Introduction

Chronic obstructive pulmonary disease (COPD) is a prevalent chronic debilitating disease and expected to be the fourth leading cause of death by 2030. Acute exacerbations of COPD (AECOPD) are a common clinically important condition observed in about 20% of COPD patients, and determine disease morbidity, mortality, healthcare utilization, and associated costs. Exacerbation is marked by coughing, shortness of breath, and increased sputum production. Mechanisms of AECOPD are different and three types of exacerbations, namely those driven by bacteria, viruses, or by enhanced eosinophilic inflammation are known. Therefore, identification of a biomarker that could help in the differentiation between COPD exacerbations caused by bacteria and those with other etiologies is very useful.

Procalcitonin (PCT), is an acute phase inflammatory protein that is known as a biomarker for bacterial infection, but not viral infections, could possibly recognize AECOPD requiring antibiotic treatment from other etiologies of respiratory attack. In normal people, the normal PCT level is 0.1 ng/ml. Previous studies have shown that administration of antibiotics can increase the PCT level in the exacerbation group.

Methods:

Patients aged from 40–80 years who were diagnosed with COPD according to the GOLD criteria and who referred to the Imam Khomeini Hospital of Ahvaz in 2016 were divided into two groups of exacerbated and stable COPD. Exacerbation of COPD is defined as worsening of the patient’s condition from the stable state and behind normal day-to-day variations that is acute in onset and may necessitate treatment in a patient with underlying COPD. BODE Index and 6MWDT were used to assess the patients, and the severity of their disease was determined based on the GOLD criteria. Subsequently, PCT testing using electrochemiluminescence (ECL) method was carried out on patients on the same day. Results: PCT level in the exacerbation group was 0.272 ± 0.586 and 0.066 ± 0.027 in the non-exacerbation group, and their difference was statistically significant with P value = 0.001. Based on the results, the cut point of differentiating between the AECOPD and the stable groups with a sensitivity of 68% and a specificity of 80% is 0.085. Conclusion: Overall, the findings of this study indicate that PCT levels could be regarded as a good diagnostic marker for patients with COPD, and for the differentiation of AECOPD patients from stable COPD patients.

Keywords: Biomarker, chronic obstructive pulmonary disease, procalcitonin
bacterial endotoxin to healthy subjects increases the PCT level 2 h after the injection, which will peak 12 h later. Subsequently, its level is steady for 12 h and begins to decrease after 20–24 h. PCT shows a rapid response to infection. Researchers have shown that PCT is a component of a complex proinflammatory response to the inherent immune system. So far, elevated PCT levels have been evaluated in other inflammatory conditions such as inflammatory bowel disease, gingival cell arthritis, polyarthritis nodosa, and systemic lupus erythromatosis. In spite of this, some studies using PCT in acute attacks for antibiotic therapy or the prognosis of using non-invasive ventilation, the PCT level in AECOPD was higher compared with stable COPD patients. Therefore, the challenge remains whether PCT can be used as a diagnostic criterion for AECOPD and whether it can be used to quickly differentiate COPD attacks from other causes especially pulmonary thromboembolism and congestive heart failure which are more likely to develop in people with COPD than others.\(^\text{[5-8]}\)

### Methods

The study population included patients with COPD aged 40–80 years, whose condition was confirmed by the GOLD criteria, and who referred to the Imam Khomeini Hospital of Ahvaz in 2016. They were divided into two groups of exacerbated COPD and stable COPD. Inclusion criteria: COPD patients who had referred to the Emergency Department of Imam Khomeini Hospital of Ahvaz with a severe attack, and their condition led to their admission. Also included in our study were COPD patients who referred to the Imam Khomeini Clinic without any attack but for periodic follow-ups as stable group. Exclusion criteria: Patients who have radiological evidence of pneumonia, and those with congestive heart failure, concurrent pulmonary embolism, concurrent pneumothorax, history of known infection over the past month, and specific infection in other organs. Data collection for all patients included the following: demographic information, history of smoking, the number of cigarettes per year, vital sign as well as pulse rate, respiratory rate, saturation of arterial O\(_2\), PCO\(_2\) change in the amount and color of sputum, increased coughing and respiratory illness, BODE Index and 6MWD test, and their severity was assessed based on the GOLD criteria. Subsequently, PCT testing carried out on patients on the same day and measured using electrochemiluminescence (ECL) method.

### Statistical methods and analysis of results

The required sample size was calculated using the NCSS and PASS sample size analysis. According to the purpose of the study, the comparison of the mean PCT between the two groups of AECOPD and stable COPD was carried out. To compare the quantitative variables (PCT) in the two groups of AECOPD and the stable COPD, independent \(t\)-test was used. First, using the descriptive statistics and then the Chi-square fit of goodness, the PCT level and the relationship between the PCT level and each of the variables was measured. Regression methods were also used if necessary. Data analysis were done using the SPSS ver. 22.

### Results

In this study, we compared two groups of patients: 25 with AECOPD and 25 with stable COPD patients. The mean age of exacerbation and stable groups was 68.04 ± 9.61 and of 68.16 ± 6.85 years, respectively. Severity of the underlying disease, measured based on FEV1, was 40.56 ± 18.60 in the exacerbation group and 47.98 ± 16.18 in the stable group. PCT level in the exacerbation group was 0.272 ± 0.586, while it was 0.066 ± 0.027 in the non-exacerbation group, and their difference was statistically significant with \(P\) value = 0.001. Baseline characteristics of individuals in both groups were the same and did not differ significantly [Table 1]. The relationship between other variables and PCT levels in patients with exacerbation shown in Table 2.

Based on the results, the cut point determining the difference between the AECOPD group and the Stable group with a sensitivity of 68% and a specificity of 80% was 0.085 [Figure 1].

### Discussion

One of the high-risk inflammatory conditions that physicians, especially internists, have to deal with are patients with exacerbated COPD requiring proper diagnosis and treatment. The PCT seems to be a good marker for the diagnosis of patients with COPD exacerbation.\(^\text{[4]}\) In the present study, we evaluated 50 patients in exacerbated COPD and stable COPD conditions. Each group included 25 patients with no significant difference in age, sex, smoking, and COPD severity in both groups. In

### Table 1: Basic characteristics of the patients

| Variable          | Exacerbation-COPD n=25 | Stable-COPD n=25 | \(P\)  |
|-------------------|------------------------|------------------|------|
| Gender            |                        |                  | 0.733|
| Male              | 20 (80%)               | 19 (76%)         |      |
| Female            | 5 (20%)                | 6 (24%)          |      |
| Age, years±SD     | 68.04±9.61             | 68.16±6.85       | 0.960|
| Smoking           |                        |                  |      |
| Current           | 19 (76%)               | 23 (92%)         | 0.247|
| Ex smoking        | 6 (24%)                | 2 (8%)           |      |
| COPD (severity) FEV1 | 40.56±18.60           | 47.98±0.027      | 0.149|
| PCT               | 0.272±0.586            | 0.066±0.027      | 0.001|

### Table 2: The relationship between variables and PCT levels in patients with exacerbation

| Variable          | Mean and standard deviation | \(P\)  |
|-------------------|----------------------------|------|
| MW6               | <149 m                     | 0.109±0.053 | 0.163|
|                   | >149 m                     | 0.448±0.825 |      |
| MMR               | 1                          | 0.369±0.813 | 0.612|
|                   | 2                          | 0.196±0.333 |      |
| BODE Index        | Score 0-4                  | 0.4±0.850   | 0.382|
|                   | 5-10 score                 | 0.187±0.323 |      |
| FEV1 hospitalization length |                  | 0.011 | 0.958|
|                   |                            | 0.264 | 0.203|
addition, by controlling these variables, there was a significant difference between the two groups of the exacerbated and stable in terms of PCT. No patients who were hospitalized required ICU and tracheal intubation.

The findings of this study indicate that PCT levels in patients with exacerbated COPD and in those with stable conditions were 0.272 and 0.066, respectively, which showed a significant difference (P-value = 0.001). These findings are consistent with those of other similar studies. In a study by Tasci et al., for example, the mean serum PCT level in patients with exacerbated COPD was 1.8 ng/mm, while in patients with stable conditions it was 0.2 ng/ml. They also found that the level of serum PCT had a significant relationship with hospitalization and ESR levels. However, in the present study, there was no significant relationship between ESR and PCT was found. This difference may be related to the sensitivity of the assessment methods.

Pazarli et al. compared PCT levels between two groups of patients with COPD, namely those with exacerbated conditions and those with stable conditions. According to their findings, the mean level of PCT in patients with exacerbation was significantly higher than that in patients with stable COPD. In another study, Rammaert et al. evaluated the relationship between PCT levels in predicting mortality rates in COPD patients. They found that PCT as an independent factor can predict mortality rates such that in patients with elevated PCT levels, higher mortality rates are predicted.

One of the strengths of our study was that we investigated the relationship between PCT levels in the exacerbation group and other variables such as length of hospitalization, body temperature, respiratory rate, heart rate, white blood cell count, ESR, CRP, as well as arterial oxygen saturation, and oxygen and CO2 levels of arterial blood. In addition, we examined the underlying condition of patients admitted for COPD such as MW6, MMR, BODE Index, underlying disease severity with PCT levels, and none of these had a significant association with the increased PCT levels in patients with exacerbation.

**Conclusion**

Overall, the findings of this study indicate that PCT levels can be regarded as an appropriate diagnostic marker in patients with exacerbated COPD and in differentiating them from patients with stable conditions, especially in cases where the patient's shortness of breath may have causes other than EXCOPD, namely pulmonary embolism or pneumothorax. Based on the results, the cut point determining the difference between the AECOPD group and the stable group with a sensitivity of 68% and a specificity of 80% was 0.085.

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**Conflicts of interest**

There are no conflicts of interest.

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