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Classification of COPD as ABCD according to GOLD 2011 and 2017 versions in COPD patients at University Medical Center in Ho Chi Minh City, Vietnam

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Abstract

In 2017, Global Initiative for Chronic Lung Disease (GOLD) made substantial changes to its ABCD group categorization. Although several studies had been conducted to assess the impact of the new GOLD category, there was no research on the change of the GOLD classification in Vietnam. This retrospective analysis was conducted at Asthma and COPD clinic at the University Medical Center in Ho Chi Minh City, Vietnam. Our study population comprised patients visiting Medical Center from January 2018 to January 2020. We categorized patients' demographic, clinical characteristics and pharmacotherapy based on GOLD 2011 and 2017 guidelines. A comparison between the two versions was also determined. A total of 457 patients were included in this study. The percentage of groups A, B, C and D according to GOLD 2011 was 5%, 20.8%, 13.1% and 61.1%; and according to GOLD 2017 was 6.1%, 34.1%, 12% and 47.8%, respectively. In terms of gender, male patients constituted nearly 95% of the study's population (433/457 patients). Regarding pharmacotherapy, approximately 20% of the low-risk group (group A-B) was overtreated with ICS components: LABA+ICS (15.8%) and LAMA+LABA+ICS (3.8%). There were 13.3% and 1.1% of patients transferred from D to B and from C to A, respectively. All of them had lower FVC% pred, FEV_1% pred and FEV_1/FVC than the patients remained in group B or A ($p<0.005$). This is the first research in Vietnam to show the distribution of COPD patients using both the GOLD 2011 and GOLD 2017 criteria. There was 14% of patients reclassified from high-risk groups to low-risk groups when changing from 2011 to 2017 version and discordance of medications between guidelines and real-life practice. Therefore, clinicians should use their clinical competence to consider patients' conditions before deciding the appropriate therapeutic approach. Consequently, further studies were required to evaluate the effect of the change in GOLD classification.

Key words: Chronic obstructive pulmonary disease (COPD); GOLD 2017 classification; University Medical Center; comparison; COPD treatment.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) was a prevalent and treatable condition that was responsible for 3.3 million deaths in 2019 [1,2]. In the South East Asia region, there were 15 million prevalent cases and 189 thousand deaths of COPD in 2019 [2]. Due to COPD morbidity and mortality, several experts decided to launch a Global Initiative for Chronic Lung Disease (GOLD) program to prevent, diagnose and manage COPD [3]. In 2001, the first GOLD summary was reported and the documents were updated every 1-5 years to respond to the heterogeneity and complexity of the disease [3].

Classification of COPD is a cornerstone in its management. There have been three versions of classification from 2001 to 2022. From 2001 to 2010, COPD was categorized as stages (I→IV) based on the %FEV Predicted. From 2011 to 2016, GOLD significantly changed its criteria for the COPD category to group classification (four groups A, B, C, and D). The GOLD 2011 guidelines indicated three parameters for The "ABCD" assessment criteria: symptoms, airflow limitation and exacerbations history [4]. The first aim was to distinguish between high-level and low-level of symptoms [4]. Patients with more symptoms had COPD Assessment Test (CAT) scores ≥ 10 or Modified British Medical Research Council (mMRC) questionnaire scores ≥ 2 [4]. The second purpose was to assess the exacerbation risk based on airflow limitation and exacerbation history [4]. For airflow limitation, patients who were in severe ($30\% \leq FEV_1 < 50\%$ predicted) or very severe stage ($FEV_1 < 30\%$ predicted) were classified as high-risk [4]. For exacerbations history, people who had at least 2 exacerbations, or 1 exacerbation that lead to hospitalization, in the previous year were classified as high-risk [4]. If the risk category was inconsistent between airflow limitation and exacerbations history, the evaluation with higher risk would be chosen [4]. In GOLD 2017, the degree of airflow limitation was removed to avoid confusion and "ABCD" groups were classified based on the remaining 2 parameters: symptoms and exacerbations history [1]. The 2017 version of the classification has been still used as the current version in 2022. The update version 2023 categorized groups C and D into group E with E standing for exacerbation [5]. The current guideline of Vietnam still uses the GOLD 2017 classification in its category.

Since the change in 2017 impacted the classification of COPD, there were many studies reported the effect of the new GOLD criteria. In Spain and US, a study on 819 COPD patients demonstrated several patients were reclassified from groups C-D to groups A-B [6]. In China, patients from the new high-risk group experienced a high risk of exacerbation or mortality compared to the low-risk group [7]. In particular, a UK study on 19,268 patients illustrated a remarkable reclassification according to GOLD 2017 and 2013 assessments [8]. The authors

found that with GOLD 2013, only 46% of patients were classified into group A or B compared to that 87% of patients when applying GOLD 2017 [8].

Although several studies analyzed the impacts of new GOLD criteria, no study was conducted in Vietnam about GOLD classification. Therefore, this study was conducted to understand the distribution of ABCD groups and the changes in these groups according to GOLD 2017 and GOLD 2011 comprehensive assessments.

Materials and Methods

Study design

This study was a retrospective analysis at Asthma and COPD clinic at the University Medical Center (UMC). Patients who met the selection criteria were recruited between January 2018 and January 2020. The study was approved by the Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City. The data collection process was permitted by the Department of Science and Training of the UMC.

Participants

Patients were extracted from the list of COPD patients of UMC if they met 2 following criteria. First, the patients with COPD were in the stable stage. Second, a post-bronchodilator ratio (FEV1/FVC) had to be lower than 70%. This value indicated the persistence of airflow limitation according to GOLD 2017 [1]. Patients were excluded from the study when they were hospitalized for COPD exacerbations or other acute conditions requiring immediate intervention such as pneumonia or asthma exacerbations. Besides, patients with missing data were excluded. The study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational studies.

Variables

The dependent variables included the patients classified to A-D groups according to GOLD 2011 and 2017 criteria. We also compared characteristics of reclassified patients from group C to group A (CA) with patients remained in group A (AA) or group C (CC); and reclassified patients from group D to group B (DB) with patients remained in group B (BB) or group D (DD).

The following independent variables were retrieved from the patients' database: age, gender, body mass index (BMI), BMI classification, dyspnea symptom, cough symptom, sputum symptom, wheezing symptom, percentage of forced expiratory volume in the first second

(FEV1% predicted), percentage of forced vital capacity (FVC% predicted), the ratio of forced expiratory volume in the first second to the forced vital capacity (FEV_1/FVC); pharmacologic therapy: long-acting beta-agonists (LABA), long-acting muscarinic antagonist (LAMA), inhaled corticosteroid (ICS), short-acting beta-agonists (SABA), short-acting muscarinic antagonist (SAMA). BMI was determined by dividing body weight (kg) by height (m^2). BMI classification was divided into underweight (under 18.5 kg), normal (18.5-23 kg), overweight (23-25 kg) and obese (over 25 kg). For those patients who had more than 2 visits, the latest visit data was collected.

Statistical analysis

Data were analyzed with SPSS (version 22.0, IBM Corporation) and R software (The R Foundation for Statistical Computing, Vienna, Austria, version 4.2.1). Categorical data were expressed as frequencies (percentage) and normal distribution data were expressed as means ± SD while data with non-normal distribution were expressed as medians (interquartile range). For the parametric test, a student *t*-test or analysis of variance (ANOVA) was used, while Mann-Whitney U or Kruskal-Wallis H was used for the non-parametric test. For categorical data, Fisher's exact test or chi-square was used. A p-value <0.05 was considered statistically significant.

Results

Study population

From 01/2018 to 01/2020, the hospital received a total of 6233 visits had COPD diagnosis. However, the number of patients that met our selection criteria was 457 patients. According to the GOLD 2011 assessment, groups A-D were comprised of 23 people (5%), 95 people (20.8%), 60 people (13.1%) and 279 people (61.1%), respectively. Meanwhile, in accordance with the GOLD 2017 classification, there were 28 people (6.1%) in group A, 156 people (34.1%) in group B, 55 people (12%) in group C and 218 people (47.8%) in group D. With this new comprehensive assessment, 5 people (1.09%) and 61 people (13.3%) were regrouped from group C to A and from group D to B, respectively. According to both year criteria, the number of patients in group D was the highest and group A was the lowest.

Demographic and clinical characteristics as determined by GOLD 2011 and GOLD 2017 classification

The final analyzed patients were classified according to GOLD 2011 and 2017 criteria as shown in Table 1. The mean age of the final analyzed patients in this study was 65.3 ± 10.2. People from group A had the lowest mean age, followed by group C, D and B. Most participants were male and the ratio of men to women was approximately 9.5:1 with 100% of men in group A and over 92% in the remaining groups. In addition, the number of people who were in the high-risk group (group C or D) had one of the symptoms was 3-4 times or 1.5-2 times higher than those in the low risk group (group A or B) according to GOLD 2011 and 2017, respectively.

Pharmacotherapy as determined by GOLD 2011 and GOLD 2017

For single medication, LABA was the most common drug with 17.5% overall used (80/457 patients) and approximately 40% in group A or B according to both year assessment criteria (Table 1). However, no single ICS was found. In terms of dual treatment, patients prescribed with LAMA + LABA accounted for 35.4% (162/457 patients) of the total medications and nearly 50% of patients in group C. Triple treatment, LAMA + LABA + ICS was most found in patients of the old group and new group D with 33.3% and 40.4%, respectively. The percentage of patients treated with SABA or SABA+SAMA was very small (2.6%).

Reclassified *versus* non-reclassified patients

According to the 2017 criteria, our study compared characteristics of reclassified patients from C to A (CA) with patients remained in group A (AA) or group C (CC); and reclassified patients from D to B (DB) with patients remained in group B (BB) or group D (DD). The information was shown in Table 2 and Table 3. In Table 2, there were 5 patients transferred from C to A according to the GOLD 2017 assessment. All of them were male and they had FVC% pred, FEV_1%pred and FEV_1/FVC significantly lower than the patients remained in the original group AA ($p<0.05$). None of the reclassified patients was prescribed drugs contained LAMA components. No statistically significant difference was found between group CA and AA in age, BMI and pharmacologic therapy. In terms of groups B and D, 61 patients were transferred from D to B, accounting for 64.2% (61/95 patients) of patients remained in group B (Table 3). The DB patients were younger (mean = 62.4 ± 9.68, $p=0.026$) and had lower FVC% pred ($p=0.001$), FEV_1%pred ($p<0.001$) and FEV_1/FVC ($p=0.002$) compared to patients group BB and DD. There was an association between the pharmacologic therapy and people from group DB and DD ($p<0.001$) but not BB ($p=0.073$). Dual or triple treatments with LAMA components were

mostly found in DB (LABA+LAMA: 42.6%) and DD group (LAMA+LABA+ICS: 40.4%), while single treatment with LABA was mostly found in BB group (45.3%).

Discussion

In this retrospective study, we described the demographic, clinical and pharmacotherapy of 457 patients as determined by GOLD 2011 and GOLD 2017 criteria. We also noticed differences between the patients' characteristics in the reclassified group and those in the non-reclassified group.

According to GOLD 2017 criteria, the percentage of patients in group D made up nearly half of the studied population (47.8%), followed by group B (34.2%), group C (12.0%) and group A (6.1%). This distribution was in accordance with a cross-sectional study of Cui et al. in China: group D (48.4%), group B (44.8%), group C (1.2%) and group A (5.6%) [9]. Other studies found different trends with patients in group D less than 20% and group B more than 50% [6, 10-12]. In contrast, group A was the most prevalent group in a prospective, ongoing cohort in Spain and US [6]. Different populations and study methods might be the main reasons for unequal distribution between A-D groups [9].

Approximately 15% of patients were reclassified from the high-risk to low-risk group. Meanwhile, a total of 22.6% -32.7% reclassified patients had been analyzed by several studies with sample sizes ranging from 571 to 1880 (Supplementary table 3) [6, 7, 13, 14]. Our low rate could be due to the level of the Medical Center. Our sampling was carried out at a tertiary-level hospital where there were patients with severe symptoms [15]. This argument was supported in a 3-year observational study in Netherlands, 56.6% of COPD patients (293/518 patients) experienced over 2 exacerbations/year visited tertiary care, while only 36% and 8% of them visited secondary and primary care, respectively [16]. In addition, through epidemiological data, most of the patients lived outside Ho Chi Minh City (84.9%) indicating treatment failure in primary or secondary care. Therefore, when evaluating the difference between GOLD 2011 and 2017, the percentage of patients shifted from group D to B or C to A was not as high as in other studies because patients with over 2 exacerbations/year were not effective. It also meant that the medical systems significantly influenced the distribution of ABCD patients [10, 15].

In terms of gender, male patients constituted nearly 95% of the COPD population. This finding was consistent with many Vietnam's COPD studies: 89.4% of male patients in the Clinical

Research Center of Lam Dong Medical College from 2015 to 2017, 89.9% of male patients in Ha Noi National Lung Hospital in 2017, 84.4% of male patients in Bach Mai Hospital in 2016 [17-19]. Compared to several East Asia studies, the percentage of male patients was also high: 90.6% in China 2016-2018, 94.5% in Taiwan 2012-2013 and 90% in Japan 2015-2017 [9, 10, 20]. Smoking was believed as a crucial risk factor for COPD [21-24]. In western regions, the number of smoking women was considerably high which could be equal to the number of smoking men in some areas [25]. This resulted in the equivalent gender proportion of COPD patients [25]. The smoking status could also be applied for explaining the high percentage of COPD male participants in Asia regions. In China, Zhang *et al*. demonstrated COPD men smoked more than women ($p<0.001$) and this result was supported by the high percentage of COPD men (64.2%) to women (35.8%) [26]. In Vietnam, a nationally representative survey was launched to evaluate the trends of tobacco use in 2010 and 2015 [27]. In both years, the percentage of male smokers was remarkably higher than female smokers (47.4%:1.4% in 2010 and 45.3%:1.1% in 2015) [27]. This was likely to be the reason why in our study, the percentage of COPD male participants was over 90%.

The mean age of our target population was roughly 65.3±10.2 with older participants in group B (65.8±10.5) or D (65.5±9.82). Several studies in Vietnam also agree with our finding: 63.9±8.5 in the study of Nguyen *et al*. about dietary intake and anthropometry of COPD patients, 66.6±8.2 in Nguyen *et al*.'s research on the pharmaceutical care for COPD patients [17,19]. Our results were also in agreement with the many articles in China (62.4±8.4), the UK (69.2±10.6) and Denmark (65.4±10·9) [9,28,29]. However, higher mean age was found in a retrospective study on 1053 patients (72.8±9.6) in Taiwan or a prospective observational study in Japan (at least 73.3±6.8 among 4 groups ABCD) [10,20]. The difference in the age value could be explained by several factors: the living quality, health care system in each country or the target population [9,10,20,28,29].

Participants were divided into 4 subgroups: 40-49, 50-59, 60-69 and over 70. It was clear that patients over 60 accounted for 71.5% of the total participants (Table 1 and supplementary Table 1). In 2022, Yang *et al*. used 4 survival Cox models to explain the COPD risk probability associated with age and concluded that people without COPD under 60 years old only suffered a mild risk (0-0.25) of getting COPD [30]. The risk rank of getting COPD leveled up every 5 years after 65 years old for COPD stage 1 and after 70 years old for COPD stage 2/3/4 [30]. This finding could explain why most participants were over 60 years old and were in a later

stage (stage 2/3/4) of COPD.

Regarding pharmacologic therapy, treatment was considerably different across ABCD groups. Among 457 patients (table 1), the number of participants prescribed LAMA+LABA made up the largest proportion at 35.4%, followed by LAMA+LABA+ICS with 22.8%. The rate of using LABA was 3 times higher than that of LAMA (17.5% vs 5%). Meanwhile, several articles summarized that LAMA was more popular than LABA: 1.7 times in Europe, 4 times in Japan and 6.6 times in Taiwan [10, 13, 20]. The physician's drug choice was influenced by the benefits of LAMA over LABA: prevention of COPD exacerbation, high trough FEV_1 and low risk of adverse events [31]. The adverse trend in our study might be due to the low price of LABA compared to LAMA (in Vietnam the price of LABA is half the price of LAMA).

Most medications followed the GOLD 2017 guidelines but there were still exceptions. Although ICS was only recommended for high-risk group (group C-D patients – supplementary table 2), roughly 20% of low-risk group (group A-B) was prescribed with ICS components: LABA+ICS (15.8%) and LAMA+LABA+ICS (3.8%) [1]. Overtreatment with ICS was also observed in several studies [9,10,20,32]. Most COPD patients were prescribed based on their real-life practice rather than GOLD treatment recommendations due to clinicians' unfamiliarity with guidelines, disbelief in treatment efficacy and overall patients' presentations [9,10,32,33]. Besides, ICS+LABA is the cheapest combination controller in Vietnam.

This might be one of the first studies in Vietnam that compared the people from the reclassified group to people who remained in the original groups. We noticed that people in group DB were younger and had lower FVC% pred ($p=0.001$), FEV_1% pred ($p<0.001$) and FEV_1/FVC (Pp=0.002) than people in groups B or in group D ($p<0.001$). In 2019, Cui *et al*. also found a difference in people between group DB and DD ($p<0.001$) but no group BB was compared [9]. In addition, people reclassified from group C to A were also significantly different from those who remained in group A in terms of FVC% pred ($p=0.003$), FEV_1% pred ($p=0.001$) and FEV_1/FVC ($p=0.002$). These differences would create discordance between groups according to GOLD 2017 standards (including patients from groups C and D who were reclassified to A and B and patients remained in the original groups according to GOLD 2011). Our findings suggested that the 2017 GOLD classification could underestimate the risk of exacerbations in patients with poor respiratory function. Although exacerbation history was a major factor and played a crucial role in the prognosis of future exacerbations, the mMRC score and the degree

of airway limitation were also risk factors for future exacerbations [34,35]. In addition, taking the history of exacerbation was not always easy in low-middle income countries where electronic medical records and the connection among health centers were lacking. Consequently, it might be difficult for clinicians to classify patients based on the GOLD 2017 assessment.

Our study had several limitations. First, the retrospective study was significantly influenced by the recorded data and the potential for bias [10]. Several common variables were missed in our analysis: educational level, smoking history, smoking pack per year, etc. [10]. Second, the availability of drugs or the clinicians' familiarity with the new guidelines should be considered [9,10]. They might affect the drug choice of clinicians and explain the discordance between guidelines and real-life practice. Third, our study was conducted at a tertiary hospital and most patients resided outside Ho Chi Minh City. As a consequence, the findings couldn't represent the Ho Chi Minh City population.

Conclusions

This is the first study in Viet Nam demonstrated the distribution of COPD patients according to both GOLD 2011 and 2017 standards. In addition, we also confirmed 14% of patients were reclassified from high-risk groups to low-risk groups. Besides, there was a discordance of medications between guidelines and real-life practice. Continuous changes in criteria for defining COPD and its severity is largely inconsistent and not based on true clinical criteria. Therefore, clinicians should use their clinical competence to consider patients' conditions before deciding the appropriate therapeutic approach. Consequently, further studies were required to evaluate the effect of the GOLD 2017 classification.

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Table 1. COPD patient characteristics as determined by the GOLD 2011 and GOLD 2017

Subjects	Total	GOLD 2011					GOLD 2017				
		A	B	C	D	p-value	A	B	C	D	p-value
	n=457	n=23	n=95	n=60	n=279		n=28	n=156	n=55	n=218	
Age (years), mean ± SD	65.3±10.2	62.3±10.6	68.1±10.5	64.2±10.4	64.8±9.86	0.016	62.2±11.4	65.8±10.5	64.4±9.96	65.5±9.82	0.313
Age group, n (%)						0.093					0.099
40-49	28 (6.1)	3 (13.0)	5 (5.26)	4 (6.67)	16 (5.73)		4 (14.3)	9 (5.77)	3 (5.45)	12 (5.50)	
50-59	102 (22.3)	6 (26.1)	16 (16.8)	17 (28.3)	63 (22.6)		8 (28.6)	40 (25.6)	15 (27.3)	39 (17.9)	
60-69	167 (36.5)	9 (39.1)	27 (28.4)	23 (38.3)	108 (38.7)		9 (32.1)	45 (28.8)	23 (41.8)	90 (41.3)	
>=70	160 (35.0)	5 (21.7)	47 (49.5)	16 (26.7)	92 (33.0)		7 (25.0)	62 (39.7)	14 (25.5)	77 (35.3)	
Male, n (%)	433 (94.7)	23 (100)	88 (92.6)	59 (98.3)	263 (94.3)	0.373	28 (100)	145 (92.9)	54 (98.2)	206 (94.5)	0.352
BMI°	21.1 (4.94)	20.8 (4.05)	21.4 (4.34)	21.3 (4.23)	20.7 (5.22)	0.551	21.1 (5.34)	21.1 (4.78)	21.3 (4.18)	20.6 (5.30)	0.739
BMI classification, n (%)						0.996					0.966
Underweight	109 (23.9)	4 (17.4)	21 (22.1)	13 (21.7)	71 (25.4)		5 (17.9)	37 (23.7)	12 (21.8)	55 (25.2)	
Normal	207 (45.3)	12 (52.2)	43 (45.3)	28 (46.7)	124 (44.4)		13 (46.4)	73 (46.8)	27 (49.1)	94 (43.1)	
Overweight	76 (16.6)	4 (17.4)	17 (17.9)	11 (18.3)	44 (15.8)		5 (17.9)	22 (14.1)	10 (18.2)	39 (17.9)	
Obese	65 (14.2)	3 (13.0)	14 (14.7)	8 (13.3)	40 (14.3)		5 (17.9)	24 (15.4)	6 (10.9)	30 (13.8)	
Dyspnea, n (%)	370 (81.0)	13 (56.5)	70 (73.7)	47 (78.3)	240 (86.0)	0.001	18 (64.3)	120 (76.9)	42 (76.4)	190 (87.2)	0.005
Cough, n (%)	378 (82.7)	15 (65.2)	74 (77.9)	49 (81.7)	240 (86.0)	0.034	18 (64.3)	125 (80.1)	46 (83.6)	189 (86.7)	0.02
Sputum, n (%)	352 (77.0)	11 (47.8)	68 (71.6)	46 (76.7)	227 (81.4)	0.001	14 (50.0)	112 (71.8)	43 (78.2)	183 (83.9)	<0.001
Wheezing, n (%)	334 (73.1)	9 (39.1)	60 (63.2)	40 (66.7)	225 (80.6)	<0.001	12 (42.9)	103 (66.0)	37 (67.3)	182 (83.5)	<0.001
FVC% pred°	70.0 (24.0)	86.0 (18.0)	80.0 (21.0)	68.0 (26.3)	64.0 (22.0)	<0.001	80.5 (20.5)	71.0 (22.0)	70.0 (26.0)	66.5 (23.0)	<0.001
FEV1% pred°	50.0 (24.0)	67.0 (14.0)	61.0 (17.0)	45.5 (18.5)	43.0 (18.0)	<0.001	65.5 (17.8)	54.5 (22.0)	46.0 (20.5)	44.0 (19.8)	<0.001
FEV1/FVC°	53.0 (13.0)	61.0 (7.00)	58.0 (10.0)	52.0 (15.0)	51.0 (11.0)	<0.001	60.0 (9.00)	55.5 (11.0)	53.0 (14.5)	52.0 (11.0)	<0.001
Pharmacologic therapy, n (%)											
LABA	80 (17.5)	10 (43.5)	43 (45.3)	3 (5.0)	24 (8.6)		11 (39.3)	59 (37.8)	2 (3.6)	8 (3.7)	
LAMA	23 (5.0)	1 (4.3)	8 (8.4)	4 (6.7)	10 (3.6)		1 (3.6)	11 (7.1)	4 (7.3)	7 (3.2)	
LABA+ICS	76 (16.6)	5 (21.7)	11 (11.6)	13 (21.7)	47 (16.8)		8 (28.6)	21 (13.5)	10 (18.2)	37 (17.0)	
LAMA+LABA	162 (35.4)	1 (4.3)	30 (31.6)	29 (48.3)	102 (36.6)		1 (3.6)	56 (35.9)	29 (52.7)	76 (34.9)	
SABA/SABA+ SAMA	12 (2.6)	6 (26.1)	1 (1.1)	2 (3.3)	3 (1.1)		7 (25.0)	2 (1.3)	1 (1.8)	2 (0.9)	
LAMA+LABA+ ICS	104 (22.8)	0 (0)	2 (2.1)	9 (15.0)	93 (33.3)		0 (0)	7 (4.5)	9 (16.4)	88 (40.4)	
GOLD stage, n (%)											
Stage 1	36 (7.9)	5 (21.7)	17 (17.9)	4 (6.67)	10 (3.58)		5 (17.9)	17 (10.9)	4 (7.27)	10 (4.59)	
Stage 2	194 (42.5)	18 (78.3)	78 (82.1)	20 (33.3)	78 (28.0)		18 (64.3)	78 (50.0)	20 (36.4)	78 (35.8)	
Stage 3	190 (41.6)	0 (0.00)	0 (0.00)	29 (48.3)	161 (57.7)		3 (10.7)	54 (34.6)	26 (47.3)	107 (49.1)	

Subjects	Total	GOLD 2011					GOLD 2017				
	n=457	A n=23	B n=95	C n=60	D n=279	p-value	A n=28	B n=156	C n=55	D n=218	p-value
Stage 4	37 (8.1)	0 (0.00)	0 (0.00)	7 (11.7)	30 (10.8)		2 (7.14)	7 (4.49)	5 (9.09)	23 (10.6)	

Categorical data were shown as frequencies (percentage). Normally distribution data were shown as means ± SD. Non-normal distribution data were expressed as medians (interquartile range); °: Non-normal distribution data; GOLD, Global Initiative for Chronic Obstructive Pulmonary Disease; SD, standard deviation; BMI, body mass index; FVC% pred, percentage of forced vital capacity; FEV1%pred, percentage of forced expiratory volume in the first second; LABA, long-acting beta agonists; ICS, inhaled corticosteroid; LAMA, long-acting muscarinic antagonist; SABA, short-acting beta agonists; SAMA, short-acting muscarinic antagonist.

Table 2. Characteristics of group A and C of reclassified versus non-reclassified patients according to GOLD 2017 criteria

Subjects	CA n=5	CC n=55	p-value	AA n=23	p-value
Age (years), mean ± SD	62.0 ± 16.1	64.4 ± 9.96	0.6317	62.3 ± 10.6	0.9641
Male, n (%)	5 (100%)	54 (98.2%)	1	23 (100%)	
BMI, mean ± SD	22.9 ± 3.88	21.2 ± 3.31	0.2904	21.6 ± 3.55	0.497
FVC% pred°	58.0 (8.00)	70.0 (26.0)	0.199	86.0 (18.0)	0.003
FEV_1% pred°	42.0 (16.0)	46.0 (20.5)	0.092	67.0 (14.0)	0.001
FEV_1/FVC°	48.0 (12.0)	53.0 (14.5)	0.12	61.0 (7.00)	0.002
Pharmacologic therapy, n (%)			0.009		0.589
LABA	1 (20.0%)	2 (3.64%)		10 (43.5%)	
LABA + ICS	3 (60.0%)	10 (18.2%)		5 (21.7%)	
LAMA	0 (0.00%)	4 (7.27%)		1 (4.35%)	
LAMA + LABA	0 (0.00%)	29 (52.7%)		1 (4.35%)	
LAMA + LABA + ICS	0 (0.00%)	9 (16.4%)		0 (0.00%)	
SABA/ SABA + SAMA	1 (20.0%)	1 (1.82%)		6 (26.1%)	

°Non-normal distribution data were expressed as medians (interquartile range). CA: patients reclassified from group C to A; CC: patients remained in group C; AA: patients remained in group A; SD, standard deviation; BMI, body mass index; FVC% pred, percentage of forced vital capacity; FEV_1%pred, percentage of forced expiratory volume in the first second; LABA, long-acting beta agonists; ICS, inhaled corticosteroid; LAMA, long-acting muscarinic antagonist; SABA, short-acting beta agonists; SAMA, short-acting muscarinic antagonist.

Table 3. Characteristics of groups B and D of reclassified *versus* non-reclassified patients according to GOLD 2017 criteria.

Subjects	DB n=61	DD n=218	p-value	BB n=95	p-value
Age (years), mean ± SD	62.4 ± 9.68	65.5 ± 9.82	0.026	68.1 ± 10.5	0.001
Male, n (%)	57 (93.4%)	206 (94.5%)	0.83	88 (92.6%)	0.883
BMI°	21.1 (4.45)	20.6 (5.30)	0.773	21.4 (4.34)	0.226
FVC% pred°	60.0 (13.0)	66.5 (23.0)	0.001	80.0 (21.0)	<0.001
FEV_1%pred°	39.0 (12.0)	44.0 (19.8)	<0.001	61.0 (17.0)	<0.001
FEV_1/FVC°	48.0 (10.0)	52.0 (11.0)	0.002	58.0 (10.0)	<0.001
GOLD_therapy:			<0.001		0.073
LABA	16 (26.2%)	8 (3.67%)		43 (45.3%)	
LABA + ICS	10 (16.4%)	37 (17.0%)		11 (11.6%)	
LAMA	3 (4.92%)	7 (3.21%)		8 (8.42%)	
LAMA + LABA	26 (42.6%)	76 (34.9%)		30 (31.6%)	
LAMA + LABA + ICS	5 (8.20%)	88 (40.4%)		2 (2.11%)	
SABA/ SABA + SAMA	1 (1.64%)	2 (0.92%)		1 (1.05%)	

°: Non-normal distribution data were expressed as medians (interquartile range). DB: patients reclassified from group D to B; DD: patients remained in group D; BB: patients remained in group B; SD, standard deviation; BMI, body mass index; FVC% pred, percentage of forced vital capacity; FEV_1%pred, percentage of forced expiratory volume in the first second; LABA, long-acting beta agonists; ICS, inhaled corticosteroid; LAMA, long-acting muscarinic antagonist; SABA, short-acting beta agonists; SAMA, short-acting muscarinic antagonist.