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The Comparison of Clinical Variables in Two Classifications: GOLD 2017 Combined Assessment and Spirometric Stage of Chronic Obstructive Pulmonary Disease

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Background: There are limited number of studies that investigate clinical variables instead of chronic obstructive lung disease (COPD) management according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 classification. The aim of the study was to investigate whether there was a difference between GOLD 2017 classification and spirometric stage in clinical variables in patients with COPD. The data of 427 male patients with stable COPD were investigated retrospectively.
Methods: Patients were allocated into combined assessment of GOLD 2017 and spirometric stage. Age, amount of smoking, pulmonary function, modified Medical Research Council (mMRC), incremental shuttle walk test (ISWT), Hospital Anxiety-Depression Scale (HADS), St. George's Respiratory Questionnaire (SGRQ), body mass index (BMI), and fat free mass index (FFMI) were recorded.
Results: Seventy-three (17%) patients were in group A, 103 (24%) constituted group B, 38 (9%) were included in group C, and 213 (50%) comprised group D according to the combined assessment of GOLD 2017. Twenty-three patients (5%) were in stage 1, 95 (22%) were in stage 2, 149 (35%) were in stage 3, and 160 (38%) were in stage 4 according to spirometric stage. According to GOLD 2017, age, amount of smoking, mMRC, BMI, FFMI, SGRQ, HADS, forced vital capacity, forced expiratory volume in 1 second (FEV_1), and ISWT were significantly different between groups. Ages, amount of smoking, FFMI, BMI, HADS of group A were different from B and D. Smiliar values of FEV_1 were found in A-C and B-D. A and C had smiliar ISWT. According to spirometric stage, BMI, FFMI of stage 4 were statistically different. mMRC, ISWT, and SGRQ of stages 3 and 4 were different from other stages, amongst themselves. FEV_1 was correlated with mMRC, SGRQ, anxiety scores, BMI, FFMI, and ISWT.
Conclusion: This study showed that the GOLD ABCD classification might not represent the severity of COPD sufficiently well in terms of lung function or exercise capacity. The combination of both spirometric stage and combined assessment of GOLD 2017 is important, especially for estimating clinical variables.

Keywords: Pulmonary Disease, Chronic Obstructive; Quality of Life; Dyspnea

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Introduction

Chronic obstructive lung disease (COPD), a progressive disease, is characterized by airflow limitation with increasing mortality and morbidity rates[1]. The accurate diagnosis of COPD is very important in terms of disease management by way of decreasing symptoms such as dyspnea, number of exacerbations, improving health status, exercise capacity, and mortality[2]. COPD has been classified by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, which appears in most literature, and is accepted and used all around the world. The first GOLD report was launched in 1997. The regurlarly revised GOLD criteria were recently updated in 2017. The 2011 GOLD report was the first to recommend the "ABCD" assessment tool instead of simple spirometric grading. The report included patient-reported outcomes and the importance of exacerbation prevention in COPD management. Some limitations were noticed over time due to the decreased prediction in mortality and other important health outcomes when it was compared with spirometric grades[3-5]. Moreover, the outcomes of group D were modified by two parameters: lung function and/or exacerbation history, which caused confusion[6]. For the purpose of clarifing concerns in the 2017 GOLD report, the ABCD classification has been adjusted and spirometric grades have been seperated from ABCD groupings. For some therapy recommendations, especially pharmacologic treatments, ABCD groups are derived exclusively from patient symptoms and their exacerbation history. However, it is still recommended that spirometry, in conjunction with patient symptoms and exacerbation history, remains vital for the diagnosis, prognostication, and consideration of other important therapeutic approaches, especially non-pharmacologic therapies[1].

The aim of the study was to investigate whether there was a difference between the GOLD 2017 classification and spirometric stage in age, smoking status (current/former), amount of smoking, body composition, dyspnea sensation, health-related quality of life, psychological status, and exercise capacity in patients with COPD.

Materials and Methods

1. Data collection

The data of patients who were referred to the outpatient pulmonary rehabilitation center of our hospital between January 2013 and May 2017 were investigated retrospectively. Male patients with stable COPD were included. Patients with comorbidities such as uncontrolled hypertension, diabetes mellitus, cognitive dysfunction, lung cancer, and also with evident bronchiectasis or sequential of tuberculosis were excluded. The data of 427 male patients with COPD were recorded after patients' informed consent and hospital approvals were obtained (Ataturk Chest Disease and Chest Surgery Education and Research Hospital Review Board, approval number: 568).

The number of exacerbations and hospitalizations were analyzed from the records of the PR center and hospital database, and also confirmed with patients' declarations. The definition of exacerbations was accepted as detailed below as the GOLD recommendation[6].

2. Definition of exacerbation

Exacerbations are defined as "an acute worsening of respiratory symptoms that result in additional therapy," the cardinal symptom is increased dyspnea, and other symptoms include increased sputum purulence and volume, together with increased cough and wheeze.

3. Classifications

The patients were allocated into the combined assessment of GOLD 2017 and spirometric stage[6].

1) Classification of combined assessment

- Group A: 0 to 1 exacerbation per year and no prior hospitalizations for exacerbation, and modified Medical Research Council (mMRC) grade 0 to 1.
- Group B: 0 to 1 exacerbation per year and no prior hospitalizations for exacerbation, and mMRC grade ≥2.
- Group C: ≥2 exacerbations per year or ≥1 hospitalization for exacerbation, and mMRC grade 0 to 1.
- Group D: ≥2 exacerbations per year or ≥1 hospitalization for exacerbation, and mMRC grade ≥2.

2) Classification based on postbronchodilator forced expiratory volume in 1 second

In patients with forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) <70%:

- Stage 1: FEV_1 ≥80% predicted.
- Stage 2: 50%≤FEV_1<80% predicted.
- Stage 3: 30%≤FEV_1<50% predicted.
- Stage 4: FEV_1 <30% predicted.

4. The measurements

The recorded measures were dyspnea, exercise capacity, psychological status, health-related quality of life, and body composition. Dyspnea was assessed using the mMRC scale[7] and exercise capacity was evaluated using the incremental shuttle walk test (ISWT). The ISWT required the patient to walk up and down a 10-m course. The course was identified by two cones inset 0.5 m from either end to avoid the need for abrupt changes in direction. The speed at which the patient

walked was dictated by an audio signal, which was increased by 0.17 m/sec each minute. The distance was recorded in meters at the end of the test[8]. Psychological status was revealed with the Hospital Anxiety and Depression Scale (HADS)[9]. Health-related quality of life was assessed using the Turkish version of a standardized St. George's Respiratory Questionnaire (SGRQ)[10,11]. For body composition, bioelectrical impedance was used with a Tanita (BIA model TBF-300; Tanita Corporation, Tokyo, Japan). Body mass index (BMI) and fat-free mass index (FFMI) were calculated using a formula in which weight (body mass for BMI, fat-free mass for FFMI) in kilograms was divided by the square of height in meters.

5. Statistical analysis

SPSS version 18.0 (SPSS, Inc., Chicago, IL, USA) for Microsoft Windows (Microsoft Corporation, Redmond, WA, USA) was used for analysis. The variables were analyzed using the Shapiro-Wilk test to evaluate distribution. Results for descriptive statistics were expressed as mean±standard deviation or median (minimum:maximum). Categorical variables were expressed as numbers and percentages (%). Statistical comparisons of continuous variables among the groups were performed using one-way analysis of variance or the Kruskal-Wallis test based on their distribution. The Tukey test was performed for *post hoc* analysis after performing the analysis of variance test. Spearman correlation analysis was performed. Statistical significance was set to a $p<0.05$.

Results

The mean age of all patients was 62.7±9 years. Three hundred sixty-nine patients (86%) were former smokers, and 58 (13%) were current smokers with a median value of 40 (0:200) pack-years among all patients (Table 1).

Seventy-three patients (17%) were in group A, 103 (24%) constituted group B, 38 (9%) were included in group C, and 213 (50%) comprised group D according to the combined as-

Table 1. Demographic features of all patients

	Value
Age, yr	
Mean±SD	62.7±9
Median (min–max)	63 (40–86)
Smoking, pack-years	
Mean±SD	44±28
Median (min–max)	40 (0–200)
Former smoker, n (%)	69 (86)
Current smoker, n (%)	58 (13)

Table 2. The recorded values of each group according to GOLD 2017

GOLD	Age (yr)	Smoking, pack-years	mMRC	BMI (kg/m^2)	FFMI (kg/m^2)	FEV_1	FVC	ISWT (m)	SGRQ	Anxiety	Depression
A											
Mean±SD	59±8	33±24	0.9±0.2	27±5	20±6	55±20	69±18	342±104	41±16	8±2.5	8±2
Median (min–max)	60 (45–78)	30 (0–120)	1 (0–1)	27 (15–39)	20 (14–26)	57 (15–99)	69 (24–100)	350 (110–520)	40 (13–84)	8 (1–15)	8 (2–14)
B											
Mean±SD	64±9	43±22	2.4±0.6	25±6	19±9	40±19	57±17	221±117	64±14	9±2	10±3
Median (min–max)	65 (43–83)	40 (0–120)	2 (2–4)	24 (15–41)	19 (14–31)	35 (13–94)	56 (25–99)	200 (30–480)	65 (31–98)	10 (3–17)	10 (3–15)
C											
Mean±SD	60±8	45±27	0.9±0.2	25±5	19±2	50±19	68±16	317±98	49±12	9±2	9±2
Median (min–max)	61 (45–73)	40 (0–107)	1 (0–1)	25 (16–35)	20 (15–25)	46 (24–92)	69 (40–99)	305 (40–450)	49 (18–76)	10 (4–13)	9 (5–13)
D											
Mean±SD	64±9	49±32	2.6±0.6	24±6	19±3	34±16	50±16	174±97	71±15	10±2	10±2
Median (min–max)	63 (40–86)	45 (0–200)	2 (2–4)	24 (14–42)	19 (13–25)	29 (13–99)	48 (13–98)	170 (30–480)	73 (31–98)	10 (2–15)	10 (3–15)

GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC: modified Medical Research Council scale; BMI: body mass index; FFMI: fat-free mass index; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; ISWT: incremental shuttle walk test distance; SGRQ: St. George's Respiratory Questionnaire.

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sessment of GOLD 2017. The recorded values of each group are given in Table 2. Age (p=0.001), mMRC scale (p<0.001), amount of cigarettes (pack-years) (p<0.001), BMI (p=0.002), FFMI (p=0.001), SGRQ score (p<0.001), HADS (p<0.001), FVC (p<0.001), FEV_1 (p<0.001), and ISWT distance (p<0.001) were significantly different between the groups (Figure 1).

The ages, amount of cigarettes, FFMI, BMI values, anxiety, depression scores of group A were found to be statistically significant different than group B (p=0.009, p=0.028, p=0.008, p=0.008, p=0.001, and p<0.001, respectively), and group D (p=0.002, p<0.001, p<0.001, p=0.001, p<0.001, and p<0.001, respectively). Group C was similar to the other groups and also groups B and D were similar in these measurements. Similar FEV_1 values were in groups A and C, and B and D. Statistically different values of FEV_1 were found in groups A and B (p<0.001), A and D (p<0.001), B and C (p=0.034), and C and D (p<0.001). In the ISWT distance, only groups A and C had similar values (significant difference between groups: A–B, p<0.001; A–D, p<0.001; B–C, p<0.001; B–D, p=0.001; C–D, p<0.001). However, SGRQ scores were different between all

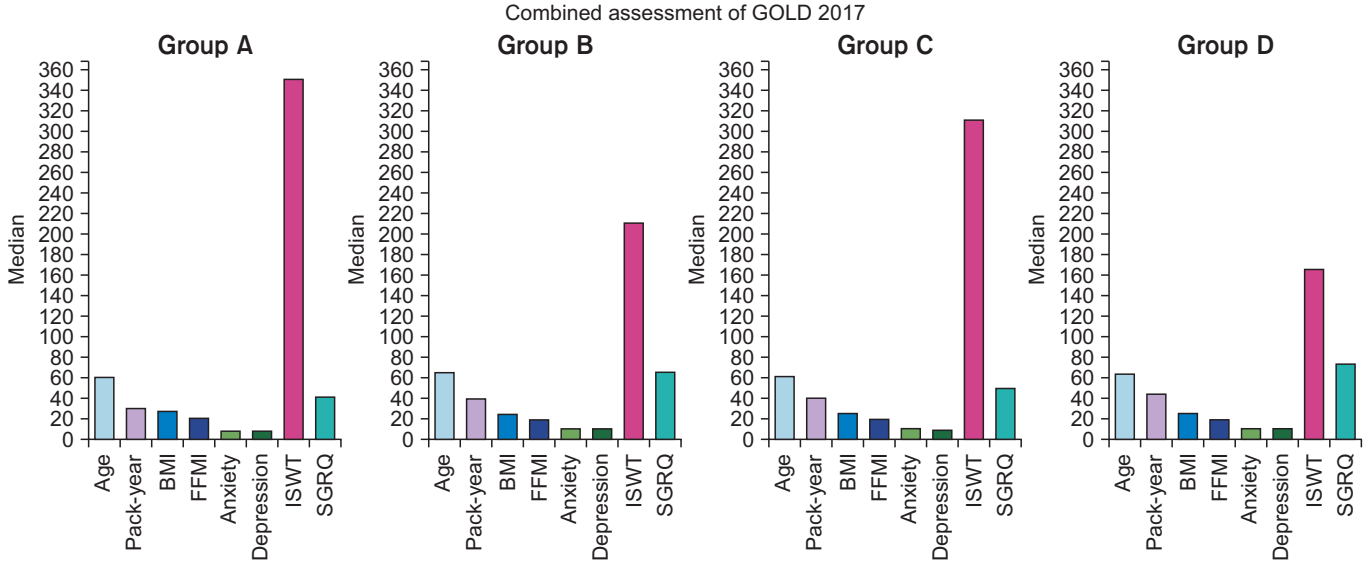

Figure 1. Statistically different parameters between the groups according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. BMI: body mass index; FFMI: fat-free mass index; ISWT: incremental shuttle walk test distance; SGRQ: St. George's Respiratory Questionnaire.

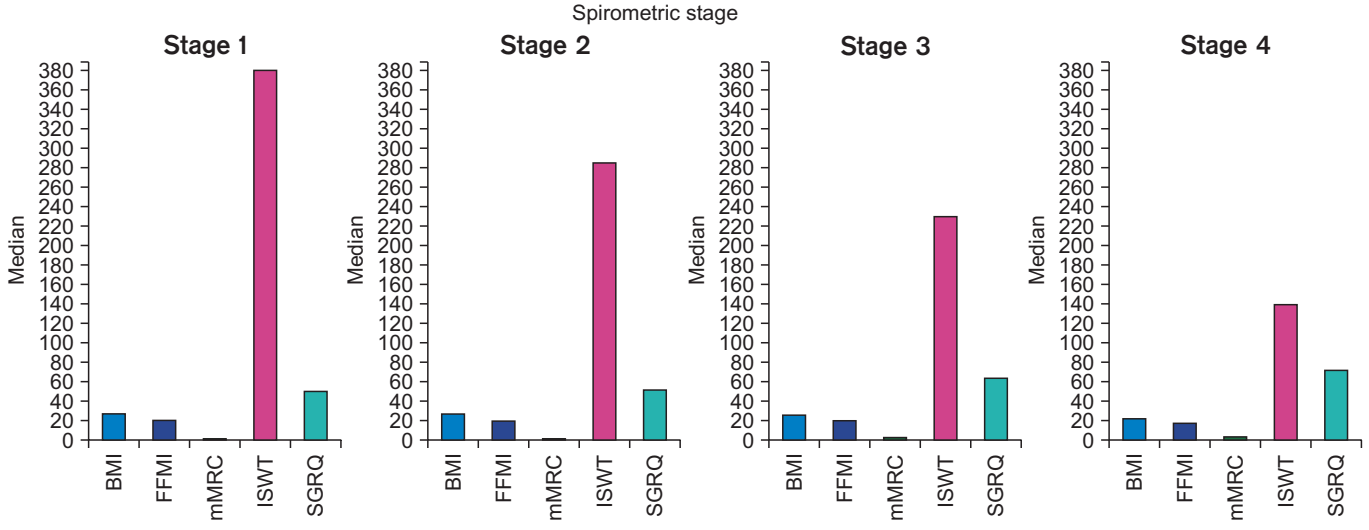

Figure 2. Statistically different parameters between the groups according to spirometric stage. BMI: body mass index; FFMI: fat-free mass index; mMRC, modified Medical Research Council; ISWT: incremental shuttle walk test distance; SGRQ: St. George's Respiratory Questionnaire.

Table 3. The recorded values of each group according to spirometric stage

Spirometric stage	Age (yr)	Smoking Pack-years	mMRC	BMI (kg/m^2)	FFMI (kg/m^2)	FEV_1	FVC	ISWT (m)	SGRQ	Anxiety	Depression
1											
Mean±SD	61±9	46±32	1.5±0.8	27±4	20±2	87±6	90±7	354±119	50±21	9±2	8±3
Median (min–max)	63 (43–76)	34 (0–120)	1 (0–3)	27 (17–36)	20 (15–24)	87 (80–99)	91 (76–99)	370 (60–520)	50 (15–92)	10 (6–14)	9 (2–12)
2											
Mean±SD	63±9	40±25	2±0.8	27±5	20±2	63±8	74±13	293±123	54±20	9±2	9±3
Median (min–max)	61 (45–86)	40 (0–107)	2 (2–4)	27 (15–42)	20 (14–26)	61 (51–79)	75 (45–99)	280 (40–520)	52 (13–96)	9 (3–13)	9 (3–15)
3											
Mean±SD	64±9	45±28	2±0.7	25±5	19±3	38±5	57±10	234±110	62±16	9±2	9±2
Median (min–max)	65 (43–83)	40 (0–165)	2 (2–4)	26 (16–41)	20 (14–31)	37 (30–49)	56 (30–80)	230 (30–480)	63 (24–98)	10 (1–15)	10 (3–14)
4											
Mean±SD	62±9	47±31	2.6±0.8	23±5	18±2	23±4	42±12	162±90	70±16	9±2	9±2
Median (min–max)	62 (40–79)	40 (0–200)	3 (0–4)	22 (14–37)	18 (13–24)	23 (13–29)	41 (13–98)	140 (30–430)	72 (25–98)	10 (3–17)	10 (2–15)

mMRC: modified Medical Research Council scale; BMI: body mass index; FFMI: fat-free mass index; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; ISWT: incremental shuttle walk test distance; SGRQ: St. George's Respiratory Questionnaire.

groups (groups A–B, p<0.001; A–C, p=0.031; A–D, p<0.001; B–C, p<0.001; B–D, p=0.002; C–D, p<0.001).

Twenty-three patients (5%) were in stage 1, 95 (22%) were in stage 2, 149 (35%) were in stage 3, and 160 (38%) were in stage 4 according to spirometric stage. The values of each group are given in Table 3.

The values of BMI and FFMI of stage 4 were found to be statistically different than other stages (stages 1–4, p<0.001, p<0.001; stages 2–4, p<0.001, p<0.001; and stages 3–4, p<0.001, p<0.001, respectively) (Figure 2).

The mMRC scale, ISWT distance, and SGRQ scores were similar between only stages 1 and 2. These measurements of stages 3 and 4 were found to be significantly different than the other stages and amongst themselves (mMRC: stages 1–3, p=0.025; 1–4, p<0.001; 2–3, p=0.006; 2–4, p<0.001; 3–4, p<0.001; ISWT: stages 1–3, p<0.001; 1–4, p<0.001; 2–3, p<0.001; 2–4, p<0.001; 3–4, p<0.001; SGRQ stages 1–3, p=0.007; 1–4, p<0.001; 2–3, p=0.002; 2–4, p<0.001; 3–4, p=0.004).

FEV_1 was negatively correlated with the mMRC scale (p<0.001, r=–0.473), SGRQ total score (p<0.001, r=–0.352), anxiety scores (p=0.032, r=–0.105), and positively correlated with BMI (p<0.001, r=0.379), FFMI values (p<0.001, r=0.391), and ISWT distance (p<0.001, r=0.499).

Discussion

This study showed that patients with low levels of dyspnea sensation and exacerbation risk had lower age and amount of cigarette smoking, were more obese, and had better psycological status than patients with higher levels of dyspnea and exacerbation risk. Patients with the same level of dyspnea sensation were found to have similar pulmonary functions, and similar exercise capacity was found in patients with less dyspnea regardless of exacerbation risk levels. Additionally, the health-related quality of life was found to be different based on both symptoms and exacerbation risks according to the new combined assessment of GOLD 2017. Furthermore, although in patients who had post-bronchodilator FEV_1 <30% (stage 4) the deterioration of body composition was found to be more evident, for patients who had post-bronchodilator FEV_1 <50% (stages 3–4), the deteriorations of dyspnea, health-related quality of life, and exercise capacity were also more evident than other stages and increased as the stage increased.

Among most patients with COPD, exacerbations could be more frequent with the progression of disease. In contrast, some patients are likely to be prone to exacerbations more frequently, yet some have them rarely[12]. The mechanisms of the discrepancy in the frequency of COPD exacerbation have not been revealed, but the associated variables have been shown in several studies. In these studies, it was suggested that the frequency of exacerbations was related to a decline in FEV_1[12-17], worsening of health-related quality of life[12,13,18], and

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increased mortality[19-21]. Therefore, exacerbations and hospitalizations have been accepted as an important outcome measure in COPD, and it seems to be useful to identify and predict patients with COPD who are at risk for frequent exacerbations and hospitalization for the purpose of improving management and variables of the disease. The number of exacerbations and hospitalizations, especially for exacerbations in the previous 12 months, are likely to be predictive for future exacerbation risk. According to the GOLD 2017 criteria, a history of zero exacerbations or one in the past 12 months suggests a low future risk of exacerbations (groups A and B), whereas two or more exacerbations or a hospitalized exacerbation suggest a higher future risk (groups C and D)[6]. After hospitalization and exacerbation, body composition and exercise capacity have also been shown to be reduced[22-24]. Contrary to these studies and current knowledge, the present study showed that age, amount of cigarette smoking, body composition, psychological status, and exercise capacity in patients with less dyspnea, and pulmonary function in patients with the same level of dyspnea, were not linked to exacerbation risk level. It was suggested that, especially in patients with fewer symptoms, the number of exacerbations and/or hospitalizations would not be appropriate predictors for most important clinical variables. Otherwise, the health-related quality of life scores were different due to exacerbation risk levels, and even these scores were worse in patients who were more dyspneic.

The most common symptom in patients with COPD is dyspnea. Although various tools for evaluating symptom severity have been developed, the GOLD guidelines suggest using the COPD Assessment Test or the mMRC scale. The latter is not able to evaluate COPD-related symptoms other than dyspnea. In a recent study in which 50 patients with COPD were enrolled, it was found that between MRC scores 3 and 4, exercise performance, SGRQ, and depression scores were major determinants of disability[25,26]. In another recent study, it was found that MRC scores revealed a negative correlation with upper limb muscle strength in patients with COPD[27]. MRC was also found to be correlated with lung function measurements and 6-minute walk distance, and it also was suggested to be a potential predictor for survival in another study[28]. The present study showed that patients who were less dyspneic and had lower exacerbation risk could have different age, amount of cigarette smoking, body composition, and psychological status than patients who are more dyspneic, whether at low or high exacerbation risk. It was suggested that these parameters could deteriorate with increased sensation of dyspnea. Pulmonary functions could be associated with dyspnea sensation, even if the patients had one or no hospitalizations. This result was contrary to the GOLD 2011 criteria and justified the exclusion of FEV_1 in the new classification of GOLD 2017. Additionally, patients with less dyspnea were able to walk a similar distance and longer than the other groups. Although both symptoms and exacerbation risks were determinant for health-related quality of life, it was found that worse health-related quality of life scores were seen in patients with high dyspnea scores. Taken together, dyspnea sensation seemed to be more determinative than exacerbations/hospitalizations in predicting the most frequently seen clinical variables, and the combined classification of GOLD 2017 was thought to be decisive grouping for health-related quality of life due to the definite difference between groups.

Although some studies found a weak correlation between FEV_1, symptoms, and health status impairment, the initial GOLD guidelines used FEV_1 to stage disease severity[29,30]. Recently, FEV_1 has been shown to be a very important parameter at the population level in the prediction of important clinical variables[6]. In the Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points (ECLIPSE) study, which included 2,164 patients with COPD, it was shown that a history of exacerbation in the year before baseline was associated with a decline in FEV_1 (–94.20 mL per year). Each 1% increase in FEV_1 was found to be associated with a decreased risk of exacerbations and increased exercise capacity, and also lower FEV_1 values were associated with increased mMRC grade, SGRQ total score, and duration of smoking[31]. Similarly, in present study, it was found that in most patients with advanced spirometric stage, dyspnea, body composition, health-related quality of life, and exercise capacity were more deteriorated than at other stages. Furthermore, FEV_1 values were correlated with dyspnea, health-related quality of life, anxiety scores, and body composition.

Although there were some limitations of present study such as the patient population consisting of only the male sex due to the low number of female patients with COPD and the retrospective design of the study, this study is one of a limited number of studies that emphasizes the difference in clinical variables according to GOLD 2017 Combined Assessment and Spirometric Stage of COPD.

According to the combined assessment of COPD in the GOLD 2017 report, clinical variables such as body composition, psychological status, pulmonary function, exercise capacity, quality of life, and patients' characteristics such as age and amount of smoking were found to be different in some groups, and the mMRC score was likely to be more determinative than risk level. It was thought that symptom control could be more important than exacerbation risk control for the purpose of predicting clinical variables. According to the spirometric stage, patients with advanced-stage clinical variables could have more deteriorated sensation of dyspnea, exercise capacity, quality life, and body composition. The present study, which outlined the combination of both spirometric stage and combined assessment of GOLD 2017, is important, especially for estimating clinical variables.

Authors' Contributions

Conceptualization: IC, DK, FT, PE, NE. Methodology: IC, PE. Formal analysis: IC, PE, DK. Data curation: IC, DK, FT, NE, PE. Software: IC, FT, NE. Validation: IC, DK, PE. Investigation: IC, DK, FT, PE, NE. Writing - original draft preparation: IC, DK, PE. Writing - review and editing: IC, PE. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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