










# Periodontitis is associated with airflow obstruction in the Malmö Offspring Dental Study

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## Abstract

**Aim:** To investigate the association between periodontitis and lung function in the Malmö Offspring Dental Study.

**Materials and Methods:** In all 1001 individuals (49.9% female, mean age: 44.6) from Malmö Offspring Dental Study were included. Periodontitis was assessed by a full-mouth examination protocol including bleeding on probing and classified according to the American Academy of Periodontology/Center for Disease Control definitions. Forced expiratory volume in 1 s (FEV<sub>1</sub>) and forced vital capacity (FVC) were expressed as absolute values and %predicted according to Global Lung Function Initiative reference values. FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC were analysed in relation to periodontal status using linear regression.

**Results:** Severe periodontitis was found in 7% of the population. Adjusted regression models showed significant associations between lung function and severe periodontitis with 2.1 unit lower FEV<sub>1</sub>/FVC ratio (95% CI: -3.91, -0.23) and odds ratio (adjusted) of 2.56 (95% CI: 1.40, 4.75, *p* = .003) for airflow obstruction (FEV<sub>1</sub>/FVC less than the lower limit of normal) if having severe periodontitis. Lower values of %predicted FEV<sub>1</sub> and %predicted FVC, but not FEV<sub>1</sub>/FVC, were found in individuals with >25% bleeding on probing.

**Conclusions:** Severe periodontitis was associated with lower FEV<sub>1</sub>/FVC ratio and airflow obstruction in the present cohort. More large-scale prospective studies and intervention studies are required for a comprehensive evaluation.

## KEYWORDS

lung function, Malmö Offspring Dental Study, periodontal disease, periodontitis, pulmonary function

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### Clinical Relevance

*Scientific rationale for study:* Periodontitis and lung diseases share common risk factors. This study aimed to explore the association between periodontitis and lung function in the Malmö Offspring Dental Study population.

*Principal findings:* This study shows that severe periodontitis is associated with lower lung function and airflow obstruction in a cohort of Swedish adults. Furthermore, bleeding on probing was associated with lower spirometry values but not with airflow obstruction.

*Practical implications:* Periodontitis and gingival inflammation in patients with compromised lung function require special attention, and periodontitis treatment may be an important factor in the prevention of further deterioration of lung function.

## 1 | INTRODUCTION

Periodontitis is a multifactorial, chronic inflammatory disease in the periodontal tissues associated with a dysbiotic plaque biofilm (Papapanou et al., 2018). In 2010, severe periodontitis was the sixth most prevalent condition worldwide, affecting 743 million people (Kassebaum et al., 2014). In milder forms, periodontitis affects 45%–50% of adults and in the severe form about 5%–10% (Eke et al., 2015), with a majority being over 65 years old (Theo Vos et al., 2015). Periodontitis is characterized by progressive destruction of the tooth-supporting apparatus, clinically manifested by periodontal pocket formation, alveolar bone resorption and, finally, tooth loss (Pihlstrom et al., 2005).

Despite the multiple causes of pulmonary disease, bacterial infection is known to be a contributing component in some cases (Murphy & Sethi, 1992). Because of the anatomical relationship between the oral cavity and the airways, microorganisms present in the oral biofilm can be aspirated into the lower airway, promoting inflammation (Hajishengallis, 2015, 2022; Imai et al., 2021). Moreover, periodontitis and some lung diseases are linked by inflammation (Gläser et al., 2012; Rasmussen et al., 2009; Shaaban et al., 2006; Thyagarajan et al., 2006; Yoshii et al., 2009). Proposed pathways also include the systemic transfer of cytokines and enzymes from periodontal inflamed tissues into the lungs (Cardoso et al., 2018) and a systemic neutrophil dysfunction that disturbs protease/anti-protease and redox state balance, predisposing inflammation and tissue destruction in both lung and periodontal tissues (Usher & Stockley, 2013).

Spirometry is widely available and used to measure lung function. Usually, the volume exhaled during the first second of a forced expiration ( $FEV_1$ ) and forced vital capacity (FVC) are recorded. The ratio between these two variables is considered a measure of airflow obstruction. Chronic obstructive pulmonary disease (COPD) and asthma are the most common obstructive lung disorders (Osadnik & Singh, 2019). Both asthma and COPD are important causes of impaired health-related quality of life and disability, worldwide (Frag et al., 2018; Juniper, 1999). Periodontitis and impaired lung function share common risk factors (Cullinan et al., 2009; Zeng et al., 2012), and epidemiological studies have confirmed that periodontitis is associated with lower levels of  $FEV_1$  (Lee et al., 2020;

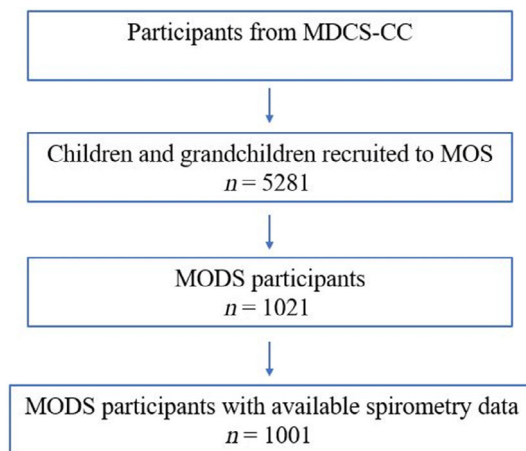
Winning et al., 2019), increased risk of airflow obstruction (Chen et al., 2022) and reduced lung volumes and airflow limitation (Holtfreter et al., 2013). A recently published systematic review showed that COPD, obstructive sleep apnea and COVID-19 complications are positively associated with periodontitis (Molina et al., 2023). Moreover, the effect of periodontitis treatment on the onset and progression of respiratory diseases in subjects with periodontitis has been investigated. Two intervention studies (Kucukcoskun et al., 2013; Zhou et al., 2014) that evaluated the effect of periodontal therapy on the number of COPD exacerbations and lung function found less frequent and severe exacerbation following periodontal therapy. Another recently published study found that advanced dental cleaning can reduce the number of exacerbations in COPD compared with non-treated controls, indicating a causal relationship between dental biofilm and COPD (Sundh et al., 2021). However, there are also studies reporting no significant association between periodontitis and COPD (Apossos et al., 2021; Jung et al., 2020; Zhou et al., 2020) and reduced lung function (Lee & Lee, 2019).

Overall, there is still uncertainty about the association between lung function and periodontitis. To our knowledge, no previous study has investigated the relationship between periodontitis and lung function in a Scandinavian population, using a full-mouth periodontal examination protocol including bleeding on probing (BoP). Thus, the aim of this study was to investigate the association between periodontitis and lung function in a cohort of Swedish adults.

## 2 | MATERIALS AND METHODS

### 2.1 | Study population

The Malmö Offspring Study (MOS) (Brunkwall et al., 2021) is a population-based cohort study inviting adult children and grandchildren (age  $\geq 18$  years) of index subjects from the Malmö Diet Cancer Study-Cardiovascular Cohort (MDCS-CC) (Berglund et al., 1993). The MOS was initiated in 2013 and recruited participants until the fall of 2021. Participants were recruited by invitation letter for a visit to the Clinical Research Unit, Skåne University Hospital, Malmö, Sweden. They were informed about the Malmö Offspring Dental Study (MODS) and thereafter recruited via phone call. Of the eligible



**FIGURE 1** Flow chart of the study enrollment.

offspring in MDCS-CC, 47% were recruited to the MOS, and 19% of the MOS participants with available spirometry and a dental clinical examination from MODS were included in this study (Figure 1). By January 2021, when the analysis for the current study was initiated, the MODS population consisted of 1021 subjects. Only a minor group, accounting for 1% ( $n = 20$ ), did not have spirometry data and were excluded from the current analysis. The most common reason for not participating in the MODS was a recent visit to the dentist. In Sweden, dental insurance is common, which indicated that these study participants already had a dental examination at reduced fee and did not see the need for another visit. Another reason for not participating was dental anxiety.

MOS and MODS were both approved by the Ethical Review Board of Lund University (MOS: Dnr. 2012/594, and MODS: Dnr. 2013/761).

## 2.2 | Data collection

### 2.2.1 | Lung function measurements

Spirometry data were used to assess lung function (primary outcome). Three acceptable and reproducible measurements of FVC and FEV<sub>1</sub> were performed using a Jaeger Masterscope spirometer according to the American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations (Miller et al., 2005) and the highest recorded values were used for further analyses. Up to eight additional trials were conducted if the spirometry criteria were not met after three manoeuvres.

The outcomes of interest in the analyses were FEV<sub>1</sub>, FVC and the FEV<sub>1</sub>/FVC ratio, the latter defined as the FEV<sub>1</sub> divided by FVC and then multiplied by 100. For spirometry, only low values are considered to be abnormal, so the lower limit of normal (LLN) is taken to be equal to the fifth percentile according to the Global Lung function Initiative (GLI) 2012 (Quanjer et al., 2012). Airflow obstruction was defined by an FEV<sub>1</sub>/FVC ratio less than LLN according to ERS/ATS technical

standard on interpretive strategies for routine lung function tests (Stanojevic et al., 2022). The %predicted values were calculated by comparing FEV<sub>1</sub> and FVC with reference values from GLI 2012. Data from healthy individuals provide meaningful reference values against which to compare an individual's pulmonary function test (PFT) results, and presenting results as %predicted lung function values aids in understanding whether the measurement falls within the expected range or deviates from it (Stanojevic et al., 2022). The %predicted lung function values were calculated by prediction equations, which consider the participant's age, sex, height and ethnicity (Caucasians). All participants in the study belonged to this ethnic group.

### 2.2.2 | Periodontal parameters

The MODS has a full-mouth periodontal examination protocol (Jönsson et al., 2020). The radiographic examination protocol includes one panoramic radiograph and four bitewing radiographs of molars and premolars. Periodontal probing depth (PD) >2 mm was recorded at six sites per tooth (mesio-buccal, mid-buccal, disto-buccal, disto-lingual, mid-lingual and mesio-lingual). PD of 1 and 2 mm is considered to constitute a healthy periodontium and was not registered. PD represents the distance (in mm) from the gingival margin to the probable base of the pockets, and clinical attachment loss (CAL) is the distance (in mm) from the cemento-enamel junction to the depth of the pocket. PD and CAL were assessed using a periodontal probe with 1 mm grading (Hu-Friedy PCPUNC157). For each patient, aggregated variables, including the number of sites measuring  $\geq 3$  mm,  $\geq 4$  mm,  $\geq 5$  mm and  $\geq 6$  mm, as well as the number of teeth with sites measuring  $\geq 3$  mm,  $\geq 4$  mm,  $\geq 5$  mm and  $\geq 6$  mm, were recorded. Additionally, the total number of teeth was recorded.

Periodontitis was classified according to the Centers for disease control and prevention/American academy of periodontology case definition (Page & Eke, 2007). BoP was assessed by gently probing six sites per tooth and registered as the proportion of sites with BoP (%) (Ainamo & Bay, 1975). In the present study, participants were categorized according to proportions of BoP  $\leq 25\%$  and  $>25\%$ . The cut-off is based on a suggested threshold of 20%–30% BoP, as this level is critical for maintaining periodontal stability (Lang et al., 1986; Ramseier et al., 2015). Five trained and experienced dentists examined the participants between 2014 and 2018. Inter-examiner agreement was set at  $\geq 90\%$  within  $\pm 1$  mm probing depth. The two-way mixed inter-class correlation coefficient with absolute agreement for inter-examiner probing depth was  $>0.75$  (0.753–0.791) (Ottoosson et al., 2022).

### 2.2.3 | Other patient-related covariate assessments

Height (cm) and weight (kg) were measured during clinical examinations according to the MOS protocol (Brunkwall et al., 2021). Body mass index (BMI) was calculated as weight/height<sup>2</sup> (kg/m<sup>2</sup>) and categorized into BMI < 18.5, BMI 18.5–25, BMI 25–30 and BMI > 30.

Blood samples were analysed at the laboratory of the Skåne University Hospital, and a diagnosis of diabetes was defined by fasting

plasma glucose (FPG)  $\geq 7$  mmol/L according to the American Diabetes Association (2020) clinical practice recommendations.

Use of snus (smokeless tobacco) and smoking status were obtained from questionnaires. Snus use was dichotomously categorized, and smoking status was categorized as never, former and current smokers. The smoking variable was based on responses to the following questions: 'Do you smoke?' and 'Have you smoked before, if yes, when did you stop?'. No information on smoking history (pack-years) was available for the (whole) cohort.

Education level was obtained from the questionnaires and categorized as follows: (I) less than 12 years of education, (II) completed 12 years education or (III) completed university education.

## 2.2.4 | Statistical analysis

Summary statistics were constructed using frequencies for categorical variables and means  $\pm$  SD for continuous variables. Association between the categorical variables was investigated using the chi-squared test, and differences in means between groups were investigated using one-way ANOVA and *t*-test.

The association between periodontitis and airflow obstruction status was investigated with logistic regression analysis, adjusting for age, sex, smoking, BMI, educational level and diabetes.

The association between periodontal disease severity and lung function was examined using covariate-adjusted linear regression models. The lung function measures, namely the %predicted FEV<sub>1</sub>, % predicted FVC and the ratio FEV<sub>1</sub>/FVC, were modelled as continuous dependent variables.

Three models of adjustment were used. Model 1 included sex and age and was used exclusively when reporting absolute values. The % predicted values were reported as 'crude', because age and sex were already taken into account in the first step. Model 2 included smoking and snus use as covariates in addition to sex and age. Model 3 was additionally adjusted for BMI, educational level and diabetes. By using this hierarchical approach, we could investigate how the included variables altered the association between the outcome of interest and the main exposure. Similar model building was applied to the analyses exploring the association between lung function and BoP. A two-sided  $p < .05$  was considered statistically significant. All statistical analyses were conducted by Stata 17.0 (Stata Corporation, College Station, TX, USA).

## 3 | RESULTS

### 3.1 | Characteristics

The mean age of the study population was 44.6 years, and 49.9% were women (Table 1). Moderate periodontitis was found in 29% of the population, whereas severe periodontitis was found in 7.0%. Significant differences were found in the categories of BMI, FPG levels, smoking habits, use of snus, educational level, number of missing

teeth and age between subjects, classified on the basis of severity of periodontitis (Table 1). The lung function indices, namely FEV<sub>1</sub> (both as absolute values and %predicted), FVC (as absolute values) and the ratio FEV<sub>1</sub>/FVC, were significantly lower in subjects with severe periodontitis. There was no difference regarding sex or FVC (%predicted). The population was dichotomously stratified by airflow obstruction FEV<sub>1</sub>/FVC < LLN. Statistically significant differences were found in sex, age, number of teeth, percentage of sites with periodontal pocket depths  $\geq 4$  mm, smoking status and the use of snus based on categories of airway obstruction (Table 1).

### 3.2 | Periodontitis and lung function

A statistically significant inverse association was found between FEV<sub>1</sub>/FVC ratio and the severity of periodontitis (Table 2). These findings were consistent after adjustment for age, sex, smoking, snus use, BMI, educational level and diabetes. The effect of BMI appeared non-linear. Hence, we added a cubic polynomial to the equation for the adjustment of BMI. This did not alter the overall finding, nor did the effects of periodontitis severity alter the outcome variables. Individuals with severe periodontitis had a 2% lower FEV<sub>1</sub>/FVC ratio compared with individuals with no/mild periodontitis. An inverse correlation was observed between the lung function indices FEV<sub>1</sub> and FVC (% predicted and absolute values) and the severity of periodontitis (Tables 2 and 3). However, this correlation did not reach statistical significance.

Compared with that of participants with mild/no periodontitis, the likelihood of having airflow obstruction was higher both in those with moderate (OR<sub>crude</sub>: 1.78, 95% CI: 1.20–2.64,  $p = .004$ ) and severe (OR<sub>crude</sub>: 4.4, 95% CI: 2.48–7.66,  $p < .001$ ) periodontitis. The findings for severe periodontitis were supported in the fully adjusted logistic regression model (OR<sub>adjusted</sub>: 2.56, 95% CI: 1.37–4.75,  $p = .003$ ).

Considering the number of missing teeth as the exposure (Table S1), statistically significant inverse associations with a 2.73 lower %predicted FEV<sub>1</sub> were found in individuals having the most severe tooth loss ( $p = .042$ ). Exchanging the exposure variable to percentage of sites  $\geq 4$  mm as a surrogate for periodontitis revealed inverse associations with %predicted FEV<sub>1</sub> (Table S2). However, these associations did not reach statistical significance in the fully adjusted model.

### 3.3 | Gingival inflammation and lung function

About 44% of the study participants had BoP > 25%. Statistically significant lower values of %predicted FEV<sub>1</sub> and %predicted FVC were detected in individuals with BoP > 25% (data not shown). Comparison between %predicted FEV<sub>1</sub>, %predicted FVC and FEV<sub>1</sub>/FVC values among categories of BoP is shown in Table 4. In the fully adjusted linear regression model, statistically significant inverse associations were seen in %predicted FEV<sub>1</sub> and %predicted FVC for individuals with BoP > 25% compared with the reference group (BoP  $\leq$  25%). This tendency was also seen in the model using bleeding as a continuous variable.

**TABLE 1** Characteristics of study population by periodontitis status (CDC/AAP 2007) and proportion of gingival inflammation (BoP).

Characteristics Variables	Total	Periodontitis status			Airflow obstruction FEV <sub>1</sub> /FVC < lower limit of normal		p-Value
		Healthy/mild	Moderate	Severe	No	Yes	
Number of participants	1001	645 (64.4)	289 (28.9)	67 (6.7)	858 (85.7)	143 (14.3)	
Sex							.104 <sup>a</sup>
Male	501 (50.0)	307 (61.3)	156 (31.1)	38 (7.6)	415 (82.8)	86 (17.2)	.009 <sup>a</sup>
Female	500 (50.0)	338 (67.6)	133 (26.6)	29 (5.8)	443 (88.6)	57 (11.4)	
Age (years)	44.63 ± 14.15	41.7 ± 13.9	48.7 ± 13.5	54.8 ± 9.2	43.7 ± 14.3	50.4 ± 11.6	<.001 <sup>c</sup>
Education	n = 999						.111 <sup>a</sup>
<12 years	39 (3.9)	13 (33.3)	14 (35.9)	12 (30.8)	29 (74.4)	10 (25.6)	
12 years	562 (56.3)	362 (64.4)	164 (29.2)	36 (6.4)	482 (85.8)	80 (14.2)	
Education at university level	398 (39.8)	269 (67.6)	110 (27.6)	19 (4.8)	345 (86.7)	53 (13.3)	
Number of teeth	n = 999 27.1 ± 1.9	27.2 ± 1.8	27.1 ± 1.9	26.0 ± 3.1	27.2 ± 0.05	26.5 ± 0.3	.001 <sup>c</sup>
Number of missing teeth	n = 999						.228 <sup>a</sup>
No missing teeth	643 (64.4)	427 (66.4)	186 (28.9)	30 (4.7)	559 (86.9)	84 (13.1)	
1–2 missing teeth	234 (23.4)	146 (62.4)	69 (29.5)	19 (8.1)	199 (85.0)	35 (15.0)	
≥3 missing teeth	122 (12.2)	71 (58.2)	34 (27.9)	17 (13.9)	99 (81.2)	23 (18.8)	
Pocket depths (PD) and clinical attachment loss (CAL)	n = 995						
Percentage of sites with PD ≥ 4 mm	5.2 ± 7.6	2.5 ± 2.8	7.6 ± 5.6	20.3 ± 18.4	4.7 ± 0.2	7.8 ± 1.0	<.001 <sup>c</sup>
Prevalence of ≥2 sites with PD ≥ 4 mm	772 (77.1)	428 (55.4)	277 (35.9)	67 (8.7)	652 (84.5)	120 (15.5)	.037 <sup>a</sup>
Prevalence of ≥2 sites with CAL ≥ 4 mm	272 (27.3)	0	216 (79.4)	56 (20.6)	150 (27.0)	122 (28.0)	.850 <sup>a</sup>
Prevalence of ≥2 sites with CAL ≥ 6 mm	67 (6.7)	0	2 (3.0)	65 (97.0)	30 (5.4)	37 (8.4)	.650 <sup>a</sup>
Bleeding on probing (%), mean ± SD	n = 997 26.9 ± 18.3	25.6 ± 17.4	28.5 ± 19.3	33.1 ± 21.5	26.8 ± 0.6	27.2 ± 1.6	.841 <sup>c</sup>
Body mass index [BMI] (kg/m <sup>2</sup> )							.923 <sup>a</sup>
BMI ≤ 25	451 (45.1)	313 (69.4)	115 (25.5)	23 (5.1)	388 (86.0)	63 (14.0)	
BMI > 25 and ≤30	352 (35.2)	225 (63.9)	105 (29.8)	22 (6.3)	302 (85.8)	50 (14.2)	
BMI > 30	198 (19.7)	107 (54.0)	69 (34.9)	22 (11.1)	168 (84.8)	30 (15.2)	
Fasting plasma glucose (mmol L <sup>-1</sup> )	n = 1000 5.51 ± 0.97	5.5 ± 0.9	5.6 ± 0.9	5.9 ± 1.5	5.5 ± 0.03	5.6 ± 0.1	.140 <sup>c</sup>
Diabetes/fasting plasma glucose > 7 mmol L <sup>-1</sup>	39 (3.9)	17 (43.6)	14 (35.9)	8 (20.5)	30 (77.0)	9 (23.0)	.110 <sup>a</sup>
Smoking status	n = 998						<.001 <sup>a</sup>
Never smoker	599 (60.0)	417 (69.6)	161 (26.9)	21 (3.5)	531 (88.6)	68 (11.4)	
Former smoker	288 (28.9)	162 (56.3)	97 (33.7)	29 (10.0)	242 (84.0)	46 (16.0)	
Current smoker	111 (11.1)	64 (57.6)	30 (27.0)	17 (15.3)	82 (73.9)	29 (26.1)	



TABLE 1 (Continued)

Characteristics Variables	Total	Periodontitis status			Airflow obstruction FEV <sub>1</sub> /FVC < lower limit of normal		p-Value
		Healthy/mild	Moderate	Severe	No	Yes	
Snus use	n = 1000						
Yes	132 (13.2)	74 (56.1)	42 (31.8)	16 (12.1)	104 (78.8)	28 (21.2)	.015 <sup>a</sup>
%predicted FEV <sub>1</sub> (%)	94.6 ± 13.7	95.1 ± 12.8	94.5 ± 15.1	90.4 ± 15.0	96.6 ± 0.4	82.8 ± 1.2	<.001 <sup>c</sup>
%predicted FVC (%)	98.7 ± 12.9	99.1 ± 12.8	98.2 ± 13.0	97.0 ± 13.5	98.3 ± 0.4	100.7 ± 1.3	.043 <sup>c</sup>
FEV <sub>1</sub> /FVC	77.3 ± 7.4	78.0 ± 6.9	76.7 ± 8.0	73.3 ± 7.4	79.4 ± 0.2	65.0 ± 0.4	<.001 <sup>c</sup>
FEV <sub>1</sub> (L)	3.4 ± 0.8	3.5 ± 0.8	3.3 ± 0.9	3.0 ± 0.8	3.5 ± 0.02	3.0 ± 0.07	<.001 <sup>c</sup>
FVC (L)	4.4 ± 1.1	4.5 ± 1.0	4.4 ± 1.1	4.2 ± 0.9	4.4 ± 0.03	4.6 ± 0.1	.030 <sup>c</sup>
Airflow obstruction FEV <sub>1</sub> /FVC < Lower limit of normal	143 (14.3)	69 (48.3)	51 (35.7)	23 (16.0)			

Note: Data are presented as n (%) or mean ± standard deviation. FEV<sub>1</sub>/FVC is unitless and has the formula FEV<sub>1</sub> (L)/FVC (L) × 100.

Abbreviations: FEV<sub>1</sub>, forced expiratory volume in the first second; FVC, forced vital capacity.

<sup>a</sup>Results from chi-squared test.

<sup>b</sup>Results from one-way ANOVA.

<sup>c</sup>Results from t-test.

## 4 | DISCUSSION

The present study investigated the association between periodontitis and lung function in a cross-sectional study of 1001 adult Swedish individuals. Severe periodontitis was consistently related to lower FEV<sub>1</sub>/FVC ratio and with airflow obstruction, which is defined as FEV<sub>1</sub>/FVC < LLN. Furthermore, gingival inflammation was linked to lower %predicted FEV<sub>1</sub> and %predicted FVC in the fully adjusted regression models.

Our findings were consistent with earlier reports on the association between periodontitis and lung function. Consistent with our findings, Holtfreter et al. found an independent inverse association between periodontitis, as indicated by the mean CAL, and airflow limitation (Holtfreter et al., 2013). Another cross-sectional study based on the Third National Health and Nutrition Examination Survey 1988–1994 (NHANES III) including 10,645 individuals revealed that values of FEV<sub>1</sub>/FVC were lower in patients with moderate and severe periodontitis compared with healthy individuals (Lee et al., 2020). These findings were confirmed by Chen et al. (2022) using more recent NHANES data (from 2009 to 2012). In our study, lung function was lower only in participants with severe periodontitis and not in those with moderate periodontitis. The classification used in the NHANES study by Chen et al. included 'mild' periodontitis, which differs from the definition used in the present study that merged the mild and no periodontitis groups. Thus, the differences observed between the studies might be due to different versions of periodontitis classification as well as differences in demographic characteristics, such as race, which can affect lung function.

A few earlier studies have described the relationship between periodontal health and lung function in Scandinavian populations. In a study from Norway, Pérez Barrionuevo et al. investigated the association between periodontal health assessed by the Community Periodontal Index (CPI) and lung function among young and middle-aged adults in two Norwegian cohorts. The mean age was in a similar range as in the present study, and despite a different case definition of periodontitis, Pérez Barrionuevo et al. supported that poorer periodontal health is associated with a significantly lower FEV<sub>1</sub>/FVC ratio (2018).

Another finding from our analysis was that severe periodontitis was significantly associated with airflow obstruction, defined as FEV<sub>1</sub>/FVC < LLN. The odds ratio for an association between severe periodontitis and airflow obstruction from the fully adjusted model is in line with findings from recent studies (Chen et al., 2022; Winning et al., 2020). According to Winning et al., subjects with periodontitis in a cohort of older Swedish individuals (median age: 72 years) had a nearly three-fold increased risk of airway obstruction, which is roughly the same as revealed by our data in cases of severe periodontitis. This may be due to a higher prevalence of severe periodontitis and airflow obstruction in older populations.

To date, the impact of periodontitis on pulmonary function is mainly indicated by observational studies. It is important to note that observational research is vulnerable to confounding factors and reverse causation, which can make it challenging to establish a clear causal inference or determine the direction of these associations. A

**TABLE 2** Covariate-adjusted linear regression analysis with %predicted lung function measurements as dependent variables.

	Periodontitis status				
	Healthy/mild periodontitis	Moderate	p-Value	Severe	p-Value
%predicted FEV <sub>1</sub> (%)					
Crude	Reference	-0.62 (-2.51, 1.27)	.521	-4.72 (-8.15, -1.28)	.007
Model 2	Reference	-0.60 (-2.50, 1.32)	.536	-3.68 (-7.16, -0.20)	.038
Model 3	Reference	-0.10 (-2.00, 1.80)	.916	-2.80 (-6.30, 0.80)	.123
%predicted FVC (%)					
Crude	Reference	-0.83 (-2.63, 0.97)	.366	-2.10 (-5.33, 1.19)	.213
Model 2	Reference	-0.90 (-2.70, 0.91)	.334	-1.52 (-4.82, 1.80)	.368
Model 3	Reference	-0.40 (-2.20, 1.39)	.659	-0.41 (-3.75, 2.92)	.807
FEV <sub>1</sub> /FVC <sup>a</sup>					
Model 1	Reference	0.04 (-0.94, 1.03)	.934	-2.32 (-4.11, -0.53)	.011
Model 2	Reference	0.12 (-0.90, 1.10)	.818	-2.00 (-3.73, -0.10)	.038
Model 3	Reference	0.13 (-0.87, 1.12)	.800	-2.10 (-3.91, -0.23)	.030

Note: Linear regression coefficients with their respective 95% confidence intervals. Model 1: Age and sex. Model 2: Model 1 + smoking + snus use. Model 3: Model 2 + BMI + education + diabetes.

Abbreviations: FEV<sub>1</sub>, forced expiratory volume in the first second; FVC, forced vital capacity.

<sup>a</sup>The FEV<sub>1</sub>/FVC variable is not based on predicted values. Hence, in Model 1 adjustments for age and sex are included. FEV<sub>1</sub>/FVC is unitless and have the formula FEV<sub>1</sub> (L)/FVC (L) × 100.

**TABLE 3** Covariate-adjusted linear regression analysis with absolute measurements of lung function as dependent variables.

	Periodontitis status				
	Healthy/mild periodontitis	Moderate	p-Value	Severe	p-Value
FEV <sub>1</sub> (L)					
Crude	Reference	-0.16 (-0.30, -0.05)	.006	-0.44 (-0.65, -0.23)	<.001
Model 1	Reference	-0.05 (-0.13, 0.03)	.230	-0.20 (-0.33, -0.05)	.005
Model 2	Reference	-0.05 (-0.13, 0.03)	.238	-0.16 (-0.30, -0.01)	.022
Model 3	Reference	-0.03 (-0.11, 0.04)	.413	-0.11 (-0.26, 0.02)	.100
FVC (L)					
Crude	Reference	-0.14 (-0.30, 0.01)	.069	-0.32 (-0.61, -0.07)	.016
Model 1	Reference	-0.06 (-0.16, 0.04)	.233	-0.15 (-0.32, 0.03)	.117
Model 2	Reference	-0.06 (-0.16, 0.03)	.213	-0.11 (-0.31, 0.06)	.215
Model 3	Reference	-0.04 (-0.14, 0.05)	.381	-0.04 (-0.22, 0.14)	.630

Note: Table shows linear regression coefficients with their respective 95% confidence intervals. The regression coefficients represent mean of lung function values in litres (L) across categories of periodontitis. Model 1: Age and sex. Model 2: Model 1 + smoking + snus use. Model 3: Model 2 + BMI + education + diabetes.

Abbreviations: FEV<sub>1</sub>, forced expiratory volume in the first second; FVC, forced vital capacity.

study by Baumeister et al. (2021), using Mendelian randomization, did not support a relationship between a genetic liability to periodontitis and worsened pulmonary function. Another approach to mitigate observational bias and enhance causal inference would be to investigate the treatment impact of periodontitis on lung function through intervention studies and randomized controlled trials (RCTs). To our knowledge, there are few clinical trials examining the effect of dental treatment on lung function. Four interventional studies, two non-randomized (Kucukcoskun et al., 2013; Shen et al., 2016) and two randomized (Sundh et al., 2021; Zhou et al., 2014), showed a positive

effect of dental treatment on lung function in patients with COPD. However, it is important to conduct additional large-scale prospective studies and RCTs, similar to that by Romero et al. (2017), to validate the association between periodontitis and lung function as observed in the present study.

BoP is considered a pivotal parameter for predicting periodontal stability and periodontitis progression, and several studies have determined a threshold of 20%–30% BoP as critical to maintain periodontal stability (Lang et al., 1986; Ramseier et al., 2015). Moreover, the proportion of BoP reflects the presence of dental plaque and has been

**TABLE 4** Covariate-adjusted linear regression analysis with lung function measurements as dependent variable.

	BoP > 25% versus BoP ≤ 25% (ref.)	p-Value	%BoP continuous	p-Value
%Predicted FEV <sub>1</sub> (%)				
Crude	-2.34 (-4.04, -0.63)	.007	-0.05 (-0.10, -0.007)	.023
Model 2	-2.11 (-3.81, -0.42)	.015	-0.05 (-0.10, -0.003)	.035
Model 3	-1.75 (-3.45, -0.10)	.042	-0.04 (-0.10, 0.003)	.068
%Predicted FVC (%)				
Crude	-2.59 (-4.20, -0.98)	.002	-0.06 (-0.11, -0.018)	.006
Model 2	-2.44 (-4.05, -0.83)	.003	-0.06 (-0.10, -0.020)	.007
Model 3	-2.10 (-3.70, -0.50)	.011	-0.05 (-0.10, -0.010)	.016
FEV <sub>1</sub> /FVC <sup>a</sup>				
Model 1	0.20 (-0.67, 1.01)	.643	0.010 (-0.02, 0.031)	.510
Model 2	0.30 (-0.60, 1.20)	.512	0.010 (-0.01, 0.034)	.393
Model 3	0.28 (-0.60, 1.16)	.538	0.010 (-0.01, 0.033)	.424

Note: Linear regression coefficients with their respective 95% confidence intervals presenting difference in means between categories of bleeding on probing (%BoP < 25 as reference) and %BoP as a continuous variable. Model 1: Age and sex. Model 2: Model 1 + smoking + snus use. Model 3: Model 2 + BMI + education + diabetes.

Abbreviations: BoP, bleeding on probing; FEV<sub>1</sub>, forced expiratory volume in the first second; FVC, forced vital capacity.

<sup>a</sup>The FEV<sub>1</sub>/FVC variable is not based on predicted values. Hence, in Model 1 adjustments for age and sex are included. FEV<sub>1</sub>/FVC is unitless and has the formula FEV<sub>1</sub>(L)/FVC(L) × 100.

implemented as a parameter in the case definitions of plaque-induced gingivitis and periodontal health (Murakami et al., 2018; Trombelli et al., 2018). The periodontal pocket provides a suitable microenvironment for both pathogenic and opportunistic species of bacteria, and this increases the risk of aspirating pathogenic bacteria into the lungs, exacerbating pulmonary inflammation and endothelial dysfunction (Imai et al., 2021). Moreover, indirect mechanisms, such as low-grade inflammation due to hematogenous spread of oral bacteria and inflammatory mediators, have been suggested to exacerbate respiratory diseases (Hajishengallis, 2022). In the present study, BoP > 25% was associated with lower %predicted FEV<sub>1</sub> and %predicted FVC, and no relationship was found between BoP and airflow obstruction. This may be related to both aspiration of periodontal bacteria and a higher level of periodontitis-induced inflammation (Hajishengallis, 2015, 2022; Imai et al., 2021).

In the population-based study conducted by Gómez Real et al. (2016), the authors found a consistent link between gum bleeding and self-reported obstructive airway disease. Even though these findings were based on self-reported gum bleeding, they measured CPI index in a subsample of the population and found that self-reported gum bleeding was strongly related to the measured CPI score. However, the above-mentioned study used only questionnaire-based data and therefore no lung function data were available. In another study by Heinrich et al. (2019), 1000 adolescents from two birth cohorts in the years 1995–1999 were followed up at the age of 15 with thorough dental examination and spirometry. The authors reported that those who had gingival bleeding in at least three out of six segments in the oral cavity had lower lung function, FEV<sub>1</sub> and FVC, compared with those who did not have any gingival bleeding. These results are consistent with our findings,

which showed that participants with BoP > 25% had lower %predicted FEV<sub>1</sub> and FVC compared with subjects having BoP < 25%.

The strength of this study includes the homogeneity of the study population with respect to ethnicity, age and sex. The population is relatively young with an average age of 44.6 years, an overall good lung function and few comorbidities. However, in an older population there are possibly more individuals with severe periodontitis but presumably also more confounding risk factors. Another strength is the full-mouth periodontal examination including registration of BoP, which is used to assess periodontitis and periodontal inflammation status. This provides accurate information about the presence and distribution of disease at the point of lung function assessment. Rather than presence or absences of disease, levels of severity give important information to understand how progression of periodontitis may impact lung health. To our knowledge, gingival inflammation has not been clinically assessed by the extent of BoP in the previously mentioned studies (Gómez Real et al., 2016; Heinrich et al., 2019) but only as self-reported gum bleeding or segment bleeding.

Using data from the Swedish Dental Health Register, we investigated whether subjects included in the MODS received a different amount of periodontitis treatment compared with those in the MOS cohort. Our findings did not reveal any statistically significant differences in the amount of periodontal treatment between the MODS and MOS participants ( $p = .1$ ) as assessed by the Mann–Whitney  $U$  test (data not shown).

Even though the MODS dataset has information on a wide range of potential confounding factors such as smoking, BMI and FPG levels, the potential of residual confounding by other factors can never be completely ruled out. One limitation of our analyses was missing information of ‘pack-years’ and ‘time since smoking’ in a subset of



the population. The 'Number of cigarettes per day' was available in current smokers only. However, using both 'smoking status' and 'cigarettes per day' as covariates would probably cause an overfitting of the regression models.

An additional weakness was that only periodontal pockets of >2 mm were recorded, and no calibration study such as repeated inter-correlation was performed prior to study initiation. Socio-economic status (SES) seems to be a significant factor in the association between periodontitis and lung function, as it has a role in access to medical and dental health care. In the present study, we adjusted for educational level as a proxy for SES. Adding SES covariates may have improved the aspect; however, it could also have caused an overfitting of the models. Unfortunately, in the present project, apart from educational level, no other SES covariates were available. Another potential limitation is the fact that we only have pre-bronchodilatory spirometry, whereas post-bronchodilatory spirometry would have been useful for assessing the association with chronic airflow limitation. This is, however, a limitation shared by all other published studies on the relation between periodontitis and lung function.

## 5 | CONCLUSIONS

In conclusion, severe periodontitis was found to be associated with lower values of FEV<sub>1</sub>/FVC in a population of middle-aged Swedish adults. Furthermore, gingival inflammation appears to be mainly associated with lower lung volumes. We can only speculate on the reason for different relations of BoP and periodontitis with impaired lung function. Potential explanations might be that different bacteria and different inflammatory mechanisms are related to BoP and periodontitis. However, this has not been specifically studied within the present study or systematically in the literature. Owing to the cross-sectional study design, a cause-effect relationship could not be established between severe periodontitis, gingival inflammation and lower lung function. The relevance of this 2% lower FEV<sub>1</sub>/FVC ratio in periodontitis patients remains to be established. However, it might be relevant, as these individuals will have lower margins until reaching the LLN and develop airflow obstruction. To validate the observed associations and gain a closer understanding of causality, future research should involve large cohort studies with extended observation periods. It is strongly recommended that these studies thoroughly consider and address potential confounders while also conducting analyses solely on never-smoking individuals. Intervention studies and RCTs are necessary to investigate whether the prevention or treatment of periodontitis could potentially yield positive effects on lung function.

### AUTHOR CONTRIBUTIONS

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### CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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