The characteristics of airflow obstruction and its association with treatment response in the real world in different GOLD groups of COPD patients

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Research

Keywords: Chronic obstructive pulmonary disease, Global Initiative for Chronic Obstructive Lung Disease, Pulmonary function, Exacerbation, Mortality.

Posted Date: January 15th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-145783/v1>

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Abstract

Background: The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 separated spirometry from combined assessment to guide treatment. We aimed to analyze the characteristics of airflow obstruction and its association with treatment response in the real world in different GOLD groups of COPD patients.

Methods: For this prospective observational study, stable COPD outpatients were enrolled and divided into Groups A, B, C and D based on GOLD 2017, and followed-up for 18 months. Data on patient demographics, pulmonary function, COPD assessment test (CAT), Clinical COPD Questionnaire (CCQ), modified Medical Research Council (mMRC), exacerbations, mortality and treatments were collected to analyze the airflow obstruction and its association with treatment response.

Results: A total of 993 subjects were classified into Groups A (n = 170, 17.1%), B (n = 360, 36.3%), C (n = 122, 12.3%), and D (n = 341, 34.3%). There were significant differences in mMRC, CAT, CCQ, exacerbations and hospitalizations among different groups ($P < 0.001$). Groups B and D had more airflow obstruction and ventilatory disorder than Groups A and C ($P < 0.05$). In the same groups with different GOLD grades, the differences were mainly observed in BMI, CAT, CCQ and treatment with long-acting muscarinic antagonist (LAMA) and LAMA + long-acting β_2 -agonist (LABA) + inhaled corticosteroid (ICS) ($P < 0.05$). After 18 months of follow-up, the number of exacerbations and hospitalizations were significantly different among different groups, with Group D having the highest values. Also, there were more frequent exacerbators and a higher mortality rate in Group D. However, in the same groups with different GOLD grades, the mortality rates and number of exacerbations, hospitalizations and frequent exacerbators showed no differences.

Conclusion: There were significant differences in pulmonary function in different groups. However, different GOLD grades had no impact on future exacerbations and mortality rate in the same groups.

Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease, characterized by respiratory symptoms and persistent airflow obstruction [1–2]. It is also the most serious chronic respiratory disease, and it becomes the fifth largest disease in the global economic burden and have the third largest fatality rate [3].

The goal of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) program is to produce recommendations for the management of COPD based on the best scientific information available. The first edition of GOLD was released in 2001 and has been revised annually [4]. Until 2011, GOLD evaluated COPD patients based on symptoms, degree of airflow obstruction, exacerbation risk. According to combined COPD assessment, patients were divided into Groups A, B, C and D [5]. However, compared with spirometry classification, the combined COPD assessment cannot better predict mortality and other important clinical outcomes [6–8]. Therefore, the GOLD 2017 revised the assessment tool and separated spirometry. ABCD groups were then only determined based on COPD assessment test (CAT) or modified Medical Research Council (mMRC), and exacerbation history [9].

Pulmonary function is an important parameter for evaluating airflow obstruction and severity in COPD patients. A post-bronchodilator ratio of forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) of < 0.70 can be interpreted as continuous airflow obstruction. FEV1 is an important pulmonary function parameter that most of the clinical trial evidence about treatment efficacy in COPD is based on [10–11]. Although GOLD 2017 separated spirometry from the old assessment tool, combining spirometry results with patient symptoms and exacerbation history remains vital for the diagnosis, treatment of COPD.

Kim et al. [12] found that there was no difference in the rate of decline in pulmonary function among different groups categorized by GOLD 2014 assessment tools. However, in the real world, the characteristics of airflow obstruction and its association with treatment response in different groups assessed according to GOLD 2017 is unclear.

Methods

Study design and subjects

This is a multicenter, prospective observational study, based on data collected as part of the Chronic Pulmonary Diseases Database setup by the Second Xiangya Hospital of Central South University (Registration number: ChiCTR-POC-17010431). Patients were enrolled from September 2017 to February 2019. All patients were followed-up for 18 months. According to criteria of GOLD 2017, COPD was confirmed when an FEV1/FVC ratio of < 0.70 was obtained, following the inhalation of 400 μg of salbutamol aerosol. Patients diagnosed with, or with a history of bronchiectasis, asthma, lung cancer or pneumonia were excluded from our study. This study was approved by the institutional ethics committee of the Second Xiangya Hospital of Central South University. All patients gave informed consent.

Data collection

The collected data included age, sex, education degree, body mass index (BMI), smoking history, biofuel and occupational exposure history, CAT, mMRC, Clinical COPD Questionnaire (CCQ), pulmonary function, exacerbations, hospitalizations and treatments. After 18 months of follow-up, data on exacerbations, hospitalizations and mortality were collected.

Definition of exacerbation

An exacerbation was defined as an acute worsening of respiratory symptoms that resulted in the need for additional therapy (including antibiotics, oral corticosteroids or require hospitalization) [13]. Frequent exacerbators were patients who suffered at least two exacerbations or one hospitalization per year or died [14].

Classification of combined COPD assessment

According to GOLD 2017, patients were assigned to four categories. Briefly, Group A, 0 to 1 exacerbation per year, no hospitalizations, CAT score < 10 or mMRC score of 0 to 1; Group B, CAT score ≥ 10 or mMRC score ≥ 2; Group C, exacerbations ≥ 2 or hospitalization ≥ 1 per year, and a CAT score < 10 or mMRC score of 0 to 1; Group D, CAT score ≥ 10 or mMRC score ≥ 2.

Classification of GOLD grades

GOLD grading was based on FEV1 % predicted as follows: GOLD grade I, ≥ 80 FEV1 % predicted; GOLD grade II, 50–79 FEV1 % predicted; GOLD grade III, 30–49 FEV1 % predicted; GOLD grade IV, < 30 FEV1 % predicted.

Pulmonary function test

Pulmonary function tests were measured by a spirometer (MasterScreen-Body/Diff, CareFusion, Germany). The following parameters were measured after a bronchodilator test: FEV1, FEV1 % predicted, FVC, FVC % predicted, FEV1/FVC, maximal expiratory flow (MEF) 25, MEF25 % predicted, MEF75, MEF75 % predicted, peak expiratory flow (PEF), PEF % predicted, and diastolic function test. The bronchodilator test was performed 20 minutes after inhaling 400 µg of salbutamol aerosol. The level of ventilatory disorder before a bronchodilator test was determined using the FEV1 % predicted value as follows: mild, ≥ 70 FEV1 % predicted; moderate, 60–69 FEV1 % predicted; moderately-severe, 50–59 FEV1 % predicted; severe, 35–49 FEV1 % predicted and very severe, < 35 FEV1 % predicted [15].

Statistical analysis

Statistical analyses were performed using SPSS 26 (IBM Corporation, Armonk, NY, USA). The data was expressed as the mean ± standard deviation, or as the median and interquartile range. The Pearson's chi-squared test was used to analyze categorical variables. Comparisons of continuous variables were performed using independent-samples t-test or one-way analysis. The least significant difference (LSD) t-test was used for pairwise comparisons. The non-parametric test was used for non-normal distribution or uneven variance. P values < 0.05 were considered statistically significant.

Results

Baseline demographic and clinical characteristics (N = 993)

993 patients were analyzed in this study (Fig. 1). According to GOLD 2017, 170 (17.1%), 360 (36.3%), 122 (12.3%) and 341 (34.3%) patients were allocated to Groups A, B, C and D, respectively. The data on demographic and clinical characteristics are shown in the Table 1. The mean age of the enrolled patients from Groups A to D were 61.5 ± 7.9, 65.1 ± 8.1, 63.0 ± 9.1 and 66.8 ± 8.0 years and were significantly different (P < 0.001). There were more current smokers in the Groups A and C (P < 0.05). There were higher CAT and CCQ scores in Groups B and D (P < 0.05). The proportion of LAMA was higher in Groups A and C, while LAMA + LABA + ICS was higher in Groups B and D (P < 0.05). There were higher numbers of exacerbations and hospitalizations in Groups C and D (P < 0.05). The proportions of patients in Groups A, B, C and D that suffered an exacerbation once per year were 13.5%, 13.1%, 50.8% and 26.7%, respectively, while the proportion of patients suffering exacerbations at least twice per year in Groups C and D were 49.2% and 3.3%. The proportion of patients who were never hospitalized in Groups A, B, C and D were 100%, 100%, 28.7% and 31.4%, respectively. However, the proportions of patients who were hospitalized at least once per year were 71.3% in Groups C and 68.6% in Group D.

Table 1
The distribution of baseline demographic and clinical characteristics in different groups (N = 993).

Variables	Group A (n = 170)	Group B (n = 360)	Group C (n = 122)	Group D (n = 341)	P- value
Age (years)	61.5 ± 7.9 *, &	65.1 ± 8.1 ¶	63.0 ± 9.1 ♦	66.8 ± 8.0 ▲	< 0.001
Sex, n (%)					0.488
Male	149 (87.6)	320 (88.9)	113 (92.6)	299 (87.7)	
Female	21 (12.4)	40 (11.1)	9 (7.4)	42 (12.3)	
Education, n (%)					
Primary school	59 (34.7) *, #, &	148 (41.1)	56 (45.9) ♦	160 (46.9) ▲	0.050
Junior high school	57 (33.5)	132 (36.7)	48 (39.3)	120 (35.2)	0.751
High school	36 (21.2) *, #, &	63 (17.5) ¶	11 (9.0) ♦	47 (13.8) ▲	0.021
University	18 (10.6) *, #, &	17 (4.7) ¶	7 (5.8) ♦	14 (4.1)	0.019
BMI (kg/m ²)	23.13 ± 3.57	22.70 ± 3.87	22.55 ± 3.44	22.24 ± 3.71	0.071
Smoke history, n (%)					
Never-smoker	30 (17.6)	65 (18.0)	19 (15.6)	69 (20.2)	0.681
Ex-smoker	43 (25.3)	119 (33.1)	36 (29.5)	126 (37.0)	0.054
Current-smoker	97 (57.1) *, &	176 (48.9) ¶	67 (54.9) ♦	146 (42.8) ▲	0.010
Smoke (pack/year) (Median, IQR)	30 (30)	32 (30)	36.5 (31.25)	30 (30)	0.357
Biofuel exposure, n (%)					< 0.001
Yes	43 (25.3) *, #, &	147 (40.8)	49 (40.2)	161 (47.2)	
No	127 (74.7) *, #, &	213 (59.2)	73 (59.8)	180 (52.8)	
Occupational exposure, n (%)					0.471
Yes	59 (34.7)	131 (36.4)	52 (42.6)	134 (39.3)	
No	111 (65.3)	229 (63.6)	70 (57.4)	207 (60.7)	
CAT (Mean ± SD)	10.32 ± 4.80 *, #, &	16.61 ± 5.09 ¶	13.57 ± 5.03 ♦	19.21 ± 5.78 ▲	< 0.001
mMRC (Median, IQR)	1 (0) *, &	2 (1) ¶	1 (0) ♦	3 (1) ▲	< 0.001
CCQ (Mean ± SD)	15.85 ± 5.89 *, #, &	22.80 ± 5.71 ¶	19.20 ± 5.73 ♦	25.45 ± 5.80 ▲	< 0.001
Treatments, n (%)					

Notes: * P < 0.05 versus group B, # P < 0.05 versus group C, & P < 0.05 versus group D, ¶ P < 0.05 versus group C, ♦ P < 0.05 versus group D, ▲ P < 0.05 versus group B.

Variables	Group A (n = 170)	Group B (n = 360)	Group C (n = 122)	Group D (n = 341)	P- value
Any COPD medication	157 (92.4) *, #, &	351 (97.5) ¶	115 (94.3)	328 (96.2) ▲	0.039
LAMA	87 (51.2) *, &	123 (34.2) ¶	60 (49.2) ◆	111 (32.6)	< 0.001
LABA + ICS	12 (7.1)	33 (9.2)	10 (8.2)	18 (5.3)	0.257
LAMA + LABA	1 (0.6)	2 (0.6)	0 (0)	4 (1.2)	0.716
LAMA + LABA +ICS	55 (32.6) *, &	190 (52.8) ¶	43 (35.3) ◆	195 (57.2)	< 0.001
Exacerbations in the past year, (Mean ± SD)	0.14 ± 0.34 #, &	0.13 ± 0.34 ¶	2.46 ± 2.55 ◆	3.46 ± 4.10 ▲	< 0.001
Exacerbations in the past year, n (%)					< 0.001
0	147 (86.5) #, &	313 (86.9) ¶	0 (0)	0 (0) ▲	
1	23 (13.5) #, &	47 (13.1) ¶	62 (50.8) ◆	91 (26.7) ▲	
≥ 2	0 (0) #, &	0 (0) ¶	60 (49.2) ◆	250 (73.3) ▲	
Hospitalizations in the past year (Mean ± SD)	0 #, &	0 ¶	0.94 ± 1.00	1.38 ± 1.49 ▲	< 0.001
Hospitalizations in the past year, n (%)					< 0.001
0	170 (100) #, &	360 (100) ¶	35 (28.7)	107 (31.4) ▲	
≥ 1	0 (0) #, &	0 (0) ¶	87 (71.3)	234 (68.6) ▲	
Notes: * P < 0.05 versus group B, # P < 0.05 versus group C, & P < 0.05 versus group D, ¶ P < 0.05 versus group C, ◆ P < 0.05 versus group D, ▲ P < 0.05 versus group B.					

Characteristics of pulmonary function

As shown in Table 2, there were significant differences across Groups A to D in FEV1, FEV1 %predicted, FVC, FVC %predicted, FEV1/FVC, MEF 25, MEF25 %predicted, MEF75, MEF75 %predicted, PEF and PEF % predicted (P < 0.001). Groups B and D had a heavier airflow obstruction than Groups A and C. Also, the proportion of patients with mild and moderate ventilatory disorder was higher in Groups A and C, while the proportion of patients with very severe disorder was higher in Groups B and D (P < 0.05). Similarly, the proportion of GOLD grade I to IV patients was significantly different across Groups A to D (P < 0.001). The proportion of GOLD grades I and II patients were higher in Group A, while GOLD grades III and IV were higher in Group D (P < 0.05).

Table 2
Characteristics of pulmonary function in different groups (N = 993).

Variables	Group A (n = 170)	Group B (n = 360)	Group C (n = 122)	Group D (n = 341)	P-value
FEV1 (L)	1.71 ± 0.57 *, #, &	1.21 ± 0.49 ¶	1.56 ± 0.64 ♦	1.08 ± 0.57 ▲	< 0.001
FEV1 (% predicted)	65.74 ± 18.44 *, #, &	49.72 ± 18.78 ¶	59.42 ± 22.18 ♦	45.71 ± 18.20 ▲	< 0.001
FEV1/FVC	54.53 ± 10.51 *, #, &	44.67 ± 12.53 ¶	50.59 ± 12.68 ♦	42.95 ± 11.81 ▲	< 0.001
FVC (L)	3.09 ± 0.76 *, &	2.70 ± 0.65 ¶	3.01 ± 0.80 ♦	2.49 ± 0.71 ▲	< 0.001
FVC (% predicted)	95.20 ± 17.29 *, &	86.57 ± 17.38 ¶	91.25 ± 18.45 ♦	82.35 ± 18.77 ▲	< 0.001
MEF25	0.32 ± 0.30 *, #, &	0.23 ± 0.27 ¶	0.30 ± 0.20 ♦	0.21 ± 0.18 ▲	< 0.001
MEF25 (% predicted)	26.14 ± 15.36 *, &	21.91 ± 14.23	24.32 ± 14.94 ♦	20.62 ± 14.88	< 0.001
MEF75	2.54 ± 1.55 *, #, &	1.46 ± 1.12 ¶	1.12 ± 1.44 ♦	1.21 ± 0.99 ▲	< 0.001
MEF75 (% predicted)	38.46 ± 23.48 *, #, &	22.88 ± 17.12 ¶	32.01 ± 21.89 ♦	19.16 ± 16.70 ▲	< 0.001
PEF (L/s)	4.47 ± 1.85 *, #, &	3.25 ± 1.32 ¶	4.02 ± 1.58 ♦	2.90 ± 1.33 ▲	< 0.001
PEF (%predicted)	62.12 ± 23.83 *, #, &	46.88 ± 18.77 ¶	54.43 ± 20.45 ♦	42.51 ± 19.44 ▲	< 0.001
Ventilatory disorder, n (%)					
Mild	44 (25.9) *, &	38 (10.6) ¶	27 (22.1) ♦	24 (7.0)	< 0.001
Moderate	44 (25.9) *, &	41 (11.4) ¶	23 (18.9) ♦	25 (7.4)	< 0.001
Moderately-severe	33 (19.4)	56 (15.5)	23 (18.8)	54 (15.8)	0.609
Severe	38 (22.4)	100 (27.8)	24 (19.7)	91 (26.7)	0.230
Very severe	11 (6.4) *, #, &	125 (34.7) ¶	25 (20.5) ♦	147 (43.1) ▲	< 0.001
Diastolic function Test, n (%)					0.121
Positive	22 (12.9)	52 (14.4)	17 (13.9)	30 (8.8)	
Negative	148 (87.1)	308 (85.6)	105 (86.1)	311 (91.2)	
GOLD grade, n (%)					
I	37 (21.7) *, &	26 (7.2) ¶	21 (17.2) ♦	18 (5.3)	< 0.001
II	104 (61.2) *, #, &	148 (41.1)	57 (46.7) ♦	105 (30.8) ▲	< 0.001

Notes: * P < 0.05 versus group B, # P < 0.05 versus group C, & P < 0.05 versus group D, ¶ P < 0.05 versus group C, ♦ P < 0.05 versus group D, ▲ P < 0.05 versus group B.

Variables	Group A (n = 170)	Group B (n = 360)	Group C (n = 122)	Group D (n = 341)	P-value
III	26 (15.3) *, #, &	130 (36.1)	33 (27.1) ♦	149 (43.7) ▲	< 0.001
IV	3 (1.8) *, #, &	56 (15.6) ¶	11 (9.0) ♦	69 (20.2) ▲	< 0.001
Notes: * P < 0.05 versus group B, # P < 0.05 versus group C, & P < 0.05 versus group D, ¶ P < 0.05 versus group C, ♦ P < 0.05 versus group D, ▲ P < 0.05 versus group B.					

Table 3
Differences in baseline demographic and clinical characteristics for different GOLD grades in Groups A, B, C and D (N = 993).

	Group A (n = 170)		P-	Group B (n = 360)		P-	Group C (n = 122)		P-	Group D (n = 341)		P-
Variables	GOLD		value	GOLD		value	GOLD		value	GOLD		value
	I- II (n = 141)	III-IV (n = 29)		I- II (n = 174)	III-IV (n = 186)		I- II (n = 78)	III-IV (n = 44)		I- II (n = 123)	III-IV (n = 218)	
Age (years)	61.0 ± 7.6	64.0 ± 8.8	0.059	66.4 ± 8.2	63.8 ± 7.9	0.003	62.9 ± 9.3	63.3 ± 8.8	0.844	66.7 ± 8.5	66.2 ± 7.7	0.108
Sex, n (%)			0.027			0.057			0.486			0.096
Male	120 (85.1)	29 (100)		149 (83.3)	171 (92.9)		71 (91.0)	42 (95.4)		103 (83.7)	196 (89.9)	
Female	21 (14.9)	0 (0)		25 (16.7)	15 (7.5)		7 (9.0)	2 (4.6)		20 (16.3)	22 (10.1)	
Education, n (%)			0.002			0.276			0.595			0.024
Primary school	45 (31.9)	14 (47.3)		80 (48.0)	68 (37.8)		36 (46.2)	20 (45.5)		71 (57.7)	89 (40.8)	
Junior high school	49 (34.8)	8 (27.6)		57 (33.3)	75 (40.4)		32 (41.0)	16 (36.4)		33 (26.8)	87 (39.9)	
High school	32 (22.7)	4 (13.8)		28 (13.3)	35 (17.9)		5 (6.4)	6 (13.6)		14 (11.4)	33 (15.2)	
University	15 (10.6)	3 (10.3)		9 (5.4)	8 (3.9)		5 (6.4)	2 (4.5)		5 (4.1)	9 (4.1)	
BMI (kg/m ²)	23.42 ± 3.50	21.69 ± 3.58	0.017	23.65 ± 3.50	21.82 ± 3.84	< 0.001	23.04 ± 3.54	21.67 ± 3.10	0.034	22.97 ± 3.79	21.65 ± 3.54	0.006
Smoke history, n (%)			0.235			0.098			0.302			0.321
Never-smoker	28 (19.9)	2 (6.9)		35 (20.1)	30 (16.1)		15 (19.2)	4 (9.1)		27 (22.0)	42 (19.3)	
Ex-smoker	34 (24.1)	9 (31.0)		48 (27.6)	71 (38.2)		21 (26.9)	15 (34.1)		39 (31.7)	87 (39.9)	
Current-smoker	79 (56.0)	18 (62.1)		91 (52.3)	85 (45.7)		42 (53.9)	25 (56.8)		57 (46.3)	89 (40.8)	
Smoke (pack/year) (Median, IQR)	30 (36.5)	40 (30)	0.248	30 (30)	34.5 (40)	0.376	36.5 (40)	35.5 (40)	0.236	30 (30)	30 (32)	0.322
Biofuel exposure, n (%)			0.875			0.676			0.201			0.181
Yes	36 (25.5)	7 (24.1)		73 (40.7)	74 (41.0)		28 (35.9)	21 (47.7)		64 (52.0)	97 (44.5)	
No	105 (74.5)	22 (75.9)		101 (59.3)	112 (59.0)		50 (64.1)	23 (52.3)		59 (48.0)	121 (55.5)	
Occupational exposure, n (%)			0.689			0.945			0.392			0.317
Yes	48 (34.0)	11 (37.9)		63 (35.3)	68 (37.8)		31 (39.7)	21 (47.7)		44 (35.7)	90 (41.3)	
No	93 (66.0)	18 (62.1)		111 (64.7)	118 (62.2)		47 (60.3)	23 (52.3)		79 (64.3)	128 (58.7)	

	Group A (n = 170)		P-	Group B (n = 360)		P-	Group C (n = 122)		P-	Group D (n = 341)		P-
CAT (Mean ± SD)	9.87 ± 4.67	12.52 ± 4.92	0.006	15.49 ± 4.76	17.66 ± 5.19	< 0.001	12.85 ± 4.86	14.86 ± 5.19	0.034	17.63 ± 5.32	20.10 ± 5.85	< 0.001
mMRC (Median, IQR)	1 (0)	1 (0)	0.814	2 (1)	3 (1)	< 0.001	1 (0)	1 (0)	0.046	3 (1)	3 (1)	< 0.001
CCQ (Mean ± SD)	15.18 ± 5.79	19.10 ± 5.29	0.001	21.60 ± 5.39	23.93 ± 5.79	< 0.001	18.15 ± 4.88	21.05 ± 6.66	0.007	23.80 ± 5.64	26.38 ± 5.69	< 0.001
Treatments, n(%)												
Any COPD medication	129 (91.5)	28 (96.6)	0.700	167 (96.0)	184 (98.7)	0.095	72 (90.3)	43 (97.7)	0.420	117 (95.1)	211 (96.8)	0.557
LAMA	77 (54.6)	10 (34.5)	0.048	87 (48.0)	36 (17.3)	< 0.001	49 (62.8)	11 (25.0)	< 0.001	69 (56.1)	42 (19.3)	< 0.001
LABA + ICS	11 (7.8)	1 (3.5)	0.693	18 (11.3)	15 (10.3)	0.454	7 (9.0)	3 (6.8)	0.677	7 (5.7)	11 (5.0)	0.798
LAMA+ LABA	1 (0.7)	0	1.000	0	2 (1.1)	0.499	0	0	-	0	4 (1.8)	0.301
LAMA+ LABA + ICS	38 (26.9)	17 (58.6)	0.001	60 (35.3)	130 (69.9)	< 0.001	14 (17.9)	29 (65.9)	< 0.001	40 (32.5)	154 (70.6)	< 0.001
Exacerbations in the past year (Mean ± SD)	0.13 ± 0.34	0.14 ± 0.35	0.964	0.13 ± 0.34	0.13 ± 0.34	0.930	2.32 ± 2.28	2.70 ± 2.98	0.427	3.39 ± 3.84	3.50 ± 4.24	0.820
Hospitalizations in the past year (Mean ± SD)	0	0	-	0	0	-	0.92 ± 1.07	0.98 ± 0.88	0.775	1.34 ± 1.42	1.40 ± 1.53	0.712

Differences in demographic and clinical characteristics for different GOLD grades

Each group was then divided into two subgroups included GOLD I-II and III-IV. In Group A, the proportions of patients in GOLD I-II and III-IV were 82.9% and 17.1%, respectively, and there were significant differences between GOLD grade I-II and III-IV in sex, BMI, CAT, CCQ, treatment with LAMA and LAMA + LABA + ICS ($P < 0.05$). However, in Group B, the proportions of patients in GOLD I-II and III-IV were 48.3% and 51.7%, respectively, and there were significant differences in age, BMI, CAT, mMRC, CCQ, treatment with LAMA and LAMA + LABA + ICS ($P < 0.05$). The proportions of patients in GOLD I-II and III-IV were 63.9% and 36.1% in group C and there were significant differences in BMI, CAT, mMRC, CCQ, treatment with LAMA and LAMA + LABA + ICS ($P < 0.05$). In contrast, in Group D, the proportions of patients in GOLD I-II and III-IV were 36.1% and 63.9%, respectively, and there were significant differences in education degree, BMI, CAT, mMRC, CCQ, treatment with LAMA and LAMA + LABA + ICS between GOLD grade I-II and III-IV ($P < 0.05$).

Differences in future exacerbations and mortality in Groups A, B, C and D after 18 months of follow-up (N = 792)

After 18 months of follow-up, 792 patients were analyzed for future exacerbations and mortality. There were significant differences in numbers of exacerbations and hospitalizations among Groups A, B, C and D ($P < 0.001$). The numbers of frequent exacerbators in Groups A, B, C and D were 15 (11.28%), 56 (18.98%), 24 (23.30%) and 92 (35.25%), respectively, while the percentage mortalities were significantly different among the four groups ($P < 0.01$) at 0.75%, 4.41%, 2.91% and 8.43%, respectively. There were more frequent exacerbators and a higher mortality in group D (Table 4).

Table 4
Exacerbations and mortality in Groups A, B, C and D after 18 months of follow-up (N = 792).

Variables	Group A (n = 133)	Group B (n = 295)	Group C (n = 103)	Group D (n = 261)	P- value
Exacerbations (Mean ± SD)	0.18 ± 0.46 &	0.33 ± 0.78	0.39 ± 0.74 ♦	0.75 ± 1.33 ▲	< 0.001
Exacerbations, n (%)					< 0.001
0	112 (84.2) *, #, &	222 (75.2)	72 (69.9) ♦	150 (57.5) ▲	
1	16 (12.0)	40 (13.6)	20 (19.4)	41 (15.7)	
≥ 2	4 (3.0) &	20 (6.8)	8 (7.8) ♦	48 (18.6) ▲	
Hospitalizations (Mean ± SD)	0.11 ± 0.36 &	0.15 ± 0.42	0.25 ± 0.59	0.32 ± 0.72 ▲	0.001
Hospitalizations, n (%)					0.001
0	119 (89.4) *, #, &	247 (83.7) ¶	80 (77.7) ♦	183 (70.1) ▲	
≥ 1	13 (9.8) *, #, &	35 (11.9) ¶	20 (19.4) ♦	56 (21.5) ▲	
Frequent Exacerbators, n (%)	15 (11.3) *, #, &	56 (19.0)	24 (23.3) ♦	92 (35.3) ▲	< 0.001
Mortality, n (%)	1 (0.8) *, #, &	13 (4.4) ¶	3 (2.9) ♦	22 (8.4)	0.005
Notes: * P < 0.05 versus group B, # P < 0.05 versus group C, & P < 0.05 versus group D, ¶ P < 0.05 versus group C, ♦ P < 0.05 versus group D, ▲ P < 0.05 versus group B;					

As showed in Table 5, we divided each group into two subgroups (GOLD I-II and III-IV). In Groups A, B, C and D, there were no significant differences in the number of exacerbations or hospitalizations between GOLD I-II and III-IV patients after 18 months of follow-up. In addition, the proportion of patients with exacerbations (0, 1, ≥ 2 times/year) or hospitalizations (0, ≥ 1 times/year) was not significantly different in the same group with different GOLD grades. The same trends could be seen in mortality rates and the proportion of frequent exacerbators in all groups.

Table 5
Exacerbations and mortality for different GOLD grades in Groups A, B, C and D after 18 months of follow-up (N = 792).

	Group A (n = 133)		P-	Group B (n = 295)		P-	Group C (n = 103)		P-	Group D (n = 261)		P-
Variables	GOLD		value	GOLD		value			value			value
	I- II (n = 109)	III-IV (n = 24)		II (n = 146)	III-IV (n = 149)		II (n = 63)	III-IV (n = 40)		II (n = 93)	III-IV (n = 168)	
Exacerbations (Mean ± SD)	0.19 ± 0.46	0.17 ± 0.48	0.859	0.31 ± 0.74	0.34 ± 0.82	0.682	0.32 ± 0.60	0.51 ± 0.91	0.240	0.64 ± 1.21	0.82 ± 1.40	0.314
Exacerbations, n (%)			0.671			0.935			0.582			0.264
0	91 (84.3)	21 (87.5)		108 (78.8)	114 (78.6)		46 (75.4)	26 (66.7)		60 (67.4)	90 (60.0)	
1	14 (13.0)	2 (8.3)		20 (14.6)	20 (13.8)		11 (18.0)	9 (23.1)		16 (18.0)	25 (16.7)	
2	3 (2.7)	1 (4.2)		9 (6.6)	11 (7.6)		4 (6.6)	4 (10.2)		13 (14.6)	35 (23.3)	
Hospitalizations, (Mean ± SD)	0.13 ± 0.39	0.04 ± 0.20	0.121	0.15 ± 0.39	0.15 ± 0.45	0.910	0.20 ± 0.44	0.33 ± 0.77	0.332	0.31 ± 0.81	0.32 ± 0.67	0.956
Hospitalizations, n (%)			0.461			0.719			0.539			0.367
0	96 (88.89)	23 (95.83)		119 (86.86)	128 (88.28)		50 (81.97)	30 (76.92)		71 (79.78)	112 (74.67)	
≥ 1	12 (11.11)	1 (4.17)		18 (18)	17 (11.72)		11 (18.03)	9 (23.08)		18 (20.22)	38 (25.33)	
Frequent exacerbator, n (%)	14 (12.84)	1 (4.17)	0.305	30 (20.55)	26 (17.45)	0.497	14 (22.22)	10 (25.00)	0.745	27 (29.03)	65 (38.69)	0.118
Mortality, n (%)	1 (0.9)	0 (0)	0.638	9 (6.16)	4 (2.68)	0.145	2 (3.17)	1 (2.50)	0.843	4 (4.30)	18 (10.71)	0.074

Discussion

In this study, stable COPD outpatients were divided into Groups A, B, C, and D based on GOLD 2017 to analyze the clinical features, the characteristics of airflow obstruction and its association with treatment response in the real world. We found that patients were older in Groups B and D. A similar result was observed in Oishi et al. [16] Smoking is a major environmental risk factors for COPD [17]. In this study, we found that compared with Group D, there were more current smoker in Groups A, B and C. Perhaps patients in Group D experienced more symptoms, which made more patients stop smoking. The number of female patients in this study was small. This may be because smoking was the main risk factor for COPD, but there were relatively few female smoking patients in China [18–19]. Biofuel exposure is another risk factor for the development of COPD that particularly affects women in developing countries [20–21]. Our research results also confirmed that Groups B to D had a higher biofuel exposure rate than Group A.

Since GOLD 2017 revised the assessment tool, the characteristics of airflow obstruction in Groups A, B, C and D were unclear. In this study, we found that there were the highest FEV1, FEV1 % predicted, FVC, FVC % predicted, FEV1/FVC, MEF 25, MEF25 % predicted, MEF75, MEF75 % predicted, PEF and PEF % predicted values in Group A. Also, there were more patients of mild and moderate ventilatory disorder and patients in GOLD grade I and II in Groups A. When compared with Group A, the airflow obstruction of Group C was higher and there were more patients of GOLD grade II and III in this group. The FEV1, FEV1 % predicted, FVC, FVC % predicted, FEV1/FVC, MEF 25, MEF25 % predicted, MEF75, MEF75 % predicted, PEF and PEF % predicted values were lowest in group D. In addition, in Group D, there were more patients with severe and very severe ventilatory disorder and patients in GOLD grade III and IV. In Group B, we could see that the airflow obstruction was lower than Group D, while higher than that in Group C. Furthermore, there were more patients with severe and very severe ventilatory disorder, and GOLD grade II and III in Groups B. Further research found that GOLD grade I and II patients were concentrated in Groups A and C, while GOLD III and IV

patients were concentrated in Groups B and D. This is consistent with the results of Cabrera et al. [22] However, the proportion of GOLD IV patients in Groups A was relatively small. This was associated with less symptoms and a lower risk in group A patients.

In the GOLD 2011 guidelines, GOLD classification of airflow obstruction was used to guide combined COPD assessment. Briefly, GOLD I-II categories indicated low risk, while GOLD III-IV indicated high risk [23]. Therefore, we divided Groups A, B, C and D into two subgroups, one for GOLD I-II patients, and one for GOLD III-IV patients. The purpose of this was to analyze the differences in demographics and clinical characteristics. The results showed that patient with GOLD III-IV had lower BMI and proportion of LAMA, but higher CAT, CCQ and proportions of LAMA + LABA + ICS. This result implied that different GOLD grades had an impact on symptoms scores and treatments in the same groups.

Since GOLD 2017 removed spirometry, there was no research of its association with treatment response in real world in different groups. Therefore, we analyzed the future exacerbations and mortality in Groups A, B, C and D, and in the same groups with different GOLD grades, after 18 months of follow-up. The period of 18 months was chosen because one-year follow-up times were not well reflective of future exacerbations in COPD patients [24]. The result showed that the exacerbations and hospitalizations were significantly different among different groups. The proportion of frequent exacerbators and mortality rates showed the same results. Further analysis found that there were more exacerbations and hospitalizations in Group D, along with a higher mortality rate. However, it was noted that the mortality rate was relatively low in this study because the patients were only followed-up for 18 months. Furthermore, we conducted analysis of the GOLD grade subgroups of Groups A, B, C and D. The results were surprising in that there were no differences in numbers of exacerbations or hospitalizations in all groups after 18 months of follow-up. Also, the mortality rates and proportions of frequent exacerbators were not significantly different. This result implied that GOLD classification of airway obstruction had no impact on the ABCD grouping in terms of future exacerbations and mortality. In other words, as described in the GOLD 2017 guidelines, combined COPD assessment should separate spirometry from the "ABCD" grouping [9].

There was still limitation in this study. The number of enrolled patients in Groups A and C was small. It may be that patients in Groups A and C have few symptoms, and typically in China, people attend hospital only once their symptoms are more severe.

Conclusions

In summary, our study revealed that there were significant differences in pulmonary function across Groups A to D, and that Groups B and D had more airflow obstruction. Also, there were significant differences in the number of exacerbations and the mortality rates among different groups after 18 months of follow-up. However, further analyzed showed there were no significant differences in exacerbations, hospitalizations and mortality rates in the same groups with different GOLD grades. In other words, GOLD classification of airway obstruction had no impact on future exacerbations and mortality rates in Groups A, B, C and D.

Abbreviations List

BMI, Body Mass Index

COPD, Chronic Obstructive Pulmonary Disease;

CAT, COPD Assessment Test

CCQ, Clinical COPD Questionnaire

FEV1, Forced Expiratory Volume in one second

FVC, Forced Vital Capacity

GOLD, Global Initiative for Chronic Obstructive Lung Disease

ICS, Inhaled Corticosteroid

LAMA, Long-Acting Muscarinic Antagonist

LABA, Long-Acting β 2-Agonist

MEF, Maximal Expiratory Flow

mMRC, Modified Medical Research Council

PTF, Pulmonary Function Tests

PEF, Peak Expiratory Flow.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional ethics committee of the Second Xiangya Hospital of Central South University. All patients gave informed consent.

Consent for publication

Not applicable

Availability of data and materials

All publications discussed in the manuscript are available from the corresponding author on request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by grants from the National Natural Science Foundation of China (NSFC, Grants 81770046 to Prof Ping Chen),

Author's contributions

Ping Chen, Yan Chen and Shan Cai were the guarantor and took responsibility for the content of this manuscript. Qing Song contributed toward data analysis, wrote this manuscript, drew the figures and tables. Yi-Yang Zhao, Yu-Qin Zeng, Wei Cheng, Cong Liu, Min-Hua Deng, Xin Li and Li-Bing Ma contributed to data collection and analysis.

Acknowledgments

The authors would like to thank the staff of the hospitals for their cooperation in collecting the study data.

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Figures

Figure 1

Flow chart of study inclusion. Note: Groups A to D were categories according to GOLD 2017. Abbreviations: GOLD, Global Initiative for Chronic Obstructive Lung Disease; PFT, Pulmonary Function Test.