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Risk of Periodontal Diseases in Patients With Chronic Obstructive Pulmonary Disease

A Nationwide Population-based Cohort Study

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Abstract: Several studies have reported an association between chronic obstructive pulmonary disease (COPD) and periodontal diseases. However, a large-scale population-based cohort study was previously absent from the literature. Therefore, we evaluated the risk of periodontal diseases in patients with COPD in a nationwide population.

From the National Health Insurance claims data of Taiwan, we identified 22,332 patients with COPD who were newly diagnosed during 2000 to 2010. For each case, two individuals without COPD were randomly selected and frequency matched by age, sex, and diagnosis year. Both groups were followed up till the end of 2011.

The overall incidence of periodontal diseases was 1.19-fold greater in the COPD group than in the comparison group (32.2 vs 26.4 per 1000 person-years; 95% confidence interval [CI] 1.15–1.24). Compared with non-COPD patients, the adjusted hazard ratios of patients with COPD increased with the number of emergency room visits (from 1.14 [95% CI 1.10–1.19] to 5.09 [95% CI 4.53–5.72]) and admissions (from 1.15 [95% CI 1.10–1.20] to 3.17 [95% CI 2.81–3.57]). In addition, the adjusted hazard ratios of patients with COPD treated with inhaled corticosteroids (1.22, 95% CI 1.11–1.34) and systemic corticosteroids (1.15, 95% CI 1.07–1.23) were significantly higher than those of patients not treated with corticosteroids.

Patient with COPD are at a higher risk of developing periodontal diseases than the general population. Our results also support that the risk of periodontal diseases is proportional to COPD control. In addition, patients who receive corticosteroid treatment are at a higher risk of developing periodontal diseases.

(*Medicine* 94(46):e2047)

Abbreviations: CAD = coronary artery disease, CD8 = cluster of differentiation 8, CI = confidence interval, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, ER = emergency room, HR = hazard ratio, ICD-9-CM = International Classification of Disease 9th Revision Clinical Modification, LHID2000 = Longitudinal Health Insurance Database 2000, NHI = National Health Insurance, NHRI = National Health Research Institutes.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by persistent and usually progressive airflow limitation and is associated with an enhanced chronic inflammatory response in the airways and the lungs. Comorbidities that occur frequently in patients with COPD include certain infections, cardiovascular diseases, diabetes, metabolic syndrome, skeletal muscle dysfunction, osteoporosis, anxiety, depression, impaired cognitive function, and lung cancer.[1] These comorbid conditions can have a significant impact on the prognosis of the disease.

Periodontal diseases are defined as any disorder of the tissues surrounding and supporting the teeth; the term usually refers to the inflammatory disorders of gingivitis and periodontitis.[2] These diseases are highly prevalent and may affect up to 90% of the worldwide population.[3] They are mainly caused by the bacterial biofilm that accumulates on the teeth, but other genetic and environmental factors also contribute to the conditions.[4,5] Compared with COPD, similar comorbid diseases such as cardiovascular diseases, diabetes, and osteoporosis have been reported in association with periodontal diseases.[6–8]

Patients who have an underlying respiratory disorder may face some special challenges in establishing and maintaining oral health. These factors include the illness itself and the associated medical therapies.[9] Several studies have reported the association between COPD and periodontal diseases.[10–14] For example, Zeng et al[12] recently performed a meta-analysis using 14 observational studies and identified a significant association between periodontal diseases and COPD (odds ratio (OR) 2.08, 95% confidence interval [CI] 1.48–2.91, $P < 0.001$).

Editor: Martin Samantha.
Received: August 20, 2015; revised: October 2, 2015; accepted: October 21, 2015.
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Funding: This study was supported in part by Taiwan Ministry of Health and Welfare Clinical Trial and Research Center of Excellence (MOHW104-TDU-B-212-113002), China Medical University Hospital (1MS1), Academia Sinica Taiwan Biobank, Stroke Biosignature Project (BM104010092), NRPB Stroke Clinical Trial Consortium (MOST 103–2325-B-039–006), Tseng-Lien Lin Foundation, Taichung, Taiwan, Taiwan Brain Disease Foundation, Taipei, Taiwan, and Katsuzo and Kiyo Aoshima Memorial Funds, Japan.
Conception and design: TCS, PYC, CHC, and CYT; administrative support: TCH, CMS, WHH, FCS, and CHK; collection and assembly of data: all authors; data analysis and interpretation: TCS, CLL, FCS, and CHK; manuscript writing: TCS, PYC, CLL, FCS, and CHK; final approval of manuscript: all authors.
There are no conflicts of interests.

ISSN: 0025-7974
DOI: 10.1097/MD.0000000000002047

However, most of these studies were cross-sectional or case-control studies. Cohort study designs were lacking in the literature and the direction from COPD to the incident periodontal diseases was rarely evaluated.

The National Health Insurance (NHI) database of Taiwan is a nationwide database with cohort data on 23 million people. These reliable data have been used for various studies, including those on COPD and periodontal diseases.[15–18] The aim of the present study was to use the data from the NHI database to determine if patients with COPD are at a higher risk of developing periodontal diseases.

MATERIALS AND METHODS

Data Source

This cohort study used outpatient and inpatient claims from the Longitudinal Health Insurance Database 2000 (LHID2000) from 1996 to 2011, which is released by the National Health Research Institutes (NHRI). The NHI is a government, compulsory-enrolment, single-payer system that had a coverage rate of >99% by the end of 2004. The LHID2000 contains all claims data of 1 million insurants (approximately 4.35% of the total population) who were randomly selected from the 2000 Registry for Beneficiaries. The age, sex, and healthcare costs of the LHID2000 dataset and all NHI enrollees did not differ significantly. Informed consent was not required because this was a secondary data analysis. This study was exempted by the Institutional Review Board of China Medical University in central Taiwan (CMUH-104-REC2–115).

Sampled Participants

The COPD group included participants with COPD (International Classification of Disease, 9th Revision, Clinical Modification [ICD-9-CM] codes 491, 492, 496) who were newly diagnosed from 2000 to 2010. The date of the first medical visit for COPD was identified as the index date. Patients with a history of periodontal diseases (ICD-9-CM code 523) before the index date and those with incomplete age or sex information were excluded from the study. The comparison group included individuals without a history of COPD or periodontal diseases who were randomly selected from the claims data. For the non-COPD comparison cohort, we used an approximately 1:2 frequency matching design for each COPD case, matching for sex, age, and index year.

Outcome and Comorbidity

The main outcome was new diagnosis with periodontal diseases during the follow-up. Participants were followed from the index date to the current date of periodontal diseases, the date of withdrawal from the insurance, to the point where they were censored because of death, or the end date of the database (December 31, 2011). For each participant, a record of comorbidities before the index date was obtained; comorbidities included hypertension (ICD-9-CM codes 401–405), diabetes (ICD-9-CM code 250), hyperlipidemia (ICD-9-CM code 272), asthma (ICD-9-CM code 493), coronary artery disease (CAD, ICD-9-CM codes 410–414), chronic kidney disease (CKD, ICD-9 code 585), and stroke (ICD-9-CM codes 430–438).

Statistical Analysis

Demographic characteristics and baseline comorbidities were compared between the COPD cohort and non-COPD comparison cohort. The chi-square test was used for categorical variables and the Student *t* test was used for continuous variables. We computed the incidence densities rate (per 1000 person-years) by dividing the number of events of current periodontal diseases by the person-years of exposure for each participant. We used univariable and multivariable models to calculate the hazard ratios (HRs) and 95% CIs, with Cox proportional-hazards regression models being applied. Multivariable models were adjusted for age, sex, and the comorbidities of hypertension, diabetes, hyperlipidemia, asthma, CAD, CKD, and stroke. We assessed the cumulative incidence of periodontal diseases between the COPD cohort and non-COPD comparison cohort by using the Kaplan–Meier method, and we estimated their differences using a log-rank test. All analyses were conducted with SAS statistical software (version 9.3 for Windows; SAS Institute, Inc., Cary, NC) and the significance level was set at $P < 0.05$ for the 2-tailed tests.

RESULTS

The demographic characteristics and comorbidities of the COPD cohort (n = 22,332) and non-COPD comparison cohort (n = 43,762) are shown in Table 1. There were more men than women in both cohorts. In the COPD cohort, approximately 54.0% of the patients were aged >65 years and the mean age was 63.9 (standard deviation [SD] 15.8). Patients with COPD had a higher prevalence of all comorbidities than did the non-COPD comparison cohort ($P < 0.001$). The mean number of follow-up years for the COPD and non-COPD cohorts was 5.49 and 5.95 years, respectively. Figure 1 shows that the cumulative incidence of periodontal diseases in the COPD cohort was

TABLE 1. Demographic Characteristics and Comorbidity in Patients With and Without Chronic Obstructive Pulmonary Disease

	COPD				
	No (n = 43762)		Yes (n = 22332)		
Variables	n	%	n	%	*P* value*
Sex					0.05
Female	18453	42.2	9238	41.4	
Male	25309	57.8	13094	58.6	
Age, y					0.07
20–49	9048	20.7	4524	20.3	
50–64	11490	26.3	5745	25.7	
≥65	23224	53.1	12063	54.0	
Mean (SD)*	62.8	(15.7)	63.9	(15.8)	<0.001
Comorbidity					
Hypertension	17414	39.8	12168	54.5	<0.001
Diabetes	4385	10.0	2873	12.9	<0.001
Hyperlipidemia	7141	16.3	4811	21.5	<0.001
Asthma	1243	2.8	3579	16.0	<0.001
CAD	7397	16.9	6524	29.2	<0.001
CKD	3493	8.0	2701	12.1	<0.001
Stroke	2728	6.2	2635	11.8	<0.001

CAD = coronary artery disease, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease.
Chi-square test.
* Two sample *t* test.

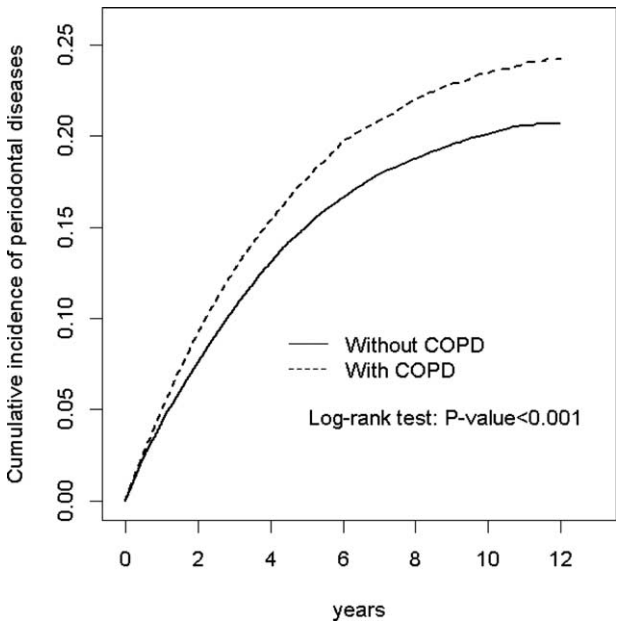

FIGURE 1. Cummulative incidence of periodontal diseases between patients with and without chronic obstructive pulmonary disease (COPD).

higher than that in the non-COPD comparison cohort (log-rank test, $P < 0.001$).

The overall incidence density of periodontal diseases was significantly higher in patients with COPD than in the non-COPD cohort (32.2 vs 26.4 per 1000 person-years), and an adjusted HR (aHR) of 1.20 (95% CI 1.15–1.25) was calculated (Table 2). The individuals with COPD were associated with a significantly increased risk of periodontal diseases relative to those without COPD according to the following factors: female sex (HR 1.18, 95% CI 1.11–1.26), male sex (HR 1.21, 95% CI 1.15–1.28), 3 age groups (HR 1.20, 1.20, and 1.18, respectively), and being with or without comorbidity (HR 1.24 and 1.10, respectively).

Compared with patients without COPD, patients with COPD tended to have an increased risk of developing periodontal diseases when they visited an emergency room (ER) less than once per year, and the risk increased significantly in patients who visited the ER more than once (HR 5.09, 95% CI 4.53–5.72) (Table 3). Compared with participants in the non-COPD comparison cohort, the risk of periodontal disease development increased from 1.15 (95% CI 1.10–1.20) in patients with COPD presenting with one or fewer hospitalization to 3.17 (95% CI 2.81–3.57) in patients hospitalized more than once.

To examine the combined effects of COPD and associated treatments, we divided the COPD cohort into 3 subgroups according to the treatment received by patients (Table 4). Compared with patients who did not receive treatment with corticosteroids, patients with COPD who inhaled corticosteroids exhibited a higher risk of periodontal diseases (HR 1.22, 95% CI 1.11–1.34), as did patients with COPD who received treatment with systemic corticosteroids (HR 1.15, 95% CI 1.07–1.23).

DISCUSSION

To the best of our knowledge, this is the first nationwide population-based cohort study evaluating patients with COPD and their subsequent risk of developing periodontal diseases. The study demonstrates that there is an increased risk of periodontal diseases in patients with COPD compared with people in the general population. Furthermore, we found that aHRs were similar in both sexes and different age groups, but aHRs were slightly higher in patients without comorbidities

TABLE 2. Incidence and Hazard Ratios of Periodontal Diseases for COPD Group Compared With Non-COPD Group by Demographic Characteristics and Comorbidity

	COPD							
	No (n = 43762)			Yes (n = 22332)				
Variables	Event	Person-years	Rate[$]	Event	Person-years	Rate[$]	Crude HR (95% CI)	Adjusted HR[*] (95% CI)
Total	6883	260374	26.4	3948	122674	32.2	1.19 (1.15–1.24)[‡]	1.20 (1.15–1.25)[‡]
Sex								
Female	3019	111741	27.0	1715	52957	32.4	1.18 (1.11–1.25)[‡]	1.18 (1.11–1.26)[‡]
Male	3864	148633	26.0	2233	69717	32.0	1.20 (1.14–1.27)[‡]	1.21 (1.15–1.28)[‡]
Age, y								
20–49	2156	57787	37.3	1280	27624	46.3	1.23 (1.15–1.32)[‡]	1.20 (1.11–1.29)[‡]
50–64	2523	73277	34.4	1432	34256	41.8	1.20 (1.12–1.28)[‡]	1.20 (1.12–1.28)[‡]
≥65	2204	129309	17.0	1236	60794	20.3	1.16 (1.08–1.24)[‡]	1.18 (1.09–1.27)[‡]
Comorbidity[†]								
No	3949	141219	28.0	1373	36887	37.2	1.31 (1.23–1.39)[‡]	1.24 (1.17–1.32)[‡]
Yes	2934	119155	24.6	2575	85787	30.0	1.21 (1.15–1.28)[‡]	1.10 (1.04–1.16)[‡]

CI = confidence interval, COPD = chronic obstructive pulmonary disease, HR = hazard ratio, Rate[$] = per 1000 person-years.

[*] Model was adjusted for age, sex, and comorbidities of hypertension, diabetes, hyperlipidemia, asthma, coronary artery disease, chronic kidney disease, and stroke.

[†] Patients with any comorbidity of hypertension, diabetes, hyperlipidemia, asthma, coronary artery disease, chronic kidney disease, and stroke were included in the comorbidity group.

[‡] $P < 0.001$.

TABLE 3. Hazard Ratios and 95% Confidence Intervals of Periodontal Diseases Associated With the Number of Annual Emergency Room Visits and Admissions for COPD

	No. Event	Crude HR (95% CI)	Adjusted HR* (95% CI)
Non-COPD	6883	1 (Reference)	1 (Reference)
Times of emergency room visit			
≤1	3625	1.12 (1.08–1.17)†	1.14 (1.10–1.19)†
>1	323	4.14 (3.70–4.63)†	5.09 (4.53–5.72)†
P for trend		<0.001	<0.001
Times of admission			
≤1	3653	1.16 (1.11–1.20)†	1.15 (1.10–1.20)†
>1	295	2.03 (1.80–2.28)†	3.17 (2.81–3.57)†
P for trend		<0.001	<0.001

CI = confidence interval, COPD = chronic obstructive pulmonary disease, HR = hazard ratio.
* Model was adjusted for age, sex, and comorbidities of hypertension, diabetes, hyperlipidemia, asthma, coronary artery disease, chronic kidney disease, and stroke.
† $P < 0.001$.

than in those with any comorbidity. Moreover, our study showed that the risk of developing periodontal diseases increased proportionately with the annual number of ER visits and admissions for COPD. In addition, our findings support the notion that patients with COPD treated with inhaled or systemic corticosteroids have a higher risk of developing periodontal diseases than those who do not receive corticosteroid treatment.

Not only is the prevalence of periodontal diseases higher in patients with COPD, but these diseases also have an important impact on COPD. Scannapieco and Ho[19] analyzed the third National Health and Nutrition Examination Survey data and reported that diminished lung function was associated with more severe periodontal attachment loss. In addition, Peter et al[20] reported a significant correlation between clinical attachment level, probing depth, and gingival index and forced expiratory volume in 1 second. Furthermore, in relation to patients with acute exacerbation, Liu et al[21] reported that higher plaque index scores were significantly correlated with COPD exacerbations. Kucukcoskun et al[22] conducted a prospective study and found that initial periodontal treatment in patients with COPD and chronic periodontitis can reduce the exacerbation frequency. In a 2-year pilot randomized controlled trial, Zhou et al[23] reported that periodontal therapy in patients with COPD and chronic periodontitis can improve lung function and decrease the frequency of exacerbation. In relation to periodontal health and the quality of life in patients with COPD, Zhou et al[24] also reported that poor periodontal health was considerably associated with low quality of life in patients with COPD. The aforementioned findings indicate the importance of screening for and promoting periodontal health in patients with COPD to improve the outcome of the disease and their quality of life.

Several hypotheses have been postulated on the relationship between COPD and periodontal diseases. The pathology of both diseases is complex and involves many cell types such as cluster of differentiation 8 (CD8)-positive cells and macrophages. The diseases are predominantly characterized by neutrophilic inflammation, which can cause the loss of local connective tissue. They potentially have similar pathophysiological processes based on the functions of the neutrophils, which include a disturbance in the protease/antiprotease activity and oxidative stress.[25] In addition, shared risk factors could contribute to the occurrence of both diseases; these may include tobacco smoking, diabetes, and socioeconomic status. In the present study, tobacco smoking is the most important potential confounding factor. Although the NHI database does not contain data on personal smoking habits, we expect that there are >50% ex-smokers or current smokers in the COPD cohort based on previous studies.[26,27] In a recent public health report from the Ministry of Health and Welfare of Taiwan, the current smoking rate in the general population is 19.8%; in males, it is 35.0%, whereas in females it is 4.1% (http://www.hpa.gov.tw). Nevertheless, we found that the incidence of periodontal diseases was similar in males and females (32.4 vs 32.0 in the COPD cohort; 27.0 vs 26.0 in the comparison cohort). We note

TABLE 4. Cox Proportional-hazards Regression Analysis Measured Hazard Ratio of Periodontal Diseases Among COPD Patients by Different Treatments

Variables	n	Event	PY	Rate$	Crude HR (95% CI)	Adjusted HR* (95% CI)
Treatments of COPD						
Nonsteroids	9574	1643	50125	32.8	1 (Reference)	1 (Reference)
Inhaled corticosteroids	3154	642	19313	33.2	1.06 (0.96–1.16)	1.22 (1.11–1.34)†
Systemic corticosteroids	9604	1663	53236	31.2	0.97 (0.91–1.04)	1.15 (1.07–1.23)†

CI = confidence interval, COPD = chronic obstructive pulmonary disease, HR = hazard ratio, PY = person-years, Rate$ = per 1000 person-years.
* Model was adjusted for age, sex, and comorbidities of hypertension, diabetes, hyperlipidemia, asthma, coronary artery disease, chronic kidney disease, and stroke.
† $P < 0.001$.

that a major limitation of the present study was the combination (or lack of separation) of COPD and smoking effects when evaluating the incidence of periodontal diseases in patients with COPD.

The effects of COPD medications, particularly corticosteroids, on periodontal diseases should also be emphasized. Corticosteroids can cause a decrease in the bone mineral density,[28,29] and systemic bone loss may have an impact on the onset and progression of periodontal diseases.[30] Komerik et al[31] reported that patients who inhaled corticosteroid treatments could experience impaired bone metabolism that may lead to a marked decrease in bone mineral density. In the present study, we found that either inhaled or systemic corticosteroids can have a significant effect on the development of periodontal diseases in patients with COPD.

Previous studies have reported that 50% to 90% of adults worldwide suffer from periodontal diseases (depending on the precise definition of the term).[2] The incidence of periodontal diseases reported herein was substantially less than this, which was probably due to the present study reflecting a ''real world'' scenario wherein periodontal diseases were diagnosed during a real medical consultation. Thus, the patients with periodontal diseases included in this study were believed to have greater disease severity. In addition, the participants in the previous studies passively received a dental survey. The prevalence of periodontal diseases has been reported to be as high as 90%; nevertheless, we consider that periodontal diseases are an underestimated problem in patients with COPD. Clinical physicians should pay more attention to this group of individuals and provide appropriate support.

The strength of this study comes from providing a longitudinal population-based evaluation of patients with COPD and assessing their risk of developing periodontal diseases. In general, it is costly to conduct a population-based prospective cohort study, but a retrospective cohort study using insurance or register data is a suitable and economical alternative. However, certain limitations should be considered in the present study. First, the diagnoses of COPD, periodontal diseases, and comorbidities were identified from ICD-9-CM, and they depend on the performance of clinical physicians. A spot check is regularly performed to prevent errors and violation. Moreover, we enrolled only disorders with repeated cares to increase the validity. Second, NHI research database does not contain detailed information on the severity of periodontal diseases and COPD, socioeconomic status, environmental factors, smoking habits, alcohol consumption, diet preference, and family history, which may be potential confounding factors. Furthermore, relevant clinical variables such as image reports, serum laboratory data, and pulmonary function information were unavailable in the database.[32]

CONCLUSIONS

Patients with COPD are at a higher risk of developing periodontal diseases than the general population. Our results also support that the risk of periodontal diseases is proportion to COPD control. In addition, patients who receive corticosteroid treatment are at a higher risk of developing periodontal diseases.

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