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High Serum YKL-40 Level in Patients with COPD Is Related to Hypoxemia and Disease Severity

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Chronic obstructive pulmonary disease (COPD) is a major health problem with increasing morbidity and mortality throughout the world. YKL-40 is a chitin-binding glycoprotein consisting of 383 amino acids, with a molecular mass of 40 kDa, and its serum level is elevated in inflammatory diseases. YKL-40 is a newly recognized biomarker of inflammation and has not been thoroughly investigated in COPD. The aim of the study is to investigate the relationship between serum YKL-40 levels and severity of COPD. The study population consisted of 52 patients with COPD with the mean age of 60.2 ± 10.1 years. The serum YKL-40 level increased significantly with increasing age (p = 0.022, r = 0.346). In COPD patients, high serum YKL-40 level is correlated to low forced expiratory volume at 1 second (FEV_1, percent of predicted) (r = −0.277, p = 0.047). Moreover, high serum YKL-40 level is correlated to low arterial oxygen pressure (PaO_2, mmHg) (r = −0.387, p = 0.005). The mean serum YKL-40 level was found as 243.1 ± 129.2 ng/ml in COPD patients with desaturation during 6-minute walk test (6MWT) and this value was higher than the mean serum YKL-40 level (155.8 ± 59.1 ng/ml) of COPD patients without desaturation during 6MWT (p = 0.004). This study demonstrated that high serum YKL-40 levels were correlated to severity of COPD. We propose that circulating YKL-40 levels could be a biomarker for hypoxemia and decline in lung function.

Keywords: chitin binding glycoprotein; chronic obstructive pulmonary disease; hypoxemia; inflammation; saturation
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Chronic obstructive pulmonary disease (COPD) is a major health problem with increasing morbidity and mortality throughout the world. It is estimated that COPD will be the third leading cause of mortality in 2020 (Anto et al. 2001). The main reasons for the increase in mortality are ageing and increase in risk factors such as smoking, air pollution, occupational diseases and advances in treatment of infections and cardiovascular disease. COPD is defined as a preventable disease and is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases (Vestbo et al. 2012). There is increasing evidence in the literature that COPD is a systemic disease that involves pathology in several extrapulmonary tissues (Agusti 2005). Inflammation is recognized as a hallmark of pathogenesis, and the mechanisms responsible for the persistent chronic inflammatory process has been investigated extensively (Agusti 2005). COPD is characterized by a specific pattern of inflammation involving an increased number of CD8+ (cytotoxic) lymphocytes present only in smokers that develop the disease (Barnes et al. 2003). The lymphocytes together with neutrophils and macrophages, release inflammatory mediators and enzymes and interact with structural cells in the airways and lung parenchyma leading to a rapid decrease in pulmonary functions (Donaldson et al. 2005). Systemic inflammation may also contribute to comorbidities such as cachexia in patients with COPD (Wagner 2008). Spirometric results of forced expiratory volume at 1 second (FEV_1, percent of predicted) and the ratio of FEV_1 to forced vital capacity (FEV_1/FVC) are the most reproducible and objective measurements of airflow limitation. In general, gas transfer of oxygen and carbon dioxide worsens as the chronic obstructive pulmonary disease progresses. Consequently, decrease in FEV_1 (percent of predicted) and arterial partial oxygen pressure (PaO_2, mmHg) level or increase in arterial partial carbon monoxide pressure ($PaCO_2$, mmHg) level demonstrates the severity of COPD.

The abbreviation YKL-40 is based on the one letter code for the first three N-terminal amino acids, tyrosine (Y),

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lysine (K) and leucine (L) and the apparent molecular weight (Hauschka et al. 1986). YKL-40 is a glycoprotein consisting of 383 amino acids with a molecular mass of 40 kDa and increases in systemic inflammation (Rathcke and Vestergaard 2009). The gene coding for YKL-40 protein is localized on 1q31-q32 of the human chromosome (Rehli et al. 2003). The structure of YKL-40 is similar to bacterial chitinase, but does not exhibit any enzymatic activity (Renkema et al. 1998). The main cells releasing YKL-40 are peritumoral macrophages in small cell lung cancer, giant cells in sarcoid lesions, vascular smooth muscle cells and liver cells in fibrotic regions of hepatic cirrhosis and, mesothelial cells in benign pleural effusions (Volck et al. 1998; Johansen et al. 2004, 2005). It is previously stated that the main cells releasing YKL-40 are neutrophils and alveolar macrophages in COPD, and the serum YKL-40 level increases in inflammatory diseases of the lungs (Volck et al. 1998).

In the previous investigations, it is demonstrated that high serum YKL-40 can be used as a biomarker of poor prognosis in patients with cancer, inflammation and increased tissue remodelling (Johansen et al. 1993, 1999, 2004, 2005; Volck et al. 1998, 2001; Nordenbaek et al. 1999, 2005; Roslind and Johansen 2009; Lin et al. 2012). The correlation analysis between YKL-40 and pulmonary functions has not been thoroughly investigated in COPD. We aimed in this study to determine the relationship between the serum YKL-40 level and the severity of COPD by the measurement of blood oxygen saturation, pulmonary function test and cardiopulmonary exercise test.

Methods

Study design and patients

Prior to the start of the study, ethical approval was obtained from the ethics committee of Recep Tayyip Erdogan University. The study was conducted between June 2012 and October 2012 in the pulmonology clinic of the medical faculty in Recep Tayyip Erdogan University. This is a prospective, observational and descriptive type study using 63 patients with stable COPD and 26 apparently healthy subjects with similar age and sex properties with the study group. They were informed about the study and provided their consents to participate in study. Eleven patients could not complete the exercise test and they were thus excluded from the study. The remaining 52 patients with COPD comprised our study group. Physical examinations and blood pressure (systolic and diastolic) measurements of the patients were performed by the physicians. All subjects including the apparently healthy control group fasted for a minimum of eight hours before arterial and venous blood samples were taken. Total blood count, biochemical analysis, serum YKL-40 measurement, arterial blood gas analysis, chest x-ray, 6 minute walk test (6MWT) and pulmonary function test (PFT) were performed on individual subjects. The spirometric classification of airflow limitation is divided into four grades based on post-bronchodilator FEV_1 levels by Global Initiative against Chronic Obstructive Lung Disease (GOLD). These are GOLD 1, Mild ($FEV_1 \geq 80\%$ predicted); GOLD 2, Moderate ($50\% \leq FEV_1 < 80\%$ predicted); GOLD 3, Severe ($50 \leq FEV_1 < 30\%$ predicted); GOLD 4, Very Severe ($FEV_1 < 30\%$ predicted) and using the fixed ratio, post-bronchodilator $FEV_1/FVC < 0.70$ to define airflow limitation (GOLD committee 2011). The study group included 2 patients in GOLD 1, 24 patients in GOLD 2, 20 patients in GOLD 3 and 6 patients in GOLD 4. Patients were divided into two groups as desaturated and normal according to the 6MWT which is a cardiopulmonary exercise test. The patients with a decrease of $\geq 4\%$ in oxygen saturation level (SaO_2) were included in the desaturated group ($n = 26$) and the others, whose saturation level did not decrease after the 6MWT were classified as the saturated group ($n = 26$). Demographic characteristics, spirometric findings and blood oxygen results were statistically matched between both groups.

Exclusion Criteria

History of an acute COPD exacerbation or hospitalization in preceding month and the administration of oral or intravenous glucocorticoids, immunosupressive agents or any antiinflammatory drugs in the last two weeks were the main exclusion criteria on the assumption that anti-inflammatory drugs like corticosteroids and cysteinyl leukotriene receptor antagonist were able to suppress elevated pulmonary levels of YKL-40 (Shuhui et al. 2009). Patients with cancer, infection, liver cirrhosis, pregnancy, chronic renal failure, bronchiectasis, obstructive sleep apnea, neuromuscular disease and decompensated cardiac failure were also excluded from the study.

Pulmonary function tests

Pulmonary function tests including FEV_1, FVC, FEV_1/FVC, mean forced expiratory flow (FEF_{25-75}) and peak expiratory flow (PEF) rates were measured using the Flowhandy ZAN 100 USB pulmonary spirometer (nSpire Health, Inc, Germany) in our clinic. Tests were repeated at least three times in the sitting position. The best test was accepted as the final result to evaluate the percentage of predicted values by a software programme that generated the knowledge according to the demographic characteristics of the patients.

Arterial blood gases

Arterial blood samples were taken from radial arteries in the sitting position after resting for 15 minutes in room air respiration. Blood gas analysis was done within the first minute of intervention by using a gas analysator **(**RAPIDLab 248/348 Systems, siemens AG healthcare, Germany).

Six-minute walk test

The test was performed in the 30-meter-long pulmonology clinic. The blood pressures and pulse rates of the participants were measured before and after the test. The parameters including the distance that the patients walked during 6 minutes, oxygen saturation levels before the test, the lowest and the highest oxygen saturation levels during the test were recorded. Oxygen level measurements were performed using the pulse oxymeter device (Choicemed MD300C12, South Korea). Decrease in oxygen saturation level $\geq 4\%$ was accepted as the existence of desaturation.

YKL-40 measurement

After taking the venous blood samples, they were centrifuged 10 minutes at 2,500/min rate. Serum was separated using Eppendorf pipettes and kept in refrigerator at −80°C. Serum YKL-40 levels were measured by the ELISA method (Biomarker Technology solutions, Santa Clara, CA, USA).

Statistical analysis

We used SPSS (SPSS version 15; SPSS Inc., Chicago, IL, USA), a statistical program to analyze the data. The relationships between the variables were examined by Pearson's and Spearman's correlation analysis. Continuous variables were determined as average ± standard deviation, and categorical variables were determined as percent. In the comparison of averages, Student's *t*-test and ANOVA test were used for parametric variables, and the Mann-Whitney U test and Kruskal-Wallis test were used for nonparametric variables. The value of $p < 0.05$ was accepted as statistically significant.

Results

We examined a total of 78 subjects comprising 52 patients with COPD and 26 apparently healthy people for control. In Table 1, the main characteristics of COPD and control groups are shown. Demographically, both groups were similar in terms of age, sex and body mass index. However, smoking level was found to be significantly higher in patients with COPD than among subjects in the control group ($p = 0.026$). The mean serum YKL-40 level was found as 199.4 ± 108.8 ng/ml in patients with COPD. In the control group, the mean serum YKL-40 level was 171.1 ± 80.0 ng/ml. Thus, there was no significant difference in the serum YKL-40 levels between the patients and control subjects. The mean age of COPD patients was 60.2 ± 10.1 years and the serum YKL-40 level increased significantly with increasing age ($r = 0.346$, $p = 0.022$). The mean age of control group (57.8 ± 9.9 years) was found to be similar to COPD patients ($p = 0.32$) and the serum YKL-40 level also increased with age in control group ($r = 0.426$, $p = 0.03$). The relation between the mean serum YKL-40 levels (ng/ml) and the age groups of the study population is shown in Table 2.

The relationship between serum YKL-40 level and the other results was examined by Spearman's correlation method. The relationship between FEV_1 (% of predicted) and other parameters was evaluated by the Pearson correlation method. The correlation analysis of YKL-40 and FEV_1 (% of predicted) according to pulmonary function tests, blood gas analysis and the other parameters in COPD patients is shown in Table 3. In COPD patients, high serum YKL-40 level is correlated to low FEV_1, ($r = -0.277$, $p = 0.047$). Moreover, high serum YKL-40 level is correlated to low PaO_2 ($r = -0.387$, $p = 0.005$), indicating that YKL-40 increases in hypoxemia. The mean serum YKL-40 level was found to be 243.1 ± 129.2 ng/ml in 26 COPD patients with desaturation during 6MWT, the value of which was higher than the mean serum YKL-40 level (155.8 ± 59.1 ng/ml) of the other 26 COPD patients without desaturation during 6MWT ($p = 0.004$). Spirometric results including FEV_1, FVC, PEF and FEF_{25-75} were found to be lower in COPD patients with desaturation during 6MWT. Comparison of the findings according to 6MWT in COPD patients is shown in Table 4. An inverse relationship between FEV_1 (% of predicted) and serum YKL-40 level in COPD patients is shown in Fig. 1. In addition, there was an inverse relation between serum YKL-40 level and PaO_2 (Fig. 2).

Table 1. General characteristics of COPD patients and control group.

	COPD	Control group	*P* value
Number	52	26	
Age	60.2 ± 10.1	57.8 ± 9.9	0.32
Sex (F/M)	4/48	3/23	0.57
BMI (kg/m²)	27.1 ± 5.2	27.1 ± 2.8	0.95
Smoking (pack/year)	36.2 ± 12.8	27.6 ± 16.8	0.026*
YKL-40 (ng/ml)	199.4 ± 108.8	171.1 ± 80.0	0.23
SBP (mmHg)	126.3 ± 16.1	128.1 ± 17.2	0.67
DBP (mmHg)	79.8 ± 12.6	74.2 ± 9.8	0.35

The results are shown as mean ± standard deviation. *$p < 0.05$ is significant. F, female; M, male; BMI, body mass index; SBP, systolic blood prerssure; DBP, diastolic blood pressure.

Table 2. The mean serum YKL-40 levels (ng/ml) according to the ages of study population.

Age (year)	COPD group (n:52)	Control group (n:26)	Total (n:78)
≤ 50	124.8 ± 58.8 (n:8)	153.4 ± 45.6 (n:6)	137.1 ± 53.7 (n:14)
51-60	206.6 ± 90.7 (n:18)	136.2 ± 54.2 (n:11)	179.9 ± 115.6 (n:29)
61-70	221.5 ± 134.2 (n:21)	205.9 ± 26.2 (n:5)	218.9 ± 90.7 (n:26)
≥ 71	229.9 ± 51.4 (n:5)	247.4 ± 155.1 (n:4)	221.1 ± 104.7 (n:9)
SC values	*p*: 0.022*, *r*: 0.346**	*p*: 0.03*, *r*: 0.426**	*p*: 0.002*, *r*: 0.346**

The mean YKL-40 levels are shown as mean ± standard deviation. SC, Spearman's correlation. *Correlation is significant at the $p < 0.05$ level (2-tailed), **Correlation is significant at $r > 0.25$ and $r < -0.25$ level (2-tailed).

Table 3. The correlation analysis of YKL-40 and FEV_1 (% of predicted) according to pulmonary function tests, blood gas analysis and the other parameters in COPD patients.

	YKL-40 (SC)		FEV_1 (PC)	
FEV_1 (% of predicted)	*p*: 0.047*	*r*: −0.277**		
FVC (% of predicted)	*p*: 0.058	*r*: −0.265**		
PEF (% of predicted)	*p*: 0.095	*r*: −0.234		
FEF_{25-75} (% of predicted)	*p*: 0.068	*r*: −0.255**		
pH	*p*: 0.371	*r*: 0.127	*p*: 0.519	*r*: −0.091
PaO_2 (mmHg)	*p*: 0.005*	*r*: −0.387**	*p* < 0.001*	*r*: 0.702**
$PaCO_2$ (mmHg)	*p*: 0.461	*r*: 0.104	*p*: 0.069	*r*: −0.254**
SaO_2 (%)	*p*: 0.052	*r*: −0.270**	*p* < 0.001*	*r*: 0.568**
Age (year)	*p*: 0.022*	*r*: 0.346**	*p*: 0.015*	*r*: −0.337
Smoking (pack/year)	*p*: 0.289	*r*: 0.122	*p*: 0.014*	*r*: −0.339**
6MWT	*p*: 0.024*	*r*: −0.312**	*p* < 0.001*	*r*: 0.445**
The highest SaO_2 (%)	*p*: 0.051	*r*: −0.272**	*p* < 0.001*	*r*: 0.580**
The lowest SaO_2 (%)	*p*: 0.058	*r*: −0.265**	*p* < 0.001*	*r*: 0.650**
Desaturation rate	*p*: 0.051	*r*: 0.272**	*p* < 0.001*	*r*: −0.634**
BMI (kg/m²)	*p*: 0.236	*r*: 0.131	*p*: 0.026*	*r*: 0.310**
Hb (gr/dl)	*p*: 0.618	*r*: −0.071	*p*: 0.126	*r*: 0.220

SC, Spearman's correlation analysis used for YKL-40 analysis; PC, Pearson correlation analysis used for FEV_1 (% of predicted). *Correlation is significant at the $p < 0.05$ level (2-tailed), **Correlation is significant at $r > 0.25$ and $r < -0.25$ level (2-tailed). FEV_1, Forced expiratory volume r in one second; FVC, Forced vital capacity rate over expected value; PEF, Peak expiratory flow; FEF_{25-75}, 25-75% of forced expiratory flow; PaO_2, Arterial partial oxygen pressure; $PaCO_2$, Arterial partial carbon dioxide pressure; SaO_2, Arterial oxygen saturation before 6 minute walk test; 6MWT, 6 minute walk test; Desaturation rate: The time interval between onset of the test and the time patient reached the lowest oxygen saturation level. BMI, Body mass index; Hb, Blood haemoglobin level.

Table 4. Comparison of the findings according to 6MWT in COPD patients.

Parameters	Desaturated patients during 6MWT ($n = 26$)	Non-desaturated patients during 6MWT ($n = 26$)	*p*
Age (year)	62.6 ± 8.5	57.8 ± 11.2	0.09
YKL-40 (ng/ml)	243.1 ± 129.2	155.8 ± 59.1	0.004*
BMI (kg/m²)	25.6 ± 4.1	28.7 ± 5.8	0.03*
Smoking (pack/year)	38.5 ± 13.9	34.1 ± 11.5	0.22
SBP (mmHg)	127.3 ± 16.1	125.4 ± 16.3	0.67
DBP (mmHg)	81.2 ± 14.1	78.5 ± 10.9	0.44
pH	7.4 ± 0.0	7.4 ± 0.0	0.200
PaO_2 (mmHg)	65.0 ± 8.4	73.8 ± 7.6	< 0.001*
$PaCO_2$ (mmHg)	40.8 ± 6.0	39.0 ± 3.8	0.202
SaO_2 (%)	94.0 ± 3.0	95.8 ± 1.8	0.012*
FEV_1 (% of predicted)	39.2 ± 11.9	59.7 ± 15.4	< 0.001*
FVC (% of predicted)	59.3 ± 14.7	77.9 ± 15.1	< 0.001*
FEV1/ FVC	51.9 ± 9.6	60.8 ± 13.3	< 0.001
FEF_{25-75} (% of predicted)	18.7 ± 6.5	32.8 ± 11.0	< 0.001*
PEF (% of predicted)	36.2 ± 11.0	47.8 ± 16.2	0.004*
The highest SaO_2 (%)	94.7 ± 3.2	96.9 ± 1.7	0.003*
The lowest SaO_2 (%)	87.1 ± 6.1	95.1 ± 2.8	< 0.001*
Hb (gr/dl)	14.7 ± 1.6	14.8 ± 1.1	0.84

Decrease in oxygen saturation level ≥ 4% during 6MWT was accepted as desaturated. Findings are shown as mean± standard deviation, *$p < 0.05$ is significant. BMI, Body mass index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; PaO_2, Arterial partial oxygen pressure; $PaCO_2$, Arterial partial carbon dioxide pressure; SaO_2, Arterial oxygen saturation; FEV_1, Expiratory volume rate at the first second of forced vital capacity over expected value; FVC, Forced vital capacity rate; FEF_{25-75} %, 25-75% of forced expiratory flow; PEF, Peak expiratory flow; Hb, Blood haemoglobin level.

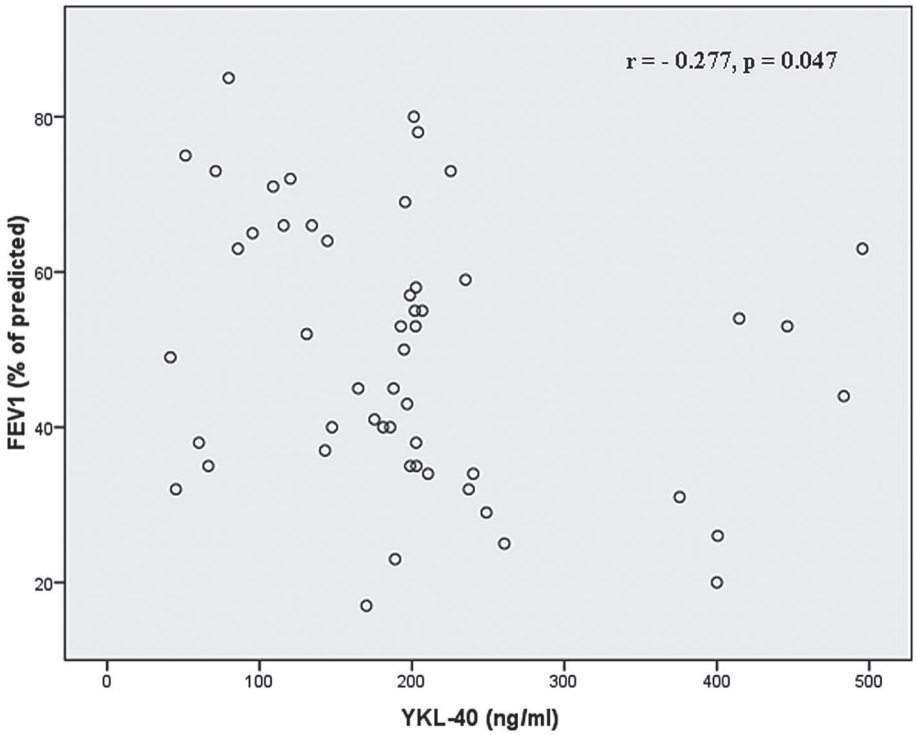

Fig. 1. Relation of YKL-40 and FEV_1 in COPD patients (n = 52).

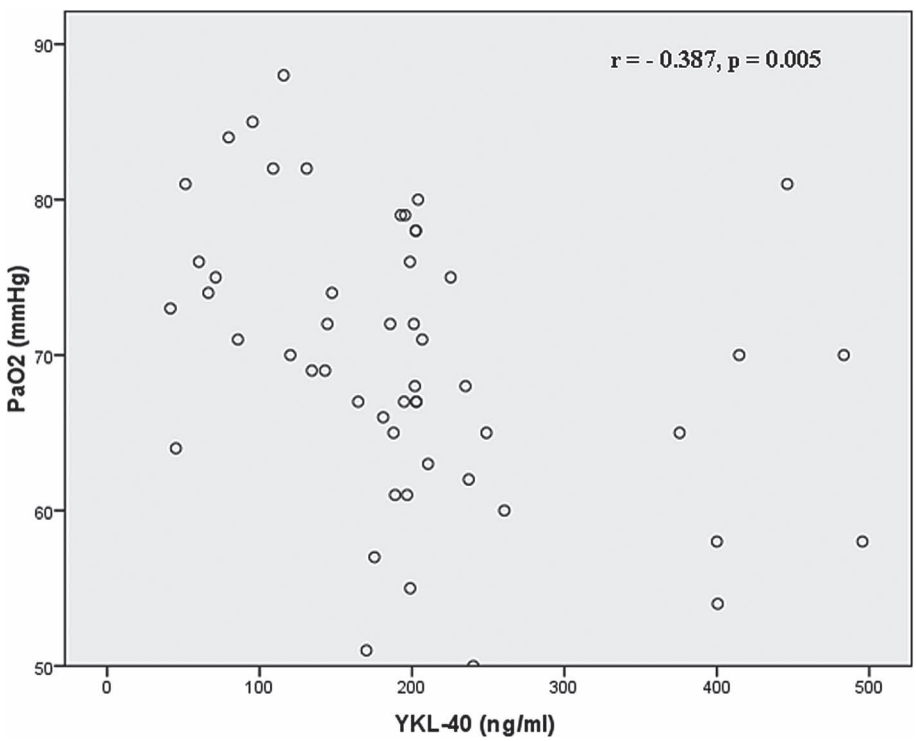

Fig. 2. Relation of YKL-40 and PaO_2 in COPD patients (n = 52).

Discussion

Recent investigations have researched the role of YKL-40 identifying it as a potential new marker in determining the severity and prognosis of many systemic diseases. YKL-40 is released from macrophages in atherosclerotic plaques, and it is released by macrophages, chondrocytes and fibroblast-like synovial cells in rheuma-

toid arthritis, ankylosing spondylitis and osteoarthritis (Boot et al. 1999; Volck et al. 2001). A high YKL-40 level is correlated with the severity of many diseases such as rheumatoid arthritis, osteoarthritis, atherosclerosis, sarcoidosis, systemic sclerosis and pneumonia, and it is found to be a risk factor for mortality in small cell lung cancer and type 2 diabetes mellitus (Boot et al. 1999; Volck et al. 2001; Johansen et al. 2004, 2005; Nordanbaek et al. 2005; Lin et al. 2012). YKL-40 concentration is increased in asthmatic serum, and is correlated with asthma severity and subepithelial membrane thickness (Bara et al. 2012). The serum YKL-40 level was also found to be higher in asthmatic patients than in patients with allergic rhinitis (Kwon et al. 2011). In systemic sclerosis, a high serum YKL-40 level is related to pulmonary involvement (Nordenbaek et al. 2005).

Johansen et al. (2010) conducted a study of 8899 people, and demonstrated that serum YKL-40 level and age have a linear relationship in both genders. Our study supports the results of this related investigation because we also found that the serum YKL-40 level increased significantly with increasing age in COPD and control groups.

There are only limited studies investigating YKL-40 levels in patients with COPD in the literature. For example, Letuve et al. (2008) found that YKL-40 serum levels increased in COPD patients in comparison to levels in healthy smokers and nonsmokers. In the other study, Sakazaki et al. (2011) reported that there was a significant positive correlation between the serum levels of YKL-40 and emphysematous changes in smokers and COPD patients. This may account for the similar levels of YKL-40 in COPD and healthy groups in our study ($p = 0.23$). In the present study, we found that smoking degrees (pack/year) were different between COPD patients and control group ($p = 0.026$), but we did not find any correlation between smoking level (pack/year) and serum YKL-40 level ($p > 0.05$). After the results of these studies, it is thought that smoking may cause an increase in serum YKL-40 level solely and the further studies is needed to investigate the effects of smoking on serum YKL-40 levels in healthy individuals and COPD patients.

Previous studies showed that YKL-40 increases in many diseases accompanied by inflammation, and that it has a prognostic factor (Volck et al. 2001; Johansen et al. 2004; Nordenbaek et al. 2005; Lin et al. 2012). COPD is also accompanied by systemic inflammation that occurs as a result of many mechanisms, particularly smoking and airway inflammation (Takabatake et al. 2000; Van Eeden and Hogg 2000; Gan et al. 2004; Agusti 2005; Tkacova et al. 2011). Tissue hypoxia and hypoxia-related mediators may also cause systemic inflammation in COPD (Kent et al. 2011). PaO_2 negatively correlated with soluble TNF alpha in COPD (Takabate et al. 2000). It was found that inflammatory cytokines increase in white adipose tissue with hypoxemia in COPD patients having obesity (Tkacova et al. 2011). Nuclear factor kappa B (NFkB) as an inflammatory mediator related to hypoxemia increases in sleep apnea syndrome (Garvey et al. 2009; Ryan et al. 2009), and also in pulmonary and heart tissue after 24 hour-long hypoxia (Fitzpatrick et al. 2011). These studies showed that COPD is characterized by systemic inflammation leading to a progressive decrease in pulmonary functions (Donaldson et al. 2005).

COPD diagnosis is based on patient history and clinical information, radiologic findings, arterial blood gas analysis and spirometric measurements. However, these diagnostic methods do not demonstrate the degree of pulmonary inflammation which plays a pivotal role in the progression and pathogenesis of chronic airway obstruction. To our knowledge, the relationship between serum YKL-40 level and pulmonary functions has not been investigated in COPD patients. In the present study, we determined an inverse relationship between serum YKL-40 level and pulmonary function test, and arterial blood oxygen level in COPD patients. The most prominent finding of our study was the existence of a negative correlation between FEV_1 (percent of predicted) and YKL-40 serum level in patients with COPD ($p = 0.047$, $r = -0.277$). Another remarkable finding of this study was the inverse relationship between serum YKL-40 levels and PaO_2 (mmHg) levels in COPD ($p = 0.005$, $r = -0.387$). YKL-40 showed a negative correlation with SaO_2 ($p = 0.052$, $r = -270$) and a positive correlation with desaturation rate ($p = 0.051$, $r = 0.272$). Moreover, serum YKL-40 level was found to be significantly higher in the desaturated group after 6MWT ($p = 0.004$). All these findings supported that, YKL-40 is a nonspecific inflammatory marker and has a potential effect on the pathogenesis of inflammation.

As a result, serum YKL-40 levels increase in many systemic inflammatory diseases. Its clinical importance is gradually increasing as a new marker in systemic inflammation that is reproducible and a predictor of prognosis in various systemic diseases. Through this investigation, we demonstrated that serum YKL-40 level increases in COPD patients with desaturation during 6MWT. There was a significant correlation between serum YKL-40 level and FEV_1 (% of predicted). Moreover, this study showed that there was a significant correlation between serum YKL-40 level and PaO_2 level. We propose that high YKL-40 level is related to hypoxemia and is a marker of systemic inflammation in COPD. To determine the clinical importance of serum YKL-40 level in COPD, further studies should be conducted that include larger patient groups and that investigate the relationship between inflammation and impairment of pulmonary functions and the correlation between serum YKL-40 level and mortality.

Conflict of Interest

The authors declare no conflict of interest.

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