

# Increased platelet-to-lymphocytes ratio is associated with poor long-term prognosis in patients with pancreatic cancer after surgery

Jinming Yu, MD<sup>a</sup>, Zhaoyan Ding, MD<sup>b</sup>, Yuanming Yang, MD<sup>c</sup>, Shanli Liu, MD<sup>d,\*</sup>

## Abstract

Several studies reported platelet-to-lymphocytes ratio (PLR), neutrophil-to-lymphocyte ratio (NLR) and red blood cell distribution width (RDW) were associated with the mid-term survival or cancer stage in pancreatic cancer. However, the relationship between these markers and the long-term prognosis of pancreatic cancer is still unknown. We investigated the relationship between PLR, NLR, RDW, and the long-term prognosis of pancreatic cancer.

We included 182 pancreatic cancer patients who received operation at Linzi District People's Hospital between August 2010 and January 2017. PLR, NLR, and RDW control data was obtained from 150 health volunteers from January 2011 to January 2017. Blood biochemical data before operation, preoperative computed tomography information, and pathological data of the pancreatic cancer patients were retrospectively collected for further analysis. Independent long-term prognostic significance of PLR, NLR, and RDW were analyzed in pancreatic cancer patients.

PLR, NLR, and RDW were significantly increased in pancreatic cancer group compared with the control. Receiver operating characteristic (ROC) curve analysis showed the optimal cut-off values of PLR, NLR, and RDW were 150, 1.73, and 13.2 respectively. Overall survival (OS) analysis showed pancreatic cancer patients with PLR $\geq$ 150 (median time, 24 vs 37.5 months,  $P=.005$ ) or RDW $\geq$ 13.2 (median time, 27 months vs 37.5 months,  $P=.018$ ) had lower postoperative 5 year OS compared with pancreatic cancer patients with PLR $<$ 150 or RDW $<$ 13.2. Univariate and multivariable Cox regression analysis for postoperative 5 year OS data showed PLR $\geq$ 150 (HR=2.451, 95% CI 1.215–4.947;  $P=.012$ ) was still associated with the OS independently. Disease free survival (DFS) analysis showed pancreatic cancer patients with PLR $\geq$ 150 (median time, 24 months vs 38 months,  $P=.002$ ) or RDW $\geq$ 13.2 (median time, 24 months vs 37.5 months,  $P=.006$ ) had lower postoperative 5 year DFS compared with pancreatic cancer patients with PLR $<$ 150 or RDW $<$ 13.2. Univariate and multivariable Cox regression analysis for postoperative 5 year DFS data showed PLR $\geq$ 150 (HR=2.712, 95% CI 1.367–5.379;  $P=.004$ ) was independently associated with the DFS.

In the present study, we find hematological biomarkers PLR $\geq$ 150 is an independently predictive risk factor for the postoperative long-term prognosis in pancreatic cancer patients. Our study may provide a convenient way for the prognostic assessment of pancreatic cancer patients.

**Abbreviations:** AUC = area under the curve, CI = confidence intervals, DFS = disease free survival, HR = hazard ratio, IL-10 = interleukin-10, NLR = neutrophil-to-lymphocyte ratio, OS = overall survival, PLR = platelet-to-lymphocytes ratio, RDW = red blood cell distribution width, ROC = receiver operating characteristic, TGF- $\beta$  = transforming growth factor- $\beta$ .

**Keywords:** long-term prognosis, operation, pancreatic cancer, PLR

## 1. Introduction

Pancreatic cancer is one of the most deadly diseases with very poor prognosis. It was reported its overall survival rate was only

about 8% at 5 years after diagnosis and pancreatic cancer would become the second leading cause of cancer death in United States in 2030.<sup>[1]</sup> Surgical intervention is the only effective treatment for pancreatic cancer<sup>[2]</sup>; however, pancreatic cancer is almost impossible to be completely cured.<sup>[3]</sup>

It was reported pancreatic cancer cells interacted with the host immune system and resulted in a decreased lymphocytes ratio and inflammatory circulating markers were associated with the outcome of pancreatic cancer.<sup>[4]</sup> Asari et al<sup>[5]</sup> reported higher preoperative platelet-to-lymphocytes ratio (PLR) predicted lower mid-term outcomes in borderline resectable pancreatic cancer patients. Piciocchi et al<sup>[6]</sup> found elevated neutrophil-to-lymphocyte ratio (NLR) was associated with poor mid-term survival in patients with metastatic pancreatic cancer. These studies indicated PLR and NLR might be related with the long-term prognosis in pancreatic cancer patients.

As a main descriptive parameter for erythrocyte variation, increased red blood cell distribution width (RDW) was associated with poor prognosis in some diseases. Li et al<sup>[7]</sup> reported increased RDW predicted higher risk for coronary heart disease induced arrhythmia. Yilmaz et al<sup>[8]</sup> found RDW was associated

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<sup>a</sup> Department of Laboratory, Linzi District People's Hospital, Zibo, <sup>b</sup> Department of Ultrasound, <sup>c</sup> Department of Blood Transfusion, Affiliated Hospital of Medical College, Qingdao University, Qingdao, <sup>d</sup> Department of Laboratory, Changle People's Hospital, Changle, China.

\* Correspondence: Shanli Liu, Department of Laboratory, Changle People's Hospital, Limin Road No. 278, Changle 262400, China (e-mail: shanliu@yeah.net).

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with the stage of pancreatic cancer. But the relation between RDW and the long-term survival in pancreatic cancer patients has not been investigated.

In the present study, we retrospectively investigated changes of PLR, NLR, and RDW and whether they were associated with the long-term prognosis in patients with pancreatic cancer.

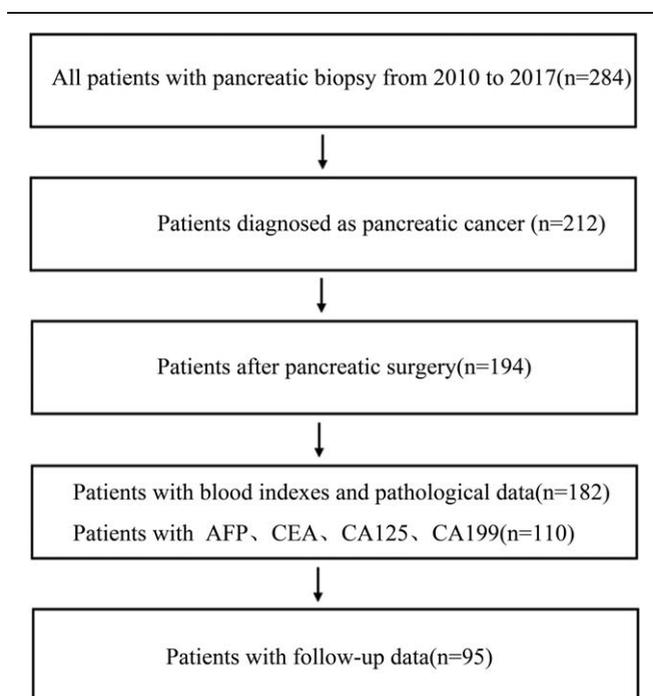
## 2. Patients and methods

### 2.1. Patients

From August 2010 to January 2017, 182 pancreatic cancer patients who received operation at Linzi District People's Hospital was included in this study, details of the patient number in each part were shown in Figure 1. PLR, NLR, and RDW control data were obtained from 150 health volunteers from January 2011 to January 2017. Pancreatic cancer was confirmed with the pathologic diagnosis from the primary pancreatic lesion. Blood biochemical data before operation, preoperative computed tomography information, and pathological data of the patients were collected for further analysis. The pathological and clinical stages were assessed according to the TNM classification system and NCCN guidelines, respectively. Survival data were collected by clinical or telephone follow-up. This study was approved by the Institutional Review Board of Linzi District People's Hospital.

### 2.2. Statistical analysis

Statistical Package for Social Sciences, version 21.0 (SPSS, Chicago, IL) was used for statistical analysis. For non-normally distributed continuous variables, non-parametric Mann-Whitney *U* test was used for 2 group comparison. For categorical variables, chi-square test was used to test statistical differences. Optimal cut-off values for PLR, NLR, and RDW were determined by receiver operating characteristic (ROC) curve



**Figure 1.** The flow chart of the study.

and the area under the curve (AUC). Disease free survival (DFS) was defined as the time from the date of pancreatic cancer diagnosis to the date of first recurrence after operation. Overall survival (OS) was defined as the time from the date of operation to the date of death or last follow-up. DFS and OS in 2 groups divided by PLR, NLR, or RDW were compared with Kaplan-Meier estimation with the log-rank test. Multivariate Cox proportional hazard model was used to examine risk factors found by the univariate analysis. Hazard ratio (HR) and 95% confidence intervals (CI) were calculated for comparison. Data were presented as mean  $\pm$  SD, n (%) or HR (95%CI).  $P < .05$  was considered statistically significant.

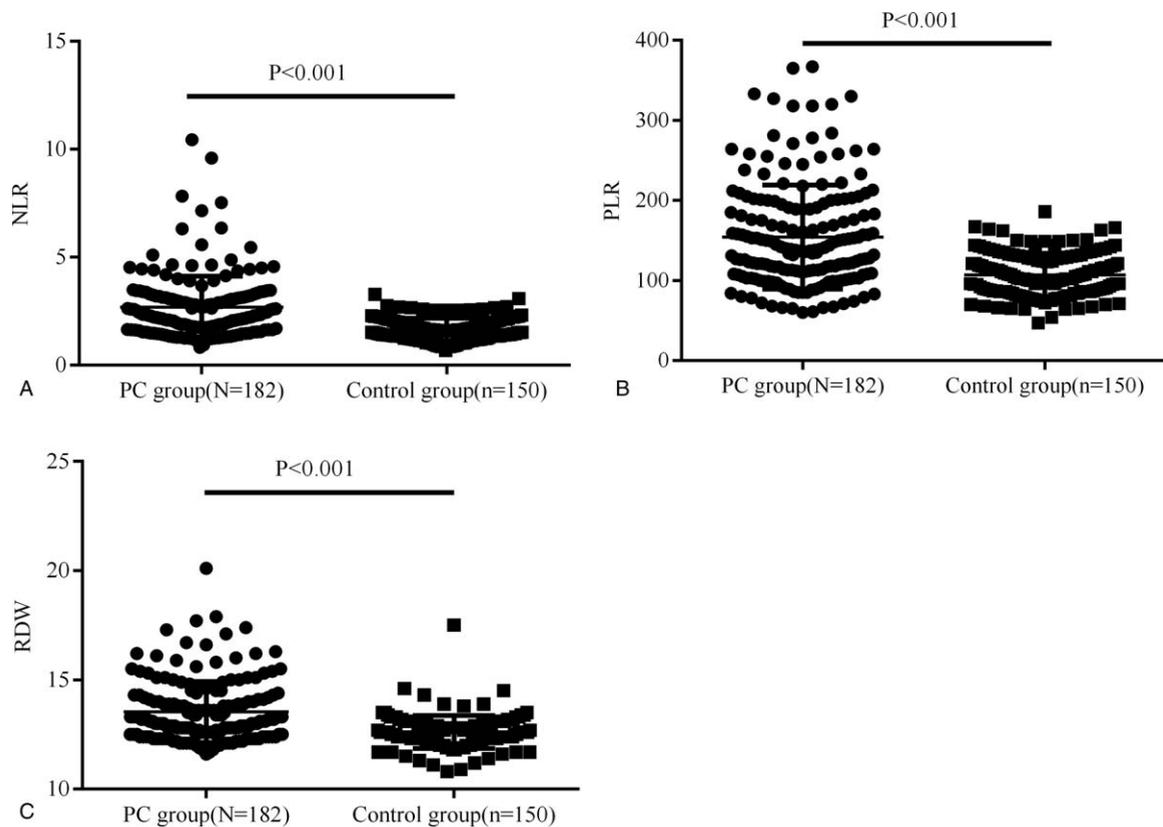
## 3. Results

### 3.1. Clinicopathological characteristics comparison and optimal cut-off values for PLR, NLR, and RDW

We first compared PLR, NLR, and RDW between pancreatic cancer group ( $n=182$ ) and the control group ( $n=150$ ). Results showed PLR, NLR, and RDW were significantly increased in pancreatic cancer group ( $154.6 \pm 64.97$  vs  $106.75 \pm 27.09$ ,  $2.69 \pm 1.44$  vs  $1.65 \pm 0.52$  and  $13.53 \pm 1.40$  vs  $12.62 \pm 0.75$ , respectively; Fig. 2). Then the optimal cut-off values of PLR, NLR, and RDW were determined by an ROC curve analysis. Around 182 pancreatic cancer patients underwent surgical resection were included in this analysis. Results showed the optimal cut-off values of PLR, NLR, and RDW were 150, 1.73, and 13.2 while the AUC of PLR, NLR, and RDW were 0.742, 0.779, and 0.708 (Fig. 3). Finally, pancreatic cancer patients were divided into 2 groups according to the cut-off values of PLR, NLR, and RDW and their clinicopathological characteristics were compared. Results showed there were no significant differences between  $PLR \geq 150$  group and  $PLR < 150$  group. For the comparison between patients grouped by NLR and RDW, results showed there were more number of patients age  $\geq 60$  in  $NLR \geq 1.73$  group compared with  $NLR < 1.73$  group ( $P = .026$ ); Patients in  $RDW \geq 13.2$  group had larger tumor size ( $P = .035$ ), worse tumor differentiation ( $P = .002$ ), more depth tumor infiltration ( $P < .001$ ), worse tumor stage ( $P < .001$ ) and higher CA199 ( $P = 0.012$ ) compared with  $RDW < 13.2$  group; there were no significant differences in other characteristics (Table 1).

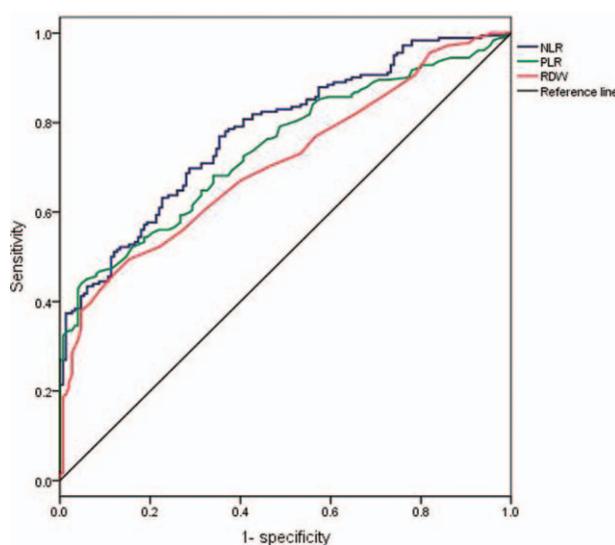
### 3.2. Overall survival analysis for patients grouped by PLR, NLR, and RDW

In this part, pancreatic cancer patients were grouped by the optimal cut-off values of PLR, NLR, and RDW and the OS analysis was performed with Kaplan-Meier estimation with the log-rank test between different groups. Results showed the 5 year OS rate (median time, 24 vs 37.5 months,  $P = .005$ ) in  $PLR \geq 150$  group ( $n = 37$ ) was significantly lower than  $PLR < 150$  group ( $n = 58$ ) (Fig. 4A). However, there were no significant differences in the 5 year OS rate (median time, 34 vs 34 months,  $P = .278$ ) between  $NLR \geq 1.73$  group ( $n = 24$ ) and  $NLR < 1.73$  group ( $n = 71$ ) (Fig. 4B). We finally assessed the 5 year OS rate between  $RDW \geq 13.2$  group ( $n = 47$ ) and  $RDW < 13.2$  group ( $n = 48$ ) and found the OS was significantly lower in  $RDW \geq 13.2$  group compared with  $RDW < 13.2$  group (median time, 27 months vs 37.5 months,  $P = .018$ ) (Fig. 4C). Results in this part showed pancreatic cancer patients with  $PLR \geq 150$  or  $RDW \geq 13.2$  had a worse 5 year OS compared with pancreatic cancer patients with



**Figure 2.** Preoperative peripheral blood NLR, PLR, and RDW between pancreatic cancer group and the control group. Results showed NLR, PLR, and RDW were significantly increased in pancreatic cancer group (N=182) compared with the control (N=150). NLR=neutrophil-to-lymphocyte ratio, PLR=platelet-to-lymphocytes ratio, RDW=red blood cell distribution.

PLR<150 or RDW<13.2 while there were no differences in the 5 year OS between pancreatic cancer patients with NLR≥1.73 and patients with NLR<1.73.



**Figure 3.** ROC analysis for survival prediction according to the preoperative NLR, PLR, and RDW. Area under ROC curves were 0.779, 0.742, and 0.708, respectively. NLR=neutrophil-to-lymphocyte ratio, PLR=platelet-to-lymphocytes ratio, RDW=red blood cell distribution, ROC=receiver operating characteristic.

**3.3. Univariate and multivariable Cox regression analysis for OS in pancreatic cancer patients**

We first did univariate Cox regression analysis for OS in pancreatic cancer patients included in the present study. Results showed the PLR ( $P=.009$ ), RDW ( $P=.025$ ), depth of tumor ( $P=.017$ ), pStage ( $P=.005$ ), carcinoembryonic antigen (CEA) ( $P=.009$ ), CA125 ( $P=.046$ ), and CA199 ( $P=.027$ ) were significantly associated with the OS. Then these 6 factors were included into the multivariable Cox regression analysis. Results showed preoperative PLR≥150 (HR=2.451, 95% CI 1.215–4.947;  $P=.012$ ) and preoperative pStage (HR=1.652, 95% CI 1.068–2.554;  $P=.024$ ) were still associated with the OS independently. Detail results in this part were shown in Table 2.

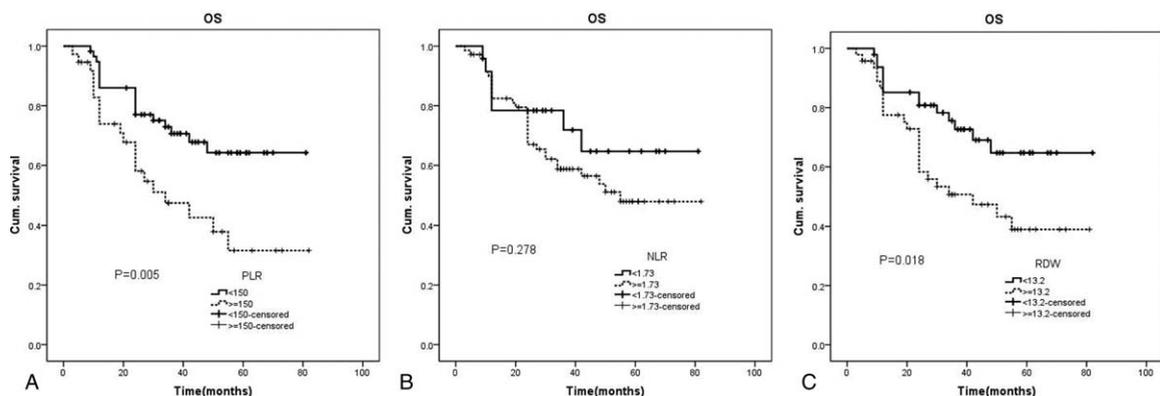
**3.4. Disease free survival analysis for patients grouped by PLR, NLR, and RDW**

In this part, we adopted Kaplan–Meier analysis with the log-rank test to analysis the DFS in patients grouped by PLR, NLR, and RDW. Results showed the 5 year DFS rates (median time, 24 months vs 38 months,  $P=.002$ ) were significantly lower in pancreatic cancer patients with PLR≥150 (n=37) than patients with PLR<150 (n=58) (Fig. 5A). No differences (median time, 34 months vs 34 months,  $P=.277$ ) were found in the 5 year DFS between patients with NLR≥1.73 (n=24) and patients with NLR<1.73 (n=71) (Fig. 5B). Patients with RDW≥13.2 (n=47) had significantly lower 5 year DFS (median time, 24 months vs 37.5 months,  $P=.006$ ) compared with patients with RDW<13.2 (n=48) (Fig. 5C).

**Table 1**  
**Association of NLR, PLR, and RDW with clinicopathological characteristics.**

Characteristics	NLR		P value	PLR		P value	RDW		P value
	<1.73	≥1.73		<150	≥150		<13.2	≥13.2	
Age			.026			.397			.183
<60	28 (66.7)	66 (47.1)		55 (54.5)	39 (48.1)		52 (56.5)	42 (46.7)	
≥60	14 (33.3)	74 (52.9)		46 (45.5)	42 (51.9)		40 (43.5)	48 (53.5)	
Gender			.871			.312			.997
Male	21 (50.0)	72 (51.4)		55 (54.5)	38 (46.9)		47 (51.1)	46 (51.1)	
Female	21 (50.0)	68 (48.6)		46 (45.5)	43 (53.1)		45 (48.9)	44 (48.9)	
Diameter			.913			.130			.035
≤4	23 (54.8)	78 (55.7)		51 (50.5)	50 (61.7)		44 (47.8)	57 (63.3)	
>4	19 (45.2)	62 (44.3)		50 (49.5)	31 (38.3)		48 (52.2)	33 (36.7)	
Differentiation			.109			.084			.002
Well+ Moderate	25 (59.5)	80 (57.1)		56 (55.4)	49 (59.8)		48 (52.2)	57 (63.3)	
Poor	17 (40.5)	60 (42.9)		45 (44.6)	32 (40.2)		44 (47.8)	33 (36.7)	
Depth of tumor			.330			.053			<.001
T1	4 (9.5)	5 (3.6)		6 (5.9)	3 (3.7)		5 (5.4)	4 (4.4)	
T2	19 (45.2)	58 (41.4)		51 (50.5)	26 (32.1)		54 (58.7)	23 (25.6)	
T3	18 (42.9)	69 (49.3)		40 (39.6)	47 (58.0)		30 (32.6)	57 (63.3)	
T4	1 (2.4)	8 (5.7)		4 (4.0)	5 (6.2)		3 (3.3)	6 (6.7)	
Lymph node metastasis			.784			.786			.111
N0	30 (71.4)	103 (73.6)		73 (72.3)	60 (74.1)		72 (78.3)	61 (67.8)	
N1	12 (28.6)	37 (26.4)		28 (27.7)	21 (25.9)		20 (21.7)	29 (32.2)	
Distance metastasis			.570			.451			.848
M0	39 (92.9)	124 (88.6)		92 (91.1)	71 (87.7)		82 (89.1)	81 (90.0)	
M1	3 (7.1)	16 (11.4)		9 (8.9)	10 (12.3)		10 (10.9)	9 (10.0)	
pStage			.209			.184			<.001
I	22 (52.4)	48 (34.3)		46 (45.5)	24 (29.6)		49 (53.3)	21 (23.3)	
II	16 (38.1)	71 (50.7)		43 (42.6)	44 (54.3)		32 (34.8)	55 (61.1)	
III	1 (2.4)	5 (3.6)		3 (3.0)	3 (3.7)		1 (1.1)	5 (5.6)	
IV	3 (7.1)	16 (11.4)		9 (8.9)	10 (12.3)		10 (10.9)	9 (10.0)	
AFP			.930			.102			.497
≤4	17 (68.0)	57 (67.1)		49 (73.1)	25 (58.1)		38 (70.4)	36 (64.3)	
>4	8 (32.0)	28 (32.9)		18 (26.9)	18 (41.9)		16 (29.6)	20 (35.7)	
CEA			.676			.577			.110
≤5	19 (76.0)	61 (71.8)		50 (74.6)	30 (69.8)		43 (79.6)	37 (66.1)	
>5	6 (24.0)	24 (28.2)		17 (25.4)	13 (30.2)		11 (20.4)	19 (33.9)	
CA125			.655			.373			.881
≤35	21 (84.0)	68 (80.0)		56 (83.6)	33 (76.7)		44 (81.5)	45 (80.4)	
>35	4 (16.0)	17 (20.0)		11 (16.4)	10 (23.3)		10 (18.5)	11 (19.6)	
CA199			.667			.796			.012
≤39	10 (40.0)	30 (35.3)		25 (37.3)	15 (34.9)		26 (48.1)	14 (25.0)	
>39	15 (60.0)	55 (64.7)		42 (62.7)	28 (65.1)		28 (51.9)	42 (75.0)	

AFP=alpha fetal protein, CEA=carcinoembryonic antigen, NLR=neutrophil-to-lymphocyte ratio, PLR=platelet-to-lymphocytes ratio, RDW=red blood cell distribution. Data presented as n (%).  $\chi^2$  test was used for statistic analysis.  $P<.05$  was considered statistically significant.



**Figure 4.** Overall survival analysis for patients grouped by PLR, NLR, and RDW. NLR=neutrophil-to-lymphocyte ratio, PLR=platelet-to-lymphocytes ratio, RDW=red blood cell distribution.

**Table 2**  
**Univariate and multivariable Cox regression analyses for OS in 182 patients with pancreatic cancer.**

Variables	Univariate*			Multivariate†		
	HR	95% CI	P value	HR	95% CI	P value
NLR (<1.73/≥1.73)	1.552	0.683–3.526	.293			
PLR (<150/≥150)	2.356	1.244–4.120	.009	2.451	1.215–4.947	.012
RDW (<13.2/≥13.2)	2.130	0.101–2.294	.025	1.379	0.640–2.970	.411
Age (<60/≥60)	1.890	0.953–3.747	.068			
Gender (Male/Female)	0.759	0.396–1.455	.406			
Tumor diameter (≤4/>4)	1.451	0.766–2.748	.253			
Differentiation (Well+Moderate/Poor)	1.521	0.793–2.917	.207			
Depth of tumor (T1/T2/T3/T4)	1.729	1.101–2.714	.017	0.871	0.473–1.604	.658
Lymph node metastasis (N0/N1)	1.284	0.657–2.512	.464			
Distance metastasis (M0/M1)	2.171	0.894–5.272	.087			
pStage (I/II/III/IV)	1.545	1.140–2.094	.005	1.652	1.068–2.554	.024
AFP (≤4/>4)	1.266	0.654–2.451	.485			
CEA (≤5/>5)	2.366	1.240–4.516	.009	2.064	0.970–4.391	.060
CA125 (≤35/>35)	2.096	1.014–4.334	.046	1.211	0.546–2.683	.683
CA199 (≤39/>39)	2.326	1.100–4.917	.027	1.904	0.878–4.130	.103

AFP = alpha fetal protein, CEA = carcinoembryonic antigen, CI = confidence interval, HR = hazard ratio, NLR = neutrophil-to-lymphocyte ratio, OS = overall survival, PLR = platelet-to-lymphocytes ratio, RDW = red blood cell distribution.

\* Performed 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.

† Performed using Cox proportional hazards models with the forward likelihood method.

**3.5. Univariate and multivariable Cox regression analysis for DFS in pancreatic cancer patients**

In order to find the independent prognostic factors for the postoperative DFS in pancreatic cancer patients. We first did univariate Cox regression analysis for DFS. Results showed PLR ( $P = .004$ ), RDW ( $P = .009$ ), age ( $P = .015$ ), depth of tumor ( $P = .007$ ), pStage ( $P = .003$ ), CEA ( $P = .002$ ), CA125 ( $P = .021$ ) and CA199 ( $P = .044$ ) were significantly associated with the DFS. Then these 8 preoperative factors were entered into the multivariable Cox regression analysis. Results showed PLR  $\geq 150$  (HR = 2.712, 95% CI 1.367–5.379;  $P = .004$ ), pStage (HR = 1.732, 95% CI 1.113–2.695;  $P = .015$ ) and CEA (HR = 2.447, 95% CI 1.180–5.077;  $P = .016$ ) were independently associated with the DFS. Details in this part were shown in Table 3.

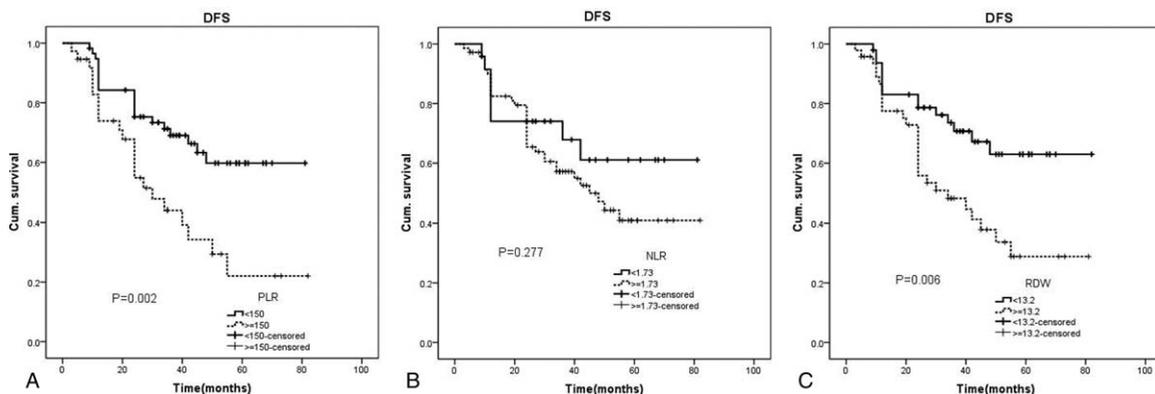
**4. Discussion**

Pancreatic cancer is a kind of serious malignant tumor with a gradual rising morbidity, it is utility to find a relatively simple marker which is associated with the prognosis. We studied the

relationship between PLR, NLR, RDW, and the long-term survival prognosis of pancreatic cancer in the present study, the results showed PLR  $\geq 150$  was independently related with poor postoperative long-term OS and DFS in pancreatic cancer patients.

PLR is a clinical common hematological markers for the assessment of the inflammatory response in cancer patients since it is relatively easy to test before operation and has no adverse effect on the treatment. Previous studies showed PLR was associated with the prognosis of several kind cancers.

Kozasa et al<sup>[9]</sup> reported the pretreatment elevated PLR was independently associated with poor OS and progression-free survival in cervical cancer patients. A meta-analysis reported by Zhou et al<sup>[10]</sup> included a total of 2392 patients with biliary tract cancer and their results showed the pretreatment high PLR was an unfavorable prognostic factor for the OS. Yang et al<sup>[11]</sup> analyzed 778 patients with hepatocellular carcinoma between 2010 and 2013 and found elevated PLR before operation was independently related with poor postoperative OS and DFS. Ma et al<sup>[12]</sup> included 2340 patients with ovarian cancer into their meta-analysis to analyze the relationship between PLR and the prognosis of ovarian



**Figure 5.** Disease free survival analysis for patients grouped by PLR, NLR, and RDW. NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocytes ratio, RDW = red blood cell distribution.

**Table 3****Univariate and multivariable Cox regression analyses for DFS in 182 patients with pancreatic cancer.**

Variables	Univariate*			Multivariate†		
	HR	95% CI	P value	HR	95% CI	P value
NLR (<1.73/≥1.73)	1.512	0.699–3.268	.293			
PLR (<150/≥150)	2.449	1.332–4.503	.004	2.712	1.367–5.379	.004
RDW (<13.2/≥13.2)	2.321	1.233–4.371	.009	1.625	0.786–3.358	.190
Age (<60/≥60)	2.293	1.172–4.485	.015	1.504	0.727–3.112	.271
Gender (Male/Female)	0.796	0.429–1.475	.468			
Tumor diameter (≤4/>4)	1.176	0.638–2.170	.603			
Differentiation (Well+Moderate/Poor)	1.641	0.880–3.060	.119			
Depth of tumor (T1/T2/T3/T4)	1.811	1.177–2.787	.007	0.796	0.432–1.465	.463
Lymph node metastasis (N0/N1)	1.081	0.562–2.082	.815			
Distance metastasis (M0/M1)	1.971	0.818–4.750	.131			
pStage (I/II/III/IV)	1.556	1.164–2.079	.003	1.732	1.113–2.695	.015
AFP (≤4/>4)	1.370	0.733–2.558	.324			
CEA (≤5/>5)	2.594	1.400–4.805	.002	2.447	1.180–5.077	.016
CA125 (≤35/>35)	2.268	1.129–4.558	.021	1.274	0.568–2.858	.557
CA199 (≤39/>39)	2.029	1.091–4.040	.044	1.644	0.807–3.350	.171

AFP = alpha fetal protein, CEA = carcinoembryonic antigen, CI = confidence interval, DFS = disease free survival, HR = hazard ratio, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocytes ratio, RDW = red blood cell distribution.

\* Performed 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.

† Performed using Cox proportional hazards models with the forward likelihood method.

cancer, results showed the elevated PLR is associated with poor OS. All these previous studies showed PLR was a potentially simple and reliable biomarkers for the prediction of cancer prognosis.

We reviewed studies on the predictive role of PLR and pancreatic cancer prognosis and found PLR was associated with its prognosis. Martin et al<sup>[13]</sup> analyzed data from 124 patients with advanced pancreatic cancer and found patients with  $PLR \geq 200$  had a median survival of 4 months while the median survival was 9.1 months in patients with  $PLR < 200$ , which indicated elevated PLR was associated with poor median survival. In the research reported by Asari et al,<sup>[5]</sup> a total of 37 pancreatic cancer patients were included in their study and the postoperative median survival was compared, results showed patients with preoperative  $PLR \leq 225$  had a median survival of 24.7 months while patients with preoperative  $PLR > 225$  had a median survival of only 10.2 months. Recently, a meta-analysis which included eight studies with 1904 pancreatic cancer patients reported by Song et al<sup>[14]</sup> showed elevated PLR was associated with decreased OS, especially in patients with  $PLR > 150$ . In our study, we analyzed data from pancreatic cancer patients who received surgical treatment in our center, the prognostic value of preoperative PLR was tested and compared with other inflammation based hematological biomarkers such as NLR, RDW, CEA, CA199, and CA125. Our results showed that only PLR was independently associated with postoperative OS and DFS. Patients with  $PLR \geq 150$  had a significantly lower 5 year OS and DFS compared with patients with  $PLR < 150$ .

In the present study, we also found PLR was significantly increased in pancreatic cancer patients compared with the control, in addition to its association with postoperative OS and DFS. Mechanisms responsible for the increased PLR in pancreatic cancer have not been fully clarified. But some studies showed pancreatic cancer cells activated thrombocytes production while suppressed lymphocytes. Khorana et al<sup>[15]</sup> reported pancreatic cancer always induced thromboembolic disease which indicated pancreatic cancer might promoted the production of thrombocytes. Hamada et al reported pancreatic cancer tissues produced large amounts of IL-6, which activated megakaryocyte proliferation and produced more thrombocytes.<sup>[16,17]</sup> A study reported by Romano et al<sup>[18]</sup>

included 22 pancreatic cancer patients, they found pancreatic cancer always accompanied by significantly decreased lymphocytes which showed a significantly immunosuppression. Bellone et al reported pancreatic cancer cells produced more transforming growth factor- $\beta$  (TGF- $\beta$ ) and interleukin-10 (IL-10), both has been demonstrated had a significant immunosuppressive effect on lymphocytes.<sup>[19,20]</sup> These studies partly explained the increased PLR in pancreatic cancer patients and the relation between PLR and the postoperative prognosis. However, the specific mechanism for the increased thrombocytes production and lymphocytes suppression still need to be further investigated.

## 5. Conclusion

In the present study, we find hematological biomarkers  $PLR \geq 150$  is an independently predictive risk factor for the postoperative long-term prognosis in pancreatic cancer patients. Our study may provide a convenient way for the prognostic assessment of pancreatic cancer patients.

## Author contributions

**Conceptualization:** Jinming Yu, Shanli Liu.

**Data curation:** Jinming Yu, Zhaoyan Ding, Yuanming Yang, Shanli Liu.

**Formal analysis:** Jinming Yu, Zhaoyan Ding, Yuanming Yang.

**Investigation:** Jinming Yu, Yuanming Yang, Shanli Liu.

**Methodology:** Jinming Yu, Zhaoyan Ding, Yuanming Yang, Shanli Liu.

**Writing – original draft:** Jinming Yu, Shanli Liu.

**Writing – review & editing:** Shanli Liu.

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