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The Relationships of Serum Prealbumin Levels With Parameters That Indicate Severity of Disease and Emphysema Pattern in Patients With Stable Chronic Obstructive Pulmonary Disease

Stabil KOAH'lı Hastalarda Serum Prealbümin Seviyelerinin Hastalığın Ağırlığını ve Amfizem Paternini Gösteren Parametreler ile İlişkisi

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Abstract

Objective: Malnutrition, which is a complication frequently observed in chronic obstructive pulmonary disease (COPD) and negatively affects prognosis, has become a parameter that must be monitored. Even though various methods are applied to assess malnutrition, biochemical parameters, especially serum prealbumin levels, are useful.

Materials and Methods: The relationships between serum prealbumin levels, which we used as an indicator of malnutrition, with the severity of disease and the parameters predicting emphysema in stable COPD patients with no additional health problems were determined in this prospective study.

Results: One hundred stable COPD patients were evaluated prospectively. Serum prealbumin levels had a negative correlation with the total number of hospitalizations due to acute exacerbation, total hospitalization time, and average number of annual hospitalizations, whereas it showed a positive correlation with FEV_1 and FEV_1/FVC% values. Serum prealbumin levels were positively correlated with the length of the line connecting the costophrenic sinus to the dome of the diaphragm, which is used to assess the presence of emphysema and was negatively correlated with retrosternal distance. Also, in COPD patients with low prealbumin levels, while the FEV_1 and FEV_1/FVC% values and the length of the line connecting the costophrenic sinus to the diaphragm dome significantly decreased, the retrosternal distance dramatically increased compared to COPD patients with normal prealbumin levels.

Conclusion: Serum prealbumin levels were convenient for monitoring malnutrition in COPD, were correlated with spirometric and anamnestic data indicating the severity of COPD, and were useful in distinguishing the subtype of COPD due to its decrease in the presence of emphysema.

Key Words: COPD, Emphysema, Malnutrition, Serum prealbumin level

Özet

Amaç: KOAH'ta sık rastlanan ve prognozu olumsuz etkileyen bir komplikasyon olan malnütrisyon, takibi zorunlu bir parametre halini almıştır. Malnütrisyonu değerlendirmede birçok yöntem kullanılsa da, biyokimyasal parametrelerin özellikle de serum prealbümin düzeyinin oldukça yararlı olduğu gösterilmiştir.

Gereç ve Yöntem: Prospektif çalışmamızda malnütrisyon belirteci olarak kullandığımız serum prealbümin düzeyinin, malnütrisyon nedeni olabilecek ek sağlık problem olmayan stabil KOAH'lı hastalarda hastalığın ağırlığı ve amfizemi predikte eden parametrelerle ilişkisi araştırıldı.

Bulgular: Yüz stabil KOAH'lı hastanın prospektif olarak değerlendirildiği çalışmada serum prealbümin değerinin KOAH akut alevlenme nedenli toplam yatış sayısı, toplam yatış günü ve ortalama yıllık yatış sayısı ile negatif; %FEV_1 ve FEV_1/FVC değerleri ile pozitif korelasyon gösterdiği saptandı. Amfizem varlığını değerlendirdiğimiz kostofrenik sinüsleri birleştiren çizginin diyafragma kubbesine uzaklığı ile pozitif, retrosternal mesafe ile negatif korelasyon mevcuttu. Prealbümin değeri normal olan KOAH'lılara oranla düşük olan KOAH'lılarda %FEV_1, FEV_1/FVC değerleri ve kostofrenik sinüsleri birleştiren çizginin diyafragma kubbesine uzaklığının anlamlı derecede azalmış, retrosternal mesafenin anlamlı derecede artmış olduğu görüldü.

Sonuç: Serum prealbümin düzeyinin KOAH'ta malnütrisyon düzeyini takip etmede kullanışlı, KOAH'ta hastalığın ağırlığını gösteren spirometrik ve anamnestik verilerle korele olduğu, amfizem varlığında düzeyinin daha çok azalması nedeniyle KOAH subtipinin ayrımında yardımcı olabileceği sonucuna varıldı.

Anahtar Kelimeler: Amfizem, KOAH, Malnütrisyon, Serum prealbümin düzeyi

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Introduction

Malnutrition in chronic obstructive pulmonary disease (COPD) is a common problem, with reported prevalences of 24% to 65% [1, 2]. The main cause of malnutrition is the need for energy that cannot be met due to the respiratory difficulty resulting from hypermetabolism and increasing respiratory exertion in COPD [3, 4]. Malnutrition has a direct effect on the central nervous system, respiratory muscles and lungs, which control respiration [2]. Respiratory minute volume is reduced in hypoxia and hypercapnia [5]. Determining the presence and severity of malnutrition has become essential due to its frequent appearance and negative impact on prognosis in COPD [6]. Although no perfect test exists to asses nutritional status in COPD [3], some features of biochemical parameters, such as reflecting chronic malnutrition properly in stable patients and detecting early changes, have allowed biochemical parameters to gain prominence [7]. In this context, prealbumin is the most frequently used and most effective parameter to assess malnutrition. Moreover, due to the more distinctive characteristics of malnutrition in patients with emphysema [8], nutritional indicators may also be used to distinguish chronic bronchitis and emphysema [9]. This study aims to explore the relationship of the serum prealbumin value, which is used as a nutritional indicator, with parameters showing the degree and severity of the illness and to assess its success in reflecting emphysematous changes.

Materials and Methods

Upon approval of the Ethics Committee of our university, patients with stable COPD who were monitored in our clinic were included in the study after signing the written informed consent. Patients who had been recently diagnosed with COPD and stable patients with a COPD diagnosis who had been monitored (on the basis that post-bronchodilator spirometric FEV_1/FVC value, as defined in the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) [10] guide for the diagnosis of COPD, was below 70%) were included in the study. Patients with a pathology or history that may have contributed to malnutrition (endocrinological pathologies such as malignity, malabsorption syndromes, diabetes mellitus, and hyperthyroidism; chronic renal failure; chronic liver diseases; active tuberculosis; collagen tissue disorders; or had recently undergone a trauma or operation), COPD patients with any kind of infection or attacks, and patients who did not agree to participate were excluded from the study. In total, 22 patients were excluded (9 declined to participate, 7 had diabetes mellitus, 2 had malignancy, 2 had chronic renal failure, 2 had a recent operation).

One hundred stable COPD patients who met the criteria were included in the study. Respiratory function tests were performed on the patients with MIR model equipment by the same technician. The obtained values (FEV_1, FVC, FEV_1/FVC, FEF_{25-75}, PEF measurements and their expected values in %) were recorded. Demographic data of the cases together with all the measured parameters were recorded and then evaluated.

Presence of Emphysema: Posterior-anterior and lateral lung graphics of all cases were taken to determine the radiological presence of emphysema. In the graphics, the length of the line connecting the costophrenic sinus to the diaphragm dome (which is reduced with the flattening of the diaphragm in the presence of emphysema due to trapped air) and the retrosternal distance were measured (In lateral graphics, the retrosternal distance is the length of the airway column between the back side of the sternum and the cardiac shadow. It increases in cases of emphysema due to trapped air).

Serum Indicators: A total of 5 cc of blood was drawn from the cases into a dry tube to determine their serum prealbumin levels. After centrifuging the drawn blood, prealbumin levels were measured in the Biochemistry Laboratory of the University (Abbott Clinical Chemistry kit, ARCHITEC / AEROSET system).

Statistical Analysis

Statistical analysis was performed at the Department of Biostatistics using SPSS 13.0 for Windows, (IBM Corporation, Route 100 Somers, NY 10589). Pearson correlation analysis was used to find correlations between parameters. The Mann-Whitney U test was applied to compare the differences in biochemical, spirometric and anthropometric values between COPD stages. Levene's test, the T test and the Mann-Whitney U test were also conducted to assess the differences in biochemical, spirometric and anthropometric values between groups who had low prealbumin levels and who did not have low prealbumin levels. Values are given as mean±standard deviation (SD). A p-value less than 0.05 was considered statistically significant.

Results

One hundred stable COPD patients (81 males, 19 females) were enrolled in this study. The average age of the cases was 65.1±9.7 years (46-84 years). The average serum prealbumin value of the cases was 0.24±0.06 g/L (Table 1). Serum prealbumin levels revealed a negative correlation with the total number of hospitalizations due to acute exacerbation (r=-0.304 p=0.002), total hospitalization time (r=-0.319 p=0.001) and the number of annual hospitalizations on average (r=-0.351 p=0.012) (Figures 1-3). However, preal-

bumin levels had a positive correlation with the values FEV_1 % (r=0.730 p<0.001) and FEV_1/FVC% (r=0.541 p<0.001), which are parameters of the respiratory function test (Figures 4, 5). Also, while serum prealbumin had a positive correlation (r=0.585 p<0.001) with the length of the line connecting the costophrenic sinus to the diaphragm dome, it showed a negative correlation (r=-0.583 p<0.001) with retrosternal distance (Figures 6,7). The average serum prealbumin value of the low prealbumin group (n=23, 23%) was 0.16±0.01 g/L, and the average serum prealbumin value of the normal prealbumin group (n=77, 77%) was 0.26 ± 0.01 g/L. Additionally, the FEV_1 % value (32.0±1.8%) in COPD patients with lower prealbumin was significantly lower than COPD patients with normal prealbumin (60.4±2.0%) (p<0.001). Similarly, the ratio of FEV_1/FVC in the low prealbumin group (48.5±1.6%) was significantly lower than in the normal prealbumin group (60.1±0.9%) (p<0.001). Moreover, retrosternal distance, which was measured to assess emphysematous changes in patients, in the low prealbumin group (32.9±1.9 mm) was significantly higher than in the normal prealbumin group (20.5±0.8 mm) (p<0.001). Finally, the distance from the sinus to the diaphragm in the low prealbumin group (11.3±0.5 mm) was significantly lower than in the normal prealbumin group (18.4±0.6 mm) (p<0.001) (Table 2).

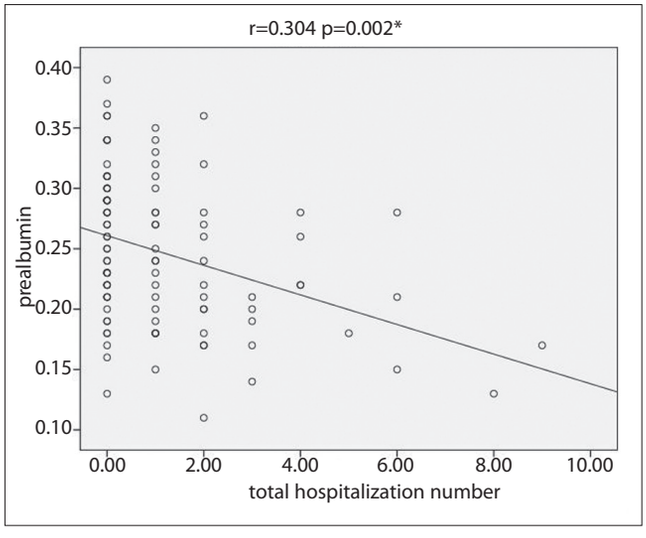

Figure 1. *Diagram of the correlation between serum prealbumin level and total number of hospitalizations related to COPD acute exacerbations.*

Discussion

Malnutrition and nutritional disorders in patients with COPD are significant factors affecting morbidity and mortality [11]. Malnutrition, which is encountered more often in COPD patients, who are particularly more subject to emphysema than patients with chronic bronchitis, and incidents of acute respiratory insufficiencies associated with these cases increase [1, 3]. Currently, the importance of studying nutritional indicators and monitoring them in COPD has become more evident [6]. For this purpose, mass measurements, anthropometric measurements and biochemical parameters are assessed [7]. Even though there may not be any ideal tests,

Table 1. Average characteristics of the cases

	AVERAGE±SD	Minimum/ Maximum
Duration of disease (years)	6.6±0.4	1/21
$\%FEV_1$	53.9±20.1	21.4/87.5
%FVC	71.4±21.1	47.5/99.4
$\%FEV_1$/FVC	57.4±9.5	48.3/67.6
$\%FEF_{2575}$	28.3±12.5	12.4/54.2
%PEF	46.5±17.8	27.8/64.1
Prealbumin (g/L)	0.24±0.06 (NR=0.20–0.40)	0.08/0.39
Retrosternal distance (mm)	23.3±9.5 (NR<35)	10.8/47.6
Distance from costophrenic sinus to dome of diaphragm (mm)	16.8±5.8 (NR>15)	9.1/41.3

(NR = normal range)

Table 2. The relations between cases with normal and low prealbumin levels

	Cases with normal prealbumin levels n=77 (0.26±0.01 g/L)	Cases with low prealbumin levels n=23 (0.16±0.01 g/L)	P value *S
$\%FEV_1$	%60.4±2.0	%32.0±1.8	p<0.001*
FEV_1/FVC	%60.1±0.9	%48.5±1.6	p<0.001*
Retrosternal distance (mm)	20.5±0.8	32.9±1.9	p<0.001*
Distance from costophrenic sinus to dome of diaphragm (mm)	18.4±0.6	11. 3±0.5	p<0.001*

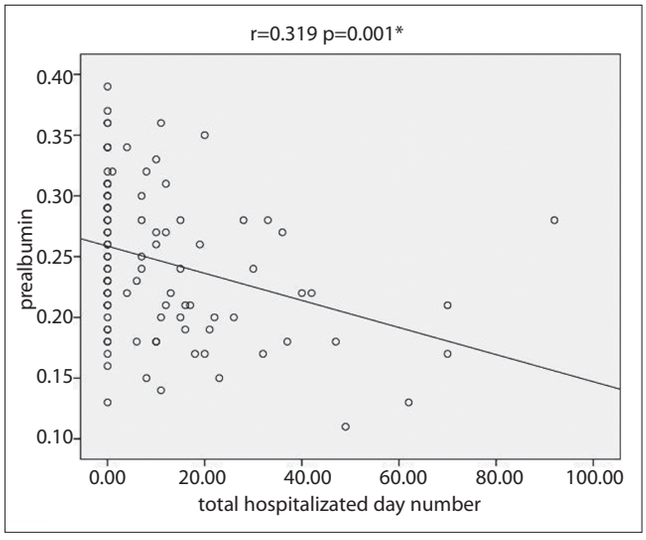

Figure 2. *Diagram of the correlation between serum prealbumin levels and total hospitalization time related to COPD acute exacerbations.*

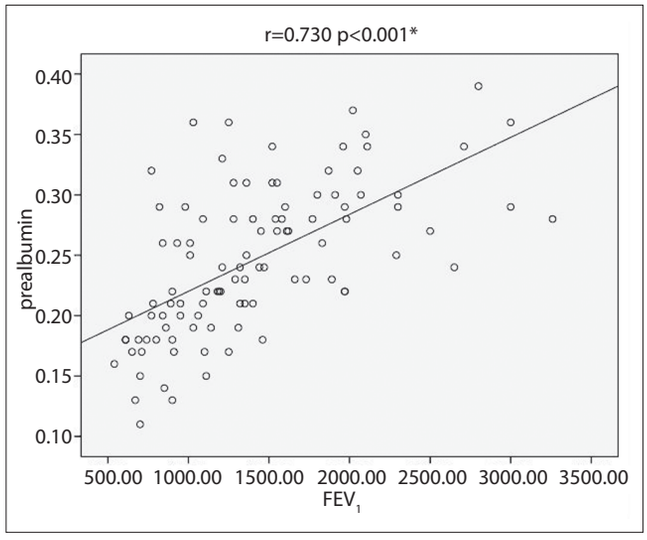

Figure 4. *Diagram of the correlation between serum prealbumin levels and the FEV_1 value.*

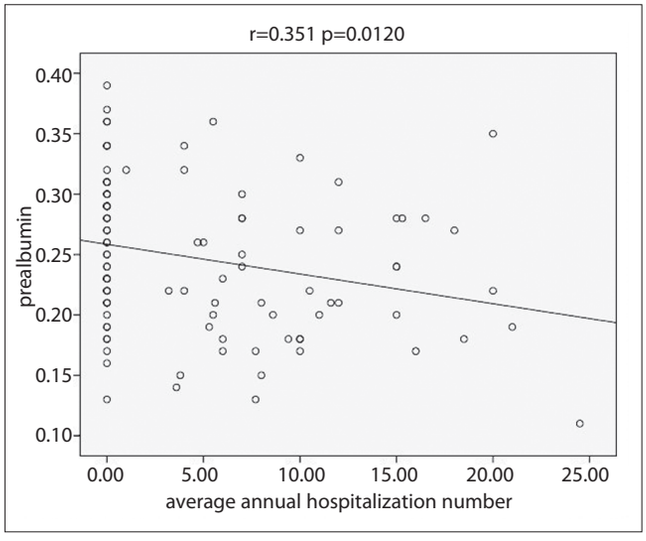

Figure 3. *Diagram of the correlation between serum prealbumin levels and average annual number of hospitalizations related to COPD acute exacerbations.*

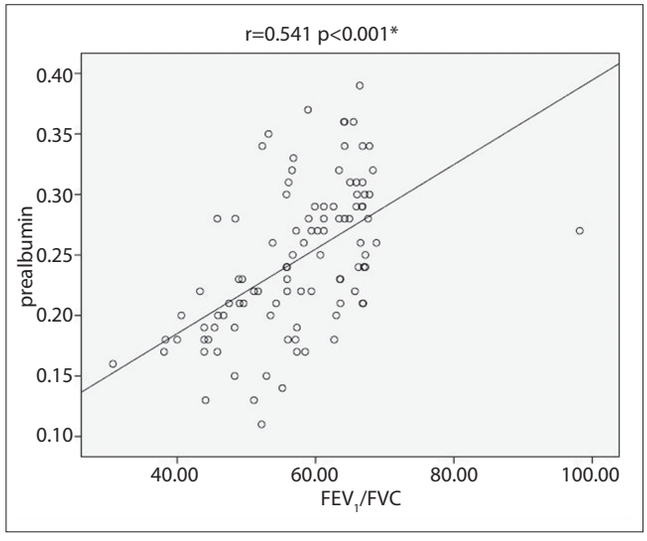

Figure 5. *Diagram of the correlation between serum prealbumin levels and the FEV_1/FVC ratio.*

certain biochemical parameters have significant advantages [1, 7]. Due to their short half-lives, some molecules are used to monitor chronic malnutrition and can easily detect acute changes in a short time [7, 12]. Importantly, measuring them is practical [12]. For this reason, the most frequently studied parameter is the serum prealbumin level [13]. Prealbumin is a protein synthesized in the liver, used in T_3 and T_4 transport, and it carries vitamin A to desired organs by forming a complex with retinol-binding protein (RBP) [14]. It is considered the best parameter to detect nutritional changes [12]. As its level decreases during inflammatory incidents, it acts as a negative acute-phase reactant, and due to its short half-life (approximately 2-3 days), it is affected at an early stage in cases of malnutrition [14]. Therefore, even at the stable stage during the ongoing systemic inflammatory process of COPD, it serves as a significant indicator of the severity of the disease and nutritional state [13, 15]. Some studies have revealed a correlation between serum prealbumin levels in COPD with the severity of the disease [16, 17]. Gil Kanada et al. found a positive correlation between serum prealbumin values and FEV_1 and PaO_2 values and a negative correlation

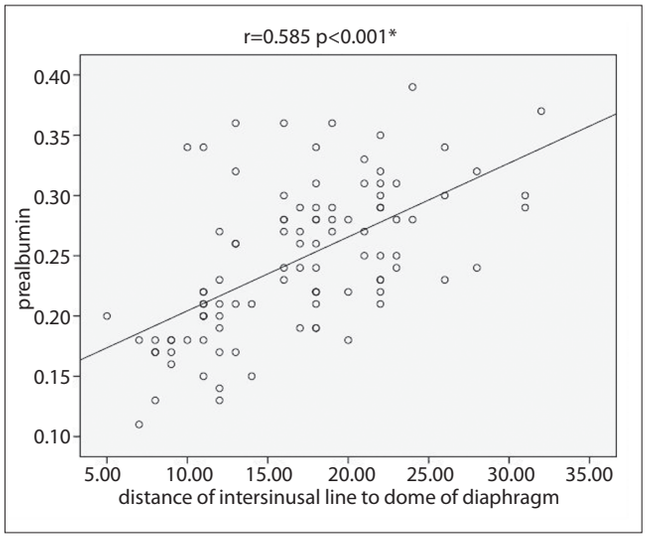

Figure 6. *Diagram of the correlation between serum prealbumin levels and the length of the line from the costophrenic sinus to the dome of the diaphragm.*

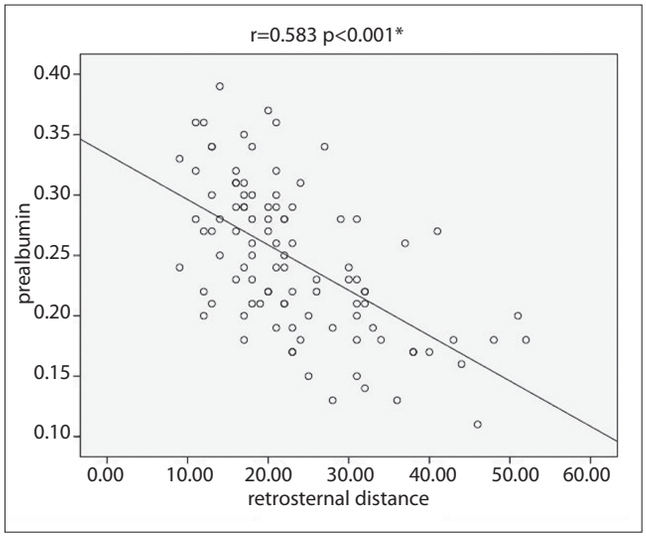

Figure 7. *Diagram of the correlation between serum prealbumin levels and the retrosternal distance.*

between the length of illness and frequency of attacks [18]. In another study, prealbumin levels of the COPD patients at stage 3 were significantly lower than in COPD patients at stage 1 [19]. Laaban found significant differences in prealbumin values between one group of COPD patients who needed mechanical ventilation due to acute respiratory insufficiency and another group who did not need mechanical ventilation [3]. Based on the data in the literature, it has been suggested that evaluation of COPD patients, particularly with regard to prealbumin levels together with a malnutritional examination, should be routinely performed [1, 3]. Our study also demonstrated that serum prealbumin levels were significantly correlated with parameters showing the spirometric and demographic severity of the illness (number of hospital stays due to attacks, length of hospital stay, and FEV_1 and FEV_1/FVC values). Moreover, in accord with previous findings, we observed that FEV_1 and FEV_1/FVC values were significantly decreased in the patients with low serum prealbumin levels compared to patients with normal serum prealbumin levels. These findings support the idea that as the severity of the illness increases, there is an increase in the number of attacks and, therefore, an increase in the frequency of hospital stays due to these attacks; as a result, the systemic inflammatory response increases and the nutritional state declines [1, 3].

Even though emphysema is a pathological diagnosis, it is currently assessed radiologically by thorax CT. Thorax CT is a successful technique in assessing emphysema [20]; however, in addition to problems with its availability and practicability compared to conventional graphics, the dose of radiation exposure is also higher. For this reason, the practicability of using conventional graphics to monitor emphysema changes is gradually being studied. Miniati et al. evaluated emphysematous changes by measuring the length of the line connecting the costophrenic sinus to the diaphragm dome and the retrosternal distance. In the quantitative evaluation where both measurements were applied, 95% of the patients were diagnosed with emphysema through thorax CT using this method, and their sensitivity and specificity were reported as 90% and 98%, respectively [21]. In another study, a success rate of more than 80% was attained with the same criteria [22]. Reich demonstrated that emphysematous changes determined according to these two parameters were correlated with respiratory functions [23]. In our study, we evaluated emphysematous changes by these two radiological parameters in a quantitative approach. As a result of this evaluation, serum prealbumin levels showed a significant correlation with the indicators of emphysema. Similarly, while retrosternal distance in patients with low serum prealbumin levels was significantly higher than in the normal serum prealbumin group, the length of the line connecting the costophrenic sinus to the diaphragm dome decreased significantly. Although various studies have shown that serum prealbumin in severe COPD patients with emphysema is low [1, 19], no similar studies that used the same measurement techniques to evaluate emphysema could be found in the literature. Therefore, we believe that this characteristic makes our study unique and interesting.

As a result, determining malnutrition in COPD and its routine monitoring are now suggested, as malnutrition is considered a common complication with a negative effect on the prognosis of the illness. To serve this purpose, using biochemical parameters is both advantageous and practical.

In particular, the serum prealbumin level is the most preferred parameter due to its sensitivity to nutritional changes. In addition to indicating the nutritional status of the illness, it is also correlated with conventional radiological findings that show emphysematous changes. Hence, it not only assists in distinguishing subtypes of the illness but also increases the reliability of radiological indicators in predicting emphysema.

Conflict of interest statement: The authors declare that they have no conflict of interest to the publication of this article.

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