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Original Article

Correlation of immune inflammatory indices and nutritional risk index with prognosis in patients with non-small cell lung cancer

Zhongmiao Shi[1*], Dawei Zheng[2*], Xiaowan Tang[3], Youyi Du[4]

[1]Department of Cardio-Thoracic Surgery, Shaoxing Shangyu Hospital of Traditional Chinese Medicine, Shaoxing 312300, Zhejiang, China; [2]Department of Respiratory, Nanyang Central Hospital, Nanyang 473000, Henan, China; [3]Department of Medical Oncology, Taizhou First People's Hospital, Taizhou 318000, Zhejiang, China; [4]Department of Respiratory Medicine, Lishui Central Hopistal, Lishui 323000, Zhejiang, China. [*]Equal contributors.

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Abstract: Objective: To investigate the relationship of lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and nutritional risk index (NRI) with the prognosis of non-small cell lung cancer (NSCLC). Methods: The clinical data of 400 NSCLC patients undergoing surgery at Shaoxing Shangyu Hospital of Traditional Chinese Medicine from January 2019 to June 2022 were collected for this retrospective analysis. The optimal cutoff values for NLR, PLR, LMR and NRI were determined using receiver operating characteristic (ROC) curves. The patients were grouped according to the optimal cutoff values, and the clinicopathological characteristics were compared between groups. The Kaplan-Meier survival curve and Cox risk model were used to identify the independent risk factors affecting the prognosis of patients with NSCLC. A nomogram risk prediction model was constructed and its effectiveness was verified. Results: ROC curve analysis revealed that the area under the curve (AUC) values for NLR, PLR, LMR and NRI in predicting overall survival of NSCLC patients were 0.827, 0.753, 0.719 and 0.770, respectively. The optimal cutoff values for NLR, PLR, LMR and NRI were 2.49, 126.32, 3.02 and 89, respectively. Survival analysis found that the survival time was shorter in patients with NLR>2.49, PLR>126.32, LMR>3.02 and NRI≤89. Results from Cox model indicated that TNM staging, NLR>2.49, LMR>3.02, NRI≤89, surgical method, intraoperative blood loss, postoperative complication, and adjuvant chemotherapy were risk factors affecting the prognosis of NSCLC patients. A nomogram was constructed based on the results of multivariate analysis. The AUC of the nomogram was 0.967 (95% CI: 0.943-0.992) and 0.948 (95% CI: 0.874-1) in the training set and the test set, respectively. The C-index was 0.90 and 0.89, respectively. The calibration curve demonstrated good agreement between the predicted values of the nomogram and the actual observed values. Conclusion: NLR, LMR and NRI are significant predictors of the prognosis of patients with NSCLC. NLR>2.49, LMR>3.02, and NRI≤89 are risk factors for the prognosis of NSCLC patients.

Keywords: NLR, LMR, NRI, NSCLC, relevance

Introduction

Lung cancer is a common malignancy with a high incidence and poor prognosis. It is classified into small cell lung cancer and non-small cell lung cancer (NSCLC), with NSCLC accounting for 80-85% of all lung cancer cases, seriously affecting human life and health [1]. For patients with early NSCLC, surgery is the first choice of treatment. However, due to no typical clinical symptoms in the early stage and rapid disease progression, NSCLC patients are often diagnosed in the middle and late stages, missing the optimal time for surgery. As a result, their 5-year survival rate is less than 15% [2]. Investigating the risk factors associated with the prognosis of NSCLC patients can help identify high-risk patients and give early intervention. Lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) are valid indicators of systemic inflammatory response and have been

proven in several studies to be indicators associated with the prognosis of many solid tumors, such as breast cancer and kidney cancer [3-5]. In recent years, it has been reported that the nutritional status of patients can affect the prognosis to a certain extent, and malnutrition can increase the adverse outcomes of lung cancer patients after surgery [6]. The nutritional status of patients can be reflected by nutritional risk index (NRI), but there are few reports on the association of inflammatory markers and NRI with the prognosis of NSCLC patients. Therefore, this study aimed to evaluate the predictive value of NLR, PLR, LMR and NRI for the prognosis of NSCLC patients.

Material and methods

Ethics statement

This study was approved by the Ethics Committee of Shaoxing Shangyu Hospital of Traditional Chinese Medicine.

General information

This is a retrospective analysis. The clinical data of 400 NSCLC patients who underwent surgical treatment in Shaoxing Shangyu Hospital of Traditional Chinese Medicine from January 2019 to June 2022 were collected. Inclusion criteria: (1) patients with NSCLC confirmed by pathological examination; (2) patients who did not receive preoperative radiotherapy, chemotherapy or targeted therapy; (3) patients with complete preoperative blood test indexes and postoperative follow-up data. Exclusion criteria: (1) patients with other malignancies; (2) patients who were suffering from mental illness; (3) patients with immune system diseases or severe infectious diseases; (4) patients with dysfunction in other major organs such as heart, liver and kidney. This study was conducted using the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) checklists (Table S1).

Methods

General data such as sex, age, height, weight, smoking history, pathological type, TNM stage, surgical method, intraoperative blood loss, postoperative complications, and postoperative adjuvant chemotherapy were collected. In addition, laboratory examination results such as platelet, neutrophil, lymphocyte, albumin and monocyte in peripheral blood were collected. PLR, NLR and LMR were calculated. NRI = 1.519 × albumin (g/L) + 0.417 × (current body weight/ideal body weight) × 100. Ideal weight = 22 × height^2. Weight was measured in kg and height in meter. The primary outcome measure was overall survival (OS), defined as time from the date of surgery to death or the end of follow-up period, December 31, 2022. The optimal cutoff values for NLR, PLR, LMR and NRI were determined by receiver operating characteristic (ROC) curves and used for grouping, so as to compare the clinicopathological features between different groups and analyze the risk factors associated with the prognosis of NSCLC patients. The predictive performance of NLR, PLR, LMR and NR was considered main outcome measures.

Statistical methods

Statistical software SPSS23.0 was used for analysis and processing. Count data were indicated by number of cases (%), and the chi-square test was applied for comparisons between groups. Quantitative data were represented by ($\bar{x}\pm$sd), and t test was applied for comparisons between groups. The ROC curve was applied to obtain the area under the curve (AUC) of NLR, PLR, LMR and NRI, as well as the cut-off values. Survival analysis was performed using the Kaplan-Meier method with a log-rank test. Analysis of risk factors was performed using Cox model. Differences were considered statistically significant at $P<0.05$. In addition, a nomogram risk prediction model was constructed by R software, and its discrimination was evaluated using the ROC curve. The fitting of the model was expressed by the calibration curve.

Results

General information

In this study, 400 patients with NSCLC were included, and the age range of patients was from 20 to 80 years. The patients' characteristics such as age, sex, smoking history, pathological type distribution, TNM stage, surgical method, intraoperative blood loss, postoperative complication, and adjuvant chemotherapy are shown in **Table 1**.

Table 1. Baseline data of the NSCLC patients [n (%)]

Factors		n = 400
Sex	Male	213 (53.25)
	Female	187 (46.75)
Age	≥60	217 (54.25)
	<60	183 (45.75)
Smoking history	Yes	209 (52.25)
	No	191 (47.75)
Pathological type	Adenocarcinoma	199 (49.75)
	Squamous carcinoma	201 (50.25)
TNM staging	I	134 (33.50)
	II	129 (32.25)
	III	137 (34.25)
Surgical method	Lobectomy	294 (73.5)
	Total pneumonectomy	106 (26.5)
Intraoperative blood loss	>200	74 (18.5)
	≤200	326 (81.5)
Postoperative complication	Yes	100 (25.00)
	No	300 (75.00)
Adjuvant chemotherapy	Yes	310 (77.5)
	No	90 (25.5)

NSCLC: non-small cell lung cancer.

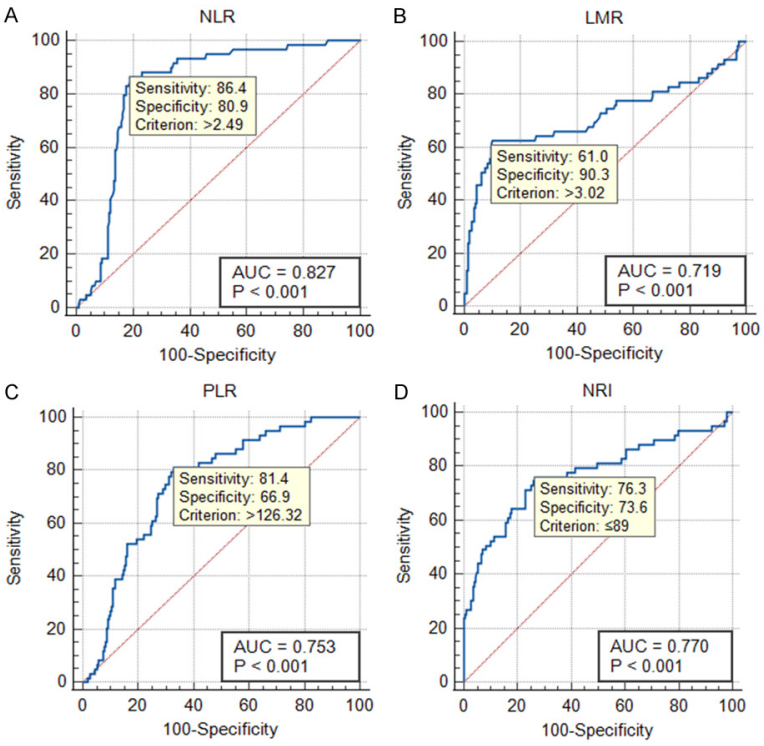

Figure 1. ROC curve analysis of different indicators. (A) The ROC curve for NLR; (B) The ROC curve for LMR; (C) The ROC curve for PLR; (D) The ROC curve for NRI. ROC: receiver operating characteristic; NLR: neutrophil-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; PLR: platelet-to-lymphocyte ratio; NRI: nutritional risk index.

Comparison of clinicopathological features between the different NLR, PLR, LMR and NRI groups

As shown in **Figure 1**, the ROC curve analysis revealed that the AUCs for NLR, PLR, LMR and NRI in predicting overall survival of NSCLC patients were 0.827, 0.753, 0.719 and 0.770, respectively. The optimal cut-off values for NLR, PLR, LMR and NRI were 2.49, 126.32, 3.02 and 89, respectively. Patients were classified according to the optimal cut-off values: NLR≤2.49 and NLR>2.49, PLR≤126.32 and PLR>126.32, LMR≤3.02 and LMR>3.02, NRI≤89 and NRI>89. The clinical data were compared between groups, as shown in **Tables 2** and **3**.

Survival analysis based on different NLR, PLR, LMR and NRI levels

Kaplan-Meier survival curves exhibited a 3-year OS rates of 70.19% and 95.40% in patients with PLR>126.32 and PLR≤126.32, respectively. Patients with NLR>2.49 and NLR≤2.49 had 3-year OS rates of 56.03% and 97.18%, respectively. The 3-year OS rates in patients with LMR>3.02 and LMR≤3.02 were 47.83% and 93.05%, respectively. The 3-year OS rates in patients with NRI>89 and NRI≤89 were 94.36% and 67.16%, respectively. See **Figure 2**.

Univariate analysis of factors affecting the prognosis of NSCLC

Data including sex, age, smoking history, pathological types, TNM stages, NLR, PLR, LMR, and NRI were incorporated into the Cox model for analysis

Table 2. Comparison of clinical characteristics of NSCLC patients with different NLR and PLR levels [n (%)]

Factors	NLR≤2.49 (n = 283)	NLR>2.49 (n = 117)	χ^2 value	*P* value	PLR≤126.32 (n = 239)	PLR>126.32 (n = 161)	χ^2 value	*P* value
Sex								
Female	139 (49.1)	48 (41)	2.177	0.140	121 (50.6)	66 (41)	3.586	0.058
Male	144 (50.9)	69 (59)			118 (49.4)	95 (59)		
Age								
<60	126 (44.5)	57 (48.7)	0.587	0.444	106 (44.4)	77 (47.8)	0.468	0.494
≥60	157 (55.5)	60 (51.3)			133 (55.6)	84 (52.2)		
Smoking history								
No	137 (48.4)	54 (46.2)	0.169	0.681	115 (48.1)	76 (47.2)	0.032	0.858
Yes	146 (51.6)	63 (53.8)			124 (51.9)	85 (52.8)		
Pathological type								
Squamous carcinoma	137 (48.4)	64 (54.7)	1.310	0.252	115 (48.1)	86 (53.4)	1.080	0.299
Adenocarcinoma	146 (51.6)	53 (45.3)			124 (51.9)	75 (46.6)		
TNM staging								
I	136 (48.1)	36 (30.8)	14.445	0.001	111 (46.4)	61 (37.9)	4.507	0.105
II	89 (31.4)	38 (32.5)			76 (31.8)	51 (31.7)		
III	58 (20.5)	43 (36.8)			52 (21.8)	49 (30.4)		
Surgical method								
Lobectomy	237 (83.7)	57 (48.7)	52.144	<0.001	201 (84.1)	93 (57.8)	34.257	<0.001
Total pneumonectomy	46 (16.3)	60 (51.3)			38 (15.9)	68 (42.2)		
Intraoperative blood loss								
≤200 ml	251 (88.7)	75 (64.1)	33.197	<0.001	213 (89.1)	113 (70.2)	22.875	<0.001
>200 ml	32 (11.3)	42 (35.9)			26 (10.9)	48 (29.8)		
Postoperative complication								
No	237 (83.7)	63 (53.8)	39.467	<0.001	195 (81.6)	105 (65.2)	13.753	<0.001
Yes	46 (16.3)	54 (46.2)			44 (18.4)	56 (34.8)		
Adjuvant chemotherapy								
Yes	237 (83.7)	73 (62.4)	21.643	<0.001	199 (83.3)	111 (68.9)	11.312	<0.001
No	46 (16.3)	44 (37.6)			40 (16.7)	50 (31.1)		

Note: NSCLC: non-small cell lung cancer; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio.

of risk factors for poor prognosis. Univariate analysis found that sex, TNM staging, NLR, PLR, LMR, NRI, surgical method, intraoperative blood loss, postoperative complication, and adjuvant chemotherapy were significant factors associated with the OS in NSCLC patients (*P*<0.05). See **Table 4**.

Multivariate analysis of factors affecting the prognosis of NSCLC

The significant variables from univariate analysis were assigned as independent variables (male = 1, female = 0; TNM staging I = 0, II = 1, III = 2; NLR>2.49 = 1, NLR≤2.49 = 0; PLR>126.32 = 1, PLR≤126.32 = 0; LMR>3.02 = 1, LMR≤3.02 = 0; NRI≤89 = 1, NRI>89 = 0; lobectomy = 0, total pneumonectomy = 1; intraoperative blood loss >200 ml = 1, intraoperative blood loss ≤200 ml = 0; postoperative complication: yes = 1, no = 0; adjuvant chemotherapy: yes = 0, no = 1). The survival status of patients was taken as the dependent variable (death = 1, survival = 0). Multivariate Cox analysis indicated that TNM staging, NLR>2.49, LMR>3.02, NRI≤89, surgical method, intraoperative blood loss, postoperative complication, and adjuvant chemotherapy were independent risk factors affecting prognosis of patients with NSCLC (**Table 5**).

Construction of a nomogram risk prediction model for NSCLC prognosis

The above four risk factors affecting the prognosis of NSCLC were included for risk assessment to establish a nomogram risk model (**Figure 3**). In order to further verify the predic-

Table 3. Comparison of clinical characteristics of NSCLC patients with different LMR and NRI levels [n (%)]

Factors	LMR≤3.02 (n = 326)	LMR>3.02 (n = 74)	χ^2 value	*P* value	NRI>89 (n = 289)	NRI≤89 (n = 111)	χ^2 value	*P* value
Sex								
Female	164 (50.3)	23 (31.1)	8.955	0.003	144 (49.8)	43 (38.7)	3.961	0.047
Male	162 (49.7)	51 (68.9)			145 (50.2)	68 (61.3)		
Age								
<60	148 (45.4)	35 (47.3)	0.088	0.767	128 (44.3)	55 (49.5)	0.894	0.344
≥60	178 (54.6)	39 (52.7)			161 (55.7)	56 (50.5)		
Smoking history								
No	159 (48.8)	32 (43.2)	0.739	0.390	136 (47.1)	55 (49.5)	0.199	0.655
Yes	167 (51.2)	42 (56.8)			153 (52.9)	56 (50.5)		
Pathological type								
Squamous carcinoma	161 (49.4)	40 (54.1)	0.526	0.468	142 (49.1)	59 (53.2)	0.518	0.472
Adenocarcinoma	165 (50.6)	34 (45.9)			147 (50.9)	52 (46.8)		
TNM staging								
I	151 (46.3)	21 (28.4)	20.972	0.001	134 (46.4)	38 (34.2)	13.093	0.001
II	108 (33.1)	19 (25.7)			96 (33.2)	31 (27.9)		
III	67 (20.6)	34 (45.9)			59 (20.4)	42 (37.8)		
Surgical method								
Lobectomy	269 (82.5)	25 (33.8)	73.532	<0.001	245 (84.8)	49 (44.1)	67.974	<0.001
Total Pneumonectomy	57 (17.5)	49 (66.2)			44 (15.2)	62 (55.9)		
Intraoperative blood loss								
≤200 ml	291 (89.3)	35 (47.3)	70.448	<0.001	259 (89.6)	67 (60.4)	45.536	<0.001
>200 ml	35 (10.7)	39 (52.7)			30 (10.4)	44 (39.6)		
Postoperative complication								
No	274 (84)	26 (35.1)	76.958	<0.001	240 (83)	60 (54.1)	35.949	<0.001
Yes	52 (16)	48 (64.9)			49 (17)	51 (45.9)		
Adjuvant chemotherapy								
Yes	271 (83.1)	39 (52.7)	32.018	<0.001	243 (84.1)	67 (60.4)	25.882	<0.001
No	55 (16.9)	35 (47.3)			46 (15.9)	44 (39.6)		

Note: NSCLC: non-small cell lung cancer; LMR: lymphocyte-to-monocyte ratio; NRI: nutritional risk index.

tion efficiency of the model, ROC curves of the training set and the test set were plotted respectively (**Figure 4**). It was found that the model exhibited high prediction accuracy in both training set and test set, with AUC of 0.967 (95% CI: 0.943-0.992) and 0.948 (95% CI: 0.874-1), respectively. The C-index was 0.96 and 0.98, respectively. Calibration curve (**Figure 5**) demonstrated that the prediction probabilities of the nomogram were consistent with the actual observations in both the training and test sets.

Discussion

The current clinical treatment regimen for early-stage NSCLC is primarily surgery with chemotherapy [7]. In recent years, with the improvement of medical technology, new treatment methods such as targeted therapy have been introduced in the clinical treatment of NSCLC [8]. However, NSCLC patients also have diverse biological behaviors such as metastasis and mutation in the process of disease progression, resulting in generally poor prognosis [9]. Clinical studies have shown that serum tumor markers (such as serum carcinoembryonic antigen) are involved in the development, progression and transformation of NSCLC, and the determination of these markers is simple and convenient, so they are often used for clinical diagnosis and prognosis evaluation in NSCLC patients [10]. However, it is found that the interference of smoking, diet and other factors in NSCLC patients could affect the sensitivity and specificity of the tumor markers [11]. Therefore, finding accurate and effective evaluation indices to assess the condition and prognosis of

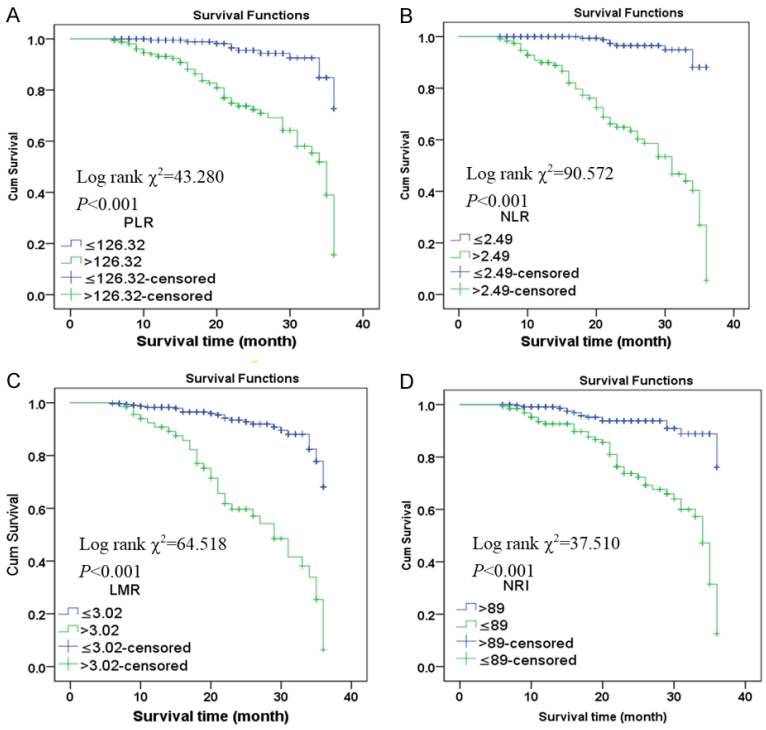

Figure 2. Survival curves of patients with different index levels. (A) The survival curves of patients with different PLR levels; (B) The survival curves of patients with different NLR levels; (C) The survival curves of patients with different LMR levels; (D) The survival curves of patients with different NRI levels. NLR: neutrophil-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; PLR: platelet-to-lymphocyte ratio; NRI: nutritional risk index.

NSCLC patients is of great significance in the formulation of personalized treatment plans and evaluating treatment efficacy.

Wang et al. [12] reported a correlation of the NLR level with the prognosis of NSCLC patients. NLR is one of the effective indicators of systemic inflammatory response. The decrease of lymphocyte count and the increase of neutrophils can lead to the increase of NLR level. Studies have shown that neutrophils can regulate lymphocytes and suppress their activity, thereby affecting tumor growth to a certain extent, while lymphocytes can induce the apoptosis of malignant cells, thus playing a key role in the defense mechanism against tumors [13-15]. A decrease in lymphocytes indicates that the body's immune mechanism is abnormal and that the anti-tumor immune ability is decreased, which can lead to a poor prognosis in patients [16]. Therefore, NLR can reflect the balance between the body's ability to inhibit or promote tumor growth, and can be used to evaluate the prognosis of tumor patients. Our results found that patients with reduced neutrophil counts and low NLR had significantly higher survival rates, suggesting that elevated NLR is associated with poor patient prognosis.

Inflammatory cells in the inflammatory environment, along with their secretion of inflammatory cytokines, such as interleukin-6 and cell growth factors, can contribute to tumor growth, invasion and metastasis. These cells and factors interact with each other to form a tumor-related inflammatory microenvironment [17]. Inflammatory microenvironment not only promotes angiogenesis, invasion and metastasis of cancers, but also changes the response of cancer cells to hormones and chemotherapy drugs. As inflammatory cells, lymphocytes and monocytes have been shown to be closely associated with the survival and prognosis of patients with malignancies [18, 19]. Our results demonstrated that patients with high LMR had a lower survival rate and that elevated LMR level is a risk factor for the prognosis of NSCLC. It is suggested that patients with high LMR may have a poor prognosis, which is consistent with the study conducted by Zhai et al. [20].

The NRI value is based on the plasma albumin level and weight loss of patients, which can reflect the nutritional status of the body [21]. Recent research found NRI to be closely related to the prognosis of several tumors, such as gastric cancer and NSCLC [22]. Shen et al. [23] conducted a systematic review of 11 studies that evaluated the use of the geriatric nutritional risk index (GNRI) in predicting NSCLC in the elderly. They concluded that GNRI has good prognostic ability for NSCLC patients. It is suggested that GNRI can serve as a simple and practical tool for the initial stratification of patients and development of targeted treatment plans. Lee et al. [24] found that low GNRI was correlated with poor prognosis in NSCLC patients. This study found a higher survival rate

Table 4. Univariate analysis of factors affecting the prognosis of NSCLC

Factors	Variable	B value	SE value	Wald value	*P* value	HR (95% CI)
Sex	Male	1.090	0.306	12.668	<0.001	2.974 (1.632-5.421)
Age	≥60	-0.143	0.262	0.298	0.585	0.867 (0.519-1.448)
Smoking history	Yes	0.111	0.264	0.177	0.674	1.118 (0.666-1.875)
Pathological type	Adenocarcinoma	0.153	0.262	0.34	0.56	1.165 (0.698-1.945)
TNM staging	I	-	-	-	<0.001	-
	II	0.723	0.434	2.776	0.096	2.061 (0.880-4.827)
	III	2.292	0.387	35.141	<0.001	9.899 (4.639-21.124)
NLR	>2.49	2.968	0.403	54.256	<0.001	19.445 (8.828-42.829)
PLR	>126.32	1.921	0.334	32.987	<0.001	6.827 (3.545-13.151)
LMR	>3.02	3.646	0.391	86.827	<0.001	38.338 (17.804-82.553)
NRI	≤89	2.764	0.348	63.174	<0.001	15.859 (8.022-31.352)
Surgical method	Total pneumonectomy	3.771	0.387	94.911	<0.001	43.423 (20.335-92.726)
Intraoperative blood loss	>200 ml	2.929	0.289	102.374	<0.001	18.711 (10.609-33)
Postoperative complication	Yes	4.177	0.455	84.209	<0.001	65.185 (26.71-159.081)
Adjuvant chemotherapy	No	2.996	0.296	102.762	<0.001	20 (11.207-35.692)

Note: NSCLC: non-small cell lung cancer; NLR: neutrophil-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; PLR: platelet-to-lymphocyte ratio; NRI: nutritional risk index.

Table 5. Multivariate analysis of factors affecting the prognosis of NSCLC

Factors	Variable	B value	SE value	Wald value	*P* value	HR (95% CI)
Sex	Male	0.392	0.344	1.301	0.254	1.48 (0.755-2.902)
TNM staging	I	-	-	7.315	0.026	-
	II	0.93	0.5	3.466	0.063	2.535 (0.952-6.752)
	III	1.2	0.444	7.311	0.007	3.321 (1.391-7.927)
NLR	>2.49	1.852	0.734	2.524	<0.012	6.375 (1.513-26.860)
PLR	>126.32	-0.196	0.385	0.259	0.610	0.822 (0.386-1.749)
LMR	>3.02	1.410	0.663	2.128	0.033	4.096 (1.118-15.010)
NRI	≤89	1.012	0.459	2.205	0.027	2.75 (1.119-6.756)
Surgical method	Total pneumonectomy	1.936	0.838	2.312	0.021	6.932 (1.343-35.796)
Intraoperative blood loss	>200 ml	0.871	0.422	2.065	0.039	2.390 (1.045-5.466)
Postoperative complication	Yes	1.293	0.586	2.207	0.027	3.644 (1.156-11.487)
Adjuvant chemotherapy	No	0.939	0.478	1.964	0.049	2.559 (1.002-6.537)

Note: NSCLC: non-small cell lung cancer; NLR: neutrophil-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; PLR: platelet-to-lymphocyte ratio; NRI: nutritional risk index.

in patients with high NRI, which is in agreement with the results of studies mentioned above, indicating that patients with low NRI may have a poor prognosis. The decrease of NRI may be due to the increased nutritional demand caused by the excessive tumor tissue proliferation in cancer patients. When patients are unable to meet the nutritional requirements, tumor cells will accelerate the deterioration of the body, leading to poor prognosis. Adequate nutritional support before surgery can significantly decrease the incidence of complications, morbidity and mortality in patients.

In this study, the correlation of NLR, PLR, LMR and NRI with the prognosis of NSCLC was analyzed. Survival analysis indicated that the survival rate was lower in patients with NLR>2.49, PLR>126.32, LMR>3.02 and NRI≤89. Cox regression analysis showed that NLR>2.49, LMR>3.02 and NRI≤89 were risk factors affecting the prognosis of NSCLC patients. In order to further clarify the prognostic value of NLR, LMR, and NRI in NSCLC patients, we constructed a nomogram risk prediction model based on the independent risk factors. The model predicted the risk through nomogram, and the dis-

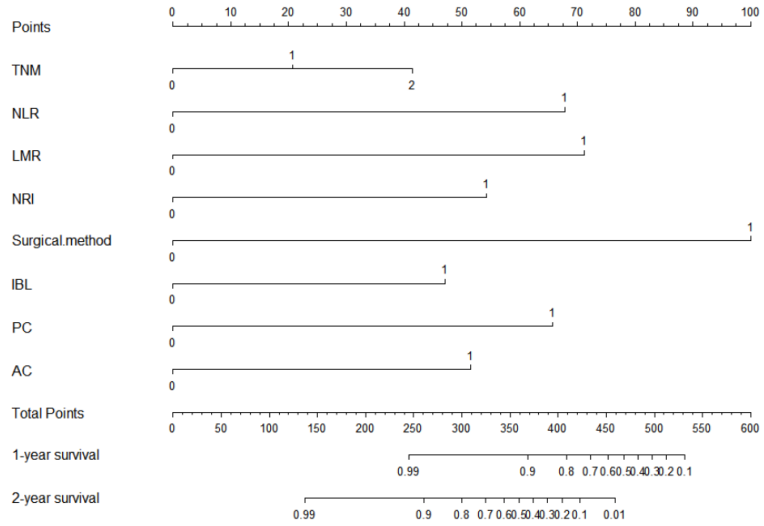

Figure 3. Nomogram of risk factors for predicting the prognosis of NSCLC. NSCLC: non-small cell lung cancer; NLR: neutrophil-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; NRI: nutritional risk index; IBL: intraoperative blood loss; PC: postoperative complication; AC: adjuvant chemotherapy.

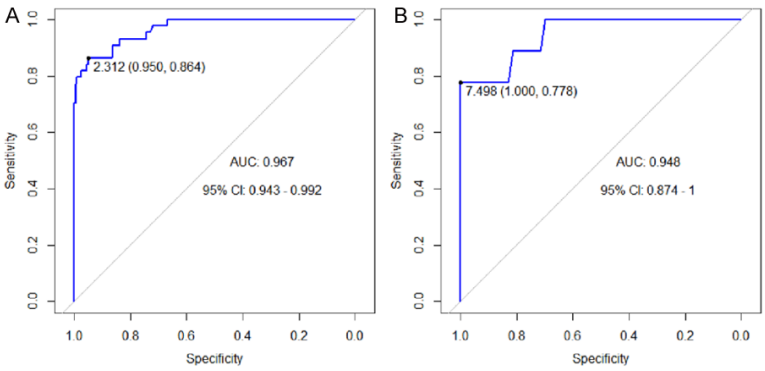

Figure 4. Predictive value of nomogram for prognosis of NSCLC. (A) ROC curve of training set; (B) ROC curve of test set. NSCLC: non-small cell lung cancer; ROC: receiver operating characteristic.

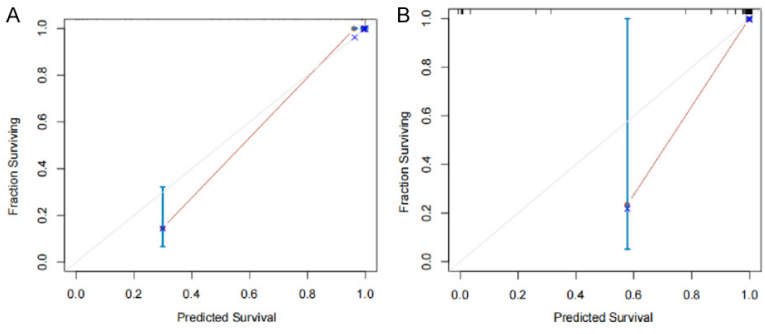

Figure 5. Calibration curve analysis. (A) Calibration curve of training set; (B) Calibration curve of test set.

crimination of the model was evaluated using an ROC curve. The nomogram is composed of TNM staging, NLR, LMR, NRI, surgical method, intraoperative blood loss, postoperative complication, and adjuvant chemotherapy, showing high reliability and clinical practicability. The nomogram highlights the relative importance of each index, suggesting that TNM stage, NLR, LMR, and NRI are significant predictors of the prognosis of patients with NSCLC, with good discrimination, calibration, and accuracy. These results indicate that changes in NLR, LMR, and NRI levels are correlated with the progression of NSCLC and can be used to evaluate the prognosis of NSCLC patients.

However, this study still has some limitations, because this is a retrospective and single-center study. A relatively large sample size was included in this study to minimize the selection bias. Nevertheless, multi-center prospective research with larger samples is required to validate the experimental results. Moreover, the analysis of prognostic indicators with more independent significance combined with other meaningful inflammatory indicators would provide a more comprehensive understanding of NSCLC prognosis.

In conclusion, TNM staging, NLR>2.49, LMR>3.02, NRI≤89, surgical method, intraoperative blood loss, postoperative complication, and adjuvant chemotherapy are independent risk factors affecting the prognosis of NSCLC patients. NLR, LMR and NRI can reflect the inflammatory and nutritional status of patients. The combined detection of NLR, LMR and NRI can effectively improve the sensitivity and specificity

of the prediction of prognosis in NSCLC patients.

Disclosure of conflict of interest

None.

Address correspondence to: Youyi Du, Department of Respiratory Medicine, Lishui Central Hopistal, No. 289, Kuocang Road, Liandu District, Lishui 323000, Zhejiang, China. Tel: +86-0578-2285242; E-mail: duyouyi0578@163.com

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Table S1. Checklist of items to include when reporting a study developing or validating a multivariable prediction model for diagnosis or prognosis*

Section/topic	Item	Development or validation	Checklist item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	1
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	2
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model, or both.	2
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	2
	4b	D;V	Specify the key study dates, including start of accrual, end of accrual, and, if applicable, end of follow-up.	3
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	3
	5b	D;V	Describe eligibility criteria for participants.	3
	5c	D;V	Give details of treatments received, if relevant.	
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	3
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	D;V	Clearly define all predictors used in developing the multivariable prediction model, including how and when they were measured.	3-4
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	D;V	Explain how the study size was arrived at.	2
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	3
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	3
	10c	V	For validation, describe how the predictions were calculated.	3
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	NA
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	NA
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	NA
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	NA
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	NA
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	4
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	NA
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	4
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	4
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	NA
	15b	D	Explain how to use the prediction model.	NA

Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	5
Model updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	NA
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, or missing data).	6
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	6
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	6
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	6
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	NA
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	NA

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.