Classification of chronic obstructive pulmonary disease as ABCD according to the GOLD 2011 and 2017 versions in patients at the University Medical Center in Ho Chi Minh City, Vietnam

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Abstract

In 2017, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) substantially changed 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 in the GOLD classification in Vietnam. This retrospective analysis was conducted at the Asthma and Chronic Obstructive Pulmonary Disease (COPD) Clinic at the University Medical Center in Ho Chi Minh City, Vietnam. Our study population comprised patients visiting the medical center from January 2018 to January 2020. We categorized patients' demographics, 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%, respectively, and according to GOLD 2017, it 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 (groups A and B) was overtreated with inhaled corticosteroid (ICS) components: long-acting β-agonists (LABA) + ICS (15.8%) and long-acting muscarinic antagonist + 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 a lower predicted percentage of forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), and FEV_1/FVC than the patients who remained in groups 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. 14% of patients were reclassified from high-risk to low-risk groups when changing from the 2011 version to the 2017 one, and there was discordance of medications between guidelines and real-life practice. Therefore, clinicians should use their clinical competence to consider patients' conditions before deciding on the appropriate therapeutic approach. Consequently, further studies were required to evaluate the effect of the change in the GOLD classification.

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 Southeast Asia region, there were 15 million prevalent cases and 189 thousand deaths of COPD in 2019 [2]. Due to COPD morbidity and mortality, sev-

eral experts decided to launch a Global Initiative for Chronic Obstructive 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].

The classification of COPD is a cornerstone of its management. There have been three versions of the classification from 2001 to 2022. From 2001 to 2010, COPD was categorized as stages (I-IV) based on the predicted percentage of forced expiratory volume in the first second (FEV_1). 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 exacerbation history [4]. The first aim was to distinguish between high-level and low-level symptoms [4]. Patients with more symptoms had COPD assessment test 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 a severe ($30\% \leq FEV_1 < 50\%$ predicted) or very severe stage ($FEV_1 < 30\%$ predicted) were classified as high-risk [4]. For exacerbation history, people who had at least two exacerbations, or one that led to hospitalization, in the previous year were classified as high-risk [4]. If the risk category was inconsistent between airflow limitation and exacerbation 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 two parameters: symptoms and exacerbation history [1]. The 2017 version of the classification was still being used as the current version in 2022. The updated version of 2023 categorized groups C and D into group E, with E standing for exacerbation [5]. The current guideline for Vietnam still uses the GOLD 2017 classification in its category.

Since the change in 2017 impacted the classification of COPD, many studies have reported the effect of the new GOLD criteria. In Spain and the US, a study on 819 COPD patients demonstrated that several patients were reclassified from groups C-D to groups A-B [6]. In China, patients from the new high-risk group experienced a higher 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 groups A or B, compared to 87% when applying GOLD 2017 [8].

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

Materials and Methods

Study design

This study was a retrospective analysis conducted at the 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 in Ho Chi Minh City. The data collection process was permitted by the Department of Science and Training at UMC.

Participants

Patients were extracted from the list of COPD patients at UMC if they met the following criteria: i) COPD patients in the stable stage; ii) a post-bronchodilator ratio [FEV_1/forced vital capacity (FVC)] lower than 70%. This value indicated the persistence of airflow limitations, 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 Strengthening the Reporting of Observational Studies in Epidemiology guidelines for observational studies.

Variables

The dependent variables included the patients classified into A-D groups according to GOLD 2011 and 2017 criteria. We also compared the characteristics of reclassified patients from group C to group A (CA), with patients who remained in group A (AA) or group C (CC), and reclassified patients from group D to group B (DB), with patients who 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 FEV_1 (FEV_1% predicted), percentage of FVC (FVC% predicted), the ratio of FEV_1 to the FVC (FEV_1/FVC); pharmacologic therapy: long-acting β-agonist (LABA), long-acting muscarinic antagonist (LAMA), inhaled corticosteroid (ICS), short-acting β-agonist (SABA), short-acting muscarinic antagonist (SAMA). BMI was determined by dividing body weight (kg) by height (m^2). The 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 two visits, the latest visit data was collected.

Statistical analysis

Data were analyzed with SPSS version 22.0 (IBM Corporation, Armonk, NY, USA) and R software version 4.2.1 (The R Foundation for Statistical Computing, Vienna, Austria). Categorical data were expressed as frequencies (%), and normal distribution data were expressed as means ± standard deviation, while data with non-normal distribution were expressed as medians (interquartile range). For the parametric test, a student *t*-test or analysis of variance 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 $p<0.05$ was considered statistically significant.

Results

Study population

From January 2018 to January 2020, the hospital received a total of 6233 visits with a COPD diagnosis. However, the number

of patients that met our selection criteria was 457. 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, following 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 the Global Initiative for Chronic Obstructive Lung Disease 2011 and 2017 classification

The final analyzed patients were classified according to GOLD 2011 and 2017 criteria, as shown in Table 1. In this study, the final analyzed patients had a mean age of 65.3±10.2. People from group A had the lowest mean age, followed by groups C, D, and B. Most participants were male, and the ratio of men to women was approx-

Table 1. Chronic obstructive pulmonary disease patient characteristics as determined by the Global Initiative for Chronic Obstructive Lung Disease 2011 and 2017.

Subjects	Total	GOLD 2011					GOLD 2017				
		A	B	C	D	p	A	B	C	D	p
	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											
FEV_1% 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											
FEV_1/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)	
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 ± standard deviation. Non-normal distribution data were expressed as medians (interquartile range). °Non-normal distribution data; GOLD, Global Initiative for Chronic Obstructive Lung Disease; 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 β-agonists; ICS, inhaled corticosteroid; LAMA, long-acting muscarinic antagonist; SABA, short-acting β-agonists; SAMA, short-acting muscarinic antagonist.

imately 9.5:1, with 100% of men in group A and over 92% in the remaining groups. In addition, the number of people in the high-risk group (group C or D) who 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 the Global Initiative for Chronic Obstructive Lung Disease 2011 and 2017 criteria

For single medication, LABA was the most common drug, with 17.5% overall use (80/457 patients) and approximately 40% in groups A or B according to both year assessment criteria (Table 1). However, no single ICS was found. In terms of dual treatment, patients prescribed 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 common in patients in 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 the characteristics of CA patients, with AA or CC patients, and DB patients with BB or DD patients. The information is shown in Tables 2 and 3.

In Table 2, there were 5 patients transferred from C to A

Table 2. Characteristics of groups A and C of reclassified *versus* non-reclassified patients according to the Global Initiative for Chronic Obstructive Lung Disease 2017 criteria.

Subjects	CA n=5	CC n=55	p	AA n=23	p
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 β-agonists; ICS, inhaled corticosteroid; LAMA, long-acting muscarinic antagonist; SABA, short-acting β-agonists; SAMA, short-acting muscarinic antagonist.

Table 3. Characteristics of groups B and D of reclassified *versus* non-reclassified patients according to the Global Initiative for Chronic Obstructive Lung Disease 2017 criteria.

Subjects	DB n=61	DD n=218	p	BB n=95	p
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, n (%)			<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 β-agonists; ICS, inhaled corticosteroid; LAMA, long-acting muscarinic antagonist; SABA, short-acting β-agonists; SAMA, short-acting muscarinic antagonist.

according to the GOLD 2017 assessment. All of them were male, and they had FVC% predicted, FEV_1% predicted and FEV_1/FVC significantly lower than the patients who remained in the original group AA ($p<0.05$). None of the reclassified patients were prescribed drugs that contained LAMA components. No statistically significant difference was found between groups 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 who 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% predicted ($p<0.001$) 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 groups DB and DD ($p<0.001$) but not BB ($p=0.073$). Dual or triple treatments with LAMA components were mostly found in the DB (LABA+LAMA: 42.6%) and DD groups (LAMA+LABA+ICS: 40.4%), while single treatment with LABA was mostly found in the BB group (45.3%).

Discussion

In this retrospective study, we described the demographic, clinical, and pharmacotherapy characteristics of 457 patients as determined by the 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%), C (12.0%), and A (6.1%). This distribution was in accordance with a cross-sectional study by Cui *et al*. in China: group D (48.4%), B (44.8%), C (1.2%), and 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 the US [6]. Different populations and study methods might be the main reasons for the unequal distribution between A-D groups [9].

Approximately 15% of patients were reclassified from the high-risk to the low-risk group. Meanwhile, a total of 22.6-32.7% of reclassified patients had been analyzed by several studies with sample sizes ranging from 571 to 1880 (*Supplementary Table 1*) [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 the Netherlands: 56.6% of COPD patients (293/518 patients) experienced over two exacerbations per year and 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 who shifted from group D to B or C to A was not as high as in other studies because patients with over two exacerbations/year were not effective. It also meant that the medical system 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 of 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, and 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 to be 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 to explain the high percentage of COPD male participants in Asian 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 that of 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 male COPD participants was over 90%.

The mean age of our target population was roughly 65.3±10.2, with older participants in groups 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, a higher mean age was found in a retrospective study on 1053 patients (72.8±9.6) in Taiwan and in 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 quality of life, the health care system in each country, or the target population [9,10,20,28,29].

Participants were divided into four 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 2*). In 2022, Yang *et al*. used four 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 three times higher than that of LAMA (17.5% *versus* 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 groups (group C-D patients; *Supplementary Table 3*), roughly 20% of the low-risk groups (group A-B) were prescribed 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 those who remained in the original groups. We noticed that people in group DB were younger and had lower FVC% predicted (p=0.001), FEV_1% predicted (p<0.001), and FEV_1/FVC (p=0.002) than people in groups B or 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 group A were also significantly different from those who remained in group A in terms of FVC% predicted (p=0.003), FEV_1% predicted (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 who 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 exacerbations was not always easy in low- to 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 could not represent the Ho Chi Minh City population.

Conclusions

This is the first study in Vietnam that demonstrated the distribution of COPD patients according to both GOLD 2011 and 2017 standards. In addition, we also confirmed that 14% of patients were reclassified from high-risk 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 are largely inconsistent and not based on true clinical criteria. Therefore, clinicians should use their clinical competence to consider patients' conditions before deciding on the appropriate therapeutic approach. Consequently, further studies were required to evaluate the effect of the GOLD 2017 classification.

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Online supplementary material:

Supplementary Table 1. Percentage of the reclassified group in some studies.

Supplementary Table 2. Comparison of patients in different Global Initiative for Chronic Obstructive Lung Disease stages.

Supplementary Table 3. Comparison of patients between low-risk group (A-B) and high-risk group (C-D) according to Global Initiative for Chronic Obstructive Lung Disease 2017 criteria.