

RESEARCH

Open Access



Comprehensive appraisal of lung function in young COPD patients: a single center observational study

Lunfang Tan^{1†}, Yun Li^{1†}, Zhufeng Wang^{1†}, Zihui Wang^{1†}, Shuyi Liu¹, Junfeng Lin¹, Jinhai Huang¹, Lina Liang¹, Kang Peng¹, Yi Gao^{1*} and Jinping Zheng^{1*}

Abstract

Purpose The present study aimed to investigate the clinical characteristics and lung function impairment in young people diagnosed with chronic obstructive pulmonary disease (COPD).

Patients and methods We retrospectively enrolled patients with COPD who underwent symptom assessment and comprehensive pulmonary function tests at the First Affiliated Hospital of Guangzhou Medical University between August 2017 and March 2022. The patients were categorized into two groups based on age: a young COPD group (aged 20–50 years) and an old COPD group (aged > 50 years).

Results A total of 1282 patients with COPD were included in the study, with 76 young COPD patients and 1206 old COPD patients. Young COPD patients exhibited a higher likelihood of being asymptomatic, lower rates of smoking, and a lower smoking index compared to old COPD patients. Although young COPD patients had higher median post-bronchodilator forced expiratory volume in 1 s (post-BD FEV₁) (1.4 vs. 1.2 L, $P=0.019$), diffusing capacity of the lung for carbon monoxide (D_LCO) (7.2 vs. 4.6, $P<0.001$), and a lower median residual volume to total lung capacity ratio (RV/TLC) compared to their older counterparts, there were no differences observed in severity distribution by GOLD categories or the proportion of lung hyperinflation (RV/TLC%pred > 120%) between two groups. Surprisingly, the prevalence of reduced D_LCO was found to be 71.1% in young COPD, although lower than in old COPD (85.2%).

Conclusion Young COPD showed fewer respiratory symptoms, yet displayed a similar severity distribution by GOLD categories. Furthermore, a majority of them demonstrated lung hyperinflation and reduced D_LCO. These results underscore the importance of a comprehensive assessment of lung function in young COPD patients.

Keywords Young COPD, Respiratory symptoms, Lung function, Diffusing capacity, Lung volume

[†]Lunfang Tan, Yun Li, Zhufeng Wang and Zihui Wang contributed equally to this work.

*Correspondence:

Yi Gao

misstall2@163.com

Jinping Zheng

jpzhenggy@163.com

Full list of author information is available at the end of the article



Introduction

Chronic obstructive pulmonary disease (COPD), characterized by persistent respiratory symptoms and airflow limitation, is usually considered a disease of the elderly and always diagnosed in the population over 60 years old [1]. However, growing evidence has shown that COPD also occurs in younger people. For example, a national cross-sectional study in China reported that the age-standardized prevalence of COPD was 1.4% in the 20–29 age group, 3% in the 30–39 age group, and 5.1% in the 40–49 age group [2]. And another Korean population-based cohort of 2236 randomly selected individuals aged 40–50 years, the prevalence of young patients with COPD was 4.2% [3]. The onset age of COPD is younger, and the prevalence of young COPD is gradually increasing. This trend suggests that we need to reassess the risk factors for COPD and pay more attention to the clinical characteristics of young individuals with COPD. Therefore, to facilitate more research on the early origins of COPD, the 2022 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines indicated that “COPD in young people” was defined as an age-dependent term for patients aged 20–50 years, who have a post-bronchodilator forced expiratory volume in 1 s (post-BD FEV₁) to forced vital capacity (post-BD FVC) ratio (post-BD FEV₁/FVC) < 0.7 regardless of the severity of airflow limitation [4].

Previous studies demonstrated that young COPD was dominated by GOLD 1 and GOLD 2 (96.7%), most of them might not go to the hospital due to the mild symptoms and airflow limitation, which resulted in insufficient attention paid to COPD in young people [5]. However, another study showed undiagnosed COPD in young people often had significant structural and functional abnormalities [6]. Moreover, young COPD patients have increased risks of exacerbations, comorbidity, and mortality compared with individuals without airflow limitation [3, 5–8]. Therefore, young individuals with COPD deserve widespread attention and research.

Pulmonary function testing (PFT) is a key tool for the assessment of COPD, which helps clinical doctors diagnose COPD and monitor disease progression by measuring spirometry, lung volume, and lung gas exchange capacity. In addition, PFT also helps to guide treatment plan adjustment, predict disease deterioration, and provide personalized management plans for patients. Therefore, it is necessary to comprehensively evaluate the lung function of young COPD patients. Although previous studies have investigated the lung function characteristics of young COPD, most of them only focused on spirometry. For example, Divo et al. demonstrated young COPD had a significantly higher FEV₁ compared to old COPD, and 15%, 33%, 33%, and 0.3% in young COPD

had GOLD 1, GOLD 2, GOLD 3, and GOLD 4, respectively, which was similar to old patients [7]. However, the other two studies showed that young COPD mainly presented GOLD1-2, and rare young subjects had more than severe airflow limitation [3, 5]. The proportion of subjects distributed among the GOLD categories remains unclear. Additionally, there are a lack of studies assessing the characteristics of lung volume and diffusing capacity in young COPD, and the changes of lung volume or diffusing capacity in such a specific population remain unknown.

Therefore, the objective of the present study was to comprehensively investigate lung function changes in young patients with COPD, including spirometry, bronchodilator responsiveness, lung volumes, and diffusing capacity. It is of interest to bring insight into the pulmonary function impairment of young COPD and provide new perspectives for future research, especially in exploring the disease mechanisms and early diagnosis of young COPD.

Materials and methods

The study protocol was performed according to the Declaration of Helsinki and approved by the First Affiliated Hospital of Guangzhou Medical University Ethics Committee (ES-2023-140-01). Informed consent was obtained from all subjects. Information of all patients was kept confidential.

Study population

Out-patients or inpatients with COPD were retrospectively enrolled from the National Center for Respiratory Medicine, National Clinical Research Center for Respiratory Disease, and the First Affiliated Hospital of Guangzhou Medical University from August 2017 to March 2022. According to the guideline of the GOLD 2022, our study defined young COPD as operationally by a post-BD FEV₁/FVC < 0.7 in patients aged 20–50 years, while those older than 50 years of age were defined as old COPD [4]. The enrolled patients should meet the criteria of completing comprehensive assessments of lung function tests and a routine questionnaire conducted before lung function tests (Supplementary Table 1). The questionnaire included age, sex, symptom assessment (cough, sputum, dyspnea), modified Medical Research Council (mMRC), self-reported smoking history, air pollution exposure, self-reported respiratory history and so on. Lung function tests included spirometry, bronchodilator responsiveness (BDR) testing, lung volume measurements, and diffusing capacity of the lung for carbon monoxide (D_LCO). Excluded criteria were as follows: (1) those with ambiguous diagnosis; (2) those diagnosed with asthma or obliterative bronchiolitis (meeting three major criteria

and at least one minor criteria. The major criteria include $FEV_1/FVC < 0.7$, negative bronchodilator responsiveness, and excluding respiratory infections [perform tests such as high-resolution CT and microbial culture based on clinical symptoms]. The minor criteria include the presence of chronic graft-versus-host disease, expiratory HRCT showed air trapping, dilatation and thickening of small airways, and $RV\%pred > 120\%$; (3) those with missing important parameters such as age, weight, FEV_1 , FVC, FEV_1/FVC and D_LCO ; (4) those with extreme values, i.e. values outside of 1.5 * interquartile range (IQR). For the subjects who have performed multiple BDR tests, only the initial report was selected.

Pulmonary function tests

The PFT equipment (Jaeger Masterscreen Body, BD, Franklin Lakes, NJ, USA; Cosmed PFT Quark, COSMED, The Metabolic Company, Rome, Italy) met the criteria of the American Thoracic Society and the European Respiratory Society (ERS/ATS). Spirometry, lung volume measurements, and single-breath diffusing capacity were conducted by trained and skilled technicians in accordance with ERS/ATS [9–12] and Pulmonary Function Group, Respiratory Diseases Society of Chinese Medical Association, [13–15] with standardization of protocols and quality control procedures across the clinical site. Only subjects with tests judged acceptable and reproducible were included. Each subject inhaled 400 µg of salbutamol (Ventolin, Glaxo Wellcome Products, France) via metered dose inhaler and repeated spirometry after 20–30 min. The lung volumes were measured by body plethysmography. D_LCO was measured by the single-breath method and was corrected for hemoglobin in those with blood routine examinations. Predicted values of spirometry, lung volume, and D_LCO were calculated from the reference equations published by Zheng and Zhong, [16] Stocks et al [17] and ATS, [18] respectively. All the lung function tests were conducted within a month.

Lung function indices and variable definitions

Spirometry, lung volume measurement, and D_LCO were standardized as percentages of predicted values as described previously. The regular indices included FEV_1 , $FEV_1\%pred$, FVC, $FVC\%pred$, FEV_1/FVC , maximal-mid expiratory flow (MMEF), $MMEF\%pred$, RV/TLC , $RV/TLC\%pred$, D_LCO , and $D_LCO\%pred$. According to the 2005 ERS/ATS criteria, the positive BDR met the change of $\geq 12\%$ and 200 mL in FEV_1 and/or FVC between the optimal value of baseline and post-bronchodilator. The grades of COPD conformed to GOLD guidelines, GOLD 1: $FEV_1\%pred \geq 80\%$, GOLD 2: $50\% \leq FEV_1\%pred < 80\%$, GOLD 3: $30\% \leq FEV_1\%pred < 50\%$,

and GOLD 4: $FEV_1\%pred < 30\%$ [19]. An abnormal ratio of RV/TLC was considered pathological and pulmonary hyperinflation was defined as $RV/TLC\%pred > 120\%$ [20]. The severity of reduced D_LCO was assessed by $D_LCO\%pred$ with 3 critical values of 80%, 60%, and 40%, namely normal: $D_LCO\%pred \geq 80\%$ or LLN, mild: $60\% \leq D_LCO\%pred < 80\%$, moderate: $40\% \leq D_LCO\%pred < 60\%$, severe: $D_LCO\%pred < 40\%$ [21].

Sample size imbalance

We supposed that the sample size of old COPD was much larger than young COPD, which might lead to bias in results. In this study, a total of 76 young COPD patients and 1206 old COPD patients were included. To ensure a balanced distribution of sample sizes between the two groups, a random under-sampling method was implemented using SPSS. Each old COPD patient was assigned a random number, and subsequently, 152 individuals were randomly selected from this group, resulting in a balanced ratio of 1:2 between the young and old COPD patients. We would compare the differences between analysis results before and after balancing the data, and the more reliable results would be mainly discussed.

Statistical analysis

All analyses were performed using SPSS version 25. Continuous variables were presented as the mean and standard deviation (SD) for normally distributed data, or the median and interquartile range (IQR) for non-normally distributed data. Categorical variables were presented as percentages. Differences between young COPD and old COPD patients were assessed by the Mann–Whitney U-tests for continuous variables with non-normal distribution, while the Student's t-test for continuous variables with normal distribution and the Chi-square test or Fisher's exact test for categorical variables. The association between each potential risk factor and the presence of reduced D_LCO in young COPD was determined using logistic regression. The relationship between risk factors and reduced D_LCO in young COPD was presented as odd ratio (OR). A two-sided $P < 0.05$ was considered statistically significant.

Result

Difference in clinical characteristics between young COPD and old COPD

Considering the analysis results after balancing the data were similar to the results based on the unbalanced data, (Supplementary Table 2) which might be more reliable due to their larger sample size, we mainly discussed the analysis results based on the unbalanced data. A total of 1282 patients with COPD were ultimately enrolled in the study, including a young COPD group ($n=76$) and an

old COPD group ($n=1206$) (Fig. 1). The clinical characteristics were shown in Table 1. The median ages of the young COPD group and old COPD group were 47 years and 66 years, respectively. The proportion of males differed between two groups (73.7% vs. 90.3%, $P<0.001$). Compared with the old COPD group, the young COPD group demonstrated a significantly lower prevalence of ever or current smokers (25.0% vs. 70.6%, $P<0.001$) and self-reported smoking history (pack-year) (4.9 ± 11.7 vs. 32.1 ± 32.2 , $P<0.001$), but the young COPD group exhibited a higher incidence of self-reported exposure to air pollution (71.4% vs. 48.8%, $P=0.007$). Significant intergroup disparities were observed in the prevalence of respiratory symptoms. The young COPD group exhibited

a notably lower incidence of individuals experiencing at least one respiratory symptom (44.7% vs. 62.0%, $P=0.003$), such as cough and dyspnea. Moreover, young COPD had a significantly higher population of mMRC < 2 (89.5% vs. 72.8%, $P \leq 0.001$).

Differences in lung function indices between young COPD and old COPD

As shown in Table 2, compared with the old COPD group, the young COPD group had higher median post-BD FEV₁ (1.4 vs. 1.2 L, $P=0.019$), post-BD FVC (2.8 vs. 2.7 L, $P=0.040$), post-BD MMEF (0.7 vs. 0.5 L/s, $P=0.001$), and D_LCO (7.2 vs. 4.6, $P<0.001$), while lower median RV (3.0 vs. 3.6 L, $P=0.001$) and RV/TLC (0.5

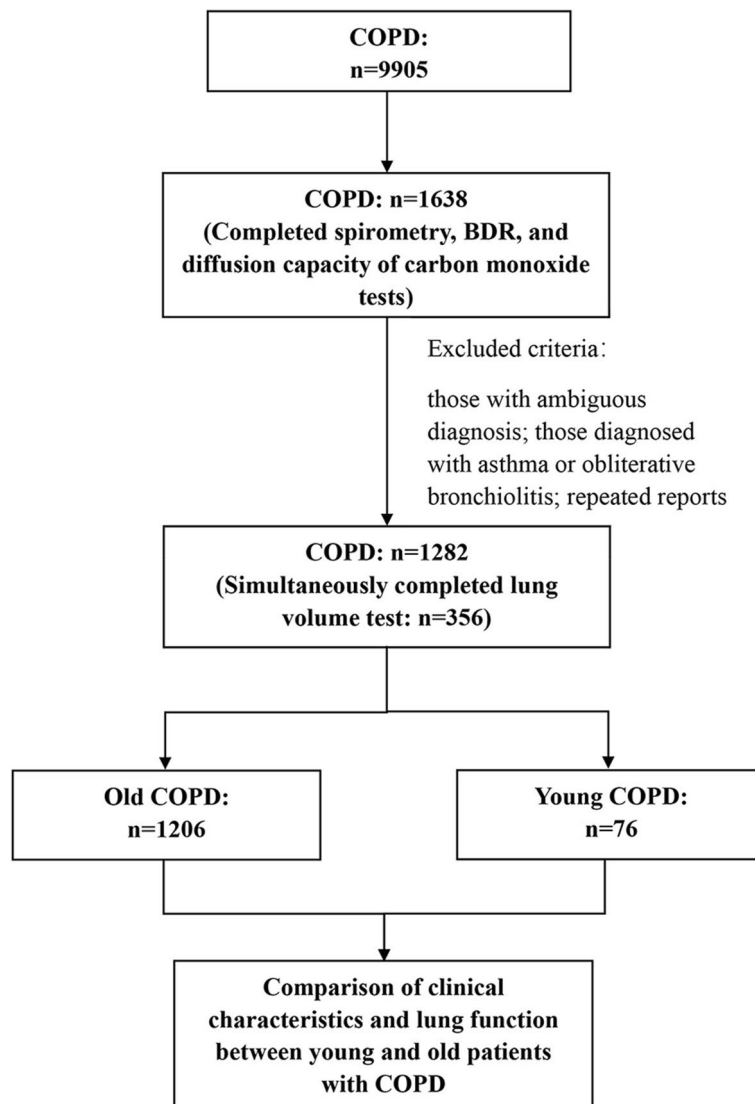


Fig. 1 Screening the lung function data of COPD from the database. COPD, chronic obstructive pulmonary disease. BDR, bronchodilator responsiveness

Table 1 Comparison of clinical characteristics between young COPD and old COPD

Variables	Young COPD (n=76)	Old COPD (n=1206)	P value
Age (years)	47.0 (43.3-49.0)	66.0 (61.0-71.0)	< 0.001
Sex			< 0.001
Female	20 (26.3)	117 (9.7)	
Male	56 (73.7)	1089 (90.3)	
BMI (kg/m ²)	22.4 (18.3-24.6)	21.7 (19.5-24.2)	0.962
BMI (%)			< 0.001
Low BMI (<18.5)	7 (3.6)	213 (19.8)	
Normal BMI (18.5-25)	122 (63.2)	702 (65.2)	
High (≥25)	64 (33.2)	162 (15.0)	
Smoking status			< 0.001
Never smoker	57 (75.0)	354 (29.4)	
Current/Ever smoker	19 (25.0)	852 (70.6)	
Pack-years	4.9±11.7	32.1±32.2	< 0.001
Air pollution exposure	25 (71.4)	391 (48.8)	0.007
History of respiratory diseases	3 (8.1)	38 (4.7)	0.591
Any symptom	34 (44.7)	748 (62.0)	0.003
Cough (%)	23 (30.3)	506 (42.0)	0.045
Sputum (%)	29 (38.2)	569 (47.2)	0.126
Dyspnea (%)	18 (23.7)	490 (40.6)	0.003
mMRC			0.001
< 2	68 (89.5)	878 (72.8)	
≥ 2	8 (10.5)	328 (27.2)	

Abbreviation: COPD chronic obstructive pulmonary disease, BMI body mass index, mMRC modified Medical Research Council. History of respiratory diseases include tuberculosis, bronchiectasis, and interstitial lung disease

vs. 0.6, $P < 0.001$). However, the severity distribution by GOLD categories was similar between the two groups (Fig. 2). In addition, the young COPD group showed a markedly lower prevalence of positive BDR compared to the older group (18.4% vs. 30.6%, $P < 0.001$). Unexpectedly, the incidence of lung hyperinflation and reduced D_LCO in young COPD were up to 86.7% and 71.1%, respectively (Fig. 3). Moreover, the proportions of reduced D_LCO for GOLD 1–4 in young COPD were 60.0%, 48.3%, 88.9%, and 86.7%, respectively (Fig. 4).

Risk factors for young COPD with reduced D_LCO

The clinical characteristics and pulmonary function in young COPD patients with reduced D_LCO were shown in Supplementary Table 3. Compared with the young COPD with reduced D_LCO , those with normal D_LCO had higher BMI and proportion of normal BMI, and exhibited better FEV_1 , FVC, MMEF, RV, and RV/TLC. However, no significant differences were observed in the prevalence of chronic respiratory symptoms between two subgroups. BMI, GOLD, $FVC\%pred < 80\%$, and post-BD FEV_1/FVC were individually included in univariable analysis. Table 3 showed that on univariable logistic regression, the BMI < 18.5 (OR = 10.50, $P = 0.029$) and $FVC\%pred < 80\%$

(OR = 2.98, $P = 0.038$) were risk factors in young COPD with reduced D_LCO , but the multivariate logistic analysis results showed that all BMI < 18.5 , BMI ≥ 25 , GOLD, $FVC\%pred < 80\%$, and post-BD FEV_1/FVC were not associated with reduced D_LCO in young COPD ($P > 0.05$).

Discussion

Our study has investigated the clinical characteristics and impairment of lung function in young individuals with COPD. The main findings indicated that young COPD patients showed a similar severity distribution by GOLD categories compared with old COPD patients and that the majority of these young patients had developed lung hyperinflation and reduced DLCO (82.1% and 71.1%, respectively).

We found that the proportion of current or ever smokers in young COPD was 25.0%, significantly lower than that of old COPD (60.6%). However, young COPD showed higher proportions of air pollution exposure and a history of respiratory diseases (including tuberculosis, bronchiectasis, and interstitial lung disease). Therefore, we speculated that in addition to smoking other risk factors may contribute to young COPD, which was supported by a previous study showing genetics,

Table 2 Comparison of lung function indices between young COPD and old COPD

Variables	Young COPD (n = 76)	Old COPD (n = 1206)	P value
Spirometry (%)			
FEV ₁ (L)			
pre-BD	1.2 (0.9–1.8)	1.1 (0.8–1.6)	0.013
post-BD	1.4 (1.0–1.8)	1.2 (0.9–1.7)	0.019
FEV ₁ %pred			
pre-BD	41.6 (29.4–54.8)	44.1 (31.3–60.0)	0.354
post-BD	45.7 (32.1–61.1)	48.5 (35.9–65.3)	0.201
FVC (L)			
pre-BD	2.7 (2.2–3.7)	2.5 (2.0–3.1)	0.007
post-BD	2.8 (2.2–3.9)	2.7 (2.2–3.2)	0.040
FVC%pred			
pre-BD	74.3 (61.8–90.9)	76.2 (64.0–90.4)	0.556
post-BD	77.5 (66.3–91.3)	82.6 (69.9–95.1)	0.101
FEV ₁ /FVC			
pre-BD	0.5 (0.4–0.6)	0.5 (0.4–0.6)	0.206
post-BD	0.5 (0.5–0.6)	0.5 (0.4–0.6)	0.121
FEV ₁ /FVC%pred			
pre-BD	62.7 (45.5–72.2)	57.1 (45.2–70.6)	0.269
post-BD	65.3 (48.9–77.7)	60.0 (47.1–74.6)	0.097
MMEF (L/s)			
pre-BD	0.5 (0.4–0.8)	0.4 (0.3–0.6)	<0.001
post-BD	0.7 (0.4–0.9)	0.5 (0.3–0.8)	0.001
MMEF%pred			
pre-BD	14.1 (9.1–21.1)	12.8 (8.6–20.3)	0.299
post-BD	17.1 (10.1–24.9)	15.9 (10.4–25.2)	0.754
Lung volume (%) ^a			
RV (L)	3.0 (2.2–3.8)	3.6 (2.9–4.6)	0.001
RV%pred	164.0 (129.5–194.0)	155.3 (126.5–203.1)	0.921
TLC (L)	5.8 (4.6–7.0)	6.4 (5.4–7.2)	0.063
TLC%pred	103.0 (94.0–114.5)	109.3 (94.5–120.6)	0.194
RV/TLC	0.5 (0.5–0.6)	0.6 (0.5–0.7)	<0.001
RV/TLC%pred	157.8 (128.7–178.5)	150.1 (126.0–174.0)	0.442
Diffusing capacity (%) ^b			
D _L CO	7.2 (5.8–9.2)	4.6 (3.2–6.4)	<0.001
D _L CO%pred	71.0 (48.1–80.8)	55.1 (40.9–70.5)	<0.001
Reduced DLCO	54 (71.1)	1028 (85.2)	0.001
Mild (60–80%)	28 (51.9)	336 (32.7)	
Moderate (40–60%)	14 (25.9)	419 (40.8)	
Severe (<40%)	12 (22.2)	273 (26.6)	

Continuous variables were presented as the median and interquartile range (IQR) and categorical variables were presented as frequency (%)

Abbreviations: FEV₁ Forced expiratory volume in the first second, FVC Forced vital capacity, FEV₁/FVC Forced expiratory volume in the first second/forced vital capacity, MMEF Maximal-mid expiratory flow, post-BD post-bronchodilator responsiveness, D_LCO Diffusion capacity of carbon monoxide, RV Residual volume, TLC Total lung capacity, RV/TLC Ratio of residual volume to total lung capacity

^a Young COPD (n = 31) and Old COPD (n = 325)

^b Young COPD (n = 76) and Old COPD (n = 1199)

pregnancy and childbirth history, history of respiratory diseases, and air pollution exposure were the risk factors for COPD [22]. Respiratory symptoms are instrumental in motivating individuals to seek medical consultation

and serve as significant predictors for early identification of individuals who are at risk for developing COPD. However, we found that most young COPD had fewer chronic respiratory symptoms, which was similar to

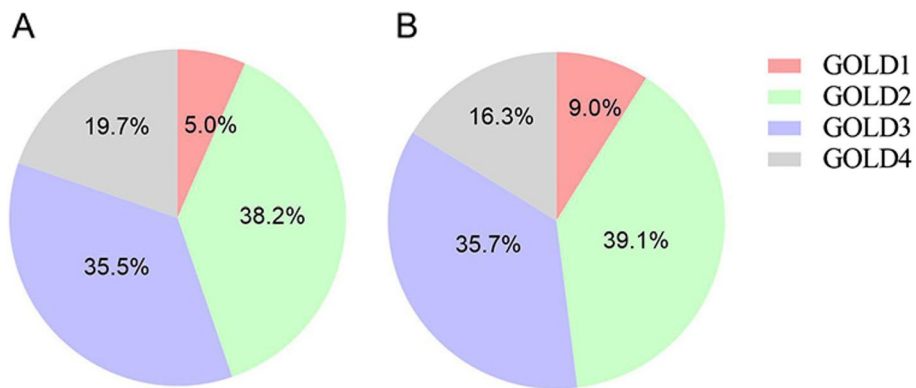


Fig. 2 The severity distribution by GOLD categories in young COPD (A) and old COPD (B). COPD, chronic obstructive pulmonary disease. GOLD, Global Initiative for Chronic Obstructive Lung Disease

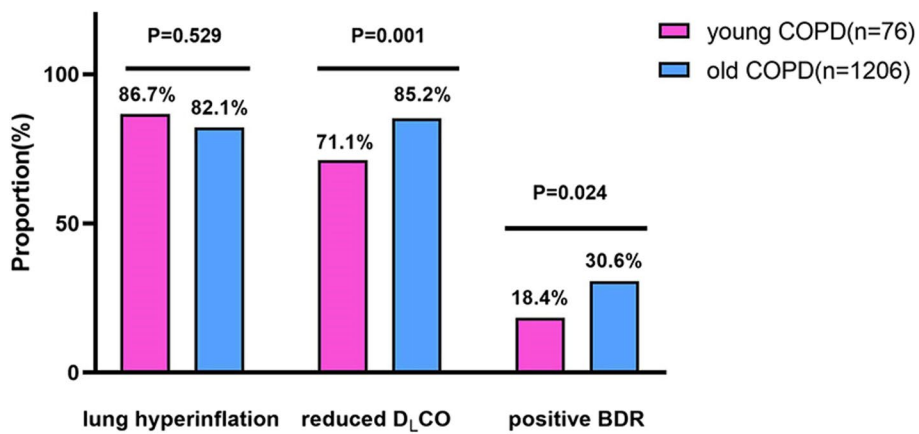


Fig. 3 The proportion of lung hyperinflation, reduced DLCO and positive BDR between young COPD and old COPD. COPD, chronic obstructive pulmonary disease; BDR, bronchodilator responsiveness; DLCO, diffusion capacity of carbon monoxide

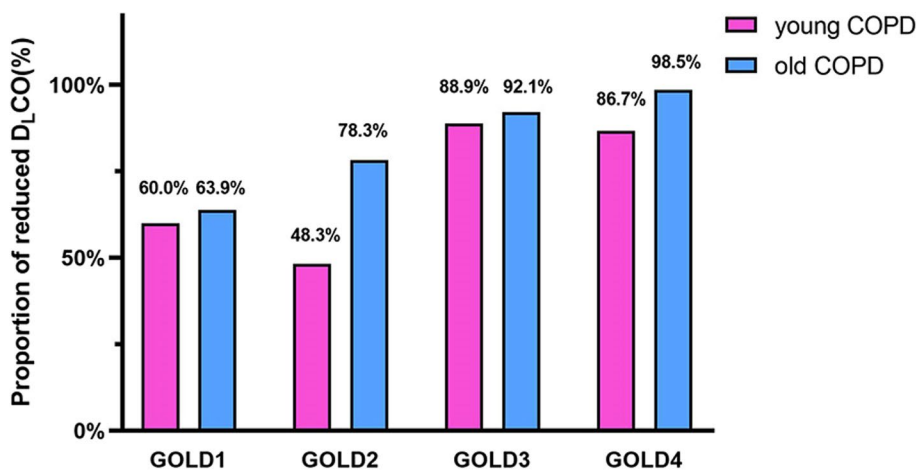


Fig. 4 The proportions of reduced DLCO among GOLD in young COPD and old COPD. COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; DLCO, diffusion capacity of carbon monoxide

Table 3 Univariate and multivariable logistic regression analysis of risk factors for young COPD with diffusing impairment

Variables	Univariable model		Multivariable model	
	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Low BMI (ref: Normal BMI)	10.50(1.27–86.93)	0.029	5.57(0.54–57.72)	0.150
High BMI (ref: Normal BMI)	0.43(0.12–1.54)	0.194	0.47(0.12–1.86)	0.279
GOLD2(ref: GOLD1)	0.62(0.09–4.29)	0.630	0.52(0.06–4.57)	0.559
GOLD3(ref: GOLD1)	5.33(0.62–45.99)	0.128	2.53(0.08–78.66)	0.597
GOLD4(ref: GOLD1)	4.33(0.42–44.43)	0.217	1.26(0.01–115.65)	0.919
FVC%pred < 80%	2.98(1.06–8.33)	0.038	1.61(0.40–6.59)	0.506
post-BD FEV ₁ /FVC	0.96(0.92–1.00)	0.068	1.01(0.93–1.11)	0.809

Abbreviation: OR Odd ratio, CI Confidence interval, BMI Body mass index, GOLD Global initiative for chronic obstructive lung disease, post-BD post-Bronchodilator responsiveness

previous observations [3, 5, 23]. For example, Çolak et al. [23] reported that as much as one-third of individuals with early COPD (FEV₁/FVC < LLN in smokers under 50 years of age with ≥ 10 pack-years) were asymptomatic. This suggested that a subset of young COPD patients with functional abnormalities might fail to go hospital and undervalue the severity of their condition due to the absence or minimal presence of symptoms. This underscores the importance of lung function testing in the early diagnosis and comprehensive assessment of young COPD patients, particularly for those who do not exhibit clinical signs.

In accordance with previous studies [7, 24], our study showed that the proportion of young COPD distributed among the GOLD categories was similar to old COPD. This might be attributed to two aspects. First, young COPD patients have a low peak lung function in early adulthood due to the following factors, including maternal tobacco smoking, maternal undernutrition, intrauterine growth restriction, preterm birth (< 37 weeks of gestation), bronchopulmonary dysplasia, air pollution exposure, lower respiratory tract infections, and active smoking during adolescence [22, 25, 26]. Second, the accelerated lung function decline in young patients with COPD. Some studies demonstrated that compared with old patients, young COPD had a higher FEV₁ and more significant space for decline [27]. FEV₁ declining at a faster rate led to the accelerated progression of COPD. Additionally, we found that more than half of young COPD was GOLD 3–4 (56.8%), which was supported by the result of Divo [7]. However, previous studies showed that young COPD was dominated by GOLD 1–2 (96.7% and 98.0%) [3, 5], and few subjects had more than severe airflow limitation. There is a possible explanation that our data was from the medical institution, whose participants were mainly patients with symptoms, while the data resources of other studies were from the National Health and Nutrition Examination Survey, including healthy

individuals and mild patients. This suggested that the severity of airflow limitation in young COPD was similar to old COPD and that severe airflow limitation would also occur in young COPD, thus we should attach great attention to lung function screening in young individuals.

It is well known that expiratory flow limitation in patients with COPD can cause an increase in lung volume (hyperinflation) and the decline in lung function varies between patients [28]. To our knowledge, this was the first study to show the differences in lung volume between young COPD and old COPD. In this study, young COPD had lower RV and RV/TLC than the elderly, as possibly the absolute values of RV and RV/TLC increase with aging. However, the medians of RV%pred and RV/TLC%pred in young COPD were higher than those of elderly patients and higher than the normal range, indicating that the gas trapped in young COPD was more severe. It might be explained by the faster decline of FEV₁ in young COPD patients, leading to aggravative gas trapping [27, 29]. Moreover, our study has revealed an interesting finding that the proportion of lung hyperinflation (RV/TLC%pred > 120%) was highly up to 86.7% in young patients. A previous study showed that lung hyperinflation was observed in mild COPD and the progressive increase in TLC and RV appeared with the worsening airflow limitation during the course of COPD [30]. Therefore, lung hyperinflation may occur from mild to more severe COPD. Moreover, RV/TLC can be used to predict the long-term change of lung function in patients with COPD and is also an independent risk factor for all-cause mortality in COPD. Lung hyperinflation is an independent predictor for frequent exacerbation and links to the quality of life of COPD [31–33]. Therefore, lung volume measurement is warranted in young COPD.

To our knowledge, the structure abnormalities in the airways, alveoli, and pulmonary circulation can lead to the imbalance of ventilation-perfusion distributions,

which are considered as main factors to reduced D_LCO in COPD. In our study, although the severity distribution of GOLD categories and the proportion of lung hyperinflation were similar between young and old COPD, the absolute and percentage predicted values of D_LCO were significantly better in young COPD than the old patients. We hypothesized that it might be attributed to a discrepancy in the small airway involvement between young and old COPD patients, which was supported by the MMEF being significantly better in the young patients. A previous study has established a correlation between functional small airways disease (fSAD) and low D_LCO in COPD patients, as fSAD corresponding to pathologic abnormality (including decreased circularity, decreased luminal area, and complete obstruction of terminal bronchioles) impairs gas exchange and leads to reduced D_LCO [34]. Moreover, a significant correlation between small airway involvement and age, smoking, and pack-years [35, 36]. Therefore, young COPD patients, due to their younger age, lower proportion of smoking, and lower pack-years, have relatively mild damage to small airways, which may lead to less damage to lung diffusing capacity. Additionally, we found that young COPD patients exhibited a more significant improvement of MMEF between the optimal value of baseline and post-BD compared to the old COPD, which was supported by a previous study [36]. This is possible because young COPD patients suffer from less pronounced bronchiolar distortion and inflammation, which results in inhaled drugs being more abundantly deposited in the small airways [37]. Therefore, we speculated that young COPD patients might benefit more from inhaled drug treatment, which needs to be validated with further studies.

Although young COPD had better D_LCO than the old patients, there was a high proportion of reduced D_LCO (71.1%) in young COPD. A previous study was similar to our study showing that approximately half of early COPD had abnormal D_LCO [6]. Of note, reduced D_LCO also appeared in young COPD with mild airflow restriction (GOLD1-2). Potential explanations for this might be that reduced D_LCO was associated with other risk factors rather than smoking in early life [38, 39]. For example, the D_LCO was persistently reduced in extremely preterm (EP) subjects, which sustained from mid-childhood to adulthood, with no signs of pubertal catch-up growth at 25 years, while the disruption of alveolar growth associated with EP birth may be linked to early-onset COPD in adult life [39]. Therefore, the association between the reduced D_LCO and the young COPD remains unclear, which needs to be explored with further studies.

In the present study, we observed that young COPD with reduced D_LCO had lower BMI and worse lung

function parameters (including FEV₁, FVC, RV, and RV/TLC). The univariable logistic regression showed that the low BMI and FVC%pred < 80% were associated with reduced D_LCO . This was supported by previous studies [40, 41]. Lim et al. revealed that low BMI is linearly correlated with reduced D_LCO [40]. In addition, the decreased FVC in the patients with COPD was caused by hyperinflation or air trapping, [42] which also worsened the effectiveness of gas exchange and declined D_LCO . However, the multivariate logistic analysis showed that all the above influence factors had no statistical significance. This biased result might be due to the small sample, thus further exploration is needed to expand the sample size in future studies.

We believe the most important aspect of this work was the first time to collect the indices of multiple lung function tests, including spirometry, bronchodilator responsiveness testing, lung volume measurements, and diffusion capacity of carbon monoxide. However, we acknowledge several limitations of this study. First, the study did not enroll healthy young individuals (20–50 years) as the control group and did not explore differences in lung function between young patients without and with COPD. Second, it was a cross-sectional study that failed to observe the changes in long-term lung function and prognosis in young COPD patients. However, the long-term follow-up, including the impairment of lung function and the characteristics of disease progression, was critical for researching the treatment in young COPD, and we hope to improve this limitation in future research. Finally, we did not obtain other important clinical characteristics, such as detailed medical history, laboratory indicators, imaging features, and so on. Due to the fact that the questionnaire involved in this study was a routine questionnaire before lung function test and not specifically designed for COPD, the information provided was very limited. Additionally, some outpatients did not undergo laboratory examinations and chest imaging scans in our hospital. In future research, we will collect data from multiple centers for screening, hoping to better address this issue.

Conclusion

In conclusion, despite having fewer respiratory symptoms and better FEV₁, FVC, RV/TLC, and D_LCO compared with old COPD, young COPD have a similar disease severity distribution by GOLD categories. In addition, most of these young people have shown lung hyperinflation and reduced D_LCO . Our findings support the need to screen airway obstruction in young COPD individuals and the preventive and treatment strategies were greatly important for improving progression and outcomes.

Abbreviations

COPD	Chronic obstructive pulmonary disease
BDR	Bronchodilator responsiveness
FEV ₁	Forced expiratory volume in 1 s
D _L CO	Diffusing capacity of the lung for carbon monoxide
RV	Residual volume
TLC	Total lung capacity
RV/TLC	Residual volume to total lung capacity ratio
GOLD	Global initiative for chronic obstructive lung disease
FVC	Forced vital capacity
FEV ₁ /FVC	Forced expiratory volume in 1 second to forced vital capacity ratio
PFT	Pulmonary function testing
mMRC	Modified Medical Research Council
IQR	Interquartile range
ERS/ATS	The American Thoracic Society and the European Respiratory Society
MMEF	Maximal- mid expiratory flow
SD	Standard deviation
BMI	Body mass index
OR	Odds ratio
CI	Confidence interval
LLN	Lower limit of normal
fSAD	Functional small airways disease
EP	Extremely preterm

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12890-024-03165-9>.

Supplementary Material 1.

Acknowledgements

Not applicable.

Authors' contributions

Lunfang Tan, Yun Li, Zhufeng Wang, and Zihui Wang had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Lunfang Tan, Yun Li, Zhufeng Wang, and Zihui Wang contributed equally as co-first authors. Lunfang Tan wrote the main manuscript text. All authors contributed to the acquisition, analysis, interpretation of data, and statistical analysis. All authors reviewed the manuscript. Yi Gao and Jinping Zheng obtained the funding. Yun Li, Zhufeng Wang, Yi Gao, and Jinping Zheng supported the administrative, technical, or material. Yi Gao and Jinping Zheng supervised the research.

Funding

This work was supported by grants from R&D Programme of Guangzhou National Laboratory [No.SRPG22-018], Zhongnanshan Meical Foundation of Guangdong Province [ZNSA-202101], the Supported by R&D Program of Guangzhou National Laboratory, [No. SRPG 22-01], Medical Scientific Research Foundation of Guangdong Province [NO: C2021073].

Availability of data and materials

The data presented in this study are available on request from the corresponding author.

Declarations**Ethics approval and consent to participate**

The study protocol was approved by the First Affiliated Hospital of Guangzhou Medical University Ethics Committee and the permit number was ES-2023-140-01. Informed consent was obtained from all subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Guangzhou National Laboratory, National Center for Respiratory Medicine, National Clinical Research Center for Respiratory Disease, State Key Laboratory of Respiratory Disease, Institute of Respiratory Health, the First Affiliated Hospital of Guangzhou Medical University, No.151 Yanjiang Road, Guangzhou, Guangdong 510120, China.

Received: 11 April 2024 Accepted: 12 July 2024

Published online: 24 July 2024

References

- (GOLD) GfCOLD: global strategy for prevention, diagnosis and management of COPD. 2024 Reprint. 2024. <https://www.goldcopd.org/2024-gold-report/>. Update 2024.
- Wang C, Xu J, Yang L, Xu Y, Zhang X, Bai C, Kang J, Ran P, Shen H, Wen F, et al. Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. *Lancet*. 2018;391(10131):1706–17. [https://doi.org/10.1016/s0140-6736\(18\)30841-9/](https://doi.org/10.1016/s0140-6736(18)30841-9/).
- Jo YS, Kim KJ, Rhee CK, Yoo KH, Jung KS, Park YB. Prevalence, characteristics, and risk of exacerbation in young patients with chronic obstructive pulmonary disease. *Respir Res*. 2022;23(1):212. <https://doi.org/10.1186/s12931-022-02144-0/>.
- (GOLD) 2022 GfCOLD: Global strategy for prevention, diagnosis and management of COPD, Reprint. <https://www.goldcopd.org/2022-gold-reports-2/>.
- Wang Z, Li Y, Lin J, Huang J, Zhang Q, Wang F, Tan L, Liu S, Gao Y, Peng S, et al. Prevalence, risk factors, and mortality of COPD in young people in the USA: results from a population-based retrospective cohort. *BMJ Open Respir Res*. 2023;10(1). <https://doi.org/10.1136/bmjresp-2022-001550/>.
- Cosío BG, Pascual-Guardia S, Borrás-Santos A, Peces-Barba G, Santos S, Vigil L, Soler-Cataluña JJ, Martínez-González C, Casanova C, Marcos PJ, et al. Phenotypic characterisation of early COPD: a prospective case-control study. *ERJ Open Res*. 2020;6(4). <https://doi.org/10.1183/23120541.00047-2020/>.
- Divo MJ, Marin JM, Casanova C, Cabrera Lopez C, Pinto-Plata VM, Marin-Oto M, Polverino F, de-Torres JP, Billheimer D, Celli BR. Comorbidities and mortality risk in adults younger than 50 years of age with chronic obstructive pulmonary disease. *Respir Res*. 2022;23(1):267. <https://doi.org/10.1186/s12931-022-02191-7/>.
- Martinez FJ, Agusti A, Celli BR, Han MK, Allinson JP, Bhatt SP, Calverley P, Chotirmall SH, Chowdhury B, Darken P, et al. Treatment trials in young patients with chronic obstructive pulmonary disease and pre-chronic obstructive pulmonary disease patients: time to move forward. *Am J Respir Crit Care Med*. 2022;205(3):275–87. <https://doi.org/10.1164/rccm.202107-1663SO/>.
- Macintyre N, Crapo RO, Viegi G, Johnson DC, van der Grinten CP, Brusasco V, Burgos F, Casaburi R, Coates A, Enright P, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J*. 2005;26(4):720–35. <https://doi.org/10.1183/09031936.05.00034905/>.
- Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, Coates A, van der Grinten CP, Gustafsson P, Hankinson J, et al. Interpretative strategies for lung function tests. *Eur Respir J*. 2005;26(5):948–68. <https://doi.org/10.1183/09031936.05.00035205/>.
- Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CP, Gustafsson P, et al. Standardisation of spirometry. *Eur Respir J*. 2005;26(2):319–38. <https://doi.org/10.1183/09031936.05.00034805/>.
- Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, Chen R, Decramer M, Fabbri LM, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. *Am J Respir Crit Care Med*. 2017;195(5):557–82. <https://doi.org/10.1164/rccm.201701-0218PP/>.
- RDSocMA PFG. Guidelines for pulmonary function tests (part I) - overview and general requirements. *Chin J Tuberc Respir Dis*. 2014;37(6):402–5.
- RDSocMA PFG. Guidelines for pulmonary function tests (part II) - spirometer examination. *Chin J Tuberc Respir Dis*. 2014;37(7):481–6.

15. Gao Y, Han J, Jiang L. Guidelines for pulmonary function tests (part IV) –bronchodilator reversibility testing. *Chin J Tuberc Respir Dis*. 2014;37(9):655–8.
16. Zheng J, Zhong N. Normative values of pulmonary function testing in Chinese adults. *Chin Med J (Engl)*. 2002;115(1):50–4.
17. Stocks J, Quanjer PH. Reference values for residual volume, functional residual capacity and total lung capacity. ATS workshop on lung volume measurements. Official statement of the European respiratory society. *Eur Respir J*. 1995;8(3):492–506. <https://doi.org/10.1183/09031936.95.08030492/>.
18. American Thoracic Society. Single-breath carbon monoxide diffusing capacity (transfer factor). Recommendations for a standard technique—1995 update. *Am J Respir Crit Care Med*. 1995;152(6 Pt 1):2185–98. <https://doi.org/10.1164/ajrccm.152.6.8520796/>.
19. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, Bourbeau J, Han MK, Martínez FJ, Montes de Oca M, et al. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. *Eur Respir J*. 2023;61(4). <https://doi.org/10.1183/13993003.00239-2023/>.
20. Chen C, Jian W, Gao Y, Xie Y, Song Y, Zheng J. Early COPD patients with lung hyperinflation associated with poorer lung function but better bronchodilator responsiveness. *Int J Chron Obstruct Pulmon Dis*. 2016;11:2519–26. <https://doi.org/10.2147/copd.S110021/>.
21. RDSocMA PFG. Guidelines for pulmonary function tests - diffusing capacity testing. *Chin J Tuberc Respir Dis*. 2015;38(3):164–9.
22. Martinez FD. Early-Life origins of Chronic Obstructive Pulmonary Disease. *N Engl J Med*. 2016;375(9):871–8. <https://doi.org/10.1056/NEJMra1603287/>.
23. Çolak Y, Afzal S, Nordestgaard BG, Vestbo J, Lange P. Prevalence, characteristics, and prognosis of early chronic obstructive pulmonary disease. The Copenhagen general population study. *Am J Respir Crit Care Med*. 2020;201(6):671–80. <https://doi.org/10.1164/rccm.201908-1644OC/>.
24. Morice AH, Celli B, Kesten S, Lystig T, Tashkin D, Decramer M. COPD in young patients: a pre-specified analysis of the four-year trial of tiotropium (UPLIFT). *Respir Med*. 2010;104(11):1659–67. <https://doi.org/10.1016/j.rmed.2010.07.016/>.
25. Tai A, Tran H, Roberts M, Clarke N, Wilson J, Robertson CF. The association between childhood asthma and adult chronic obstructive pulmonary disease. *Thorax*. 2014;69(9):805–10. <https://doi.org/10.1136/thoraxjnl-2013-204815/>.
26. Sears MR, Greene JM, Willan AR, Wiecek EM, Taylor DR, Flannery EM, Cowan JO, Herbison GP, Silva PA, Poulton R. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. *N Engl J Med*. 2003;349(15):1414–22. <https://doi.org/10.1056/NEJMoa022363/>.
27. Dransfield MT, Kunisaki KM, Strand MJ, Anzueto A, Bhatt SP, Bowler RP, Criner GJ, Curtis JL, Hanania NA, Nath H, et al. Acute exacerbations and lung function loss in smokers with and without chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2017;195(3):324–30. <https://doi.org/10.1164/rccm.201605-1014OC/>.
28. Leith DE, Brown R. Human lung volumes and the mechanisms that set them. *Eur Respir J*. 1999;13(2):468–72. <https://doi.org/10.1183/09031936.99.13246899/>.
29. Park J, Lee CH, Lee YJ, Park JS, Cho YJ, Lee JH, Lee CT, Yoon HI. Longitudinal changes in lung hyperinflation in COPD. *Int J Chron Obstruct Pulmon Dis*. 2017;12:501–8. <https://doi.org/10.2147/copd.S122909/>.
30. Deesomchok A, Webb KA, Forkert L, Lam YM, Ofir D, Jensen D, O'Donnell DE. Lung hyperinflation and its reversibility in patients with airway obstruction of varying severity. *Copd*. 2010;7(6):428–37. <https://doi.org/10.3109/15412555.2010.528087/>.
31. Capozzolo A, Carratù P, Dragonieri S, Falcone VA, Quaranta VN, Liotino V, D'Alba G, Castellana G, Resta O. Clinical and functional lung parameters associated with frequent exacerbator phenotype in subjects with severe COPD. *Respir Care*. 2017;62(5):572–8. <https://doi.org/10.4187/respcare.05278/>.
32. Kang J, Oh YM, Lee JH, Kim EK, Lim SY, Kim WJ, Yoon HI, Kim TH, Park TS, Kim SO, et al. Distinctive patterns of pulmonary function change according to baseline lung volume and diffusing capacity. *Int J Tuberc Lung Dis*. 2020;24(6):597–605. <https://doi.org/10.5588/ijtld.19.0401/>.
33. Shin TR, Oh YM, Park JH, Lee KS, Oh S, Kang DR, Sheen S, Seo JB, Yoo KH, Lee JH, et al. The prognostic value of residual volume/total lung capacity in patients with chronic obstructive pulmonary disease. *J Korean Med Sci*. 2015;30(10):1459–65. <https://doi.org/10.3346/jkms.2015.30.10.1459/>.
34. Criner RN, Hatt CR, Galbán CJ, Kazerooni EA, Lynch DA, McCormack MC, Casaburi R, MacIntyre NR, Make BJ, Martínez FJ, et al. Relationship between diffusion capacity and small airway abnormality in COPD. *Respir Res*. 2019;20(1):269. <https://doi.org/10.1186/s12931-019-1237-1/>.
35. Harvey BG, Strulovici-Barel Y, Kaner RJ, Sanders A, Vincent TL, Mezey JG, Crystal RG. Risk of COPD with obstruction in active smokers with normal spirometry and reduced diffusion capacity. *Eur Respir J*. 2015;46(6):1589–97. <https://doi.org/10.1183/13993003.02377-2014/>.
36. Xiao D, Chen Z, Wu S, Huang K, Xu J, Yang L, Xu Y, Zhang X, Bai C, Kang J, et al. Prevalence and risk factors of small airway dysfunction, and association with smoking, in China: findings from a national cross-sectional study. *Lancet Respir Med*. 2020;8(11):1081–93. [https://doi.org/10.1016/s2213-2600\(20\)30155-7/](https://doi.org/10.1016/s2213-2600(20)30155-7/).
37. Sandek K, Bratel T, Lagerstrand L. Effects on diffusing capacity and ventilation–perfusion relationships of budesonide inhalations for 2 months in chronic obstructive pulmonary disease (COPD). *Respir Med*. 2001;95(8):676–84. <https://doi.org/10.1053/rmed.2001.1124/>.
38. Hakulinen AL, Järvenpää AL, Turpeinen M, Sovijärvi A. Diffusing capacity of the lung in school-aged children born very preterm, with and without bronchopulmonary dysplasia. *Pediatr Pulmonol*. 1996;21(6):353–60. [https://doi.org/10.1002/\(sici\)1099-0496\(199606\)21:6%3C353::doi%3E3.0.CO;2-1/](https://doi.org/10.1002/(sici)1099-0496(199606)21:6%3C353::doi%3E3.0.CO;2-1/).
39. Sattrell E, Clemm H, Røksund OD, Hufthammer KO, Thorsen E, Halvorsen T, Vollseter M. Development of lung diffusion to adulthood following extremely preterm birth. *Eur Respir J*. 2022;59(5). <https://doi.org/10.1183/13993003.04103-2020/>.
40. Lim JU, Lee JH, Kim JS, Hwang YI, Kim TH, Lim SY, Yoo KH, Jung KS, Kim YK, Rhee CK. Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients. *Int J Chron Obstruct Pulmon Dis*. 2017;12:2465–75. <https://doi.org/10.2147/copd.S141295/>.
41. Divo MJ, Cabrera C, Casanova C, Marin JM, Pinto-Plata VM, de-Torres JP, Zulueta J, Zagaceta J, Sanchez-Salcedo P, Berto J, et al. Comorbidity distribution, clinical expression and survival in COPD patients with different body Mass Index. *Chronic Obstr Pulm Dis*. 2014;1(2):229–38. <https://doi.org/10.15326/jcopdf.1.2.2014.0117/>.
42. Alter P, Orszag J, Kellner C, Kahnert K, Speicher T, Watz H, Bals R, Welte T, Vogelmeier CF, Jörres RA. Prediction of air trapping or pulmonary hyperinflation by forced spirometry in COPD patients: results from COSYCONET. *ERJ Open Res*. 2020;6(3). <https://doi.org/10.1183/23120541.00092-2020/>.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.