Original Article

How to Utilize CAT and mMRC Scores to Assess Symptom Status of Patients with COPD in Clinical Practice?

Klinikte KOAH Hastalarının Semptom Durumlarını Değerlendirmede CAT ve mMRC Skorlarını Nasıl Kullanmalı?

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ABSTRACT

Objective: In this study, we aimed to investigate the compatibility of modified Medical Research Council (mMRC) and COPD assessment test (CAT) scores of chronic obstructive pulmonary disease (COPD) patients in terms of evaluation of their symptom status.

Methods: The study was planned as a single-center, cross-sectional study. Statistically four separate receiver operating characteristic (ROC) curves of CAT scoring were generated for mMRC scores of 1 to 4.

Results: Two hundred twenty eight patients with stable COPD, mean age 64.2±8.2 and 88.6% male were included. A strong positive correlation was detected between CAT and mMRC (r=0.60, p<0.001). However, it was observed that 32 patients had mMRC<2 but CAT≥10, while 21 patients had CAT<10 but mMRC≥2. Thus, in 53 patients CAT and mMRC scores were not identical in terms of assessed symptom status. According to the ROC analysis, the mMRC scores of 1 to 4 were most compatible with the CAT scores of 10, 10, 15, and 20, respectively.

Conclusions: Expanding current data represents that CAT score of 10 could be more compatible with mMRC score of 1. Moreover we think although a high mMRC or CAT score may be sufficient to assign patients to high symptom groups, it is needed to evaluate mMRC and CAT together to assign a patient to a low symptom group. In this way misclassification of the patients with high symptoms due to insufficient symptom evaluation as if they have low symptoms can be prevented.

Keywords: CAT, COPD, GOLD, mMRC, symptom assessment

ÖZ

Amaç: Bu çalışmada kronik obstrüktif akciğer hastalığı (KOAH) hastalarının semptom durumlarını değerlendirme bakımından, modifiye Tıbbi Araştırma Konseyi (mMRC) ve KOAH değerlendirme testi (CAT) skorlarının uyumluluğunu araştırmayı amaçladık.

Yöntemler: Tek merkezli kesitsel bir çalışma olarak planlandı. İstatistiksel olarak birden dörde kadar olan mMRC skorları için dört ayrı CAT skorlaması alıcı işlem karakteristikleri (ROC) eğrisi üretildi.

Bulgular: Çalışmaya ortalama yaşı 64,2±8,2 yıl olan ve %88,6'sı erkek 228 stabil KOAH hastası dahil edildi. CAT ve mMRc skorları arasında güçlü pozitif bir ilişki saptandı (r=0,60, p<0,001). Ancak 32 hastada mMRC<2 iken CAT≥10 ve 21 hastada CAT<10 iken mMRC≥2 olduğu gözlemlendi. Böylece 53 hastada CAT ve mMRC skorları semptom durumlarını değerlendirmek bakımından benzer değildi. ROC analizine göre 1'den 4'e kadar olan mMRC skorları sırasıyla en çok CAT 10, 10, 15 ve 20 ile uyumlu bulundu.

Sonuçlar: Artmakta olan veriler CAT skorundaki 10 değeri ile mMRC skorundaki bir değerinin daha uyumlu olabileceğine işaret etmektedir. Ayrıca semptom skoru yüksek olan hastaları belirlemek için mMRC veya CAT skorlarından birinin yüksek olması yeterli iken hastayı düşük semptom skoru olan gruba atamak için mMRC ve CAT'nin birlikte değerlendirilmesi gerektiği düşüncesindeyiz. Böylece semptomlarının yetersiz değerlendirilmesi nedeniyle yüksek semptom skoruna sahip hastaların, düşük semptom skorlu olarak yanlış gruplandırılması önlenebilir.

Anahtar kelimeler: CAT, KOAH, GOLD, mMRC, semptom değerlendirmesi

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an important and rising reason for morbidity and mortality, a major global health problem worldwide[1]. Symptomatic burden of COPD is closely interrelated with quality of life, exacerbations, hospital admissions, and mortality[2,3]. Dyspnea is the most common symptom of COPD, and it is defined by the American Thoracic Society as "subjective experience of breathing discomfort that consists of qualitatively distinct sensation that vary in intensity.[4]" Objective evaluation of dyspnea is as difficult as to comprehend its definition. The modified Medical Research Council (mMRC) dyspnea score is used to assess breathlessness and is based on five stages of dyspnea owing to exertion[5]. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommend that the cutoff point of "more symptoms" is mMRC≥2, but this value has not been validated in patients with COPD[2]. In addition, previous studies indicated that many COPD patients with mMRC<2 had a St. George's Respiratory Questionnaire score greater than 25, which shows significant levels of impairment in their health status[6,7].

While dyspnea is the most common symptom of COPD, it should be borne in mind that cough is often the first COPD symptom. Chronic cough and sputum are related to the annual decline in the forced expiratory volume in 1 s (FEV_1), increased hospitalization, and mortality in COPD[8]. For this reason, a more comprehensive and useful questionnaire is needed to evaluate other symptoms besides dyspnea. The COPD assessment test (CAT) includes eight items related to the severity of dyspnea, exercise capacity, cough, sputum, chest tightness, sleep quality, self-confidence, and energy levels. The CAT is a short and simple instrument to evaluate COPD patients, and its validated translations are present in a broad range of languages in the world. Additionally, the CAT is correlated with quality of life[9,10].

According to the GOLD guidelines, patients with CAT score of ≥10 or mMRC score of ≥2 represents have more prominent symptoms (Figure 1). The cutoff point of more symptoms for CAT score ≥10 was validated in COPD. This threshold has been detected to have an important impact on the daily lives of patients with COPD[11].

In clinical practice, it is common to ask the question corresponding to mMRC grade 2 "On level ground, I walk slower than people of the same age because of breathlessness, or I have to stop for breath when walking at my own pace on the level" when evaluating the symptom status of the patient with COPD. However, previous studies have shown that some patients with mMRC<2 have more symptoms based on their CAT score[12-14].

Our study aimed to investigate the correlation between CAT and mMRC scores, as well as examine each mMRC score regarding the compatibility to relevant CAT scores. In the light of our results and literature, we present the discussion for using mMRC or CAT scores to evaluate the symptom status in accordance with the GOLD recommendations. In addition, we would like to unveil some new suggestions in this article. First, the most concordant mMRC score with a CAT score of 10 may be reevaluated. Second, mMRC or CAT can be used to assign patients to groups B and D, but both tests should be assessed together to admit less symptom, which would assign patients to groups A and C (Figure 1). Therefore, the misclassification rates of patients with high symptom scores in groups A and C may be substantially prevented. Lastly, the GOLD 2019 guideline recommends combined long-acting bronchodilator therapy as the first-line treatment for patients with high symptoms (CAT>20) in group D. We believe that an mMRC score corresponding to the CAT score >20 should be suggested for the physicians who do not have enough time to assess CAT scoring in their clinical practice.
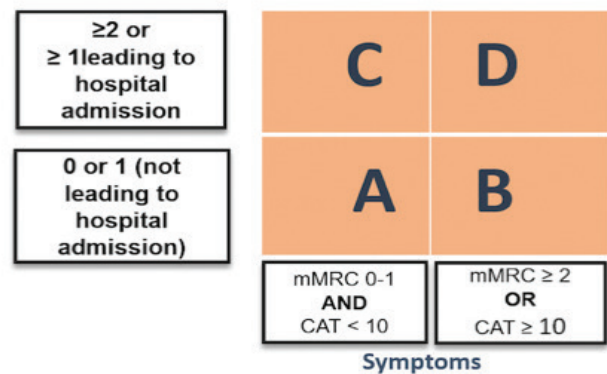

Figure 1. mMRC or CAT can be used to assign patients to groups B and D, but both sets should be assessed together to admit less symptom, which would assign patients to groups A and C.

mMRC: Modified Medical Research Council, CAT: COPD assessment test, COPD: Chronic obstructive pulmonary disease

MATERIALS and METHODS

The study was a single-center, observational, and cross-sectional, comprising the stable COPD patients who were admitted to outpatient clinics consecutively. Inclusion criteria were as follows: COPD diagnosis had been confirmed (post-bronchodilator FEV_1/forced vital capacity ratio of <70%) for at least 1-yr diagnosis, participants were aged ≥40 yr, with smoking history of ≥10 pack-yr. Patients who were unable to complete the case report form or whose pulmonary function tests (PFTs) were not compatible or experiencing COPD exacerbations within the previous 6 weeks of enrollment were excluded from the study. The case report form covered patient demographics and clinical and laboratory attributes (gender, age, smoking and exacerbation history, mMRC, CAT, and PFTs). If the patient's latest test was not within 6 months or the test was interpreted as invalid, the PFT was performed. According to the GOLD guideline, it was performed with a Sensor Medics model 2400 (Yorba Linda, California, USA). Patients' FEV_1% classified spirometric severity of the disease predicted value: FEV_1≥80%, mild (Stage 1); 50%≥FEV_1<80%, moderate (Stage 2); 30%≥FEV_1<50%, severe (Stage 3); and FEV_1<30%, very severe (Stage 4)[15]. All patients were classified into four categories in terms of risk/symptom status according to GOLD 2017 report: less symptoms, low risk (Category A); more symptoms, low risk (Category B); less symptoms, high risk (Category C); more symptoms, high risk (Category D). Based on this classification, the cutoff points for symptoms were CAT scores ≥10 and/or mMRC≥2, whereas the cutoff points for risks were the number of exacerbation in the previous year ≥2 or ≥1 leading to hospitalization[2].

The written informed consent was taken from each patient. The Ethics Committee Biruni University approved the study protocol (decision no: 2018/24-05, date: 28.12.2018).

Statistical Analysis

Statistical analyses were performed using the IBM SPSS version 22 software (SPSS Inc., Chicago, Illinois, USA). The data were descripively expressed as mean and standard deviation for continuous variables and as numbers and percentages for categorical variables. Spearman's nonparametric correlation analysis was used to analyze the bivariate correlations among CAT score, mMRC score, and FEV_1%. Association between dichotomized CAT scores and mMRC scores was examined using Somers' D statistics. Four separate receivers operating characteristic (ROC) curves of the CAT score were generated for an mMRC scores of 1 to 4. The area under the curve (AUC) with their standard error and 95% confidence interval (CI) is presented. Maximum Youden's index (sensitivity + specificity - 1) was used to find a cutoff point for the best combination of sensitivity and specificity. P-values less than 0.05 are considered statistically significant.

RESULTS

The study comprised 228 stable COPD patients, with a mean age of 64.2±8.2 yr and 88.6% of male patients. The mean FEV_1% predicted CAT and mMRC scores were 46.2±18, 12.2±8.6, and 1.6±1.2, respectively. The distribution of patients according to GOLD Stages 1, 2, 3, and 4 were 10 (4.4%), 80 (35.1 %), 88 (38.6%), and 50 (21.9%), respectively. Table 1 shows the baseline characteristics of the patients. The correlation between CAT and mMRC scores was strongly positive (r=0.60, p<0.001) (Figure 2). The CAT and mMRC scores of 53 patients were not identical to assess symptom status according to GOLD. Thirty-two (14%) patients had mMRC of 0-1, but CAT≥10, and in 21 (9%) patients, CAT score was <10, but mMRC was ≥2. Table 2 shows the distribution of patients according to CAT and mMRC scores.

The ROC curve was used to identify which CAT score was most compatible with the mMRC scores. For an mMRC score of 1, a CAT score of 10, showed the maximum value of Youden's index (0.52) with a sensitivity 0.57, specificity 0.96, AUC: 0.82 (0.77-0.88; 95% CI). For an mMRC score of 2, a CAT score of 10 showed the maximum value of Youden's index (0.54) with a sensitivity of 0.75, specificity 0.79, AUC: 0.85 (0.80-0.90; 95% CI). For an mMRC score of 3, a CAT score of 15 showed the maximum value of Youden's index (0.64) with a sensitivity of 0.80, specificity 0.83, AUC: 0.89 (0.84-0.94; 95% CI), and finally for an mMRC score of 4, a CAT score of 20 showed the maximum value of Youden's index (0.75) with a sensitivity 0.88, specificity 0.88, AUC: 0.91 (0.86-0.96; 95% CI). The ROC curves for each mMRC and CAT scores are shown in Figure 3.

DISCUSSION

Our study reveals that CAT and mMRC scores were strongly correlated. Although there was a strong correlation between CAT and mMRC scores, they were not identical to assess symptom status according to the GOLD in 53 patients. Thirty-two (14%) patients had mMRC of 0-1, but CAT scores ≥10, and 21 (9%) patients had CAT scores <10, but mMRC was ≥2. According to the ROC analysis, the mMRC scores 1 to 4 were most compatible with the CAT scores of 10, 10, 15, and 20, respectively.

| Table 1. The baseline characteristics of patients (n=228).	
Patient characteristics	Mean ± SD or n (%)
Age (yr)	64.2±8.2
Male patient	202 (88.6%)
Smoking (pack/yr)	46.2±25.6
COPD duration (yr)	7.7±5.2
FEV_1 (L)	1.3±0.6
FEV_1% predicted	46.2±18.1
FVC (L)	2.3±2.5
FVC, % predicted	60.1±18.2
FEV_1/FVC	55.4±10.4
The number of exacerbations in the previous year	3.9±4.3
CAT score	12.2±8.6
mMRC score	1.6±1.2
The categorization according to GOLD 2017	
Group A; n (%)	64 (28.2)
Group B; n (%)	65(28.5)
Group C; n (%)	15 (6.6)
Group D; n (%)	84 (37)
The categorization according to FEV_1% predicted	
GOLD Stage 1; n (%)	10 (4.4)
GOLD Stage 2; n (%)	80 (35.1)
GOLD Stage 3; n (%)	88 (38.6)
GOLD Stage 4; n (%)	50 (21.9)
SD: Standard deviation, FEV_1: Forced expiratory volume in 1 s, FVC: Forced vital capacity, CAT: COPD assessment test, mMRC: Modified Medical Research Council, GOLD: Global Initiative for Chronic Obstructive Lung Disease	
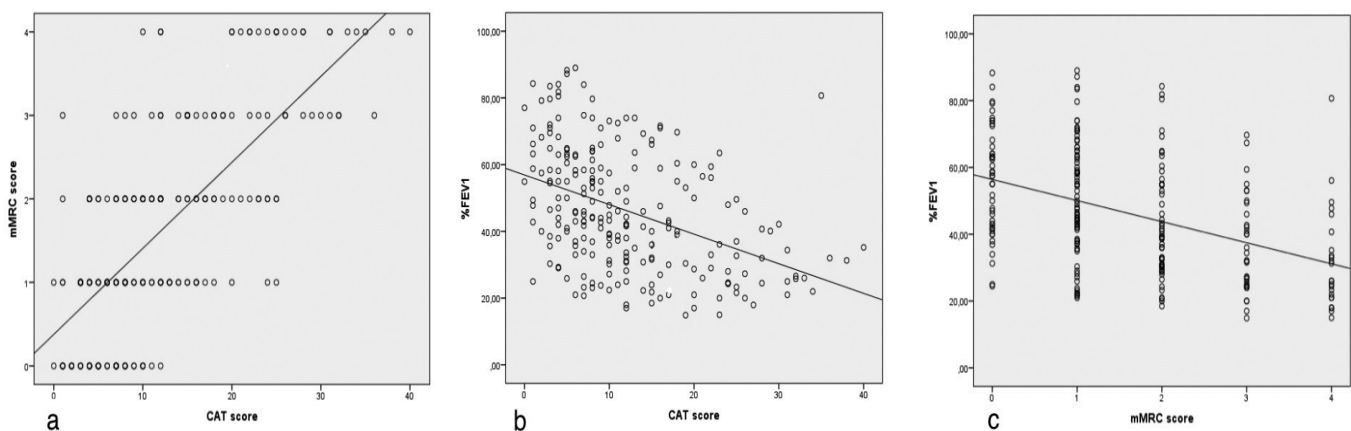
Figure 2. a. The correlation between CAT and mMRC scores was strongly positive (r=0.60). **b.** There was a weak to moderately negative correlation for FEV_1% and CAT score (r=0.45). **c.** There was a weak to moderately negative correlation for FEV_1% and mMRC score (r=0.44).

mMRC: Modified Medical Research Council, CAT: COPD assessment test, COPD: Chronic obstructive pulmonary disease, FEV_1: Forced expiratory volume in 1 s

Table 2. Distribution of patient numbers according to CAT and mMRC scores.

| | mMRC score | | | | | |
	0	1	2	3	4	Total
CAT<10	39	49	17	4	0	109
CAT≥10	5	27	35	28	24	119
Total	44	76	52	32	24	228
CAT<15	44	66	33	8	3	154
CAT≥15	0	10	19	24	21	74
Total	44	76	52	32	24	228
CAT: COPD assessment test, mMRC: Modified Medical Research Council, COPD: Chronic obstructive pulmonary disease						
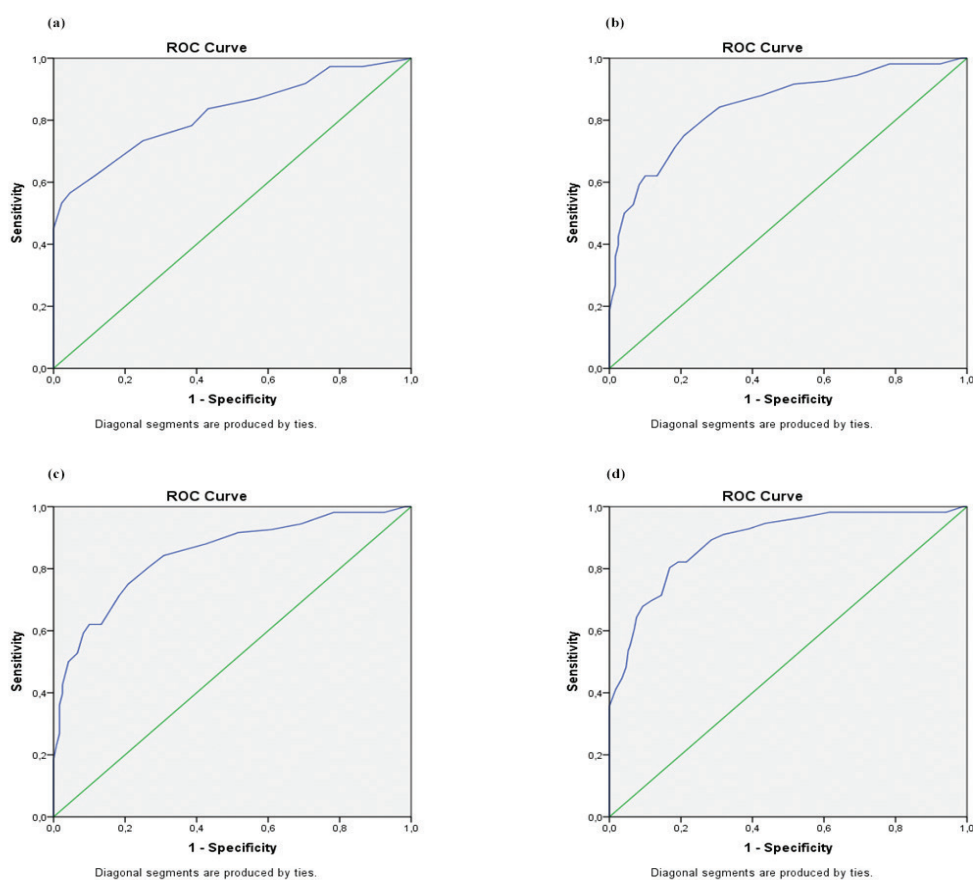
Figure 3. The symptom assessment performance of CAT score compatible with mMRC scores; ROC analysis.

(a) The symptom assessment performance of CAT score when mMRC≥1 is set as positive value. A CAT score of ≥10 is compatible with an mMRC score ≥1; sensitivity 0.57, specificity 0.96 AUC: 0.82 (0.77-0.88; 95% CI). **(b)** The symptom assessment performance of CAT score when mMRC≥2 is set as positive value. A CAT score of ≥10 is compatible with an mMRC score ≥2; sensitivity 0.75, specificity 0.79 AUC: 0.85 (0.80-0.90; 95% CI). **(c)** The symptom assessment performance of CAT score when mMRC≥3 is set as positive value. A CAT score of ≥15 is compatible with an mMRC score ≥3; sensitivity 0.80, specificity 0.83 AUC: 0.89 (0.84-0.94; 95% CI). **(d)** The symptom assessment performance of CAT score when mMRC≥4 is set as positive value. A CAT score of ≥20 is compatible with an mMRC score ≥4; sensitivity 0.88, specificity 0.88, AUC: 0.91 (0.86-0.96, 95% CI).

mMRC: Modified Medical Research Council, CAT: COPD assessment test, COPD: Chronic obstructive pulmonary disease, ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval

Some studies have found a weak to moderate correlation between CAT and mMRC scores[12,13,16-18]. A previous study that included 1,817 patients demonstrated a significant relationship between mMRC and CAT scores similar to our research[19]. Although we have exhibited a strong correlation between CAT and mMRC scores, 14% of the patients had mMRC 0-1, but CAT≥10, and 9% had CAT<10, but mMRC≥2. Many studies indicated that COPD group assignment was not identical regarding the cut points of CAT score ≥10 and mMRC score ≥2, which are the purposed thresholds by GOLD 2011[7,14,18]. A retrospective study of 757 COPD patients showed that 11% of patients had mMRC 0-1, but CAT≥10, and 27% of patients had CAT<10, but mMRC≥2. In terms of concordant group assessment, they could not find a perfect agreement presented between the cut point CAT score ≥10 and each mMRC cut point[18]. Kim et al.[13] demonstrated that a significant number of patients with mMRC score below 2 were in the more symptoms group according to the CAT score. The percentage of CAT score over than 10 was 68.5%, but mMRC score of 2 was 38.1% in this study[13]. Rieger-Reyes et al.[14] revealed that more than 25% of patients were reclassified into different groups according to an mMRC score of 2 and a CAT score of 10[14]. The US multicenter cross-sectional study obtaining data from 445 patients who had a spirometry-confirmed diagnosis that, as compared with the traditional system, the GOLD CAT system reclassifies 41%, and GOLD mMRC system reclassifies 47% of the patients, but the distributions are very different in each reclassification[20]. The GOLD guideline recommends that the cutoff point of more symptoms are mMRC score ≥2 and CAT score ≥10. The cutoff point of more symptoms with CAT score was validated, but the cut point of mMRC score has yet to be validated in COPD patients[11]. Many studies suggested that COPD group placement was not the same regarding the cut points of CAT score ≥10 and mMRC scale ≥2[12,13,18,19]. A study that analyzed data collected from the Korean COPD Subgroup Study cohort detected that a CAT score of 10 was most concordant with an mMRC score of 1 contrarily to the GOLD recommendation[12]. Other studies support the result of this analysis too[19,21,22]. Similarly, we founded a high concordance between a CAT score of 10 and an mMRC score of 1. Effective and early management of symptoms remains the primary treatment goal in stable COPD. Failure to control dyspnea in the early stages results in decreased exercise capacity, decondition, deterioration in health perception, anxiety, depression, and social isolation over time[2]. There is expanding evidence suggesting that early bronchodilator therapy in COPD may change the course of the disease[23,24]. However, the mMRC is frequently used alone to evaluate dyspnea in clinical practice. This approach may result in the undertreatment of some patients who actually would require long-acting bronchodilators. According to a cross-sectional study including 450 primary care COPD patients, mMRC and CAT were not compatible regarding the COPD group assignment. When evaluated with CAT, more patients were included in groups B and D. A key finding was that 20% of patients were undertreated in this study[25]. The GOLD 2019 report recommends combined long-acting bronchodilator therapy as the first choice initial treatment to patients with more symptoms (CAT>20) in group D. Although it is used more frequently than CAT, a cutoff value was not given for the mMRC scale[26]. ROC analysis revealed that a CAT score of 20 was most concordant with an mMRC score of 4. Our study had several limitations. This study was cross-sectional and conducted with a single center. Our results may not reflect the general population of COPD patients since the recruitment was limited to our tertiary hospital. Finally, the total number of patients and, in particular, female patients enrolled in the study were low.

CONCLUSIONS

We would like to bring forward some suggestions based on our results and the literature. First, the most concordant mMRC score with a CAT score of 10 may be reevaluated. Second, mMRC or CAT can be used to assign patients to groups B and D. Still, both tests should be assessed together to admit less symptom, which would assign patients to groups A and C. Therefore, the misclassification rates of patients with high symptom scores in groups A and C may be substantially prevented. The last, GOLD 2019 guideline recommends combined long-acting bronchodilator therapy as the first choice initial treatment to patients with high symptoms (CAT>20) in group D. We believe that an mMRC score corresponding to the CAT score >20 should be suggested for the physicians who do not have enough time to assess CAT scoring in their clinical practice.

Ethics

Ethics Committee Approval: The Ethics Committee Biruni University approved the study protocol (decision no: 2018/24-05, date: 28.12.2018).

Informed Consent: The written informed consent was taken from each patient.

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Author Contributions

Surgical and Medical Practices: E.E.Y., E.Y.N., B.Y., M.B., Concept: E.E.Y., Design: E.E.Y., E.Y.N., Data Collection and/or Processing: E.E.Y., B.Y., M.B., Analysis and/or Interpretation: E.E.Y., B.Y., M.B., Literature Search: E.E.Y., E.Y.N., B.Y., M.B., Writing: E.E.Y., E.Y.N., B.Y., M.B.

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