

## Original Research

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## Smoking Duration and Cessation in Relation to DLCO Among Patients with Stable COPD

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**ABSTRACT:** Smoking contributes to airway, parenchymal, and pulmonary vascular abnormalities in chronic obstructive pulmonary disease (COPD). Diffusing capacity of the lung for carbon monoxide (DLCO) provides complementary information on alveolar–capillary gas transfer beyond conventional spirometry. This cross-sectional study compared DLCO between current and former smokers with stable COPD and evaluated the relationships of smoking duration and smoking cessation duration with DLCO % predicted. Fifty patients with stable COPD were included, comprising 25 current smokers and 25 former smokers. Demographic characteristics, smoking history, hemoglobin concentration, spirometry, and DLCO were assessed. Absolute DLCO values were compared between groups using an independent-samples t-test, while Pearson correlation was used to assess relationships with DLCO % predicted. Mean absolute DLCO was significantly lower in current smokers than in former smokers ( $14.27 \pm 4.36$  vs  $16.78 \pm 4.09$  mL/min/mmHg;  $p=0.041$ ). Among current smokers, smoking duration showed a moderate negative correlation with DLCO % predicted ( $r=-0.445$ ;  $p=0.026$ ), whereas among former smokers, smoking cessation duration showed a strong positive correlation with DLCO % predicted ( $r=0.608$ ;  $p=0.001$ ). Former smokers with stable COPD had higher absolute DLCO than current smokers, while longer smoking duration and longer smoking cessation duration showed opposite associations with DLCO % predicted. These findings highlight the relationship between smoking history and pulmonary gas-transfer capacity in stable COPD.

## 1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a heterogeneous respiratory condition characterized by persistent respiratory symptoms and airflow obstruction resulting from abnormalities of the airways and/or alveoli.<sup>[1]</sup> Cigarette smoking remains a major risk factor for COPD and contributes to chronic airway inflammation, oxidative stress, parenchymal destruction, and pulmonary vascular injury. Although smoking cessation is a fundamental component of COPD management, structural and functional abnormalities may persist after cessation because of cumulative tobacco exposure.<sup>[2, 3]</sup> Consequently, pulmonary impairment in current and former smokers may extend beyond the degree of airflow obstruction detected by conventional spirometry.

The *diffusing capacity of the lung for carbon monoxide* (DLCO) provides complementary physiological information by assessing gas transfer across the alveolar–capillary interface.<sup>[4]</sup> In COPD, reduced DLCO may reflect emphysematous destruction, loss of effective alveolar surface area, and abnormalities of the pulmonary microvasculature. DLCO may therefore identify clinically relevant impairment that is not fully captured by forced expiratory volume in one second (FEV<sub>1</sub>). Smoking can also influence DLCO through both cumulative structural damage and ongoing exposure-related effects, including increased carboxyhemoglobin and alterations in pulmonary gas exchange.<sup>[4, 5]</sup>

Previous studies have demonstrated impaired DLCO among individuals with substantial smoking exposure, while current smokers may exhibit greater diffusion impairment than former smokers.<sup>[6]</sup> However, smoking history encompasses several dimensions, including smoking status, duration of exposure, cumulative exposure, and duration of smoking cessation.<sup>[7]</sup> The relationships between these characteristics and DLCO remain clinically relevant, particularly among patients with established stable COPD. Evaluating smoking duration among current smokers and cessation duration among former smokers may provide additional insight into the relationship between tobacco exposure history and alveolar–capillary gas transfer.<sup>[4, 8]</sup>

Therefore, this study aimed to compare DLCO between current and former smokers with stable COPD and to evaluate the relationship between smoking duration and DLCO among current smokers, as well as the relationship between smoking cessation duration and DLCO among former smokers. We hypothesized that former smokers would have higher DLCO than current smokers, that longer smoking duration would be associated with lower DLCO, and that longer smoking cessation duration would be associated with higher DLCO. These findings may provide further physiological evidence supporting the relevance of smoking history and smoking cessation in the assessment of patients with stable COPD.

## 2. MATERIALS AND METHODS

### 2.1 Study Design and Setting

This analytical observational study employed a cross-sectional design to evaluate the relationship between smoking history and diffusing capacity of the lung for carbon monoxide (DLCO) in patients with stable chronic obstructive pulmonary disease (COPD). The study was conducted at the Pulmonology Outpatient Clinic of Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia, a tertiary referral center with facilities for comprehensive pulmonary function testing, including DLCO measurement. Participants were recruited between April and August 2026.

### 2.2 Study Participants

Patients with stable COPD attending the pulmonology outpatient clinic were screened for eligibility. COPD was defined by a post-bronchodilator forced expiratory volume in one second to forced vital capacity ratio ( $FEV_1/FVC$ )  $<0.70$ . Stable COPD was defined as the absence of an acute exacerbation for at least four weeks before enrollment. Eligible participants were classified into two groups: current smokers and former smokers. Current smokers were defined as individuals who continued to smoke regularly at the time of enrollment and had a smoking exposure of at least 10 pack-years, whereas former smokers were defined as individuals who had stopped smoking for at least six months and had a smoking exposure of at least 10 pack-years.

A total of 50 participants who met the eligibility criteria were included, comprising 25 current smokers and 25 former smokers. Participants underwent assessment of demographic and clinical characteristics, smoking history, hemoglobin concentration, spirometry, and DLCO. Individuals with other pulmonary conditions that could substantially affect DLCO were excluded according to the predefined study criteria. Chest radiography was performed to identify relevant pulmonary abnormalities and support exclusion of other lung diseases.

### 2.3 Smoking Exposure and Smoking Status

Smoking history was obtained through direct interviews and included smoking status, smoking duration, average number of cigarettes smoked per day, cumulative smoking exposure, and smoking cessation duration. Participants were classified as current smokers if they continued to smoke regularly at the time of enrollment and had a cumulative smoking exposure of at least 10 pack-years. Former smokers were defined as participants who had ceased smoking for at least six months before enrollment and had a cumulative smoking exposure of at least 10 pack-years.

Cumulative smoking exposure was expressed in pack-years and calculated based on the average number of cigarettes smoked per day and smoking duration. Smoking duration was recorded in years for both groups, whereas smoking cessation duration was recorded in months for former smokers. These smoking-related variables were subsequently evaluated in relation to DLCO according to the predefined statistical analysis.

### 2.4 Pulmonary Function and DLCO Assessment

Pulmonary function was assessed using spirometry and measurement of diffusing capacity of the lung for carbon monoxide (DLCO). Spirometry was performed to obtain forced expiratory volume in one second ( $FEV_1$ ), forced vital capacity (FVC),

and the FEV<sub>1</sub>/FVC ratio. COPD was confirmed by a post-bronchodilator FEV<sub>1</sub>/FVC ratio <0.70, and FEV<sub>1</sub> was expressed as a percentage of the predicted value.

DLCO was measured using the single-breath technique with a Q-Box pulmonary function testing system (COSMED, Rome, Italy) operated through OMNIA software version 2.5. DLCO was recorded as an absolute value (mL/min/mmHg) and as a percentage of the predicted value. Hemoglobin concentration was measured on the same day as DLCO testing; DLCO values were not adjusted for hemoglobin concentration. Current smokers were instructed to abstain from smoking for at least 24 hours before DLCO measurement to minimize the acute influence of cigarette smoking and elevated carboxyhemoglobin.

## 2.5 Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics. Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed data were presented as mean  $\pm$  standard deviation (SD), whereas non-normally distributed data were presented as median with minimum and maximum values. Categorical variables were summarized as frequencies and percentages.

Baseline characteristics were compared between current and former smokers using the independent-samples t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. DLCO absolute values were compared between current and former smokers using the independent-samples t-test. Pearson correlation analysis was used to assess the relationship between smoking duration and DLCO % predicted among current smokers and between smoking cessation duration and DLCO % predicted among former smokers. Correlation coefficients ( $r$ ) were used to determine the direction and strength of the associations.

## 3. RESULTS AND DISCUSSION

### 3.1 Participant Characteristics

A total of 50 patients with stable COPD were included in the analysis, comprising 25 current smokers and 25 former smokers. Baseline characteristics included age, body mass index (BMI), smoking duration, number of cigarettes smoked per day, cumulative smoking exposure expressed as pack-years, hemoglobin concentration, and forced expiratory volume in one second (FEV<sub>1</sub>). Participant characteristics are summarized in Table 1.

**Table 1.** Baseline Characteristics of Current and Former Smokers With Stable COPD

| Variable                       | Current Smokers (n=25) | Former Smokers (n=25) | p-value |
|--------------------------------|------------------------|-----------------------|---------|
| Age, years                     | 57.00 $\pm$ 6.24       | 54.80 $\pm$ 5.24      | 0.184*  |
| BMI, kg/m <sup>2</sup>         | 21.27 $\pm$ 1.39       | 21.38 $\pm$ 1.37      | 0.783*  |
| Smoking duration, years        | 41.00 (29.00–50.00)    | 39.00 (28.00–49.00)   | 0.392** |
| Cigarettes, number/day         | 20.00 (12.00–24.00)    | 20.00 (12.00–24.00)   | 1.000** |
| Pack-years                     | 39.07 $\pm$ 12.10      | 37.61 $\pm$ 11.59     | 0.664*  |
| Hemoglobin, g/dL               | 14.22 $\pm$ 0.66       | 14.20 $\pm$ 0.57      | 0.927*  |
| FEV <sub>1</sub> , % predicted | 60.44 $\pm$ 19.27      | 61.44 $\pm$ 19.23     | 0.855*  |

Data are presented as mean  $\pm$  SD or median (minimum–maximum), as appropriate. \*Independent-samples t-test; \*\*Mann–Whitney U test. Abbreviations: BMI, body mass index; FEV<sub>1</sub>, forced expiratory volume in one second.

The two groups showed comparable baseline characteristics. No statistically significant differences were observed in age, BMI, smoking duration, cigarettes smoked per day, pack-years, hemoglobin concentration, or FEV<sub>1</sub> between current and former smokers (all  $p > 0.05$ ). These findings indicate no statistically significant baseline differences in the measured characteristics between the two groups.

## 3.2 DLCO in Current and Former Smokers

The mean diffusing capacity of the lung for carbon monoxide (DLCO) was  $14.27 \pm 4.36$  mL/min/mmHg in current smokers and  $16.78 \pm 4.09$  mL/min/mmHg in former smokers. The mean difference between the groups was 2.51 mL/min/mmHg, with higher DLCO observed among former smokers. The independent-samples t-test demonstrated a statistically significant difference in DLCO between current and former smokers ( $p=0.041$ ) (Table 2).

**Table 2.** Comparison of DLCO Between Current and Former Smokers With Stable COPD

| Variable          | Current Smokers (n=25) | Former Smokers (n=25) | p-value |
|-------------------|------------------------|-----------------------|---------|
| DLCO, mL/min/mmHg | $14.27 \pm 4.36$       | $16.78 \pm 4.09$      | 0.041*  |

Data are presented as mean  $\pm$  SD. \*Independent-samples t-test;  $p<0.05$  was considered statistically significant. Abbreviation: DLCO, diffusing capacity of the lung for carbon monoxide.

The distribution of DLCO values in current and former smokers is illustrated in Figure 1. The distribution was shifted toward higher DLCO values among former smokers compared with current smokers.

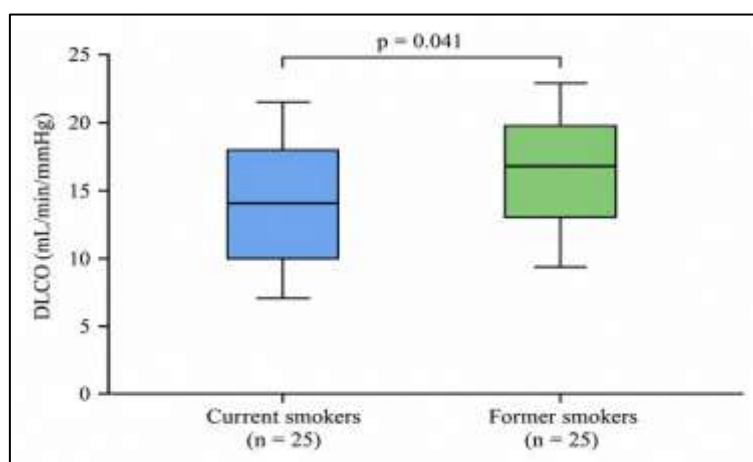


**Figure 1.** Distribution of DLCO Values in Current and Former Smokers With Stable COPD.

## 3.3 Association Between Smoking Duration and DLCO in Current Smokers

Among current smokers, Pearson correlation analysis demonstrated a moderate negative correlation between smoking duration and DLCO % predicted ( $r=-0.445$ ,  $p=0.026$ ). This correlation was statistically significant, indicating that longer smoking duration was associated with lower DLCO % predicted among current smokers with stable COPD (Table 3).

**Table 3.** Correlation Between Smoking Duration and DLCO (% Predicted) Among Current Smokers With Stable COPD

| Variable                                | n  | r      | p-value |
|-----------------------------------------|----|--------|---------|
| Smoking duration and DLCO (% predicted) | 25 | -0.445 | 0.026*  |

Data were analyzed using Pearson correlation. \* $p<0.05$  was considered statistically significant. Abbreviation: DLCO, diffusing capacity of the lung for carbon monoxide.

The relationship between smoking duration and DLCO % predicted is further illustrated in Figure 2. The scatter plot demonstrates a downward trend in DLCO % predicted with increasing smoking duration, consistent with the negative correlation observed in the statistical analysis.

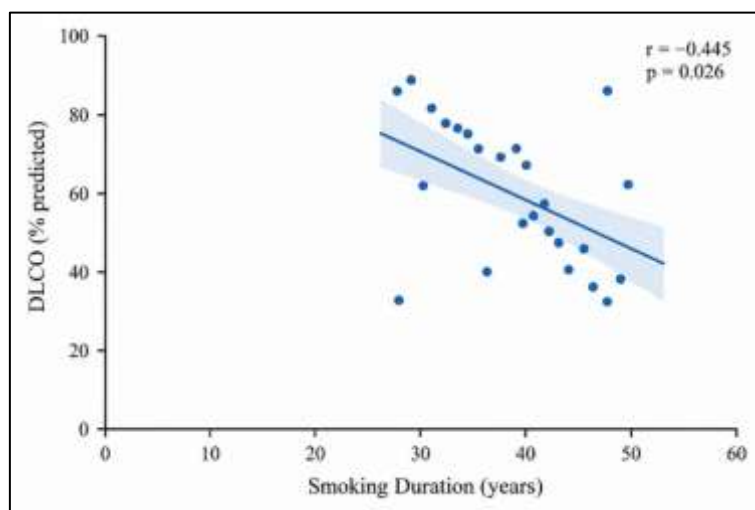


**Figure 2.** Correlation Between Smoking Duration and DLCO (% Predicted) Among Current Smokers With Stable COPD.

### 3.4 Association Between Smoking Cessation Duration and DLCO in Former Smokers

Among former smokers, Pearson correlation analysis demonstrated a strong positive correlation between smoking cessation duration and DLCO % predicted ( $r=0.608$ ,  $p=0.001$ ). This correlation was statistically significant, indicating that longer smoking cessation duration was associated with higher DLCO % predicted among former smokers with stable COPD (Table 4).

**Table 4.** Correlation Between Smoking Cessation Duration and DLCO (% Predicted) Among Former Smokers With Stable COPD

| Variable                                 | n  | r     | p-value |
|------------------------------------------|----|-------|---------|
| Smoking cessation and DLCO (% predicted) | 25 | 0.608 | 0.001*  |

Data were analyzed using Pearson correlation. \* $p<0.05$  was considered statistically significant. Abbreviation: DLCO, diffusing capacity of the lung for carbon monoxide.

The relationship between smoking cessation duration and DLCO % predicted is illustrated in Figure 3. The scatter plot demonstrates an upward trend in DLCO % predicted with increasing smoking cessation duration, consistent with the positive correlation observed in the statistical analysis.

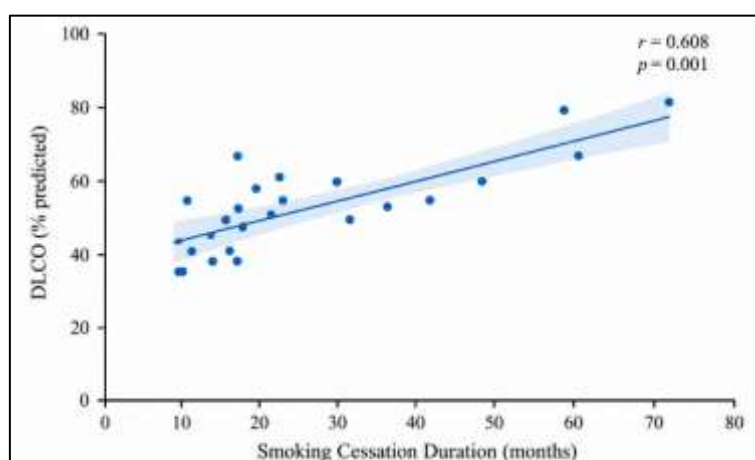


**Figure 3.** Correlation Between Smoking Cessation Duration and DLCO (% Predicted) Among Former Smokers With Stable COPD.

## 4. DISCUSSION

This study provides three principal findings regarding smoking history and *diffusing capacity of the lung for carbon monoxide* (DLCO) in patients with stable COPD. First, former smokers had significantly higher DLCO than current smokers, despite comparable age, body mass index, cumulative smoking exposure, hemoglobin concentration, and FEV<sub>1</sub> between the groups.<sup>[7]</sup> Second, longer smoking duration was significantly associated with lower DLCO among current smokers.<sup>[9]</sup> Third, longer smoking cessation duration was significantly associated with higher DLCO among former smokers. Together, these findings suggest that smoking history is associated with variation in pulmonary gas-transfer capacity beyond the information provided by conventional spirometric measures.<sup>[4]</sup>

The higher DLCO observed among former smokers is consistent with previous evidence demonstrating greater impairment of pulmonary diffusing capacity among individuals with ongoing cigarette exposure.<sup>[10]</sup> In the present study, mean DLCO was  $14.27 \pm 4.36$  mL/min/mmHg in current smokers compared with  $16.78 \pm 4.09$  mL/min/mmHg in former smokers, corresponding to a mean difference of 2.51 mL/min/mmHg. Importantly, the groups showed no statistically significant differences in pack-years, hemoglobin concentration, or FEV<sub>1</sub>. This relative comparability is relevant because cumulative tobacco exposure, hemoglobin concentration, and the severity of airflow obstruction may influence the interpretation of DLCO.<sup>[11]</sup> The observed difference therefore supports an association between current smoking status and impaired gas transfer in stable COPD, although the cross-sectional design does not establish causality.

Several mechanisms may contribute to lower DLCO among current smokers.<sup>[12]</sup> Chronic cigarette smoke exposure promotes oxidative stress, persistent inflammatory responses, protease–antiprotease imbalance, destruction of alveolar structures, and abnormalities within the pulmonary microvasculature.<sup>[13, 14]</sup> Loss of alveolar surface area and pulmonary capillary bed reduces the effective interface available for carbon monoxide transfer. In addition to these structural abnormalities, active smoking may exert acute physiological effects through increased carboxyhemoglobin, which can interfere with DLCO measurement and gas-transfer efficiency.<sup>[6]</sup> In the present study, current smokers were instructed to abstain from smoking for at least 24 hours before DLCO testing to minimize this acute effect, making persistent smoking-related pulmonary abnormalities particularly relevant to interpretation of the observed difference.

Smoking duration was moderately and negatively correlated with DLCO among current smokers ( $r = -0.445$ ,  $p = 0.026$ ). This finding suggests that prolonged exposure to cigarette smoke is associated with progressively greater impairment of alveolar–capillary gas transfer. Duration of smoking may reflect cumulative biological exposure that is not completely represented by the number of cigarettes smoked at a single point in time. Repeated exposure over decades may contribute to progressive emphysematous destruction and pulmonary vascular injury, both of which are important determinants of reduced DLCO.<sup>[15, 16]</sup> Nevertheless, the moderate magnitude of the correlation indicates that smoking duration alone does not account for all variability in DLCO. Other factors, including cumulative smoking intensity, emphysema burden, pulmonary vascular involvement, and individual susceptibility, may also contribute.

A distinct pattern was observed among former smokers, in whom smoking cessation duration showed a strong positive correlation with DLCO ( $r = 0.608$ ,  $p = 0.001$ ). Participants with longer periods of smoking cessation tended to have higher DLCO values. Previous physiological studies have reported improvement in carbon monoxide transfer after smoking cessation, particularly during the early period after discontinuation, suggesting that a component of smoking-related DLCO impairment may be reversible.<sup>[17]</sup> Potential mechanisms include reduction in carboxyhemoglobin, attenuation of ongoing smoke-related inflammatory and oxidative effects, and improvement in physiological conditions affecting alveolar–capillary gas transfer. However, established emphysematous destruction is generally considered structurally irreversible, indicating that higher DLCO after longer cessation should not be interpreted as complete restoration of damaged lung parenchyma.

The opposing directions of the correlations observed in current and former smokers provide a coherent physiological pattern. Longer smoking duration was associated with lower DLCO during continued smoking, whereas longer cessation duration was associated with higher DLCO after smoking discontinuation. These findings reinforce the potential value of incorporating detailed smoking history into physiological assessment of patients with COPD. They also highlight DLCO as a complementary measure to spirometry. FEV<sub>1</sub> primarily characterizes expiratory airflow limitation, whereas DLCO provides information regarding alveolar–capillary gas transfer and may therefore capture abnormalities related to emphysema and pulmonary vascular involvement that are not directly reflected by FEV<sub>1</sub>.<sup>[18]</sup>

From a clinical perspective, these findings support the relevance of smoking cessation in patients with COPD and suggest that assessment of smoking status alone may not fully characterize tobacco-related physiological impairment.<sup>[19,20]</sup> Duration of active smoking and duration since cessation may provide additional context when interpreting DLCO. The significant difference in DLCO despite similar FEV<sub>1</sub> between current and former smokers further illustrates that comparable degrees of airflow obstruction do not necessarily imply comparable gas-transfer function.<sup>[18]</sup> Incorporating DLCO into pulmonary function assessment may therefore provide additional physiological information, particularly in patients with substantial smoking exposure.<sup>[5, 21]</sup>

## Strengths and Limitations

A strength of this study is the simultaneous evaluation of smoking status, smoking duration, cessation duration, spirometric function, hemoglobin concentration, and DLCO in a clinically defined stable COPD population. The current and former smoker groups were also relatively comparable across the measured baseline characteristics, including pack-years and FEV<sub>1</sub>. However, several limitations should be considered. The cross-sectional design precludes assessment of within-person changes in DLCO over time and does not permit causal inference regarding smoking cessation and improvement in diffusing capacity.

The sample size was relatively small and participants were recruited from a single tertiary referral center, which may limit generalizability. Smoking exposure and cessation duration were based on participant-reported histories and were therefore susceptible to recall bias. Quantitative computed tomography was not performed to characterize emphysema burden, which could have provided structural correlates of reduced DLCO. Future longitudinal, multicenter studies incorporating serial DLCO measurements and quantitative imaging could clarify the temporal relationship between smoking cessation and pulmonary gas-transfer function.

## 5. CONCLUSION

Former smokers with stable COPD had significantly higher absolute DLCO than current smokers. Among current smokers, longer smoking duration was associated with lower DLCO % predicted, whereas among former smokers, longer smoking cessation duration was associated with higher DLCO % predicted. These findings demonstrate that smoking status, smoking duration, and duration of smoking cessation are associated with pulmonary gas-transfer capacity in stable COPD. DLCO may provide complementary physiological information beyond spirometry, particularly when interpreted alongside detailed smoking history. Longitudinal studies are warranted to evaluate changes in DLCO over time following smoking cessation.

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## AUTHOR CONTRIBUTIONS

**Pujia Cahya Amalia:** Conceptualization, methodology, investigation, data curation, formal analysis, visualization, and writing original draft.

**Nur Ahmad Tabri:** Conceptualization, methodology, supervision, validation, and writing review and editing.

**Erwin Arief:** Methodology, supervision, validation, and writing review and editing.

All authors read and approved the final manuscript.

## CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

## ETHICS STATEMENT

This study was approved by the Health Research Ethics Committee, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia (No. 822/UN4.6.4.5.31/PP36/2026). Written informed consent was obtained from all participants prior to enrollment. Participant confidentiality was maintained throughout the study.

## DATA AVAILABILITY STATEMENT

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

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