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SERUM KLF5 AND CXCL12 LEVELS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE COMPLICATED WITH TYPE II RESPIRATORY FAILURE

NIVOI KLF5 I CXCL12 U SERUMU KOD PACIJENATA SA HRONIČNOM OPSTRUKTIVNOM BOLEŠĆU PLUĆA SA KOMPLIKACIJAMA U VIDU RESPIRATORNE INSUFICIJENCIJE TIPA II

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Summary

Background: To explore the changes in the serum levels and significance of Kruppel-like factor 5 (KLF5) and chemokine ligand 12 (CXCL12) in individuals suffering from type II respiratory failure (II-RF) in conjunction with an acute exacerbation of chronic obstructive pulmonary disease (AECOPD).
Methods: The observation group consisted of 164 patients with AECOPD and II-RF who were admitted to the hospital between January 2022 and January 2025. There were two groups in the observation group: one with a good prognosis and the other with a bad prognosis. The control group consisted of an additional 90 healthy people who were examined physically in the hospital throughout that time. The levels of serum KLF5 and CXCL12 in all research subjects were determined via enzyme-linked immunosorbent assay (ELISA). The associations between the blood levels of KLF5 and CXCL12 in patients with AECOPD combined with II-RF, along with associated lung function indicators and the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, were examined using Pearson correlation analysis. The predictive value of serum KLF5 and CXCL12 for the prognosis of patients with AECOPD and II-RF was analysed.
Results: Serum KLF5 and CXCL12 levels were substantially higher in the observation group than in the control group ($P<0.05$). Compared with those in the group with a good prognosis, the levels of serum KLF5 and CXCL12, partial pressure of carbon dioxide (PCO_2), and APACHE II score in the poor prognosis group were increased ($P<0.05$), both the arterial partial pressure of oxygen (PO_2) and the forced expi-

Kratak sadržaj

Uvod: Cilj je bio da se ispitaju promene u nivou seruma i klinički značaj faktora tipa Kruppel 5 (KLF5) i hemokin liganda 12 (CXCL12) kod pacijenata sa respiratornom insuficijencijom tipa II (II-RF) u okviru akutnog pogoršanja hronične opstruktivne bolesti pluća (AECOPD).
Metode: Ispitivana grupa je obuhvatila je 164 pacijenta sa AECOPD i II-RF, koji su hospitalizovani između januara 2022. i januara 2025. godine. Ova grupa je podeljena na pacijente sa dobrom i lošom prognozom. Kontrolnu grupu je činilo 90 zdravih ispitanika koji su u istom periodu prošli rutinske preglede. Nivoi KLF5 i CXCL12 u serumu su određeni pomoću enzimski povezane imunoadsorpcione analize (ELISA). Korelacija između nivoa KLF5 i CXCL12 u serumu, parametara plućne funkcije i APACHE II skora procenjena je Pirsonovom korelacionom analizom. Analizirana je i prediktivna vrednost KLF5 i CXCL12 za prognozu kod pacijenata sa AECOPD i II-RF.
Rezultati: Nivoi KLF5 i CXCL12 u serumu bili su značajno viši kod pacijenata u grupi ispitanika u poređenju sa kontrolnom ($P<0,05$). Kod pacijenata sa lošom prognozom registrovani su viši nivoi KLF5 i CXCL12, povišen parcijalni pritisak ugljen-dioksida (PCO_2) i viši APACHE II skor, dok su parcijalni pritisak kiseonika (PO_2), forsirani ekspiratorni volumen u jednoj sekundi (FEV_1), odnos FEV_1/forisani vitalni kapacitet (FEV_1/FVC) i procenat predviđenog FEV_1 (FEV_1%Pred) bili ni i u poređenju sa grupom sa dobrim ishodom ($P<0,05$). FEV_1, FEV_1/FVC, FEV_1% Pred i PO_2 negativno su korelisali sa nivoima KLF5 i

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ratory volume in one second (FEV_1), volume in one/forced vital capacity (FEV_1/FVC%), and the percentage of the FEV_1%PR to the expected value dropped ($P<0.05$). FEV_1, FEV_1/FVC, FEV_1%Pred, and PO_2 had a negative correlation ($P<0.05$) with serum KLF5 and CXCL12 levels, whereas PCO_2 and the APACHE II score were positively correlated with the levels of serum KLF5 and CXCL12 ($P<0.05$). The results of the ROC curve analysis revealed that the area under the curve (AUC) for the combined detection of serum KLF5 and CXCL12 for predicting poor prognosis in patients with AECOPD combined with II-RF was 0.947 (95% CI: 0.913–0.981), which was significantly greater than the AUC predicted by the individual detection of KLF5 and CXCL12 [0.870 (95% CI: 0.816–0.923), 0.843 (95% CI: 0.770–0.915)], and the differences were statistically significant ($Z=2.413$, $P=0.016$; $Z=2.554$, $P=0.011$).

Conclusions: The levels of serum KLF5 and CXCL12 in patients with AECOPD combined with II-RF were significantly increased. Additionally, detecting both of these indicators together provides substantial prognostic value for patients with II-RF and AECOPD. Therefore, serum KLF5 and CXCL12 can serve as serum markers to predict poor prognosis in patients with AECOPD combined with II-RF, and may help guide clinical diagnosis and treatment.

Keywords: chronic obstructive pulmonary disease, Kruppel-like factor 5, chemokine ligand 12, respiratory failure, acute exacerbation period

CXCL12 ($P<0,05$), dok su PCO_2 i APACHE II skor pozitivno korelisali sa ovim markerima ($P<0,05$). Analiza ROC krive je pokazala da kombinovano određivanje KLF5 i CXCL12 ukazuje na lošu prognozu sa površinom ispod krive (AUC) od 0,947 (95% CI: 0,913–0,981), što je značajno više u odnosu na pojedinačno određivanje KLF5 [0,870 (95% CI: 0,816–0,923)] ili CXCL12 [0,843 (95% CI: 0,770–0,915)] ($Z=2,413$, $P=0,016$; $Z=2,554$, $P=0,011$).

Zaključak: Nivoi KLF5 i CXCL12 u serumu su značajno povišeni kod pacijenata sa AECOPD i II-RF. Kombinovano određivanje ova dva markera pru a značajnu prognostičku vrednost i mo e pomoći u kliničkoj dijagnostici i lečenju pacijenata sa AECOPD komplikovanom respiratornom insuficijencijom tipa II.

Ključne reči: hronična opstruktivna bolest pluća, faktor tipa Kruppel 5 (KLF5), hemokin ligand 12 (CXCL12), respiratorna insuficijencija, akutno pogoršanje

Introduction

Airflow obstruction in the lungs, damage to tiny airways, and reduced airflow are the hallmarks of chronic obstructive pulmonary disease (COPD), a common respiratory disorder (1–3). It has a high incidence and mortality rate. Acute exacerbation of COPD (AECOPD) is the most dangerous stage of COPD in clinical practice (4). Clinically, it is usually accompanied by type II respiratory failure (II-RF), causing patients to have breathing difficulties/shortness of breath, which poses a serious threat to patients' safety. Therefore, effective monitoring and evaluation of AECOPD are vital for improving patient prognosis (5). Angiogenesis, inflammatory responses, cell proliferation, differentiation, development, and death are all regulated. Research has shown that miR-145-5p prevents airway epithelial apoptosis and inhibits inflammatory responses by targeting KLF5. Chemokine ligand 12 (CXCL12) is a type of chemokine that plays a significant role in infectious diseases and inflammatory responses. Another study (6) reported that CXCL12 was highly expressed in the serum of elderly patients with AECOPD.

It has a high prevalence rate, high disability and mortality rates and imposes a heavy burden on global public health (7–9). Some COPD patients progress to the advanced stage of the disease and often develop type II respiratory failure (characterised mainly by hypercapnia and hypoxemia), which is the main cause of repeated hospitalisations, severe decline in quality of life and death (10). A thorough clarification of the complex pathophysiological mechanisms of COPD, including type II respiratory failure, and the search for effective biomarkers are vital for the early identification of high-risk populations, guiding individualised treatment and improving prognosis. One significant transcription factor that helps control the expression of several genes linked to oxidative stress, cell division, fibrosis, and the inflammatory response is Kruppel-like factor 5 (KLF5) (11–13). Its role in airway remodelling and inflammation in COPD is attracting attention. Moreover, CXC chemokine ligand 12 (CXCL12), a key chemokine, plays a significant role in recruiting inflammatory cells (such as neutrophils and lymphocytes) to the lungs and in promoting chronic inflammation and tissue damage (14).

Nevertheless, there is still a lack of studies on the evolving trends, connections, and clinical relevance of serum KLF5 and CXCL12 levels in patients with COPD, particularly those with severe consequences of type II respiratory failure (15). Clarifying the expression patterns of these two indicators at different stages of the disease (especially when combined with respiratory failure) will help reveal the potential molecular mechanisms by which COPD progresses to respiratory failure and provide new ideas (16). The heterogeneity of COPD itself, the diversity of complications, and the complexity and stability control of biomarker detection.

To explore the associations between the levels of KLF5 and CXCL12 in the serum of patients with stable COPD, patients with COPD complicated with type II respiratory failure, and healthy controls and to evaluate their value as potential biomarkers, to deepen

the understanding of this complication, this study provides a theoretical basis for future risk prediction and intervention research.

Materials and Methods

General information

A total of 164 patients with AECOPD and II-RF who visited our hospital between January 2022 and January 2025 were selected for the observation group. The average age of these individuals was 58.14±5.47 years, with 88 males and 76 females, aged 43 to 82. The average age of people with COPD was 7.33±2.17 years, and the duration ranged from 4 to 12 years. Twenty people had diabetes. A total of 29 patients had a history of alcohol intake, 35 patients had a history of smoking, and 26 patients had hypertension.

In the same time frame, 90 more healthy people were examined physically at our hospital, including 48 males and 42 females aged 40–83 years, with an average age of 58.09±5.69 years, were selected as the control group. There was no statistically significant difference in sex or age between the two groups ($P>0.05$).

This study has been approved by the Medical Research Ethics Committee (No. AZWJC18068).

Inclusion criteria and exclusion criteria

Inclusion criteria: (1) Met the relevant diagnostic criteria for AECOPD; (2) Had a normal respiratory tract structure; (3) Conscious and able to cooperate with the relevant diagnosis and treatment work.

Exclusion criteria: (1) Liver or kidney dysfunction; (2) A combination of malignant tumours; (3) Blood system diseases; (4) An autoimmune disease.

Determination of serum KLF5 and CXCL12 levels

Laboratory testing methods

Quantitative analysis of key biomarkers was conducted on serum samples collected from included patients and healthy controls. All serum samples were left to stand at room temperature for 30 minutes after collection to solidify fully. Then, they were separated at 3000 RPM for 15 minutes at 4 °C to obtain the serum, which was immediately aliquoted and frozen at -80 °C for testing. The concentrations of KLF5 protein and CXCL12 (SDF-1α) cytokine in serum were determined by enzyme-linked immunosorbent assay (ELISA) technology. The detection of KLF5 concentration uses the commercial human KLF5 ELISA test kit provided by Cloud-Clone Corp from the United States (catalogue number:). The detection of CXCL12 concentration was carried out using the commercial human CXCL12/SDF-1 alpha Quantikine ELISA kit (item number: DSA00) provided by R&D Systems from the United States. This involves adding standard and quality control substances, as well as diluted serum samples, to microplates precoated with specific antibodies, followed by incubation and washing to remove unbound substances. Add the biotin-labelled detection antibody, horseradish peroxidase (HRP) -labelled Streptavidin-HRP and the chromogenic substrate solution (TMB) in sequence. The colour development reaction was carried out under light-protected conditions. Immediately after the reaction was terminated, the absorbance (OD) of each well was measured at 450 nm using an automatic microplate reader (BioTek Synergy H1). The standard curve was drawn based on the concentration of the standard substance and its corresponding OD value. The specific concentration values of KLF5 and CXCL12 in each serum sample were calculated through the four-parameter logistic (4-PL) curve fitting method. To ensure the accuracy and reliability of the test results, all samples were subjected to double-well repeated determination, and the average value was calculated as the final result.

Laboratory reagents and equipment

(1) The determination of KLF5 protein concentration in serum samples was carried out using the human KLF5 ELISA detection kit provided by Cloud-Clone Corp from the United States (product number: SEB514Hu). The determination of CXCL12 (SDF-1α) cytokine concentration was carried out using the human CXCL12/SDF-1 alpha Quantikine ELISA Kit (product number: DSA00) provided by R&D Systems from the United States.

(2) The absorbance (OD value) was read in the experimental operation on the BioTek Synergy H1 multifunctional microplate reader (Manufacturer: BioTek Instruments, Inc., USA), which is the core equipment for concentration quantification.

Assessment of Acute Physiology and Chronic Health Evaluation II (APACHE II) scores and indicators associated with pulmonary function

(1) The pulmonary function of the patients in the observation group was measured via the KOKO pulmonary function instrument (PDS Company, USA). Forced expiratory volume in one second (FEV_1) and volume in one second/forced vital capacity (FEV_1/FVC%) are its primary components; airflow limitation is defined as less than 70%.

(2) An ABL80 arterial blood gas analyser (bought from Radomite, Denmark) was used to measure the partial pressures of carbon dioxide (PCO_2) and oxygen (PO_2) in each subject's arterial blood.

(3) APACHE II scores were evaluated for patients in the observation group.

Prognosis and assessment grouping

Prognosis judgment: Patients with AECOPD combined with II-RF do not require mechanical ventilation after treatment. The symptoms of respiratory failure improved. These patients transition from AECOPD to COPD. The PO_2, PCO_2 and pH values returned to the normal range, and there was no acid-base balance or water or electrolyte imbalance. Patients with the above conditions were included in the good prognosis group. In contrast, those in the poor prognosis group had diseases that either did not develop or even got worse after treatment.

Statistical methods

The statistical program SPSS 25.0 was utilised to manage and examine the data. The χ^2 test was used to compare groups. The normally distributed data are shown as $\bar{x}\pm s$, and two groups were compared using an independent-samples t-test. Lung function markers, the APACHE II score, and serum KLF5 and CXCL12 levels were examined using Pearson correlation analysis. The prognostic significance of serum KLF5 and CXCL12, both alone and in combination, for poor prognosis in patients with AECOPD and II-RF was examined using receiver operating characteristic (ROC) curves.

Results

Comparison of serum KLF5 and CXCL12 levels between the control group and the observation group

The levels of serum KLF5 and CXCL12 in the observation group were both greater than those in the control group ($P<0.05$).

The levels of serum KLF5 and CXCL12 in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) complicated with type II respiratory failure (II-RF) (observation group, n=164) were significantly higher than those in the control group who underwent a healthy physical examination during the same period (n=90). The difference was statistically significant ($P<0.05$). In the pathological state of AECOPD combined with severe type II respiratory failure, the expressions of KLF5 and CXCL12 in the circulatory system of patients are significantly upregulated. KLF5 and CXCL12 may play essential roles in the development and progression of AECOPD associated with II-RF. The increase in their serum levels may reflect disease activity and severity (*Table I*).

General data comparison between the groups with poor and favourable prognoses

There were 112 patients in the favourable-prognosis group and 52 in the poor-prognosis group. When comparing the two groups' general data, no statistically significant difference was found ($P>0.05$) (*Table II*).

There was no significant difference between the two groups of patients in basic demographic and dis-

Table I Comparison of serum KLF5 and CXCL12 levels between the control group and the observation group ($\bar{x}\pm s$).

Group	n	KLF5 (μg/L)	CXCL12 (pg/L)
Control group	90	3.84±1.03	1.22±0.31
Observation Group	164	6.93±1.51	3.52±0.90
t	-	-17.320	-23.474
P	-	<0.001	<0.001

Table II Comparison of general data between the poor prognosis group and the good prognosis group (n/n or $\bar{x}\pm s$).

Group	n	Gender (Male/ Female)	Age (Years)	Body Mass Index (kg/m^2)	COPD time (Years)	Combined diabetes (Yes/No)	Combined hypertension (Yes/No)	Smoking history (Yes/No)	Drinking history (Yes/No)
Good prognosis group	112	61/51	58.18±5.51	22.21±1.52	7.28±2.20	12/100	15/97	20/92	17/95
Poor prognosis group	52	27/25	58.06±5.38	22.37±1.41	7.43±2.12	8/44	11/41	15/37	12/40
t		0.092	0.131	-0.642	-0.411	0.723	1.603	2.555	1.522
P		0.761	0.896	0.522	0.682	0.395	0.205	0.110	0.217

Table III Comparison of serum KLF5 and CXCL12 levels between the good prognosis group and the poor prognosis group ($\bar{x}\pm s$).

Group	n	KLF5 (μg/L)	CXCL12 (pg/L)
Good prognosis group	112	6.22±1.45	3.11±0.83
Poor prognosis group	52	8.45±1.63	4.41±1.06
t	-	-8.807	-8.525
P	-	<0.001	<0.001

Table IV Comparison of lung function-related indicators and APACHE II scores between patients with good prognosis and those with poor prognosis ($\bar{x}\pm s$).

Group	n	FEV (L)	FEV /FVC (%)	FEV % pred (%)	PO_2 (mmHg)	PCO_2 (mmHg)	APACHE II score (points)
Good prognosis group	112	1.39±0.36	57.83±5.42	57.62±5.39	69.57±10.21	40.39±8.22	21.23±4.79
Poor prognosis group	52	1.07±0.29	42.59±5.07	41.37±5.11	43.09±9.62	57.61±9.48	33.42±6.71
t	-	5.617	17.096	18.259	15.736	-11.882	-13.286
P	-	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

ease characteristics, such as age, gender composition, and the course of chronic obstructive pulmonary disease (P>0.05), indicating that the two groups were comparable in terms of underlying disease status. However, there were significant differences between the two groups in key clinical and laboratory indicators. The levels of serum KLF5 and CXCL12 in the poor prognosis group were significantly higher than those in the good prognosis group (P<0.05). Meanwhile, blood gas analysis indicators reflecting the severity of respiratory failure showed that the arterial partial pressure of carbon dioxide (PCO2) in the poor-prognosis group was significantly elevated, while the arterial partial pressure of oxygen (PO2) was significantly decreased (P<0.05).

Comparison of serum KLF5 and CXCL12 levels between the good-prognosis group and the poor-prognosis group

The group with a poor prognosis had greater serum KLF5 and CXCL12 levels than the group with a favourable prognosis (P<0.05) (*Table III*).

Prognosis analysis of 164 patients with AECOPD complicated by type II respiratory failure revealed significant differences in serum KLF5 and CXCL12 levels across prognostic groups. The serum KLF5 concentration in the poor prognosis group was significantly higher than that in the good prognosis group (P<0.05). Similarly, serum CXCL12 levels increased significantly in the poor-prognosis group (P<0.05). The expression levels of serum KLF5 and CXCL12 are closely associated with patient prognosis. The overexpression of KLF5 and CXCL12 may jointly be involved in the pathophysiological process of disease deterioration and poor prognosis in patients with AECOPD combined with II-RF. Therefore, serum levels of KLF5 and CXCL12 can serve as important biological indicators to predict the prognosis of patients with AECOPD combined with II-RF.

Comparison of pulmonary function-related indicators between the good prognosis group and the poor prognosis group

Compared with those in the good prognosis group, the FEV_1, FEV_1/FVC, FEV_1%Pred, and PO_2 in the poor prognosis group were significantly lower (P<0.05), and the PCO2 and APACHE II scores were significantly greater (P<0.05) (*Table IV*).

The poor prognosis group had more severe airflow limitation and ventilation/exchange disorders, manifested as a decrease in forced expiratory volume in one second, an increase in airway obstruction, and a reduction in the predicted percentage of lung function. At the same time, it was accompanied by more obvious hypoxemia and carbon dioxide retention. The differences in the above indicators between the two groups showed consistent directionality and statistical significance, suggesting that decreased lung function is closely related to abnormal gas exchange and adverse outcomes.

Table V Correlation between serum KLF5, CXCL12 levels and lung function-related indicators and APACHE II score in AECOPD combined with II-RF patients.

Indicator	KLF5		CXCL12	
	r	P	r	P
FEV_1	-0.426	<0.001	-0.408	<0.001
FEV_1/FVC	-0.583	<0.001	-0.687	<0.001
FEV_1 %pred	-0.603	<0.001	-0.58	<0.001
PO_2	-0.467	<0.001	-0.471	<0.001
PCO_2	0.408	<0.001	0.417	<0.001
APACHE II rating	0.480	<0.001	0.548	<0.001

Table VI Predictive efficacy of serum KLF5, CXCL12 single and combined detection for poor prognosis in AECOPD patients with II-RF.

Indicator	AUC	95% confidence interval of AUC	Sensitivity (%)	Specificity (%)	Best Truncation Value	Youden index	P
KLF5	0.870	0.816~0.923	94.2	63.8	6.57 μg/L	0.477	<0.001
CXCL12	0.843	0.770~0.915	75.0	67.0	3.94 pg/L	0.420	<0.001
Two joint projects	0.947	0.913~0.981	90.4	76.1	-	0.735	<0.001

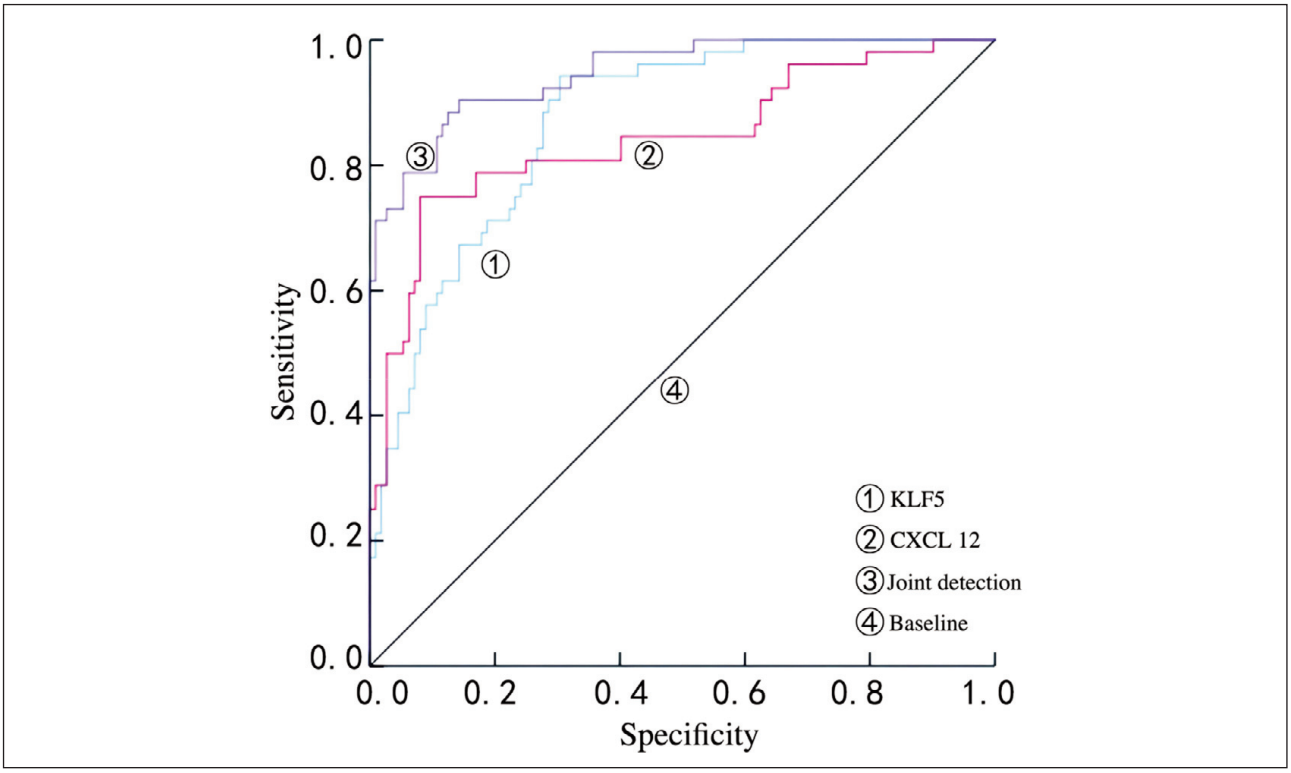

Figure 1 ROC curves for the detection of serum KLF5 and CXCL12 alone and in combination to forecast a bad outcome in patients with AECOPD complicated by II-RF.

Correlations between the levels of serum KLF5 and CXCL12 and pulmonary function-related indicators, as well as the APACHE II score, in patients with AECOPD combined with II-RF

Serum KLF5 and CXCL12 in patients with AECOPD combined with II-RF were negatively correlated with FEV_1, FEV_1/FVC, FEV1%Pred and PO_2 ($P<0.05$) and positively correlated with PCO_2 and the APACHE II score ($P<0.05$).

Pearson correlation analysis was used to explore the relationships among serum KLF5 and CXCL12 levels, lung function, and disease severity in patients with AECOPD complicated by type II respiratory failure. The results showed that both KLF5 and CXCL12 were significantly negatively correlated with FEV_1, FEV_1/FVC%, FEV_1%PRED and arterial PO_2 (all $P<0.05$), and significantly positively correlated with PCO2 and APACHE II score (all $P<0.05$). That is, the higher the levels of the two indicators, the more severe the patient's airflow limitation, the more pronounced the hypoxemia and carbon dioxide retention, and the higher the overall physiological load and disease severity (*Table V*).

Serum KLF5 and CXCL12 detection alone and in combination are predictive of a poor prognosis in patients with AECOPD complicated by II-RF

The prognostic value of serum KLF5 and CXCL12 in patients with AECOPD and II-RF was evaluated using ROC curves. The area under the curve (AUC) for the combined detection of serum KLF5 and CXCL12 for predicting poor prognosis in patients with AECOPD combined with II-RF was 0.947 (95% CI: 0.913–0.981), which was significantly greater than the AUC predicted by the individual detection of KLF5 and CXCL12 [0.870 (95% CI: 0.816–0 923), 0.843 (95% CI: 0.770–0.915)], and the differences were statistically significant ($Z=2.413$, $P=0.016$; $Z=2.554$, $P=0.011$) (*Table VI* and *Figure 1*).

Discussion

Chronic small airway inflammation in patients with COPD can cause lung parenchymal damage and a continuous decline in lung function, and repeated attacks can further aggravate airway damage, thereby narrowing peripheral small airways, increasing airway resistance, and impairing respiratory muscle contractility, leading to respiratory muscle fatigue (17–19). This, in turn, causes hypoxia and carbon dioxide retention, leading to respiratory failure. Frequent acute exacerbations in patients with COPD cause a rapid decline in lung function, increasing the hospitalisation and mortality rates of COPD patients. Respiratory failure is a common complication in patients with AECOPD (20). Patients with combined II-RF have rapid disease progression, a high mortality rate, and a poor prognosis (21). Therefore, it is imperative to assess the prognosis of patients with AECOPD combined with II-RF as early as possible.

Previous studies (22–24) have suggested that airway inflammatory responses, airway damage, chemokines, and cytokines are closely associated with the occurrence and progression of AECOPD combined with II-RF. KLF5 is a zinc-finger transcription factor widely expressed throughout the body and plays a significant role in regulating gene expression. Under the stimulation of inflammatory factors, KLF5 can activate inflammatory signalling pathways, thereby exacerbating inflammatory responses. Research (25–27) has shown that histone deacetylase 4 (HDAC4) promotes airway remodelling and the progression of asthma by deacetylating KLF5 and upregulating CXCL12. Another study revealed that miR-9-5p can negatively regulate interleukin-1 levels through KLF5, thereby participating in airway remodelling and inflammation in asthma (28). These findings further indicate that serum KLF5 levels are associated with impaired lung function in patients with AECOPD and II-RF (29). A possible reason for this finding is that KLF5, an inducer of the respiratory system, can promote inflammation in human tracheal epithelial cells and the proliferation and migration of bronchial smooth muscle cells, thereby aggravating the progression of AECOPD combined with II-RF and affecting the prognosis of patients (30).

The chemokine family includes CXCL12, which is widely expressed in the stromal cells of organs such as the liver and lungs. By binding to its receptor CXCR4, CXCL12 regulates downstream signalling pathways, thereby participating in various biological and pathological processes and playing a significant role in the body's inflammatory response. Studies (31–33) have shown that CXCL12 may indicate active pulmonary infection and is associated with disease severity. Moreover, compared with the good-prognosis group, the serum CXCL12 level in the poor-prognosis group was even higher, suggesting that CXCL12, combined with II-RF, is closely associated with the malignant progression of AECOPD patients. It is speculated that this may be due to elevated CXCL12 levels, which promote the aggregation and infiltration of mononuclear macrophages and lymphocytes, thereby intensifying the local inflammatory response. In addition, CXCL12 is widely expressed in fibroblasts and smooth muscle cells. The interaction between airway epithelial cells and subcutaneous fibroblasts during inflammatory responses is a driving factor for respiratory failure. Elevated CXCL12 levels can induce smooth muscle cell contraction and promote fibroblast proliferation, thereby increasing airway hyperresponsiveness (34). ROC curve analysis revealed that, when paired with II-RF, KLF5 and CXCL12 showed some predictive value for a poor prognosis in patients with AECOPD, and their combined detection yielded the highest AUC. These

findings suggest that the combined detection of KLF5 and CXCL12 can improve the predictive efficacy for the poor prognosis of patients with AECOPD, particularly in combination with II-RF, and compensate for the limitations of single serum factor detection.

Conclusion

Patients with AECOPD and II-RF have higher serum levels of KLF5 and CXCL12, and these elevated levels are closely associated with lung function impairment and poor patient prognosis. Furthermore, combined detection of serum KLF5 and CXCL12 has high predictive efficacy for a poor prognosis in patients with AECOPD and II-RF.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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