Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1537054
J Health Sci Med. 2024;7(6):658-663

Chronic obstructive pulmonary disease and malnutrition: severity of the disease and controlling nutritional status (CONUT) score

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Cite this article as: Bardakçı Mİ, Albayrak GA, Gediz R. Chronic obstructive pulmonary disease and malnutrition: severity of the disease and controlling nutritional status (CONUT) score. *J Health Sci Med.* 2024;7(6):658-663.

Received: 22.08.2024 ◆ **Accepted**: 20.10.2024 ◆ **Published**: 27.10.2024

ABSTRACT

Aims: The definition for chronic obstructive pulmonary disease (COPD) is abnormalities of the or alveoli, that can cause chronic respiratory symptoms. A significant number of COPD patients have malnutrition. We aimed to demonstrate the correlation between the Control of Nutritional Status (CONUT) score and the severity of the disease, the number of hospitalizations, and emergency department visits due to acute exacerbations of COPD. **Methods:** Patients over 65 years of age diagnosed with COPD were included in this study. Smoking habits, systemic and pulmonary comorbidities, Modified British Medical Research Council (mMRC) survey score and COPD assessment test (CAT) score, number of COPD exacerbations, number of hospitalizations due to COPD in the last year were recorded. CONUT score was calculated by looking at blood albumin, total cholesterol and lymphocyte levels. **Results:** This study was carried out with 112 COPD patients. The mean age of our patients was 72.28±7.3 (64-96). Of the 112 patients, 26 (23.2%) were female and 86 (76.8%) were male. Forced expiratory volume in 1 second (FEV1%) was 42.31% (13.00-75.00%), CAT 17.83±6.8 (7-34), mMRC 2.19±1.1 (0-4), COPD attack count 2.30±2.1 (0-9) and 35 patients were hospitalized due to COPD attacks. The CONUT score determined as 2.71±2.3 (0-9), 45 (40.1%) patients were normal, 36 (32.1%) were light, 29 (25.9%) were moderate, and 2 (1.8%) patients were severe. There was a statistically significant, correlation between CONUT values and FEV1 (%), CAT and mMRC values. The patients were divided into 2 groups as low (values 4 and below) and high (values 5 and above). A statistically significant difference was found between the CONUTs high and low groups in terms of CAT, mMRC and FEV 1 (%). The number of high CONUT attacks was statistically significantly higher than the number of low CONUT attacks. High CONUTs hospitalization rates are significantly higher than low CONUTs hospitalization rates. **Conclusion:** The CONUT score is accepted as a promising tool for the assessment of malnutrition. In our study, CONUT scores were high in COPD patients over 65 years of age with low FEV1%, high CAT and high mMRC values. This high level suggests that the CONUT score may be a new prognostic predictor. And again, we found that the CONUT score was associated with a high number of attacks and hospitalizations. These results suggest that the use of the CONUT score may help adapt patients' follow-up and treatment strategies.

Keywords: COPD, CONUT, malnutrition

INTRODUCTION

The definition for chronic obstructive pulmonary disease (COPD) is abnormalities of the airways (bronchitis/bronchiolitis) or alveoli (emphysema), that can cause chronic respiratory symptoms (dyspnea, cough, sputum). It's a heterogeneous condition and causes persistent and often progressive airway obstruction.[1] COPD is a significant cause of mortality and morbidity worldwide and is the third leading cause of all deaths.[2] Worsening of symptoms of cough, sputum and/or dyspnea accompanied by tachypnea and/or tachycardia within the last 14 days as a result of local and systemic inflammation due to infection, air pollution or other exposure are defined as acute exacerbations in COPD.[1] COPD exacerbations cause an increase in the need for hospitalization and an increase in secondary mortality rates.[3] Exacerbation of COPD is the cause of a significant portion of health care costs attributable to COPD.

A significant number of COPD patients have malnutrition. Studies have reported a strong link between body weight and respiratory muscle mass, and have shown that progressive respiratory disorders develop with malnutrition.[4,5] Malnutrition is detected in 25% of COPD patients followed in outpatient clinics and 50% of COPD patients treated in hospitals.[6] This rate reaches 60% in critically ill COPD patients with acute respiratory failure.[7] COPD patients with protein energy malnutrition also have Weight loss. Weight loss and loss of lean body mass affect respiratory function capacity negatively and life expectancy in COPD patients.[8]

Monitoring of body weight reduction in COPD patients has been identified as a poor prognostic factor.[9] Weight loss in COPD patients is an independent risk factor and is caused by malnutrition, high metabolic rate and/or inappropriate

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nutritional intake.[10] Patients with advanced COPD often have a decrease in body weight. It is stated that there is a decrease in body weight in about half of all COPD patients; in particular, one-fourth of people with severe disease and one-third of patients with extremely severe disease also have losses in free fat mass index.[11] In COPD patients, normal daily respiratory energy expenditure increases 10-fold, and this increase in energy expenditure cannot be replaced by proportional energy intake and may lead to malnutrition.[12] Higher mortality in COPD patients has been associated with malnutrition.[10] A study based on the European Society of Clinical Nutrition and Metabolism (ESPEN) showed that malnutrition has a significant effect on prognosis at two years. In addition, this study stated that free fat mass index is more significant in the diagnosis of malnutrition and COPD prognosis.[13] According to data from many studies, it is seen that 30-60% of patients hospitalized with COPD have impaired nutritional status, which increases the risk of hospitalization, decreases exercise tolerance and has a negative effect on mortality.[14] Although a wide variety of therapeutic approaches can be used, malnutrition in COPD patients is underdiagnosed and undertreated.

The Control of Nutritional Status (CONUT) score is a simple nutritional marker that allows the assessment of a patient's nutritional status.[15] Although the CONUT score was initially developed to predict acute deterioration in surgical patients, it has a high prognostic value in certain populations such as the elderly, cancer patients, patients affected by gastroenterological or heart failure or ischemic stroke.[16]

The poor prognosis observed in elderly patients with COPD may be related to an impaired nutritional status. Therefore, as with many diseases, it is important to evaluate the nutritional status of the patient in COPD to take corrective measures. Malnutrition in COPD patients is underdiagnosed and therefore untreated. Based on this information, we wanted to evaluate our elderly patients with COPD with the Nutritional Status Control scale. We aimed to show the relationship between CONUT score and severity scores, the number of hospitalizations and emergency department admissions due to acute exacerbation of COPD.

METHODS

Ethical Approval

This study was approved by the Şişli Hamidiye Etfal Training and Research Hospital Ethics Committee (Date: 28.05.2024, Decision No: 2661). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population and Design

This cross-sectional retrospective study included patients diagnosed with COPD over 65 years of age. Patients who came to the Chest Diseases Outpatient Clinic of our hospital between 01.01.24 and 01.06.24 for control were included in our study.

All COPD patients over the age of 65 who applied to the outpatient clinic within the specified period were evaluated. Patients over the age of 65 whose diagnosis of COPD was confirmed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) diagnostic criteria, who did not have a known chronic disease other than COPD, and who had laboratory tests within the last 6 months were admitted to our study.[1] Patients under the age of 65, with missing file and laboratory information, with previously known chronic diseases other than COPD, with insufficient information for identification criteria, patients with sleep breathing disorder, patients with neurological diseases such as advanced dementia, Alzheimer's, cerebrovascular disease, and patients with a history of orthopedic or other surgical operations were not included in this study.

Data Collection

Detailed anamnesis, pulmonary function tests and posterior anterior chest radiographs are routinely performed in COPD patients admitted to the outpatient clinic. All COPD patients over the age of 65 who applied to the outpatient clinic within the specified period were re-evaluated by the physicians participating in the study. Patients whose diagnosis of COPD was confirmed and laboratory data were found in the system were recorded in the study excel file. Smoking habits, systemic and pulmonary comorbidities, Modified British Medical Research Council (mMRC) survey score and COPD Assessment Test (CAT) score, number of COPD exacerbations, number of hospitalizations due to COPD in the last year were recorded. Blood sampling was saved on all patients to determine glucose, albumin, total cholesterol, creatinine, hemoglobin, white blood cells (WBCs), lymphocytes, and C-reactive protein (CRP).

Scale

Nutritional status was evaluated using the the CONUT score. The CONUT score, first used by Ignacio de Ulíbarri et al.[15,] is a new nutritional marker based on serum albumin value, absolute lymphocyte count and serum cholesterol value. Values between 0-12 can be detected; 0-1: normal, 2-4: light, 5-8: moderate, and 9-12: severe are considered high.

Statictical Analysis

IBM SPSS 26.0 package program was used in the statistical analysis of the study. Descriptive statistics (frequency, percentage, min-max values, median, mean, standard deviation, etc.) of the demographic data, clinical values, laboratory results of the study participants were calculated. Before all statistical analyses, the normal distribution of the parameters was determined by the Shapiro-Wilk test. Parametric tests were used for the analysis of normally distributed variables, and non-parametric tests were used for the analysis of normally distributed variables. Accordingly, pearson correlation analysis was used for normally distributed parameters and Spearman correlation analysis was used for non-normally distributed parameters in relationship analysis. In the comparison of CONUT low/high groups in terms of related parameters, independent samples t test, which is one of the parametric tests, was used for the parameters that were not normally distributed, and Mann-Whitney U test, which was one of the nonparametric tests, was used for the parameters

that were not normally distributed. Chi-square test was used to compare categorical data. All statistical analyses were evaluated at 95% confidence interval and significance was evaluated at p<0.05.

RESULTS

Demographic Characteristics and Laboratory Findings

This study was carried out with 112 COPD patients without distinction between men and women. The mean age of our patients was 72.31±7.27 (65-96). Of the 112 patients, 26 (23.2%) were female and 86 (76.8%) were male. The body-mass index (BMI) of the patients was 29.75 (26.51-31.23). Smoking pack-year history 39.53±6.1 (25-56). The laboratory parameters were: glucose 102.4±19.7 (67-197) mg/dl, urea 42.63±19.5 (17-153) mg/dl, creatinine 1.1±0.4 (0.32-3.82) mg/dl, alanine aminotransferase 18.69±10.7 (7-71) U/L, aspartate aminotransferase 22.68±9.4 (6-62) U/L, albumin 3.81±4.7 (2.79-5.36) g/dl, total cholesterol 173±36.3 (114-316) mg/dl, C-reactive protein 10.47±13.9 (0.5-90.43) mg/L, hemoglobin 13.26±1.7 (8.6-17.5), hematocrit 40.35±4.9 (26.7-52.6), platelet 250.07±85.4 (108-713) 10^9/L, lymphocytes 1730±700 (490-3660) n/mm^3 (Table 1).

Table 1. Baseline demographic and laboratory findings of the study population

Characteristics	Patients (n=112)
Gender, n(%)	
Female	26 (23.2%)
Male	86 (76.8%)
Age, year, mean±SD (min-max)	72.31±7.27 (65-96)
BMI, year, mean±SD (min-max)	26.24±5.1 (15.7-44.44)
Smoking habit	
Pack-years (min-max)	39.53±6.1 (25-56)
Laboratory parameters, mean±SD	
White blood cell (10^9/ml)	8.33±2.1
Hemoglobin (g/dl)	13.26±1.7
C-reaktive protein (mg/L)	10.47±13.9
Lymphocytes (n/mm^3)	1.73±0.7
Albumin (g/dl)	3.81±0.47
Total cholesterol (mg/dl)	173.53±36.3

SD: Standard deviation, min: Minimum, max: Maximum, BMI: Body-mass index

Pulmonary Function Test, CAT, mMRC, CONUT

When the pulmonary function tests of one hundred and twelve patients were examined, forced expiratory volume in 1 second (FEV1%) was 42.31% (13.00-75.00%) and forced vital capacity (FVC%) was 46.50 (15.00-80.00). CAT 17.83±6.8 (7-34), mMRC 2.19±1.1 (0-4), COPD attack count 2.30±2.1 (0-9) and 35 patients were hospitalized due to COPD attacks. The CONUT score of all our patients was calculated and determined as 2.71±2.3 (0-9). When the CONUT score was evaluated according to severity, 45 (40.1%) patients were normal, 36 (32.1%) were light, 29 (25.9%) were moderate, and 2 (1.8%) patients were severe (Table 2).

Table 2. Pulmonary function test, CAT, mMRC, CONUT score data of all patients

Characteristics	Patients (n=112) Mean±SD (min-max)
Pulmonary function test	
FVC (L)	1.53±0.6 (0.42-3.07)
FVC (%)	46.5±14.6 (15-80)
FEV1 (L)	1.08±0.4 (0.29-2.14)
FEV1 (%)	42.31±13.1 (13-75)
FEV1/FVC	71.6±13.2 (38-100)
CONUT	2.71±2.3 (0-9)
Number of exacerbations	2.3±2.1 (0-9)
Hospitalization, n (%)	35 (31.25)
CAT	17.83±6.8 (7-34)
mMRC	2.19±1.1 (0-4)

SD: Standard deviation, min-max: minimum-maximum, FEV1: forced expiratory volume in 1 second, FVC: forced vital capacity, CONUT: Controlling nutritional status, CAT: COPD assessment test, mMRC: Modified medical research council

Patients' CONUT scores were compared with pulmonary function test, CAT, and mMRC values. There was a statistically significant, negative, low-level correlation between CONUT values and FEV1 (%) values of the participants (p=0.0001<0.01). When FEV1 (%) decreases, CONUT increases. There was a statistically significant, positive, low-level correlation between CONUT values and CAT and mMRC values of the participants (p=0.0001<0.01). CONUT increases or decreases along with CAT and mMRC (Table 3).

Table 3. Correlation of CONUT with FEV1 (%), CAT and mMRC

		CONUT	FEV1 (%)	CAT	mMRC
CONUT	r	1.000	-.310**	.357**	.365**
	p		0.001	0.0001	0.0001
	n	112	112	112	112
FEV1 (%)	r		1.000	-.748**	-.774**
	p			0.0001	0.0001
	n		112	112	112
CAT	r			1.000	.723**
	p				0.0001
	n			112	112
mMRC	r				1.000
	p				
	n				112

CONUT: Controlling Nutritional Status, FEV1: Forced expiratory volume in 1 second, CAT: COPD assessment test, mMRC: Modified Medical Research Council

The patients were divided into 2 groups as low (values 4 and below) and high (values 5 and above) according to the results of the CONUT score. There were 81 (72.3%) patients in the low CONUT group and 31 (27.7%) patients in the high group. The mean number of attacks was 1 (0-7) in the low CONUT group and 4 (0-9) in the high group.

According to the high and low CONUT levels, the groups were compared with CAT, mMRC and FEV1%. A statistically significant difference was found between the CONUTs high and low groups in terms of CAT, mMRC and FEV1% (Table 4) (Figure).

Table 4. Comparison of CONUT with CAT, mMRC and FEV 1 (%) according to high and low			
CONUTs	**Low CONUT(≤4) n=81**	**High CONUT (≥5) n=31**	**p**
Median (Min-max)			
CAT	16 (7-33)	21 (9-34)	0.001**[2]
mMRC	2 (0-4)	3 (1-4)	0.001**[2]
Mean±SD (Min-max)			
FEV 1 (%)	44.63±13.1 (15-75)	36.26±11.1 (13-58)	0.002**[1]

SD: Standard deviation, min-max: minimum-maximum, CONUT: Controlling Nutritional Status, FEV1: Forced expiratory volume in 1 second, CAT: COPD assessment test, mMRC: Modified medical research council, [1]: Independent samples t test; [2]: Mann-Whitney U test; **: p<0.01

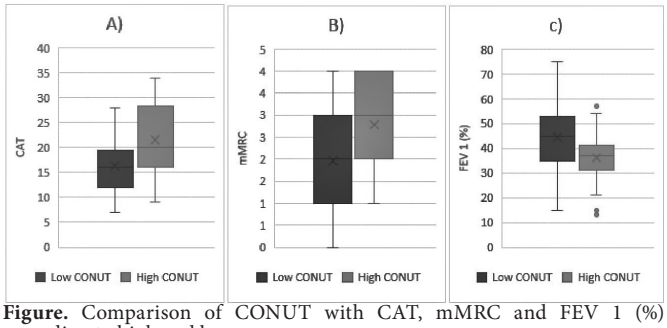

Figure. Comparison of CONUT with CAT, mMRC and FEV 1 (%) according to high and low

CONUT: Controlling nutritional status, CAT: COPD assessment test, mMRC: Modified medical research council, FEV1: Forced expiratory volume in 1 second

There is a statistically significant difference in the number of attacks between the CONUT high and low groups. (Mann-Whitney U test; U=594.5; Z=-4.383; p=0.0001<0.01). The number of high CONUT attacks was statistically significantly higher than the number of low CONUT attacks. There is a statistically significant difference between the CONUT high and low groups and the number of hospitalizations (Chi-square test; X^2=27.425; p=0.0001<0.01). High CONUTs hospitalization rates are significantly higher than low CONUTs hospitalization rates (Table 5).

Table 5. Comparison of the number of hospitalizations and the number of attacks according to CONUT high and low			
CONUTs	**Low CONUT (≤4) n=81**	**High CONUT (≥5) n=31**	**p**
n, median (min-max)			
Number of exacerbations n (%)	1 (0-7)	4 (0-9)	0.0001**[1]
Number of hospitalizations			
0	65 (80.2)	12 (38.7)	0.0001**[2]
1	13 (16)	7 (22.6)	
2	3 (3.7)	9 (29)	
3	0 (0)	2 (6.5)	
4	0 (0)	1 (3.2)	

min: Minimum, max: Maximum, CONUT: Controlling nutritional status, [1]: Mann-Whitney U test; [2]: Chi-square test; **: p<0.01

DISCUSSION

COPD is a heterogeneous disease characterized by persistent and often progressive air way obstruction.[1] Being an important cause of fatality all around the world, COPD ranks third among all deaths.[2] COPD exacerbations cause an increased need of hospitalization and an increased risk of death in patients with COPD.[3] It's been shown that a significant number of patients with COPD had malnutrition and progressive respiratory disorders developed due to malnutrition.[4,5] Although it was researched in many systemic diseases the CONUT score was not quite evaluated with COPD and its parameters. We think our study is important in this aspect.

In our study we compared the CONUT score, one of the indications of malnutrition and COPD parameters. The CONUT score was high in one third of our patients. Correlation existed between the CONUT score and FEV1%, CAT and mMRC values. As FEV1% value of our patients decreased, the CONUT score increased. Also, as CAT and mMRC values increased CONUT score increased. The second aim of our study was to assess the correlation between the COPD exacerbations and the numbers of hospitalizations along with the CONUT score. We found relation among these values.

Assessing malnutrition and supporting the assessment is vital for the management of patients with COPD.[17] There is no gold standard method to assess the nutritional status of patients with COPD. BMI is a simple method for assessing the nutritional status and a low BMI is related to a worse prognosis.[18] Along with this, BMI may not reflect the nutritional status of patients with COPD correctly.[19] In a very small portion of our patients too had low BMI. Therefore we did not use BMI to assess malnutrition.

Malnutrition causes negative effects on exercising and muscle function along with lung function, increases exacerbations, mortality and expenses.[20] In their studies Gea et al.[21] associated the status of inflammations with increased exacerbations in COPD, anorexia and increased work of breathing. They indicated that it had a direct effect on muscle dysfunction and caused an increased risk of hospitalization due to exacerbations. They added that in the end the loss of muscle mass would cause a negative functional effect by compromising the functioning of respiratory muscles. In a similar way Silvestre also indicated that malnutrition played an important role by reducing muscle mass, strength and durability of respiratory muscles in patients with COPD and also, malnutrition is related to the severity of illness and the duration of increased exacerbations, hospitalization and long-term hospitalization.[22] In a recently published article, it was stated that malnutrition in COPD caused frequent attacks in patients and it was shown that there was an increase in the number of hospitalizations and duration of stay.[23] Law et al.[24] researched malnutrition in patients hospitalized for AECOPD. They detected malnutrition in one fifth of the patients and wrote this group of patients had worse results compared to the patients without malnutrition, both during and after hospitalization. In a review article published in 2022 it was stated that malnutrition was common among patients with COPD and this existing malnutrition is associated with an increased number of attacks in COPD patients, an increased number of hospitalizations and longer hospitalization periods.[25] Similarly, in our study, we found an increase in the number of hospital admissions due to acute attacks and

therefore hospitalizations in our patients with high CONUT scores. This is related to the deterioration of the respiratory level scores (FEV1%, CAT and mMRC) of the patients due to malnutrition.

One of the three parameters of the CONUT score is albumin. Yamaya et al.[26] stated in their studies that malnutrition is associated with severe emphysema, airflow limitation, attacks related to infection and mortality. Also in this study total protein, serum albumin and lymphocyte levels were detected to be low. In a study examining malnutrition albumin level was found to be low in patients with severe COPD. It was shown that nutritional parameters of patients during exacerbation were related to length of hospital stay and duration of readmission.[27] Other than ours only one study examining the relation between malnutrition and COPD by using the CONUT score was encountered. In a study Lo Buglio et al.[28] conducted, they found the CONUT score to be high nearly in two third of COPD patients over 65 years old. In this study they detected correlation among the CONUT score and FEV1%, CAT and mMRC values. Again in this study, Lo Buglio et al. detected relation between the CONUT score and numbers of COPD attacks with the numbers of hospitalizations. We found the CONUT score to be high in nearly one third of our patients. We found negative correlation in our elderly patients' CONUT score and FEV1% value and positive correlation between CAT and mMRC values. We found a correlation between the number of exacerbations and the number of hospitalizations in our elderly COPD patients in the last year. The results of our and a limited number of other studies have shown that malnutrition, which can be prevented if attention is paid, is directly related to the respiratory scores of the patients and thus to the quality of life. Especially in the outpatient clinic, we can evaluate the patient's malnutrition and reduce the respiratory problems that may develop.

Limitations

This study was a relatively small-scale study with 112 patients. This may have influenced the statistical power to detect significant effects. In addition, since it was a single-center retrospective study, it covered a certain segment of the society. The results cannot be generalized to the entire population. Our study is the second study showing the relationship between malnutrition and COPD. Prospective and multicenter studies on more patients are needed to confirm our findings. In addition, malnutrition treatment studies with COPD can be performed to show improvements in respiratory scores.

CONCLUSION

The CONUT score is accepted as a promising tool for the assessment of malnutrition. By applying it easily in outpatient clinics, the risks that may develop in the patient can be predicted. In addition, treatment success can be increased by stopping malnutrition at an early stage. In our study the CONUT score was detected to be high in COPD patients over 65 years old who had severe symptoms, low FEV1%, high CAT and high mMRC values. This high level suggests that the CONUT score may be a new prognostic predictor. And again, we found the CONUT score to be related to the high numbers of attacks and hospitalizations in elderly patients affected by COPD. These results suggest that the use of the CONUT score may help tailor patients' follow-up and treatment strategies. We think that supporting the validity of the CONUT score in patients with COPD with studies involving a higher number of patients.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by the Şişli Hamidiye Etfal Training and Research Hospital Ethics Committee (Date: 28.05.2024, Decision No: 2661).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Acknowledgments

I would like to thank my colleagues who contributed to all stages of the article.

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