CORRELATION OF LEVELS OF CA19-9, CA15-3, CA12-5 WITH THE SEVERITY AND OUTCOMES OF IDIOPATHIC INTERSTITIAL PNEUMONIA (IIP)

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ABSTRACT

Objective: *To investigate the correlation of levels of carbohydrate antigens 19-9 (CA19-9), 15-3 (CA15-3), and 12-5 (CA12-5) with the disease severity and outcomes of idiopathic interstitial pneumonia (IIP) patients.*

Methods: *We selected as the observation group a total of 98 patients with IIP admitted to the Department of Respiratory Medicine of our hospital from January 2019 to January 2020. In the same period, healthy people selected for examination in our hospital's examination center were selected as the control group. The observation group was divided into mild, moderate, and severe groups according to the severity of the patient's condition and divided into a survival group and a death group according to their prognosis. We collected 4ml of fasting venous blood from all subjects in the morning, and the levels of serum CA19-9, CA15-3, and CA12-5 were detected by immunoradiometric assay. For each group of subjects, we recorded and compared the forced expiratory volume in 1 second as a percentage of the predicted value (FEV1%), the ratio of FEV1 and forced vital capacity (FEV1/FVC), and the percentage of the lung carbon monoxide diffusion as a percentage of the predicted value (DLCO%). The Spearman's Rank Order Correlation Test was used to analyze the correlation between levels of CA19-9, CA15-3, and CA12-5, and the values for FEV1%, FEV1/FVC, and DLCO%. Multifactor logistic regression analysis was used to analyze the factors influencing the prognosis of IIP patients. The relationship between the levels of CA19-9, CA15-3, and CA12-5 in IIP patients and the severity and outcome of the disease were analyzed.*

Results: *The serum CA19-9, CA15-3, CA12-5 levels were significantly higher in the observation group than in the control group. The serum CA19-9, CA15-3, CA12-5 levels in the moderate and severe groups were significantly higher than those in the mild and severe groups. The serum CA19-9, CA15-3, and CA12-5 levels were significantly higher than those in the syndrome group, and the difference was statistically significant (P<.05). The levels of FEV1%, FEV1/FVC, and DLCO% in the moderate and severe groups were significantly lower than those in the mild group, and the levels of serum FEV1%, FEV1/FVC, and DLCO% in the severe group were significantly lower than those in the moderate group, the difference was statistically significant (P<.05). Spearman's Rank-Order Correlation analysis indicates that CA19-9 was negatively correlated with FEV1%, FVC%, and DLCO% (r=- 0.586, r=- 0.579, and r=- 0.561, respectively, and P<.05 or P<.01 for all). CA15-3 was negatively correlated with FEV1%, FVC%, and DLCO% (r=- 0.469, r=- 0.521, and r=- 0.584, respectively, and P<.05 or P<.01 for all). CA12-5 was negatively correlated with FEV1%, FVC%, and DLCO% (r=- 0.502, r=- 0.506, and r=- 0.618, respectively, and P < .05 or P < .01 for all). The levels of serum CA19-9, CA15-3, and CA12-5 in the death group were significantly higher than those in the survival group, and the difference was statistically significant (P<.01). Multivariate logistic regression analysis showed that CA19-9, CA15-3, and CA12-5 were all factors affecting the prognosis of IIP patients (P<. 05 or P<.01).*

Conclusions: *The serum CA19-9, CA15-3, and CA12-5 levels in IIP patients were significantly higher than those in healthy subjects. These levels were negatively correlated with changes in lung function and were influencing factors in the prognosis of IIP patients. The changes in CA19-9, CA15-3, and CA12-5 levels can reflect the disease severity and prognosis of IIP patients.*

Keywords: *Idiopathic interstitial pneumonia, CA19-9, CA15-3, CA12-5, severity, outcomes.*

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Introduction

Idiopathic interstitial pneumonia (IIP) is diffuse interstitial fibrosis of unknown cause, which is a relatively common and progressive lower respiratory tract disease. IIP can occur at any age and is more common among middle-aged and elderly people[1]. The pathological process is progressive diffuse alveolitis and (or) alveolar structural disorder. This eventually leads to the destruction of the alveolar structure, forming complete fibrosis and vesicular honeycomb in the alveolar cavity, and progressive clinical dyspnea often occurs[2]. Most patients experience chronic disease, and the early course of

the disease is hidden and not easily detected. The prognosis of this disease is poor, and the mortality rate is very high; the disease often results in death due to pulmonary insufficiency and heart failure[3]. Therefore, early detection, diagnosis, and treatment are key to improving the efficacy and prognosis of patients with IIP[4]. Glycoantigens 19-9 (CA19-9), 15-3 (CA15-3), and 12-5 (CA12-5) are tumor markers that have a high expression in the serum of tumor patients[5]. In recent years research has shown that the levels of CA19-9, CA15-3, and CA12-5 are abnormally expressed in the serum of IIP patients[6]. In this paper, 98 cases of IIP patients admitted to the Department of Respiratory Medicine of our hospital from January 2019 to January 2020 were adopted as observation objects to analyze the correlation of levels of CA19-9, CA15-3, CA12-5 with the severity and outcomes of IIP. opportunity.

Materials and methods

Materials

A total of 98 patients with IIP admitted to the Department of Respiratory Medicine of our hospital from January 2019 to January 2020 were collected as the observation group according to the following inclusion criteria:

• All patients meet the diagnostic criteria for IIP in the IIP diagnosis and treatment guidelines jointly developed by the American Thoracic Society (ATS), European Respiratory Society (ERS), Japanese Respiratory Society (JRS), and Latin American Thoracic Society (ALAT)[7];

• Patients and their families agree and sign an informed consent form.

The exclusion criteria are the following:

• The patient has other lung diseases;

• The patient's heart, liver, kidney, and other important organs have serious dysfunction;

• The patient has an immune system disease such as leukemia or other autoimmune diseases;

• The patient has a malignant tumor;

• The patient refuses participation in the experiment or terminated the experiment for other reasons.

During the same period, 52 healthy individuals were selected as the control group from those examined in our hospital examination center.

The inclusion criteria are as follows:

• The individual has no lung disease;

• The important organs such as heart, liver, and kidney function normally;

• The individual agrees and signs an informed consent form.

The observation group was divided into the mild, moderate, and severe groups according to the severity of the patients' condition and divided into the survival and death groups according to their prognosis. There were 34 cases in the mild group, including 18 males and 16 females, with an average age of (45.15±5.10) years and an average body mass index (BMI) value of (21.12±1.45) kg/m^2. A total of 33 patients in the syndrome group, including 17 males and 16 females, had an average age of (45.13±5.08) years and an average BMI of (21.15±1.34) kg/m^2.

A total of 31 patients in the severe group, including 16 males and 15 females, had an average age of (45.09±5.51) years and an average BMI of (21.24±1.23) kg/m^2. There were 56 patients in the survival group, including 29 males and 27 females, with an average age of (45.25±5.01) years and an average BMI of (21.33±1.45) kg/m^2. There were 42 cases in the death group, including 22 males and 20 females. The average age was (45.65±5.27) years old, and the average BMI value was (21.00±1.72) kg/m^2. There were 52 cases in the control group, including 27 males and 25 females. The average age was (45.33±5.18) years old, and the average BMI value was (21.20±1.41) kg/m^2. There was no statistically significant difference in age, gender, and BMI values among the patients in each group (P>.05).

Observation index

Serum index

Collect 4ml of fasting venous blood of all subjects in the morning, stand at room temperature for 30min, centrifuge at 3500r/min for 10min, carefully separate the supernatant, and store at -80^{o}C to avoid repeated freeze-thaw. Serum levels of CA19-9, CA15-3, and CA12-5 are detected by immunoradiometric assay. Critical values: CA19-9 <33U/ml, CA15-3 <31U/ml, CA12-5 <35U/ml.

Lung function index

The subject's forced expiratory volume in the first second as a percentage of the predicted value (FEV 1%). The ratio of FEV1 to forced vital capacity (FEV1/FVC). The percentage of carbon monoxide diffusion volume in the predicted value (DLCO%) of the subject's lungs.

Statistical method

The data of this experiment were analyzed

by SPSS20.0 software. All measurement data is represented by ($\bar{x}\pm s$), and the t-test is used for comparison between groups; count data is represented by (%), and the χ^2 test is used. The Spearman's Rank-Order Correlation test was used to analyze the correlation between CA19-9, CA15-3, and CA12-5 levels with FEV1%, FEV1/FVC, and DLCO%. Multifactor logistic regression analysis was used to analyze the influencing factors of the prognosis of IIP patients. The statistical results are statistically significant, with P<.05.

Results

Comparison of serum tumor marker levels between patients with different severity IIP and healthy people

Serum CA19-9, CA15-3, and CA12-5 levels in the observation group were significantly higher than those in the control group. Serum CA19-9, CA15-3, and CA12-5 levels in the moderate and severe groups were significantly higher than those in the mild and severe groups.

Serum levels of CA19-9, CA15-3, and CA12-5 were significantly higher than those in the syndrome group, and the difference was statistically significant (P<.05). The results are shown in Table 1.

Group		n	CA19-9 (u/ml)	CA15-3 (u/ml)	CA12-5 (u/ml)
Control Group		52	9.45±6.12	7.32±5.16	10.26±6.18
Observation Group	Mild Group	34	52.46±15.46[a]	41.79±7.19[a]	54.19±10.51[a]
	Moderate Group	33	86.49±20.45[ab]	50.49±10.33[ab]	70.46±15.46[ab]
	Severe Group	31	110.46±30.48[abc]	67.49±12.42[abc]	86.49±17.45[abc]

Table 1: Comparison of serum tumor marker levels in healthy individuals and patients with different levels of idiopathic interstitial pneumonia disease severity ($\bar{x}\pm s$). *Note: here, [a] is compared with the control group, P<.05; [b] is compared with the mild group P<.05; and [c] is compared with the moderate group, P<.05.*

Comparison of lung function in patients with different levels of IIP severity

The levels of FEV1%, FEV1/FVC, and DLCO% were significantly lower in the moderate and severe groups than those in the mild group.

The levels of serum FEV1%, FEV1/FVC, and DLCO% were significantly lower in the severe than in the moderate group, and the difference was statistically significant (P<0.05). The results are shown in Table 2.

Group	n	FEV1%	FVC%	DLCO%
Mild Group	34	89.46±2.16	79.46±3.12	77.43±2.06
Moderate Group	33	59.46±12.45[b]	56.49±12.43[b]	75.49±12.08[b]
Severe Group	31	48.21±3.45[bc]	45.79±5.18[bc]	65.49±6.42[bc]

Table 2: Comparison of lung function in patients with different levels of idiopathic interstitial pneumonia disease severity ($\bar{x}\pm s$).
Note: [b] is compared with the mild group, P<.05; [c] is compared with the syndrome group, P<.05.

Correlation analysis of serum tumor marker levels and lung function

Spearman's Rank-Order Correlation analysis showed that CA19-9 was negatively correlated with FEV1%, FVC%, and DLCO% (r=-0.586, r=-0.579, and r=-0.561, respectively, and P<.05 or P<.01 for all). CA15-3 was negatively correlated with FEV1%, FVC%, and DLCO% (r=-0.469, r=-0.521, and r=-0.584, respectively, and P<.05 or P<.01 for all).

CA12-5 was negatively correlated with FEV1%, FVC%, and DLCO% (r=-0.502, r=- 0.506, and r=-0.618, respectively, and P<.05 or P<.01 for all). The results are shown in Table 3.

Index		FEV1%	FVC%	DLCO%
CA19-9	*r*	- 0.586	- 0.579	- 0.561
	P	.012	< .001	< .001
CA15-3	*r*	- 0.469	- 0.521	- 0.584
	P	< .001	<.001	.024
CA12-5	*r*	- 0.502	- 0.506	- 0.618
	P	.016	.031	.015

Table 3: Correlation analysis of serum tumor marker levels and lung function.

Comparison of serum tumor marker levels in patients with different IIP prognoses

The levels of serum CA19-9, CA15-3, and CA12-5 in the death group were significantly higher than those in the survival group, and the difference was statistically significant (P<.01). The results are shown in Table 4.

Group	n	CA19-9 (u/ml)	CA15-3 (u/ml)	CA12-5 (u/ml)
Survival Group	56	75.46±12.48	45.13±8.46	60.18±11.43
Death Group	42	105.43±25.46	61.43±10.46	81.79±14.76
t		7.673	8.525	8.170
P		< .001	< .001	< .001

Table 4: Comparison of serum tumor marker levels in patients with differing idiopathic interstitial pneumonia prognoses ($\bar{x}\pm s$).

Analysis of factors influencing the prognosis of patients with IIP

Multivariate logistic regression analysis showed that CA19-9, CA15-3, and CA12-5 were all influencing factors for the prognosis of IIP patients (P<.05 or <.01). The results are shown in Table 5.

Influencing factors	β	*SE*	*P*	*OR*	*95% CI*
CA19-9	0.979	0.051	<.001	2.930	1.711–4.152
CA15-3	0.869	0.481	.025	2.081	1.681–2.485
CA12-5	0.842	0.359	.010	1.645	1.249–2.075

Table 5: Analysis of factors influencing the prognosis of patients with idiopathic interstitial pneumonia.

Discussion

IIP is a common progressive lung disease, and its pathogenesis has not been fully clarified. However, according to some studies, it is closely related to damage of the alveolar epithelium, the formation of fibroblast foci, and the excessive accumulation of extracellular matrix[8].

CA19-9 exists in the form of salivary mucin in serum and is distributed in the normal fetal pancreas, gallbladder, liver, and intestine, and the normal adult pancreas and bile duct epithelium. It is a gastrointestinal tumor-associated antigen present in the blood circulation[9, 10] CA15-3 is the most important specific marker for breast cancer. The levels of CA15-3 in 30%-50% of breast cancer patients are significantly increased, and the change in its content is closely related to the therapeutic effect. For breast cancer patients, CA15-3 is the best indicator for diagnosing and monitoring postoperative recurrence and efficacy[11]. CA12-5 is a glycoprotein derived from body-cavity epithelial cells and can be expressed in normal tissues. It is typically used as a tumor marker for ovarian epithelial cancer, and its increase can also be seen in some non-gynecological diseases[12].

Recent studies suggest that the development of IIP has a certain relationship with the induction of epithelial-mesenchymal transition. Serum CA19-9, CA15-3, CA12-5, and other tumor markers in IIP patients are higher than in individuals without IIP. The decrease in tumor markers after lung transplantation in IIP patients indicates that the tumor markers are derived from lung tissue[13]. The extensive proliferation and regeneration of bronchioloalveolar epithelium in patients with IIP is the cause of elevated tumor markers. In other words, the increase of serum CA19-9, CA15-3, CA12-5, and other tumor markers can be used as a marker for airway alveolar epithelial damage and metaplasia[14, 15]. In this experiment, the serum CA19-9, CA15-3, CA12-5 levels were significantly higher in the observation group than those in the control group. The levels of serum CA19-9, CA15-3, and CA12-5 in the moderate and severe groups were significantly higher than those in the mild group. The levels of serum CA19-9, CA15-3, and CA12-5 in the severe group were significantly higher than those in the moderate group. The difference was statistically significant (P<.05). The levels of serum CA19-9, CA15-3, and CA12-5 in the death group were significantly higher than those in the survival group, and the difference was statistically significant (P<.01). It is suggested that the changes of serum CA19-9, CA15-3, and CA12-5 levels have a certain relationship with the severity and prognosis of the disease and may reflect different levels of disease severity and prognosis.

Spearman's Rank-Order Correlation analysis was conducted to further analyze the relationship between CA19-9, CA15-3, CA12-5 and the severity and prognosis of IIP patients. CA19-9 was negatively correlated with FEV1%, FVC%, and DLCO% (r=-0.586, r=-0.579, and r=-0.561, respectively, and P<.05 or P<.01). CA15-3 was negatively correlated with FEV1%, FVC%, and DLCO% (r=-0.469, r=-0.521, and r=-0.584, respectively, and P<.05 or P<.01). CA12-5 was negatively correlated with FEV1%, FVC%, and DLCO% (r=-0.502, r=-0.506, and r=-0.618, respectively, and P<.05 or P<.01). Multivariate logistic regression analysis showed that CA19-9, CA15-3, and CA12-5 were all factors affecting the prognosis of IIP patients (P<.05 or P<.01). The analysis further shows that the CA19-9, CA15-3, and CA12-5 levels can be used as markers to evaluate the disease severity and prognosis of IIP patients and provide test support for accurate analysis of patients and interventions. In summary, the serum CA19-9, CA15-3, and CA12-5 levels in IIP patients were significantly higher than those in healthy individuals, were negatively correlated with changes in lung function, and were factors affecting the prognosis of IIP patients. The changes of CA19-9, CA15-3, and CA12-5 levels can reflect the disease severity and prognosis of IIP patients. However, because of this study's short research time and small sample size, we will continue to clarify the value of serum CA19-9, CA15-3, CA12-5 in assessing the severity of IIP and prognosis.

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