in prostate cancer (PCa).

Methods: A total of 226 PCa patients who were diagnosed at our institution from 2011 to 2016 were analyzed retrospectively. We compared the clinicopathological features, survival curves, and prognosis of the PCa patients between the high and low groups according to the cutoffs of NLR, PLR, and RDW.

Results: The pretreatment NLR, PLR, and RDW values were significantly higher in the patients with PCa than those in the controls ($P < .05$). Increased NLR and PLR values were significantly associated with high risk of progression, including higher Gleason scores, cell proliferation antigen 67 (Ki-67) indexes, and prostate-specific antigen (PSA) levels ($P < .05$), whereas an elevated RDW was only associated with an older age. An increased NLR was correlated with both overall survival (OS) ($P = .025$) and disease-free survival (DFS) ($P = .017$). In addition, a higher PLR only showed a significantly worse DFS ($P = .040$). Pretreatment NLR was an independent prognostic indicator of DFS.

Conclusions: The pretreatment NLR and PLR might be beneficial to predict the progression and prognosis of PCa. Furthermore, NLR was more effective than PLR acting as an independent prognostic indicator for PCa.

KEYWORDS

inflammatory biomarkers, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, prognostic indicators, prostate cancer, red blood cell distribution width

1 | INTRODUCTION

Prostate cancer (PCa) is the most common urological malignant tumors and the second leading cause of cancer-related death in males after lung cancer.¹ As a result of aging population, altered lifestyle, and increased detection level, PCa continuously increases in China.² Most PCa patients are diagnosed at early stage using PSA screening and imaging modalities and can receive promising outcomes through

the standard treatment, such as radical prostatectomy or radiotherapy. However, a large amount of PCa patients still present at advanced stage. Because cancer cells have the tendency of distant metastasis, especially bones metastasis, PCa can have detrimental effect on patients' life.³ Therefore, efficient indicators are urgently required to predict the progression and prognosis of PCa, thus to assess risk, choose reasonable treatment, and make an appropriate surveillance method. The inflammatory response plays a significant role in the initiation and

progression of the tumors,⁴ and the predictive value of inflammation markers in tumor prognosis is of interest to academia.

Neutrophil-to-lymphocyte ratio (NLR) is equal to the absolute value of neutrophils divided by the absolute value of lymphocytes, therefore, a high NLR indicated the increased number of neutrophils or the decreased number of lymphocytes. On the one hand, neutrophilia can promote the growth, invasion, and migration of tumor by reconstructing the extracellular matrix and secreting reactive oxygen species, which inhibit the T-cell anti-tumor immunity and cause mutagenesis.⁵ Furthermore, neutrophilia can suppress the activity of lymphocyte, thus, countervailing the anti-tumor immunoreaction.⁶ On the other hand, tumor cells can produce granulocyte colony-stimulating factor, tumor necrosis factor α , interleukin1, and interleukin6, which may improve the number of neutrophil around the tumor.^{7,8} Studies have proved that an increased NLR value is significantly connected with an adverse prognosis in esophageal cancer,⁵ breast cancer,⁹ and colorectal cancer.¹⁰

Platelet-to-lymphocyte ratio (PLR) is calculated as the number of platelets divided by the number of lymphocytes. As is known to all, platelets play an important role in hemostasis and thrombosis.¹¹ Besides, platelets promote tumor growth, metastasis, and angiogenesis. Conversely, tumor cells mediate platelet aggregation.¹² Platelet can release cytokines, such as platelet-derived growth factor and transforming growth factor which can promote the tumor growth.¹³ Szkandera et al.¹⁴ indicated that a higher PLR was significantly related to a poor OS rate in patients with advanced colon cancer. Koh et al.¹⁵ indicated that an increased PLR was independently related to an increased risk of mortality in breast cancer.

Red cell distribution width (RDW) is a detection parameter of the heterogeneity of peripheral red blood cell size. RDW has a strong association with inflammatory factors, such as C-reactive protein, erythrocyte sedimentation rate, and fibrinogen.¹⁶ One study indicated that RDW was an effective indicator of all-cause mortality, including cancer-associated deaths.¹⁷ Seretis et al.¹⁸ showed that patients with invasive breast cancer had significantly higher RDW values compared to patients with fibroadenomas.

Therefore, we carried out the systematic study to acquire a more comprehensive evaluation of prognostic values of inflammatory indicators in patients with PCa, such as NLR, PLR, and RDW. In our study, the first objective was to analyze the abilities of the pretreatment NLR, PLR, and RDW in identification of the PCa group and the control group; the second objective was to analyze the relationship between the pretreatment NLR, PLR, and RDW values and the clinicopathological parameters; our third objective was to evaluate the impact of pretreatment NLR, PLR, and RDW on prognosis of PCa.

2 | SUBJECTS AND METHODS

2.1 | Subjects

A total of 450 men who underwent transrectal ultrasound (TRUS)-guided prostate needle biopsy in the second hospital of Shandong University between January 2011 and November 2016 were

collected. Of these, 384 patients were diagnosed as PCa by two pathologists. After exclusion standard screening, 87 patients were excluded for the reasons, including hematological disorders, chronic inflammation, or other diseases. Of these, 226 patients who had both blood and urine routine indexes were eventually included in our study (Figure 1). Meanwhile, we selected 100 age-matched men as healthy controls for comparison analysis. The inclusion criteria for healthy controls were that those examination indicators of the prostate were normal. The exclusion criteria for PCa and healthy controls were: benign prostatic hyperplasia (BPH), prostatitis, chronic inflammation, hematological disorders, autoimmune diseases, blood transfusion, neoadjuvant therapy, and other cancers. A prostate biopsy may be done when appear the following indications: (i) A digital rectal examination finds an abnormal prostate or a lump (ii) A blood test shows PSA>10 ng/mL, regardless of the f/tPSA value (iii) When the PSA level is 4-10 ng/mL and the f/tPSA level is abnormal. The PSA threshold value is 0-4 ng/mL.

2.2 | Data collection

We consulted the medical records of 226 patients with prostate biopsy. Data regarding age, biopsy Gleason score, Ki-67 indexes, PSA levels, pre-biopsy routine blood indexes, and routine urine indexes in patients who were diagnosed as PCa were analyzed. Blood indexes were detected with an automated hematology analyzer XE-2100 (Sysmex, Kobe, Japan). PSA was measured with a Cobas e601 analyzer (Roche Diagnostics, Mannheim, Germany). Urine routine test was detected with automated urine analyzer (Sysmex, UF-1000i).

FIGURE 1 Flowchart of patients included and excluded in this study

2.3 | Follow-up

Posttreatment regular telephone follow-up was carried out after 226 PCa patients were treated by radical prostatectomy, hormone therapy, radiotherapy, or endocrine therapy. The last follow-up proceeded in December 2016. The first research end-point was overall survival (OS), which was defined as the time from the initiation of treatment to the date of death for any reason. The second study end-point was disease-free survival (DFS), which was defined as the time from the date of curative treatment to the date of identification of disease recurrence, either radiological or histological. Radiological recurrence was defined as a size increase in an existing lesion, new metastatic lesions, or disease-related symptoms. Histological recurrence was considered as cancerous cells, local invasion, vascular invasion, lymph node invasion by the repeat biopsy after treatment. This study was approved by the Ethics Committee of the Second Hospital of Shandong University. Informed consent forms were written by all patients.

2.4 | Statistical methods

We performed statistical analysis using SPSS statistical software version 19.0 (SPSS Inc., Chicago, IL, USA). Continuous variables conformed to normal distributions were presented as mean $\pm$ SD and the difference was compared using Student's *t* test, whereas continuous variables violated normal distribution were shown as median (P25, P75) and the difference was compared using Mann-Whitney *U*-test. Categorical variables were expressed as frequencies or percentages and the difference was compared using the χ^2 test. Receiver operating characteristic (ROC) curves were established for NLR, PLR, and RDW, and the optimal cut-off values were calculated. Patients were divided

into high and low groups according to the cut-off values. The survival rate curves were determined using the Kaplan-Meier analysis, and was compared using the log-rank test. The multivariate Cox proportional hazards model was used to determine independent prognostic factors. Logistic regression analysis was used to detect the NLR-associated risk factors. *P* values <.05 were considered as statistical significance.

3 | RESULTS

3.1 | Comparison of characteristics between the PCa patients and the controls

The general characteristics of the patients and the controls are shown in Table 1. No statistical difference was found in age when comparing the PCa patients with the controls. The mean values of RBC ($\times 10^{12}/L$) and HGB (g/L) in the patients with PCa were 4.6 and 140.0, respectively, which were significantly lower than 4.9 and 153.5, respectively, in the controls ($P<.001$ and $P<.001$, respectively). The median of neutrophils ($\times 10^9/L$) in the patients with PCa was 3.7 which was significantly higher than 3.4 in the controls ($U=9702.5$, $P=.042$). The median values of lymphocytes ($\times 10^9/L$) and PDW (fL) in the patients with PCa were 1.7 and 12.0 which were significantly lower than 2.1 and 12.9 in the controls ($P<.001$ and $P<.001$, respectively). The median PSA value was significantly higher in the PCa patients than in the healthy controls ($P<.001$). No significant differences were detected in WBC and PLT ($P=.632$ and $P=.108$, respectively). As shown in Figure 2, comparisons of NLR, PLR, and RDW values between the PCa patients and the controls were conducted. The median (P25, P75) values of NLR, PLR, and RDW in the PCa patients were 2.3 (1.7, 3.3), 129.0 (96.8, 159.3), and 13.1% (12.7%, 13.5%), respectively, which were significantly higher than 1.6 (1.3, 2.0), 99.0 (86.0, 122.5), and

TABLE 1 Characteristics of the patients with PCa and the controls

Characteristics	PCa patients (n=226)	Controls (n=100)	$\chi^2/t/U$	<i>P</i> values
Age, n (%)				
<70	110 (48.7)	54 (54.0)	0.8	.375 ^a
≥ 70	116 (51.3)	46 (46.0)		
Age, mean $\pm$ SD (years)	68.5 $\pm$ 8.4	68.6 $\pm$ 6.5	0.2	.872 ^b
RBC, mean $\pm$ SD ($\times 10^{12}/L$)	4.6 $\pm$ 0.6	4.9 $\pm$ 0.4	6.8	<.001 ^b
HGB, mean $\pm$ SD (g/L)	140.0 $\pm$ 18.1	153.3 $\pm$ 11.5	8.0	<.001 ^b
PLT, mean $\pm$ SD ($\times 10^9/L$)	207.4 $\pm$ 59.1	218.3 $\pm$ 49.4	1.6	.108 ^b
WBC, median (P25, P75) ($\times 10^9/L$)	6.0 (5.1, 7.3)	6.3 (5.3, 7.0)	11 675.5	.632 ^c
Neutrophil, median (P25, P75) ($\times 10^9/L$)	3.7 (2.9, 4.7)	3.4 (2.9, 4.2)	9702.5	.042 ^c
Lymphocyte, median (P25, P75) ($\times 10^9/L$)	1.7 (1.2, 1.9)	2.1 (1.8, 2.5)	17 325.5	<.001 ^c
PDW, median (P25, P75) (fL)	12.0 (10.8, 13.1)	12.9 (12.1, 13.6)	14 876.0	<.001 ^c
PSA, median (P25, P75) (ng/mL)	30.3 (9.3, 100)	0.7 (0.3, 1.8)	1386.5	<.001 ^c

WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; PLT, platelet; PDW, platelet distribution width; PSA, prostate-specific antigen.

^aValue was calculated by χ^2 test.

^bValue was calculated by *t*-test.

^cValue was calculated by Mann-Whitney *U*-test.

12.7% (12.4%, 13.1%), respectively, in the controls. The differences were statistically significant ($P<.001$, $P<.001$, and $P<.001$, respectively).

3.2 | The ROC curves

According to the ROC curve analysis, the optimal cutoffs of NLR, PLR, and RDW were determined to be 2.31 (a sensitivity of 51.3% and a specificity of 86.0%), 134 (a sensitivity of 46.9% and a specificity of 86.0%), and 12.9% (a sensitivity of 63.3% and a specificity of 65.0%), respectively. The area under the curves (AUCs) of NLR, PLR, and RDW were 0.739 (95%CI=0.685-0.792, $P<.001$), 0.682 (95%CI=0.625-0.739, $P<.001$), and 0.675 (95%CI=0.614-0.736, $P<.001$), respectively, for predicting the presence of PCa (Figure 3).

3.3 | Comparisons of clinicopathological parameters of 226 patients with PCa

The clinicopathological features stratified by the cut-offs of NLR, PLR, and RDW are shown in Table 2. We defined a high risk of progression as an age ≥ 70 , a Gleason score >6 , a Ki-67 index $\geq 20\%$, a PSA level

>10 ng/mL,¹⁹ urine red blood cell (URBC) $\geq 25/\mu\text{L}$ and urine white blood cell (UWBC) $\geq 30/\mu\text{L}$. A higher NLR group was significantly connected with a higher Gleason score, Ki-67 index, and PSA level

FIGURE 3 The ROC curves grouped by NLR, PLR, and RDW. ROC, receiver operating characteristic. Notes: The red line represents NLR, the green line PLR, and the blue line RDW

FIGURE 2 Comparison of NLR, PLR and RDW levels in the PCa group and the control group. NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; RDW, red blood cell distribution width. Note: The data of NLR, PLR and RDW in the patients with PCa and the controls were abnormal distributions and the comparisons of the two groups were conducted by Mann-Whitney U-test

($P=.031$, $P=.001$ and $P=.001$, respectively). Similarly, statistically significant differences were detected between a higher PLR group and a higher Gleason score, Ki-67 index, and PSA level ($P=.008$, $P=.030$, and $P=.003$, respectively). A higher RDW was only significantly related to an older age ($P=.003$). The above results showed that an increased value of NLR, PLR, and RDW could predict a high risk of progression.

3.4 | The prognosis analysis of the patients with PCa

For the 226 patients, the median follow-up time was 24 months (range from 1 to 73). Loss of follow-up and death occurred in 55 and 21 patients, respectively. The Kaplan-Meier curves for OS and DFS of 171 PCa patients are presented in Figure 4. Patients with an increased NLR value possessed a significantly poor OS ($P=.025$) and adverse DFS ($P=.017$). Similarly, the higher PLR group only showed a significantly worse DFS than the lower group ($P=.040$). However, the value of RDW seemingly had no significant connection with OS and DFS ($P=.815$ and 0.827 , respectively). To obtain prognostic factors that affect the OS and DFS of patients with PCa, univariate and multivariate survival analysis were conducted (Table 3). Multivariate analysis revealed that Gleason score and URBC were independent prognosis factors for OS ($P=.049$ and $P=.030$, respectively), but NLR and PLR were not related to OS. Moreover, NLR and Gleason score became the independent predictors for DFS ($P=.039$, $P=.023$).

3.5 | Logistic regression analysis of the NLR-associated risk factors

To evaluate the clinical data that likely led to the increased NLR, logistic regression analysis was executed. The results indicated that Ki-67 and PLR were independent risk factors that caused the increased of the NLR level ($P=.024$, $P<.001$, respectively) (Table 4).

4 | DISCUSSION

In recent years, with the deeper understanding of the inflammatory microenvironment of tumors, the correlation between inflammation and cancers has become an advanced research hotspot. Many studies have demonstrated that the invasion ability of malignant tumor cells not only depends on the biological behavior of the tumor cells, but also on the tumor microenvironment, especially the interaction of various kinds of inflammation factors.²⁰ Inflammatory response plays an important role in the occurrence, progression, prognosis of several tumors through stimulating or suppressing tumor cells.²¹ Therefore, a lot of inflammatory biomarkers, such as NLR, PLR, RDW, or other hematological parameters, have become progressive and prognostic indicators for many tumors.²² In this study, we first systematically evaluated the relationship between the NLR, PLR, RDW, and the prognosis of PCa.

Firstly, in our study, we demonstrated that the median values of NLR, PLR, and RDW in the PCa patients were significantly higher than those in the controls, implying that the NLR, PLR, and RDW could act

as indicators for the differential diagnosis of the PCa and the control. Kawahara et al.²³ verified that NLR was significantly higher in men with prostate cancer than in those without prostate cancer. Yuksel et al.²⁴ revealed that there was a remarkably increase in the PLR value in the PCa group compared to the benign prostatic hyperplasia (BPH) group, and PLR values were higher in the PCa group in comparison with the prostatitis group though not statistically significant. Another study also showed that PLR in PCa patients was significantly higher than that of healthy individuals and BPH patients.²⁵ Albayrak et al.²⁶ reported that the RDW values were significantly higher in patients with PCa than those in healthy controls. The results of the three studies above were in accordance with ours.

At present, the occurrence mechanism of the above law has not been confirmed. It is generally believed that the onset of PCa in the starting point is the infection or inflammatory response. NLR, PLR, and RDW are a kind of sensitive indicators which reflect the activation of the inflammatory system and involve in the inflammatory response. When the NLR, PLR, and RDW values elevate means that the body effective defense is weakened and the barrier against malignant cells is destroyed, which ultimately leads to the poor survival prognosis of PCa. The mechanism of the above analysis is consistent with the results of the study. In addition, the ROC curve analysis also proved the effective predictive values of the three indicators and NLR possessed more effective predictive ability than PLR and RDW.

Secondly, the PCa patients with an increased NLR or PLR were inclined to own more clinicopathological features related to a high risk of progression, including older age, a bigger Gleason score, a higher Ki-67, and a higher PSA level, whereas an increased RDW was only significantly connected with an older age. The results above indicated that increased NLR and PLR can be used as indicators of malignant progression in PCa. Zhang et al.²⁷ reported that patients with PCa in the high NLR group had a significant higher age, higher incidence of pT3-4 disease, greater lymph node involvement, and a borderline higher PSA than those in the low-NLR group which was consistent with ours. Kawahara et al.²³ revealed that for PCa patients, a higher NLR value tended to own a high risk of progression though not statistically significant, including an older age, Gleason score (≥ 8), and a higher initial PSA. Li et al.²⁵ showed that comparing to the low PLR group with PCa, the high PLR group had older age, bigger Gleason score, organ involvement, and advanced tumor stage which was in accordance with ours. However, Wang et al.²⁸ found that the differences in age, serum PSA level, Gleason score, risk stratification, and incidence of metastasis between low PLR group and high PLR group were not significant for PCa patients. Albayrak et al.²⁶ showed that PCa patients with a higher RDW value had an increased risk of progression, whereas a lower RDW had a decreased risk of progression.

Thirdly, the patients with a higher NLR possessed a significantly poorer OS and DFS compared to those with a lower NLR and the patients with a higher PLR only possessed a significantly worse DFS than a lower PLR. Furthermore, a multivariate analysis revealed that NLR was effective independent prognostic factor for DFS. Although high PLR and RDW lost their independent prognostic significance for OS and DFS in multivariate analysis, it still offered considerable

TABLE 2 Comparisons of clinicopathological parameters of 226 PCa patients

Characteristics	Cases (n)	NLR<2.31 n (%)	RDW>2.31 n (%)	P value	PLR<134 n (%)	PLR≥134 n (%)	P value	RDW<12.9 n (%)	RDW≥12.9 n (%)	P value
Age (years)										
<70	110	56 (52.3)	54 (45.4)	.296	57 (48.7)	53 (48.6)	.989	51 (61.4)	59 (41.3)	.003
≥70	116	51 (47.7)	65 (54.6)		60 (51.3)	56 (51.4)		32 (38.6)	84 (58.7)	
Gleason score										
≤6	55	33 (30.8)	22 (18.5)	.031	37 (31.6)	18 (16.5)	.008	23 (27.7)	32 (22.4)	.368
>6	171	74 (69.2)	97 (81.5)		80 (68.4)	91 (83.5)		60 (72.3)	111 (77.6)	
Ki-67 (%)										
<20	172	92 (86.0)	80 (67.2)	.001	96 (82.1)	76 (69.7)	.030	69 (83.1)	103 (72.0)	.059
≥20	54	15 (14.0)	39 (32.8)		21 (17.9)	33 (30.3)		14 (16.9)	40 (28.0)	
PSA (ng/mL)										
≤10	62	40 (37.4)	22 (18.5)	.001	42 (35.9)	20 (18.3)	.003	22 (26.5)	40 (28.0)	.812
>10	164	67 (62.6)	97 (81.5)		75 (64.1)	89 (81.7)		61 (73.5)	103 (72.0)	
URBC (count/μL)										
≤25	139	71 (66.4)	68 (57.1)	.155	76 (65.0)	63 (57.8)	.269	54 (65.1)	85 (59.4)	.403
>25	87	36 (33.6)	51 (42.9)		41 (35.0)	46 (42.2)		29 (34.9)	58 (40.6)	
UWBC (count/μL)										
≤30	174	87 (81.3)	87 (73.1)	.144	96 (82.1)	78 (71.6)	.061	68 (81.9)	106 (74.1)	.179
>30	52	20 (18.7)	32 (26.9)		21 (17.9)	31 (28.4)		15 (18.1)	37 (25.9)	

Ki-67, cell proliferation antigen 67; PSA, prostate-specific antigen; URBC, urine red blood cell; UWBC, urine white blood cell. P values were calculated by χ^2 test.

FIGURE 4 Kaplan-Meier survival curves according to NLR, PLR, and RDW. Notes: NLR: overall survival (A) and disease-free survival (B); PLR: overall survival (C) and disease-free survival (D); RDW: overall survival (E) and disease-free survival (F). The survival curves were determined using the Kaplan-Meier analysis, and were compared using the log-rank test

TABLE 3 Univariate and multivariate survival analysis of 171 patients with PCa

Clinicopathological feature	Univariate ^a (OS)		Multivariate ^b (OS)		Univariate ^a (DFS)		Multivariate ^b (DFS)	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
NLR (<2.31/≥2.31)	2.8 (1.1-7.2)	.033	2.0 (0.8-5.4)	.150	2.1 (1.1-4.1)	.021	2.0 (1.0-3.8)	.039
PLR (<134/≥134)	2.1 (0.8-4.9)	.110			1.9 (1.0-3.5)	.045	1.3 (0.6-2.8)	.429
RDW (<12.9/≥12.9)	1.1 (0.5-2.7)	.817			1.1 (0.6-2.0)	.828		
Age (<70/≥70)	1.6 (0.6-3.7)	.329			0.8 (0.5-1.5)	.565		
Gleason score (≤6/>6)	8.3 (1.1-62.3)	.039	7.6 (1.0-56.9)	.049	3.2 (1.3-8.3)	.015	3.0 (1.2-7.7)	.023
Ki-67 (<20%/≥20%)	1.5 (0.6-3.7)	.378			0.8 (0.4-1.7)	.551		
PSA (≤10/>10)	0.8 (0.3-1.9)	.563			1.0 (0.5-1.9)	.955		
URBC (≤25/>25)	2.9 (1.2-6.9)	.017	2.6 (1.1-6.3)	.030	1.7 (0.9-3.2)	.080	1.5 (0.8-2.8)	.253
UWBC (≤30/>30)	0.9 (0.3-2.6)	.793			1.647 (0.836-3.243)	.149		

Ki-67, cell proliferation antigen 67; PSA, prostate-specific antigen; URBC, urine red blood cell; UWBC, urine white blood cell; HR, hazard ratio; CI, confidence interval.

^aPerformed using the Kaplan-Meier analysis model and the log-rank test; values of $P < .05$ in the univariate analysis were entered into a multivariate analysis.

^bPerformed using Cox proportional hazards models with the forward likelihood method.

TABLE 4 Logistic regression analysis of NLR-associated risk factors

Clinicopathological feature	B	SE	Wals	HR	95%CI	P value
Age (years) (<70/≥70)	0.101	0.407	0.061	1.106	0.498-2.457	.805
Gleason score (≤6/>6)	-0.322	0.467	0.478	0.724	0.290-1.808	.489
Ki-67 (<20%/≥20%)	1.104	0.488	5.126	3.017	1.160-7.846	.024
PSA (≤10/>10)	0.222	0.451	0.243	1.249	0.516-3.022	.622
URBC (≤25/>25)	0.361	0.456	0.627	1.435	0.587-3.506	.428
UWBC (≤30/>30)	0.450	0.524	0.737	1.568	0.561-4.381	.391
PLR (<134/≥134)	2.503	0.429	34.069	12.224	5.247-28.332	<.001
RDW (<12.9/≥12.9)	-0.019	0.403	0.002	0.981	0.445-2.161	.962

Ki-67, cell proliferation antigen 67; PSA, prostate-specific antigen; URBC, urine red blood cell; UWBC, urine white blood cell; HR, hazard ratio; CI, confidence interval.

information on PLR and RDW for clinical prognosis. Combined with the result of ROC curve analysis, the above results indicated that NLR is superior to PLR as a prognosis indicator for PCa. Previous research has shown that inflammatory response led to the malignant conversion and poor prognosis of PCa.²⁹ Langsenlehner et al.³⁰ reported that elevated NLR could act as an independent prognostic factor of OS and progression-free survival (PFS) in patients with PCa. Yin et al.³¹ demonstrated that increased NLR was not significantly related to the poor OS or recurrence-free survival of patients with localized PCa, whereas increased NLR was a strong predictor of worse prognosis of patients with metastatic castration resistant prostate cancer (mCRPC). Li et al.²⁵ found that 3 years survival rate of patients in high PLR group was significantly reduced, additionally, PLR was a possible risk factor associated with mortality and an independent predictor of all-cause mortality during follow-up. Wang et al.²⁸ also reported that the PCa patients with high PLR had a significantly worse survival than those with low PLR with regard to cancer-specific survival (CSS), PFS, and OS. The relationship between the NLR, PLR, RDW, and poor prognosis of PCa has not been

illustrated so far. However, the association may be caused by inflammatory condition and poor nutritional state.

Lastly, we conducted logistic regression to evaluate the risk clinicopathological factors which led to the increased NLR and found that Ki-67 and PLR were independent risk indicators that caused increased NLR. Ki-67 represented the proliferation activity of tumor cells. The above results confirmed that NLR and PLR were beneficial to predict prostate cancer outcome.

In this study, several limitations need to be noted. Inevitably, there may be erroneous data collection which will occur in most retrospective studies. In addition, the subject number in our study was relatively small and the follow-up duration was not sufficiently long. Thus, our findings should be validated in further investigations with a larger subject size and longer follow-up duration.

On the basis of the results of this study, we concluded that pre-treatment NLR and PLR, very simple, cheap, and convenient indicators, might be helpful to predict the progression and prognosis of PCa. Notably, NLR was detected to be more effective than PLR acting as an independent prognostic indicator for PCa.

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