Pulmonary Pharmacology & Therapeutics 85 (2024) 102298

Contents lists available at ScienceDirect

Pulmonary Pharmacology & Therapeutics

journal homepage: www.elsevier.com/locate/ypupt

Suboptimal peak inspiratory flow rate in dry-powder inhaler users for chronic obstructive pulmonary disease in Korea

Ji-Yong Moon [a,1], Sang Hyuk Kim [b,1], Youlim Kim [c], Hyun Lee [a], Chin Kook Rhee [d], Seung Won Ra [e], Chang Youl Lee [f], Joo Hun Park [g], Yong Bum Park [h,**,2], Kwang Ha Yoo [c,*,2]

[a] Department of Internal Medicine, Hanyang University College of Medicine, Seoul, South Korea
[b] Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Internal Medicine, Dongguk University Gyeongju Hospital, Dongguk University College of Medicine, Gyeongju, South Korea
[c] Department of Internal Medicine, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, South Korea
[d] Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea
[e] Department of Internal Medicine, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea
[f] Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Hallym University Chuncheon Sacred Heart Hospital, Chuncheon-si, Gangwon-do, South Korea
[g] Department of Pulmonary and Critical Care Medicine, Ajou University School of Medicine, Suwon, South Korea
[h] Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Hallym University Kangdong Sacred Heart Hospital, Seoul, South Korea

ARTICLE INFO

Keywords:
Obstructive disease
Chronic pulmonary
Administration
Inhalation
Inhalation devices
Inspiratory capacity
Respiratory function tests

ABSTRACT

Background: A suboptimal peak inspiratory flow rate (PIFR) in dry-powder inhaler (DPI) users can lead to insufficient therapeutic effects in the treatment of chronic obstructive pulmonary disease (COPD). However, few data on the prevalence of and factors associated with suboptimal PIFR in Korean patients with COPD are available.

Methods: We conducted a cross-sectional study of patients with COPD who had been using DPIs for more than three months. PIFR was measured using an In-Check DIAL G16 device. Suboptimal PIFR was defined as below the resistance-matched threshold. Multivariable logistic regression analysis was used to determine factors associated with suboptimal PIFR.

Results: Of 444 DPI users with COPD, the rate of suboptimal PIFR was 22.0 % (98/444). In a multivariable analysis, significant factors associated with suboptimal PIFR were age (adjusted odds ratio [aOR] = 1.06 by 1-year increase; 95 % confidence interval [CI] = 1.02–1.09), male sex (aOR = 0.28; 95 % CI = 0.11–0.73), body mass index (BMI) (aOR = 0.91 by 1 kg/m^2 increase; 95 % CI = 0.85–0.99), post-bronchodilator forced vital capacity (FVC) %pred (aOR = 0.97 by 1%pred increase; 95 % CI = 0.95–0.99), and In-Check DIAL R2-type inhaler [medium-low resistance] use (aOR = 3.70 compared with R1-type inhalers [low resistance]; 95 % CI = 2.03–7.03).

Conclusions: In Korea, more than one-fifth of DPI users with COPD had a suboptimal PIFR. The factors associated with suboptimal PIFR were age, female gender, low BMI, low FVC, and R2-type inhaler use. Therefore, clinicians should carefully evaluate the possibility of suboptimal PIFR when prescribing DPIs.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic respiratory disease that substantially burdens affected patients and healthcare systems [1]. Current guidelines recommend inhaled bronchodilators as the most important treatment modality for COPD; inhaled bronchodilators are associated with better treatment outcomes by improving the quality of life and lung function and by preventing future

* Corresponding author.
** Corresponding author.
E-mail addresses: bfspark2@gmail.com (Y.B. Park), 20010025@kuh.ac.kr (K.H. Yoo).
[1] J-Y. Moon and S.H. Kim contributed equally as co-first authors.
[2] Y.B. Park and K.H. Yoo contributed equally as co-corresponding authors.

https://doi.org/10.1016/j.pupt.2024.102298
Received 17 December 2023; Received in revised form 17 March 2024; Accepted 31 March 2024
Available online 10 April 2024

exacerbation of COPD [2–4]. Currently, inhalers are available in three different systems: pressurized metered-dose inhalers, dry-powder inhalers (DPIs), and soft-mist inhalers [5].

A commonly utilized inhaler is the DPI, in which the medication is formulated as a powder and combined with carrier particles [6]. Successful utilization of a DPI relies on the patient's ability to generate adequate inspiratory flow, which is essential for disaggregating and dispersing the powder into particles smaller than 5 μm in diameter [7]. These smaller particles can then be inhaled and deposited into the lower respiratory tract, which is a site of action, for optimal therapeutic effect [8]. To deliver the medication effectively, a sufficient inhalation power, known as peak inspiratory flow rate (PIFR), is necessary [9]. In addition to the patient's inhalation ability, internal resistance generated by the drug-delivery device itself can also affect the PIFR [10]. Therefore, when a suitable inhaler is prescribed to appropriate patients, we can anticipate therapeutic efficacy.

One of the most prevalent errors associated with DPI use is an insufficient PIFR [11]. Previous studies have demonstrated that a suboptimal PIFR can diminish the effectiveness of the medication, leading to poor outcomes [12,13]. However, there is a lack of data regarding this issue in Korea, and patient education or treatment strategies based on PIFR have yet to be widely implemented. This study aims to evaluate the prevalence of and factors associated with suboptimal PIFR in Korean patients with moderate to severe COPD who used DPIs.

2. Methods

2.1. Study design and study population

We conducted a cross-sectional observational study at seven hospitals in Korea. Eligibility criteria for the study were (1) an age of 40 years or more, (2) a diagnosis of COPD before the past year, and a post-bronchodilator forced expiratory volume in 1 s (FEV_1) to a forced vital capacity (FVC) ratio < 70 % at diagnosis, (3) outpatient status with moderate to very severe COPD (defined as Global Initiative for Chronic Obstructive Lung Disease [GOLD] stage 2–4), including patients improved to GOLD stage 1 from stage 2–4, (4) a documented history of the presence or absence of the acute exacerbation, (5) consistent use of a long-acting bronchodilator using DPIs (of any type) for at least three consecutive months without switching to other DPIs, and (6) a recorded pulmonary function test within the last 12 months.

Prescription of the inhaler was made at the discretion of attending physicians, without a PIFR assessment. Exclusion criteria included a history of bronchial asthma, a current diagnosis of bronchial asthma or asthma-COPD overlap, the presence of significant diseases other than COPD, unstable or life-threatening cardiac arrhythmias, hospitalization for heart failure or myocardial infarction within the previous year, regular daytime oxygen therapy use exceeding 1 h per day, and acute exacerbation within the last three months. Acute exacerbation comprises both moderate and severe exacerbations. Moderate exacerbation was an event that required the prescription of steroids or antibiotics in the outpatient department. Severe exacerbation was an emergency room visit or hospitalization due to deterioration of respiratory symptoms. Based on these criteria, we enrolled 449 patients, and 5 patients were excluded. As a result, 444 patients were analyzed per protocol.

2.2. Peak inspiratory flow rate

Peak inspiratory flow was evaluated using the In-Check DIAL G16 device, a tool designed to measure the PIFR against specific resistance levels. This is a disposable, single-patient mouthpiece equipped with a one-way valve to prevent patients from exhaling into the device. The resistance levels are categorized from R1 (low resistance) to R5 (high resistance), each corresponding to different device types and the minimally required PIFR. Device resistance was adjusted to match the resistance of the patient's inhaler.

A trained nurse measured the PIFR three times, and the highest recorded value was recorded. A suboptimal PIFR was defined as a measured PIFR below the threshold that matched the set resistance level (Table 1). In patients using multiple inhaler devices, a PIFR below the threshold for any device was considered suboptimal.

2.3. Outcomes

The primary outcome of this study was the proportion of patients with a suboptimal PIFR among DPI users with COPD. The secondary outcome was factors associated with suboptimal PIFR.

2.4. Statistical analysis

We expressed normally distributed continuous variables, non-normally distributed continuous variables, and categorical variables as means ± standard deviation, medians with interquartile range (IQR), and numbers with percentages, respectively. To evaluate the prevalence of suboptimal PIFR, patients were divided into optimal and suboptimal PIFR groups. In a comparison of optimal and suboptimal PIFRs, statistically significant differences were assessed using a χ^2 test, Student's t-test, or Mann–Whitney *U* test according to their normality. Post hoc analysis of the χ^2 test was conducted with a Bonferroni adjustment to account for multiple comparisons. Multivariable logistic regression analysis was performed to evaluate the factors associated with suboptimal PIFR. In the multivariable analysis, demographic variables (age, sex, height, and weight), lung function (post-bronchodilator FEV_1% pred), and In-Check dial resistance were included. We used three multivariable analysis models with the following variables: model 1 included age, sex, body mass index (BMI), post-bronchodilator FEV_1, and In-Check dial resistance; model 2 included age, sex, BMI, post-bronchodilator FVC, and In-Check dial resistance; and model 3 included age, sex, BMI, post-bronchodilator FVC, GOLD stage, and In-Check dial resistance. A *p*-value < 0.05 was considered statistically significant. All statistical analyses were conducted using R software version 4.2.2 (R core Team 2019; R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Baseline characteristics of the study population

The baseline characteristics of the study population are summarized in Table 2. The mean age of the study population was 71.5 ± 8.1 years, and the majority of participants (93.2 %) were men. Comparing patients with a suboptimal PIFR against those with an optimal PIFR revealed that the former were older (74.2 ± 8.1 vs. 70.7 ± 7.9 years, p < 0.001), more likely to be women (85.7 % vs. 95.4 %, p = 0.002), and had a lower BMI (22.6 [IQR, 21.5–24.8] vs. 24.0 [IQR, 21.6–25.7] kg/m^2, p = 0.015). Regarding smoking status, patients with a suboptimal PIFR reported a higher cumulative number of PYs than those with a suboptimal PIFR (43 [IQR, 30–50] vs. 40 [IQR, 25–48] PYs, *p* = 0.044). However, there was no significant difference in the proportion of ever-smokers (current or

Table 1
Definition of suboptimal peak inspiratory flow rate for each dry powder inhaler.

Resistance	Device type	Minimally required PIFR (L/min)
R1 (Low)	Breezhaler	<50
R2 (Medium-low)	Ellipta, Diskus	<60
R3 (Medium)	Turbohaler, Symbicory	<45
R4 (Medium-high)	NEXTHaler, Turbohaler Pulmicort	<45
R5 (High)	Handihaler	<30

Abbreviations: PIFR = peak inspiratory flow rate.

Table 2
Clinical characteristics of the study population.

	Optimal PIFR (n = 346)	Suboptimal PIFR (n = 98)	Total (n = 444)	*p*-value*
Age, years	70.7 ± 7.9	74.2 ± 8.1	71.5 ± 8.1	<0.001
40–49	3 (0.9 %)	0 (0.0 %)	3 (0.7 %)	<0.001
50–59	21 (6.1 %)	6 (6.1 %)	27 (6.1 %)	<0.001
60–69	135 (39.0 %)	19 (19.4 %)	154 (34.7 %)	0.015
70–79	141 (40.8 %)	47 (48.0 %)	188 (42.3 %)	
≥80	46 (13.3 %)	26 (26.5 %)	72 (16.2 %)	
Gender				0.002
Female	16 (4.6 %)	14 (14.3 %)	30 (6.8 %)	
Male	330 (95.4 %)	84 (85.7 %)	414 (93.2 %)	
Height, cm	165.5 ± 6.8	161.9 ± 7.9	164.7 ± 7.2	<0.001
Weight, kg	65.3 ± 10.3	60.0 ± 9.6	64.1 ± 10.4	<0.001
Body mass index, kg/m^2	24.0 (21.6–25.7)	22.6 (21.5–24.8)	23.7 (21.5–25.6)	0.015
Smoking status				0.063
Current smoker	70 (20.2 %)	14 (14.3 %)	84 (18.9 %)	
Ex-smoker	267 (77.2 %)	77 (78.6 %)	344 (77.5 %)	
Never smoker	9 (2.6 %)	7 (7.1 %)	16 (3.6 %)	
Smoking amount, pack-years	38.0 (25.0–48.0)	43.0 (30.0–50.0)	40.0 (26.0–50.0)	0.044
CAT score	8.0 (5.0–13.0)	10.0 (6.0–16.0)	8.0 (5.0–14.0)	0.007
Lung function				
Post-BD FVC, % pred	82.4 ± 16.3	74.0 ± 15.7	80.5 ± 16.5	<0.001
Post-BD FEV$_1$, % pred	65.7 ± 16.8	58.2 ± 16.9	64.0 ± 17.1	<0.001
Post-BD FEV$_1$/FVC ratio	0.6 (0.5–0.6)	0.5 (0.4–0.6)	0.6 (0.5–0.6)	0.254
Acute exacerbation				
Moderate exacerbation, n (%)	48 (13.9)	19 (19.4)	67 (15.1)	
Severe exacerbation, n (%)	4 (1.2)	8 (8.2)	12 (2.7)	0.001
Modified charlson comorbidity index	1.0 (1.0–2.0)	1.0 (1.0–3.0)	1.0 (1.0–2.0)	0.026

Values are presented as numbers (%) for categorical variables and median with interquartile range or mean ± standard deviation according to their normality for continuous variables. *p-values for categorical variables were calculated with the χ^2 test; p-values for continuous variables were estimated with the Student t-test or Mann–Whitney U test.
Abbreviations: mMRC = modified Medical Research Council, CAT = COPD Assessment Test, BD = bronchodilator, FVC = forced vital capacity, FEV$_1$ = forced expiratory volume in 1 s.

ex-smokers) between the two groups (92.9 % vs. 97.4 %, $p = 0.063$). Regarding lung function, patients with a suboptimal PIFR had a lower FVC (74.0 ± 15.7 vs. 82.4 ± 16.3 %pred, p < 0.001) and FEV$_1$ (58.2 ± 16.9 vs. 65.7 ± 16.8 %pred, p < 0.001) compared with patients with a suboptimal PIFR.

3.2. Peak inspiratory flow rate and devices

Among the total population, the median PIFR was 70 L/min, with an IQR of 55–90 L/min (Table 3). The most frequently used inhaler type was R2 (medium-low resistance, 52.5 %), followed by R1 (low resistance, 35.4 %), and approximately 11.3 % of patients used multiple inhalers. Patients with a suboptimal PIFR had a lower highest PIFR, were more likely to use an R2-type (medium-low resistance) inhaler, and were more likely to use multiple inhalers.

Table 3
Peak inspiratory flow rate and devices.

	Optimal PIFR (n = 346)	Suboptimal PIFR (n = 98)	Total (n = 444)	*p*-value[a]
Highest PIFR value, L/min	80.0 (65.0–95.0)	40.0 (30.0–50.0)	70.0 (55.0–90.0)	<0.001
Devices				<0.001
R1 (Breezhaler)	141 (40.8 %)	16 (16.3 %)	157 (35.4 %)	
R2 (Ellipta, Diskus)	165 (47.7 %)	68 (69.4 %)	233 (52.5 %)	
R3 (Turbohaler, Genuair)	33 (9.5 %)	5 (5.1 %)	38 (8.6 %)	
R4 (NEXTHaler)	4 (1.2 %)	4 (4.1 %)	8 (1.8 %)	
R5 (Handihaler)	3 (0.9 %)	5 (5.1 %)	8 (1.8 %)	
Duration of inhaler use, days	893.5 (504.0; 1520.0]	884.0 (364.0; 1366.0)	885.0 (483.5–1494.0)	0.274
Use of multiple inhalers[b]	32 (9.2 %)	18 (18.4 %)	50 (11.3 %)	0.019
Suboptimal PIFR in the second inhaler	0 (0.0 %)	10 (55.6 %)	10 (20.0 %)	

Values are presented as numbers (%) for categorical variables and median (interquartile range) for continuous variables.
Abbreviations: PIFR = peak inspiratory flow rate.
[a] p-values for categorical variables were calculated with the χ^2 test; p-values for continuous variables were estimated with the Mann–Whitney U test.
[b] Multiple inhaler users all used triple therapy (inhaled corticosteroid, long-acting beta-agonist, and long-acting muscarinic antagonist).

3.3. Prevalence of suboptimal PIFR

Of 444 patients, the proportion with a suboptimal PIFR was 22.1 % (Fig. 1). Among sex subgroups, a significantly higher rate of suboptimal PIFRs was observed in women compared with men (46.7 % vs. 20.3 %, $p = 0.002$). Across different age subgroups, there was a statistically significant difference ($p < 0.001$), with the highest rate of suboptimal PIFRs seen in patients aged ≥ 80 years (36.1 %), followed by those aged 70–80 years (25.0 %) and < 60 years (20.0 %). In a stratification analysis based on lung function, the prevalence of suboptimal PIFRs increased stepwise, corresponding to the increase in GOLD severity. However, no significant differences were observed between the GOLD severity subgroups. Among In-Check dial resistance subtypes, the R1 type (low resistance) was associated with the lowest suboptimal PIFR rate (10.2 %).

3.4. Factors associated with suboptimal PIFR

The factors associated with a suboptimal PIFR are presented in Table 4. In model 1, which included post-bronchodilator FEV$_1$, BMI was statistically insignificant (adjusted odds ratio [aOR] = 0.96; 95 % confidence interval [CI] = 0.88–1.03), but the odds of age (per each 10-year increase; aOR = 2.02; 95 % CI = 1.45–2.80) and female sex (aOR = 4.06; 95 % CI = 1.65–10.01) were the highest among all models. In model 2, R2 (medium-low resistance, aOR = 4.74; 95 % CI = 2.51–8.95), R4 (medium-high resistance, aOR = 9.12; 95 % CI = 1.69–49.29), and R5 type (high resistance, aOR = 16.61; 95 % CI = 2.91–94.92) In-Check dial resistance had the highest odds ratios for a suboptimal PIFR. In model 3, a suboptimal PIFR was significantly associated with post-bronchodilator FVC (per each 10%pred decrease; aOR = 1.47; 95 % CI = 1.23–1.74), but with the GOLD stage (aOR = 1.60; 95 % CI = 0.93–2.74).

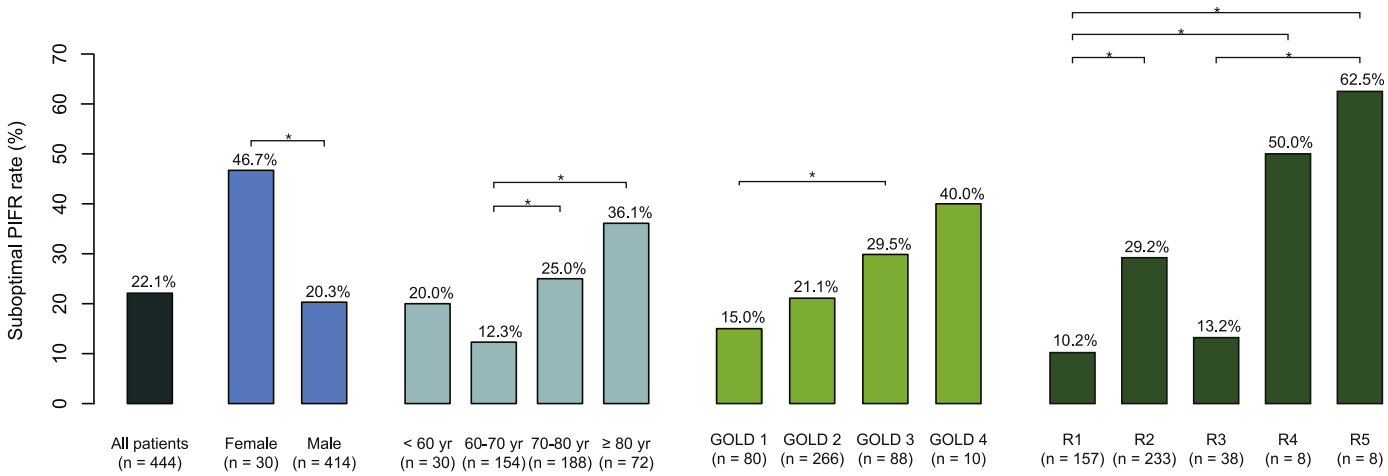

Fig. 1. The prevalence of suboptimal PIFR among patients with moderate to severe chronic obstructive pulmonary disease
*Indicates *p*-value < 0.05 in the post hoc analysis. ***Abbreviations:*** PIFR = peak inspiratory flow rate, GOLD = Global Initiative for Chronic Obstructive Lung Disease.

Table 4
Factors associated with suboptimal peak inspiratory flow rate.

	Univariable	Model 1	Model 2	Model 3
	OR (95 % CI)	aOR (95 % CI)	aOR (95 % CI)	aOR (95 % CI)
Age, per 10-year increase	1.77 (1.31–2.38)	2.02 (1.45–2.80)	1.67 (1.21–2.31)	1.61 (1.16–2.22)
Sex				
Male	Reference	Reference	Reference	Reference
Female	3.44 (1.61–7.32)	4.06 (1.65–10.01)	3.80 (1.53–9.43)	3.86 (1.53–9.72)
Height, per 10-cm increase	0.50 (0.36–0.69)	–	–	–
Weight, per 10-kg increase	0.59 (0.47–0.75)	–	–	–
BMI, per 1 kg/m^2 increase	0.92 (0.86–0.98)	0.96 (0.88–1.03)	0.90 (0.83–0.97)	0.91 (0.84–0.98)
Post-BD FVC, 10% pred decrease	1.40 (1.20–1.63)	–	1.48 (1.24–1.76)	1.47 (1.23–1.74)
Post-BD FEV_1, 10% pred decrease	1.30 (1.14–1.49)	1.32 (1.13–1.55)	–	–
GOLD stage				
A	Reference	–	–	Reference
B or E	2.35 (1.45–3.79)	–	–	1.60 (0.93–2.74)
InCheck dial resistance				
R1	Reference	Reference	Reference	Reference
R2	3.63 (2.01–6.55)	4.42 (2.37–8.25)	4.74 (2.51–8.95)	4.40 (2.33–8.34)
R3	1.34 (0.46–3.91)	1.18 (0.38–3.62)	1.10 (0.36–3.43)	1.00 (0.32–3.15)
R4	8.81 (2.01–38.68)	6.15 (1.13–33.49)	9.12 (1.69–49.29)	8.42 (1.53–46.31)
R5	14.69 (3.21–67.28)	14.70 (2.62–82.55)	16.61 (2.91–94.92)	13.65 (2.37–78.76)

In the multivariable analysis, the following variables were included: model 1: age, sex, BMI, post-BD FEV_1, and Incheck Dial Resistance, model 2: age, sex, BMI, post-BD FVC, and Incheck dial resistance, and model 3: age, sex, BMI, post-BD FVC, GOLD stage, and Incheck dial resistance.
Abbreviations: BMI = body mass index, BD = bronchodilator, GOLD = Global Initiative for Chronic Obstructive Lung Disease, FEV_1 = forced expiratory volume in 1 s, FVC = forced vital capacity.

4. Discussion

A substantial proportion of DPI users with moderate to severe COPD in this observational multicenter study had a suboptimal PIFR related to the resistance of their device. This rate was significantly higher in women and the elderly. Age, sex, lung function, BMI, and the use of an R2 (medium-low resistance), R4 (medium-high resistance), and R5-type (high resistance) inhaler were associated with a suboptimal PIFR.

A significant proportion of stable patients with COPD using DPIs reported a lack of sufficient inspiratory power to achieve optimal drug inhalation [14]. Among outpatients with COPD using DPIs, this suboptimal PIFR ranged from 19 % to 78 % in the previous investigations [12–18]. We found that nearly a quarter of stable patients with moderate to severe COPD had a suboptimal PIFR in Korea. This persistent issue has been discussed for decades, suggesting that certain patients with COPD may struggle to properly utilize DPIs due to insufficient inhalation ability [13,19,20]. Furthermore, suboptimal PIFR may coincide with other inhaler technique errors, particularly correct breathing-holding time, which also could lead to poor drug delivery [21]. When the initial inspiratory effort is insufficient, it may not only affect the initial distribution of the medication within the lungs but also limit the patient's ability to hold their breath effectively.

The aging population presents a significant global challenge [22]. Our stratified analysis revealed that the proportion of suboptimal PIFR increased with increased age, consistent with findings from the previous study [23]. Notably, over one-third of patients aged over 80 exhibited suboptimal PIFR. Although the small sample size limited statistical significance across all GOLD severity groups, a stepwise increase in suboptimal PIFR rate was also observed as GOLD severity increased. Elderly patients with COPD often had decreased lung function, and comorbid cognitive disorders could further complicate the use of inhalers [24,25]. It is time to establish a holistic management strategy beyond optimizing inhaler use in elderly patients with COPD.

Another important finding of this study is that a suboptimal PIFR was significantly more likely to be reported among female patients than male patients, as in previous studies [13,15,16,18,20]. In Korea, the majority of patients diagnosed with COPD have been men [26–28]. However, this gender gap has been closing, indicating a rising proportion of female patients with COPD [29]. Additionally, it is widely recognized that female patients experience a more progressive disease course in terms of decline in lung function, decreased quality of life, and higher susceptibility to exacerbations [30]. In this regard, identifying female patients with COPD is challenging [31], and even those diagnosed may struggle to use DPIs properly.

We found that female sex, increased age, lower body weight, and

decreased lung function were all linked to a suboptimal PIFR, which aligns with the findings of previous studies [13,15,16,18,20,32]. This result indicates that elderly underweight female patients with decreased lung function would be the most likely to be unsuitable candidates for DPI use. Additionally, the type of DPI device, particularly R2 (medium-low resistance), R4 (medium-high resistance), and R5-type (high resistance) inhalers, had an association with a suboptimal PIFR. Despite technological advancements, achieving optimal drug delivery with DPIs remains challenging for certain populations. For these patients, pressurized metered-dose inhalers (pMDIs) or soft mist inhalers (SDIs) may represent more suitable options.

Several limitations of this study are worth discussing. First, it relied on a limited type of measurement of PIFR using a single device without assessing reproducibility using spirometry. Multiple measurements using various other techniques would have provided more reliable data on PIFR. Second, the reason for the suboptimal PIFR remains unclear, as we did not assess PIFR against zero resistance. Consequently, the cause might stem from either the device resistance or the inadequate inspiratory effort of patients. Furthermore, the study did not investigate other potential causes, such as inappropriate inhaler technique. Third, PIFRs were measured at a single time point each day, and no follow-up data were obtained. It is possible that actual PIFRs vary throughout the day. Continuous monitoring would allow for a more accurate assessment of suboptimal PIFRs. Fourth, because only patients with a history of moderate to very severe COPD were included, the study population did not represent the entire COPD population. Our results may not be applicable to those with mild COPD.

In conclusion, more than one-fifth of Korean DPI users in this study had a suboptimal PIFR. The factors associated with suboptimal PIFR included older age, female sex, low BMI, low post-bronchodilator FVC, and use of an R2-type (medium-low resistance) inhaler. To optimize patient care, clinicians should carefully evaluate the possibility of suboptimal PIFR when prescribing DPIs.

Ethics statement

The protocol of this study was approved by the institutional review board (IRB) of Konkuk University Hospital (IRB number: 2021-06-008). All participants provided written informed consent.

Funding

This was an independent, investigator-initiated study supported by Boehringer Ingelheim (BI). BI had no role in the design, analysis or interpretation of the results in this study; BI was given the opportunity to review the manuscript for medical and scientific accuracy as it relates to BI substances, as well as intellectual property considerations.

CRediT authorship contribution statement

Ji-Yong Moon: Writing – original draft, Conceptualization. **Sang Hyuk Kim:** Writing – original draft, Formal analysis, Data curation. **Youlim Kim:** Writing – review & editing. **Hyun Lee:** Writing – review & editing. **Chin Kook Rhee:** Writing – review & editing. **Seung Won Ra:** Writing – review & editing. **Chang Youl Lee:** Writing – review & editing. **Joo Hun Park:** Writing – review & editing. **Yong Bum Park:** Writing – review & editing, Supervision, Conceptualization. **Kwang Ha Yoo:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

None.

Data availability

Data will be made available on request.

Acknowledgments

None.

References

[1] S.A. Christenson, B.M. Smith, M. Bafadhel, N. Putcha, Chronic obstructive pulmonary disease, Lancet 399 (10342) (2022) 2227–2242.
[2] M. Miravitlles, S. Baek, V. Vithlani, R. Lad, Optimal bronchodilation for COPD patients: are all long-acting β_2-agonist/long-acting muscarinic antagonists the same? Tuberc Respir Dis (Seoul) 81 (3) (2018) 198–215.
[3] Y.S. Jo, Long-term outcome of chronic obstructive pulmonary disease: a review, Tuberc Respir Dis (Seoul) 85 (4) (2022) 289–301.
[4] Y.B. Park, C.K. Rhee, H.K. Yoon, Y.M. Oh, S.Y. Lim, J.H. Lee, K.H. Yoo, J.H. Ahn, C. G. Committee of the Korean, Revised, COPD clinical practice guideline of the Korean academy of tuberculosis and respiratory disease: a summary, Tuberc Respir Dis (Seoul) 81 (4) (2018) 261–273, 2018.
[5] O.S. Usmani, Choosing the right inhaler for your asthma or COPD patient, Therapeut. Clin. Risk Manag. 15 (2019) 461–472.
[6] M.J. Telko, A.J. Hickey, Dry powder inhaler formulation, Respir Care 50 (9) (2005) 1209–1227.
[7] M.T. Leving, S. Bosnic-Anticevich, J. van Cooten, J.C. de Sousa, B. Cvetkovski, R. Dekhuijzen, L. Dijk, M.G. Pardo, A. Gardev, R. Gawlik, I. van der Ham, Y. Janse, F. Lavorini, T. Maricoto, J. Meijer, B. Metz, D. Price, M. Roman-Rodriguez, K. Schuttel, N. Stoker, I. Tsiligianni, O. Usmani, R. Emerson-Stadler, J.W.H. Kocks, Clinical recommendations for dry powder inhaler use in the management of COPD in primary care, NPJ Prim Care Respir Med 32 (1) (2022) 59.
[8] J. Heyder, Deposition of inhaled particles in the human respiratory tract and consequences for regional targeting in respiratory drug delivery, Proc Am Thorac Soc 1 (4) (2004) 315–320.
[9] A.R. Clark, A.M. Hollingworth, The relationship between powder inhaler resistance and peak inspiratory conditions in healthy volunteers–implications for in vitro testing, J Aerosol Med 6 (2) (1993) 99–110.
[10] A.R. Clark, The role of inspiratory pressures in determining the flow rates though dry powder inhalers; A review, Curr. Pharmaceut. Des. 21 (27) (2015) 3974–3983.
[11] F. Lavorini, A. Magnan, J.C. Dubus, T. Voshaar, L. Corbetta, M. Broeders, R. Dekhuijzen, J. Sanchis, J.L. Viejo, P. Barnes, C. Corrigan, M. Levy, G. K. Crompton, Effect of incorrect use of dry powder inhalers on management of patients with asthma and COPD, Respir Med 102 (4) (2008) 593–604.
[12] C.H. Loh, S.P. Peters, T.M. Lovings, J.A. Ohar, Suboptimal inspiratory flow rates are associated with chronic obstructive pulmonary disease and all-cause readmissions, Ann Am Thorac Soc 14 (8) (2017) 1305–1311.
[13] G. Sharma, D.A. Mahler, V.M. Mayorga, K.L. Deering, O. Harshaw, V. Ganapathy, Prevalence of low peak inspiratory flow rate at discharge in patients hospitalized for COPD exacerbation, Chronic Obstr Pulm Dis 4 (3) (2017) 217–224.
[14] D.A. Mahler, Peak inspiratory flow rate as a criterion for dry powder inhaler use in chronic obstructive pulmonary disease, Ann Am Thorac Soc 14 (7) (2017) 1103–1107.
[15] J. van der Palen, Peak inspiratory flow through diskus and turbuhaler, measured by means of a peak inspiratory flow meter (In-Check DIAL), Respir Med 97 (3) (2003) 285–289.
[16] L.P. Malmberg, P. Rytilä, P. Happonen, T. Haahtela, Inspiratory flows through dry powder inhaler in chronic obstructive pulmonary disease: age and gender rather than severity matters, Int. J. Chronic Obstr. Pulm. Dis. 5 (2010) 257–262.
[17] D.A. Mahler, L.A. Waterman, A.H. Gifford, Prevalence and COPD phenotype for a suboptimal peak inspiratory flow rate against the simulated resistance of the Diskus(R) dry powder inhaler, J. Aerosol Med. Pulm. Drug Deliv. 26 (3) (2013) 174–179.
[18] S. Ghosh, R.A. Pleasants, J.A. Ohar, J.F. Donohue, M.B. Drummond, Prevalence and factors associated with suboptimal peak inspiratory flow rates in COPD, Int. J. Chronic Obstr. Pulm. Dis. 14 (2019) 585–595.
[19] R.A. Al-Showair, W.Y. Tarsin, K.H. Assi, S.B. Pearson, H. Chrystyn, Can all patients with COPD use the correct inhalation flow with all inhalers and does training help? Respir Med 101 (11) (2007) 2395–2401.
[20] D.A. Mahler, L.A. Waterman, A.H. Gifford, Prevalence and COPD phenotype for a suboptimal peak inspiratory flow rate against the simulated resistance of the Diskus® dry powder inhaler, J. Aerosol Med. Pulm. Drug Deliv. 26 (3) (2013) 174–179.
[21] N. Ding, W. Zhang, Z. Wang, C. Bai, Q. He, Y. Dong, X. Feng, J. Zhang, S. Gao, Prevalence and associated factors of suboptimal daily peak inspiratory flow and technique misuse of dry powder inhalers in outpatients with stable chronic airway diseases, Int. J. Chronic Obstr. Pulm. Dis. 16 (2021) 1913–1924.
[22] L. Partridge, J. Deelen, P.E. Slagboom, Facing up to the global challenges of ageing, Nature 561 (7721) (2018) 45–56.
[23] S. Jarvis, P.W. Ind, R.J. Shiner, Inhaled therapy in elderly COPD patients; time for re-evaluation? Age Ageing 36 (2) (2007) 213–218.
[24] W. Janssens, P. VandenBrande, E. Hardeman, E. De Langhe, T. Philps, T. Troosters, M. Decramer, Inspiratory flow rates at different levels of resistance in elderly COPD patients, Eur. Respir. J. 31 (1) (2008) 78–83.
[25] J. Wang, X. Li, S. Lei, D. Zhang, S. Zhang, H. Zhang, J. Li, Risk of dementia or cognitive impairment in COPD patients: a meta-analysis of cohort studies, Front. Aging Neurosci. 14 (2022) 962562.

[26] Y.I. Hwang, Y.B. Park, K.H. Yoo, Recent trends in the prevalence of chronic obstructive pulmonary disease in Korea, Tuberc Respir Dis (Seoul) 80 (3) (2017) 226–229.
[27] J.Y. Choi, S. Milne, F. Yunus, C.K. Rhee, K. Matsunaga, Current chronic obstructive pulmonary disease treatment status in asia: a position statement of the asian pacific society of respirology, Tuberc Respir Dis (Seoul) 85 (3) (2022) 279–282.
[28] J.G. Jang, K.H. Lee, J.H. Chung, K.C. Shin, E.Y. Choi, H.J. Jin, J.H. Ahn, Assessment of inhaler satisfaction and determinants of high satisfaction among Korean COPD patients, J. Kor. Med. Sci. 37 (46) (2022) e327.
[29] S.H. Kim, H. Lee, Y. Kim, C.K. Rhee, K.H. Min, Y.I. Hwang, D.K. Kim, Y.B. Park, K. H. Yoo, J.Y. Moon, Recent prevalence of and factors associated with chronic obstructive pulmonary disease in a rapidly aging society: Korea national health and nutrition examination survey 2015-2019, J. Kor. Med. Sci. 38 (14) (2023) e108.
[30] D.L. DeMeo, S. Ramagopalan, A. Kavati, A. Vegesna, M.K. Han, A. Yadao, T. K. Wilcox, B.J. Make, Women manifest more severe COPD symptoms across the life course, Int. J. Chronic Obstr. Pulm. Dis. 13 (2018) 3021–3029.
[31] J. Ancochea, M. Miravitlles, F. García-Río, L. Muñoz, G. Sánchez, V. Sobradillo, E. Duran-Tauleria, J.B. Soriano, Underdiagnosis of chronic obstructive pulmonary disease in women: quantification of the problem, determinants and proposed actions, Arch. Bronconeumol. 49 (6) (2013) 223–229.
[32] D.A. Mahler, H. Watz, R. Emerson-Stadler, J. Ritz, A. Gardev, A. Shaikh, M. B. Drummond, Clinical implications of peak inspiratory flow in COPD: post hoc analyses of the TRONARTO study, Int. J. Chronic Obstr. Pulm. Dis. 18 (2023) 1729–1740.