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Analysis of the Value of Interleukin-6 in Assessing the Severity and Prognosis of Interstitial Lung Disease

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Abstract

Objective: To observe the expression level of interleukin-6 in patients with interstitial lung disease and its evaluation effect on the severity and prognosis of the patients. **Methods:** A total of 100 patients with interstitial lung disease who visited our hospital from January 2024 to January 2025 were screened, and their clinical data were retrospectively analyzed. **Results:** The level of interleukin gradually increases as the severity of the disease increases. It can be seen that the level of procalcitonin is proportional to the severity of the disease.Interleukin-6 was negatively correlated with pulmonary function indicators. The higher the level, the lower the pulmonary function. This relationship showed a significant differential trend ($P < 0.05$). **Conclusion:** Serum interleukin-6, as a key indicator for effectively evaluating the severity and prognosis of interstitial lung disease, can provide comprehensive data support and guidance for clinical diagnosis and treatment when jointly detected with procalcitonin indicators.

Keywords

Interstitial Lung Disease, Interleukin-6, Severity, Prognosis

1. Background

Interstitial lung disease, as a heterogeneous disorder characterized by pulmonary interstitial fibrosis and abnormal alveolar structure, has a rather complex etiology and involves various factors such as the environment, genetics, autoimmunity and infection [1]. The clinical manifestations of interstitial lung disease are diverse. Progressive dyspnea, dry cough and fatigue are common symptoms. Some pa-

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tients also have symptoms such as arthralgia and clubbing of fingers. Clinical imaging examinations revealed diffuse honeycomb lung and ground-glass opacity in both lungs, while pulmonary function tests mostly showed reduced diffusion function and restrictive ventilation dysfunction [2]. Despite the continuous in-depth research on interstitial lung disease in recent years, its prognosis remains poor. Some patients experience rapid disease progression, which can lead to respiratory failure and even death. Therefore, early diagnosis and accurate assessment of the severity of the disease can positively improve the prognosis of patients.

Inflammation plays a key role in the pathogenesis of interstitial lung disease. The abnormal expression of inflammatory factors is closely related to pulmonary tissue fibrosis and injury. Interleukin-6 is a versatile pleipotent cellular inflammatory factor and an important member of the interleukin family. It is a small molecule glycoprotein with a molecular weight of 19 to 28 kDa, composed of 184 amino acids forming a four-helical structure, and usually exists in monomer form. It is produced by fibroblasts, monocytes/macrophages, lymphocytes, B lymphocytes, epithelial cells, keratinocytes, and various tumor cells [3]. Interleukin-6 can activate various inflammatory cells, accelerate the release of inflammatory factors, and thereby promote lung tissue damage and intensify inflammatory responses. In addition, interleukin-6 can also stimulate collagen synthesis and fibroblast proliferation, accelerating the formation of pulmonary fibrosis. Therefore, an increase in the level of this indicator can serve as a key sign for assessing the aggravation of the severity of interstitial lung disease. Procalcitonin is a type of broad-spectrum inflammatory marker and is mainly used in the diagnosis and determination of bacterial infections. Studies have shown that the expression level of procalcitonin in various infectious diseases is closely related to the severity of the diseases [4]. However, a single inflammatory marker has shortcomings in assessing the severity and prognosis of interstitial lung disease. In recent years, researchers have attempted to combine various inflammatory markers for detection to enhance the accuracy of assessing the severity and prognosis of diseases [5]. Therefore, this study focused on evaluating the expression level of interleukin-6 in patients with interstitial lung disease and its assessment effect on the severity and prognosis of the patients' conditions, providing comprehensive data support and reference for clinical diagnosis and treatment, in order to improve the prognosis of patients and promote the improvement of their living standards. For details, please refer to the following.

2. Materials and Methods

Materials

A total of 176 patients with interstitial lung disease who visited our hospital from January 2024 to January 2025 were screened. Among them, patients who did not undergo the IL-6 test or pulmonary function test were excluded, and a total of 100 patients with interstitial lung disease were included. The average age of the study population was 68.1 years, among which 65.1% were male patients. The

content of this research is in line with the principles of ethics and can be studied. Inclusion criteria: (1) Consistent with the diagnostic criteria for interstitial lung disease [6]; (2) Age 18 or above, gender not limited; (3) The applicant or his/her family member signs the informed consent form. Exclusion conditions: (1) Accompanied by other serious lung diseases, such as lung cancer and tuberculosis, etc. (2) Those with severe organic diseases; (3) Those who have recently received hormone or immunosuppressive therapy.

Methods

The determination method of interleukin-6: After admission, 5ml of fasting venous blood was collected from all patients. The blood was then centrifuged at 3000 revolutions per minute for 10 minutes to extract the upper layer of serum. The level of interleukin-6 in the serum was determined by enzyme-linked immunosorbent assay. Meanwhile, basic data of the patients were collected, covering their gender, age, disease duration, physical signs, symptoms, pulmonary function indicators (forced expiratory volume in one second, forced vital capacity and diffusion function, etc.) and imaging examination results. Assess the severity of the patient's disease: Based on the patient's clinical symptoms, imaging examination results, and pulmonary function index data, the patients were divided into three groups: mild, moderate, and severe. All patients were followed up for a period of 12 months, and the number of acute exacerbations, hospitalizations and deaths of the patients were recorded in detail.

Observation Indicators

1. Compare the levels of interleukin-6 and procalcitonin in patients with different severity levels.

2. Analyze the correlation between interleukin-6, procalcitonin and pulmonary function indicators.

3. Analysis of the Correlation Between Interleukin-6 and Procalcitonin with Hospitalization Frequency, Acute Exacerbations, and Mortality.

4. Receiver Operating Characteristic (ROC) curve of IL-6 to predict AE.

Statistical Methods

Data were processed using SPSS 26.0. Measurement data were analyzed using t-tests and expressed as ($\overline{x} \pm s$). Count data were analyzed using chi-square tests and expressed as n (%). Correlation analysis was performed using Pearson correlation coefficient. A difference was considered statistically significant when $P < 0.05$.

Results

1. Comparison of Interleukin-6 and Procalcitonin Levels in Patients with Different Disease Severities

The level of procalcitonin gradually increases under the trend that the severity of the disease increases. It can be seen that the level of procalcitonin is proportional to the severity of the disease. At the same time, the interleukin levels were measured. Similarly, as the severity of the disease continuously intensified, the index levels significantly increased.

Detailed data are shown in **Table 1**.

Table 1. Comparison of interleukin-6 and procalcitonin levels in patients with different disease severities.

Order of severity	interleukin6 (pg/ml)	Procalcitonin (ng/ml)
Mild	10.52 ± 2.36	0.68 ± 0.23
Moderate	25.84 ± 4.61	1.32 ± 0.36
Severe	45.21 ± 7.62	2.64 ± 0.51
P	<0.05	<0.05

2. Analyze the correlation between interleukin-6, procalcitonin and pulmonary function indicators

Interleukin-6 showed a negative correlation with pulmonary function indicators; the higher the IL-6 level, the lower the lung function, with this relationship demonstrating a significant difference ($P < 0.05$). Procalcitonin also showed a negative correlation with pulmonary function indicators, but the correlation was weak ($P > 0.05$), indicating that higher procalcitonin levels were associated with lower lung function, though the correlation was not strong. Specific data are detailed in Table 2.

Table 2. Analysis of the correlation between interleukin-6 and procalcitonin with pulmonary function indicators.

Index	interleukin6 (r, P)	Procalcitonin (r, P)
FVC	−0.654, $P < 0.01$	−0.512, $P < 0.05$
FEV1	−0.621, $P < 0.01$	−0.481, $P < 0.05$
DLco	−0.584, $P < 0.01$	−0.451, $P < 0.05$

3. Analysis of the Correlation Between Interleukin-6 and Procalcitonin with Hospitalization Frequency, Acute Exacerbations, and Mortality

As shown in Table 3, higher levels of interleukin-6 and procalcitonin were associated with poorer patient prognosis ($P < 0.05$).

Table 3. Analysis of the correlation between interleukin-6 and procalcitonin with hospitalization frequency, acute exacerbations, and mortality.

Index	interleukin6	Procalcitonin	Number of hospitalizatians	Number of acute exacerbation	Death rate
Number of hospitalizatians	>30	>1.0	High	-	-
Number of acute exacerbation	>40	>1.5	-	High	-
Death rate	>50	>2.0	-	-	High
P	<0.05	<0.05	<0.05	<0.05	<0.05

4. In multivariate analysis, a high serum IL-6 level during the follow-up period

(OR 1.014, 95% CI: 1.001 - 1.027, p = 0.036) was an independent predictor of acute exacerbation (Figure 1). In the characteristic curve analysis of the subjects, a high level of serum IL-6 could be used to predict AE in patients with ILD (area under the curve = 0.88, 95% CI: 0.704 - 0.927, p < 0.001). The optimal cut-off value was 28.50 pg/mL, with a sensitivity of 83.3% and a specificity of 77.1%.

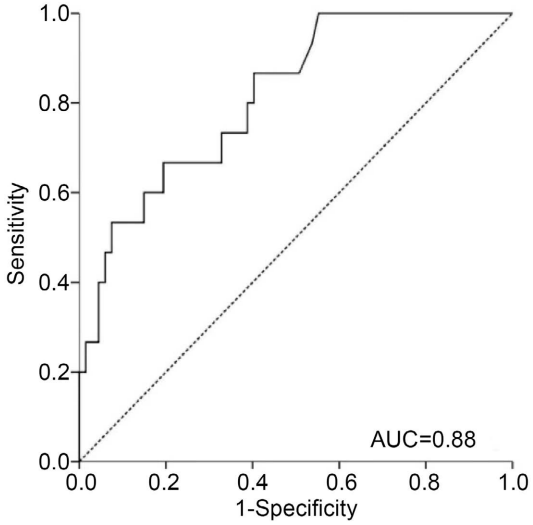

Figure 1. Receiver operating characteristic (ROC) curve of IL-6 to predict AE.

3. Discussion

Interstitial lung disease, as a type of disorder characterized by abnormal alveolar structure and interstitial fibrosis of the lungs, has a complex etiology and diverse clinical manifestations, with a poor prognosis for patients. In recent years, inflammatory factors have played a very crucial role in the pathogenesis of interstitial lung disease and have continuously attracted much attention. Interleukin-6 is a key inflammatory factor and plays an especially crucial role in various inflammatory diseases. Therefore, this study mainly monitored the levels of serum procalcitonin and interleukin-6 in patients with interstitial lung disease, and analyzed their association with the severity and prognosis of the disease.

In this study, it is not difficult to find that under the increasing trend of the severity of interstitial lung disease, the level of interleukin-6 in the patients' serum has significantly increased. This is closely related to the pro-inflammatory effect of interleukin-6 in the inflammatory response. IL-6 can directly or indirectly act on fibroblasts, activating, proliferating them and synthesizing excessive extracellular matrix components, thereby promoting the process of pulmonary fibrosis. IL-6 can indirectly enhance the expression of TGF-β; Shochet et al. reported in an experimental study between patients with idiopathic pulmonary fibrosis and normal healthy donors that IL-6 indirectly leads to an increase in the expression of TGF-β, thereby causing pulmonary fibrosis [7]. On the other hand, IL-6 can induce fibroblasts into a pro-fibrotic phenotype and increase the expression of α-

smooth muscle actin. In order to study the connection between IL-6 and pulmonary fibrosis, Penumatsa KC performed α-smooth muscle actin antibody staining on lung fibroblasts isolated from IL-6+ mice and wild-type control mice that had grown on coverslips for 72 hours to detect the myofibroblast phenotype. It was found that the IL-6+ mouse group was compared with the wild-type mouse group. The expression of α-smooth muscle actin significantly increased [8]. Therefore, an elevated level of interleukin-6 serves as a key indicator of the aggravation of the severity of interstitial lung disease. Compared with the single procalcitonin level test, the combination of interleukin-6 can comprehensively and accurately assess the severity of the disease.

In addition, the research shows that only high interleukin-6 levels are independent risk factors for death. Patients with high interleukin-6 levels have a significantly increased number of acute exacerbations and hospitalizations, and have a very high mortality rate. A previous study supported our results. Among 67 patients with IPF (stable IPF 20 and AE IPF 47), Collard et al. found that IL-6 in the AE IPF group was higher than that in the stable IPF group (10.1 pg/mL vs 5.3 pg/mL, $p = 0.004$). IL-6 was not associated with high mortality (OR 0.26, 95% CI: 0.06 - 1.24, $p = 0.09$) [9]. Our research results indicate that high interleukin-6 levels are associated with the occurrence of AE and a high mortality rate. However, it remains unclear whether high levels of IL-6 are a direct risk factor for death or a predictor of the severity of AE, as all deaths occurred in both the AE group and the group with high interleukin-6 levels. Further research is needed to clarify the relationship between the degree of IL-6 and the severity of AE, and the severity of AE suggests a high mortality rate.

In addition, the research results also revealed that serum interleukin-6 levels, as a key indicator for evaluating the severity and prognosis of interstitial lung disease, the combined detection of procalcitonin and interleukin-6 can provide very comprehensive guidance and reference for clinical diagnosis and treatment. In clinical practice, the determination of procalcitonin and interleukin-6 levels can provide effective references for the diagnosis, condition analysis and treatment of interstitial lung disease. For patients with high levels of both of these indicators, early anti-inflammatory treatment regimens, such as immunosuppressants and glucocorticoids, can be considered to alleviate the patient's inflammatory levels and delay the progression of the disease [10]. In addition, regular measurement of procalcitonin and interleukin-6 levels can be used to evaluate the effectiveness of clinical treatment and make timely adjustments to treatment plans.

Procalcitonin is a type of broad-spectrum inflammatory marker and is often used in the diagnosis and monitoring of bacterial infections. In this study, monitoring procalcitonin alone can to some extent reflect the degree of inflammation and prognosis of interstitial lung disease, but its clinical diagnostic efficacy is relatively low. Combined detection of interleukin-6 can effectively make up for the limitations of a single indicator, thereby improving the accuracy of clinical diagnosis and prognosis assessment [11].

In conclusion, serum interleukin-6, as a key indicator for effectively assessing the severity and prognosis of interstitial lung disease, when combined with procalcitonin indicators for detection, can provide comprehensive data support and guidance for clinical diagnosis and treatment, facilitating the early identification of high-risk patients in clinical practice, the timely implementation of effective intervention plans, and promoting the improvement of patient prognosis. Future research still needs to conduct an in-depth analysis of the specific role of interleukin-6 in the pathogenesis of interstitial lung disease, and at the same time, combine the diagnostic and evaluation value of other indicators in lung diseases.

This study has some limitations. Firstly, this is a retrospective study conducted in a single center, with a limited number of ILD patients. Furthermore, the number of AE cases and deaths is too small to assess the risk factors for AE and death. However, the baseline characteristics, morbidity and mortality of our subjects were similar to those of the patients reported previously.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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