The Significance of Procalcitonin and Biomarkers for Patients Who are Treated in Intensive Care Unit with COPD Diagnosis

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ABSTRACT

Objective: Patients with diagnosis of chronic obstructive pulmonary disease (COPD) in the intensive care unit have high mortality rate between 14% and 41%. Therefore, markers to predict mortality and morbidity in the early period of intensive care hospitalization are important for these patients. In this study, we aimed to evaluate the biochemical markers in predicting mortality, morbidity, and possible complications in the intensive care follow-up of patients with COPD diagnosis.

Materials and Methods: Demographic data, laboratory results, treatments, complications, length of stay, mortality, and morbidity of COPD patients treated in intensive care unit between January 2012 and January 2019 were recorded. To assess the sensitivity of C-reactive protein, procalcitonin, white blood cells, and lactate in predicting mortality and complications, patients were divided into two main groups as "deceased" and "discharge."

Results: In this study, the "procalcitonin 1st day" values of the "exitus" patient group were higher than the "discharged" group (p<0.01). Between "Procalcitonin 1st day" and "COPD stages according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria," the relationship was statistically significant (p<0.05). Procalcitonin measured on admission day to intensive care unit of patients who are later discharged with tracheostomies were found to be statistically significantly higher.

Conclusion: In this study, procalcitonin was found to be the most valuable biomarker in predicting mortality and morbidity. Procalcitonin levels measured on the day of hospitalization were found to be statistically associated with COPD stages according to GOLD criteria. Therefore, we think that for those kinds of patients, procalcitonin may be used as an early predictor of bad prognosis.

Keywords: Chronic obstructive pulmonary disease, CRP, GOLD criteria, intensive care unit, lactate, procalcitonin, white cells

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INTRODUCTION

Intensive care units are multidisciplinary centers, where high-risk patients who are hospitalized for many different reasons are treated. Among these patients, those who are diagnosed with chronic obstructive pulmonary disease (COPD), both as the primary cause and as an additional disease, have a significant proportion. Therefore, blood markers which can be used to predict mortality and morbidity for COPD patients, who are treated in intensive care units are the subject of many recent studies.[1,2]

According to the global initiative for chronic obstructive lung disease (GOLD) report, COPD is a common, preventable, and treatable disease characterized by persistent airflow limitation and respiratory symptoms due to airway and/or alveolar abnormalities usually caused by severe exposure to harmful particles or gases. Post-bronchodilator FEV1/FVC <70% with the presence of clinical symptoms indicates persistent airflow limitation, which is necessary for the diagnosis of COPD.[3]

Since procalcitonin is predominantly synthesized by the C-cells of the thyroid gland and, to a lesser extent, by the

neuroendocrine tissue of other organs such as the lungs and gastrointestinal tract, normal levels of procalcitonin in the blood are very low. However, production can be stimulated by inflammatory cytokines and especially bacterial endotoxins in almost any organ, with an increase in procalcitonin levels within 3–4 h of stimulation and reaching a peak in 24 h.[4] C-reactive protein (CRP) is an acute phase protein, which elevates in many cases such as infection, inflammation, malignancy, and autoimmune diseases and has a plasma half-life of up to 19 h. It is synthesized in the liver under the control of TNF and IL-6. Patients with CRP levels above 10 mg/L at the intensive care unit admission have been reported to have high mortality and morbidity rates.[5] Lactate is produced as a result of anaerobic metabolism in most of the tissues of human body (skeletal muscle, brain, erythrocytes, and kidneys). It is rapidly metabolized in the liver, kidneys (10–20%) and, to a lesser extent, skeletal muscle.[4,5] White blood cells have a role in both acute and chronic phase of inflammation. Its normal values in adults are between 4400 and 11.000/mm³. Serum levels may increase in many conditions such as hematological diseases, inflammatory processes, autoimmune diseases, infectious diseases, and gastrointestinal system diseases.[4–6]

In this study, patients with COPD diagnosis who were followed up and treated for various reasons in the 3rd level intensive care unit of the Anesthesiology and Reanimation Clinic between the years 2012 and 2019 were examined retrospectively. Demographic characteristics, stages of COPD according to the 2018 GOLD Criteria (mild (1), moderate (2), severe (3), and very severe (4)), duration of intensive care unit stays, comorbidities, mortality, and risk factors that may affect mortality were determined. We aimed to compare white cells, lactate, procalcitonin, and CRP measurements of the patients with those data and investigate whether they are correlated relevantly.

MATERIALS and METHODS

After the approval of the ethics committee (decision no: KAEK/2019. 01. 17) had been obtained, the study was started.

Patients with COPD diagnosis who were treated in the Anesthesia and Reanimation Intensive Care Unit between January 2012 and January 2019 were included to this study. Patients who did not have pulmonary function tests, therefore could not be staged according to GOLD criteria were excluded from the study. Patients who had positive blood, urine, or bronchoalveolar lavage cultures, which were sent on the 1st day of intensive care unit admission were excluded from the study. Thus, it was aimed to minimize the possible effect of infection on CRP, procalcitonin, white blood cell, and lactate values.

The data were retrospectively examined on the hospital's existing computer recording system PANATES.

Thirty-four patients were included to the study. Patients were compared in two groups as deceased and discharge. Age, gender, indications for admission to intensive care, the ward in which they were admitted to intensive care from, their comorbidities, smoking history, COPD stages according to GOLD criteria, Glasgow Coma Scale scores, prognosis, procalcitonin, CRP, white blood cell, and lactate values measured in the first and last days of intensive care unit admission of the patients were recorded.

IBM SPSS Statistics 21 package program was used for statistical analysis of the data. Descriptive statistics (frequency, percentage, mean, standard deviation, and median) were obtained. Chi-square test for the analysis of qualitative data, Mann–Whitney you, and Wilcoxon Sign Sequencing test in the analysis of quantitative data were used. When the results were evaluated, p<0.05 was considered to be statistically significant.

RESULTS

A total of 34 patients, 15 females and 19 males, whose demographic data, clinical features, and complications during their follow-up are summarized in Table 1, were included in the study. Twenty-seven patients were admitted to the intensive care unit after surgery, while seven patients were admitted from various services due to exacerbation of COPD. Of the 26 discharged patients, four were discharged with home ventilator support with tracheostomy.

The comparison of demographic data, clinical characteristics, and laboratory values of the patients between deceased and discharge groups are summarized in Table 2.

When the procalcitonin values were compared between the deceased and discharged patient groups, both the 1st day (U=29 p<0.01) and the last day (U=12 p<0.001) value of procalcitonin was found to be statistically significantly higher in the deceased group. When the discharged patients were compared within themselves, the procalcitonin values measured on the 1st day of intensive care unit hospitalization were found to be statistically significantly higher in patients who were discharged with tracheostomy (p<0.05).

When CRP last day values were compared between the two groups, the values of the deceased patient group were found to be statistically significantly higher (U=49, p<0.05).

The relationship between the procalcitonin values and COPD stages according to the GOLD criteria based on spirometry values measured within the 3 months of admission date to the intensive care unit was summarized in Figures 1 and 2.

Table 1. Demographic and clinical characteristics of the patients

	n	%
Total	34	
Gender		
Female	19	
Male	15	
Smoking	20	59
GOLD stage		
1	8	24
2	10	29
3	6	18
4	10	29
Deceased	8	24
Discharged	26	76
Age (year)	71±11	
Height (cm)	163±9	
Weight (kg)	77±18	
COPD history (year)	19±8	
Niv (day)	2 (1–4)	
Imv (day)	0 (0–3)	
ICU follow-up (day)	4 (2–11)	
Complication		
Pneumonia	15	44
Pulmonary edema	3	8
Pneumothorax	1	2
ARDS	2	5

Values were written as; number, mean±SD (standard deviation), median (25–75th percentile). F: Female; M: Male; GOLD: Global Initiative for Chronic Obstructive Lung Disease; COPD: Chronic obstructive pulmonary disease; Niv: Non-invasive mechanical ventilation, Imv: Invasive Mechanical Ventilation; ICU: Intensive care unit; ARDS: Acute respiratory distress syndrome

DISCUSSION

Similar to the literature, the median age of the patients examined in our study was 71 years and the median procalcitonin value in intensive care unit admission was 2.053 ng/mL.[7]

Similar to the literature, the procalcitonin values of the deceased patient group on the day of intensive care unit admission and the last day of intensive care unit follow-up were higher than the discharged group.[8] When the studies, which were conducted with the laboratory results obtained in the routine follow-up of COPD patients were examined in the literature, it was seen that procalcitonin values did not have a significant relationship with mortality.[9–12]

In our study, the higher "CRP Day 1" values measured on the day of admission to the intensive care unit were not found to be significant in terms of mortality. However, CRP values measured on the past day of intensive care follow-up were found to be significantly higher in the deceased group. Among the patients included in our study, 27 were admitted to the intensive care unit after surgery. Therefore, the high CRP values on the 1st day of admission to the intensive care unit were not found to be significant in terms of mortality; it can be explained by the post-operative elevation of CRP, which is an acute phase reactant. [13] When similar studies in the literature were examined, higher CRP result in a single measurement was not found to be significant in terms of mortality for patients with COPD; however, an increase or decrease of the CRP values in serial measurements was found to be useful in determining the prognosis.[10,11,14]

When the white blood cell values of the patients in our study were examined, values on the 1st day of hospitalization and on the past day of intensive care follow-up were not found to be significant in a single measurement. However, the decrease in white blood cell values was found to be significant in terms of showing good prognosis; nevertheless, white blood cell elevation was not significant in terms of increased risk of mortality. There are similar studies supporting the data in our study.[9,10]

When the COPD stages according to GOLD criteria and the procalcitonin values of the patients on the day of admission were compared, high procalcitonin values were found to be significant in terms of showing high stage COPD disease. When similar studies in the literature were examined, it was seen that high procalcitonin values measured in both routine follow-up and hospitalization of patients with COPD were associated with higher COPD stages.[15,16]

CONCLUSION

When all patients participating in the study were examined, CRP elevation was found to be the most observed finding; however, the decrease or increase in serial CRP measurements was not found to be significant in predicting prognosis. When the white blood cell and lactate values were examined, it was seen that; according to our study, they were not strong markers that alone could predict the prognosis in patients with COPD.

Procalcitonin values were found to be significant in predicting mortality in all measurements, similar to the literature. Similarly, the procalcitonin values measured on the 1st

Table 2. Comparison of deceased and discharge group in terms of demographic data and variables

	Discharged	Deceased	p
Year	70±12	72±8	0.98
Height	164±9	160±9	0.31
Weight	78±17	74±19	0.64
COPD history (year)	21 (10–28)	20 (16–22)	0.68
Niv (day)	2 (0–5)	2.5 (1–4.5)	0.62
Imv (day)	0 (0–0)	8 (1–20)	**<0.001**
ICU follow-up (day)	4 (2–8.5)	12.5 (3–25)	0.14
Procalcitonin 1st day	0.97 (0.37–2.69)	4.3 (3.3–11.7)	**0.002**
Procalcitonin past day	0.4 (0.16–2.14)	20.4 (4.2–126.3)	**<0.001**
CRP 1st day	47 (19.25–105.8)	57.2 (23.3–170.3)	0.69
CRP past day	38 (14–78)	95 (58–167)	**0.026**
White blood cells 1st day	14.9 (10.8–17.4)	10.6 (5.8–16.5)	0.22
White blood cells past day	11.2 (7.8–14.5)	11.8 (10.3–17.2)	0.52
Lactate 1st day	1.7 (1.2–2.6)	1.9 (0.9–3)	0.97
Lactate past day	1.5 (1–2)	1.8 (1.2–2.8)	0.52

Values were written as; number, mean±SD (standard deviation), median (25–75th percentile). P<0.05 was considered significant in the analysis between groups. COPD: Chronic obstructive pulmonary disease; CRP: C-reactive protein, Niv: Non-invasive mechanical ventilation, Imv: Invasive Mechanical Ventilation; ICI: Intensive care unit
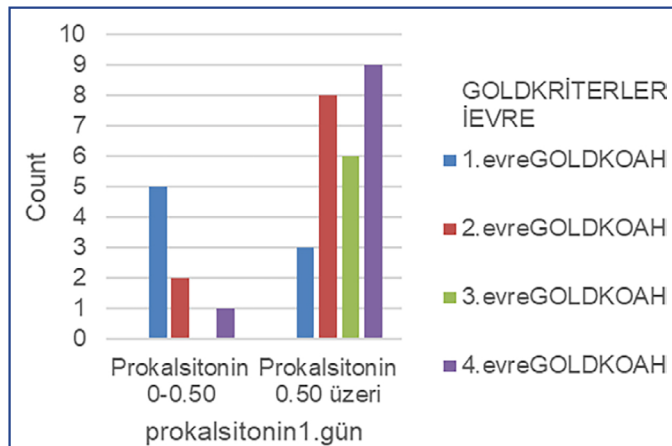

Figure 1. The relationship between patients' COPD stage according to GOLD criteria and procalcitonin

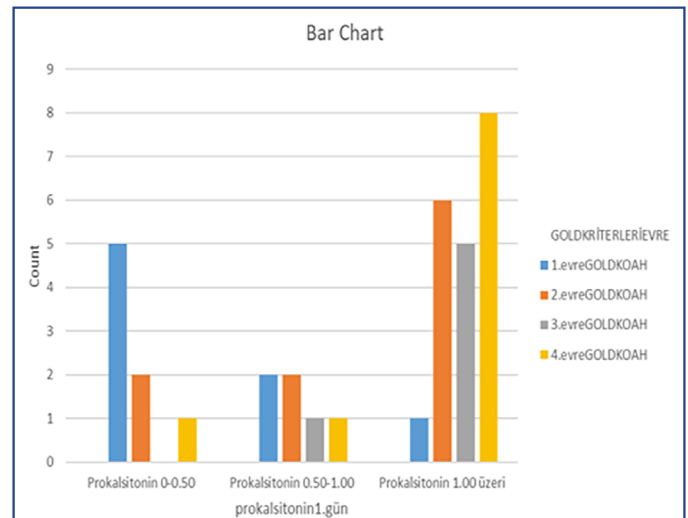*COPD: Chronic obstructive pulmonary disease; GOLD: Chronic obstructive lung disease*

Figure 2. The relationship between patients' COPD stage according to GOLD criteria and procalcitonin

day in the intensive care unit of the patients who were discharged with tracheostomies were found to be significantly higher than the other discharged patients. Apart from its success about predicting the prognosis in intensive care unit, it was also shown in our study that, high procalcitonin values on the 1st day of intensive care unit admission were associated with low pulmonary function tests in spirometry performed in the previous 3 months.

Similar literature data supporting the results of our study suggest that, procalcitonin can be used in the determination of prognosis both for patients being followed in the intensive care unit and for stable COPD diagnosed patients.

Disclosures

Ethics Committee Approval: The study was approved by the University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee (No: KAEK/2019. 01. 17, Date: 20/06/2019).

Informed Consent: Written informed consent was obtained from all patients.

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