Effect of a Three-Month Salmeterol/Fluticasone Regimen on Forced Expiratory Volume in One Second and Forced Vital Capacity in Chronic Obstructive Pulmonary Disease

WPŁYW TRZYMIESIĘCZNEGO SCHEMATU LECZENIA SALMETEROLEM/FLUTYKAZONEM NA WYMUSZONĄ OBJĘTOŚĆ WYDECHOWĄ W CIĄGU JEDNEJ SEKUNDY I WYMUSZONĄ POJEMNOŚĆ ŻYCIOWĄ W PRZEWLEKŁEJ OBTURACYJNEJ CHOROBIE PŁUC

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Streszczenie

Wprowadzenie: Przewlekła obturacyjna choroba płuc (POChP) jest postępującą chorobą układu oddechowego, charakteryzującą się utrwalonym, w dużej mierze nieodwracalnym ograniczeniem przepływu powietrza. Natężona objętość wydechowa pierwszosekundowa (FEV_1) oraz natężona pojemność życiowa (FVC) są podstawowymi parametrami spirometrycznymi służącymi do oceny ciężkości choroby i odpowiedzi na leczenie. Jednak wpływ terapii salmeterol/flutikazon w warunkach rzeczywistej praktyki klinicznej POChP nie jest w pełni poznany.
Cel: Ocena zmian FEV_1 i FVC po trzymiesięcznej terapii salmeterolem/flutikazonem u pacjentów z POChP.
Materiał i metody: Retrospektywne badanie obserwacyjne typu pre–post obejmowało dokumentację medyczną 61 pacjentów z POChP w Szpitalu Delta Surya w Surabaya, Indonezja. Kryterium włączenia stanowiło rozpoznanie POChP według GOLD oraz stosowanie salmeterolu/flutikazonu przez co najmniej trzy miesiące z kompletnymi danymi spirometrycznymi. Wykluczono pacjentów z niekompletną dokumentacją, astmą nakładającą się na POChP, ostrymi zaostrzeniami, zapaleniem płuc lub ciężkimi chorobami współistniejącymi wpływającymi na czynność płuc. Normalność rozkładu oceniano testem Shapiro–Wilka. FVC analizowano testem t dla prób zależnych, a FEV_1 testem rang Wilcoxona. Istotność statystyczną przyjęto na poziomie $p<0,05$.
Wyniki: FVC wykazała niewielki, nieistotny statystycznie spadek po leczeniu (43,39±11,88 vs 42,23±13,44; p=0,437; d Cohena=0,10). FEV_1 wykazała niewielki, nieistotny wzrost (43,75±15,97 vs 45,21±16,90; p=0,331). W ujęciu opisowym FEV_1 poprawiła się u 49,2% pacjentów, pogorszyła u 41,0%, a u 9,8% pozostała bez zmian.
Wnioski: Trzymiesięczna terapia salmeterolem/flutikazonem nie spowodowała istotnych zmian parametrów spirometrycznych w tej rzeczywistej kohorcie chorych na POChP, co sugeruje stabilizację funkcji płuc zamiast ich mierzalnej poprawy

Słowa kluczowe: *przewlekła obturacyjna choroba płuc, objętość wydechowa wymuszona, pojemność życiowa wymuszona, salmeterol, spirometrii*

Summary

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disease characterized by persistent, largely irreversible airflow limitation. Forced Expiratory Volume in one second (FEV_1) and Forced Vital Capacity (FVC) are key spirometric parameters for assessing disease severity and therapeutic response. However, the effect of salmeterol/fluticasone on spirometric outcomes in real-world COPD practice remains incompletely defined.
Aim: To evaluate changes in FEV_1 and FVC after a three-month salmeterol/fluticasone regimen in COPD patients.
Materials and Methods: This retrospective pre–post observational study used medical records of 61 COPD patients at Delta Surya Hospital, Surabaya, Indonesia. Eligible patients had COPD diagnosed according to GOLD criteria and received salmeterol/fluticasone for at least three consecutive months with complete spirometry data. Patients with incomplete records, asthma-COPD overlap, acute exacerbation, pneumonia, or severe comorbidities affecting lung function were excluded. Normality was tested using Shapiro–Wilk. FVC was analyzed using paired t-test, while FEV_1 was analyzed using Wilcoxon signed-rank test. Significance was set at $p<0.05$.
Results: FVC showed a slight non-significant decrease after treatment (43.39±11.88 vs. 42.23±13.44; p=0.437; Cohen's d=0.10). FEV_1 showed a small non-significant increase (43.75±15.97 vs. 45.21±16.90; p=0.331). Descriptively, FEV_1 improved in 49.2% of patients, declined in 41.0%, and remained stable in 9.8%.
Conclusion: Three-month salmeterol/fluticasone therapy did not produce significant spirometric improvement in this real-world COPD cohort, suggesting clinical stability rather than measurable lung function recovery, particularly in predominantly severe disease.

Key words: Chronic Obstructive Pulmonary Disease, Forced Expiratory Volume, Forced Vital Capacity, Salmeterol, Spirometr

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms including dyspnoea, cough, and sputum production with progressive and largely irreversible airflow obstruction resulting from a combination of small airway disease and parenchymal emphysema [1]. The GOLD 2024 report defines COPD as a preventable and treatable disease, with airflow limitation confirmed by post-bronchodilator FEV_1/FVC < 0.70 on spirometry [1,5].

The disease is driven by chronic inflammation dominated by neutrophils, macrophages, and, in a subset of patients, eosinophils. This inflammatory heterogeneity underlies variability in treatment response and underpins contemporary guideline recommendations for phenotype-guided therapy [5]. Comorbidities, smoking history, and baseline lung function further modulate clinical trajectories, making comprehensive characterization of patients essential for interpreting therapeutic outcomes.

Pulmonary function testing via spirometry remains the cornerstone of COPD diagnosis and monitoring. FEV_1 reflects the degree of airway obstruction, FVC assesses total expiratory lung volume, and the FEV_1/FVC ratio defines obstruction severity according to GOLD staging [5]. Serial spirometric measurements are widely used to track disease progression and evaluate pharmacological interventions.

Among pharmacological options, the combination of an Inhaled Corticosteroid (ICS) and a Long-Acting Beta-2 Agonist (LABA) has been established as an important therapeutic strategy for patients with symptomatic COPD, particularly those with a history of exacerbations or elevated blood eosinophil counts. The salmeterol/fluticasone fixed-dose combination (FSC) is one of the most extensively studied ICS/LABA regimens. Clinical trials have demonstrated that FSC reduces exacerbation rates, improves health-related quality of life, and produces modest improvements in FEV_1 compared with placebo or bronchodilator monotherapy [3,4,6]. The landmark TORCH trial reported a modest reduction in the annual rate of FEV_1 decline and a trend toward improved survival with FSC, particularly in patients with higher eosinophil counts [9].

However, evidence from real-world settings often diverges from randomized controlled trial (RCT) findings, as clinical practice involves heterogeneous populations that may not meet strict RCT eligibility criteria. Furthermore, the current GOLD guidelines emphasize that ICS should be prescribed in a phenotype-guided manner, primarily in patients with frequent exacerbations and/or elevated blood eosinophils (≥300 cells/μL), rather than universally across all COPD patients [5]. The optimal duration of observation to detect meaningful spirometric change remains debated, with most landmark trials using follow-up periods of one to three years.

Despite these considerations, real-world observational data on short-term spirometric outcomes with FSC in routine clinical settings remain limited, particularly from Southeast Asian populations. This study, conducted at a pulmonary outpatient clinic in Surabaya, Indonesia, aimed to evaluate changes in FEV_1 and FVC following three months of salmeterol/fluticasone therapy in COPD patients, within the constraints of routine medical record data.

METHODS

Study Design

This study employed a retrospective pre–post observational design using secondary data from medical records of COPD patients. The primary comparison was spirometric parameters FEV_1 and FVC measured before and after three months of salmeterol/fluticasone combination therapy. No interventions were performed; all data were derived from routine clinical care. The study was conducted in accordance with the ethical standards of the institutional review board and the Declaration of Helsinki (Ethical Approval Number: 0082/EC/KEPK/UNUSA/2026).

Study Setting and Period

The study was conducted at Delta Surya Hospital, Surabaya, Indonesia, at the pulmonary outpatient clinic. Medical record data covered the period from January 2023 to December 2025. Data analysis was performed from January to April 2026.

Study Population and Sample

The study population comprised all patients with a confirmed COPD diagnosis who received salmeterol/fluticasone therapy during the study period and had available spirometry data at both time points. A total of 61 patients fulfilled the inclusion criteria after applying the exclusion criteria described below.

Inclusion Criteria

Patients were included if they: (1) had a confirmed COPD diagnosis based on GOLD criteria (post-bronchodilator FEV_1/FVC < 0.70); (2) received salmeterol/fluticasone combination inhalation therapy continuously for at least three months; (3) had complete spirometric data recorded before initiating therapy and after three months of therapy; and (4) had accessible, complete medical records.

Exclusion Criteria

Patients were excluded if they: (1) had incomplete or missing medical records; (2) had a concurrent diagnosis of asthma or asthma–COPD overlap (ACO); (3) experienced acute severe exacerbation or pneumonia during the observation period that may have confounded spirometric results; or (4) had severe comorbid conditions known to independently impair lung function, including chronic heart failure or pulmonary fibrosis.

Clinical Phenotyping and Data Limitations

It is important to acknowledge that detailed clinical phenotyping data were not available from the medical records used in this study. Specifically, smoking history (pack-years), GOLD subgroup classification (A–D or ABCD assessment), blood eosinophil counts, mMRC/CAT symptom scores, inhaler adherence, inhaler technique assessment, BMI, concomitant medications, and exacerbation history during follow-up were not systematically documented in the records. This limitation precludes phenotype-based subgroup analyses and must be considered when interpreting the results. Future studies should prospectively collect these variables to enable phenotype-stratified analyses and more robust interpretation of treatment response.

Justification for ICS/LABA Therapy

The GOLD guidelines recommend ICS/LABA therapy for COPD patients with persistent symptoms despite bronchodilator monotherapy, particularly those with a history of exacerbations or elevated eosinophil counts [5]. In the present cohort, salmeterol/fluticasone was prescribed as part of routine clinical care at the treating physicians' discretion, based on clinical assessment of symptom burden, exacerbation risk, and standard institutional practices at Delta Surya Hospital during the study period. While the specific clinical rationale for ICS/LABA initiation in each patient could not be extracted from the retrospective records, it is reasonable to assume that prescribing physicians applied clinical judgment consistent with guideline recommendations for symptomatic patients with moderate-to-severe COPD. This represents a real-world prescription pattern rather than a protocol-driven RCT exposure.

Justification for Three-Month Observation Period

Although longer observation periods of 12 months or more are preferable for detecting meaningful FEV_1 decline trajectories in COPD, a three-month evaluation period captures the short-term pharmacodynamic response to ICS/LABA initiation, which is relevant in routine clinical monitoring. Several prior studies and guideline documents have used 12-week (three-month) spirometric assessments as a standard short-term endpoint following therapy initiation [3,4]. Furthermore, in resource-limited real-world settings, spirometric data availability at three months represents the most practically accessible time point for retrospective analysis. This study therefore serves as an initial observational evaluation of short-term effects, with the explicit acknowledgment that longer-term follow-up studies are needed to assess disease trajectory.

Statistical Analysis

The Shapiro–Wilk test was used to assess normality of paired differences (ΔFVC and ΔFEV_1), defined as post-treatment minus pre-treatment values. For normally distributed differences, a paired t-test was applied; otherwise, the Wilcoxon signed-rank test was used.

Effect size for FVC was estimated using Cohen's d (d = mean difference / pooled SD). The Minimal Clinically Important Difference (MCID) for FEV_1 in COPD has been established at approximately 100–140 mL in the literature [5]. Confidence intervals (95% CI) for the mean FVC difference were calculated from paired t-test output. Multivariable regression analysis was not performed due to the absence of phenotype variables and the retrospective single-cohort design; this represents a recognized statistical limitation. A post-hoc power analysis was not conducted due to the exploratory nature of this study. These statistical limitations are acknowledged and should be addressed in future prospective designs

Results

Descriptive Characteristics

The study included 61 COPD patients, all of whom were male (n = 61; 100%). The mean age was 65.5 ± 8.3 years, indicating an elderly population consistent with typical COPD epidemiology. Baseline spirometric values demonstrated reduced lung function, consistent with moderate-to-severe airflow limitations across the cohort.

Descriptive Statistics of Spirometric Variables

This study included 61 COPD patients who fulfilled the inclusion and exclusion criteria and had complete spirometric data at both time points. All four spirometric measurements (FVC at first examination, FVC at third examination, FEV_1 at first examination, and FEV_1 at third examination) had 100% data completeness with no missing values. Descriptive statistics are presented in Table 1.

The mean FVC at the first examination was 43.39 ± 11.88 (median 45.00; range 17–68), which slightly decreased to 42.23 ± 13.44 (median 42.00; range 15–79) at the third examination. The mean FEV_1 at the first examination was 43.75 ± 15.97 (median 44.00; range 16–69), which showed a slight increase to 45.21 ± 16.90 (median 46.00; range 15–80) at the third examination. These values indicate that both spirometric parameters were below 50% of predicted at baseline, consistent with moderate-to-severe COPD (GOLD stage 2–3) [5].

Table 1. Descriptive Statistics of the Research Variables

Variable	Mean ± SD	Median	Min–Max	IQR
FVC First Examination	43.39 ± 11.88	45.00	17–68	18
FVC Third Examination	42.23 ± 13.44	42.00	15–79	17
FEV_1 First Examination	43.75 ± 15.97	44.00	16–69	29
FEV_1 Third Examination	45.21 ± 16.90	46.00	15–80	27

Note: SD = standard deviation; IQR = interquartile range. All values represent percentage of predicted. FVC = Forced Vital Capacity; FEV_1 = Forced Expiratory Volume in one second.

Normality Testing (Shapiro–Wilk)

The Shapiro–Wilk test was applied to assess the distribution of FVC and FEV_1 data at both time points (Table 2). FVC data at the first and third examinations both showed normal distribution ($p = 0.552$ and $p = 0.688$, respectively). In contrast, FEV_1 data at the first examination failed the normality assumption ($p = 0.005$), while the third examination showed borderline normality ($p = 0.063$). Based on these results, FVC was analyzed using a paired t-test (parametric), whereas FEV_1 was analyzed using the Wilcoxon signed-rank test (non-parametric).

Comparison of FVC Values (Paired t-test)

The The paired t-test showed no statistically significant difference in FVC when calculated as Δ = FVC_follow-up − FVC_baseline (mean difference = 1.164; 95% CI: −1.8 to 4.1; $t = 0.782$; $df = 60$; $p = 0.437$; Cohen's $d = 0.10$, very small) (Table 3).

Comparison of FEV_1 Values (Wilcoxon Signed-Rank Test)

The Wilcoxon signed-rank test showed no statistically significant difference in FEV_1 between the first and third examinations ($Z = -0.973$; $p = 0.331$). Descriptively, 30 patients (49.2%) showed an increase in FEV_1, 25 patients (41.0%) experienced a decrease, and 6 patients (9.8%) showed no change. The mean FEV_1 increased from 43.75 to 45.21, representing an absolute change of approximately 1.46 percentage points of predicted. This change is below the established MCID threshold of approximately 100–140 mL for FEV_1 in COPD and therefore is not considered clinically meaningful [5]. All comparative results are summarized in Table 3.

Table 2. Results of the Normality Test (Shapiro–Wilk)

Variable	Statistic	p-Value
FVC First Examination	0.983	0.552
FVC Third Examination	0.986	0.688
FEV_1 First Examination	0.939	0.005*
FEV_1 Third Examination	0.963	0.063

Note: *$p < 0.05$ indicates significant departure from normality. FVC data (both time points) met the assumption of normal distribution; FEV_1 at the first examination did not, necessitating non-parametric analysis

Table 3. Comparative Statistical Analysis of Spirometric Parameters Before and After Three-Month Salmeterol/Fluticasone Therapy

Variable	Statistical Test	Mean Difference	Test Statistic	df	p-Value	Effect Size
FVC	*Paired t-test*	1.164 (95% CI: −1.8 to 4.1)	$t = 0.782$	60	0.437	Cohen's $d = 0.10$ (very small)
FEV_1	*Wilcoxon Signed-Rank Test*	1.46	$Z = -0.973$	–	0.331	Not calculated (non-parametric)

Note: A p-value < 0.05 was considered statistically significant. Effect size for FVC estimated by Cohen's d = mean difference / pooled SD. The MCID for FEV_1 in COPD is approximately 100–140 mL; the observed change does not reach this threshold. 95% CI for FVC mean difference is approximate based on t-distribution parameters. FVC = Forced Vital Capacity; FEV_1 = Forced Expiratory Volume in one second.

DISCUSSION

This retrospective pre–post observational study evaluated the short-term effects of three-month salmeterol/fluticasone therapy on spirometric outcomes in 61 COPD patients in a real-world clinical setting. The primary findings were that neither FVC nor FEV_1 demonstrated statistically significant changes following therapy (FVC: $p = 0.437$; FEV_1: $p = 0.331$), with very small effect sizes (Cohen's $d = 0.10$ for FVC). These results are interpreted in the context of a predominantly severe COPD population with mean baseline FEV_1 of 43.75%, consistent with GOLD stage 3, wherein irreversible structural changes substantially constrain the achievable range of spirometric improvement.

COPD is characterized by chronic inflammatory and structural changes including small airway remodeling, mucous hypersecretion, and emphysematous parenchymal destruction that are largely irreversible with current pharmacological therapy [12] [13]. Unlike asthma, airflow limitation in COPD is dominated by neutrophilic and macrophage-driven inflammation that exhibits relative corticosteroid resistance, explaining why ICS components do not consistently produce large FEV_1 improvements across unselected COPD populations [15][11]. In patients with advanced disease and extensive airway remodeling, the magnitude of pharmacological bronchodilation is constrained by fixed structural obstruction, placing a biological ceiling on short-term spirometric response [5].

In this study, the salmeterol/fluticasone combination was prescribed strictly as part of routine clinical care based on the clinical judgment of the treating physicians. However, due to the retrospective nature of this research and the lack of systematic phenotypic data documentation (such as blood eosinophil counts and exacerbation history) it cannot be definitively confirmed whether these prescriptions were appropriately indicated or fully concordant with current GOLD guidelines [5]. The decision to initiate ICS/LABA therapy in this cohort purely reflects real-world empirical prescribing patterns for patients with a symptomatic burden, rather than a strictly protocol-driven exposure like those in randomized controlled trials (RCTs) [11]. Therefore, definitive mechanistic conclusions regarding the responsiveness to ICS therapy in this population cannot be drawn and remain speculative [14]

The three-month observation period employed in this study is a recognized limitation. Landmark COPD trials such as TORCH [9] and FLAME [10] used follow-up periods of one to three years to detect clinically meaningful changes in FEV_1 decline and exacerbation rates. However, shorter-duration evaluations of 12 weeks are clinically relevant for assessing initial symptomatic and functional responses to therapy and are commonly used as standard short-term endpoints in bronchodilator studies [3]. A three-month real-world dataset represents a pragmatic observational window in resource-limited settings, where longer prospective follow-up is logistically challenging. The absence of spirometric improvement at three months is therefore not equivalent to treatment futility; sustained effects on exacerbation reduction and symptom stabilization are expected to emerge over longer follow-up periods [11]. Future studies with 12-month or longer observational windows are essential to evaluate the trajectory of lung function under continued therapy.

The absence of significant FVC change (mean difference = 1.164; Cohen's $d = 0.10$) is physiologically consistent with the mechanisms of airflow limitation in advanced COPD. FVC reflects total expiratory lung volume and is reduced in the context of hyperinflation and air trapping secondary to emphysematous destruction and loss of elastic recoil [Lee et al., 2024]. ICS/LABA therapy does not reverse parenchymal destruction, and studies using triple therapy (LABA/LAMA/ICS) have demonstrated superior improvement in lung hyperinflation through the addition of a long-acting muscarinic antagonist (LAMA) that reduces dynamic hyperinflation more effectively [7]. The dual therapy evaluated here appears insufficient to produce significant FVC changes in patients with substantial structural lung damage, which is consistent with systematic review evidence [6].

The small increase in mean FEV_1 from 43.75 to 45.21 (absolute change approximately 1.46 percentage points of predicted) is below the established MCID for FEV_1 in COPD (approximately 100–140 mL) and did not reach statistical significance. However, in the context of a disease that characteristically follows a progressive decline, the no statistically significant change in FEV_1 observed over three months may represent a descriptive observation only in certain patients. Vestbo et al. (2020) emphasized that real-world spirometric changes are often smaller and more heterogeneous than those observed in RCTs due to greater variability in adherence, technique, and disease heterogeneity. The distribution of individual FEV_1 responses 49.2% improving, 41.0% declining, and 9.8% stable is consistent with the known heterogeneity of treatment response in unselected COPD populations and underscores the need for phenotype stratification to identify responders [14].

Contemporary literature establishes blood eosinophil counts as a practical and validated biomarker for predicting ICS responsiveness in COPD. Patients with eosinophil counts ≥300 cells/μL consistently demonstrate greater reductions in exacerbation rates and more favourable spirometric responses to ICS-containing regimens, while those with low eosinophil counts or neutrophil-predominant inflammation often show limited benefit and may face increased infection risk [11] [14]. In the present study, eosinophil data were not available for systematic analysis, which represents a significant phenotypic gap. It is plausible that the absence of significant spirometric improvement reflects, in part, the inclusion of a mixed eosinophil-profile population in which ICS efficacy varies substantially. Without stratification by eosinophil phenotype, mechanistic conclusions about ICS responsiveness cannot be drawn, and this interpretation remains speculative.

Several statistical limitations merit acknowledgment. First, the sample size of 61 patients limits statistical power to detect modest but clinically relevant spirometric changes, particularly for non-parametric analyses. Based on reported MCID estimates for FEV_1 (≈100–140 mL), a study detecting such an effect with 80% power at $\alpha = 0.05$ would typically require larger sample sizes. Second, multivariable regression analysis was not performed due to the absence of phenotype and confounding variables in the retrospective records. Uncontrolled confounders including ongoing smoking, environmental pollutant exposure, unreported exacerbations, concomitant medications, and BMI may have biased the results in either direction. Third, the retrospective design cannot control for inhaler adherence or technique, both of which significantly influence pharmacological efficacy [16][17].

A further limitation is the exclusive reliance on spirometric parameters as outcome measures. The

present study did not assess patient-reported clinical outcomes including dyspnoea scores (mMRC scale), symptom burden (CAT questionnaire), exacerbation frequency, hospitalization rates, rescue medication use, or exercise tolerance. These outcomes are widely recognized as essential indicators of COPD therapeutic benefit and may be more sensitive to ICS/LABA effects than FEV_1 in short-term studies [11]. The absence of such data is a significant limitation of this retrospective study and constrains the clinical conclusions that can be drawn. Future studies should systematically incorporate patient-reported outcomes and clinical event data alongside spirometry.

The scientific contribution of this study, while methodologically limited, lies in providing real-world observational data from a regional hospital in Indonesia context where COPD management evidence is predominantly derived from Western or large urban Asian populations. Short-term spirometric outcomes from community-level clinical practice in resource-limited settings are underrepresented in the literature. This study demonstrates the feasibility of conducting structured retrospective spirometric analyses using routine outpatient records and provides a methodological template for future prospective studies in similar settings. The consistent finding of no significant change observed, rather than deterioration, in a predominantly severe COPD cohort over three months is a preliminary signal warranting further investigation with appropriate prospective design, phenotype stratification, and comprehensive clinical outcome assessment.

Future research in this clinical setting should employ prospective cohort designs with standardized data collection protocols including eosinophil counts, GOLD subgroup classification, symptom scores, exacerbation recording, adherence monitoring, and longer observational periods of at least 12 months. Phenotype-stratified analyses comparing ICS/LABA with LABA/LAMA or triple therapy (LABA/LAMA/ICS) would allow identification of patient subgroups most likely to benefit from ICS-containing regimens, in alignment with precision medicine principles endorsed by GOLD 2024 and the treatable traits framework [13].

CONCLUSIONS

In this retrospective real-world study of 61 COPD patients, a three-month course of salmeterol/fluticasone combination therapy did not produce statistically significant improvements in FEV_1 or FVC. The absence of significant spirometric change is consistent with the predominantly irreversible structural pathology of advanced COPD, the modest and heterogeneous spirometric effects of ICS/LABA documented in controlled trials, and the limitations of short-term retrospective evaluation. The descriptive pattern of no significant change observed particularly the slight increase in mean FEV_1 without clinically significant deterioration may represent a descriptive observation only in a predominantly severe (GOLD 3) population, where disease progression typically produces ongoing FEV_1 decline.

These findings must be interpreted with caution given the retrospective design, small sample size, absence of phenotype data, lack of clinical outcome measures, and inability to control for adherence and confounding variables. They do not support or refute the efficacy of salmeterol/fluticasone in COPD broadly but rather reflect the complexity of demonstrating short-term spirometric benefit in an unselected, predominantly severe real-world cohort. Future prospective studies with phenotype stratification, eosinophil-guided prescription, comprehensive clinical outcome assessment, and longer follow-up are essential to better define the role of ICS/LABA therapy in COPD management in regional Indonesian clinical settings.

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