Original Paper

Chronic Respiratory Disease

The association between dental health and nutritional status in chronic obstructive pulmonary disease

Chronic Respiratory Disease
2017, Vol. 14(4) 334–341

DOI: 10.1177/1479972316643076
journals.sagepub.com/home/crd
SAGE

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Abstract

Chronic obstructive pulmonary disease (COPD) and periodontitis are chronic inflammatory systemic diseases with common risk factors (smoking and aging). In COPD, poor periodontal health could result in inadequate nutrition, potentially causing loss of muscle volume. The purpose of this case-control study was to examine our hypothesis that COPD patients have poorer periodontal health and poorer nutritional status than non-COPD patients. Periodontal status was assessed using bleeding on probing (BOP), pocket depth (PD), and plaque–control ratio (PCR). Nutritional status was assessed using body mass index, lean body mass, and serum albumin levels. The COPD group ($n = 60$) had fewer remaining teeth, greater BOP, greater PD, and lower serum albumin levels compared with smokers without COPD ($n = 41$) and nonsmokers ($n = 35$; $p < 0.001$). COPD was an independent risk factor for poor periodontal health, demonstrated by fewer remaining teeth (relative risk (RR), 5.48; $p = 0.0024$), BOP (RR, 12.8; $p = 0.0009$), and having >30% of remaining teeth with a PD $\geq$ 4 mm (RR, 4.82; $p = 0.011$). A significant negative correlation existed between the number of teeth with a PD $\geq$ 4 mm and serum albumin level ($r^2 = 0.127$; $p = 0.013$). We demonstrated that poor periodontal health was associated with hypoalbuminemia, suggesting poor nutritional status and inflammation in COPD.

Keywords

Periodontitis, COPD, pocket depth, bleeding on probing, hypoalbuminemia

Introduction

Chronic obstructive pulmonary disease (COPD) is currently considered a systemic inflammatory disease. COPD manifests not only as airflow limitations but also as systemic symptoms related to various comorbidities such as cardiovascular diseases, psychiatric diseases, and osteoporosis that potentially worsen quality of life (QOL). The goal for COPD management should be improving QOL in addition to physiological state and lung function.

Periodontitis is a chronic inflammatory reaction induced by bacterial infections, which results in destruction of the supporting connective tissue and ultimately leads to tooth loss. Recent reports have indicated that periodontitis is associated with several other systemic diseases including diabetes and cardiovascular diseases.[1,2] Further, smoking is one of the most common contributing factors in the pathogenesis

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of COPD and periodontitis. Although previous studies have investigated the association between COPD and periodontitis,[3] the findings remain inconclusive.[4]

Several factors have been linked with health status in COPD. Body mass index (BMI) has been shown to be an independent prognostic factor for COPD.[5] Further, body composition has been shown to be associated with exercise performance in COPD patients,[6] and exercise tolerance has been associated with serum albumin concentrations.[7] Good oral health is likely important in maintaining adequate nutrition; conversely, poor oral health could result in inadequate nutrition and therefore decreased muscle volume in COPD patients.

We hypothesized that COPD patients have poorer periodontal health than people without COPD and that COPD patients who have poor periodontal health have poorer nutritional status. Therefore, we conducted a case-control study to examine the association between periodontal status and COPD and between periodontal status and nutritional status in COPD patients.

Materials and methods

Study population and design

Patients with COPD were recruited from Tokyo Dental College, Ichikawa General Hospital. Current or previous smokers with a forced expiratory volume in 1 second ($FEV_{1.0}$)/forced vital capacity < 0.7 constituted the COPD group. All COPD patients ($n = 60$) were clinically diagnosed by pulmonary physicians, and their diagnosis was confirmed with a pulmonary function test. From the same hospital, nonsmokers ($n = 35$) and smokers ($n = 41$) without COPD were selected from participants who had normal pulmonary function. The nonsmoking group included never-smokers and those with no pulmonary disease history. Meanwhile, we also created a group of smokers without COPD that comprised current or previous smokers without any pulmonary disease history. Patients who had diabetes, malignant neoplasms within the past 3 years, or other serious diseases were excluded.

Ethics statement

The ethics committee of Tokyo Dental College (No. 268) approved the study protocol, and written informed consent was obtained from each patient.

Pulmonary function and clinical examinations

Spirometry was performed for all patients who were in a stable condition using an electronic spirometer (Auto spirometer system 7, Minato Medical Science Corporation, Osaka, Japan) according to the guidelines of the American Thoracic Society.[8]

The nurses measured the anthropometric variables including height and weight, which were used to calculate BMI. The body fat ratio was also measured using a body composition monitor (Inner Scan 50, Tanita Corporation, Tokyo, Japan). Lean body mass (LBM) was calculated by subtracting fat weight from total body weight. For the COPD patients, the degree of dyspnea was evaluated using the Medical Research Council (MRC) dyspnea scale, which was scored from 0 to 4, and severity was based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage.[8]

Blood examinations

Serum albumin levels were used to assess nutritional status and were measured using the bromocresol green method (LSI Medience, Tokyo, Japan), with a detection limit of 0.1–6 g/dL. C-reactive protein (CRP) was assessed using a latex-enhanced immunoturbidimetric assay (Nittobo Medical, Tokyo, Japan) with a lower detection limit of 0.01 mg/dL.

Chest radiography and computed tomography

Chest images were obtained using a computed radiography technique. Patients with COPD underwent a 64-slice helical computed tomography (CT) examination of the chest. As already mentioned, COPD was diagnosed based on airway limitation, as assessed using spirometry. Chest radiograph and CT characteristics were used to confirm the COPD diagnosis and exclude differential diagnoses such as bronchiectasis and diffuse panbronchiolitis.

Dental examination

Trained dentists who were blinded to the patients' pulmonary function conducted the dental examinations, which focused on periodontal health status and included assessments regarding the number of remaining teeth, periodontal pocket depth (PD), gingival bleeding, and dental plaque as measures for oral hygiene standards. PD was measured with a millimeter-graduated probe. According to the classifications of periodontitis used in the US Third

National Health and Nutrition Examination Survey, a PD $\geq$ 4 mm was arbitrarily chosen as a cutoff point to define periodontitis for a tooth, and patients with >30% of their remaining teeth with a PD $\geq$ 4 mm were designated as having moderate or severe periodontitis.[9,10] The plaque–control ratio (PCR) was assessed following erythrosine staining on four supragingival surfaces per tooth and expressed as a percentage of plaque-positive surfaces. Estimations of gingival inflammation severity were based on the gingival bleeding propensity upon probing in conjunction with the PD measurement. The presence or absence of bleeding on probing (BOP) was assessed within 30 seconds following probing with gentle pressure.

Statistical analysis

Data are presented as mean $\pm$ standard deviation. Group means for PCR and PD were based on intraindividual means (case means). Statistical analysis was performed for comparisons among the three groups using a multifactorial analysis of variance and Tukey–Kramer honestly significant difference test for post hoc multiple comparisons. Categorical variables were tested following a χ^2distribution with Pearson's correction.

The relative risk (RR) was estimated using both univariable and multivariable logistic regression analyses including the number of remaining teeth (<20 or $\geq$20), BOP (yes or no), and PD (<30% or $\geq$30% of remaining teeth with a PD $\geq$ 4 mm) as dependent variables. Age (<65, 65–74, and $\geq$75 years), smoking index (0, 0–30, 30–60, and >60 pack-years), and COPD (yes or no) were the independent variables.

The associations between the periodontal indices and BMI, LBM, albumin level, and CRP level were assessed using linear regression analyses. In addition, the relationship between serum albumin level and CRP level was assessed.

A p value <0.05 was considered significant. All data were analyzed using JMP software, version 9.0.2, for Windows (SAS Institute Japan, Tokyo, Japan).

Results

Basic characteristics and demographics

The basic demographic characteristics of the study population are presented in Table 1. The COPD patients were significantly older than the patients in the other two groups. The proportions of men were significantly higher in the COPD and smokers without COPD groups than in the nonsmoking group. The COPD group included 2 current smokers, 57 ex-smokers, and 1 never-smoker. The cumulative tobacco smoke exposure was higher in the COPD group than in the smokers without COPD group. As expected, the $FEV_{1.0}$% predicted in the COPD group was significantly lower than that of the other two groups. The $FEV_{1.0}$% predicted did not differ between smokers and nonsmokers without COPD. No differences existed in the mean BMIs for the three groups. The LBM of the nonsmokers was significantly lower than that of the other two groups. The serum level of albumin, but not CRP, in the COPD group was significantly lower than that of the other two groups.

The basic characteristics of the COPD patients are presented in Table 2. Based on the GOLD stage,[8] we identified 21 mild COPD (stage I), 25 moderate COPD (stage II), 9 severe COPD (stage III), and 5 very severe COPD (stage IV) patients. Smoking index, BMI, LBM, and serum albumin levels did not differ among the COPD stages. The mean MRC dyspnea scale for stage III patients was significantly greater than that with stages I and II.

Dental status and periodontal status

The dental status of the three groups is presented in Table 3. Compared with the other two groups, the number of remaining teeth was significantly lower in the COPD group, the percentage of patients with a positive BOP was significantly higher, and the mean PD was significantly greater in the COPD group. Although there were no significant differences in the number of teeth with a PD $\geq$ 4 mm, the percentage of teeth with a PD $\geq$ 4 mm was higher in the COPD group than in the other two groups.

Based on the univariable logistic regression analysis, the unadjusted RRs for <20 remaining teeth were 13.7 (95% confidence interval (95% CI), 4.74–44.2; $p < 0.0001$) for age $\geq$75 years, versus <65 years; 8.33 (95% CI, 2.96–26.6; $p < 0.0001$) for a smoking index >60 versus an index of 0; and 11.3 (95% CI, 5.15–26.4; $p < 0.0001$) for COPD, versus without COPD. The unadjusted RRs for a positive BOP were 0.45 (95% CI, 0.13–1.35) for age $\geq$75 years, versus <65 years; 4.00 (95% CI, 1.22–15.7; $p = 0.02$) for a smoking index >60, versus an index of 0; and 6.05 (95% CI, 2.32–19.0; $p < 0.0001$) for COPD, versus without COPD. The unadjusted RRs for having >30% of remaining teeth with a PD $\geq$ 4 mm were 5.50 (95%

Table 1. Basic characteristics of the study population.[a]

Characteristics	COPD ($n = 60$)	Smokers ($n = 41$)	Nonsmokers ($n = 35$)
		Non-COPD ($n = 76$)	
Age (years)	73.9 ± 7.6[b,c]	66.2 ± 5.8	63.9 ± 5.7
		65.1 ± 5.8	
Gender (male/female)	55:5[c]	37:4[c]	12:23
		49:27	
Smoking (pack-years)	68.9 ± 36.6[b,c]	34.7 ± 26.9[c]	0
		18.7 ± 26.3	
$FEV_{1.0}$% predicted	70 ± 28[b,c]	104 ± 16	108 ± 17
		106 ± 17	
FEV1.0/FVC	54.1 ± 10.5[b,c]	78.5 ± 4.6	79.8 ± 5.1
		79.1 ± 4.8	
BMI (kg/m^2)	23.0 ± 3.3	24.4 ± 4.0	23.5 ± 3.0
		24.0 ± 3.6	
LBM (kg)	47.8 ± 8.0[d]	49.9 ± 8.6[d]	42.6 ± 7.9
		46.6 ± 9.0	
Serum albumin (g/dL)	4.13 ± 0.35[b,c]	4.32 ± 0.23	4.42 ± 0.18
		4.37 ± 0.21	
Serum CRP (mg/dL)	0.15 ± 0.14	0.13 ± 0.13	0.13 ± 0.17
		0.13 ± 0.15	

COPD: chronic obstructive pulmonary disease; $FEV_{1.0}$: forced expiratory volume in 1 second; FVC: forced vital capacity; BMI: body mass index; LBM: lean body mass; CRP: C-reactive protein.
[a]Data are presented as mean ± standard deviation. p values were obtained from one-way ANOVA for continuous variables and χ^2 tests for categorical variables.
[b]$p < 0.0001$, compared with smokers without COPD.
[c]$p < 0.0001$, compared with nonsmokers.
[d]$p < 0.05$, compared with nonsmokers.

Table 2. Basic characteristics of patients with COPD.[a]

Characteristics	GOLD COPD stage			
	I: Mild ($n = 21$)	II: Moderate ($n = 25$)	III: Severe ($n = 9$)	IV: Very severe ($n = 5$)
Smoking index (pack-years)	61.1 ± 40.1	65.8 ± 33.5	91.3 ± 28.9	78.7 ± 40.1
MRC dyspnea scale	1.0 ± 0.8	1.2 ± 1.1	3.0 ± 1.0[b]	2.0 ± 1.6
BMI (kg/m^2)	23.8 ± 2.8	22.3 ± 2.9	22.5 ± 4.3	23.0 ± 5.0
LBM (kg)	49.3 ± 6.8	46.7 ± 9.1	46.3 ± 9.2	49.4 ± 5.7
Serum albumin (g/dL)	4.20 ± 0.29	4.00 ± 0.37	4.23 ± 0.39	4.33 ± 0.22

COPD: chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Lung Disease; MRC: Medical Research Council; BMI: body mass index; LBM: lean body mass; ANOVA: analysis of variance.
[a]Data are presented as mean ± standard deviation. p values were obtained from one-way ANOVA for comparisons among the groups.
[b]$p < 0.001$, compared with stages I and II.

CI, 2.00–16.2; $p = 0.0008$) for age ≥75 years, versus <65 years; 5.81 (95% CI, 2.10–17.3; $p = 0.0005$) for a smoking index >60, versus an index of 0; and 6.18 (95% CI, 2.85–14.0; $p < 0.0001$) for COPD, versus without COPD.

In the multivariable regression analysis, COPD was the only statistically significant factor for poor dental status (Table 4): <20 remaining teeth (adjusted RR, 5.48; 95% CI, 1.81–17.9; $p = 0.0024$), positive BOP (adjusted RR, 12.8; 95% CI, 2.64–97.9; $p = 0.0009$), and having >30% of remaining teeth with a PD ≥ 4 mm (adjusted RR, 4.82; 95% CI, 1.43–17.6; $p = 0.011$).

In the linear regression analysis, there were no significant correlations between any of the periodontal indices and BMI or LBM (Table 5). A significant

Table 3. Dental status.[a]

Characteristics	COPD ($n = 60$)	Smokers ($n = 41$)	Nonsmokers ($n = 35$)	Non-COPD ($n = 76$)
Number of remaining teeth	12.3 ± 9.7[b,c]	22.1 ± 7.2	23.4 ± 6.3	22.7 ± 6.8
Percentage of patients with a positive BOP	90.6[b,c]	57.5	65.7	61.3
PD (mm)	3.8 ± 1.1[b,c]	3.0 ± 0.6	2.9 ± 1.1	3.0 ± 0.9
Number of teeth with a PD $\geq$ 4 mm	5.8 ± 5.2	4.4 ± 3.7	4.4 ± 4.8	4.4 ± 4.2
Percentage of teeth with a PD $\geq$ 4 mm	49.2 ± 34.3[b,c]	20.2 ± 17.2	19.8 ± 22.6	20.0 ± 19.7
Percentage of patients with >30% of remaining teeth with a PD $\geq$ 4 mm	70.0[b,c]	25.6	29.4	27.4

BOP: bleeding on probing; PD: pocket depth; ANOVA: analysis of variance; COPD: chronic obstructive pulmonary disease.
[a]Data are presented as mean ± standard deviation. p values were obtained from one-way ANOVA for continuous variables and χ^2 tests for categorical variables.
[b]$p < 0.001$, compared with smokers without COPD.
[c]$p < 0.001$, compared with nonsmokers.

Table 4. Multivariable logistic regression analysis to identify significant factors for poor dental health.

	<20 remaining teeth		Positive BOP		Having >30% of remaining teeth with a PD $\geq$ 4 mm	
	RR [95% CI]	p Value	RR [95% CI]	p Value	RR [95% CI]	p Value
Age						
$\geq$75 versus <65 years	3.27 [0.84–13.3]	0.08	0.27 [0.03–1.59]	0.15	1.50 [0.37–6.01]	0.57
Versus 65–74 years	1.61 [0.51–5.25]	0.42	0.32 [0.04–1.71]	0.19	0.75 [0.21–2.61]	0.65
Smoking index (pack-years)						
>60 versus 0	1.57 [0.39–6.40]	0.53	1.14 [0.28–5.24]	0.86	1.54 [0.40–5.92]	0.53
Versus 0–30	2.01 [0.59–6.95]	0.26	1.42 [0.33–6.62]	0.64	2.35 [0.64–8.72]	0.19
Versus 30–60	0.73 [0.22–2.29]	0.59	2.46 [0.59–11.4]	0.22	2.34 [0.70–8.03]	0.17
COPD, yes/no	5.48 [1.81–17.9]	0.0024	12.8 [2.64–97.9]	0.0009	4.82 [1.43–17.6]	0.011

BOP; bleeding on probing; PD: pocket depth; RR: relative risk; CI: confidence interval.

correlation existed between serum albumin level and the number of teeth with a PD $\geq$ 4 mm ($r^2 = 0.127$; $p = 0.013$; Table 6). CRP level was not significantly correlated with any of the periodontal indices or with serum albumin ($p = 0.65$). Correlations between the periodontal indices and serum albumin or CRP level were not observed in the nonsmokers or smokers without COPD.

Discussion

To our knowledge, this is the first study to evaluate the association between periodontal status and nutritional status in patients with COPD. Poor periodontal status was associated with a low serum albumin level in COPD patients, suggesting relationships between periodontal status and nutritional status and inflammation in COPD patients. Furthermore, COPD itself was a significant factor for periodontitis.

The rate of albumin synthesis is affected by both nutrition and inflammation. Therefore, hypoalbuminemia could be the result of inadequate protein and caloric intake and/or inflammation in patients with chronic disease.[11] In patients with COPD, serum albumin levels have been associated with exercise tolerance and the length of hospitalization.[7,12] Reduced protein intake by COPD patients who have reduced chewing function secondary to periodontitis might

Table 5. Linear regression analysis for body composition based on periodontal indices in patients with COPD.

	BMI		LBM	
Periodontal index	r^2	p	r^2	p
Number of remaining teeth	0.004	0.628	0.008	0.517
PCR	0.081	0.052	0.072	0.067
BOP	0.043	0.155	0.022	0.316
Number of teeth with a PD $\geq$ 4 mm	0.005	0.645	0.0002	0.936

COPD: chronic obstructive pulmonary disease; BMI; body mass index; LBM: lean body mass; PCR: plaque–control ratio; BOP: bleeding on probing; PD: pocket depth.

Table 6. Linear regression analysis for serum albumin and CRP levels based on periodontal indices in patients with COPD.

	Serum albumin level		Serum CRP level	
Periodontal index	r^2	p	r^2	p
Number of remaining teeth	0.019	0.344	0.001	0.926
PCR	0.002	0.795	0.005	0.633
BOP	0.021	0.324	0.012	0.479
Number of teeth with a PD $\geq$ 4 mm	0.127	0.013	0.002	0.786

COPD: chronic obstructive pulmonary disease; CRP: C-reactive protein; PCR: plaque–control ratio; BOP: bleeding on probing; PD: pocket depth.

explain the correlation between periodontal status and serum albumin levels.[13,14] Another possible explanation is oral deep-pocket bacterial inflammation. However, inadequate protein was more likely the reason for hypoalbuminemia in the present study, because CRP was not associated with the periodontal indices or serum albumin levels in the COPD group. To explore this possibility further, other inflammatory markers, such as interleukin-6, should be measured.

In our case-control study, periodontal status was assessed using the number of remaining teeth, a positive BOP, and the degree of PD. The COPD group had a poorer periodontal status than non-COPD smokers and nonsmokers. These findings were consistent with previous studies that demonstrated an association between periodontal status and COPD.[15,16] Moreover, in our study, COPD was the only independent risk factor for poor periodontal status after adjusting for established risk factors such as age and smoking index. Given that most of the patients with COPD were ex-smokers, the pathophysiology of COPD, rather than the direct effects of smoking exposure, might have contributed to the periodontitis.[15]

Although the precise mechanisms regarding the association between periodontitis and COPD remain uncertain, the proposed mechanisms include the colonization of dental plaque by respiratory pathogens, followed by aspiration, periodontitis-induced chronic inflammatory mediators, and host susceptibility to cigarette smoke.[15] Furthermore, personal dental care is a surrogate marker for general health behavior, and patients with less interest in health might have little motivation to stop smoking or to maintain appropriate dental care. To that end, Wang et al. reported that COPD patients had a decreased level of personal dental care such as frequency of tooth brushing and number of dental visits as well as less dental health knowledge.[16] In addition to aging and cigarette smoke exposure, little interest in self-health and poor personal health behaviors may be common risk factors for both COPD and periodontitis. However, our study was not designed to elucidate the involved mechanisms; therefore, further investigation is needed.

The COPD group in the present study also had fewer remaining teeth, as compared with the other two groups. Additionally, COPD was an independent risk factor for patients to have <20 remaining teeth, after controlling for age and smoking index. For elderly Japanese persons, dietary intake is lower in patients with <20 remaining teeth.[14] In another report that surveyed adults aged $\geq$65 years, patients with $\geq$21 natural teeth had a greater daily intake of nutrients.[17] Therefore, fewer remaining teeth may result in underweight or malnutrition in COPD patients;

however, the number of remaining teeth was not significantly associated with BMI or serum albumin level in our study. It is difficult to evaluate periodontal status with few remaining teeth because severe periodontitis is the primary reason for missing teeth, but the focus of inflammation disappears after the teeth are lost. We believe that missing teeth influences dietary intake and the degree of periodontitis of the remaining teeth would contribute to the inflammation.

In the present study, PD was the main determinant of periodontal disease because PD is most commonly used as a periodontal disease variable.[9] To assess periodontal health status, we divided PD into two categories: <4 mm or ≥4 mm. According to a review by Greenstein, a PD ≥ 4 mm increases bacterial proliferation and is associated with an environment that is highly positive for bacteria.[18]

The main strength of this study was that pulmonary physicians clinically diagnosed the patients with COPD, which was confirmed with a pulmonary function test, and chest images were used to exclude differential diagnoses. Further, senior dentists precisely assessed dental status. To our knowledge, this is the first study demonstrating an association between periodontitis and nutritional status in COPD.

This study had some limitations. First, periodontal status demonstrated no association with BMI or LBM in our study. One explanation is that the COPD population consists of a subgroup of patients with depleted LBM and a subgroup of patients with obesity and metabolic syndrome.[19] Second, as a case-control study, the results of our study could not provide evidence of a causal effect between periodontal health and nutritional status in COPD. For COPD patients, recent studies demonstrated that periodontal therapy could prevent a decline in pulmonary function and decrease exacerbation frequency.[20,21] To prove whether periodontal interventions could improve nutritional status and affect the progression of COPD, randomized controlled trials should be conducted. Third, we cannot exclude the possibility of residual and confounding effects or effect modification by other healthy lifestyle variables. Fourth, other inflammatory markers should be measured to clarify the contribution of inflammation to hypoalbuminemia.

Conclusion

Our study showed that COPD was an independent risk factor for poor periodontal health status, as assessed by fewer remaining teeth, a positive BOP, and a greater PD. Moreover, to our knowledge, this is the first study to describe that poor periodontal health was associated with lower serum albumin levels in patients with COPD. Our findings suggest that periodontal status may be associated with the natural course of COPD via nutritional status and inflammation.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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