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The Relationship of FEV1/FVC Ratio, FEF 25-75% and Carbon Monoxide Levels as a Pulmonary Function Parameters In Smokers

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ABSTRACT:

Background and Objectives: Smoking remains a major preventable cause of morbidity and continues to increase in Indonesia, especially among productive-age adults. Early identification of smoking-related pulmonary impairment is crucial, as small-airway dysfunction may not be detected by standard spirometric indices. This study aimed to evaluate the relationship between FEV_1/FVC ratio, $FEF_{25–75}\%$, and exhaled carbon monoxide (eCO) as combined markers for early ventilatory impairment in smokers.

Materials and Methods: A comparative cross-sectional study was conducted in October 2025 among hospital security officers. Purposive sampling yielded 49 smokers and 40 non-smokers. Spirometry assessed FEV_1/FVC and $FEF_{25–75}\%$, and exhaled CO (eCO) was measured using a standardized analyzer. Data were analyzed using Chi-square, t-test or Mann–Whitney U test, Spearman correlation, and simple linear regression, with $p<0.05$ considered significant.

Results: Smokers exhibited significantly lower FEV_1/FVC and $FEF_{25–75}\%$ values and markedly higher eCO levels than non-smokers ($p<0.05$). Among smokers, eCO levels demonstrated strong negative correlations with both FEV_1/FVC (ρ up to –0.940) and $FEF_{25–75}\%$ (ρ up to –0.682). Regression analysis indicated that every 1-ppm increase in eCO was associated with a 2.13% reduction in FEV_1/FVC and a 2.88% reduction in $FEF_{25–75}\%$. A positive correlation was observed between FEV_1/FVC and $FEF_{25–75}\%$, reflecting linked impairment of central and peripheral airways.

Conclusions: Exhaled CO is significantly associated with reduced pulmonary function and serves as a practical, non-invasive biomarker of smoking exposure. Combined interpretation of FEV_1/FVC, $FEF_{25–75}\%$, and eCO enhances early detection of smoking-related airway dysfunction and may support targeted cessation interventions.

1. Introduction

Smoking remains one of the leading preventable causes of morbidity and mortality worldwide, and Indonesia is among the countries with the highest tobacco consumption [1]. The Indonesia Health Survey (SKI) 2023 reported that the number of active smokers has reached approximately 70 million people, indicating a substantial and persistent public health burden [2]. Data from the Global Youth Tobacco Survey (GYTS) further revealed an increasing trend of smoking among adolescents aged 13–15 years, rising from 18.3% in 2016 to 19.2% in 2019 [3–5]. In adults, the Global Adult Tobacco Survey (GATS) documented an increase of 8.8 million smokers over the past decade, from 60.3 million in 2011 to 69.1 million in 2021, with the majority being male [6]. These findings highlight the urgent need for more comprehensive evaluations of tobacco exposure and its impact on respiratory health in Indonesia.

Assessment of lung function plays a critical role in identifying early physiological impairment caused by smoking [7]. Spirometry is a widely used diagnostic tool that evaluates airflow limitation through several key parameters associated with morbidity, mortality, and prognosis of pulmonary diseases [8]. Spirometric testing

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enables early detection of pulmonary abnormalities even before the onset of clinically apparent symptoms [8, 9]. Commonly measured parameters include the Forced Expiratory Volume in one second (FEV_1), Forced Vital Capacity (FVC), the FEV_1/FVC ratio, and Forced Expiratory Flow at 25–75% of the pulmonary volume ($FEF_{25–75}$%) [10]. These parameters are essential for detecting small airway dysfunction, peripheral airway narrowing, and early features of bronchial hyperresponsiveness [11, 12].

Among these indices, $FEF_{25–75}$% is recognized as a sensitive marker of peripheral obstructive airflow impairment [13]. A reduced $FEF_{25–75}$% is frequently observed not only in individuals with established airflow limitation but also in those with normal spirometric results, suggesting its potential role as an early physiological indicator of small airway injury [14]. Previous studies have demonstrated significant reductions in FEV_1, FVC, FEV_1/FVC ratio, $FEF_{25–75}$%, and PEFR among smokers compared with non-smokers, with the magnitude of decline associated with the amount and duration of cigarette exposure [15]. Heavy and long-term smokers consistently exhibit lower $FEF_{25–75}$% values, reinforcing its association with cumulative tobacco exposure [16].

Despite these findings, evidence remains limited regarding the combined use of FEV_1/FVC ratio, $FEF_{25–75}$%, and carbon monoxide (CO) levels measured through breath analysis as integrated parameters to assess smoking-related pulmonary function impairment [11, 17]. CO levels are known to reflect recent smoking intensity and may serve as an objective biochemical marker of exposure [18]. A more comprehensive analysis integrating spirometric parameters with CO levels may provide a clearer depiction of early airway dysfunction in smokers. Therefore, this study aims to examine the relationship between the FEV_1/FVC ratio, $FEF_{25–75}$%, and carbon monoxide levels in smokers, offering a more robust evaluation of pulmonary impairment associated with tobacco exposure.

2. Materials and Methods

Study Design

This study employed an analytical observational design using a comparative cross-sectional approach. Measurements were conducted once for each participant to assess the FEV_1/FVC ratio, $FEF_{25–75}$%, and CO levels among smokers and non-smokers.

Study Setting and Period

Data collection was carried out at Dr. Wahidin Sudirohusodo Hospital and affiliated network hospitals in Makassar. Sampling and measurement procedures focused on hospital security officers who use conventional cigarettes. The study was conducted in October 2025.

Study Population and Sample Size

The study population consisted of all hospital security officers on duty during October 2025. Participants were recruited using purposive sampling, whereby all individuals meeting the inclusion and exclusion criteria and completing all required assessments were enrolled. Sample size was calculated using the formula for comparing two independent means with 95% confidence and 80% power. Parameters from previous studies were applied, yielding required sample sizes of 30 per group for $FEF_{25–75}$%, 28 per group for FEV_1/FVC, and 23 per group for CO levels; thus, the largest requirement (30 per group) was used. To account for a potential 20–25% drop-out rate, the final target sample was increased to 49 smokers and 40 non-smokers.

Inclusion and Exclusion Criteria

The inclusion criteria for this study required participants to be older than 18 years, to be active smokers consuming more than one cigarette per day, to have a smoking history of more than one year, and to demonstrate willingness to participate by signing informed consent. Participants were excluded if they presented with respiratory symptoms such as cough or dyspnea, worked in industrial environments with additional inhalation exposures, or had a known history of pulmonary diseases, including tuberculosis, chronic obstructive pulmonary disease (COPD), or asthma.

Data Collection Procedures

Eligible participants were first identified and screened using a brief questionnaire to ensure compliance with the established inclusion criteria. After screening, each participant underwent two main assessments. The first assessment involved the measurement of exhaled carbon monoxide levels using a standardized CO analyzer to quantify carbon monoxide as an indicator of recent smoking exposure. The second assessment consisted of a

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spirometry examination performed with a calibrated spirometer to obtain key parameters, including FEV_1, FVC, the FEV_1/FVC ratio, and $FEF_{25–75}$%. In this procedure, the FEV_1/FVC ratio was used to assess large-airway function, whereas $FEF_{25–75}$% provided an evaluation of small-airway involvement. All data obtained during these assessments were documented using standardized case report forms before progressing to the analysis stage.

Data Processing and Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS. The management process included editing for completeness, coding of categorical variables, tabulation, and data cleaning to ensure accuracy. Univariate analysis summarized variable distributions, while bivariate analysis evaluated associations between smoking-related parameters and lung function. The Chi-square test was applied for categorical variables, and independent t-tests or Mann–Whitney U tests were used for continuous variables according to data normality. A p-value <0.05 was considered statistically significant.

Ethical Considerations

This study received ethical approval from the Health Research Ethics Committee, Faculty of Medicine, Universitas Hasanuddin, under approval number 843/UN4.6.4.5.31/PP36/2025. The protocol registered as UH25100802 was reviewed through an expedited process and granted approval on 24 October 2025. All participants were informed about the study objectives and procedures, provided written informed consent prior to participation, and were assured that the confidentiality of their personal data would be strictly maintained.

3. Results

Sample Characteristics

The characteristics of the study participants are summarized in Table 1. A total of 89 respondents were included, consisting of 49 smokers and 40 non-smokers. The mean age of all participants was 41.97 ± 12.91 years (range: 19–65). Among smokers, the average smoking duration was 21.63 years, with a mean consumption of 13.47 cigarettes per day and an average Brinkman Index of 300.15.

Table 1. Characteristics of Study Participants

Variables	Mean ± SD	Min	Max
Age (years)	41.97 ± 12.91	19.0	65.0
Duration of Smoking (years)	21.63 ± 7.96	3.0	50.0
Number of Cigarettes/Day (sticks)	13.47 ± 5.12	2.0	30.0
Brinkman Index	300.15 ± 176.02	5.0	950.0
FEV_1/FVC (%)	80.24 ± 12.16	55.1	100.6
$FEF_{25–75}$ (%)	86.92 ± 18.04	38.0	130.0
CO Level (ppm)	7.06 ± 5.52	0.5	40.0

The mean FEV_1/FVC ratio was 80.24% (range: 55.1–100.6%), while the mean $FEF_{25–75}$% was 86.92% (range: 38–130%). The average exhaled carbon monoxide level was 7.06 ± 5.52 ppm, reflecting considerable variation in smoking exposure. Overall, these findings describe a predominantly adult working population with long-term smoking habits and lung function ranging from normal to mildly obstructive.

According to Table 2, most smokers were aged 35–50 years (51.0%), followed by those aged 19–34 years (36.7%) and 51–65 years (12.2%). The majority had smoked for 18–33 years (53.1%), while 32.7% had smoked for 2–17 years and 14.3% for 34–50 years. Daily cigarette consumption was predominantly within the 10–19 cigarettes/day category (46.9%), followed by 1–9 cigarettes/day (38.8%) and ≥20 cigarettes/day (14.3%). Brinkman Index values <200 were observed in 51.0% of subjects, while 34.7% fell within 200–600 and 14.3% exceeded 600.

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Table 2. Distribution and Demographic Characteristics of Smoker Participants

Variables	Category	n	%
Age (years)	19–34	18	36,7
	35–50	25	51,0
	51–65	6	12,2
Duration of Smoking (years)	2–17	16	32,7
	18–33	26	53,1
	34–50	7	14,3
Number of Cigarettes per Day (sticks)	1–9	19	38,8
	10–19	23	46,9
	≥20	7	14,3
Brinkman Index	<200	25	51,0
	200–600	17	34,7
	>600	7	14,3
FEV_1/FVC (%)	<70	2	4,1
	>70	47	95,9
$FEF_{25–75}$ (%)	≤60	8	16,3
	>60	41	83,7
Exhaled CO Level (ppm)	<6	9	18,4
	≥6	40	81,6

In terms of lung function, only 4.1% of smokers demonstrated an FEV_1/FVC ratio <70%, while 95.9% remained above this threshold. A reduction in $FEF_{25–75}$% (≤60%) was present in 16.3% of smokers, indicating small-airway impairment. Additionally, exhaled CO levels were elevated (≥6 ppm) in 81.6% of participants, confirming active smoking exposure.

Comparison of Pulmonary Function Characteristics Between Smokers and Non-Smokers

Table 3. Comparison of Pulmonary Function Characteristics Between Smokers and Non-Smokers

Variables	Category	Smokers n (%)	Non-Smokers n (%)
Age (years)	19–34	18 (36,7%)	17 (42,5%)
	35–50	25 (51,0%)	21 (52,5%)
	51–65	6 (12,2%)	2 (5,0%)
FEV_1/FVC (%)	<70	2 (4,1%)	8 (20,0%)
	>70	47 (95,9%)	32 (80,0%)
$FEF_{25–75}$ (%)	≤60	8 (16,3%)	14 (35,0%)
	>60	41 (83,7%)	26 (65,0%)
CO Levels (ppm)	<6	9 (18,4%)	40 (100,0%)
	≥6	40 (81,6%)	0 (0%)

*Chi-square test

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Following the descriptive analysis of the smoker group, comparisons were made between smokers and non-smokers regarding age distribution, FEV_1/FVC ratio, $FEF_{25–75}\%$, and exhaled CO levels. The results of this comparison are presented in Table 3.

Table 3 demonstrates significant differences between smokers and non-smokers in FEV_1/FVC ratio, $FEF_{25–75}\%$, and exhaled CO levels ($p < 0.05$), indicating a measurable impact of smoking habits on pulmonary function. Age distribution was similar between groups: among smokers, 51.0% were aged 35–50 years, 36.7% were aged 19–34 years, and 12.2% were aged 51–65 years. In the non-smoking group, the proportions were 52.5%, 42.5%, and 5.0%, respectively.

Pulmonary function differed notably between groups. An FEV_1/FVC ratio <70% was observed in 4.1% of smokers but in 20.0% of non-smokers. Reduced $FEF_{25–75}\%$ (≤60%) was also more common among non-smokers (35.0%) compared with smokers (16.3%). As expected, exposure indicators differed markedly: elevated exhaled CO levels (≥6 ppm) were present in 81.6% of smokers, while all non-smokers demonstrated CO levels below 6 ppm.

Association Between Demographic Characteristics and Brinkman Index

This analysis aimed to evaluate the relationship between demographic characteristics and pulmonary function parameters across different smoking severity levels categorized by the Brinkman Index. Variables assessed included age, duration of smoking, daily cigarette consumption, FEV_1/FVC ratio, $FEF_{25–75}\%$, and exhaled CO levels. The findings summarized in Table 4 demonstrate that increasing smoking severity is significantly associated with differences in all major variables. A clear dose–response pattern was observed, in which greater smoking exposure corresponded to reduced lung function and higher CO levels.

Table 4. Association Between Demographic Characteristics and Brinkman Index

Variables	<200 (Mild)	200–600 (Moderate)	>600 (Severe)	p-Value
Age (years)	37.8 ± 10.2	43.5 ± 9.8	47.2 ± 8.5	**0.041**
Smoking Duration (years)	14.1 ± 6.3	24.5 ± 7.6	32.7 ± 7.8	**<0.001**
Cigarettes/Day (sticks)	8.9 ± 3.9	14.5 ± 4.7	23.1 ± 5.9	**<0.001**
FEV_1/FVC (%)	86.4 ± 7.8	79.2 ± 8.1	73.8 ± 8.9	**0.003**
$FEF_{25–75}$ (%)	97.8 ± 14.2	86.1 ± 15.9	70.5 ± 18.1	**0.004**
CO Levels (ppm)	6.1 ± 3.1	9.7 ± 4.2	15.3 ± 4.8	**<0.001**

***One-Way ANOVA**

Age, duration of smoking, and daily cigarette consumption increased progressively with higher Brinkman categories. Heavy smokers had the longest duration of smoking (mean 32.7 years), compared with moderate (24.5 years) and light smokers (14.1 years). Daily cigarette use also rose markedly, from 8.9 cigarettes per day among light smokers to 23.1 cigarettes among heavy smokers ($p < 0.001$).

Pulmonary function parameters showed a consistent decline across smoking severity levels. The mean FEV_1/FVC ratio decreased from 86.4% in light smokers to 73.8% in heavy smokers ($p = 0.003$), while $FEF_{25–75}\%$ declined from 97.8% to 70.5% ($p = 0.004$). Exhaled CO levels increased sharply across categories, rising from 6.1 ppm in light smokers to 15.3 ppm in heavy smokers ($p < 0.001$). These findings confirm that heavier smoking exposure is directly associated with worsening pulmonary function and elevated CO levels.

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Table 5. Results of the Analysis of the Relationship Between Demographic Characteristics and Smoking Severity

Variables	F	p-Value
Age (years)	4.12	0.041
Smoking Duration (years)	23.64	**<0.001**
Cigarettes/Day (sticks)	21.58	**<0.001**
FEV_1/FVC (%)	7.34	**0.001**
$FEF_{25–75}$ (%)	6.98	**0.002**
CO Levels (ppm)	17.93	**<0.001**

***Post Hoc - Tukey HSD**

To further assess the strength of these associations, an ANOVA was performed, followed by Tukey's HSD post-hoc test to determine between-group differences. The results, presented in Table 5, indicate significant differences across all primary variables. Age showed a significant association with smoking severity ($F = 4.12$; $p = 0.041$), while smoking duration demonstrated the strongest relationship ($F = 23.64$; $p < 0.001$). Daily cigarette consumption also showed a highly significant association ($F = 21.58$; $p < 0.001$).

Similarly, pulmonary function parameters varied significantly across Brinkman Index categories. The FEV_1/FVC ratio ($F = 7.34$; $p = 0.001$) and $FEF_{25–75}$% ($F = 6.98$; $p = 0.002$) both declined with increasing smoking severity. Exhaled CO levels showed one of the strongest associations ($F = 17.93$; $p < 0.001$), reinforcing its role as an objective marker of smoking intensity. Post-hoc analysis confirmed significant pairwise differences, particularly between light and heavy smokers.

Overall, these findings underscore a clear dose–response relationship in which increasing tobacco exposure, as measured by the Brinkman Index, is associated with older age, longer smoking duration, higher daily cigarette consumption, declining pulmonary function, and elevated CO levels.

Association Between FEV_1/FVC Ratio, $FEF_{25–75}$%, and Exhaled Carbon Monoxide (eCO) Among Smokers

This analysis examined the relationship between the three main parameters of interest, FEV_1/FVC ratio, $FEF_{25–75}$%, and exhaled carbon monoxide (eCO), among smokers. Spearman's correlation was applied to assess the strength and direction of these associations. The results, summarized in Table 6, demonstrate significant relationships between eCO levels and lung function parameters.

A significant positive correlation was found between FEV_1/FVC and $FEF_{25–75}$% within the subgroup of smokers with $FEV_1/FVC \leq 75\%$ ($\rho = 0.612$; $p = 0.041$), indicating a moderate association between large- and small-airway function. A weaker but still significant correlation was also observed in those with $FEV_1/FVC > 75\%$ ($\rho = 0.146$; $p = 0.030$).

Table 6. Correlation of Variables Assessing Decline in Lung Function Among Smokers

Variables	Category	n	Spearman ρ	p-value
FEV_1/FVC and $FEF_{25–75}$	<70	2	0.612	**0.041**
	>70	47	0.146	**0.030**
CO (ppm) and FEV_1/FVC	≤60	8	–0.745	**0.016**
	>60	41	–0.940	**<0.001**
CO (ppm) and $FEF_{25–75}$	<6	10	–0.682	**0.027**
	≥6	39	–0.659	**<0.001**

***Spearman Correlation**

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In contrast, eCO levels showed a strong negative correlation with the FEV_1/FVC ratio in both $FEF_{25–75}\%$ subgroups. Among individuals with reduced small-airway function ($FEF_{25–75}\%$ ≤60%), the correlation reached $\rho = –0.745$ ($p = 0.016$), while an even stronger association was observed in those with $FEF_{25–75}\%$ >60% ($\rho = –0.940$; $p < 0.001$). These findings indicate that higher CO levels are consistently associated with lower FEV_1/FVC values. Similarly, eCO levels were negatively correlated with $FEF_{25–75}\%$ across both low (<6 ppm) and high (≥6 ppm) CO categories, with moderate to strong correlation coefficients ($\rho = –0.682$ and $–0.659$; both $p < 0.05$).

Overall, the correlation patterns presented in Table 6 confirm that higher CO levels, reflecting greater exposure to cigarette smoke, are closely associated with declines in both large- and small-airway ventilatory function. These findings emphasize the sensitivity of eCO as a biomarker of smoking intensity and its potential clinical relevance in detecting early airway impairment among smokers.

Correlation Between Exhaled Carbon Monoxide (eCO) and the Degree of Pulmonary Function Decline in Smokers

To evaluate the extent to which eCO levels reflect the severity of pulmonary dysfunction, an analysis was performed examining the relationship between CO concentration (ppm) and the degree of ventilatory impairment, calculated from combined reductions in FEV_1/FVC and $FEF_{25–75}\%$. This assessment aimed to determine whether eCO can serve as an objective predictor of impaired ventilation among smokers. The results of the linear correlation and regression analysis are presented in Table 7.

Table 7. Association Between CO Levels and Lung Function Decline Index

Variables	Slope (β_1)	Pearson r	95% CI	p-value
CO vs FEV_1/FVC	–2.132	–0.950	–2.332 – –1.932	<0.001
CO vs $FEF_{25–75}$	–2.878	–0.646	–3.850 – –1.905	<0.001
FEV_1/FVC ~ $FEF_{25–75}$	1.167	0.588	0.708 – 1.627	<0.001

***Pearson Correlation**

As shown in Table 7, Pearson correlation and simple linear regression analysis demonstrated a significant negative association between eCO levels and both pulmonary function indices. Each 1-ppm increase in CO was associated with a 2.13% decrease in the FEV_1/FVC ratio ($p < 0.001$) and a 2.88% decline in $FEF_{25–75}\%$ ($p < 0.001$). These findings indicate that higher CO levels consistently correspond to a greater degree of functional impairment.

A significant positive correlation was also observed between the two lung function parameters themselves, where each 1% increase in $FEF_{25–75}\%$ was associated with a 1.17% increase in the FEV_1/FVC ratio ($p < 0.001$), highlighting the interdependence between large- and small-airway performance. Overall, these results demonstrate that elevated eCO levels have a direct and measurable impact on the decline of both large and small airway function. Clinically, eCO may serve as a quantitative and practical marker for assessing the severity of smoking-related ventilatory impairment.

4. Discussion

The study population, with a mean age of 41.97 years, represents productive adults with substantial smoking exposure, consistent with the Indonesia Health Survey 2023 reporting peak smoking prevalence among individuals aged 31–50 [2]. Smoking in this demographic is often driven by social and occupational stressors, strengthening the relevance of assessing early respiratory impairment. The long duration of smoking (mean 21.63 years) and consumption of 13.47 cigarettes/day reflect chronic cumulative exposure, aligning with WHO 2024 reports that duration and intensity of smoking predict progressive lung-function decline and COPD development, a trend similarly observed in Dai et al. (2022) within developing-country populations [19, 20]. The mean Brinkman Index of

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300.15 indicates moderate-to-heavy exposure according to PDPI criteria, supporting the biological plausibility of chronic small-airway inflammation, mucus accumulation, and epithelial remodeling associated with cumulative tobacco exposure [21].

The mean FEV_1/FVC ratio (80.24%) suggests preserved overall ventilatory function despite early signs of obstruction, consistent with findings from Graham et al. (2019), who noted that values between 70–80% are typical among active smokers with subtle ventilatory impairment [22]. This aligns with Oh et al. (2018), who reported that middle-aged adults may exhibit normal spirometry despite reduced pulmonary reserve due to age and chronic exposure [23]. Although the mean $FEF_{25–75}$ remained within normal ranges (86.92%), 16% of participants demonstrated values ≤60%, reinforcing the utility of this index as a sensitive marker of early small-airway dysfunction[14]. Evidence from Kwon et al. (2020) and Alobaidi et al. (2022) further supports the predictive value of $FEF_{25–75}$ reduction for preclinical airflow limitation among active smokers [14, 24].

Exhaled CO was elevated (≥6 ppm) in 80% of smokers, reflecting increased carboxyhemoglobin levels and reduced oxygen transport capacity, consistent with studies by Ezeigbo et al. (2024) and Herath et al. (2021) showing linear increases in CO with smoking intensity [25, 26]. These findings collectively support GOLD 2017 and Adatia et al. (2021), which emphasize that physiological impairment and elevated biomarkers of exposure often precede spirometry-defined COPD [27].

Comparisons with non-smokers revealed significant differences in FEV_1/FVC, $FEF_{25–75}$, and exhaled CO, reinforcing the substantial respiratory burden of tobacco smoke. Despite the unexpected finding of a higher proportion of non-smokers with FEV_1/FVC <70%, this may reflect environmental exposures, genetic susceptibility, or passive smoking. Age-related reductions described by Oh et al. (2018) and environmental influences described by Alobaidi et al. (2022) may further explain variations in non-smoker spirometry [14, 23]. The strong discriminatory capacity of CO, elevated in 81.6% of smokers and absent in non-smokers, supports its role as a robust biomarker of recent tobacco exposure, as established in earlier studies [25, 26].

The Brinkman Index demonstrated a clear dose–response gradient: increasing smoking levels were associated with longer smoking duration, higher daily cigarette consumption, lower FEV_1/FVC and $FEF_{25–75}$ values, and rising CO levels. This gradient is consistent with national epidemiology, PDPI 2024 recommendations, and global descriptions of cumulative tobacco burden [1, 20]. The progressive decline in FEV_1/FVC across smoking categories mirrors ATS/ERS-defined airflow obstruction and emerging evidence that gradual declines often precede diagnostic thresholds [23]. Similarly, reductions in $FEF_{25–75}$ reflect early small-airway disease, a well-documented precursor to COPD [28, 29]. The steep rise in CO (6.1 to 15.3 ppm) across severity groups parallels international findings and reflects increased oxidative stress, impaired mucociliary clearance, and epithelial–mesenchymal transition associated with chronic smoke exposure [21, 30]. These mechanisms align with GOLD's conceptualization of persistent inflammation as the driver of progressive airflow limitation [31, 32].

Correlation analyses demonstrated a moderate positive association between FEV_1/FVC and FEF_{25-75} (ρ=0.612), reflecting their shared mechanical underpinnings in global and peripheral airway resistance [22, 29]. Evidence indicates that $FEF_{25–75}$ declines earlier due to the vulnerability of terminal bronchioles to inflammatory and oxidative damage [28, 29]. Negative correlations between exhaled CO and both FEV_1/FVC and $FEF_{25–75}$, particularly at higher CO levels, underscore the deleterious impact of tobacco exposure on central and peripheral airway function, consistent with GOLD 2017 and mechanisms involving carboxyhemoglobin-induced hypoxia, ROS accumulation, and airway remodeling [21, 30]. These findings are supported by Sukmawati & Amin (2016) and by population studies demonstrating linear CO increases with smoking intensity [25, 26].

Regression analysis further confirmed the linear effect of CO on ventilatory decline, with each 1-ppm CO increment associated with a 2.13% reduction in FEV_1/FVC and a 2.88% reduction in $FEF_{25–75}$, reinforcing earlier findings [13, 32]. Similar associations were reported by Dutt S et al. (2021) and Anand et al. (2014), who consistently documented lower spirometric values among smokers with elevated CO [33, 34]. These findings further support CO as a quantitative marker of tobacco exposure and a useful adjunct to spirometry for

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early detection and cessation monitoring, as emphasized in PDPI 2024 [35].

Overall, the results provide consistent evidence linking smoking exposure with early declines in both central and peripheral airway function. The combined use of FEV_1/FVC, $FEF_{25–75}$, and exhaled CO enhances early detection of smoke-induced impairment and supports the integration of these indices in smoking-cessation programs and routine screening, particularly among productive-age adults at high risk of cumulative exposure.

5. Limitation

This study has several limitations that should be considered when interpreting the findings. First, the use of a cross-sectional design limits the ability to establish causal relationships between smoking exposure, spirometric parameters, and CO levels; the results only reflect associations at a single point in time. Second, the study population consisted exclusively of hospital security officers, which may reduce generalizability to broader or more diverse populations with different occupational exposures or lifestyle patterns. Third, smoking status and history relied partly on self-reported data, which may introduce recall bias or underreporting, particularly regarding cigarette consumption and duration of smoking. Fourth, lung function was assessed using single-time spirometry measurements, which may be influenced by participant effort or short-term physiological variations. Additionally, the study did not account for potential environmental confounders, such as passive smoking, air pollution, or recent respiratory infections, which may affect FEV_1/FVC and $FEF_{25–75}$% values. Finally, carbon monoxide levels primarily reflect recent smoking behavior rather than long-term exposure, thereby limiting their ability to fully represent cumulative tobacco burden. Despite these limitations, the study provides important insights into early pulmonary function changes associated with smoking.

6. Conclusion

This study demonstrates that eCO is significantly associated with impaired pulmonary function among active smokers. Elevated CO levels show a strong negative correlation with both FEV_1/FVC and $FEF_{25–75}$, indicating that increased tobacco exposure directly contributes to declining ventilatory capacity in both central and peripheral airways. The earlier decline of $FEF_{25–75}$ compared with FEV_1/FVC supports the concept that small-airway dysfunction represents the initial phase of smoking-induced ventilatory impairment. The positive association between FEV_1/FVC and $FEF_{25–75}$ across all smoking categories further illustrates the progressive continuum from peripheral obstruction toward global airflow limitation. The dose–response pattern observed across Brinkman Index categories reinforces the cumulative impact of smoking on lung function and CO accumulation. Overall, eCO serves as a practical and non-invasive biomarker that correlates strongly with spirometric decline, making it a valuable tool for early detection of smoking-related ventilatory impairment and for monitoring smoking-cessation programs.

7. Declarations

Conflict of Interest

The authors declare no conflict of interest related to the conduct, analysis, or reporting of this study.

Author's Contributions

MB and SN conceptualized the study and developed its overall design. HI and MI established the methodology and conducted the data analysis. ID, BN, and MI supported data validation and interpretation. MB and SN performed the investigation, while EA and ID provided key resources and supervision. Data curation and management were completed by HI and MI. MB drafted the initial manuscript, with SN and BN providing critical revisions and editing. MB also prepared the visualization, and SN oversaw project administration. All authors reviewed and approved the final manuscript.

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Abbreviations

FEV_1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; $FEF_{25–75}$%: Forced Expiratory

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Flow 25–75%; eCO: exhaled Carbon Monoxide; CO: Carbon Monoxide; COPD: Chronic Obstructive Pulmonary Disease.

References

[1] Effendi DE, Ardani I, Handayani S, Agustiya RI, Nugroho AP, Oktriyanto O, Paramita A, Febriyanty D, Novita R, Yulianto A. Factors associated with quitting smoking among males: Findings from Indonesian national health survey. Clinical Epidemiology and Global Health. 2024 [accessed 2025 Nov 5];28:101672. https://www.sciencedirect.com/science/article/pii/S2213398424001684. doi:10.1016/J.CEGH.2024.101672

[2] Taufik FF. The unseen struggle to curb the country's smoking addiction - Academia - The Jakarta Post. The Jakarta Post. 2024 Sep 26 [accessed 2025 Nov 5]. https://www.thejakartapost.com/opinion/2024/09/26/the-unseen-struggle-to-curb-the-countrys-smoking-addiction.html

[3] Rachmani E, Handayani S, Saptorini KK, Nurjanah, Kusuma D, Ahsan A, Kusuma EJ, Atique S, Jumanto J. Why do youths initiate to smoke? A data mining analysis on tobacco advertising, peer, and family factors for Indonesian youths. Computer Methods and Programs in Biomedicine Update. 2024 [accessed 2025 Nov 5];6:100168. https://www.sciencedirect.com/science/article/pii/S2666990024000351. doi:10.1016/J.CMPBUP.2024.100168

[4] Megatsari H, Astutik E, Gandeswari K, Sebayang SK, Nadhiroh SR, Martini S. Tobacco advertising, promotion, sponsorship and youth smoking behavior: The Indonesian 2019 Global Youth Tobacco Survey (GYTS). Tobacco Induced Diseases. 2023 [accessed 2025 Nov 5];21(December):163. https://pmc.ncbi.nlm.nih.gov/articles/PMC10714413/. doi:10.18332/TID/174644

[5] Lucia SS, Yetiani N, Suwarni L, Rusmitasari H, Maretalinia M, Suyitno S. The determinants of adolescent smokers in Indonesia. International Journal of Public Health Science. 2022 [accessed 2025 Nov 5];11(3):808–814. doi:10.11591/IJPHS.V11I3.21510

[6] Suyitno S, Cahyati WH. Type of Occupation and Smoking Behavior: A Multinomial Analysis of Global Adults Tobacco Survey (GATS) Indonesia. JURNAL INFO KESEHATAN. 2025 [accessed 2025 Nov 5];23(2):301–308. doi:10.31965/INFOKES.VOL23.ISS2.1984

[7] Gao H, Song Y, Liu K, Lu X, Shen J, Wei S, Jiang H, Xu N. The Impact of Different Smoking Behavior on Pulmonary Function and Pulmonary Hypertension Among Chinese Male Patients with Chronic Obstructive Pulmonary Disease. International Journal of Chronic Obstructive Pulmonary Disease. 2024 [accessed 2025 Nov 5];19:1315. https://pmc.ncbi.nlm.nih.gov/articles/PMC11185172/. doi:10.2147/COPD.S455323

[8] Liu W, Gong T, Chen S, Liu Y. Spirometry. Molecular Medical Microbiology, Third Edition. 2023 Aug 17 [accessed 2025 Nov 5]:3181–3189. https://www.ncbi.nlm.nih.gov/books/NBK560526/. doi:10.1016/B978-0-12-818619-0.00020-4

[9] Yoshida A, Kai C, Futamura H, Oochi K, Kondo S, Sato I, Kasai S. Spirometry test values can be estimated from a single chest radiograph. Frontiers in Medicine. 2024 [accessed 2025 Nov 5];11:1335958. https://pmc.ncbi.nlm.nih.gov/articles/PMC10953498/. doi:10.3389/FMED.2024.1335958

[10] Katare S, Kanagalla MB, Harsha A, Jayaprakash G, BS R, Koshy L, Roy R, Thomas S, A SZ. Comparative Analysis of Non-Diabetic and Diabetes-Associated Pulmonary Function Impairment in Treated Pulmonary Tuberculosis Patients Using Spirometry. European Journal of Cardiovascular Medicine. 2025 [accessed 2025 Nov 5];15:455–461. https://healthcare-bulletin.co.uk/article/comparative-analysis-of-non-diabetic-and-diabetes-associated-pulmonary-function-impairment-in-treated-pulmonary-tuberculosis-patients-using-spirometry-4210/. doi:10.61336/EJCM/25-09-74

[11] David S, Goldin J, Edwards CW. Forced Expiratory Volume. Definitions. 2024 Oct 14 [accessed 2025 Nov 5]. https://www.ncbi.nlm.nih.gov/books/NBK540970/. doi:10.32388/i7tpmz

[12] Raz-Maman C, Borochov-Greenberg N, Lefkowitz RY, Portnov BA. Ambient exposure to nitrogen dioxide and lung function: a multi-metric approach. Environmental Monitoring and Assessment 2025 197:4. 2025 [accessed 2025 Nov 5];197(4):1–13. https://link.springer.com/article/10.1007/s10661-025-13871-4. doi:10.1007/S10661-025-13871-4

[13] Kwon DS, Choi YJ, Kim TH, Byun MK, Cho JH, Kim HJ, Park HJ. FEF25-75% Values in Patients with Normal Lung Function Can Predict the Development of Chronic Obstructive Pulmonary Disease. International Journal of Chronic Obstructive Pulmonary Disease. 2020 [accessed 2025 Nov 5];15:2913. https://pmc.ncbi.nlm.nih.gov/articles/PMC7669499/. doi:10.2147/COPD.S261732

[14] Alobaidi NY, Almeshari M, Stockley J, Stockley RA, Sapey E. Small airway function measured using forced expiratory flow between 25% and 75% of vital capacity and its relationship to airflow limitation in symptomatic ever-smokers: a cross-sectional study. BMJ open respiratory research. 2022 [accessed 2025 Nov 5];9(1). https://pubmed.ncbi.nlm.nih.gov/36202407/. doi:10.1136/BMJRESP-2022-001385

[15] Khan DrZH, Sumaiya DrJ, Nath DrMC, Nath DrMC, Rupa DrSN, Jolly DrSS. Evaluation of Lung Function Test (FEV1, FVC, FEV1/FVC ratio, PEFR) among Smokers and Nonsmokers. Scholars Journal of Applied Medical Sciences. 2022 [accessed 2025 Nov 5];10(6):1006–1011. https://www.researchgate.net/publication/361629449_Evaluation_of_Lung_Function_Test_FEV1_FVC_FEV1FVC_ratio_PEFR_among_Smokers_and_Nonsmokers. doi:10.36347/SJAMS.2022.V10I06.022

[16] Inoue-Choi M, Liao LM, Reyes-Guzman C, Hartge P, Caporaso N, Freedman ND. Association of Long-term, Low-Intensity Smoking With All-Cause and Cause-Specific Mortality in the National Institutes of Health–AARP Diet and Health Study. JAMA internal medicine. 2017 [accessed 2025 Nov 5];177(1):87. https://pmc.ncbi.nlm.nih.gov/articles/PMC5555224/. doi:10.1001/JAMAINTERNMED.2016.7511

[17] Tang L, Wu F, Zhang S, Ou J, Liang J, Peng R, Liao S, Zhou Q, Chen Y, Guo X, et al. Association between FEV1/FVC levels and all-cause mortality in the general population. BMC Pulmonary Medicine. 2025 [accessed 2025 Nov 5];25(1):108. https://pmc.ncbi.nlm.nih.gov/articles/PMC11895258/. doi:10.1186/S12890-025-03573-5

[18] Arpa M, Şen B, Kazancıoğlu L, Kılıç H. Assessment of smoking exposure by urine cotinine levels in severe COVID-19 patients: a case-control study. Scientific Reports. 2025 [accessed 2025 Nov 5];15(1):31696. https://pmc.ncbi.nlm.nih.gov/articles/PMC12394487/. doi:10.1038/S41598-025-17768-7

[19] WHO. More than 100 reasons to quit tobacco - PAHO/WHO | Pan American Health Organization. 2024 [accessed 2025 Nov 5]. https://www.paho.org/en/more-100-reasons-quit-tobacco

[20] Dai X, Gakidou E, Lopez AD. Evolution of the global smoking epidemic over the past half century: strengthening the evidence base for policy action. Tobacco control. 2022 [accessed 2025 Nov 5];31(2):129–137. https://pubmed.ncbi.nlm.nih.gov/35241576/. doi:10.1136/TOBACCOCONTROL-2021-056535

[21] Cha SR, Jang J, Park SM, Ryu SM, Cho SJ, Yang SR. Cigarette Smoke-Induced Respiratory Response: Insights into Cellular Processes and Biomarkers. Antioxidants (Basel, Switzerland). 2023 [accessed 2025 Nov 5];12(6). https://pubmed.ncbi.nlm.nih.gov/37371940/. doi:10.3390/ANTIOX12061210

[22] Graham BL, Steenbruggen I, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, Kaminsky DA, McCarthy K, McCormack MC, Miller MR, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. American journal of respiratory and critical care medicine. 2019 [accessed 2025 Nov 5];200(8):E70–E88. https://www.atsjournals.org/doi/pdf/10.1164/rccm.201908-1590ST?download=true. doi:10.1164/RCCM.201908-1590ST

[23] Oh DK, Baek S, Lee SW, Lee JS, Lee S Do, Oh YM. Comparison of the fixed ratio and the Z-score of FEV1/FVC in the elderly population: a long-term mortality analysis from the Third National Health and Nutritional Examination Survey. International journal of chronic obstructive pulmonary disease. 2018 [accessed 2025 Nov 5];13:903–915. https://pubmed.ncbi.nlm.nih.gov/29559774/. doi:10.2147/COPD.S148421

[24] Kwon DS, Choi YJ, Kim TH, Byun MK, Cho JH, Kim HJ, Park HJ. FEF25-75% Values in Patients with Normal Lung Function Can Predict the Development of Chronic Obstructive Pulmonary Disease. International journal of chronic obstructive pulmonary disease. 2020 [accessed 2025 Nov 5];15:2913–2921.

https://pubmed.ncbi.nlm.nih.gov/33209020/. doi:10.2147/COPD.S261732

[25] Omoyemwen Osakue N, Okonkwo CW, Onah EC, Onyenekwe CC, Osakue NE, Njoku CM, Ehiaghe FA, Obi CU, Ihim AC, Onyenekwe AJ. Evaluation of Blood Levels of Carbon Monoxide in Smokers in Nnewi Metropolis. International Journal of Research and Innovation in Applied Science. 2024 [accessed 2025 Nov 5];IX(VII):706–710. doi:10.51584/IJRIAS.2024.907059

[26] Herath P, Wimalasekera SW, Amarasekara TD, Fernando MS, Turale S. Adverse effects of cigarette smoking on exhaled breath carbon monoxide, blood carboxyhemoglobin, and hematological parameters amongst Sri Lankan adult tobacco smokers: A descriptive study. Population Medicine. 2021 [accessed 2025 Nov 5];3. doi:10.18332/POPMED/143076

[27] Adatia A, Wahab M, Shahid I, Moinuddin A, Killian KJ, Satia I. Effects of cigarette smoke exposure on pulmonary physiology, muscle strength and exercise capacity in a retrospective cohort with 30,000 subjects. PloS one. 2021 [accessed 2025 Nov 5];16(6). https://pubmed.ncbi.nlm.nih.gov/34166381/. doi:10.1371/JOURNAL.PONE.0250957

[28] Almeshari MA;, Alobaidi, Nowaf Y;, Sapey E;, Stockley RA;, Stockley JA. Small airways dysfunction. 2023 [accessed 2025 Nov 5]. https://doi.org/10.1016/j.heliyon.2023.e20744. doi:10.1016/j.heliyon.2023.e20744

[29] Amin M. Pemeriksaan Saluran Napas Kecil. Dalam Buku Ajar Pulmonologi dan Kedokteran Respirasi Jilid I. Jakarta: UI Publishing; 2023.

[30] Su X, Wu W, Zhu Z, Lin X, Zeng Y. The effects of epithelial-mesenchymal transitions in COPD induced by cigarette smoke: an update. Respiratory research. 2022 [accessed 2025 Nov 5];23(1). https://pubmed.ncbi.nlm.nih.gov/36045410/. doi:10.1186/S12931-022-02153-Z

[31] Akwe J, Fair N, Fongeh T. Overview of epidemiology, pathophysiology, diagnosis and staging with 2020 Updates. Medical Research Archives. 2020 [accessed 2025 Nov 5];8(2). https://esmed.org/MRA/mra/article/view/2046. doi:10.18103/MRA.V8I2.2046

[32] Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, Chen R, Decramer M, Fabbri LM, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report. GOLD Executive Summary. American journal of respiratory and critical care medicine. 2017 [accessed 2025 Nov 5];195(5):557–582. https://pubmed.ncbi.nlm.nih.gov/28128970/. doi:10.1164/RCCM.201701-0218PP

[33] Dutt S, Gogia T, Gupta M. A comparative study on pulmonary function tests in smokers & nonsmokers. Indian Journal of Clinical Anatomy and Physiology. 2021 [accessed 2025 Nov 5];8(1):53–56. doi:10.18231/J.IJCAP.2021.012

[34] Mistry A, Tyagi R, Kagathara J, Dholakiya U, Shah Chirag. Comparative Study of Pulmonary Function Tests in Smokers and Non-Smokers. GCSMC J Med Sci. 2014;3(1):22–7.

[35] Fitriani F, Harlivasari AD, Susanto AD. Pedoman Diagnosis dan Penatalaksanaan Berhenti Merokok di Indonesia. 1st ed. Jakarta: Perhimpunan Dokter Paru Indonesia (PDPI); 2024.