Original Article

Predictors of dynamic hyperinflation during the 6-minute walk test in stable chronic obstructive pulmonary disease patients

Rui Chen[1*], Lin Lin[1*], Jing-Wei Tian[1], Bin Zeng[2], Lei Zhang[2], Xin Chen[3], Hai-Yan Yan[4]

[1]Department of Respiratory Diseases, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou 510120, China; [2]Laboratory of Rehabilitation, Guangdong Provincial Hospital, Guangzhou 510055, China; [3]Department of Respiratory Diseases, Zhujiang Hospital, Southern Medical University, Guangzhou 510280, China; [4]Department of Clinical Laboratory, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou 510120, China

*These authors contributed equally to this work.

Contributions: (I) HY Yan and X Chen conceived and designed the experiments; (II) R Chen, L Lin, JW Tian, L Zhang performed the experiments; (III) R Chen, L Lin, JW Tian analyzed the data; (IV) R Chen, B Zeng, L Zhang contributed materials and analysis tools; (V) R Chen, HY Yan, X Chen composed the manuscript.

Correspondence to: Hai-Yan Yan, MM. Department of Clinical Laboratory, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, #107 Yan Jiang Rd, Guangzhou 510120, China. Email: yanhaiyanwu@sina.com; Xin Chen, PhD. Department of Respiratory Diseases, Zhujiang Hospital, Southern Medical University, Guangzhou 510280, China. Email: beijixingmiler@qq.com.

Background: Dynamic hyperinflation (DH) is a major contributor to exercise limitation in chronic obstructive pulmonary disease (COPD). Therefore, we aimed to elucidate the physiological factors responsible for DH development during the 6-minute walk test (6MWT) in COPD patients and compare ventilatory response to the 6MWT in hyperinflators and non-hyperinflators.

Methods: A total of 105 consecutive subjects with stable COPD underwent a 6MWT, and the Borg dyspnea scale, oxygen saturation (S_pO_2), breathing pattern, and inspiratory capacity (IC) were recorded before and immediately after walking. The change in IC was measured, and subjects were divided into hyperinflators (ΔIC >0.0 L) and non-hyperinflators (ΔIC ≤0.0 L). Spirometry, the Modified Medical Research Council (MMRC) dyspnea scale and St George's Respiratory Questionnaire (SGRQ) were also assessed.

Results: DH was present in 66.67% of subjects. ΔIC/IC was significantly and negatively correlated with the small airway function. On multiple stepwise regression analysis forced expiratory flow after exhaling 50% of the forced vital capacity ($FEF_{50\%}$) was the only predictor of ΔIC/IC. Non-hyperinflators had a higher post-walking V_T (t=2.419, P=0.017) and post-walking V_E (t=2.599, P=0.011) than the hyperinflators did. Age and resting IC were independent predictors of the 6-minute walk distance (6MWD) in hyperinflators.

Conclusions: DH was considerably common in subjects with COPD. Small airway function may partly contribute to the DH severity during walking. The ventilator response to the 6MWT differed between hyperinflators and non-hyperinflators. Resting hyperinflation is an important predictor of functional exercise capacity in hyperinflators.

Keywords: Chronic obstructive pulmonary disease (COPD); dynamic hyperinflation (DH); exercise capacity; inspiratory capacity (IC)

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Introduction

Exercise intolerance is a cardinal complaint of patients with chronic obstructive pulmonary disease (COPD) (1). Although the underlying mechanism of exercise intolerance is complex and multifactorial, dynamic hyperinflation (DH) remains a major contributor to exercise limitation in COPD (2). The relationship between DH and exercise capacity has been documented using cardiopulmonary

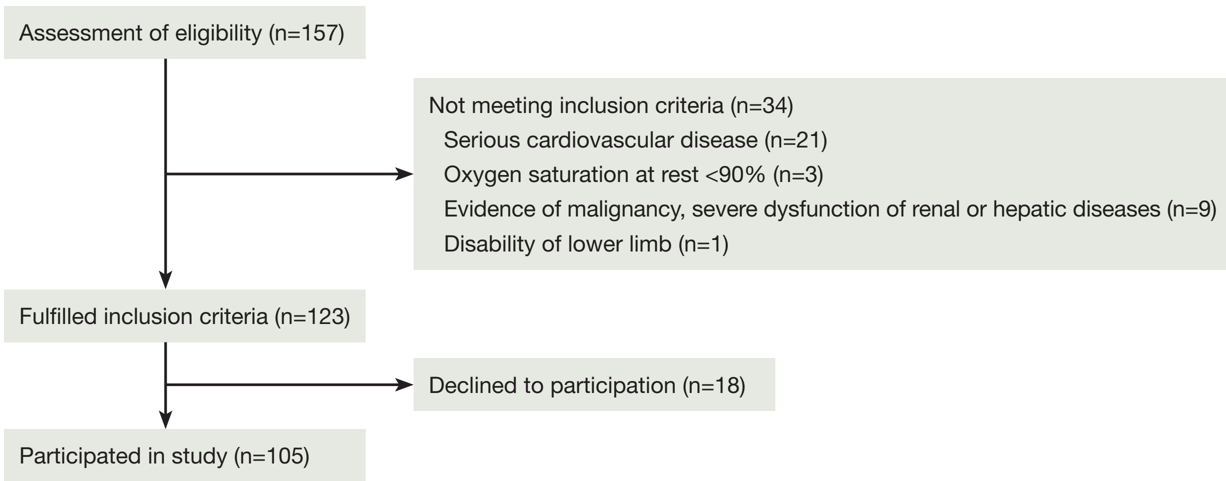

Figure 1 The flowchart illustrating participant eligibility, exclusion and enrollment.

exercise test (CPET) (3-5). In the clinical setting, CPET is often impractical because it requires specialized equipment, trained technicians, and physician supervision. Recent studies demonstrated that the 6-minute walk test (6MWT) provide a simple, safe, and well-tolerated method to detect DH in patients with COPD (6,7). However, the physiological factors responsible for DH development during the 6MWT have not been adequately evaluated. In addition, the effects of DH on ventilatory response to the 6MWT in COPD patients remain largely unknown. Finally, it is unclear whether the contribution to functional exercise capacity from resting lung function, demographic characteristics, exertional dyspnea and DH differs in COPD according to the DH status.

The aims of this study were: (I) to elucidate the physiological factors responsible for DH development during the 6MWT; (II) to compare physiological response to the 6MWT in hyperinflators and non-hyperinflators with COPD; and (III) to delineate the predictors of functional exercise capacity in hyperinflators and non-hyperinflators.

Methods

Participants

This prospective cross-sectional study was conducted between March 2013 and July 2014. Consecutive subjects with mild to very severe COPD from a pulmonary clinic at the Sun Yat-sen Memorial Hospital, Guangzhou, China were eligible for enrollment. COPD was diagnosed based on clinical manifestations, self-reported smoking history, and presence of persistent airflow limitation. Persistent flow limitation was defined as a post-bronchodilator forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) ratio <70% (8). The COPD severity was determined according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.

The inclusion criteria were: (I) a history of COPD; (II) aged over 40 years; (III) pulse oximetric saturation (S_pO_2) at rest >90% on ambient air; and (IV) no change in medication dosage or symptoms during the preceding 4 weeks.

The exclusion criteria were: (I) serious cardiovascular diseases (including uncontrolled hypertension, unstable angina pectoris, recent myocardial infarction, or congestive heart failure); (II) a diagnosis of obstructive sleep apnea (OSA) by polysomnography (PSG) before enrollment; (III) evidence of malignancy or severe renal or hepatic dysfunction; and (IV) lower limb disability. *Figure 1* summarizes the participant eligibility, exclusion, and enrollment process.

The study protocol was approved by the Ethics Committee, Sun Yat-sen Memorial Hospital, Guangzhou, China. All participants gave written informed consent. The study was registered at the Chinese Clinical Trial Registry (Registration Number: ChiCTR-TNRC-15006234, website: http://www.chictr.org/en/).

Group allocation

The study was performed at the Rehabilitation Laboratory of Guangdong Provincial Hospital, Guangzhou, China. Subjects were assigned to two groups based on occurrence of DH, defined as a decline in inspiratory capacity (IC) from baseline greater than zero (ΔIC >0.0 L) after 6MWT (9,10). Patients with a ΔIC >0.0 L in this study were diagnosed with DH (hyperinflators), and those with a ΔIC ≤0.0 L were considered DH negative (non-hyperinflators).

Measurements

Prior to examination, subjects were instructed to avoid strenuous exercise for 24 h. Demographic and clinical data were collected, followed successively by the pulmonary function test, 6MWT, assessment of quality of life and dyspnea. All measurements were obtained by a well-trained technician blinded to the study protocol.

Demographic and clinical data

The age, gender, smoking status, smoking history, body mass index (BMI), comorbidities, medication history, and use of oxygen therapy were recorded in each subject.

Pulmonary function tests

Standard forced expiratory spirometry was performed according to the American Thoracic Society guidelines using an electronic spirometer (CHEST GRAPH HI-101, Tokyo, Japan) before and after administering 400 µg salbutamol sulfate aerosol (Ventolin, GlaxoSmithKline, Shanghai, China) (11). The normal predicted values were determined according to the equations proposed by the European Coal and Steel Community with certain correction coefficients (12). Maximal voluntary ventilation (MVV) was estimated by multiplying FEV_1 by 35.

Inspiratory capacity (IC) maneuvers

The IC was measured with the patient seated after fully explaining the procedure to each subject (13). Satisfactory and consistent technique for the IC maneuvers was established with the subject at rest. After four to six consistent normal breaths, the subject was instructed to inspire the total lung capacity (TLC) and then return to normal breathing. The two largest IC measurements of at least three acceptable trials were required to agree within 5%. The better of two reproducible maneuvers was recorded for analysis.

6-minute walk test (6MWT)

The 6MWT followed the recommendations from American Thoracic Society guidelines (14). Patients were given standardized instructions to walk as fast as possible for 6 min. IC was measured at rest and immediately after walking (within 60 s). The heart rate, breathing pattern, S_pO_2, and the modified Borg dyspnea scale (15) and leg fatigue ratings were recorded before and after walking. We measured lung volume by plethysmography in five subjects before and after the 6MWT. The results showed no significant changes in TLC, which indicated that TLC did not change during walking test. Assuming that TLC does not change during exercise, changes in the IC are used to indirectly reflect the level of DH (16,17).

Dyspnea and quality of life assessment

The degree of dyspnea was assessed using the Modified Medical Research Council (MMRC) dyspnea scale (18). The health-related quality of life (HRQL) was evaluated using the St George's Respiratory Questionnaire (SGRQ) (19).

Statistical analysis

Data were expressed as the mean ± standard deviation. Statistical analyses were conducted using the Statistical Package for Social Sciences version 18.0. Chi-square analysis was applied to test discrete variables between the both groups. The independent samples *t*-test or Mann-Whitney *U*-test was used to compare continuous variables between the two groups. Pearson or spearman correlation coefficients were calculated for relationship between the ΔIC/IC or the 6-minute walk distance (6MWD) and other variables. Stepwise linear regression was performed to identify the factors independently associated with ΔIC/IC or the 6MWD. Variables were selected for use with the stepwise regression model based on the results of univariate analysis (*Tables S1*,*S2* in the supplementary file). A $P<0.05$ was considered statistically significant.

Results

Subject characteristics

Table 1 displays the population characteristics. A total of 105 subjects with stable COPD were included in this study. The

Table 1 Clinical and anthropometric characteristics of the subjects

Characteristics	Total (n=105)	DH negative group (n=35)	DH positive group (n=70)	P
Sex (M:F)	90:15	30:5	60:10	0.954*
Age (years)	71.30±7.91	71.03±8.64	71.54±7.63	0.757
BMI (kg/m^2)	21.50±3.21	22.23±3.28	21.17±3.15	0.114
MMRC dyspnea scale	1.23±0.70	1.20±0.58	1.24±0.76	0.810
6MWD (m)	486.39±81.50	486.84±74.95	486.15±85.41	0.969
Smoking index (pack-years)	35 (15, 50)	43 (12, 60)	31.75 (17.33, 47)	0.508#
Smoking status (active:prior)	26:79	8:27	19:51	0.636*
SGQR score				
Symptom score	46.72±21.01	43.84±22.15	48.46±20.43	0.293
Activity score	45.92±18.27	46.36±17.35	45.83±18.95	0.890
Impact score	19.54±16.82	16.43±14.17	21.34±17.94	0.162
Total score	32.04±14.36	30.05±12.63	33.26±15.16	0.286
Lung function				
FEV_1 (L)	1.39±0.51	1.38±0.53	1.40±0.50	0.823
FEV_1 (% pred)	58.29±18.90	58.27±19.64	58.31±18.65	0.992
FEV_1/FVC	50.66±13.46	53.85±14.54	49.01±12.67	0.084
ΔIC (L)	0.07±0.30	0.21±0.17	-0.24±0.19	0.000
ΔIC/IC (%)	0.89±19.56	11.36±9.1	-19.44±18.42	0.000
Small airway function				
MMF (L/s)	0.67±0.56	0.76±0.65	0.63±0.51	0.253
$FEF_{50\%}$ (L/s)	0.84±0.73	0.97±0.86	0.78±0.66	0.206
$FEF_{75\%}$ (L/s)	0.28±0.20	0.31±0.23	0.27±0.18	0.334
MMF (% pred)	26.82±20.62	29.88±25.09	25.27±17.95	0.290
$FEF_{50\%}$ (% pred)	26.50±23.21	30.59±29.28	24.42±19.36	0.208
$FEF_{75\%}$ (% pred)	28.42±16.83	30.13±19.69	27.55±15.27	0.471

*, Chi-square test was used to compare data between the two groups; #, Mann-Whitney U-test was used to compare data between the two groups. DH, dynamic hyperinflation; BMI, body mass index; MMRC, the Modified Medical Research Council; 6MWD, 6-minute walk distance; S_PO_2, oxygen saturation; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; IC, inspiratory capacity; MMF, maximal mid-expiratory flow; $FEF_{50\%}$, forced expiratory flow after 50% of the FVC has been exhaled; $FEF_{75\%}$, forced expiratory flow after 75% of the FVC has been exhaled.

numbers of patients diagnosed with GOLD stages I, II, III, and IV were 16 (15.2%), 50 (47.6%), 31 (29.5.1%), and 8 (7.6%), respectively. The mean age was 71.34±7.95 years, and men comprised 85.71% of the sample. DH was present in 70 subjects (66.67%), with 10 subjects (10/16) at GOLD stage I, 34 subjects (34/50) at GOLD stage II, 20 subjects (20/31) at GOLD stage III, and 6 subjects (6/8) at GOLD stage IV. Although there were decreasing trends of small airway function and FEV_1/FVC in hyperinflators, no significant differences were observed between the two groups.

Multiple regression analysis of DH

The univariate analysis of ΔIC/IC and ΔIC is shown in *Table S1*. Among the variables, only the maximal mid-expiratory flow (MMF) (% pred) (r=−0.256, P=0.010), the forced expiratory flow after exhaling 50% of the FVC ($FEF_{50\%}$) (% pred) (r=−0.279, P=0.005) and forced expiratory flow after exhaling 75% of the FVC ($FEF_{75\%}$) (% pred) (r=−0.212, P=0.033) were negatively correlated with the ΔIC/IC. No significant correlation was observed between FEV_1 and ΔIC/IC (r=0.031, P=0.755). On multivariate regression analysis,

Table 2 Multivariate linear regression for ΔIC and 6MWD

Variable	Standardized coefficients	P
Dependent variable: ΔIC (L)*		
$FEF_{50\%}$ (L/s)	−0.225	0.024
Dependent variable: ΔIC/IC (%)*		
$FEF_{50\%}$ (L/s)	−0.279	0.005
Dependent variable: 6MWD		
DH negative group#		
Age (years)	−0.462	0.002
MMRC dyspnea scale	−0.405	0.007
DH positive group#		
Age (years)	−0.359	0.003
Resting IC (L)	0.242	0.044

*, included variables if the P value was <0.30 in the univariate analysis; #, included variables if the P value was <0.10 in the univariate analysis. IC, inspiratory capacity; $FEF_{50\%}$, forced expiratory flow after 50% of the FVC has been exhaled; 6MWD, 6-min walk distance; MMRC, the Modified Medical Research Council.

the $FEF_{50\%}$ was the only predictor of ΔIC/IC (*Table 2*). For the ΔIC/IC, the $FEF_{50\%}$ uniquely contributed 27.9% of the variance.

The effects of DH on response to the 6MWT

The response to the 6WMT in both groups is summarized in *Table 3*. There were no significant differences in the 6WMD between the two groups. IC decreased by 0.24±0.19 L at the end of walking in hyperinflators. The non-hyperinflators had a higher post-walking V_T (t=2.419, P=0.017) and post-walking V_E (t=2.599, P=0.011) than the hyperinflators did. No obvious difference was observed in the post-walking breathing frequency, Borg dyspnea scale, heart rate, and ΔS_PO_2 between the two groups. After the 6MWT, the decrease of inspiratory reserve volume (IRV) in hyperinflators was significant higher than those of non-hyperinflators (t=-6.226, P<0.001). In addition, the post-walking V_T was significantly and positively correlated with the resting IC (r=0.293, P=0.004) and post-walking IC (r=0.456, P<0.001).

Multiple regression analysis of 6MWD

The univariate analysis of the 6MWD is shown in *Table S2*. In hyperinflators, age and resting IC were independent predictors of the 6MWD. These two factors contributed 60.1% of the variance for the dependent variable. In non-hyperinflators, age and MMRC dyspnea scale were the predictors of the 6MWD. These factors contributed 86.7% of the variance for the dependent variable (*Table 2*).

Discussion

There were several significant findings in this study. First, DH was common in the subjects with COPD and was easily detected using IC maneuvers during the 6MWT. Second, $FEF_{50\%}$ was the only predictor of DH during the 6MWT in subjects with COPD. Third, the ventilatory response to the 6MWT differed between hyperinflators and non-hyperinflators. Finally, resting hyperinflation was an important predictor of functional exercise capacity in hyperinflators.

We found that 66.67% of subjects with COPD developed DH during the 6MWT. It indicated that DH was considerably common during the 6MWT for subjects with COPD. We did not observe any adverse events related to the IC maneuvers during the 6MWT, which suggests that performing IC maneuvers during the 6MWT is a simple, safe, and well-tolerated method of detecting DH. In this study, there was no significant difference in the airflow obstruction between hyperinflators and non-hyperinflators. In addition, no obvious correlation was observed between airflow obstruction and the severity of DH. These findings imply that airflow obstruction is a poor predictor of the DH, echoing previous findings by Hannink (20).

Many factors are reportedly associated with the occurrence of DH such as age (21), obesity (22), exertional desaturation (23), smoking history (24), and systemic inflammation, etc. However, few studies have focused on the effect of small airway function on DH. Stewart (25) reported that small airway inflammation and structural damage preceded a marked decrease of airflow obstruction, leading to air-trapping even in mild COPD patients. Interestingly, we also observed DH in subjects with mild COPD. Hence, we speculate that small airway obstruction may be related to DH. In the current study, there was a weak but significantly negative relationship between the small airway function and the extent of DH. Moreover, $FEF_{50\%}$ was the only predictor of the DH severity. Our results suggest that small airway function may be partly responsible for the development of DH in patients with COPD. Further studies are warranted to demonstrate whether interventions to improve small

Table 3 The ventilatory response to walking in DH positive and negative group

Items	DH negative group (n=35)	DH positive group (n=70)	P
6MWD (m)	486.84±74.95	486.15±85.41	0.969
Pre-exertion V_E (L)	13.12±6.53	13.31±6.06	0.886
Post-exertion V_E (L)	20.91±9.20	16.81±7.25	0.011
Pre-exertion RR (bpm)	17.88±1.48	17.68±1.47	0.514
Post-exertion RR (bpm)	21.84±1.73	22.48±1.81	0.788
Pre-exertion V_T (L)	0.74±0.37	0.75±0.35	0.814
Post-exertion V_T (L)	0.94±0.32	0.74±0.40	0.017
ΔIC (L)	−0.21±0.17	0.24±0.19	<0.001
Pre-exertion IC (L)	1.55±0.54	1.93±0.57	0.002
Post-exertion IC (L)	1.76±0.55	1.69±0.48	0.528
Pre-exertion V_E/MVV	27.8±14.29	28.9±14.61	0.724
Post-exertion V_E/MVV	44.61±23.65	39.67±20.17	0.285
Pre-exertion IRV (L)	0.87±0.48	1.22±0.53	0.002
Post-exertion IRV (L)	0.93±0.48	0.93±0.45	0.998
ΔIRV (L)	−0.05±0.22	0.29±0.27	<0.001
Pre-exertion Borg dyspnea score	0.12±0.3	0.09±0.23	0.617
Post-exertion Borg dyspnea score	4.99±1.64	4.75±1.47	0.481
Pre-exertion Borg leg fatigue score	0.03±0.13	0.08±0.17	0.134
Post-exertion Borg leg fatigue score	3.29±1.48	3.38±1.37	0.682
Pre-exertion HR (bpm)	78.42±11.38	74.97±11.47	0.154
Post-exertion HR (bpm)	98.6±17.8	101.44±15.81	0.433
Pre-exertion S_pO_2 (%)	96.21±1.94	97.05±1.64	0.032
Post-exertion S_pO_2 (%)	93.62±10.36	96.61±5.18	0.023
ΔSpO_2 (%)	2.59±9.68	0.40±5.23	0.351[#]

[#], Mann-Whitney U-test was used to compare data between the two groups. DH, dynamic hyperinflation; 6MWD, 6-minute walk distance; V_E, minute ventilation; RR, respiratory rate; V_T, tidal volume; MVV, Maximal Minute Ventilation; IC, inspiratory capacity; HR, heart rate; IRV, inspiratory reserve volume; S_pO_2, oxygen saturation.

airway function can reduce DH in patients with COPD. We did not observe the relationship between DH and age, BMI, exertional desaturation and smoking index. Zafar *et al.* (23) reported that DH strongly correlated with exertional desaturation during the 6MWT and could be a reason for this desaturation. Our result did not agree with those of Zafar *et al.* (23).The inconsistency might be underlain by the exclusion of the subjects with resting S_pO_2 less than 90% in our study. The resting S_pO_2 of our subjects was significantly higher than those of Zafar *et al.*

Patients with COPD experience increased ventilatory demand during exercise. O'Donnell (26) reported that during a high-intensity exercise test, the occurrence of DH constrains increases in tidal volume (V_T). When close to minimal IRV, further increase of ventilatory demands is satiated through an increase in breathing frequency. However, the shortened expiratory time further exacerbates DH, creating a vicious circle. Our results showed that the post-walking V_T was significantly and positively correlated with the resting IC and post-walking IC, which is consistent with previous findings (26). In addition, we observed a remarkable increase in the post-walking V_T in non-hyperinflators instead of hyperinflators. There was an obvious increase in breathing frequency in both two groups. It indicated that the ventilatory response to the walking test differed between the two groups. In hyperinflators, the increased ventilatory demand was met primarily by the increase of breathing frequency. However, in non-hyperinflators, the increased ventilatory demand was satisfied by increasing both the breathing frequency and V_T. Guenette (27) showed that IRV provided a better index of ventilation than hyperinflation during a high-intensity exercise test. However, we did not observe such relationships. Noticeably, we observed an obvious decrease of IRV at the end of walking in hyperinflators. In contrast, there was no obvious change of IRV in non-hyperinflators. This implied that hyperinflators was prone to appear V_T constraint than non-hyperinflators during the 6MWD. O'Donnell (2) demonstrated that the ΔIC was significantly associated with exercise endurance under controlled laboratory conditions in COPD. In this study, although no obvious correlation was observed between the ΔIC and the 6WMD, both the resting IC and post-walking IC were positively correlated with the 6WMD. This suggests an indirect link between DH and exercise performance. We speculate that the inconsistency between our and previous findings is due to the different modes of exercise. The subjects didn't reach their maximal exercise capacity and ventilatory response during the 6WMT.

The 6MWT is commonly used to assess functional exercise capacity in patients with COPD. In this study, there was no significant difference in the 6MWD between hyperinflators and non-hyperinflators. However, the regression equation for 6MWD is different between the two groups. Age and resting hyperinflation were the predictors of functional exercise capacity in hyperinflators, while age and MMRC dyspnea scale was the predictors of functional exercise capacity in non-hyperinflators. Our results are consistent with the findings of Callens (6). Potentially, interventions improving resting hyperinflation may improve the exercise capacity in hyperinflators, while interventions to alleviate dyspnea may improve exercise capacity in non-hyperinflators. Additional studies are needed to confirm the hypothesis.

This study has some limitations. First, we did not measure the TLC in all patients; therefore, it is unknown whether the TLC was unchanged during the walking test. Despite this, we measured TLC with plethysmography in five subjects before and after the 6MWT. The results showed no significant changes in TLC. Hence, we supposed that TLC did not change after the 6MWT. Second, the decrease in the IC during exercise was quickly resolved (6). Hence, IC maneuvers after the walking test may actually underestimate the true severity of DH, though in our study, post-walking IC was measured within 60 s after completing the walking test. Third, there was only a weak correlation between small airway function and the level of DH. Nevertheless, the relationship was of significantly statistical significance. Additional studies are required to validate our findings, using more accurate methods to detect small airway function, such as late-phase sputum (28), peripheral airway resistance (29), alveolar nitric oxide concentrations (30), and HRCT (31). Finally, other factors known to be associated with impaired exercise capacity in patients with COPD, such as anxiety, depression, skeletal muscle function (32), and cardiovascular abnormalities (33), were not assessed.

In conclusion, DH was common in patients with COPD and easily detected by performing IC maneuvers during the 6MWT. The $FEF_{50\%}$ was the only predictor of DH during the 6MWT, and the ventilatory response to the 6MWT differed between hyperinflators and non-hyperinflators. Resting hyperinflation is an important predictor of functional exercise capacity in hyperinflators.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Table S1 Univariate analysis of ΔIC

Univariate	ΔIC		ΔIC/IC	
	Correlation coefficient	P	Correlation coefficient	P
Pearson correlation				
Age (years)	0.037	0.712	0.062	0.532
BMI (kg/m^2)	–0.041	0.680	–0.076	0.442
Smoking index (pack-years)	–0.084	0.405	–0.043	0.667
6MWD (m)	0.025	0.800	–0.008	0.933
SGRQ score				
Symptom score	0.065	0.517	0.088	0.378
Activity score	–0.063	0.527	–0.072	0.468
Impact score	0.049	0.621	0.079	0.430
Total score	0.022	0.826	0.042	0.674
Lung function				
FEV_1 (L)	0.033	0.737	0.031	0.755
FEV_1 (% pred)	–0.011	0.911	0.019	0.846
FEV_1/FVC	–0.176	0.075	–0.152	0.126
Small airway function				
MMF (L/s)	–0.192	0.054	–0.219*	0.028
$FEF_{50\%}$ (L/s)	–0.203*	0.042	–0.233*	0.019
$FEF_{75\%}$ (L/s)	–0.172	0.085	–0.210*	0.035
MMF (% pred)	–0.215*	0.031	–0.256**	0.010
$FEF_{50\%}$ (% pred)	–0.225*	0.024	–0.279**	0.005
$FEF_{75\%}$ (% pred)	–0.188	0.059	–0.212*	0.033
Spearman correlation				
Smoking status (active:prior)	–0.077	0.442	–0.091	0.359
ΔS_pO_2 (%)	–0.106	0.291	–0.070	0.485
ΔBorg dyspnea score	0.171	0.085	0.163	0.103
Gender (M:F)	0.036	0.717	0.078	0.435
MMRC	–0.002	0.988	0.021	0.831

*, Correlation is significant at the 0.05 level (2-tailed); **. Correlation is significant at the 0.01 level (2-tailed); IC, inspiratory capacity; BMI, Body Mass Index; 6MWD, 6 minute walk distance; SGRQ, St George's Respiratory Questionnaire; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; MMF, maximal mid-expiratory flow; $FEF_{50\%}$, forced expiratory flow after 50% of the FVC has been exhaled; $FEF_{75\%}$, forced expiratory flow after 75% of the FVC has been exhaled; S_PO_2, oxygen saturation; MMRC, the Modified Medical Research Council.

Table S2 Univariate analysis of 6MWD

Univariate	6MWD			
	DH positive group		DH negative group	
	Correlation coefficient	P	Correlation coefficient	P
Pearson correlation				
Age (years)	–0.448**	0.000	–0.475**	0.005
BMI (kg/m^2)	0.187	0.127	–0.034	0.850
Lung function				
FEV_1 (L)	0.374**	0.002	0.133	0.455
FEV_1 (% pred)	0.164	0.183	0.068	0.704
FEV_1/FVC	0.134	0.277	–0.006	0.972
Pre-evertion IC (L)	0.309*	0.010	0.074	0.675
Post-exertion IC (L)	0.338**	0.005	0.133	0.452
ΔIC (L)	0.022	0.858	–0.198	0.262
ΔIC/IC (%)	–0.097	0.429	–0.073	0.681
MMF (L/s)	0.257*	0.036	0.044	0.806
Spearman correlation				
Gender (M:F)	–0.151	0.218	–0.085	0.634
MMRC dyspnea scale	–0.338**	0.005	–0.306	0.078
Pre-exertion S_pO_2 (%)	–0.080	0.517	0.372	0.030
Post-exertion S_pO_2 (%)	–0.159	0.195	0.150	0.399
ΔS_pO_2 (%)	0.022	0.857	–0.042	0.814
Pre-exertion Borg score	–0.164	0.181	0.104	0.558
Post-exertion Borg score	0.029	0.812	–0.088	0.619
ΔBorg dyspnea score	0.066	0.591	–0.168	0.342

*, correlation is significant at the 0.05 level (2-tailed); **, correlation is significant at the 0.01 level (2-tailed). 6MWD, 6 minute walk distance; DH, dynamic hyperinflation; BMI, body mass index; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; IC, inspiratory capacity; MMF, maximal mid-expiratory flow; MMRC, the Modified Medical Research Council; S_PO_2, oxygen saturation.