ASSOCIATION BETWEEN LOW PEAK INSPIRATORY FLOW RATE AND ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN RECENTLY HOSPITALIZED PATIENTS

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Abstract

Introduction: Peak inspiratory flow rate (PIFR) is an important determinant of effective drug delivery with dry powder inhalers in patients with chronic obstructive pulmonary disease (COPD). Reduced PIFR is frequently observed following acute exacerbations of COPD (ECOPD), but its role in predicting early post-discharge re-exacerbation remains incompletely defined.

Methods: This prospective cohort study enrolled patients aged ≥40 years who were hospitalized for ECOPD at a tertiary hospital in Thailand between October 2024 and June 2025. PIFR was measured at hospital discharge using the In-Check Dial G16 device (Clement Clarke International, Harlow, UK) configured to a medium-resistance DPI setting. Suboptimal PIFR was defined as <60 L/min. The primary outcome was time to first moderate-to-severe COPD re-exacerbation within 56 days, evaluated by Kaplan–Meier and Cox proportional hazards analyses. The secondary outcome was the incidence of moderate-to-severe re-exacerbation within 56 days, evaluated by logistic regression with modified Poisson regression as a sensitivity analysis.

Results: Of 41 enrolled patients, 36 were included in the final analysis (mean age 66.4 years; all male), of whom 17 (47.2%) had suboptimal PIFR at discharge. During 56 days of follow-up, moderate-to-severe re-exacerbations occurred in 35.3% of patients with PIFR <60 L/min, compared with 5.3% in those with PIFR ≥60 L/min. Time-to-event analysis demonstrated a higher and earlier risk of re-exacerbation in the suboptimal PIFR group (log-rank p=0.024), with an adjusted hazard ratio of 13.52 (95% CI 1.14–159.93). Schoenfeld residuals confirmed the proportional hazards assumption. For the 56-day secondary outcome, suboptimal PIFR was associated with increased odds of re-exacerbation in univariable logistic regression (OR 9.82, 95% CI 1.04–92.78; p=0.046); the corresponding unadjusted risk ratio from modified Poisson regression was 6.71 (95% CI 0.90–50.22; p=0.064). PIFR improved over time in the overall cohort; however, patients who experienced re-exacerbation showed persistently lower or unstable PIFR trajectories.

Conclusion: Suboptimal PIFR at hospital discharge was associated with an increased risk of early COPD re-exacerbation. Assessment of PIFR may help identify patients at higher risk during the post-discharge period and support more individualized inhaler management strategies.

Keywords: Chronic obstructive pulmonary disease; Peak inspiratory flow rate; Acute exacerbation; Dry powder inhaler.

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation accompanied by chronic respiratory symptoms. Acute exacerbations of COPD (ECOPD) play a central role in disease progression and are associated with increased hospital admissions, higher healthcare costs, and excess mortality.[1, 2] Beyond their immediate clinical consequences, exacerbations contribute to sustained declines in lung function, deterioration in health-related quality of life, and an increased risk of subsequent exacerbations and death.[3]

Inhaled pharmacotherapy, particularly bronchodilators with or without inhaled corticosteroids, remains the foundation of COPD treatment and is commonly delivered via dry powder inhalers (DPIs).[4] The effectiveness of DPIs depends on the patient's ability to generate sufficient peak inspiratory flow rate (PIFR) to disperse the powdered medication. When inspiratory flow is inadequate, pulmonary drug deposition is reduced, potentially compromising symptom control and increasing susceptibility to further exacerbations.[5] A PIFR of at least 60 L/min is generally regarded as the minimum threshold required for reliable DPI performance, with delivery efficiency declining below this level.[6]

Reduced PIFR has been increasingly reported among patients with COPD, particularly in the period following an acute exacerbation. Studies have shown that a substantial proportion of patients discharged after ECOPD are unable to achieve adequate inspiratory flow for optimal DPI use.[7] This limitation has been associated with poorer clinical outcomes, including higher rates of hospital readmission and persistent symptom burden.[5]

Insufficient inspiratory flow may therefore limit the clinical benefit of prescribed inhaled therapies, resulting in suboptimal disease control and a higher likelihood of recurrent exacerbations.[8] Increasing attention has been directed toward routine assessment of PIFR in clinical practice to guide inhaler selection and optimize medication delivery.[9] Evidence suggests that tailoring inhaler choice according to measured PIFR is associated with improved clinical outcomes.[6]

Despite growing recognition of PIFR's relevance to inhaler effectiveness, its role as a predictor of short-term COPD re-exacerbation after hospital discharge remains inadequately defined. This study investigates the association between PIFR measured at discharge and the risk of re-exacerbation within 56 days among patients recovering from ECOPD. Improved identification of patients at risk due to suboptimal inspiratory flow may support more individualized post-discharge management strategies and better clinical outcomes.

Methods

Study design and setting

This prospective cohort study examined the association between peak inspiratory flow rate (PIFR) measured at hospital discharge and the risk of acute exacerbations of chronic obstructive pulmonary disease (COPD) within 56 days after discharge. The study was conducted at Phramongkutklao Hospital, Bangkok, Thailand, between October 2024 and June 2025. Ethical approval was obtained from the Institutional Review Board of the Royal Thai Army Medical Department (approval number R023h/67), and all participants provided written informed consent prior to enrollment.

Participants

Patients were recruited from the emergency department and inpatient wards of Phramongkutklao Hospital. Eligible participants were adults aged 40 years or older who were hospitalized for an acute exacerbation of COPD (ECOPD).

Inclusion criteria required a diagnosis of ECOPD made by an emergency physician or intern in accordance with the 2022 Thai COPD Clinical Practice Guideline,[13] clinical stability prior to discharge, and an anticipated discharge within 48 hours of admission. Clinical stability was defined as a respiratory rate below 24 breaths per minute and an oxygen saturation of at least 92% while breathing room air, consistent with criteria used in prior ECOPD studies.[14]

Patients were excluded if they had undergone tracheostomy, were diagnosed with heart failure during hospitalization, or had been admitted for ECOPD within the preceding 30 days. Additional exclusion criteria included inability to communicate effectively or follow instructions, terminal illness as determined by the attending physician, or receipt of palliative care. Participants were withdrawn from the study if they were unable to complete PIFR measurements despite repeated attempts, withdrew consent, died during the study period, or failed to attend two consecutive follow-up visits. A participant flowchart is presented in **Figure 1**.

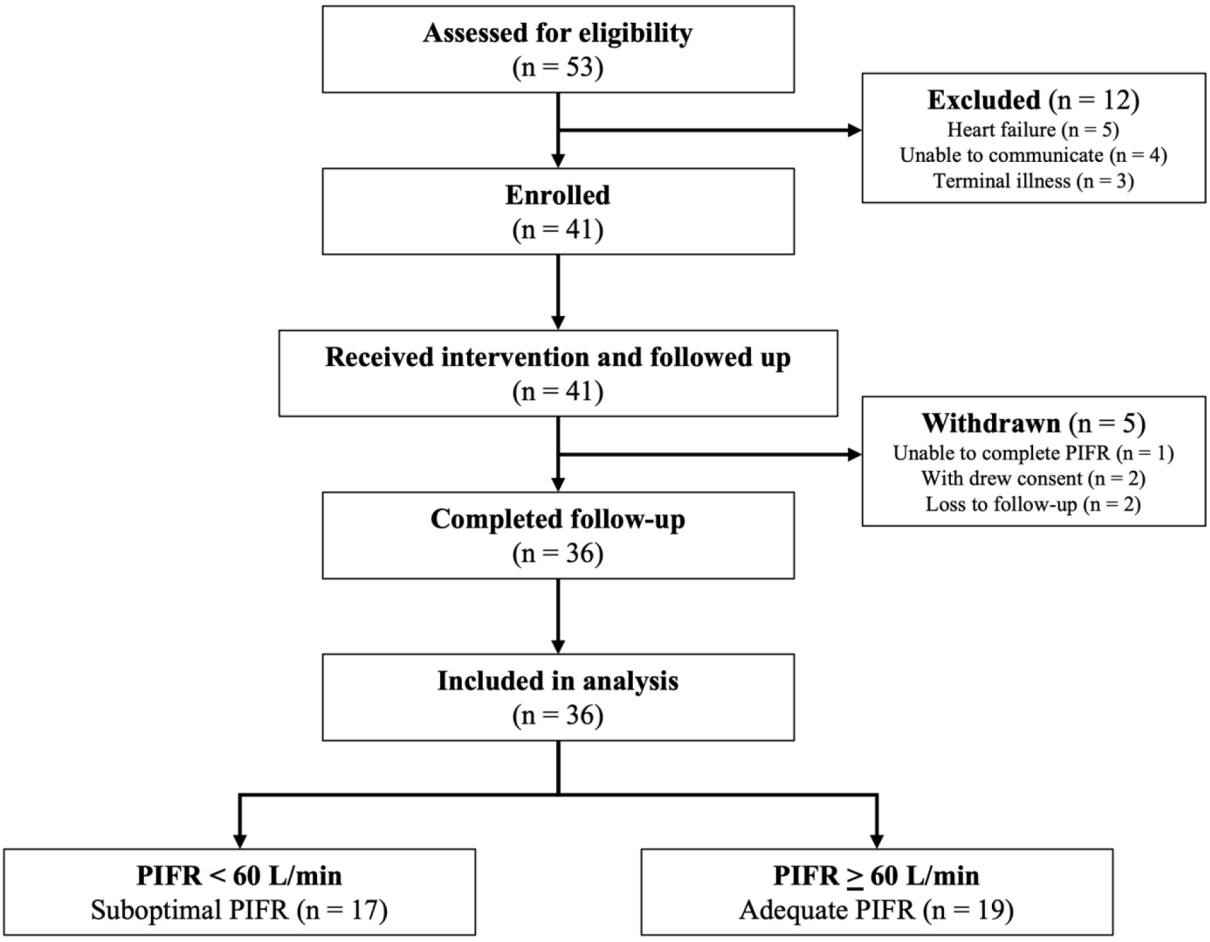

Figure 1. Study participant flowchart

Data collection

Baseline assessment

At enrollment, demographic and clinical data were collected, including age, sex, smoking status (current or former), body mass index (BMI), and comorbid conditions such as cardiovascular disease, diabetes mellitus, and hypertension. Lung function parameters, including forced expiratory volume in one second (FEV_1) and percentage of predicted FEV_1, were obtained from the most recent spirometry recorded in the medical records prior to the index admission; new spirometry was not performed at the time of the ECOPD visit. Information regarding the severity of the index exacerbation, prior exacerbations, and the inhaler devices used at the time of admission was also recorded.

PIFR measurement

PIFR was measured at hospital discharge using the In-Check Dial G16 device (Clement Clarke International, Harlow, UK), which simulates the internal resistance of different inhaler devices. The device was configured to resistance position 3, corresponding to a medium-resistance dry powder inhaler setting, consistent with the resistance profiles of commonly prescribed DPIs.[6] All measurements were performed by trained respiratory nurses and physicians who had received standardized instruction in device use and patient coaching prior to study commencement. Participants were seated upright, instructed to exhale fully, and then asked to perform a rapid and forceful maximal inspiratory maneuver through the device. Three measurements were obtained, with rest intervals of 1–2 minutes between attempts to minimize fatigue. The highest recorded value was used for analysis. A PIFR below 60 L/min was classified as suboptimal and considered insufficient for effective use of dry powder inhalers.[6]

Follow-up

Participants were scheduled for follow-up visits at 28 and 56 days after discharge at the pulmonary outpatient clinic. During in-person visits, PIFR measurements were repeated using the same protocol applied at discharge. Clinical information was collected regarding the occurrence of COPD exacerbations, changes in medication regimens, and adherence to prescribed inhaler therapy. Participants were also queried about hospital readmissions, emergency department visits, and the use of systemic corticosteroids or antibiotics for worsening respiratory symptoms. For participants unable to attend in-person visits, structured telephone interviews were conducted to document exacerbation events and medication use; PIFR measurements were not obtained during telephone follow-up.

Outcomes

The primary outcome was time to first moderate-to-severe COPD exacerbation within 56 days after discharge, evaluated by time-to-event analysis. Moderate exacerbations were defined as episodes requiring treatment with systemic corticosteroids and/or antibiotics. In contrast, severe exacerbations were defined as those requiring hospitalization or emergency department visits, in accordance with published definitions.[15]

Secondary outcomes included the incidence of moderate-to-severe COPD exacerbations within 56 days after discharge and their association with suboptimal PIFR, evaluated by logistic regression. Additional analyses explored other factors potentially associated with exacerbation risk, including comorbid conditions, prior exacerbation history, and inappropriate inhaler device use.

Statistical analysis

All analyses were performed using STATA version 17. A two-sided p-value of <0.05 was considered statistically significant. Continuous variables, including age, body mass index (BMI), forced expiratory volume in one second (FEV_1), and PIFR, were summarized as means with standard deviations for normally distributed data and as medians with interquartile ranges for non-normally distributed data. Categorical variables, such as smoking status, comorbidities, and prior exacerbation history, were presented as frequencies and percentages.

Normality of continuous variables was assessed using the Shapiro–Wilk test and support-

ed by visual inspection of histograms and Q–Q plots. Comparisons between groups defined by PIFR at discharge (<60 L/min vs ≥60 L/min) were performed using the Student's t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test when expected cell counts were fewer than five.

For the primary outcome, time to first moderate-to-severe COPD exacerbation within 56 days was evaluated using Kaplan–Meier analysis with the log-rank test for group comparison, and Cox proportional hazards regression to estimate hazard ratios. Participants were censored at the time of loss to follow-up, death, or the end of the 56-day observation period, whichever occurred first. The proportional hazards (PH) assumption was evaluated using Schoenfeld residuals; if violated, time-varying exposure or alternative approaches would be considered. Covariates for multivariable Cox regression were selected based on clinical relevance and univariable p-value <0.10, including age, baseline CAT score, baseline FEV_1, and inappropriate inhaler device use. For the secondary outcome, factors associated with COPD exacerbations within 56 days after discharge were evaluated using logistic regression. Univariable models were first constructed, and variables with p-values < 0.10 were entered into multivariable logistic regression models. Modified Poisson regression with robust standard errors was additionally performed as a sensitivity analysis to estimate risk ratios, which may be more interpretable than odds ratios for non-rare binary outcomes. Variables considered for multivariable analysis included age, PIFR at discharge (<60 L/min vs ≥60 L/min), percentage predicted FEV_1, COPD Assessment Test (CAT) score, history of exacerbations in the preceding year, comorbid conditions (including cardiovascular disease and diabetes), and inappropriate inhaler device use. Results are reported as odds ratios and risk ratios with 95% confidence intervals.

A prespecified subgroup analysis examined the association between inappropriate inhaler device use and exacerbation risk among patients with suboptimal PIFR, to assess whether mismatches between inspiratory flow and inhaler device influenced outcomes within 56 days after discharge. Missing data were handled using complete case analysis. If missingness exceeded 5% for key variables, multiple imputation was planned to minimize bias and preserve statistical power.

Given the exploratory nature of this prospective cohort study and the lower-than-anticipated number of eligible ECOPD admissions during the study period, a formal a priori sample size calculation was not performed. The study was designed to generate preliminary evidence regarding short-term clinical associations.

Results

Study population

Of 53 patients screened for eligibility, 12 were excluded: five had heart failure diagnosed during hospitalization, four were unable to communicate or follow instructions, and three had terminal illness or were receiving palliative care. Forty-one patients were enrolled. During follow-up, five patients were withdrawn: one was unable to complete PIFR measurements, two withdrew consent, and two failed to attend two consecutive follow-up visits. A total of 36 patients were included in the final analysis.

Baseline characteristics

A total of 36 patients hospitalized for acute exacerbation of COPD were included in the baseline analysis. Participants were categorized by peak inspiratory flow rate (PIFR) measured at discharge into PIFR <60 L/min (n=17) and PIFR ≥60 L/min (n=19). The cohort's mean age was 66.4 years, and all participants were male. Patients with PIFR <60 L/min were older than those with PIFR ≥60 L/min (73.0 vs 60.4 years; p<0.001). Mean body mass index was comparable between groups (21.5 vs 22.9 kg/m²; p=0.28). Smoking status did not differ significantly (p=0.12). (**Table 1**)

Comorbidities were common and similar between groups, including hypertension (72.2%), dyslipidemia (58.3%), diabetes (19.4%), cerebrovascular accident (5.6%), and dementia (5.6%). Symptom burden was higher in the low

Table 1. Baseline characteristics of patients at hospital discharge

Characteristic	Overall (N=36)	PIFR < 60 L/min (N=17)	PIFR ≥ 60 L/min (N=19)	*p*-value
Age (years), mean (SD)	66.4 (9.9)	73.0 (6.9)	60.4 (8.5)	**< 0.001**
Male gender, N (%)	36 (100)	17 (100)	19 (100)	1.00
BMI (kg/m^2), mean (SD)	22.2 (3.9)	21.5 (3.7)	22.9 (4.0)	0.28
Smoking status, N (%)				
- Current smoker	16 (44.4)	5 (29.4)	11 (57.9)	0.12
- Former smoker	20 (55.6)	12 (70.6)	8 (42.1)	
Comorbidity, N (%)				
- Hypertension	26 (72.2)	13 (76.5)	13 (68.4)	0.72
- Dyslipidemia	21 (58.3)	12 (70.6)	9 (47.4)	0.19
- Diabetes	7 (19.4)	3 (17.7)	4 (21.1)	1.00
- CVA	2 (5.6)	2 (11.8)	0 (0)	0.22
- Dementia	2 (5.6)	2 (11.8)	0 (0)	0.22
mMRC, median (IQR)	2 (1-2.5)	2 (1-3)	2 (1-2)	0.07
CAT score, mean (SD)	15.1 (9.0)	18.6 (8.9)	11.8 (8.0)	**0.02**
History of prior exacerbation, N (%)				**0.02**
- No AE	8 (22.2)	1 (5.9)	7 (36.8)	
- Mild AE	8 (22.2)	2 (11.8)	6 (31.6)	
- Moderate AE	15 (41.7)	10 (58.8)	5 (26.3)	
- Severe AE	5 (13.9)	4 (23.5)	1 (5.3)	
FEV_1 (L), mean (SD)	1.5 (0.5)	1.3 (0.4)	1.6 (0.6)	0.13
FEV_1 (%predicted), mean (SD)	56.9 (17.4)	56.7 (17.2)	57.2 (18.0)	0.94
Peak inspiratory flow rate (L/min), mean (SD)	57.3 (13.7)	48.5 (9.7)	68.9 (8.6)	**< 0.001**
Inhaler devices (controller), N (%)				0.19
- pMDI	6 (16.7)	4 (23.5)	2 (10.5)	
- Accuhaler	2 (5.6)	2 (11.8)	0 (0)	
- Turbuhaler	1 (2.8)	1 (5.9)	0 (0)	
- Ellipta	15 (41.7)	5 (29.4)	10 (52.6)	
- Handihaler	1 (2.8)	1 (5.9)	0 (0)	
- SMI	11 (30.6)	4 (23.5)	7 (36.8)	

Data are presented as mean (SD), median (IQR), or number (%), as appropriate.
p-values were calculated using Student's t-test or Mann–Whitney U test for continuous variables, and chi-square test or Fisher's exact test for categorical variables.
Abbreviations: BMI, body mass index; CAT, COPD Assessment Test;
CVA, cerebrovascular accident; FEV1, forced expiratory volume in 1 second;
mMRC, modified Medical Research Council; PIFR, peak inspiratory flow rate;
pMDI, pressurized metered-dose inhaler; SMI, soft mist inhaler.

PIFR group. Mean CAT score was 18.6 points in the PIFR <60 L/min group compared with 11.8 points in the PIFR ≥60 L/min group (p=0.02). Median mMRC was 2, with a numerically higher distribution in the low PIFR group (IQR 1–3 vs 1–2; p=0.07).

Prior exacerbation history differed between groups (p=0.02). Moderate exacerbations in the previous year were more frequent among patients with PIFR <60 L/min (10/17, 58.8%) than among those with PIFR ≥60 L/min (5/19, 26.3%).

Lung function was similar between groups: mean FEV_1 was 1.3 (0.4) L in the PIFR <60 L/min group and 1.6 (0.6) L in the PIFR ≥60 L/min group (p=0.13), and mean FEV_1 % predicted was 56.7 (17.2) versus 57.2 (18.0), respectively (p=0.94). As expected, mean PIFR differed between groups (48.5 [9.7] vs 68.9 [8.6] L/min; p<0.001).

Controller inhaler devices at baseline did not differ significantly between groups (p=0.19). Ellipta was the most frequently used device overall (15/36, 41.7%), followed by soft mist inhaler (SMI) (11/36, 30.6%) and pressurized metered-dose inhaler (pMDI) (6/36, 16.7%).

Incidence of exacerbations

During the 56-day follow-up period, moderate-to-severe COPD re-exacerbations occurred more frequently among patients with suboptimal peak inspiratory flow rate (PIFR <60 L/min) than among those with adequate PIFR. Re-exacerbations were observed in 6 of 17 patients (35.3%) in the PIFR <60 L/min group compared with 1 of 19 patients (5.3%) in the PIFR ≥60 L/min group. **(Table 2)**

In univariable logistic regression analysis, suboptimal PIFR at discharge was associated with a higher likelihood of re-exacerbation within 56 days, with an odds ratio of 9.82 (95% CI 1.04–92.78; p=0.046).

Table 2. Incidence of primary and secondary outcomes stratified by peak inspiratory flow rate

Outcome	PIFR < 60 L/min (n=17)	PIFR ≥ 60 L/min (n=19)
Primary outcome		
Time to first moderate-to-severe COPD exacerbation within 56 days		
Patients with exacerbation, n (%)	6 (35.3)	1 (5.3)
Cumulative incidence at 28 days, % (95% CI)	17.7 (6.0–45.3)	0
Cumulative incidence at 56 days, % (95% CI)	29.4 (13.4–56.9)	5.3 (0.8–31.9)
Descriptive 28-day exacerbation count ¶		
Patients with exacerbation, n (%)	3 (17.6)	0 (0)

Data are presented as numbers (%) or cumulative incidence (95% CI).

Abbreviations: CI, confidence interval; PIFR, peak inspiratory flow rate.

§ Cumulative incidence estimated by the Kaplan–Meier method at time of last observed event within the 56-day window; the observed event proportion (6/17, 35.3%) reflects all events regardless of exact timing.

¶ Early descriptive 28-day event count shown for clinical context; the prespecified secondary inferential analysis used the 56-day binary outcome **(Table 4).**

Time to first moderate-to-severe exacerbation Kaplan–Meier analysis demonstrated a higher cumulative incidence of first moderate-to-severe COPD exacerbation among patients with suboptimal peak inspiratory flow rate (PIFR <60 L/min) compared with those with adequate PIFR. Over the 56-day follow-up period, the PIFR <60 L/min group showed earlier and more frequent exacerbation events than the PIFR ≥60 L/min group. The difference between groups was statistically significant (log-rank test, p=0.024) (**Figure 2**). The median time to first exacerbation was not reached in either group during the follow-up period, reflecting the limited number of events within 56 days.

At 28 days after discharge, the cumulative incidence of exacerbation was 17.7% (95% CI 6.0–45.3) in the PIFR <60 L/min group, whereas no exacerbation events were observed in the PIFR ≥60 L/min group. By 56 days, the cumulative incidence increased to 29.4% (95% CI 13.4–56.9) in the PIFR <60 L/min group compared with 5.3% (95% CI 0.8–31.9) in the PIFR ≥60 L/min group. (**Table 2**)

In Cox proportional hazards analysis adjusted for age, baseline CAT score, baseline FEV_1, and inappropriate inhaler device use, suboptimal PIFR at discharge was associated with a significantly increased risk of moderate-to-severe exacerbation within 56 days (adjusted hazard ratio 13.52, 95% CI 1.14–159.93) (**Table 3 and Figure S1).**

Logistic regression analysis

In univariable logistic regression analysis, suboptimal PIFR (<60 L/min) was associated with an increased risk of COPD re-exacerbation within 56 days (OR 9.82, 95% CI 1.04–92.78; p=0.046). Inappropriate inhaler device use, defined as the use of a dry powder inhaler in patients with PIFR <60 L/min, was also associated with re-exacerbation (OR 6.56, 95% CI 1.05–40.95; p=0.044) (**Table 4**).

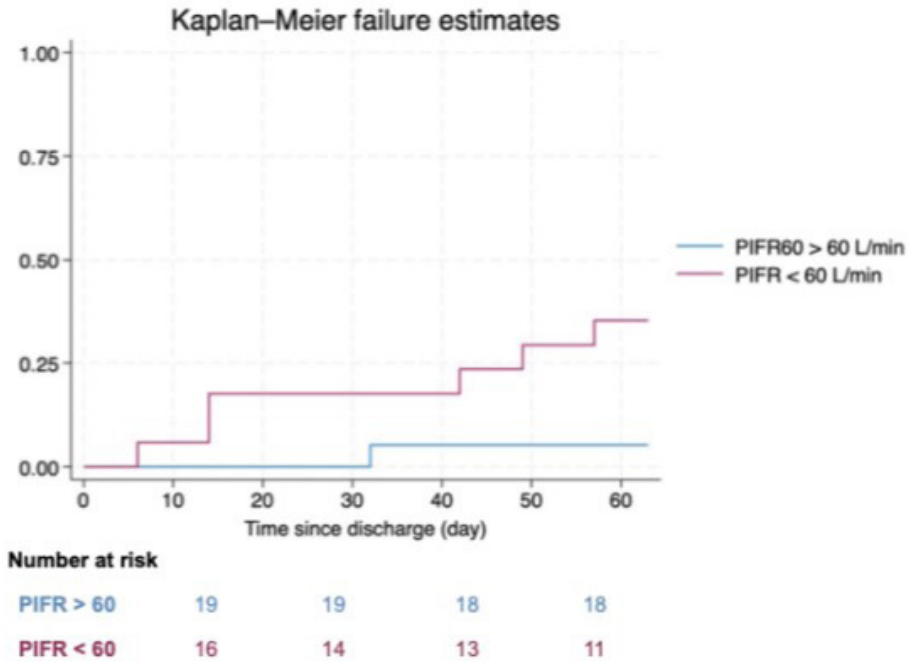

Figure 2. Kaplan–Meier curve showing time to first moderate-to-severe COPD exacerbation stratified by peak inspiratory flow rate at discharge. The number at risk at each time point is shown below the x-axis. The difference between groups was statistically significant (log-rank test, $p = 0.024$).

Table 3. Univariable and multivariable Cox proportional hazards regression for time to first moderate-to-severe COPD exacerbation within 56 days (primary outcome)

Characteristic	Unadjusted HR (95% CI)	*p*-value	Adjusted HR* (95% CI)	*p*-value	In model
PIFR <60 L/min (vs ≥60)	9.24 (1.06–80.6)	0.044	13.52 (1.14–159.93)	0.039	Yes
Age (per year)	1.07 (0.99–1.16)	0.08	1.05 (0.97–1.14)	0.25	Yes
CAT score (per point)	1.09 (1.01–1.18)	0.03	1.06 (0.97–1.16)	0.19	Yes
FEV_1% predicted (per %)	0.98 (0.94–1.02)	0.32	0.99 (0.95–1.03)	0.52	Yes
Inappropriate inhaler use†	5.38 (0.97–29.8)	0.054	3.21 (0.48–21.3)	0.23	Yes
Prior exacerbation in the preceding year	2.14 (0.42–10.9)	0.36	—	—	No

Abbreviations: CI, confidence interval; HR, hazard ratio; CAT, COPD Assessment Test; FEV_1, forced expiratory volume in 1 second; PIFR, peak inspiratory flow rate.

* Adjusted for age, baseline CAT score, baseline FEV_1, and inappropriate inhaler device use. Proportional hazards assumption verified by Schoenfeld residuals (all $p > 0.05$).

† Inappropriate inhaler device defined as use of a DPI in patients with PIFR <60 L/min.

In multivariable logistic regression analysis adjusting for prior exacerbation history, PIFR <60 L/min, and inappropriate inhaler device use, neither suboptimal PIFR (Adjusted OR 7.18, 95% CI 0.29–179.37; p=0.230) nor inappropriate inhaler device use (Adjusted OR 1.96, 95% CI 0.15–25.00; p=0.605) remained statistically significant (Table 4). As a sensitivity analysis, a modified Poisson regression was performed to estimate risk ratios when the outcome incidence exceeded 20%. The unadjusted risk ratio for suboptimal PIFR was 6.71 (95% CI 0.90–50.22; p=0.064), consistent with the logistic regression estimate in direction but borderline non-significant, with the lower confidence bound approaching unity, likely reflecting limited power due to the small number of outcome events.

PIFR progression over time

Over the 56-day follow-up period, the proportion of patients achieving an adequate peak inspiratory flow rate (PIFR ≥60 L/min) increased progressively. At hospital discharge, 52.78% of patients had a PIFR ≥60 L/min, while 47.22% had a PIFR <60 L/min. By day 28, the proportion with adequate PIFR increased to 61.11%, with 38.89% remaining below the threshold. At day 56, 72.22% of patients achieved a PIFR ≥60 L/min, whereas 27.78% maintained suboptimal PIFR (**Figure 3**).

When PIFR trajectories were examined by exacerbation status, patients without re-exacerbation showed a gradual increase in mean PIFR over the follow-up period. In contrast, patients who experienced re-exacerbation showed lower mean PIFR values throughout follow-up, with an initial improvement by day 28 followed by a subsequent decline by day 56 (**Figure S2**).

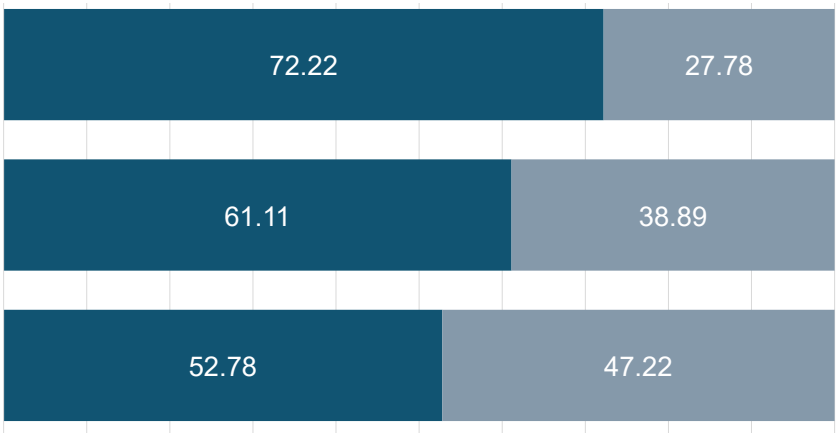

Figure 3. Changes in the proportion of patients with suboptimal peak inspiratory flow rate over 56 days

The proportion of patients achieving an adequate peak inspiratory flow rate (PIFR ≥ 60 L/min) increased from hospital discharge to days 28 and 56 after discharge. Values represent percentages of patients in each PIFR category at each time point.

Table 4. Univariable and multivariable logistic regression and modified Poisson regression for moderate-to-severe COPD re-exacerbation within 56 days (secondary outcome)

Characteristic	Unadjusted OR (95% CI)	*p*- value	Adjusted OR* (95% CI)	*p*- value	Unadjusted RR† (95% CI)	*p*- value
PIFR <60 L/min	9.82 (1.04–92.78)	0.046	7.18 (0.29–179.37)	0.230	6.71 (0.90–50.22)	0.064
Inappropriate inhaler use‡	6.56 (1.05–40.95)	0.044	1.96 (0.15–25.00)	0.605	—	—
Prior exacerbation (moderate or severe)	2.33 (0.39–14.04)	0.355	0.67 (0.07–6.53)	0.732	—	—
Age > 65 years	1.76 (0.29–10.66)	0.536	—	—	—	—
FEV_1 < 50% predicted	2.53 (0.47–13.61)	0.279	—	—	—	—

Abbreviations: OR, odds ratio; RR, risk ratio; CI, confidence interval; DPI, dry powder inhaler; PIFR, peak inspiratory flow rate.

* Multivariable logistic regression adjusted for prior exacerbation history, PIFR <60 L/min, and inappropriate inhaler device use.

† Risk ratio from modified Poisson regression with robust standard errors, performed as a sensitivity analysis to estimate risk ratios for the binary outcome.

‡ Inappropriate inhaler device defined as use of a DPI in patients with PIFR <60

Figure 2. Kaplan–Meier curve showing time to first moderate-to-severe COPD exacerbation stratified by peak inspiratory flow rate at discharge. The number at risk at each time point is shown below the x-axis. The difference between groups was statistically significant (log-rank test, $p = 0.024$).

Discussion

In this prospective cohort study, suboptimal peak inspiratory flow rate (PIFR <60 L/min) measured at hospital discharge was associated with a higher risk of early moderate-to-severe COPD re-exacerbation within 56 days. Patients with low PIFR experienced a greater cumulative incidence of re-exacerbation and earlier events compared with those who achieved adequate inspiratory flow. These findings indicate that PIFR assessed at discharge may identify a vulnerable subgroup during the immediate post-discharge period following ECOPD.

The observed association is consistent with prior evidence showing that a substantial proportion of patients recovering from ECOPD are unable to generate sufficient inspiratory flow for effective use of dry powder inhalers and that low PIFR may compromise treatment response.10 Observational studies in hospitalized and ambulatory COPD populations have reported frequent suboptimal PIFR and suggested an association with poorer clinical outcomes, including treatment failure and readmission.7 Reviews have further proposed PIFR as a practical therapeutic biomarker, particularly relevant when inhaler devices with intrinsic flow resistance are prescribed.[5, 6]

In the present study, patients with suboptimal PIFR were older, more symptomatic, and more likely to have experienced prior exacerbations, despite similar baseline spirometric severity; this suggests that PIFR may capture functional or physiological limitations not fully reflected by FEV_1 alone, a concept supported by prior physiological and clinical analyses of inspiratory flow performance in COPD.[6] The persistence of a significant association in time-to-event analysis after adjustment for age, symptom burden, and lung function supports the clinical relevance of PIFR in this setting. In contrast, suboptimal PIFR did not remain independently associated with re-exacerbation in multivariable logistic regression. Given the small number of outcome events and the short follow-up duration, this attenuation is likely attributable to limited statistical power and collinearity with established risk factors rather than the absence of an underlying relationship.

Inappropriate inhaler device use, defined as prescribing a dry powder inhaler to patients with suboptimal PIFR, was associated with re-exacerbation in univariable analysis. This finding is biologically plausible and aligns with prior reports emphasizing the importance of matching inhaler device resistance to patient inspiratory capability.[5] Although this association did not persist after adjustment, the direction of effect supports the hypothesis that device–patient mismatch may contribute to early post-discharge instability in selected patients.

PIFR improved over time in the overall cohort, with an increasing proportion of patients achieving PIFR ≥60 L/min during follow-up, consistent with physiological recovery after exacerbation. However, patients who experienced re-exacerbation demonstrated persistently lower or unstable PIFR trajectories. Similar patterns of persistently suboptimal inspiratory flow have been reported among selected COPD subgroups, particularly among users of dry powder inhalers.[11, 12] While causal inference cannot be drawn, this pattern suggests that failure to recover or maintain adequate inspiratory flow may mark ongoing vulnerability and help explain early relapse despite standard therapy.

Several limitations warrant consideration. The sample size was modest, reflecting lower-than-anticipated recruitment due to fewer ECOPD admissions during the study period, limiting statistical power for adjusted analyses and resulting in wide confidence intervals. The multivariable Cox model included 5 covariates with only 7 outcome events (events-per-variable =1.4, far below the recommended minimum of 10), resulting in a very low events-per-variable ratio and likely model instability, as reflected by the wide confidence intervals and the marked change between unadjusted and adjusted estimates. Multivariable Cox estimates should be interpreted as hypothesis-generating only. As this study was designed as an exploratory cohort to assess short-term clinical associations, the sample size was determined by the availability of real-world patients rather than a predefined power calculation. The single-center design and all-male cohort may restrict generalizability. PIFR measurements were obtained only during in-person visits, whereas exacerbation outcomes were also captured by telephone follow-up, potentially introducing measurement asymmetry. Residual confounding from unmeasured factors, including medication adherence and inhaler technique quality, cannot be excluded. Finally, the 56-day follow-up period precludes assessment of longer-term outcomes.

Despite these limitations, the findings have important clinical implications. Assessment of PIFR at hospital discharge may provide additional

risk stratification beyond conventional spirometric measures and support more individualized post-discharge management. Identification of patients with suboptimal PIFR may prompt reconsideration of inhaler device selection, reinforcement of inhaler technique, or closer follow-up during a high-risk period. These findings support the feasibility of incorporating PIFR assessment into routine discharge evaluation following ECOPD, particularly in settings where DPI use is common.

Conclusion

In patients hospitalized for acute exacerbation of COPD, suboptimal peak inspiratory flow rate measured at hospital discharge was associated with a higher risk and earlier occurrence of moderate-to-severe re-exacerbation within 56 days. PIFR provided clinically relevant information beyond conventional spirometric indices and symptom measures, particularly in the early post-discharge period. Assessment of PIFR at discharge may help identify patients at increased risk and support more individualized inhaler selection and follow-up strategies.

Author contributions

PA: Conceptualization, Formal analysis, Methodology, Project administration, Writing — original draft, Writing — review & editing. TM: Data curation, Investigation.

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