

Original Research

Received 16 June 2026

Revised 25 July 2026

Accepted 08 Aug 2026

Natural Resources for Human Health 2026, Vol. 6 (16s): 640–650

KEYWORDS:

Pneumonia, Smoking, Carbon Monoxide, Spirometry, Respiratory Function Tests, Severity of Illness Index

Cumulative Versus Recent Smoking Exposure and Community-Acquired Pneumonia Severity: A Cross-Sectional Study

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ABSTRACT: Cigarette smoking may influence the severity of community-acquired pneumonia (CAP), but the relative contributions of cumulative smoking exposure, recent exposure, and pulmonary function remain unclear. This study examined associations of pack-years, exhaled carbon monoxide (eCO), and spirometric parameters with CAP severity. This analytical cross-sectional study included 57 adults hospitalised with CAP in Makassar, Indonesia, from June to July 2026. Smoking exposure, eCO category, spirometry, and Pneumonia Severity Index (PSI) were assessed. Associations with PSI score and ordinal CAP severity were evaluated using Spearman correlation and proportional-odds ordinal logistic regression. Thirty-nine participants were active smokers and 18 had passive smoke exposure. Among active smokers, pack-years correlated positively with PSI score ($\rho=0.405$, $p=0.010$) and ordinal CAP severity ($\rho=0.398$, $p=0.012$). After adjustment for FEV₁, body mass index, and occupational dust/smoke exposure, each 5-pack-year increase was associated with higher CAP severity (adjusted odds ratio [aOR] 1.32, 95% CI 1.05–1.67; $p=0.017$). eCO distribution differed significantly between active and passive exposure groups ($p<0.001$), but eCO was not independently associated with CAP severity (aOR 2.30, 95% CI 0.89–5.94; $p=0.086$). Most spirometric parameters were not associated with severity. Cumulative smoking burden showed the most consistent association with CAP severity, whereas recent eCO exposure and acute spirometric measurements were less informative.

1. INTRODUCTION

Community-acquired pneumonia (CAP) remains a common and clinically important cause of acute respiratory morbidity, hospitalisation, and death in adults. Disease severity and clinical outcomes are influenced by both infection-related factors and host characteristics, including age, underlying lung disease, immune status, and smoking history [1,2]. Early risk stratification is therefore central to clinical management. The Pneumonia Severity Index (PSI) and CURB-65 are established prognostic tools, with PSI providing mortality-risk stratification and supporting decisions regarding treatment setting [3].

Cigarette smoking is a potentially modifiable host factor associated with respiratory infection. Tobacco smoke disrupts airway epithelial integrity, impairs mucociliary clearance, and alters innate and adaptive immune responses, thereby weakening pulmonary host defence [4,5]. Large population-based data further demonstrate dose-response associations between increasing pack-years and the risks of pneumonia, intensive-care admission, and pneumonia-related mortality [6].

Smoking exposure, however, can be characterised in different ways. Pack-years reflect cumulative exposure, whereas exhaled carbon monoxide (eCO) is more sensitive to recent combustion exposure and may vary according to time since smoking and

other environmental CO sources [7]. Higher eCO has also been associated with smoking intensity and nicotine dependence [8,9].

Spirometry provides complementary physiological information, although suspected restriction based on reduced FVC with preserved FEV₁/FVC requires confirmation by lung-volume measurement [10]. Notably, eCO may correlate with cumulative smoking indices without corresponding directly to pulmonary-function impairment [11]. This study therefore examined the associations of pack-years, eCO category, and spirometric parameters with PSI score and ordinal CAP severity among adults hospitalised with CAP in Makassar, Indonesia.

2. MATERIALS AND METHODS

2.1 Study design and setting

This analytical cross-sectional study was conducted at Dr. Wahidin Sudirohusodo General Hospital and affiliated hospitals in Makassar, Indonesia, from June to July 2026. Patients with community-acquired pneumonia (CAP) who fulfilled the eligibility criteria were recruited consecutively during the study period.

2.2 Study participants

Patients were eligible if they were aged ≥ 18 years, had CAP diagnosed on the basis of clinical and radiological findings, had a history of active smoking or passive cigarette-smoke exposure, and provided written informed consent. Patients with hospital-acquired pneumonia or ventilator-associated pneumonia, severe chest pain or other conditions precluding spirometry, or incomplete clinical or examination data were excluded.

Participants were classified as having active or passive cigarette-smoke exposure according to their smoking and exposure history. Among active smokers, smoking duration and the average number of cigarettes smoked per day were recorded. Cumulative cigarette exposure was expressed in pack-years and calculated as:

$$\text{Pack – years} = \frac{(\text{cigarettes smoked per day} \times \text{years of smoking})}{20}$$

Pack-years were calculated only among active smokers and analysed as a continuous measure of cumulative smoking exposure [12].

2.3 Exhaled carbon monoxide assessment

Exhaled carbon monoxide (eCO) was assessed as an objective indicator of recent cigarette-smoke exposure. eCO values were classified into four ordinal categories: 0–6 ppm, 7–10 ppm, 11–20 ppm, and >20 ppm, corresponding to minimal/non-smoking exposure, light exposure, moderate exposure, and heavy exposure, respectively [13]. For statistical analyses, eCO was treated as an ordinal variable, with categories ordered from minimal to heavy exposure.

2.4 Pulmonary function assessment

Pulmonary function was assessed using spirometry. The parameters analysed were forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), the FEV₁/FVC ratio, and forced expiratory flow between 25% and 75% of FVC (FEF_{25–75}). FEV₁, FVC, and FEF_{25–75} were expressed as percentages of predicted values. FEV₁ and FVC values $\geq 80\%$ predicted, an FEV₁/FVC ratio $\geq 70\%$, and FEF_{25–75} $\geq 65\%$ predicted were considered within the normal range.

Spirometric patterns were classified on the basis of FVC and the FEV₁/FVC ratio. A reduced FVC with a preserved FEV₁/FVC ratio was classified as a suspected restrictive pattern, whereas concomitant reductions in FVC and FEV₁/FVC were classified as a mixed pattern [10,14].

2.5 Assessment of CAP severity

CAP severity was assessed using the Pneumonia Severity Index (PSI). PSI was analysed both as a continuous score and as an ordinal measure of CAP severity. Participants were classified as having mild CAP for PSI classes I–III (score ≤ 90), moderate CAP for class IV (score 91–130), and severe CAP for class V (score >130) [3,15]. For ordinal analyses, CAP severity was ordered as mild $<$ moderate $<$ severe.

2.6 Covariates

Demographic and clinical variables included age, sex, body mass index (BMI), educational level, comorbidity burden, occupational exposure to dust or smoke, white blood cell count, and radiological involvement. BMI was calculated as body weight in kilograms divided by height in metres squared. Comorbidity burden was categorised according to the number of documented comorbid conditions. Occupational dust or smoke exposure was recorded as a binary variable.

2.7 Sample size

The minimum sample size was calculated for a two-sided test of correlation using Fisher's z transformation. An expected correlation coefficient of $r=0.40$ was used for sample-size estimation [16–18]. With a two-sided α of 0.05 and 80% statistical power, a minimum of 47 participants was required. After allowing for 10% incomplete data, the minimum required sample size was increased to 53 participants. The final analysis included 57 participants.

2.8 Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 30.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed variables are presented as mean $\pm$ standard deviation, whereas non-normally distributed variables are presented as median with the first and third quartiles [median (Q1–Q3)]. Categorical variables are presented as frequency and percentage.

Differences in eCO category between active and passive smoke-exposure groups were examined using the Fisher–Freeman–Halton exact test. Spirometric-pattern distributions were compared using Fisher's exact test. Continuous spirometric parameters were compared between active and passive exposure groups using independent-samples t-tests, with Welch's t-test applied when appropriate.

Among active smokers, associations of cumulative smoking exposure, eCO category, and pulmonary-function parameters with PSI score and ordinal CAP severity were examined using Spearman's rank correlation coefficient.

Multivariable proportional-odds ordinal logistic regression was used to examine factors associated with increasing CAP severity among active smokers. Two models were constructed to distinguish cumulative from recent smoking exposure. Model 1, representing cumulative exposure, included pack-years, FEV₁, BMI, and occupational dust/smoke exposure. Model 2, representing recent exposure, included eCO category, FEV₁, BMI, and occupational dust/smoke exposure. Pack-years were scaled per 5-pack-year increase and FEV₁ per 10-percentage-point increase in predicted value.

Regression results are presented as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). The proportional-odds assumption was evaluated using the test of parallel lines, model convergence was examined, and overall model fit was assessed using likelihood-ratio and goodness-of-fit statistics. All statistical tests were two-sided, and $p<0.05$ was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Baseline characteristics of the study population

A total of 57 patients with community-acquired pneumonia were included. The median age was 58 years (Q1–Q3, 49–65), and 70.2% were male. Median BMI was 21.09 kg/m² (19.57–23.44), while the median WBC count was $11.79 \times 10^3/\mu\text{L}$ (9.88–15.90). Active smokers accounted for 68.4% of the study population, and 31.6% had occupational exposure to dust or smoke. Bilateral pneumonia was the predominant radiologic finding (66.7%). The mean PSI score was 91.11 ± 23.98 , with CAP severity classified as mild in 49.1%, moderate in 43.9%, and severe in 7.0% of patients (Table 1).

Table 1. Baseline characteristics of the study population

Variable	Overall (n=57)
Age, years	58 (49–65)
Sex	
Male	40 (70.2)
Female	17 (29.8)

BMI, kg/m²	21.09 (19.57–23.44)
Education	
Primary school	14 (24.6)
Junior high school	21 (36.8)
Senior high school	7 (12.3)
University	15 (26.3)
Occupational dust/smoke exposure	
No	39 (68.4)
Yes	18 (31.6)
Comorbidity burden	
None	19 (33.3)
One comorbidity	21 (36.8)
Two comorbidities	16 (28.1)
≥3 comorbidities	1 (1.8)
WBC, ×10³/μL	11.79 (9.88–15.90)
Radiologic involvement	
Unilateral pneumonia	17 (29.8)
Bilateral pneumonia	38 (66.7)
Nonspecific location	2 (3.5)
Smoking exposure status	
Active smoking	39 (68.4)
Passive smoke exposure	18 (31.6)
PSI score	91.11 ± 23.98
CAP severity	
Mild	28 (49.1)
Moderate	25 (43.9)
Severe	4 (7.0)

Notes: Values are presented as mean ± SD, median (Q1–Q3), or n (%), according to variable type and distribution. Abbreviations: BMI, body mass index; WBC, white blood cell count; PSI, Pneumonia Severity Index; CAP, community-acquired pneumonia.

3.2 Smoking exposure, exhaled carbon monoxide, and pulmonary function

Among active smokers, the median smoking duration was 30.0 years (Q1–Q3, 12.5–40.0), with a median consumption of 12.0 cigarettes/day (6.0–16.0) and cumulative exposure of 18.0 pack-years (4.75–30.0). eCO distribution differed significantly between active smokers and participants with passive smoke exposure ($p < 0.001$), with moderate-to-heavy eCO levels occurring predominantly among active smokers. Pulmonary function parameters did not differ significantly between exposure groups, and suspected restrictive spirometric pattern was the predominant pattern in both groups (Table 2).

Table 2. Smoking exposure, exhaled carbon monoxide, and pulmonary function according to smoking exposure status

Variable	Overall (n=57)	Active smokers (n=39)	Passive exposure (n=18)	p value
Smoking duration, years	—	30.0 (12.5–40.0)	—	—
Cigarettes/day	—	12.0 (6.0–16.0)	—	—
Pack-years	—	18.0 (4.75–30.0)	—	—
eCO category				<0.001^{a*}
Minimal, 0–6 ppm	4 (7.0)	0 (0.0)	4 (22.2)	

Mild, 7–10 ppm	26 (45.6)	13 (33.3)	13 (72.2)	
Moderate, 11–20 ppm	20 (35.1)	19 (48.7)	1 (5.6)	
Heavy, >20 ppm	7 (12.3)	7 (17.9)	0 (0.0)	
FEV1, % predicted	57.43 ± 16.49	58.74 ± 15.28	54.59 ± 19.02	0.383 ^b
FVC, % predicted	52.10 ± 14.65	52.53 ± 12.85	51.17 ± 18.34	0.779 ^c
FEV1/FVC, %	85.05 ± 9.58	84.57 ± 9.92	86.10 ± 8.99	0.580 ^b
FEF25–75, % predicted	59.26 ± 19.82	56.91 ± 18.75	64.35 ± 21.65	0.190 ^b
Spirometric pattern				0.646^d
Suspected restrictive	52 (91.2)	36 (92.3)	16 (88.9)	
Mixed	5 (8.8)	3 (7.7)	2 (11.1)	

Notes: Values are presented as mean ± SD, median (Q1–Q3), or n (%), according to variable type and distribution. Smoking duration, cigarette consumption, and pack-years apply only to active smokers. ^a Fisher–Freeman–Halton exact test. ^b Independent-samples t-test. ^c Welch’s t-test. ^d Fisher’s exact test. *p<0.05. Abbreviations: eCO, exhaled carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; FEF25–75, forced expiratory flow at 25–75% of FVC.

3.3 Association of smoking exposure and pulmonary function with pneumonia severity

Among active smokers (n=39), CAP severity was classified as mild in 17 patients (43.6%), moderate in 18 (46.2%), and severe in 4 (10.3%). Pack-years showed a significant positive correlation with both PSI score ($\rho=0.405$, $p=0.010$) and ordinal CAP severity ($\rho=0.398$, $p=0.012$). eCO category was not significantly correlated with either severity measure. Among pulmonary function parameters, FEV1/FVC was positively correlated with ordinal CAP severity ($\rho=0.347$, $p=0.031$), although its correlation with PSI score did not reach statistical significance. No significant associations were observed for FEV1, FVC, or FEF25–75 (Table 3).

Table 3. Association of cumulative smoking exposure, eCO, and pulmonary function with pneumonia severity among active smokers

Variable	PSI score, ρ	p value	CAP severity, ρ	p value
Pack-years	0.405	0.010*	0.398	0.012*
eCO category	0.223	0.173	0.285	0.079
FEV1, % predicted	0.191	0.245	0.100	0.543
FVC, % predicted	−0.011	0.947	−0.163	0.323
FEV1/FVC, %	0.305	0.059	0.347	0.031*
FEF25–75, % predicted	−0.082	0.621	−0.182	0.269

Notes: Analyses were restricted to active smokers (n=39). Correlations were assessed using Spearman’s rank correlation coefficient (ρ). CAP severity was coded ordinally as mild, moderate, and severe. *p<0.05. Abbreviations: PSI, Pneumonia Severity Index; CAP, community-acquired pneumonia; eCO, exhaled carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; FEF25–75, forced expiratory flow at 25–75% of FVC.

Cumulative smoking exposure was positively associated with pneumonia severity among active smokers. As shown in Figure 1, higher pack-year exposure tended to correspond with higher PSI scores, although substantial interindividual variability was observed. The association was moderate and statistically significant (Spearman’s $\rho=0.405$, $p=0.010$).

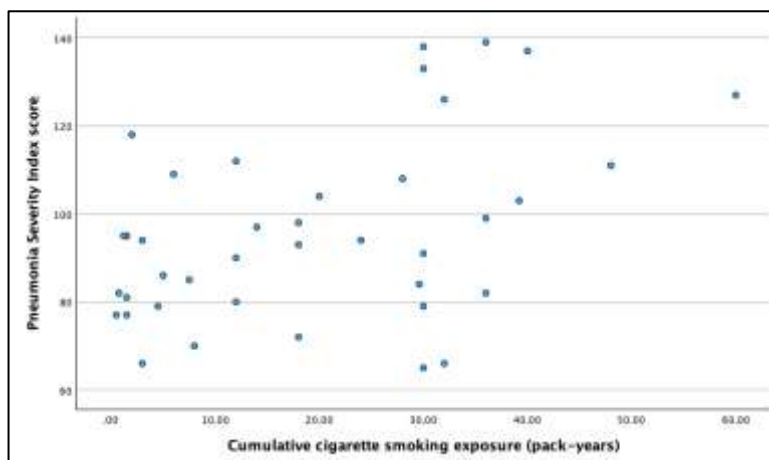


Figure 1. Association between cumulative smoking exposure and Pneumonia Severity Index (PSI) score among active smokers. Each point represents one participant. Cumulative smoking exposure was expressed in pack-years. Spearman's rank correlation showed a positive association between pack-years and PSI score ($\rho=0.405$, $p=0.010$).

3.4 Multivariable ordinal logistic regression for CAP severity

In the cumulative exposure model, the overall ordinal logistic regression was statistically significant (likelihood-ratio $\chi^2=9.870$, $p=0.043$), and the proportional-odds assumption was not violated (parallel-lines test $p=0.610$). After adjustment for FEV1, BMI, and occupational dust/smoke exposure, cumulative smoking exposure remained independently associated with greater CAP severity. Each 5-pack-year increase was associated with 1.32-fold higher odds of being in a more severe CAP category (aOR 1.32, 95% CI 1.05–1.67; $p=0.017$). FEV1, BMI, and occupational exposure were not independently associated with CAP severity.

In the recent-exposure model, eCO category was not independently associated with CAP severity (aOR 2.30, 95% CI 0.89–5.94; $p=0.086$), and the overall model was not statistically significant ($p=0.171$). Although the parallel-lines test was non-significant ($p=0.368$), interpretation of this diagnostic should be cautious because the general model did not achieve full convergence (Table 4).

Table 4. Multivariable ordinal logistic regression for CAP severity among active smokers

Variable	Adjusted OR	95% CI	p value
Model 1: cumulative smoking exposure			
Pack-years, per 5-pack-year increase	1.32	1.05–1.67	0.017*
FEV1, per 10%-predicted increase	1.04	0.68–1.61	0.845
BMI, per 1 kg/m ² increase	1.16	0.98–1.37	0.080
Occupational dust/smoke exposure	0.87	0.23–3.24	0.833
Model 2: recent exposure			
eCO, per category increase	2.30	0.89–5.94	0.086
FEV1, per 10%-predicted increase	1.04	0.68–1.59	0.855
BMI, per 1 kg/m ² increase	1.15	0.99–1.33	0.069
Occupational dust/smoke exposure	0.91	0.25–3.34	0.889

Notes: Ordinal logistic regression was performed among active smokers ($n=39$), with CAP severity ordered as mild < moderate < severe. Model 1 included cumulative smoking exposure, FEV1, BMI, and occupational dust/smoke exposure; model fit

$p=0.043$ and parallel-lines test $p=0.610$. Model 2 included eCO category, FEV₁, BMI, and occupational dust/smoke exposure; model fit $p=0.171$ and parallel-lines test $p=0.368$. The parallel-lines diagnostic for Model 2 should be interpreted cautiously because the general model did not fully converge. Adjusted ORs were obtained by exponentiating the regression coefficients. * $p<0.05$. Abbreviations: OR, odds ratio; CI, confidence interval; CAP, community-acquired pneumonia; eCO, exhaled carbon monoxide; FEV₁, forced expiratory volume in 1 second; BMI, body mass index.

The adjusted associations from the two ordinal logistic regression models are illustrated in Figure 2. In the cumulative exposure model, increasing pack-year exposure was the only predictor independently associated with higher CAP severity, with the confidence interval remaining above the null value. In contrast, eCO category in the current exposure model showed a larger point estimate but a wider confidence interval crossing 1.0, indicating substantial uncertainty and no statistically significant independent association.

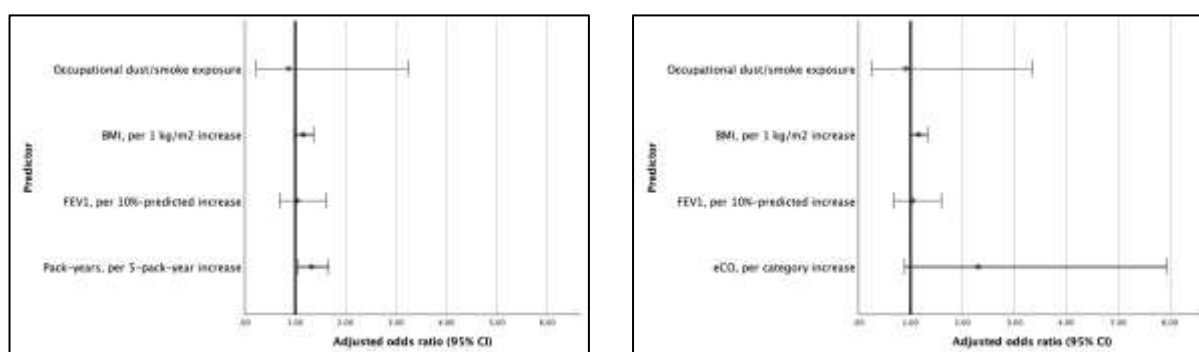


Figure 2. Forest plots of multivariable ordinal logistic regression models for increasing CAP severity among active smokers. (A) Cumulative-exposure model. (B) Recent-exposure model. Values are adjusted odds ratios with 95% confidence intervals. Pack-years were scaled per 5-pack-year increase and FEV₁ per 10-percentage-point increase in predicted value.

3.5 Discussion

The principal finding of this study was that cumulative cigarette exposure, expressed as pack-years, showed the most consistent association with CAP severity among active smokers. Pack-years correlated positively with both continuous PSI score ($\rho=0.405$, $p=0.010$) and ordinal CAP severity ($\rho=0.398$, $p=0.012$). This association persisted after adjustment for FEV₁, BMI, and occupational dust or smoke exposure. Clinically, the aOR of 1.32 indicates that, among active smokers with otherwise similar values for these covariates, each additional 5 pack-years was associated with 32% higher odds of being in a higher CAP-severity category (95% CI 1.05–1.67). Importantly, the pack-year analyses were restricted to active smokers, whereas participants with passive smoke exposure contributed to the between-group comparisons of eCO and pulmonary function. The association between cumulative smoking exposure and CAP severity therefore pertains specifically to active smokers. This finding is consistent with population-based evidence demonstrating dose-response relationships between increasing pack-years and the risks of pneumonia, ICU admission, and pneumonia-related mortality [6]. In an Indonesian hospital population, Karisma et al. (2023) similarly found an association between smoking status and PSI-based CAP severity, although smoking degree itself was not significantly associated with severity [19]. The present findings therefore extend this evidence by identifying cumulative exposure as the more consistent smoking-related measure within active smokers.

The relationship with cumulative exposure is biologically plausible. Chronic cigarette-smoke exposure compromises airway epithelial integrity and mucociliary clearance, increases oxidative stress, and alters macrophage, neutrophil, and adaptive immune responses, potentially weakening pulmonary host defence against lower respiratory tract infection [4,5]. Among 1,501 patients hospitalised with CAP, Crisafulli et al. (2020) found higher systemic inflammatory responses in current smokers and an independently increased risk of pleural complications [20]. These observations provide a plausible context in which cumulative smoking exposure may reflect long-standing host vulnerability beyond that captured by a single contemporaneous exposure measure.

In contrast, eCO clearly differentiated active from passive smoke exposure in the present cohort but was not significantly associated with PSI score or ordinal CAP severity. In the adjusted current-exposure model, increasing eCO category produced an aOR of 2.30, but the 95% CI was wide (0.89–5.94) and crossed unity. eCO should therefore be interpreted differently from pack-years. Vinnikov et al. (2020) demonstrated that breath CO is strongly influenced by recent smoking behaviour [7], while Pan et al. (2021) estimated a mean eCO half-life of approximately 4.6 hours [21]. Associations between eCO and smoking intensity or nicotine dependence have also been reported by Güden et al. [8] and Raffael et al [9]. More recently, Binny et al. (2024) demonstrated substantially higher CO and carboxyhaemoglobin levels in smokers than nonsmokers [22], supporting its role as an exposure biomarker. Thus, eCO measured after hospital presentation may not represent the cumulative biological burden accrued over years of smoking.

Pulmonary-function measures showed a different pattern. FEV₁, FVC, and FEF_{25–75} were not significantly associated with CAP severity, whereas FEV₁/FVC showed a modest positive correlation with ordinal severity. This finding should not be interpreted as indicating that a higher FEV₁/FVC ratio causes or protects against severe pneumonia. A preserved or relatively high ratio may coexist with reduced FVC and a restrictive-appearing spirometric pattern. ERS/ATS standards emphasise that spirometry characterises physiological patterns and that true restriction requires confirmation by reduced total lung capacity [10]. Myrberg et al. (2022) likewise demonstrated imperfect correspondence between spirometric restrictive patterns and restriction confirmed by lung-volume measurements [14]. Because spirometry in the present study was performed during acute CAP, these measurements are best considered contemporaneous physiological findings rather than stable pre-infection pulmonary function. This interpretation is also compatible with Khairani et al. (2023), who found that eCO correlated strongly with cumulative smoking indices but neither eCO nor smoking degree was significantly correlated with pulmonary function [11].

BMI and occupational exposure were not independently associated with increasing CAP severity in either adjusted model. This does not necessarily indicate that these factors lack clinical relevance. In 7,449 hospitalised patients with CAP, Kim et al. (2021) demonstrated a non-linear relationship between BMI and mortality [23], while Viasus et al. (2022) summarised evidence linking undernutrition with adverse CAP outcomes and showing heterogeneous findings across overweight and obese populations [24]. Hammond et al. (2021) also identified underweight status among factors associated with acquisition of community respiratory infection [25]. For occupational exposure, Riccò et al. (2023) reported increased pneumococcal disease risk specifically among workers exposed to welding and metal fumes [26]. However, those findings cannot be directly extrapolated to the broader binary dust/smoke occupational category used in the present study.

The use of PSI as both a continuous score and an ordered severity outcome provided complementary representations of CAP severity. PSI and CURB-65 remain established prognostic frameworks [3,15]. More recent prospective evidence showed that PSI had the highest discrimination for 30-day mortality, whereas IDSA/ATS minor criteria performed better for predicting respiratory ICU admission [27]. Clinical deterioration remains multifactorial; Xu et al. (2024), for example, identified age, BMI, cardiovascular comorbidity, respiratory rate, and several laboratory markers as independent predictors of deterioration in initially non-severe CAP [28].

Several limitations should be considered. The cross-sectional design establishes association rather than causation. Adjusted analyses involved only 39 active smokers, including four patients with severe CAP, resulting in limited precision for some estimates. In addition, the current-exposure model generated an incomplete-convergence warning; its estimates, particularly for eCO, should therefore be regarded as exploratory. Nevertheless, the consistent relationships of pack-years with continuous PSI, ordinal CAP severity, and the adjusted model indicate that cumulative smoking burden was more consistently associated with CAP severity than either recent eCO category or spirometric parameters measured during the acute episode.

4. CONCLUSION

Among active smokers with community-acquired pneumonia, greater cumulative smoking exposure measured in pack-years was consistently associated with higher CAP severity, including after adjustment for FEV₁, BMI, and occupational dust or smoke exposure. In contrast, eCO and spirometric parameters showed no consistent associations with severity. These findings suggest that cumulative smoking burden may be more informative than recent eCO exposure or acute spirometric measurements, but require confirmation in larger prospective studies.

ACKNOWLEDGEMENTS

The authors would like to express their sincere gratitude to Dr. Wahidin Sudirohusodo General Hospital and affiliated hospitals in Makassar for their institutional support and assistance throughout this study. The authors also thank the clinical staff, laboratory personnel, and all participants whose cooperation made this research possible.

AUTHOR CONTRIBUTIONS

All authors approved the submitted manuscript and agreed to be accountable for their respective contributions.

Nurhikma: conceptualization, methodology, investigation, data curation, formal analysis, visualization, project administration, and preparation of the original manuscript draft.

Jamaluddin Madolangan: conceptualization, methodology, supervision, validation, interpretation of findings, and critical review and editing of the manuscript.

Nur Ahmad Tabri: methodology, validation, supervision, interpretation of findings, and critical review and editing of the manuscript.

Irawaty Djaharuddin: validation, clinical interpretation, and critical review and editing of the manuscript.

Erwin Arif: validation, interpretation of findings, and critical review and editing of the manuscript.

Bulkis Natsir: validation, clinical interpretation, and critical review and editing of the manuscript.

All authors critically reviewed the manuscript, approved the final version, and agreed to be accountable for the integrity and accuracy of the work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

This research received no external funding.

ETHICS STATEMENT

The study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Hasanuddin University, Makassar (approval no. 411/UN4.6.4.5.31/PP36/2026), with research permission from Dr. Wahidin Sudirohusodo General Hospital (no. 36DP.04.03/D.XVIII.2/11253/2026). Written informed consent was obtained from all participants before enrolment.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and institutional restrictions.

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