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Original Article

Prognostic value of immunoinflammatory indicators and tumor markers for first-line chemotherapy in patients with non-small cell lung cancer

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Abstract: Objective: To evaluate the prognostic significance of immunoinflammatory indicators and tumor markers in patients with non-small cell lung cancer (NSCLC) undergoing first-line chemotherapy. Methods: This retrospective study included 306 NSCLC patients treated with first-line chemotherapy between January 2022 and January 2023. Clinical data, including demographic information, clinicopathological features, immunoinflammatory markers, and tumor markers, were collected. Survival was analyzed using Kaplan-Meier curves and compared with the log-rank test. Cox proportional hazards models were used to identify factors associated with overall survival (OS). Logistic regression was applied to predict 2-year mortality risk, and model performance was evaluated using receiver operating characteristic curves, area under the curve (AUC), calibration plots, and decision curve analysis. Results: By the end of follow-up, 183 patients had died (mortality rate: 59.80%). Univariate analysis showed that high neutrophil-to-lymphocyte ratio (NLR), high platelet-to-lymphocyte ratio (PLR), low lymphocyte-to-monocyte ratio (LMR), and elevated levels of CEA, CA125, and CYFRA 21-1 were significantly associated with worse prognosis (all $P<0.001$). Multivariate analysis identified high PLR (HR=1.94, P=0.041) and high CEA (HR=2.13, P=0.002) as independent risk factors, while high LMR (HR=0.52, P=0.043) was protective. A logistic model combining CEA, PLR, and LMR showed high predictive accuracy for 2-year mortality (AUC=0.926). Conclusion: Combined assessment of immunoinflammatory and tumor markers improves prognostic accuracy in NSCLC patients receiving first-line chemotherapy and may guide individualized treatment strategies.

Keywords: Non-small cell lung cancer, immunoinflammatory indicators, tumor markers, prognostic value, first-line chemotherapy

Introduction

Non-small cell lung cancer (NSCLC) is one of the most common malignancies worldwide in terms of both incidence and mortality, accounting for approximately 85% of all lung cancer cases [1]. According to a 2023 report by the World Health Organization, NSCLC ranks among the most prevalent cancers in both men and women [2]. Due to its high fatality rate, it remains a leading cause of cancer-related death. Epidemiological data suggest that NSCLC incidence varies across regions and populations, with risk factors including smoking, air pollution, and occupational exposures [3].

NSCLC typically progresses insidiously, with few clinical symptoms in its early stages, but becomes aggressive and fast-growing once advanced [4]. Despite advances in screening and diagnostic technologies, a majority of patients are diagnosed at locally advanced or metastatic stages, thereby missing the window for curative surgery [5, 6]. Current oncology guidelines recommend first-line chemotherapy as the standard treatment for advanced NSCLC [7], aiming to control tumor progression, relieve symptoms, and extend survival. However, significant variability exists in treatment response and prognosis: while some patients benefit from chemotherapy and achieve prolonged survival, others experience limited efficacy or severe toxicity [8]. These prognostic differences are influenced not only by tumor biology and staging but also by individual patient factors,

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including immune function and tumor microenvironment dynamics [9].

In this context, identifying reliable prognostic biomarkers is essential for guiding personalized treatment, optimizing therapeutic strategies, and improving patient outcomes. Recently, immunoinflammatory indicators and tumor markers have gained attention as potential prognostic tools [10, 11]. Inflammation and immune responses play critical roles in tumor initiation, progression, and metastasis. Systemic inflammation not only enhances tumor proliferation and invasion but may also suppress anti-tumor immunity, contributing to immune evasion [12]. NSCLC progression is closely linked to disruptions in the immune-inflammatory microenvironment: tumor cells release immunosuppressive signals to escape immune surveillance, while chronic inflammation promotes angiogenesis, invasion, and metastasis [13, 14].

Therefore, tracking changes in immunoinflammatory markers may provide insights into disease progression and chemotherapy response. In parallel, serum tumor markers such as carcinoembryonic antigen (CEA), cytokeratin 19 fragment (CYFRA 21-1), and carbohydrate antigen 125 (CA125) are widely used for diagnosis, therapeutic monitoring, and prognostication in NSCLC [15]. Given that prognosis in NSCLC is multifactorial, relying on a single marker may be insufficient. A combined approach integrating immunoinflammatory and tumor markers could offer a more comprehensive and accurate prognostic evaluation.

Although the individual prognostic value of these markers has been previously explored, their combined application in predicting the outcomes of first-line chemotherapy in NSCLC remains under-investigated. This study aims to assess the prognostic utility of multiple immunoinflammatory and tumor markers in NSCLC patients undergoing first-line chemotherapy. By analyzing clinical and follow-up data through multivariate statistical methods, we evaluated their association with survival outcomes and identified independent and combined prognostic factors. We hope this study offers novel insights for improving prognostic assessment and supports clinicians in developing more precise, individualized treatment strategies.

Materials and methods

Patient population

This retrospective study included 306 patients with NSCLC treated at the Affiliated Hospital of Nantong University between January 2022 and January 2023. All patients underwent comprehensive clinical evaluation prior to treatment, including medical history, physical examination, imaging studies (e.g., chest CT, abdominal ultrasound), and hematological tests. The patients were divided into a deceased group (183 cases) and a surviving group (123 cases) based on their 2-year survival status.

Inclusion criteria were: (1) age ≥18 years; (2) confirmed diagnosis of NSCLC based on tissue or cytopathological examination (e.g., bronchoscopic or percutaneous lung biopsy) [16]; (3) clinical stage IIIB-IV; (4) no prior antitumor treatment and initiation of platinum-based first-line chemotherapy upon admission; and (5) expected survival of ≥3 months with willingness to undergo follow-up.

Exclusion criteria included: (1) concurrent malignancies; (2) severe organ dysfunction; (3) autoimmune disease or long-term immunosuppressive therapy; and (4) loss to follow-up or incomplete survival data.

The study was approved by the Ethics Committee of the Affiliated Hospital of Nantong University.

Data collection

Data were retrospectively extracted from the hospital's electronic medical record system, including demographic information, clinicopathological characteristics, immunoinflammatory indices, and tumor marker levels. Demographic data included age, sex, smoking history, and alcohol consumption. Clinicopathological variables included tumor location, stage, histological type, and presence of distant metastases. Immunoinflammatory markers included neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR). Tumor markers included CEA, CA125, and CYFRA 21-1.

Patient follow-up

Patients were followed every 3 months for at least 8 visits. Follow-up was conducted via telephone or outpatient review, covering survival status, disease progression, and subsequent treatments. Follow-up began at the initiation of chemotherapy. The endpoint was defined as death, with the last follow-up conducted in January 2025. The primary prognostic outcome was overall survival (OS), defined as the time from chemotherapy initiation to death or last follow-up.

Statistical analysis

All analyses were performed using SPSS version 26.0. Continuous variables were expressed as median (interquartile range), and compared using Mann-Whitney U tests. Categorical variables were expressed as frequencies (percentages) and compared using chi-square tests.

Receiver operating characteristic (ROC) curves were used to determine optimal cutoff values using the Youden index, which was then used to convert continuous variables into categorical ones. Kaplan-Meier survival curves were generated, and differences between groups were tested using the log-rank test. Univariate and multivariate Cox regression analyses were performed to identify independent prognostic factors, reported as hazard ratios (HR) with 95% confidence intervals (CI).

Additionally, logistic regression models were constructed to predict 2-year survival status based on significant prognostic indicators. Model performance was evaluated using ROC curves, AUC, and 95% CI. Calibration was assessed using calibration curves and the Hosmer-Lemeshow test. Decision curve analysis (DCA) was used to evaluate clinical utility. Furthermore, model accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were calculated. All statistical tests were two-sided, with $P<0.05$ considered statistically significant.

Results

Comparison of general patient characteristics

At the end of follow-up, 183 patients had died, resulting in a mortality rate of 59.80%. Baseline characteristics of the deceased and surviving patients are summarized in **Table 1**. The proportion of patients with stage IV NSCLC was significantly higher in the deceased group compared to the surviving group ($P=0.010$). No statistically significant differences were observed between the two groups for other baseline characteristics ($P>0.05$).

Comparison of immunoinflammatory and tumour indicators

The levels of neutrophils, platelets, and monocytes were significantly higher in the deceased group, while lymphocyte levels were significantly lower, compared with the surviving group (all $P<0.001$; **Table 2**). Regarding composite indices, NLR and PLR were significantly higher, and LMR significantly lower, in the deceased group than in the surviving group (all $P<0.001$).

Among tumor markers, serum levels of CEA, CA125, and CYFRA 21-1 were significantly elevated in the deceased group compared to the surviving group (all $P<0.001$).

Determination of cut-off values

Cut-off values for immunoinflammatory and tumor markers were determined using the Youden index derived from logistic regression, with survival status as the dependent variable. The optimal Youden index was used to categorize each indicator. The accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Youden index for NLR, PLR, LMR, CEA, CA125, and CYFRA 21-1 are presented in **Table 3**.

Kaplan-Meier survival analysis for immunoinflammatory indicators

The low NLR group exhibited significantly better survival than the high NLR group (Log-rank $P<0.001$; **Figure 1**). Similarly, patients with low PLR had improved survival compared to those with high PLR (Log-rank $P<0.001$). Conversely, the high LMR group had significantly better survival than the low LMR group (Log-rank $P<0.001$).

Kaplan-Meier survival analysis for tumour indicators

Survival analyses based on tumor markers revealed that patients with low levels of CEA,

Table 1. Comparison of baseline features

Variables	Total (n=306)	Surviving group (n=123)	Deceased group (n=183)	Statistic	*P*
Age, n (%)				χ^2=3.29	0.070
<65	118 (38.56)	55 (44.72)	63 (34.43)		
≥65	188 (61.44)	68 (55.28)	120 (65.57)		
Gender, n (%)				χ^2=0.29	0.590
Female	49 (16.01)	18 (14.63)	31 (16.94)		
Male	257 (83.99)	105 (85.37)	152 (83.06)		
Smoking history, n (%)				χ^2=1.71	0.191
No	68 (22.22)	32 (26.02)	36 (19.67)		
Yes	238 (77.78)	91 (73.98)	147 (80.33)		
Drinking history, n (%)				χ^2=0.27	0.604
No	119 (38.89)	50 (40.65)	69 (37.70)		
Yes	187 (61.11)	73 (59.35)	114 (62.30)		
Tumor site, n (%)				χ^2=0.76	0.383
Right lung	140 (45.75)	60 (48.78)	80 (43.72)		
Left lung	166 (54.25)	63 (51.22)	103 (56.28)		
Pathological stage, n (%)				χ^2=6.67	0.010
III	108 (35.29)	54 (43.90)	54 (29.51)		
IV	198 (64.71)	69 (56.10)	129 (70.49)		
Pathological type, n (%)				χ^2=1.05	0.306
Non adenocarcinoma	110 (35.95)	40 (32.52)	70 (38.25)		
Adenocarcinoma	196 (64.05)	83 (67.48)	113 (61.75)		
Transfer, n (%)				χ^2=1.56	0.211
No	209 (68.30)	89 (72.36)	120 (65.57)		
Yes	97 (31.70)	34 (27.64)	63 (34.43)		

Table 2. Comparison of immunoinflammatory and tumor markers

Variables	Total (n=306)	Surviving group (n=123)	Deceased group (n=183)	Statistic	*P*
Neutrophil, M (Q_1, Q_3)	4.62 (3.34, 6.83)	3.47 (2.95, 4.39)	6.11 (4.40, 7.65)	Z=-10.03	<0.001
Lymphocyte, M (Q_1, Q_3)	1.39 (0.93, 2.00)	2.02 (1.59, 2.46)	1.05 (0.72, 1.40)	Z=-10.79	<0.001
Platelet, M (Q_1, Q_3)	223.09 (196.10, 259.88)	202.16 (179.14, 224.07)	246.46 (208.99, 278.11)	Z=-8.00	<0.001
Monocyte, M (Q_1, Q_3)	0.38 (0.29, 0.51)	0.30 (0.24, 0.36)	0.48 (0.36, 0.59)	Z=-9.83	<0.001
NLR, M (Q_1, Q_3)	3.24 (1.77, 6.93)	1.74 (1.37, 2.28)	6.06 (3.51, 9.41)	Z=-11.90	<0.001
PLR, M (Q_1, Q_3)	171.13 (98.95, 274.76)	98.19 (80.38, 128.40)	226.84 (171.46, 350.91)	Z=-11.72	<0.001
LMR, M (Q_1, Q_3)	3.47 (2.04, 6.74)	6.77 (5.34, 8.26)	2.22 (1.39, 3.10)	Z=-12.15	<0.001
CEA, M (Q_1, Q_3)	15.57 (8.79, 23.95)	8.25 (6.28, 11.84)	22.22 (16.94, 29.67)	Z=-12.53	<0.001
CA125, M (Q_1, Q_3)	36.04 (21.62, 59.80)	22.64 (17.03, 30.91)	52.50 (33.22, 76.44)	Z=-10.00	<0.001
CYFRA 21-1, M (Q_1, Q_3)	4.37 (2.82, 6.11)	3.29 (2.10, 4.54)	5.20 (3.82, 7.30)	Z=-7.22	<0.001

Note: M, Median; Q_1, First Quartile; Q_3, Third Quartile; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; LMR, Lymphocyte-to-Monocyte Ratio; CEA, Carcinoembryonic Antigen; CA125, Carbohydrate Antigen 125; CYFRA 21-1, Cytokeratin 19 Fragment.

CA125, and CYFRA 21-1 had significantly improved survival outcomes (all Log-rank P< 0.001; **Figure 2**).

Cox regression analysis of prognostic factors

Univariate Cox regression analysis identified NLR (HR=5.72, P<0.001), PLR (HR=6.49, P< 0.001), LMR (HR=0.14, P<0.001), CEA (HR= 5.79, P<0.001), CA125 (HR=3.69, P<0.001), and CYFRA 21-1 (HR=2.07, P<0.001) as significant prognostic factors (**Table 4**).

Multivariate Cox regression analysis indicated that high PLR (HR=1.94, P=0.041) and high CEA (HR=2.13, P=0.002) were independent

Table 3. Selection of cutoff value (Based on the Optimal Youden Index)

Variable	AUC (95% CI)	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	cut off
NLR	0.90 (0.87-0.94)	0.85 (0.80-0.88)	0.93 (0.88-0.97)	0.79 (0.73-0.85)	0.75 (0.68-0.82)	0.94 (0.90-0.98)	3.21
PLR	0.90 (0.86-0.93)	0.85 (0.81-0.89)	0.85 (0.78-0.91)	0.86 (0.81-0.91)	0.80 (0.73-0.87)	0.89 (0.85-0.94)	147.49
LMR	0.91 (0.88-0.94)	0.13 (0.10-0.18)	0.08 (0.03-0.13)	0.17 (0.12-0.22)	0.06 (0.02-0.10)	0.22 (0.15-0.28)	3.73
CEA	0.92 (0.89-0.95)	0.85 (0.80-0.89)	0.96 (0.92-0.99)	0.78 (0.72-0.84)	0.74 (0.67-0.81)	0.97 (0.94-1.00)	16.40
CA125	0.84 (0.79-0.88)	0.78 (0.73-0.83)	0.80 (0.73-0.87)	0.77 (0.70-0.83)	0.70 (0.62-0.77)	0.85 (0.80-0.91)	32.81
CYFRA 21-1	0.74 (0.69-0.80)	0.67 (0.62-0.73)	0.82 (0.75-0.89)	0.57 (0.50-0.65)	0.56 (0.49-0.64)	0.83 (0.76-0.89)	4.93

Note: AUC, Area Under the Curve; CI, Confidence Interval; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; LMR, Lymphocyte-to-Monocyte Ratio; CEA, Carcinoembryonic Antigen; CA125, Carbohydrate Antigen 125; CYFRA 21-1, Cytokeratin 19 Fragment.

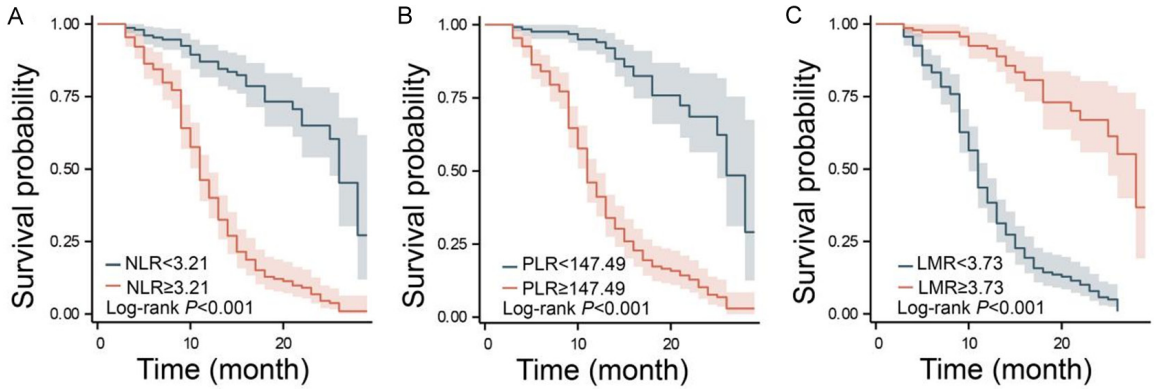

Figure 1. Kaplan-Meier survival curve analysis grouped according to immunoinflammatory markers. A. NLR; B. PLR; C. LMR. Note: NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; LMR, Lymphocyte-to-Monocyte Ratio.

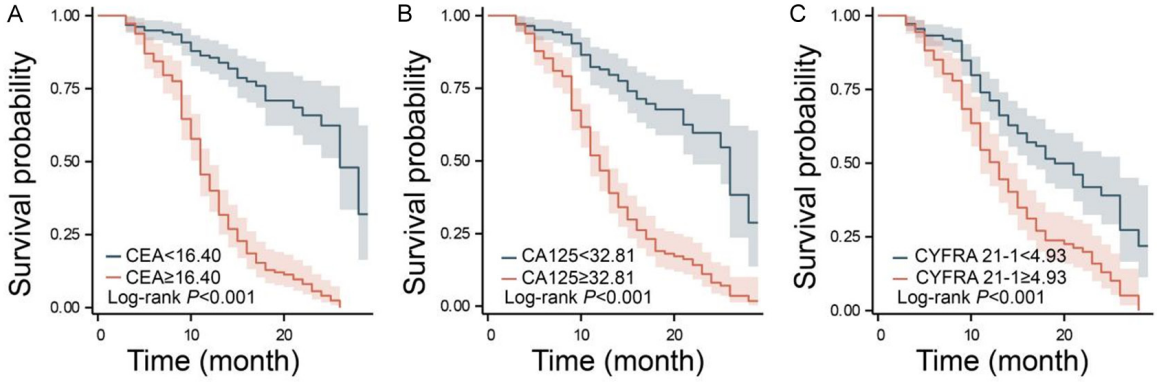

Figure 2. Kaplan-Meier survival curve analysis grouped according to tumor markers. A. CEA; B. CA 125; C. CYFRA 21-1. Note: CEA, Carcinoembryonic Antigen; CA125, Carbohydrate Antigen 125; CYFRA 21-1, Cytokeratin 19 Fragment.

risk factors, while high LMR (HR=0.52, P= 0.043) served as an independent protective factor.

Prediction of 2-year mortality risk

A logistic regression model was developed using 2-year survival status as the dependent variable (death =1, survival =0), with independent prognostic factors as covariates. The analysis identified CEA (OR=12.34, P<0.001), PLR (OR=5.77, P<0.001), and LMR (OR=0.29, P=0.014) as significant predictors of 2-year mortality (**Table 5**).

The multivariate logistic regression equation was: Logit (p) =-0.99+2.51*CEA+1.75* PLR-1.24*LMR.

Table 4. Cox regression analysis

Variables	Univariate Cox					Multifactor Cox				
	β	S.E	Z	*P*	HR (95% CI)	β	S.E	Z	*P*	HR (95% CI)
NLR										
Low					1.00 (Reference)					1.00 (Reference)
High	1.74	0.18	9.48	<0.001	5.72 (3.99-8.20)	0.31	0.29	1.09	0.277	1.36 (0.78-2.38)
PLR										
Low					1.00 (Reference)					1.00 (Reference)
High	1.87	0.21	8.77	<0.001	6.49 (4.27-9.85)	0.66	0.32	2.05	0.041	1.94 (1.03-3.67)
LMR										
Low					1.00 (Reference)					1.00 (Reference)
High	-1.94	0.20	-9.53	<0.001	0.14 (0.10-0.21)	-0.65	0.32	-2.02	0.043	0.52 (0.28-0.98)
CEA										
Low					1.00 (Reference)					1.00 (Reference)
High	1.76	0.18	9.61	<0.001	5.79 (4.05-8.28)	0.76	0.24	3.12	0.002	2.13 (1.33-3.43)
CA125										
Low					1.00 (Reference)					1.00 (Reference)
High	1.31	0.17	7.46	<0.001	3.69 (2.62-5.20)	0.12	0.21	0.55	0.580	1.13 (0.74-1.71)
CYFRA										
Low					1.00 (Reference)					1.00 (Reference)
High	0.73	0.15	4.87	<0.001	2.07 (1.55-2.78)	-0.00	0.16	-0.02	0.985	1.00 (0.73-1.36)

Note: SE, Standard Error; HR, Hazard Ratio; CI, Confidence Interval; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; LMR, Lymphocyte-to-Monocyte Ratio; CEA, Carcinoembryonic Antigen; CA125, Carbohydrate Antigen 125; CYFRA 21-1, Cytokeratin 19 Fragment.

Table 5. Multivariate logistic regression analysis predicting 2-year mortality risk

Variables	β	S.E	Z	*P*	OR (95% CI)
CEA					
Low					1.00 (Reference)
High	2.51	0.44	5.67	<0.001	12.34 (5.18-29.44)
PLR					
Low					1.00 (Reference)
High	1.75	0.47	3.69	<0.001	5.77 (2.28-14.61)
LMR					
Low					1.00 (Reference)
High	-1.24	0.50	-2.47	0.014	0.29 (0.11-0.77)

Note: SE, Standard Error; OR, Odds Ratio; CI, Confidence Interval; PLR, Platelet-to-Lymphocyte Ratio; LMR, Lymphocyte-to-Monocyte Ratio; CEA, Carcinoembryonic Antigen.

Evaluation of logistic model

The ROC curve for the combined indicators is shown in **Figure 3A**. The model demonstrated good discriminative ability with an AUC of 0.926. The calibration curve (**Figure 3B**) showed good agreement between predicted and observed outcomes, with a non-significant Hosmer-Lemeshow test (P=0.954), indicating good model fit.

DCA analysis (**Figure 3C**) suggested that the model provides a positive net benefit when the risk threshold exceeds 10%.

The model's performance metrics were as follows: accuracy 0.89 (95% CI: 0.84-0.92), sensitivity 0.90 (95% CI: 0.85-0.95), specificity 0.87 (95% CI: 0.82-0.92), PPV 0.85 (95% CI: 0.79-0.90), and NPV 0.92 (95% CI: 0.88-0.96).

Discussion

As one of the most prevalent malignancies worldwide, NSCLC exhibits both high incidence and mortality, making its prognostic assessment a key focus of clinical research [17]. Although substantial advancements have been made in lung cancer screening and diagnostic technologies in recent years, most patients are still diagnosed at locally advanced or metastatic stages [18]. For these individuals, first-line chemotherapy remains the standard treatment, but outcomes vary significantly across patients. Therefore,

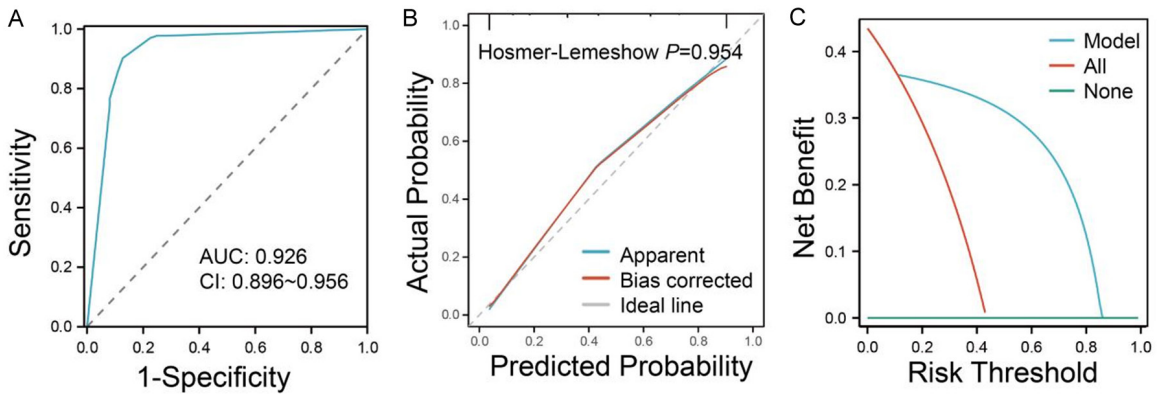

Figure 3. Evaluation of Logistic regression model. A. ROC curve; B. Calibration curve analysis; C. Clinical decision curve. Note: ROC, Receiver Operating Characteristic; AUC, Area Under the Curve; CI, Confidence Interval.

identifying reliable biomarkers to predict prognosis in NSCLC patients undergoing first-line chemotherapy is of great clinical significance.

In this retrospective study of 306 NSCLC patients treated with first-line chemotherapy, we evaluated the prognostic value of systemic immune-inflammatory markers (e.g., NLR, PLR, LMR) and tumour markers (e.g., CEA, CA125, CYFRA 21-1). The results demonstrated that elevated PLR and CEA levels were independent predictors of poor prognosis, while a higher LMR was associated with improved survival. Moreover, integrating these markers into a composite prognostic model significantly enhanced the ability to predict 2-year mortality risk.

Immune-inflammatory indicators (NLR, PLR and LMR) were significantly associated with patient outcomes. NLR and PLR levels were markedly higher in the deceased group, while LMR was lower. A retrospective analysis of 400 lung cancer patients by Shi et al. identified elevated NLR and reduced LMR as adverse prognostic factors [19]. Similarly, Huai et al. reported significant associations between inflammatory markers (including NLR and PLR) and prognosis in 189 NSCLC patients [20]. These findings align with our results.

NLR reflects the balance between neutrophils and lymphocytes [21]. Elevated NLR may indicate systemic inflammation or immune suppression, both of which can promote tumour progression and metastasis [22]. Neutrophils release reactive oxygen species and proteolytic enzymes, such as matrix metalloproteinases, which degrade the extracellular matrix and facilitate tumour invasion [23]. Moreover, neutrophils secrete pro-inflammatory cytokines (e.g., IL-6, IL-8, TNF-α), further supporting tumour growth and survival [24].

Conversely, lymphopenia may signal impaired immune surveillance, as lymphocytes - particularly cytotoxic T lymphocytes and natural killer cells - are crucial for tumour eradication [25]. A reduced lymphocyte count may reflect enhanced immune evasion within the tumour microenvironment.

The PLR combines information from two immune components. Elevated PLR suggests increased platelet activity per lymphocyte. Platelets promote angiogenesis by releasing growth factors, thereby fueling tumour proliferation and metastasis [26]. Additionally, platelets can interact directly with tumour cells to enhance invasiveness and help them evade immune detection via the release of adenosine diphosphate and thromboxane A2 [27].

The LMR reflects the relative abundance of anti-tumour lymphocytes to pro-tumour monocytes. A low LMR usually indicates both lymphopenia and monocytosis. Monocytes can differentiate into tumour-associated macrophages (TAMs), particularly the M2 phenotype, which promotes immune suppression via secretion of IL-10 and arginase-1 and facilitates immune escape [28, 29]. M2 TAMs also contribute to angiogenesis, extracellular matrix remodelling, and tumour migration through various cytokines and proteases [30].

Additionally, this study affirmed the prognostic utility of tumour markers. Jiang et al. found that elevated levels of CEA and CYFRA 21-1 in 3272 NSCLC patients were indicative of tumour metastasis [31]. Yang et al. reported significant correlations between CEA, CA125, CYFRA 21-1 and OS in 716 NSCLC patients [32], which is consistent with our findings.

CEA is a glycoprotein minimally expressed in adult gastrointestinal and respiratory tissues under normal conditions. In NSCLC, deregulated proliferation and differentiation of tumour cells lead to CEA overexpression [33]. Elevated CEA levels reflect increased tumour cell activity and are known to enhance invasion and migration by modulating cell adhesion, thereby increasing the risk of metastasis [34].

Although originally a marker for ovarian cancer, CA125 also plays a role in NSCLC. Elevated CA125 levels promote vascular endothelial cell proliferation and neovascularisation, thereby sustaining tumour growth and metastasis [35].

CYFRA 21-1 is a soluble fragment of cytokeratin-19. During tumour progression, massive tumour cell turnover leads to increased levels of CYFRA 21-1 in circulation [36, 37]. Elevated CYFRA 21-1 is often associated with more aggressive disease and abnormal cellular metabolism related to invasion and metastasis [38].

In summary, high levels of CEA, CA125, and CYFRA 21-1 correlate with poor prognosis in NSCLC patients receiving first-line chemotherapy. While CA125 and CYFRA 21-1 were not independent predictors in multivariate analysis, their prognostic value remains clinically relevant and should not be overlooked.

Multivariate Cox regression analysis revealed that elevated PLR and CEA levels were independent risk factors, while high LMR was a protective factor. Combining immune-inflammatory and tumour markers yielded superior prognostic accuracy. Our multifactorial logistic regression model, incorporating CEA, PLR and LMR, showed strong predictive performance for 2-year mortality (AUC=0.926), indicating good discrimination.

This study has several limitations. First, as a retrospective analysis, it is subject to potential selection and information biases. Although baseline assessments were conducted prior to treatment, residual confounding factors such as viral infections and unmeasured clinical variables cannot be entirely excluded. Second, the relatively small sample size may limit the generalisability of the findings. Third, important prognostic factors - such as gene mutation status, treatment adherence, and nutritional status - were not included in the analysis. These variables should be incorporated in future prospective, multicentre studies to develop a more comprehensive and robust prognostic model.

In conclusion, NSCLC remains a highly aggressive malignancy with poor prognosis, especially in advanced stages. This study identified elevated PLR and CEA as independent risk factors, while high LMR was associated with improved survival. A prognostic logistic model based on these markers demonstrated strong predictive value for 2-year mortality risk. Despite its limitations, the model offers a useful tool to support clinical decision-making. Future studies should validate and refine this model by integrating additional clinical and molecular markers, thereby improving its utility for personalised treatment strategies in NSCLC.

Disclosure of conflict of interest

None.

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