Original Paper

Neutrophil-to-Lymphocyte Ratio and Platelet Count Predict Long-Term Outcome of Stage IIIC Epithelial Ovarian Cancer

Mingyi Zhou Liankun Li Xiaobin Wang Chunyan Wang Danbo Wang

Department of Gynecology, Cancer Hospital of China Medical University, Liaoning Cancer Hospital & Institute, Shenyang, Liaoning Province, PR China

Key Words

Epithelial ovarian cancer • Neutrophil-to-lymphocyte ratio • Platelet count • Progression-free survival • Overall survival

Abstract

Background/Aims: Prognostic value of neutrophil-to-lymphocyte ratio (NLR) and platelet count (PC) in patients with International Federation of Gynecology and Obstetrics (FIGO) stage IIIC epithelial ovarian cancer (EOC) is controversial. **Methods:** A total of 370 stage IIIC EOC patients who underwent primary debulking surgery (PDS) at the Department of Gynecology of Liaoning Cancer Hospital and Institute between January 2003 and August 2016 and had full information were involved. Patients were stratified into a high NLR (H-NLR) group versus a low NLR (L-NLR) group and a high PC (H-PC) group versus a low PC (L-PC) group according to cut-off values calculated through receiver operating characteristic (ROC) curves. Prognostic values of NLR and PC for progression-free survival (PFS) and overall survival (OS) were assessed. **Results:** We identified the optimal cut-off value of 3.08 for NLR and $289.5 \times 10^9/L$ for PC. The median PFS and OS of the patients with H-NLR were shorter than L-NLR (PFS: 16.9 months vs. 19.5 months, hazard ratio [HR] 1.3, 95% confidence interval [CI] 1.03–1.63, $P = 0.022$; OS: 33.5 months vs. 46.8 months, HR 1.3, 95% CI 1.01–1.66, $P = 0.001$). The median PFS and OS of the patients with H-PC were shorter than L-PC (PFS: 15.3 months vs. 21.6 months, HR 1.3, 95% CI 1.04–1.63, $P < 0.001$; OS: 37.3 months vs. 46.1 months, HR 1.14, 95% CI 0.89–1.46, $P = 0.306$). **Conclusions:** H-NLR and H-PC could predict poor long-term outcome of patients with FIGO stage III EOC.

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Introduction

Epithelial ovarian cancer (EOC) has a poor prognosis. There were 22, 440 estimated new cases and 14, 080 deaths in the United States in 2017 [1] and 52, 100 estimated new cases and 22, 500 deaths in China in 2015 [2]. Even though optimal primary debulking surgery (PDS) and carboplatin-based chemotherapy have improved survival, the 5-year

Danbo Wang,
Chunyan Wang
and Xiaobin Wang

Department of Gynecology, Cancer Hospital of China Medical University,
Liaoning Cancer Hospital & Institute (PR China)
E-Mail wangdanbo@cancerhosp-ln-cmu.com, wangchunyan@cancerhosp-ln-cmu.com,

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overall survival rate of FIGO stage III ovarian cancer (OC) is 24.26% [3]. Specific and effective biomarkers for predicting the treatment outcome of advanced EOC are urgently needed.

Tumor-associated neutrophils and thrombocytosis have been demonstrated to play important roles in tumor progression, angiogenesis, and invasion of EOC [4]. Increased neutrophil to lymphocyte ratio (NLR) and platelet count (PC) are associated with the disease severity and poor prognosis of several kinds of malignant tumor [5-8]. Two meta-analyses about the prognostic significance of neutrophil to lymphocyte ratio in ovarian cancer were published in 2017 [9, 10]. The results showed the high NLR (H-NLR) were associated with unfavorable overall survival (OS) and progression-free survival (PFS). But extreme heterogeneity existed among studies (heterogeneity of OS: I^2 80.2%, $P < 0.001$; heterogeneity of PFS: I^2 85.2%, $P < 0.001$). The subgroup analyses of both two meta-analyses according to ethnicity showed that H-NLR was associated with shorter OS for Asian patients but not Caucasian patients. Furthermore, difference of incidence and mortality of cancer existed between the patients in North and South China [2]. And the characteristics of ovarian cancer patients between North and South China were not consistent [11]. In Chen's meta-analysis, there were five Chinese studies and all of them were sponsored by the institutes in South China. In Zhou's meta-analysis, there were six Chinese studies. Among these six studies, five studies were sponsored by the institutes in South China. Only one study was sponsored by an institute in North China. And only 80 patients with FIGO stage III-IV ovarian cancer were included this retrospective study [12]. So the correlation between NLR and the prognosis of FIGO stage IIIC EOC patients in Northeast China needed further investigation.

Materials and Methods

Clinical Data

This retrospective study was approved by the ethics committees of Liaoning Cancer Hospital and Institute (Cancer Hospital of China Medical University). Written informed consent was obtained from each patient included in this study.

A total of 370 patients with FIGO stage IIIC EOC who underwent primary debulking surgery (PDS) were retrospectively investigated between January 2003 and August 2016 at the Department of Gynecology of Liaoning Cancer Hospital and Institute. All enrolled patients met the following criteria: (1) diagnosis of FIGO stage IIIC EOC; (2) performance of PDS without neoadjuvant chemotherapy; (3) suspicion of intra-abdominal diffuse disease based on preoperative radiological assessments (computed tomography/ultrasonography); (4) use of platinum-based chemotherapy as postoperative adjuvant chemotherapy; (5) availability of data including neutrophil count, lymphocyte count, and PC; and (6) availability of other data including age, preoperative serum CA125 concentration, volume of ascites, histology and grade of tumor, Gynecologic Oncology Group performance status, and maximum size of residual disease. The 2014 FIGO guidelines removed patients with only positive retroperitoneal lymph nodes from the definition of stage IIIC EOC [13]. Therefore, we reassessed the cancer stage for all patients before 2014 according to their pathological reports. NCCN guideline was followed during the diagnosis and treatment of patients. All patients were followed up until April 30, 2017.

Optimal PDS was defined as residual disease (RD) ≤ 1 cm, and suboptimal PDS was defined as RD > 1 cm. PFS was defined as the time interval from the date of PDS to the date of disease progression or recurrence. OS was defined as the time interval from the date of PDS to the date of death or the last follow-up.

NLR was defined as neutrophil count divided by lymphocyte count. PC was defined as the absolute value of platelet count. Preoperative peripheral blood samples from the patient were drawn within 5 days prior to surgery.

Statistical Analyses

The optimal cut-off values of NLR and PC for predicting OS were calculated through receiver operating characteristic (ROC) curves. A total of 370 patients were stratified as H-NLR group versus low NLR (L-NLR) group and as high PC (H-PC) group versus low PC (L-PC) group according to cut-off values. H-NLR and H-PC were each assigned a score of 1, and peripheral blood index value (PBIV) was defined as the total score

according to the status of NLR and PC. The optimal cut-off value of PBIV predicting OS was calculated through ROC curves.

The categorical data were compared with chi-square tests. PFS and OS were analyzed using the Kaplan-Meier method. Univariate analyses were performed using log-rank tests. Multivariate analyses were performed using Cox regression analysis to assess the effects of the prognostic factors, which were expressed as hazard ratios. $P < 0.05$ was considered statistically significant, and all P values were two-sided. Some factors, such as pre-operative ascites volume, belonged to multiple categorical variables. When $<1000\text{ml}$ group was considered as the reference group, two dummy variables associated with $1000\text{--}3000\text{ml}$ and $>3000\text{ml}$ groups, respectively, were included in the COX model. Hence, the hazard ratios were estimated between the pairs of the groups [14]. All data analyses were performed using SPSS 16.0 (SPSS Inc., Chicago, IL).

Results

Cut-off values of NLR and PC

A total of 370 patients with stage FIGO III EOC were finally included in our retrospective study according to the inclusion criteria. Table 1 shows the characteristics of the patients. In 238 patients with serous carcinoma, 16 patients had low grade serous carcinoma and the other 222 patients had high grade serous carcinoma.

The following optimal cut-off values were identified: 3.08 for NLR (area under curve [AUC] 0.66, $P < 0.001$, sensitivity 0.62, specificity 0.65) and $289.5 \times 10^9/\text{L}$ for PC (AUC 0.61, $P < 0.001$, sensitivity 0.52, specificity 0.67) (Fig. 1). Therefore, H-NLR referred to patients with $\text{NLR} > 3.08$ and H-PC referred to patients with $\text{PC} > 289.5 \times 10^9/\text{L}$.

Correlation between NLR and PC and clinicopathological variables

The associations between NLR and PC and the main clinicopathological variables of patients with FIGO stage IIIC EOC were investigated (Table 2). H-NLR was observed more often in younger patients ($P = 0.034$), patients with more preoperative ascites ($P < 0.001$), higher preoperative CA125 value ($P = 0.004$), lower differentiation of tumor ($P = 0.009$), longer period of stay in hospital ($P = 0.012$), patients had blood transfusion ($P = 0.001$), and patients had plasma transfusion ($P < 0.001$). H-PC was more often observed in patients with more preoperative ascites ($P < 0.001$) and those with higher preoperative CA125 value ($P = 0.001$).

NLR and PC and survival analysis

PFS and OS according to the main clinicopathological variables, NLR, and PC are shown in Table 3.

Regarding PFS, from univariate analysis the variables associated with a shorter PFS included menopause status, volume of preoperative ascites, histology of tumor, grade of tumor,

Table 1. Characteristics of the patients. *Grade 1 referred to the well-differentiated epithelial ovarian cancer; Grade 2 referred to the moderately-differentiated epithelial ovarian cancer; Grade 3 referred to the poorly-differentiated epithelial ovarian cancer. Abbreviations: RD, residual disease; GOG, Gynecological Oncology Group; PFS, progression free survival; OS, overall survival

Variable	Data
Number of patients	370
Size of RD (cm)	
RD=0	112 (30.4%)
RD≤1	93 (25.0%)
RD>1	165 (44.6%)
Age	54.3±8.7
Menopause	
No	145 (39.2%)
Yes	225 (60.8%)
GOG performance status	
0-1	302(81.6%)
2	59(15.9%)
3	9(2.5%)
Preoperative ascites volume (ml)	2600±1679.5
Preoperative CA125 level (U/ml)	3300±688.7
Grade of tumor*	
1	24 (6.5%)
2	133 (35.9%)
3	213 (57.6%)
Histotype of tumor	
Serous	238 (64.3%)
Endometriod	46 (12.4%)
Mucinous	3 (0.8%)
Clear cell	4 (1.1%)
Adenocarcinoma, not otherwise specified	79 (21.4%)
Regimen of adjuvant chemotherapy	
Docetaxel/Paclitaxel plus cisplatin	123 (33.2%)
Docetaxel/Paclitaxel plus carboplatin	247 (66.8%)
Cycle of adjuvant chemotherapy	
<6	56 (15.1%)
≥6	314 (84.9%)
Second debulking surgery	
No	299 (80.8%)
Yes	71 (19.2%)
Median PFS (months)	17.7 (12.4-25.9)
Median OS (months)	34.5 (26.3-50.7)

stay in hospital, RD, regimen of adjuvant chemotherapy, second debulking surgery, NLR, and PC. Furthermore, from multivariate analysis by Cox regression the independent variables associated with a shorter PFS were histology of tumor, grade of tumor, RD, NLR, and PC. Patients with serous carcinoma mucinous had shorter PFS than endometrioid carcinoma but longer PFS than mucinous carcinoma. Patients with poor differentiation of tumor, RD >1 cm, NLR >3.08, and PC >289.5*10⁹/L had shorter PFS and were more likely to relapse after the initial treatment. The median PFS of patients with NLR >3.08 was 2.6 months shorter than that of patients with NLR <3.08 (16.9 months vs. 19.5 months, HR 1.3, 95% CI 1.03–1.63, *P* = 0.022). The median PFS of patients with PC >289.5*10⁹/L was 6.3 months shorter than that of patients with PC <289.5*10⁹/L (15.3 months vs. 21.6 months, HR 1.3, 95% CI 1.04–1.63, *P* < 0.001) (Fig. 2 and Table 3).

Regarding OS, from univariate analysis the variables associated with a shorter OS included histology of tumor, grade of tumor, RD, blood transfusion, regimen and cycles of adjuvant chemotherapy, second debulking surgery, NLR, and PC. Multivariate analysis by Cox regression showed that the independent variables associated with a shorter OS were histology of tumor, grade of tumor, RD, cycle of adjuvant chemotherapy and NLR. Patients with serous carcinoma mucinous had shorter OS than endometrioid carcinoma but longer OS than mucinous carcinoma. Patients with ≥6 cycles of adjuvant chemotherapy had longer OS than <6 cycles. Patients with poor differentiation of tumor, RD >1 cm, and NLR >3.08 had shorter OS. The median OS of patients with NLR >3.08 was 13.3 months shorter

Fig. 1. ROC curves of NLR (A) and PC (B) as predictors of OS.

Table 2. Correlations between NLR and PC and main clinicopathological variables for the patients. *Grade 1 referred to the well-differentiated epithelial ovarian cancer; Grade 2 referred to the moderately-differentiated epithelial ovarian cancer; Grade 3 referred to the poorly-differentiated epithelial ovarian cancer. Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PC, platelet count; RD, residual disease; PDS, primary debulking surgery

	No. of patients	H-NLR	L-NLR	P of NLR	H-PC	L-PC	P of PC
Age (y)				0.034			0.229
<65	315	169(53.7%)	146(46.3%)		184(58.4%)	131(41.6%)	
≥65	55	21(38.2%)	34(61.8%)		28(50.9%)	27(49.1%)	
Menopause				0.908			0.055
No	145	75(51.7%)	70(48.3%)		92(63.4%)	53(36.6%)	
Yes	225	115(51.1%)	110(48.9%)		120(53.3%)	105(46.7%)	
Pre-operative ascites volume (ml)				<0.001			<0.001
<1000	153	55(35.9%)	98(64.1%)		64(41.8%)	89(58.2%)	
1000–3000	127	77(60.6%)	50(39.4%)		79(62.2%)	48(37.8%)	
>3000	90	58(64.4%)	32(35.6%)		69(76.7%)	21(23.3%)	
Pre-operative CA125 value				0.004			0.001
<1000	269	124(46.1%)	145(53.9%)		141(52.4%)	128(47.6%)	
1000–5000	86	57(66.3%)	29(33.7%)		57(66.3%)	29(33.7%)	
>5000	15	9(60%)	6(40%)		14(93.3%)	1(6.7%)	
Histology of tumor				0.835			0.061
Serous	238	123(51.7%)	115(48.3%)		145(60.9%)	93(39.1%)	
Endometrioid	46	23(50%)	23(50%)		24(52.2%)	22(47.8%)	
Mucinous	3	2(66.7%)	1(33.3%)		1(33.3%)	2(66.7%)	
Clear cell	4	3(0.8%)	1(49.4%)		2(50.0%)	2(50.0%)	
Adenocarcinoma, not otherwise specified	79	39(49.4%)	40(50.6%)		40(50.6%)	39(49.4%)	
Grade of tumor				0.009			0.733
G1	24	10(41.7%)	14(58.3%)		12(50%)	12(50%)	
G2	133	56(42.1%)	77(57.9%)		78(58.6%)	55(41.4%)	
G3	213	124(58.2%)	89(41.8%)		122(57.3%)	91(42.7%)	
Stay in hospital (d)				0.012			0.517
≤30	306	148(48.4%)	158(51.6%)		173(56.5%)	133(43.5%)	
>30	64	42(65.6%)	22(34.4%)		39(60.9%)	25(39.1%)	
RD (cm)				0.372			0.909
≤1	205	101(49.3%)	104(50.7%)		118(57.6%)	87(42.4%)	
>1	165	89(53.9%)	76(46.1%)		94(57%)	71(43%)	
Surgical procedure (min)				0.071			0.536
≤240	305	150(49.2%)	155(50.8%)		177(58.0%)	128(42.0%)	
>240	65	40(61.5%)	25(38.5%)		35(53.8%)	30(46.2%)	
Blood loss during PDS (ml)				0.361			0.051
<1000	336	170(50.6%)	166(49.4%)		198(58.9%)	138(41.1%)	
>1000	34	20(58.8%)	14(41.2%)		14(41.2%)	20(58.8%)	
Blood transfusion				0.001			0.84
No	122	48(39.3%)	74(60.7%)		69(56.6%)	53(43.4%)	
Yes	248	142(57.3%)	106(42.7%)		143(57.7%)	105(42.3%)	
Plasma transfusion				<0.001			0.37
No	294	137(46.6%)	157(53.4%)		165(56.1%)	129(43.9%)	
Yes	76	53(69.7%)	23(30.3%)		47(61.8%)	29(38.2%)	
Regimen of adjuvant chemotherapy				0.286			0.059
Docetaxel/Paclitaxel plus cisplatin	123	68(55.3%)	55(44.7%)		62(50.4%)	61(49.6%)	
Docetaxel/Paclitaxel plus carboplatin	247	122(49.4%)	125(50.6%)		150(60.7%)	97(39.3%)	
Cycle of adjuvant chemotherapy*				0.826			0.136
<6	56	28(50%)	28(50%)		27(48.2%)	29(51.8%)	
≥6	314	162(51.6%)	152(48.4%)		185(58.9%)	129(41.1%)	
Second debulking surgery				0.361			0.654
No	299	157(52.5%)	142(47.5%)		173(57.9%)	126(42.1%)	
Yes	71	33(46.5%)	38(53.5%)		39(54.9%)	32(45.1%)	

Fig. 2. NLR predicted PFS and OS (A and B); PC predicted PFS and OS (C and D).

Table 3. NLR and PC predicted PFS and OS. *Grade 1 referred to the well-differentiated epithelial ovarian cancer; Grade 2 referred to the moderately-differentiated epithelial ovarian cancer; Grade 3 referred to the poorly-differentiated epithelial ovarian cancer. Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PC, platelet count; PFS, progression free survival; OS, overall survival; HR, hazard ratio; RD, residual disease; PDS, primary debulking surgery

	No. of patients	Univariate analysis, P	PFS Multivariate analysis, P	HR(95%CI)	Univariate analysis, P	OS Multivariate analysis, P	HR(95%CI)
Age (y)							
<65	315	Referent			Referent		
≥65	55	0.797			0.561		
Menopause							
No	145	Referent	Referent		Referent		
Yes	225	0.052	0.586		0.947		
Pre-operative ascites volume (ml)							
<1000	153	Referent	Referent		Referent		
1000-3000	127	0.001	0.128		0.002	0.132	
>3000	90	0.014	0.537		0.071	0.974	
Pre-operative CA125 value (U/ml)							
<1000	269	Referent	Referent		Referent		
1000-5000	86	0.145			0.176		
>5000	15	0.306			0.684		
Histology							
Serous	238	Referent	Referent		Referent	Referent	
Endometrioid	46	0.006	0.017	0.67(0.48-0.93)	0.146	0.041	0.69(0.48-0.99)
Mucinous	3	<0.001	<0.001	29.41(8.53-101.45)	0.009	0.017	5.73(1.36-24.09)
Clear cell	11	0.981	0.343	1.63(0.60-4.45)	0.958	0.584	1.38(0.44-4.39)
Adenocarcinoma, not otherwise specified	72	0.098	0.364	1.13(0.87-1.49)	0.074	0.189	1.21(0.91-1.62)
Grade of tumor*							
G1	24	Referent	Referent		Referent	Referent	
G2	133	<0.001	<0.001	2.65(1.66-4.23)	<0.001	0.002	2.42(1.40-4.18)
G3	213	<0.001	<0.001	3.00(1.89-4.75)	<0.001	<0.001	2.69(1.56-4.65)
Stay in hospital (d)							
≤30	306	Referent	Referent		Referent		
>30	64	0.074	0.664		0.155		
RD (cm)							
≤1	205	Referent	Referent		Referent	Referent	
>1	165	<0.001	<0.001	2.09(1.65-2.65)	<0.001	<0.001	1.73(1.36-2.21)
Surgical procedure (min)							
≤240	305	Referent			Referent		
>240	65	0.499			0.480		
Blood loss during PDS (ml)							
<1000	336	Referent			Referent		
>1000	34	0.884			0.967		
Blood transfusion							
No	122	Referent			Referent	Referent	
Yes	248	0.115			0.013	0.903	
Plasma transfusion							
No	294	Referent			Referent		
Yes	76	0.102			0.141		
Regimen of adjuvant chemotherapy							
Docetaxel/Paclitaxel plus cisplatin	123	Referent	Referent		Referent	Referent	
Docetaxel/Paclitaxel plus carboplatin	247	0.002	0.050	0.79(0.63-1.00)	0.041	0.058	
Cycle of adjuvant chemotherapy							
<6	56	Referent			Referent	Referent	
≥6	314	0.637			0.033	0.021	0.66(0.46-0.94)
Second debulking surgery							
No	299	Referent	Referent		Referent	Referent	
Yes	71	0.053	0.164		0.033	0.228	
NLR							
<3.08	180	Referent	Referent		Referent	Referent	
≥3.08	190	0.022	0.005	1.38(1.10-1.72)	0.001	0.010	1.38(1.08-1.77)
PC							
<289.5*10 ⁹ /L	158	Referent	Referent		Referent	Referent	
≥289.5*10 ⁹ /L	212	<0.001	0.014	1.33(1.06-1.66)	0.086	0.099	1.23(0.96-1.58)

than that of patients with NLR <3.08 (33.5 months vs. 46.8 months, HR 1.3, 95% CI 1.01–1.66, $P = 0.001$). The median OS of patients with PC >289.5*10⁹/L was shorter than that of patients with PC <289.5*10⁹/L, but the difference was not significant (37.3 months vs. 46.1 months, HR 1.14, 95% CI 0.89–1.46, $P = 0.306$) (Fig. 2 and Table 3).

Peripheral blood index value by combined NLR and PC

The PBIV of each patient was calculated. The optimal cut-off value of PBIV predicting OS was 0.5 (AUC 0.66, $P < 0.001$, sensitivity 0.38, specificity 0.87) (Fig. 3A).

The median PFS of patients with PBIV >0.5 was 7.9 months shorter than that of patients with PBIV <0.5 (16.2 months vs. 24.1 months, $P = 0.002$) (Fig. 3B). The median OS of patients with PBIV >0.5 was 14.0 months shorter than that of patients with PBIV <0.5 (37.3 months vs. 51.3 months, $P = 0.011$) (Fig. 3C).

Subgroup analyses for serous and non-serous EOC patients

For serous EOC patients, the median PFS of patients with NLR >3.08 was 6.7 months shorter than that of patients with NLR <3.08 (15.6 months vs. 22.3 months, $P = 0.001$) (Fig. 4A). The median OS of patients with NLR >3.08 was 13.7 months shorter than that of patients with NLR <3.08 (34.9 months vs. 48.6 months, $P = 0.002$) (Fig. 4B). The median PFS of patients with PC $>289.5 \times 10^9/L$ was 2.2 months shorter than that of patients with PC $<289.5 \times 10^9/L$, but the difference was not significant (17.9 months vs. 20.1 months, $P = 0.156$) (Fig. 4C). The median OS of patients with PC $>289.5 \times 10^9/L$ was 9.5 months shorter than that of patients with PC $<289.5 \times 10^9/L$, but the difference was not significant (38.2 months vs. 47.7 months, $P = 0.126$) (Fig. 4D).

For non-serous EOC patients, the median PFS of patients with NLR >3.08 was 5.4 months shorter than that of patients with NLR <3.08 (14.9 months vs. 20.3 months, $P = 0.045$) (Fig. 5A). The median OS of patients with NLR >3.08 was 11.7 months shorter than that of patients with NLR <3.08 , but the difference was not significant (33.5 months vs. 45.2 months, $P = 0.154$) (Fig. 5B). The median PFS of patients with PC $>289.5 \times 10^9/L$ was 1.9 months shorter than that of patients with PC $<289.5 \times 10^9/L$ (15.8 months vs. 17.7 months, $P = 0.048$) (Fig. 5C). The median OS of patients with PC $>289.5 \times 10^9/L$ was 6.1 months shorter than that of patients with PC $<289.5 \times 10^9/L$, but the difference was not significant (36.8 months vs. 42.9 months, $P = 0.390$) (Fig. 5D).

Discussion and Conclusion

The results of our retrospective study suggested that H-NLR and H-PC could predict poor long-term outcome of patients with FIGO stage III EOC who live in Northeast China. The median PFS and OS of the patients with H-NLR and H-PC were significantly shorter than those of patients with L-NLR and L-PC. We identified the optimal cut-off values of 3.08 for NLR and $289.5 \times 10^9/L$ for PC.

Moreover, H-NLR was associated with earlier onset age, more preoperative ascites, higher preoperative CA125 value, lower differentiation of tumor, and longer period of

Fig. 3. ROC curves of PBIV model as predictor of OS (A); PBIV model predicted PFS (B); PBIV model predicted OS (C).

Fig. 4. NLR predicted PFS and OS of serous EOC patients (A and B); PC predicted PFS and OS of serous EOC patients (C and D).

stay in hospital, whereas H-PC was associated with more preoperative ascites and higher preoperative CA125 value. Consistent with our results, other papers reported that the elevated NLR and PC were corresponding to the elevated preoperative CA125 value [15, 16].

Recently published papers demonstrated that gastric cancer, esophageal cancer, myeloma, small cell lung cancer, and non-small cell lung cancer patients with H-NLR and H-PC showed poor OS [5-8, 17]. Six Chinese institutes have investigated and indicated the correlation between NLR and long-term outcome of EOC [12][18-22]. Most studies included only about 100 patients. Compared with these studies, we specifically analyzed the data of FIGO stage IIIC EOC patients, which avoided heterogeneity caused by tumor stage. Moreover, among these six studies, five studies were sponsored by the institutes in South China [18-22]. Only one retrospective study analyzing the data of 80 FIGO stage III-IV ovarian cancer patients was sponsored by an institute in North China [12]. The results suggested that H-NLR was associated with poor prognosis. Our study is the first to provide data for patients from Northeast China with advanced EOC. Other published studies analyzing the data of foreign patients outside China had the consistent conclusion with us [4, 15, 16, 23-25].

Patients with H-PC were characterized as having thrombocytosis. H-PC was correlated with the OS of TNM stage IV colorectal cancer [26]. Watrowski R, et al. retrospectively analyzed 172 malignant and 584 benign primary adnexal tumors and indicated that H-PC predicted malignancy [27]. Several papers suggested that thrombocytosis was associated with poor prognosis of EOC patients, which was the logical consequence of the role of platelets in the pathogenesis of ovarian cancer [28-32]. However, the number of patients involved in the published papers was insufficient. Moreover, subgroup analysis of advanced EOC patients was limited. Our study was the first to investigate the relationship between H-PC and prognosis for the patients from Northeast China with advanced EOC.

Tumor-associated neutrophils have been demonstrated in the cancer microenvironment. Neutrophils play important roles in tumor progression, angiogenesis, and invasion [33], and a lack of tumor-infiltrating lymphocytes is associated with poor prognosis of ovarian cancer [34, 35]. These results further support our finding that EOC patients with H-NLR had poor long-term outcome.

Our study had some strengths. First, all 370 patients involved were diagnosed with FIGO stage IIIC EOC, which eliminated bias due to stage. Second, the median follow-up period of this study exceeded 10 years. Third, NLR and PC are both easily available biomarkers. Moreover, PC is a better variable than platelet-to-lymphocyte ratio as it eliminates bias due to different lymphocyte counts. However, this study still has some limitations. As this was a mono-institutional study, a multi-institutional study investigating the predictive effect of NLR and PC in advanced EOC is needed. Moreover, this retrospective study depended on accurate documentation and a prospective study without recall bias should be performed.

In conclusion, H-NLR and H-PC could predict poor long-term outcome of patients with FIGO stage III EOC.

Fig. 5. NLR predicted PFS and OS of non-serous EOC patients (A and B); PC predicted PFS and OS of non-serous EOC patients (C and D).

Disclosure Statement

No conflict of interests exists.

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