The Relationship Between Peak Inspiratory Flow and Hand Grip Strength Measurement in Men with Mild Chronic Obstructive Pulmonary Disease

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Abstract

Backgrounds: Chronic obstructive pulmonary disease (COPD) decreases quality of life and muscular strength. Inspiratory flow is important for inhalants in the bronchi but is complicated to measure in routine practice. We hypothesized that hand grip strength (HGS) would correlate with inhalation rate in patients with mild COPD.

Methods: The COPD patients were recruited at the St. Marianna University School of Medicine, Yokohama Seibu Hospital, from 2015 to 2018. We measured peak inspiratory flow (PIF) through an In-Check flow meter attached with Diskus [PIF(D)] and Turbuhaler [PIF(T)] inhalers. The 6-minute walking test (6MWT), and the fraction of exhaled nitric oxide (FENO), spirometry, HGS, or forced oscillation technique (FOT) parameters were measured.

Results: Forty-four subjects were enrolled. All were men, with a mean age ($\pm$ SD) of 77.8 ± 9.36 years. Thirty-nine patients had mild COPD. PIF(D) was 110 (80, 140) L/min (median, interquartile range), PIF(T) was 80 (70, 90) L/min, and HGS was 28.7 (13.8, 43.6) kgf. PIF(D) and PIF(T) were significantly correlated ($r = 0.443$, $p = 0.003$). PIF(D) was significantly correlated with age ($r = -0.327$, $p = 0.030$) and HGS ($r = 0.326$, $p = 0.031$). PIF(T) was significantly correlated with age ($r = -0.328$, $p = 0.030$), FVC ($r = 0.351$, $p = 0.019$), 6MWT distance ($r = 0.392$, $p = 0.011$), and HGS ($r = 0.328$, $p = 0.030$).

Conclusion: HGS might be more useful for predicting PIF than other parameters. Also, elderly COPD patients need to be taught inhaled methods carefully.

Introduction

Chronic obstructive pulmonary disease (COPD) is caused by cigarette smoke or other hazardous substances and results in airflow obstruction.¹ COPD has a high prevalence and is often managed by a general physician. Treatment of COPD primarily involves inhaled drugs, such as long-acting muscarinic antagonists, long-acting beta2-agonists, inhaled corticosteroids, or combinations of these drugs. When using a dry-powder inhaler, inspiratory flow is important for effective deposition in the bronchi, but it is complicated for general physicians to measure the inhalation rate in daily clinical practice.

COPD reduces the quality of life and muscular strength, and the prognosis of COPD correlates with activity in life (2, 3). The six-minute walk test (6MWT) is used to assess response to treatment, activity level, and prognosis (4, 5). However, it is difficult to perform a 6MWT in primary care clinics in Japan. Easy-to-understand indicators are required.

Recent studies showed that hand grip strength (HGS) reflects activity levels, and low HGS is associated with mortality (6). In COPD patients, HGS is associated with the antioxidant indicators serum club-cell protein 16 (CC16) and total sialic acid, which also predict forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) (7). HGS is also associated with the distance walked in the 6MWT, frequency of COPD exacerbation, and inspiratory flow rate (8), suggesting that the HGS may reflect not only upper

body muscle strength but also COPD activity and severity. In addition, there are reports that grip strength and inhalation flow rate are related (9), and also in acute exacerbation (10). However, evidence in this area is insufficient.

We explored whether HGS is associated with inhalation rate in mild COPD and could therefore be a simple method of determining inhalation rates in COPD patients managed by general physicians.

Patients And Methods

Subjects

We recruited COPD patients from outpatients who visited St. Marianna School of Medicine, Yokohama City Seibu Hospital, from 2015 through 2018. We measured the peak inspiratory air velocity with In-Check.

We diagnosed COPD according to the COPD Guidelines for Diagnosis and Treatment Fifth Edition in Japan (2018): 40 years or older; over 20 pack-years of smoking history; cough, sputum, or dyspnea; and FEV1/FVC < 70% by spirometry after inhalation of a bronchodilator (1). The stages of COPD were classified as follows depending on the state of airflow obstruction: Stage I, %FEV1 $\geq$ 80%; II, 50% $\leq$ %FEV1 < 80%; III, 30% $\leq$ %FEV1 < 50%; IV, %FEV1 < 30%. Patients were excluded when they had an obvious thoracic deformity, had acute exacerbation of COPD when the assessment was performed, required treatment for a lower airway infection, or were unable to complete the 6MWT in room air due to hypoxia or difficulty walking. Asthma-COPD overlap (ACO) was diagnosed based on the JRS Guidelines for ACO Management 2018 (11), when a patient met any two or more of the following criteria: 1) fluctuating or episodic respiratory symptoms, 2) asthma since before age 40, 3) FENO > 35 ppb, or 4) any two or more of (i) concomitant perennial allergic rhinitis, (ii) airway reversibility (change in FEV1 of > 200 mL and 20%), (iii) peripheral eosinophils in blood (> 5% or > 300/ μ L), or (iv) elevated IgE or positive specific IgE to a perennial inhaled antigen.

The study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of St. Marianna University School of Medicine (University No. 2883) on April 21, 2015. Written consent was obtained from all participants.

HGS

HGS was measured with a Jamar hydraulic dynamometer (Preston, IL) twice alternately for the left and right hands with the patient standing.

6MWT

The 6MWT was conducted in accordance with the American Thoracic Society standards (5).

FENO, FOT, and spirometry

Physiological laboratory technicians performed each measure according to the operation manual. The tests were performed in the order FENO, FOT, and spirometry to avoid having one test influence the results of the subsequent tests.

Spirometry measurements were carried out by one of our hospital's experienced physiological technicians using a CHESTAC-8800 (Chest M.I., Inc., Tokyo, Japan) following the JRS Guidelines for Respiratory Function Testing (12). FVC, %FVC, FEV1, FV1/FVC%, and %FEV1 were measured by spirometry. Diffusing capacity of the lungs for carbon monoxide (DLCO) was measured by having patients inhale CO-containing gas and exhale it 10 s later, measuring the concentration of exhaled air, and calculating the %DLCO and %DLCO divided by alveolar volume (%DLCO/VA).

FENO was measured with a NIOX-VERO (Chest M.I., Inc.). In accordance with the instruction manual, after maximum inhalation, patients were asked to exhale at 50 mL/s. Only samples for which measurable values of NO were detected were used for the analysis.

FOT measurements were carried out with a MostGraph-01 (Chest M.I., Inc.). While patients were engaged in stable resting ventilation, respiratory resistance at 5 Hz (R5) and 20 Hz (R20), respiratory reactance at 5 Hz (X5), resonant frequency (Fres), and the area of low reactance were measured, and their average values, values during expiration and inspiration, and the difference between the values during expiration and inspiration were evaluated.

Inhalation flow rate

We attached either the Diskus or Turbuhaler adaptor to the In-Check flow meter (Clement Clark International, UK). The flow was measured three times, and the highest value was adopted.

Intake muscle strength

The patients were measured using a respiratory dynamometer (CHEST, VITAL POWER KH-101). Maximum inspiration from the residual capacity was maintained for 3 seconds. The measurement was performed three times, and the maximum value was adopted.

Statistical analysis

Statistical analysis was conducted using JMP version 14 (SAS, Japan). All parameters were expressed as frequencies or medians and interquartile ranges. Correlations between parameters were indicated in terms of Spearman's correlation coefficient (r), with $p < 0.05$ regarded as significant. The multivariate analysis was used to investigate the relationships among PIF (D) or PIF (T) and other parameters.

Results

Forty-four patients were enrolled in the study, all of whom were men. Their backgrounds and parameters were showed at Table 1. The COPD stage of the patients in this study had comparatively mild (I: 28 patients (63.6%), II: 11 patients (25%), III: 5 patients (11.4%), and IV: none) and no patients had

hypoxemia. The peak inspiratory flow (PIF) with the Diskus adaptor [(PIF(D))] was 110 (80, 140) L/min (median, interquartile range) and the PIF with the Turbuhaler [PIF(T)] was 80 (70, 90) L/min. PIF(D) of all subjects were above 60 (L/min), and PIF(T) of only one subject was below 60(L/min). HGS was 28.7 (13.8, 43.6) (kgf). There was a significant correlation between PIF(D) and PIF(T) ($r = 0.443$, $p = 0.003$). Both PIF(D) and PIF(T) were correlated with age and HGS (Table 2, Fig. 1). PIF(T) was also significantly correlated with FVC ($r = 0.351$, $p = 0.019$) and the distance walked in the 6WMT ($r = 0.392$, $p = 0.011$) (Table 2). Moreover, there was significant relationship between age and HGS ($r = -0.667$, $p < 0.001$).

Further to investigate the relationships between PIF(D) or PIF(T) and other parameters, we performed multiple regression analysis (Table 3). Age and HGS were not significantly associated with PIF(D) or PIF(T) independently.

Discussion

In male patients with mild COPD, higher PIF(D) and PIF(T) were associated with lower age and higher HGS. Although the relationship of PIF to age is a well-established theory, the correlation between inhalation flow rate and HGS in mild COPD patients is a new finding.

All the cases that happened to participate in this study happened to be male. This is due to the fact that men have more COPD. Men tend to have higher muscle strength than women, so that this study shows a tendency in men.

The level of inhalation flow is important for COPD management because it is associated with the distribution of inhaled dry-powder drugs. In a clinical situation, the type of inhalation drug is often selected with reference to the respiratory function and guidance on inhalation techniques. In our study, it is difficult to predict inhalation flow rate from the results of spirometry. This is because that spirometry is excellent for determining airway stenosis but is not a direct indicator of inhalation. The inhalation flow rate should be measured directly for each patient, but the flow rate and timing required are different for each device, so drug selection and inhalation guidance are required for each device. It would be more convenient to have an objective, simple, and easy-to-understand index for predicting the inhalation flow rate.

Devices of dry powder inhaler are divided into low resistance and medium and high resistance, Diskus is low resistance inhaler, and Turbuhaler is a inhaler categorized in medium and high resistance (13). If PIF exceeds 60 (L/min), any device will have sufficient flow rate for treatment. In this study, effective inhalation was performed in all cases. If HGS exceeds 20 (kgf), it is assumed that effective inhalation for DPI is possible. In addition, multiple regression analysis did not find an independent association between age and grip strength with PIF(D) or PIF(T). Although it is thought to reflect the decrease in activity due to aging, one recent study (10) showed that there was significant correlation between HGS and PIF independently of gender and age. It is considered that the number of subjects in this study is small. Frohnhafer et al showed that HGS and inhalation flow velocity are directly correlated, and effective inhalation is not possible in patients with COPD if their HGS is less than 10 (kgf)(10). In our study, there

were no patients with HGS below 10 (kgf), but our results are generally in agreement with those of this previous study. Most of the COPD managed by primary care physicians is mild, so the results of our study are likely to be useful in primary care settings.

The inspiratory muscles, such as the diaphragm or external intercostal muscles are important for inhalation, but it is difficult to measure inspiratory muscle strength clinically. We measured maximum inspiratory mouth pressure (P_Imax) in 35 patients, but there was no significant relationship between PIF(D) or PIF(T) and P_Imax (Table 2). P_Imax is not measured in all cases and may affect the results, but this suggests that not only muscle strength but the timing of inspiration are required for predicting PIF. Although HGS reflects the muscle strength of the upper limbs and does not directly indicate the muscle strength of the lower limbs or inspiration, it does reflect the overall strength of muscles used in daily life. Thus, it is not surprising that the evaluation of muscle strength required for COPD management can be performed with HGS. In fact, there was one recent report showing significant correlation between 6MWT and HGS in COPD (8). Although HGS has not yet been used in general medical care for COPD, because of its simplicity—it can be measured simply by grasping the grip-strength meter—it may become a useful evaluation method in the future.

A limitation of this study is that it included only a small number of men at a single institution. Women's muscle strength tends to be weaker than men and require new research about women. In addition, there were relatively many cases of ACO, which may affect the results. P_Imax, 6MWT, DLCO had not been measured in all cases, and may affect results. Diskus and Turbuhaler were old Devices, so that the results with new devices were unknown. As a cross-sectional study, the results cannot be used to determine causal relationships, which would require a multicenter prospective study.

Conclusions

In conclusion, both PIF (D) and PIF (T) correlated with HGS and age. HGS predicted inhalation flow better than lung function tests and may predict therapeutic efficacy and prognosis.

Abbreviations

6MWT

the distance of 6 minutes walking test

BMI

body-mass index

COPD

chronic obstructive pulmonary disease

DLCO

Diffusing capacity of the lungs for carbon monoxide

FENO

The fraction of exhaled nitric oxide

FEV1

forced expiratory volume in 1 s

FOT

the forced oscillation technique

Fres

resonant frequency

HGS

hand grip strength

PIF

peak inspiratory flow

PI_{max}

maximum inspiratory mouth pressure

Declarations

Acknowledgement

This research was presented at 30th International Congress of the European Respiratory Society (Wien, 2020 September).

Conflict of Interest

The authors have no conflict of interest to disclose associated with this manuscript.

Ethics approval and consent to participate

The study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of St. Marianna University School of Medicine (University No. 2883) on April 21, 2015. Written consent was obtained from all participants.

Consent for publication

Written consent was obtained from all participants.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

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Authors Contributions

TT and YK designed the study. TT wrote the manuscript. TT, YK, HT, BO, HM, NH, TK and SM contributed to data collection. TT performed the statistical analysis. TK and SM performed 6MWT. All authors read and approved the final manuscript.

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Tables

Due to technical limitations, table 1,2,3 is only available as a download in the Supplemental Files section.

Figures

Figure 1

There was a significant correlation between PIF(D) and PIF(T) ($r = 0.443$, $p = 0.003$). Both PIF(D) and PIF(T) were correlated with age and HGS (Table 2, Fig. 1).

Supplementary Files

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- [Table1.jpg](#)
- [Table2.jpg](#)
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