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Original Article

Expression of CXCL8 and its relationship with prognosis in patients with non-small cell lung cancer

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Abstract: To determine the expression of chemokine 8 (CXCL8) in non-small cell lung cancer (NSCLC) patients and analyze its correlation with tumor characteristics and patient prognosis. We conducted a retrospective analysis of 149 NSCLC patients treated between January 2016 and April 2018, measuring serum CXCL8 expression upon admission or prior to treatment. The clinical characteristics, including lymph node metastasis and staging, based on CXCL8 expression levels, were analyzed. Receiver Operating Characteristic (ROC) curves was drawn to assess its predictive value for lymph node metastasis and staging in NSCLC patients. Furthermore, the Kaplan-Meier curve was plotted to assess the impact of CXCL8 on 5-year survival in NSCLC Patients. NSCLC patients exhibited significantly higher serum CXCL8 levels than those with benign tumors ($P<0.001$), with the high CXCL8 expression group showing a higher incidence of lymph node metastasis or stage III NSCLC ($P<0.01$). CXCL8 was identified as an independent predictor of lymph node metastasis (AUC=0.730) and higher TNM stage (AUC=0.708), as well as a validated biomarker for predicting five-year survival in NSCLC patients. This study highlights the strong association between CXCL8 expression in NSCLC and patient prognosis, particularly regarding lymph node metastasis and clinical staging, suggesting the need for further research to explore CXCL8's specific role in the tumor microenvironment and its impact on different NSCLC subtypes.

Keywords: CXCL8, non-small cell lung cancer, prognosis, lymph node metastasis, clinical staging

Introduction

Malignant tumors pose a significant threat to human life and overall health [1]. Despite advancements in immunotherapy and targeted therapy, the prognosis for patients with advanced non-small cell lung cancer (NSCLC) remains poor, with a dismal 5-year survival rate of less than 15% [2, 3]. Smoking is recognized as the primary risk factor for lung cancer (LC), and the incidence of the disease is rising in countries with increasing smoking rates [4]. Early-stage LC can often be effectively managed through surgical resection, leading to a potential cure [5]. Some patients with advanced diseases may also benefit from preoperative chemotherapy and/or radiotherapy, which can reduce tumor staging and improve operability [6]. However, current treatment strategies for LC do not guarantee a cure for all patients. Despite advancements in diagnosis and treatment technologies, LC remains one of the deadliest cancer worldwide [7]. In many regions, particularly in China, the reported incidence and mortality rates of LC are progressively increasing [8]. Early detection of LC is challenging because of the lack of specific clinical manifestations. Patients with LC who present with weight loss, late clinical stage, and low physical strength scores at the time of diagnosis often have a poorer prognosis [9].

Chemokines and their receptors play crucial roles in tumor initiation, progression, metastasis, and interactions with the immune system within the tumor microenvironment [10]. Among these chemokines, CXCL8 (interleukin-8) is of particular importance. It can attract and activate various immune cells, especially neutrophils and specific subsets of T cells [11]. In non-

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neoplastic diseases, CXCL8 is primarily involved in inflammatory reaction and immune regulation [12]. However, in tumor biology, the function of CXCL8 is more complicated, which is closely linked to tumor proliferation, angiogenesis, invasion, and metastasis [13, 14]. Recent studies have shown demonstrated that CXCL8 and its receptor are upregulated in various cancers, including gastric cancer [15], colorectal cancer [16], and breast cancer [17]. Although some studies have explored the role of CXCL8 in NSCLC, research into CXCL8's role in NSCLC is limited and its potential as a prognostic marker remains unclear.

This study aims to evaluate CXCL8 expression in NSCLC patients compared to healthy controls, and its correlation with tumor characteristics and prognosis. By doing so, we hope to establish CXCL8's potential as a biomarker and its role in NSCLC development and treatment strategy formulation.

Materials and methods

Sample source

A retrospective analysis was carried out on NSCLC patients treated at The Affiliated BenQ Hospital of Nanjing Medical University between January 2016 and April 2018. Furthermore, patients with benign lung lesions who treated surgically at the same hospital during the same period were included as the benign tumor group.

Inclusion and exclusion criteria for NSCLC patients

Inclusion criteria: patients who were diagnosed with NSCLC based on histopathological examination and met the diagnostic criteria outlined in the eighth edition of the American Joint Committee on Cancer (AJCC) staging system published in 2018 [18]; patients who had not undergone any form of anti-tumor treatment, including chemotherapy, radiotherapy, and targeted therapy, prior to enrolment in the study; patients aged 18 years or above; patients who were scheduled for surgical resection and successfully underwent the surgical procedure; patients with good functional status, as indicated by a Karnofsky Performance Status (KPS) score of 70 or above [19]; patients with complete clinical available for analysis (complete survival follow-up records, baseline data, and laboratory indicators at the time of initial diagnosis); patients with an expected survival time of more than 6 months.

Exclusion criteria: patients with active malignant tumors or a history of any other malignant tumors within the past five years; patients with active infections, systemic inflammatory diseases, or other serious medical conditions that may significantly affect the serum CXCL8 expression; patients with severe liver or renal dysfunction; patients with persistent hematological diseases.

Inclusion criteria for benign tumor patients

The patients underwent lung surgery at our hospital and were diagnosed with benign lung tumors. Included patients with benign lung lesions had no comorbidities of cancer, active infections, systemic inflammatory diseases, or other serious medical conditions, and had a complete medical history (complete survival follow-up records, baseline data, and laboratory indicators at the time of initial diagnosis).

Collection of clinical data

Relevant data were collected from the patient's clinical electronic medical records, mainly including clinical information and laboratory indices. Clinical information mainly included age, sex, degree of tumor differentiation, maximum diameter of tumor, lymph node metastasis, clinical stage and case type. Laboratory indices included high sensitivity C-reactive protein (hs-CRP), carcinoembryonic antigen (CEA), cytokeratin 19 fragment (CYFRA21-1) and CXCL8. The laboratory indices of patients were obtained from the first measurement taken either upon admission to the hospital or before treatment initiation. The expression of serum CXCL8 in patient was measured using the ELISA method (E-EL-H6008) with kits purchased from Elabscience Biotechnology Co., Ltd., (Wuhan, Hubei Province, China).

Follow-up record

To collect survival data, telephone follow-ups were conducted until April 2023. Data was deemed lost if no relevant follow-up information was available within the past six months or if the contact information had changed and

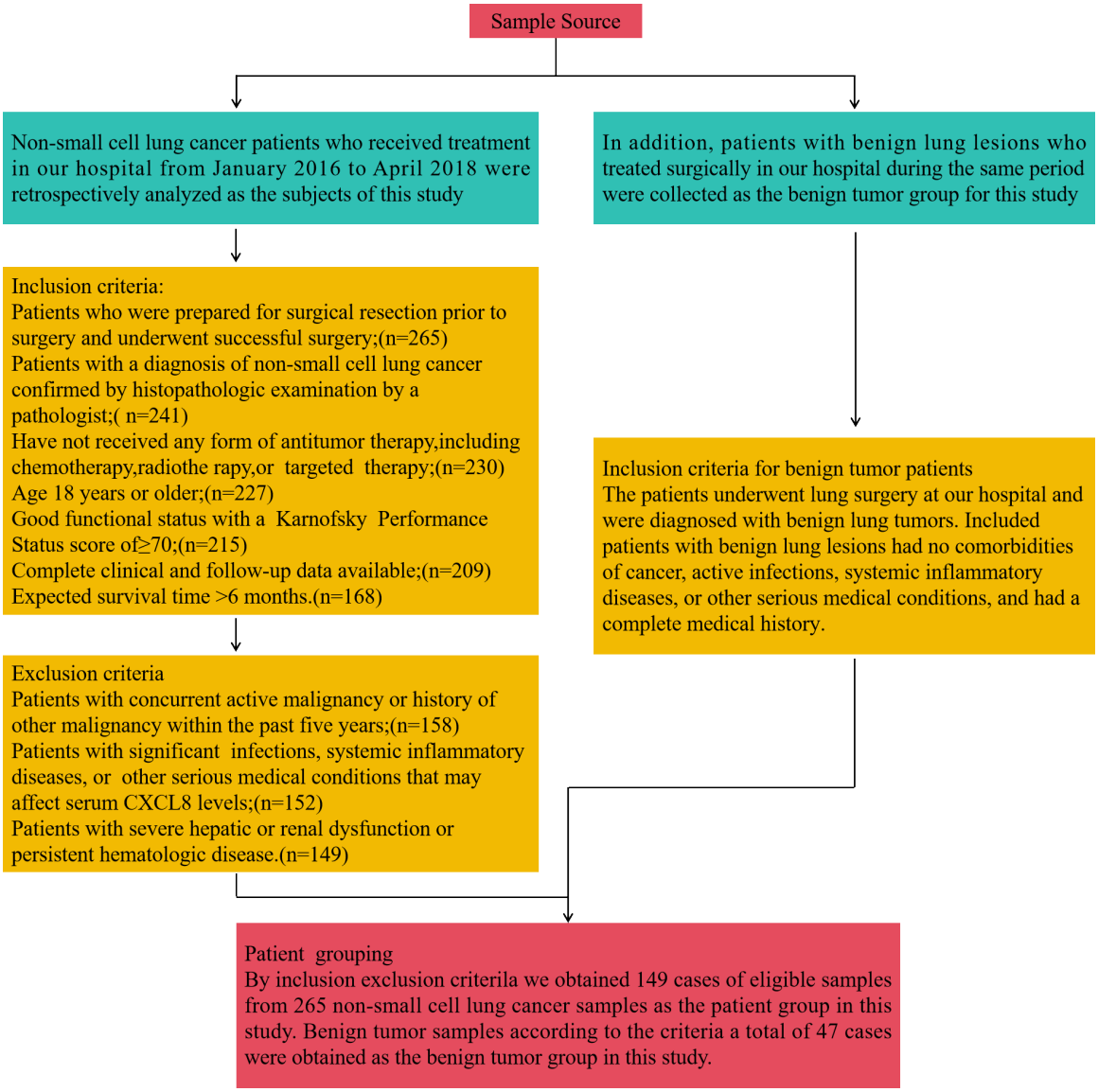

Figure 1. Inclusion process of both NSCLC and benign tumor patients.

could be updated. The 5-year survival rate of patients was counted. The follow-up frequency was once every 3 months in the first year every four months in the second year, and subsequently every six months.

Patient grouping

From January 2016 to April 2018, a total of 573 patients with NSCLC were admitted to our department. Among them, 265 patients voluntarily underwent CXCL8 testing. By applying the inclusion and exclusion criteria, we identified 149 eligible samples, forming the patient group. During the same period, 218 patients were treated surgically and diagnosed with benign lung lesions on pathologic findings. Among those, 98 volunteered for CXCL8 testing, and 47 were selected as the benign tumor group for comparison with the patient group (**Figure 1**) in accordance with the study criteria. This group comprised of cases with inflammatory pseudotumor (8 cases), lung misshapen tumor (19 cases), lung fibroma (12 cases) and lung lipoma (8 cases).

Result measurement

1. The CXCL8 expression was compared between the benign tumor group and patient

Table 1. Comparisons of CXCL8, tumor markers and inflammatory factors between NSCLC and benign tumor patients

Variable	Patient group (n=149)	Benign tumor group (n=47)	T/Z	P
CEA (ng/mL)	3.80 [2.77, 4.79]	2.36 [1.38, 3.00]	5.587	<0.001
CXCL8 (pg/mL)	321.18±97.03	149.07±23.01	19.947	<0.001
CYFRA21-1 (ng/mL)	4.61 [2.82, 6.95]	2.06 [1.29, 3.46]	5.477	<0.001
hs-CRP (mg/L)	14.44 [10.42, 22.45]	10.22 [7.13, 12.48]	4.417	<0.001

Notes: CXCL8: chemokine 8; hs-CRP: high sensitivity C-reactive protein; CEA: carcinoembryonic antigen; CYFRA21-1: cytokeratin 19 fragment.

group. 2. The correlation between CXCL8 and tumor markers was analyzed. 3. According to the average CXCL8 expression, the patients were divided into high expression group and low expression group, and the differences of clinical data between the two groups were analyzed. 4. The predictive value of CXCL8 and tumor markers for lymph node metastasis and clinical staging of patients was analyzed. 5. The Kaplan-Meier (K-M) survival curve of prognostic factors was drawn.

Statistical analyses

Statistical analysis was carried out using the SPSS 26.0 software. The qualitative data was described by the number of cases (%), and the quantitative data was analyzed by normal distribution. The data in normal distribution were represented by mean ± SD, and those in non-normal distribution were represented by quartile. Pearson's correlation coefficient was utilized to analyze the correlation between CXCL8 and tumor markers. Receiver operating characteristic (ROC) curves were generated, and the area under curve (AUC) was calculated. The AUC ranged from 0 to 1, where a higher value indicated a greater diagnostic accuracy. The K-M method was employed to construct survival curves to compare inter-group differences in survival. To determine the optimal cutoff value for continuous measurement data, X-tile software was applied [20]. P<0.05 was considered with statistical difference.

Results

Expressions of CXCL8, tumor markers and inflammatory factors in patients with NSCLC

The serum levels of CXCL8, tumor markers and inflammatory factors were compared between the benign tumor group and patient group. The levels of CXCL8, hs-CRP, CEA, and CYFRA21-1 were significantly higher in NSCLC patients compared to the benign tumor patients (all P<0.001, **Table 1**).

Correlations of CXCL8 with tumor markers and inflammatory factors

The correlations of CXCL8 with tumor markers (hs-CRP, CEA) and inflammatory factor (CYFRA21-1) were analyzed. The results revealed significant positive correlations between CXCL8 and the examined tumor markers and inflammatory factor (P<0.001) (**Figure 2**).

Correlation of CXCL8 with clinical data of tumor patients

The relationship between CXCL8 and clinical data of NSCLC patients was analyzed, and patients were divided into high- and low-expression group according to the average CXCL8 expression (313 pg/mL). According to the results, the high expression group showed a notably higher proportion of patients with lymph node metastasis and clinical stage III than the low expression group (P<0.01) (**Table 2**).

Predictive value of CXCL8, tumor markers and inflammatory factors for lymph node metastasis

The comparison revealed significantly higher levels of CXCL8, CEA and CYFRA21-1 in patients with lymph node metastasis compared to those without lymph node metastasis (all P<0.05, **Table 3**); however, no association was found between hs-CRP and lymph node metastasis. Subsequent analysis of the diagnostic value of the significant indices in predicting lymph node metastasis revealed that the AUC of CXCL8 was 0.730, whereas the AUCs of CEA and CYFRA21-1 were both 0.602. The Delong test showed no significant differences in AUC between CXCL8 and CEA, but CXCL8 demon-

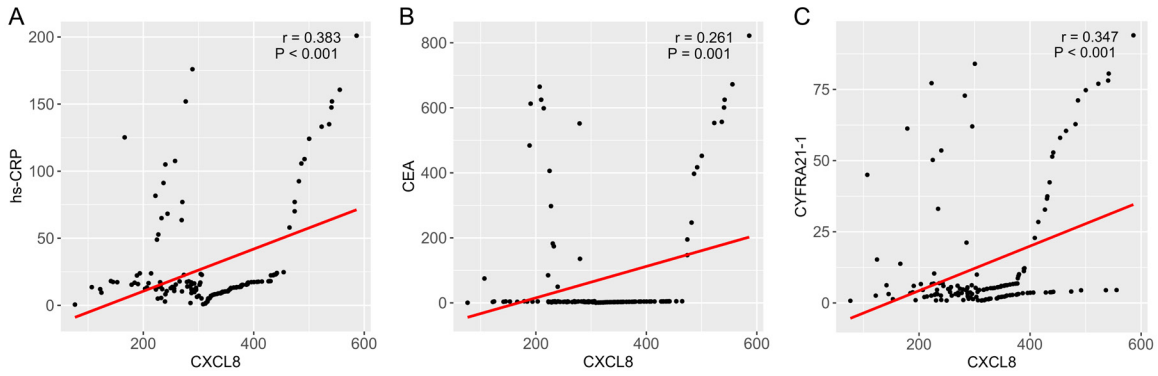

Figure 2. Correlation analysis of CXCL8 with tumor markers and inflammatory factors. A: Correlation analysis of CXCL8 with hs-CRP; B: Correlation analysis of CXCL8 with CEA; C: Correlation analysis of CXCL8 with CYFRA21-1. Notes: CXCL8: chemokine 8; hs-CRP: high sensitivity C reactive protein; CEA: carcinoembryonic antigen; CYFRA21-1: cytokeratin 19 fragment.

Table 2. Correlation of CXCL8 with clinical data of tumor patients

Factors	High expression group (n=71)	Low expression group (n=78)	x^2	P
Age				
≥65 years old	44	45	0.283	0.595
<65 years old	27	33		
Sex				
Male	46	55	0.558	0.455
Female	25	23		
Tumor differentiation				
High differentiation	20	16	1.189	0.276
Medium and low differentiation	51	62		
Maximum tumor diameter				
≥5 cm	40	37	1.18	0.277
<5 cm	31	41		
Lymph node metastasis				
Yes	53	39	9.56	0.002
No	18	39		
Clinical stages				
Stage I-II	21	41	8.083	0.004
Phase III	50	37		
Pathological type				
Adenocarcinoma	36	43	0.292	0.589
Squamous carcinoma	35	35		

Note: CXCL8: Chemokine 8.

strated a notably larger AUC than CYFRA21-1 (**Figure 3A**; **Tables 4**, **5**).

Predictive value of CXCL8, tumor markers and inflammatory factors for clinical staging

The analysis of clinical data revealed a relationship between CXCL8 expression and clinical staging in NSCLC patients. Upon further analysis, it was observed that the expressions of CXCL8, CEA, CYFRA21-1, and hs-CRP were significantly higher in patients with stage III than those with stages I-II (all P<0.05, **Table 6**). In the subsequent analysis, the diagnostic value of the significant indices in predicting clinical staging was compared. The study found

Table 3. Expression of CXCL8, tumor markers and inflammatory factors in the diagnosis of lymph node metastasis

Variable	Patients with lymph node metastasis (n=92)	Patients without lymph node metastasis (n=57)	T/Z	P
CEA	3.95 [3.02, 4.84]	3.51 [2.41, 4.56]	2.094	0.036
CXCL8	350.72±92.56	273.50±84.91	5.211	<0.001
CYFRA21-1	5.20 [3.08, 11.45]	4.48 [2.20, 6.05]	2.080	0.038
hs-CRP	15.13 [11.92, 22.82]	13.74 [8.92, 17.89]	1.674	0.095

Notes: CXCL8: chemokine 8; hs-CRP: high sensitivity C-reactive protein; CEA: carcinoembryonic antigen; CYFRA21-1: cytokeratin 19 fragment.

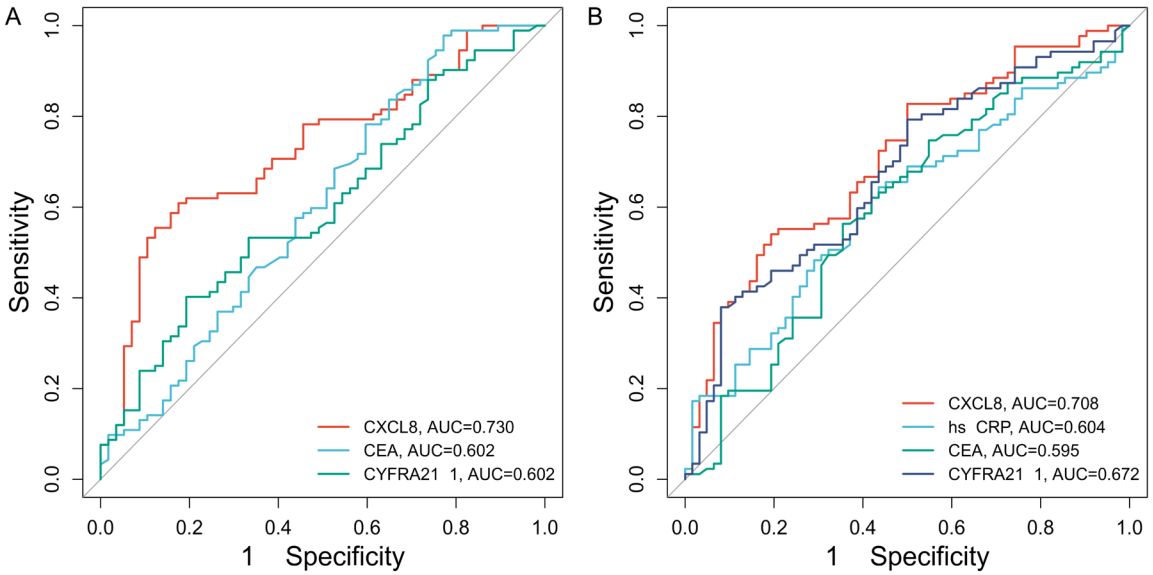

Figure 3. ROC curves of CXCL8, tumor markers and inflammatory factors in predicting lymph node metastasis and clinical staging. A: ROC curve of CXCL8, tumor markers and inflammatory factors in predicting lymph node metastasis; B: ROC curve of CXCL8, tumor markers and inflammatory factors in predicting clinical staging. Notes: CXCL8: chemokine-8; hs-CRP: high sensitivity C-reactive protein; CEA: carcinoembryonic antigen; CYFRA21-1: Cytokeratin 19 fragment; ROC: receiver operating characteristic curve.

that the AUC of CXCL8 was 0.708, while the AUC values of CEA, CYFRA21-1, and hs-CRP were 0.595, 0.672, and 0.604, respectively. However, no significant difference was observed in the AUC values among the four indices according to the Delong test (P>0.05, **Figure 3B**; **Tables 7**, **8**).

Predictive value of CXCL8 for the 5-year survival of NSCLC patients

NSCLC patients with lymph node metastasis, at clinical stage III, and with high CXCL8 levels had significantly decreased five-year survival rates (**Figure 4**).

Discussion

Despite the widespread use of radiotherapy, chemotherapy, and surgery in the treatment of NSCLC, the 5-year survival rate remains relatively low, ranging from 60% to 80%. This is largely because most patients are diagnosed in advanced stage or with metastasis [21]. Therefore, there is a pressing need to identify new therapeutic targets that can improve the prognosis and increase the survival rate of NSCLC patients. Tumor growth and metastasis are complex processes affected by various factors, including cancer cell migration, angiogenesis, and interactions within the tumor microen-

Table 4. ROC curve parameters of CXCL8 and tumor markers in predicting lymph node metastasis

Marker	AUC	95% CI	Specificity	Sensitivity	Youden index	Cut off
CXCL8	0.730	0.648-0.730	82.46%	60.87%	43.33%	328.975
CEA	0.602	0.505-0.602	22.81%	97.83%	20.63%	2.075
CYFRA21-1	0.602	0.509-0.602	80.70%	40.22%	20.92%	6.23

Notes: CXCL8: chemokine-8; CEA: carcinoembryonic antigen; CYFRA21-1: cytokeratin 19 fragment; ROC: receiver operating characteristic curve.

Table 5. AUC difference between CXCL8 and tumor markers in predicting lymph node metastasis

Marker 1	Marker 2	Z	P	AUC difference	CI lower upper
CEA	CYFRA21-1	0.012	0.991	0.001	-0.110-0.112
CXCL8	CEA	1.909	0.056	0.127	-0.003-0.258
CXCL8	CYFRA21-1	2.230	0.026	0.128	0.016-0.241

Notes: CXCL8: chemokine-8; CEA: carcinoembryonic antigen; CYFRA21-1: Cytokeratin 19 fragment; AUC: area under the curve.

Table 6. Value of CXCL8, tumor markers and inflammatory factors in clinical staging

Variable	Patients at stage III (n=87)	Patients at stage I-II (n=62)	T/Z	P
CEA	4.14 [3.06, 4.83]	3.35 [2.54, 4.48]	1.978	0.048
CXCL8	349.79±93.37	281.02±88.00	4.584	<0.001
CYFRA21-1	5.50 [3.54, 18.22]	3.47 [2.17, 5.86]	3.574	<0.001
hs-CRP	15.79 [11.31, 23.64]	13.12 [9.71, 17.39]	2.157	0.031

Notes: CXCL8: chemokine 8; hs-CRP: high sensitivity C-reactive protein; CEA: carcinoembryonic antigen; CYFRA21-1: cytokeratin 19 fragment.

Table 7. AUC parameters of CXCL8, tumor markers and inflammatory factors in clinical staging

Marker	AUC	95% CI	Specificity	Sensitivity	Youden index	Cut off
CEA	0.595	0.501-0.595	64.52%	56.32%	20.84%	3.895
CXCL8	0.708	0.625-0.708	80.65%	54.02%	34.67%	343.085
CYFRA21-1	0.672	0.585-0.672	91.94%	37.93%	29.87%	6.935
hs-CRP	0.604	0.513-0.604	56.45%	64.37%	20.82%	13.705

Notes: CXCL8: chemokine-8; hs-CRP: high sensitivity C-reactive protein; CEA: carcinoembryonic antigen; CYFRA21-1: cytokeratin 19 fragment; ROC: receiver operating characteristic curve.

Table 8. AUC differences of CXCL8, tumor markers and inflammatory factors in clinical staging

Marker 1	Marker 2	Z value	*P* value	AUC difference	CI lower upper
CEA	CYFRA21-1	-1.345	0.179	-0.077	-0.224
CXCL8	hs-CRP	1.751	0.080	0.104	-0.233
CXCL8	CEA	1.734	0.083	0.113	-0.256
CXCL8	CYFRA21-1	0.605	0.545	0.036	-0.234
hs-CRP	CEA	0.198	0.843	0.009	-0.171
hs-CRP	CYFRA21-1	-1.142	0.253	-0.068	-0.234

Notes: CXCL8: chemokine 8; hs-CRP: high sensitivity C-reactive protein; CEA: carcinoembryonic antigen; CYFRA21-1: cytokeratin 19 fragment; AUC: area under the curve.

vironment [22, 23]. Chemokines play a crucial regulatory role in these processes. CXCL8, as a prominent chemokine with the glutamic acid-leucine-arginine (ELR) motif, is essential in various biological processes such as chemotaxis, angiogenesis, wound healing, and immune cell

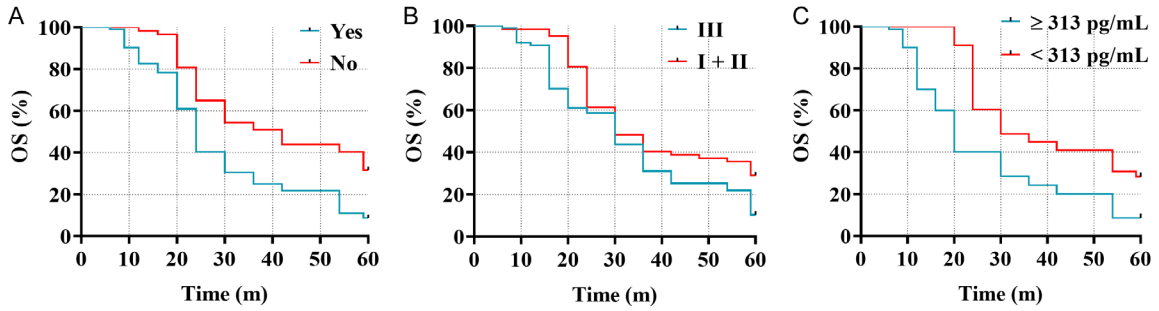

Figure 4. Associations of CXCL8, lymph node metastasis and clinical stage with 5-year survival curve. A: Five-year survival curve of patients with lymph node metastasis and those without; B: Five-year survival curve of patients at stage I-II and those at III; C: Five-year survival curve based on the expression of CXCL8. Note: CXCL8: Chemokine 8.

inflammation. It exerts its effects by binding to specific receptors on the cell surface, namely CXCR1 and CXCR2, which are G-protein coupled receptors (GPCRs) [24, 25]. The abnormal expression of CXCL8 has been implicated in the development of various chronic diseases and cancers [26], and it is closely associated with tumor cell proliferation and migration. These factors are crucial in determining the prognosis and postoperative recurrence of NSCLC patients [27].

However, there is currently some debate on the expression of CXCL8 in NSCLC. While some studies reported no significant difference in CXCL8 expression between cancer tissues and adjacent tissues of LC patients using immunohistochemical methods [28], others have demonstrated a correlation between high CXCL8 expression in NSCLC and poor prognosis [29]. There is also a view that CXCL8 may have a dual role in tumor, which can not only promote tumor growth, but also fight against tumor. The dominant role of CXCL8 in tumor development and progression remains a subject of ongoing research and requires further confirmation [30].

This study aims to delve into the expression of CXCL8 within the context of NSCLC pathogenesis and its potential link to patient outcomes. By analyzing the serum CXCL8 expression of 149 NSCLC patients and comparing them with those of with benign lesions, a significant increase in serum CXCL8 expression was observed in NSCLC patients before surgery. Additionally, CXCL8 was found to be positively correlated with hs-CRP, CEA and CYFRA21-1 through correlation analysis. These findings provide valuable insights into the significant role of CXCL8 in the development of NSCLC and its association with other biomarkers. The increase of CXCL8 expression may reflect the biological activity and tumor burden. As a pro-inflammatory chemokine, CXCL8 can promote inflammatory reactions, angiogenesis, and the proliferation and migration of tumor cells within the tumor microenvironment [31, 32]. Consequently, the elevated serum expression of CXCL8 in NSCLC patients may be associated with tumor progression and deterioration. Additionally, the positive correlation between CXCL8 and hs-CRP, CEA, and CYFRA21-1 further supports this notion. hs-CRP is an inflammatory marker, and its elevated level typically indicates the presence of inflammation within the body. CEA and CYFRA21-1 are tumor markers that are frequently used in clinical practice to monitor tumor activity and assess treatment response in cancer patients [33]. The positive correlation observed between CXCL8 and these markers suggests that CXCL8 may play a role in tumor-related inflammatory responses and tumor progression.

Prior research conducted by Yang et al. [34] has demonstrated a significant increase in CXCL8 expression in hepatocellular carcinoma cases, highlighting its close association with the clinical stage and tumor invasion. In addition, Huang et al. [35] have found that the serum expression of CXCL-8, CEA and CA19-9 in patients with colorectal cancer was significantly higher than those in healthy controls, and the diagnostic sensitivity of CXCL-8 was higher than CEA and CA19-9, suggesting that CXCL8 may serve as a superior biomarker for the diagnosis of colorectal cancer. Identifying effective biomarkers like CXCL8 for predicting lymph node

metastasis in NSCLC patients could positively impact treatment customization and outcome enhancement, especially in early stages where intervention is most effective. For example, Kobayashi et al. [36] found that high variant allele frequencies in preoperative ctDNA were closely related to the occurrence of lymph node metastasis in NSCLC patients, aiding surgical planning and scope determination. Moreover, Zhang et al. [37] reported a strong association between low lymphocyte counts and lymph node metastases in NSCLC patients, indicating a need for more potent preoperative adjuvant treatment regimen to manage the progression of lymph node metastases. However, there is no clear report on the relationship between CXCL8 and pathological conditions in NSCLC. Accordingly, we further analyzed the relationship between CXCL8 expression and the clinicopathological features of NSCLC patients. We observed that patients with high CXCL8 expression were more prone to lymph node metastasis and clinical stage III compared to those with low expression. This finding suggests a potential correlation between CXCL8 expression in NSCLC and pathological features, as well as disease progression. The increased proportion of lymph node metastasis and advanced clinical stage in the high expression group indicates that CXCL8 expression may be closely associated with tumor invasion and severity, aligning with the expression patterns in liver cancer and colorectal cancer, which further strengthens the value of CXCL8 as a potential tumor marker. To evaluate the diagnostic value of CXCL8 in lymph node metastasis and clinical staging of NSCLC patients, we analyzed ROC curves. The results demonstrated that the AUC of CXCL8 was significantly higher than that of CYFRA21-1 in detecting lymph node metastasis. However, there was no significant difference between CXCL8 and CEA in this regard. Moreover, there was no significant difference in the AUC values among the four indices for clinical staging. This suggests that while CXCL8 may have specific value in diagnosing lymph node metastasis in NSCLC, its utility in clinical staging may be limited. These findings underscore the significance of employing a comprehensive approach that incorporates multiple biomarkers in clinical practice. By doing so, we can enhance the accuracy of diagnosis and improve prognosis prediction in clinical practice.

CXCL8 plays a critical role in regulating the tumor microenvironment and promoting tumor cell proliferation, invasion, and angiogenesis [13]. Numerous studies have reported that CXCL8 is associated with the prognosis of esophageal cancer [38], cervical cancer [39], and breast cancer [40]. However, in the context of NSCLC, the relationship between CXCL8 and patient prognosis remains less reported. We initially examined the impact of lymph node metastasis and TNM staging on long-term survival in NSCLC patients and found that patients with lymph node metastasis and those in stage III had significantly lower 5-year survival rates. Lymph node metastasis and clinical staging are often indicative of the extent of tumor invasion and progression. Lymph node metastasis signifies the spread of cancer within the body, and higher clinical stages are typically associated with a more advanced disease state and poorer prognosis [41, 42]. These factors are directly linked to the biological behavior and treatment response of tumors, making them crucial prognostic factors that impact patient survival. Considering that CXCL8 is closely related to lymph node metastasis and TNM staging in NSCLC patients, it is plausible to that CXCL8 affects the long-term survival of NSCLC patients, and our results also confirmed that patients with high CXCL8 levels had a worse long-term prognosis. The specific role of CXCL8 in NSCLC may be attributed to its diverse functions within the tumor microenvironment, including regulating immune cells, directly promoting tumor cell activity, and influencing the surrounding microenvironment. As a result, CXCL8 level may reflect the physical diffusion, pathological stage of development, and molecular-level biological activity, serving as an effective biomarker for the long-term prognosis of NSCLC patients.

While our research contributes to the discussion on the role and clinical application of CXCL8 in NSCLC, there are certain limitations that should be acknowledged. Firstly, the study primarily relies on the correlation analysis of serum marker levels, which may not fully capture the complex role of CXCL8 within the tumor microenvironment. Secondly, the study did not encompass a broader range of patient samples or include multi-center data, which may restrict the generalizability of its findings. Future research should aim to incorporate

more comprehensive biomarker analyses, along with the integration of molecular biology and clinical data, to assess the role of CXCL8 more accurately in different subtypes of NSCLC. Additionally, conducting multi-center and large-scale clinical research would be beneficial in validating and expanding upon these findings. Such studies would provide a more robust scientific foundation for the development of individualized treatment approaches for NSCLC.

Conclusion

CXCL8 expression in NSCLC is strongly associated with patient prognosis, particularly in relation to lymph node metastasis and clinical staging. Although the role of CXCL8 is multifaceted in different types of cancer, in the case of NSCLC, elevated expression of CXCL8 is associated with tumor invasion and severity. These findings offer valuable insights for future clinical practice, highlighting the potential of CXCL8 as a valuable biomarker for the diagnosis and prognosis evaluation of NSCLC. Additionally, these results suggest future research avenues, emphasizing the need to investigate the specific role of CXCL8 in the tumor microenvironment and its impact on different subtypes of NSCLC.

Disclosure of conflict of interest

None.

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