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The Association between Periodontal Disease and Renal Disease Occurrence : A Retrospective Cohort Study

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1. INTRODUCTION

Chronic kidney disease (CKD) is a progressive, non-communicable disease that occurs by abnormal kidney changes triggered by various causes[1]. According to the Global Burden of Disease Study 2017 report, the prevalence of CKD was estimated to be 9.1% of the world population, and it is a crucial risk factor for cardiovascular disease, leading to high morbidity and mortality[2]. The number of CKD patients in Korea is 4.6 million, increasing by an average of 8.7% per year, and managing the burden of CKD is becoming a substantial challenge for the health care system[3].

Traditional risk factors for the development of progression of CKD are known to be physical inactivity, smoking, hypertension, diabetes mellitus, and obesity[4], but it has recently been shown that periodontitis may be a potential risk factor[5,6]. Although the biological pathway is still unclear, it is speculated that periodontal pathogens and inflammatory cytokines are speculated to spread through the bloodstream, leading to abnormal function of the nephron's endothelium[7].

Several epidemiological studies have demonstrated contradictory results regarding the association between periodontitis and the progression of renal disease[8,9]. Furthermore, although there is evidence for the association between the two diseases in human studies, it was difficult to confirm the mechanism in the rat periodontitis model[10,11]. Inflammation caused by periodontal disease can lead to an increase in systemic inflammatory markers and changes in renal tissue, which may contribute to the onset and progression of chronic kidney disease. Through various studies, the biological plausibility of the association between periodontal disease and chronic kidney disease can be explained by these inflammatory responses and interactions within the immune system[10,11,32].

Not only CKD but also glomerular diseases,

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including Immunoglobulin (Ig)A nephropathy (IgAN), can exacerbate the progression to end-stage renal disease (ESRD). IgAN is the most general form of primary glomerulonephritis, and it is a disease that causes renal failure in 20~40% of patients within 20 years of diagnosis[12-15]. It was reported that the involvement of periodontal pathogens in IgAN was confirmed in patient16 and mouse models[16,17]. Association between nephropathy and periodontal disease can be explained through several mechanisms. Periodontal disease, characterized by chronic inflammation of the gums and surrounding tissues, can lead to elevated systemic inflammatory markers like CRP and IL-6. This chronic inflammation and immune activation contribute to endothelial dysfunction, vascular damage, and the development of nephropathy[16,17]. Therefore, the biological plausibility between periodontal disease and renal or glomerular diseases may be similar through inflammatory responses, activation of the immune system, and shared risk factors.

Nevertheless, since the scope of the previous studies has mainly tended to be limited to CKD, it is necessary to examine both CKD and glomerular disease with high prevalence using long-term accurate medical records for periodontal disease and renal disease.

We hypothesized that periodontal disease is associated with a higher risk of renal disease. This retrospective follow-up study aimed to investigate whether the presence of periodontal disease and the number of dental visits due to periodontal disease are associated with an occurrence of renal disease and to explore the strength of this association within possible risk factors using the Korea national sample cohort data.

2. MATERIALS AND METHODS

2. 1. Study design and ethical consideration

This retrospective follow-up was conducted using the National Health Insurance Service-National Sample Cohort (NHIS-NSC), a population-based cohort recruited by the National Health Insurance Service (NHIS) in South Korea. From 2002 to 2015, the NHIS-NSC cohort consisted of a random sampling of approximately 1,000,000 individuals each year, accounting for 2.2 percent of the total Korean population. Because this study used the National Health Insurance Service database, which only includes anonymized secondary data, patient consent was not required. This study was approved by the Baekseok University Institutional Review Board (BUIRB-202001-HR-025).

2. 2. Study population

The total number of participants enrolled in the NHIS-NSC from 2002 to 2015 was 1,108,369. Participants were excluded from this study based on the following criteria: (1) participants under the age of 20 (n=388,677); (2) participants with renal diseas before the follow-up (n=20,471); (3) participants with no periodontal status diagnosis due to a lack of periodontal health records from 2002 to 2004 (n=355,804); (4) participants with incomplete data in confounders (n=159,879). After that, 203,538 participants (age range: age 20-89) were included in the final analysis (Fig. 1). This study was a retrospective cohort study, with the baseline established from 2002 to 2004 and the participants followed for 11 years from 2005 to 2015. The newly developed renal disease was identified from 2005 to 2015. This design was used to establish

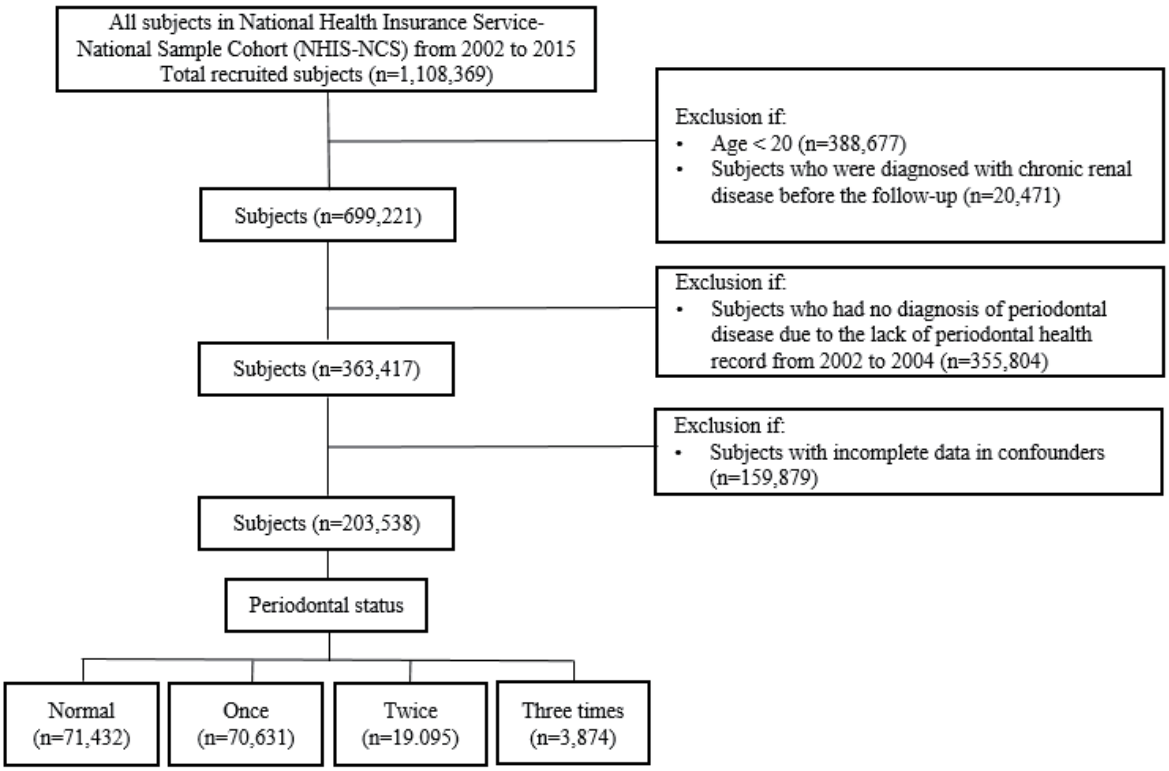

Fig. 1. Flowchart of the inclusion and exclusion of the study population in National Health Insurance Service–National Sample Cohort

a distinct causality to confirm the possibility of the occurrence of renal disease due to periodontal status and the number of dental visits.

2. 3. Assessment of periodontal disease

The presence of periodontal disease was assessed by a dentist and recorded using the following ICD−10 codes. These codes were created using clinical signs, oral examination, and radiographic evaluation by a dentist who is qualified to perform a dental check−up, as recommended by the Centers for Disease Control and the American Academy of Periodontology[18].

- Acute gingivitis (ICD−10 code K05.0)
- Chronic gingivitis (ICD−10 code K05.1)
- Aggressive periodontitis (ICD−10 code K05.2)
- Chronic periodontitis (ICD−10 code K05.3)
- Periodontitis (ICD−10 code K05.4)
- Other periodontal disease (ICD−10 code K05.5)
- Unspecified periodontal disease (ICD−10 code K05.6)

The periodontal condition was grouped into normal and periodontal disease. Participants not included in the diagnostic ICD−10 codes (International Statistical Classification of Diseases and Related Health Problems, 10th revision), were considered normal groups. Periodontal status was determined using two different definitions based on the periodontal record of the baseline[19−21]. The number of dental visits due to periodontal disease during the baseline was calculated and then divided into four categories: none, once, twice, and three times[22]. During the baseline period of 3 years, the number of dental visits due to periodontal disease was counted, and then categorized into four groups. This refers to visits to the dentist for periodontal disease over a

period of three years, each year representing whether periodontal disease was diagnosed. If the frequency of visits is high, it can be considered that the individual has been afflicted with periodontal disease for a long time. This variable was chosen as an independent variable in health insurance data analysis based on its use primarily as an independent variable related to the frequency of dental visits due to periodontal disease[19-22]. According to the Centers for Disease Control and the American Academy of Periodontology, normal group is defined as having no alveolar bone loss, healthy gingiva and alveoolar bone levels, no gingival bleeding, and a probing depth of 1-2mm (no mobility and no furcation). Individuals who do not fall into this healthy category were classified as periodontal disease patients.

2. 4. Assessment of renal disease

The diagnosis of renal disease was defined based on ICD-10 codes. Renal diseases registered in ICD-10, excluding acute conditions (N 00, N 01, & N 17) and genetic diseases (N 07), were used as the main outcome variable of this study. The specific disease names are as follows:

- Recurrent and persistent hematuria (IgA nephropathy) (ICD-10 code N02)
- Chronic nephritic syndrome (ICD-10 code N03)
- Nephrotic syndrome (ICD-10 code N04)
- Unspecified nephritic syndrome (ICD-10 code N05)
- Isolated proteinuria with a specified morphological lesion (ICD-10 code N06)
- Glomerular disorders in diseases classified elsewhere (ICD-10 code N08)
- Chronic kidney disease (ICD-10 code N18) (National Kidney Foundation, 2002)
- Kidney damage with normal or increased GFR (≥ 90mL/min), stage 1 (ICD-10 code N18.1)
- Kidney damage with mild decreased GFR (60-89 mL/min), stage 2 (ICD-10 code N18.2)
- Kidney damage with moderately decreased GFR (30-59 mL/min), stage 3 (ICD-10 code N18.3)
- Kidney damage with severely decreased GFR (15-29 mL/min), stage 4 (ICD-10 code N18.4)
- End-stage kidney disease, renal retinitis, uraemic, stage 5 (ICD-10 code N18.5)
- Unspecified kidney failure (ICD-10 code N19)

2. 5. Assessment of confounders

Traditional variables used in previous studies on renal disease were selected in the study, particularly those related to systemic diseases involving inflammation, which may have associations with periodontal disease or influence the outcome variables.

Potential confounders included sociodemographic characteristics (age, gender, and family income), health lifestyle factors (smoking, alcohol consumption), systemic health status (diabetes mellitus, hypertension, obesity, hypercholesterolemia, and ischemic heart disease), and advanced periodontal treatment. The household income was divided into quintiles as a result of the insurance payment. Smoking status (no versus yes) and average alcohol consumption (almost non-drink, 2-3 times per month, 1-2 times per week, 4 times or less per week, almost every day) were questioned using self-reported questionnaires during health checkup examinations. We also inquired about participants' physical activity levels by posing the question, "How frequently do you engage in exercise to the point of sweating each week?" Responses were categorized as follows: none, 1 - 4 times per week, and 5 or more times per week.

Diabetes mellitus (ICD-10 codes E10, E11, E12, E13, and E14), hypertension (ICD-10 codes I10, I15, and

I27), and ischemic heart disease (ICD-10 codes I20, I21, I22, I23, I24, and I25) were identified from the subject's health insurance claim record. Obesity was classified as having a BMI of 25.0 kg/m2 or higher23. Hypercholesterolemia was defined as a total cholesterol level of more than 240 mg/dL24.

Advanced periodontal treatment confirmed the records of participants who had undergone root planning (ICD-10 code U2240) or subgingival curettage (ICD-10 code U1010) or surgery (ICD-10 codes U1020, U1051, U1052, U1071, U1072, U1081, U1082, U1100). After that, the frequency of advanced periodontal treatment over 14 years was divided into three groups: none, once, two or more times.

2. 6. Statistical analysis

In the statistical analysis, possible confounders used in existing literature related to kidney disease were applied. After an 11-year follow-up, the risk of developing kidney disease was evaluated based on the presence of periodontal disease and the frequency of dental visits due to periodontal disease. First, the unadjusted association between the two variables was assessed, followed by adjustments for sociodemographic factors, health-related behaviors, systemic disease-related factors, and finally, advanced periodontal treatment. The risk was then calculated accordingly.

The chi-square provides basic characteristics according to periodontal status and the number of dental visits as numbers and percentages for categorical variables.

The incidence rate of renal disease was calculated per 100,000 person-years based on the number of dental visits. Kaplan-Meier survival curves were created to determine the cumulative survival probability of renal disease over 11 years and the mean survival time depending on the number of dental visits. To explore the differences in renal disease occurrence among the groups, the log-rank test was used. Over an 11-year follow-up period, Cox proportional hazard models were used to determine the hazard ratio and the number of dental visits for renal disease. The crude hazard ratio (cHR), adjusted hazard ratio (aHR), and 95 % confidence interval (CI) were calculated using a sequential model that included the confounders. We sequentially added socioeconomic variables, health-related variables, systemic disease variables, and advanced periodontal treatment to identify whether the number of dental visits increases the incidence of renal disease in the future. Finally, a subgroup analysis was performed for age, gender, smoking status, diabetes, and periodontal treatment. An SPSS statistical program was used to conduct all statistical tests (IBM, Chicago, IL).

3. RESULTS

3. 1. Baseline characteristics of the study participants

At baseline, the distribution of the number of dental visits was 42.4% for none, 43% for once, 12.1% for twice, and 2.5% for three times (Table 1). There were considerable disparities in the number of dental visits based on the characteristics of participants. Those who had a higher number of dental visits were more likely to be older, male, low-income, and smokers ($p<0.001$ for all). Compared to those who never had a dental visit, those who attended three visits were detected among the group almost every day, ≤ 4 times/week, and almost non-drink ($p<0.001$). The percentage of participants with frequent dental visits was higher in

Table 1. Baseline characteristics of the study participants according to periodontal status (N=203,538)

Variables	Total N	The number of dental visits due to periodontal disease				*P-value**
		None (n=71,432)	Once (n=70,631)	Twice (n=19,095)	Three times (n=3,874)	
Age group						
20 to 39	76,412	38777 (44.9)	30828 (35.2)	602 (24.5)	78 (15.2)	<0.001
40 to 59	92,735	3554 (41.2)	4101 (46.9)	1309 (53.3)	3091 (60.0)	
≥60	34,391	1198 (13.9)	15686 (17.9)	5447 (22.2)	1276 (24.8)	
Gender						
Male	103,723	41937 (48.6)	45247 (51.7)	13406 (54.6)	3133 (60.8)	<0.001
Female	99,815	44366 (51.4)	42277 (48.3)	1153 (45.4)	2019 (39.2)	
Household income quintiles						
First quintile	27,557	12247 (14.2)	11758 (13.4)	3018 (12.3)	534 (10.4)	<0.001
Second quintile	31,393	13872 (16.1)	13568 (15.5)	3334 (13.6)	619 (12.0)	
Third quintile	43,792	19002 (22.0)	18894 (21.6)	4931 (20.1)	965 (18.7)	
Fourth quintile	46,141	19323 (22.4)	199442 (22.8)	5687 (23.2)	1189 (23.1)	
Fifth quintile	54,655	21859 (25.3)	23362 (26.7)	7589 (30.9)	1845 (35.8)	
Smoking status						
No	138934	59433 (68.9)	59398 (67.9)	16644 (67.8)	3459 (67.1)	<0.001
Yes	64604	26870 (31.1)	28126 (32.1)	7915 (32.2)	1693 (32.9)	
Alcohol consumption **						
Almost Non-drink	107,692	45009 (52.2)	46456 (53.1)	13393 (54.5)	2834 (55.0)	<0.001
2-3 times/ month	39,166	17711 (20.5)	16392 (18.7)	4225 (17.2)	838 (16.3)	
1-2/week	37,490	16249 (18.8)	16011 (18.3)	4318 (17.6)	912 (17.7)	

diabetes (p<0.001), hypertension (p<0.001), obesity (p<0.001), hypercholesterolemia (p=0.034), and ischemic heart disease (p<0.001). The number of dental visits was also related to the frequency of advanced periodontal treatments (p<0.001).

3. 2. Association of periodontal disease with renal disease

Table 2 shows the incidence rate, HR, and 95% CIs of renal disease by the number of dental visits after adjustments with confounders. During the 11-year follow-up period, the occurrence of renal disease was identified as 19,868 (9.8%) among the total of 203,538 participants. The incidence rate of renal disease events was 8.7% for none, 10.0% for once, 11.9% for twice, and 13.5% for three times according to the number of dental visits. That is, the renal disease incidence rate per 100,000 person-years was higher in those who frequently visited dental offices (843.16 for none, 973.09 for once, 1171.64 for twice, and 1341.51 for three times).

Through the univariate Cox proportional hazard regression model, the risk of renal disease gradually increased as the number of dental visits increased (HR: 1.15, 95%CI: 1.12-1.19 for once; HR: 1.39, 95%CI: 1.33-1.45 for twice; HR: 1.59, 95%CI: 1.47-1.72 for three times). After adjusting for sociodemographic factors, health behavior factors, and systemic health variables, the risk for renal disease slightly decreased but remained significant. In the fully multivariate hazard regression model, we confirmed that the incidence of renal disease for the number of dental visits still exists. In addition, the risk of developing renal disease was highest among those who had three

≤4 times/week Almost every day	19,190	7334 (8.5)	8665 (9.9)	2623 (10.7)	568 (11.0)	
Physical activity **						
No	114,428	49262 (57.1)	49197 (56.2)	13383 (54.5)	2586 (50.2)	<0.001
1−4 times/week	71813	30305 (35.1)	30792 (35.2)	8722 (35.5)	1994 (38.7)	
5≥times/week	17297	6736 (7.8)	7535 (8.6)	2454 (10.0)	572 (11.1)	
Diabetes mellitus						
No	178294	77672 (90.0)	76183 (87.0)	20367 (82.9)	4072 (79.0)	<0.001
Yes	25244	8631 (10.0)	11341 (13.0)	4192 (17.1)	1080 (21.0)	
Hypertension						
No	174,392	76077 (88.2)	74391 (85.0)	19930 (81.2)	3994 (77.5)	<0.001
Yes	29,146	10226 (11.8)	13133 (15.0)	4629 (18.8)	1158 (22.5)	
Obesity						
No	138,659	59494 (68.9)	59386 (67.9)	16400 (66.8)	3379 (65.6)	<0.001
Yes	64,879	26809 (31.1)	28138 (32.1)	8159 (33.2)	1773 (34.4)	
Hypercholesterolemia						
No	189,462	80499 (93.3)	81352 (92.9)	22816 (92.9)	4795 (93.1)	0.034
Yes	14,076	5804 (6.7)	6172 (7.1)	1743 (7.1)	357 (6.9)	
Ischemic heart disease						
No	152,174	67395 (78.1)	64640 (73.9)	16854 (68.6)	3285 (63.8)	<0.001
Yes	51,364	18908 (21.9)	22884 (26.1)	7705 (31.4)	1867 (36.2)	
Advanced periodontal treatment						
None	105,527	55079 (63.8)	41771 (47.7)	7716 (31.4)	961 (18.7)	<0.001
Once	48,111	18460 (21.4)	22653 (25.9)	6045 (24.6)	953 (18.5)	
Twice or more	49,900	12764 (14.8)	23100 (26.4)	10798 (44.0)	3238 (62.8)	

Data are presented as number and percentage.
* Obtained from chi−square test
Bold denotes statistical significance at $P < 0.05$

dental visits (HR: 1.03, 95%CI: 1.00−1.06 for once; HR: 1.08, 95%CI: 1.04−1.13 for twice; HR: 1.12, 95%CI: 1.03−1.21 for three times), with a dose−response trend.

Figure 2 compares the overall trend of renal disease incidence according to the number of dental visits. Those who had more frequent dental visits had a considerably lower survival rate for renal disease by the end of 11 years of follow−up (Log−Rank test, p<0.001).

3. 3. Association of periodontal disease with renal disease in subgroups analysis

Table 3 demonstrates the results of specific subgroup analysis for renal disease risk. In the age group of 20 to 39 years, those with three dental visits had the highest risk for renal disease (HR: 1.46, 95%CI: 1.14−1.88). In current smokers and non−periodontal treatments, the HR of renal disease was higher than that of total participants (HR: 1.25, 95%CI: 1.09−1.45 for smokers; HR: 1.21, 95%CI: 1.02−1.43).

4. DISCUSSION

This study investigated the risk of periodontal disease on the development of renal disease over 11 years using the Korean cohort sample. The present study found additional evidence that periodontal disease increases the risk of renal disease after adjusting for

Table 2. Association of periodontal disease with the incidence of renal disease in the Cox proportional hazards models (n=203,538)

	Number of participants	Number of events	Hazard ratio (95% Confidence Interval)				
			Model 1	Model 2	Model 3	Model 4	Model 5
Periodontal status							
No	86303	7517	ref	ref	ref	ref	ref
Yes	117235	12351	1.22 (1.19–1.26)	1.09 (1.06–1.13)	1.09 (1.06–1.13)	1.06 (1.03–1.09)	1.04 (1.01–1.08)
The number of dental visits due to periodontal disease							
None	86303	7517	ref	ref	ref	ref	ref
Once	87524	8731	1.15 (1.12–1.19)	1.06(1.03–1.09)	1.06 (1.03–1.09)	1.04 (1.01–1.07)	1.02 (1.00–1.06)
Twice	24559	2924	1.39 (1.33–1.45)	1.17 (1.12–1.22)	1.17 (1.12–1.22)	1.11 (1.06–1.16)	1.08 (1.04–1.13)
Three times	5152	696	1.59 (1.47–1.72)	1.26 (1.16–1.38)	1.25 (1.16–1.35)	1.15 (1.06–1.24)	1.11 (1.03–1.21)

Model 1: unadjusted association
Model 2: age, gender, household income
Model 3: age, gender, household income, smoking status, alcohol consumption, physical activity
Model 4: : age, gender, household income, smoking status, alcohol consumption, physical activity, diabetes, hypertension, obesity, hypercolesterolemia, and ischemic heart disease
Model 5: : age, gender, household income, smoking status, alcohol consumption, physical activity, diabetes, hypertension, obesity, hypercolesterolemia, ischemic heart disease, and advanced periodontal treatment
Bold denotes statistical significance at $P < 0.05$

age, gender, income, smoking, drinking, diabetes, hypertension, obesity, hypercholesterolemia, ischemic heart disease, and periodontal treatment. In addition, the more frequent dental visits due to periodontal disease, the higher the risk of renal disease, with a dose–response trend. These findings suggest that the risk of developing renal disease increases progressively with the duration of periodontal disease.

Our study has several strengths. First, this study was conducted over a long period of 11 years to demonstrate overall renal disease and periodontal disease. The existing studies have primarily addressed narrow concepts such as end–stage renal disease (ESRD) and chronic kidney disease. In contrast, this study represents the first comprehensive investigation into renal diseases, encompassing glomerular diseases that impact the kidneys. Second, the data utilized in this research relies on objective diagnostic criteria provided by healthcare professionals and dentists, based on diagnoses associated with health insurance coverage, ensuring high diagnostic reliability. Third, as a 11–year retrospective study, it leverages epidemiological data to measure the long–term risk of renal disease associated with periodontal conditions. Fourth, the data presented reveals the occurrence of renal disease based on regular periodontal treatment, providing meaningful insights into the relationship between periodontal care and the development of renal diseases.

Despite extensive investigations into the association between renal disease and periodontitis, a definitive conclusion has not yet been reached. In the four cohort studies[8,9,25,26] examined thus far, three[8,25,26] have confirmed concordance with the findings of our study. In the outcomes of the retrospective study known as the Jackson Heart Study[25], participants with severe periodontal disease, compared to those without severe periodontal disease, exhibited a fourfold higher incidence rate of CKD. In another cohort study involving 761 elderly men[26], the research suggests that the presence of severe periodontal disease may be

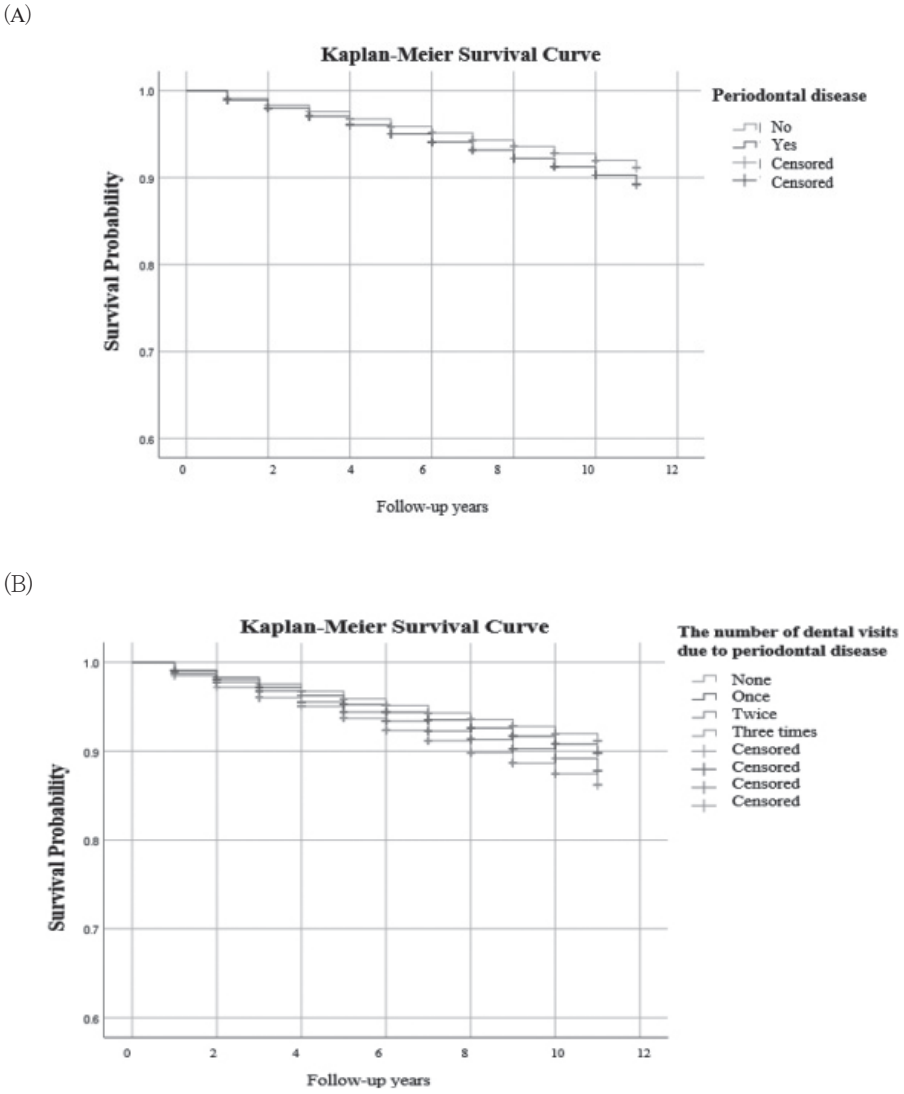

Fig. 2. Kaplan–Meier survival curves for survival probability according to periodontal disease on the occurrence of renal disease across 11–years follow–up: (A) periodontal disease (yes or no) (B) the number of dental visits due to periodontal disease (none, once, twice, three times)

associated with a clinically significant decline in kidney function.

In contrast to our study, Tai et al.[9] reported divergent outcomes in their findings from a 12–year longitudinal study using national health insurance data. Their investigations did not reveal a link between outcomes related to CKD and either periodontal therapy or dental scaling. In other words, there is inadequate evidence supporting the beneficial impact of periodontal care on kidney function and the survival of CKD patients. Even in various stratified analyses, no discernible association was evident.

The existing studies thus far exhibit various limitations, including constraints related to gender and sample size, definition of periodontal disease, as well as the utilization of cohorts that may not adequately represent the general population. Therefore, there is a need for more high–quality cohort study outcomes, and this study is considered to potentially contribute additional evidence relevant to the topic.

Table 3. Cox proportional hazards models in subgroup by age, gender, smoking status, diabetes, mellitus, advanced periodontal treatment

		Periodontal status (no vers yes) *	The number of dental visits due to periodontal disease †		
		aHR (95% CI)	aHR (95% CI)		
Stratum	N	Yes	Once	Twice	Three times
Age group					
20 to 39	76,412	1.08 (1.02−1.15)	1.05 (0.98−1.12)	1.21 (1.08−1.35)	1.46 (1.14−1.88)
40 to 59	92,735	1.01 (0.97−1.29)	1.00 (0.95−1.04)	1.03 (0.97−1.10)	1.06 (0.952−1.18)
≥60	34,391	1.08 (1.02−1.14)	1.07 (1.01−1.13)	1.11 (1.03−1.20)	1.12 (0.98−1.28)
Gender					
Male	103,723	1.03 (0.99−107)	1.01 (0.97−1.06)	1.06 (1.00−1.13)	1.12 (1.01−1.24)
Female	99,815	1.06 (1.02−1.11)	1.05 (1.01−1.10)	1.10 (1.03−1.17)	1.09 (0.96−1.24)
Smoking status					
No	138,934	1.05 (1.01−1.08)	1.04 (1.00−1.08)	1.07 (1.02−1.13)	1.06 (0.96−1.17)
Yes	64,604	1.04 (0.98−1.10)	1.01 (0.95−1.07)	1.11 (1.02−1.21)	1.25 (1.09−1.45)
Diabetes mellitus					
No	178,294	1.03 (1.00−1.07)	1.02 (0.98−1.05)	1.07 (1.02−1.13)	1.11 (1.01−1.23)
Yes	25,244	1.08 (1.02−1.15)	1.07 (1.00−1.14)	1.10 (1.02−1.20)	1.12 (0.97−1.28)
Advanced periodontal treatment					
None	105,527	1.05 (1.01−1.10)	1.04 (1.00−1.09)	1.10 (1.02−1.18)	1.21 (1.02−1.43)
Once	48,111	1.05 (0.99−1.12)	1.03 (0.96−1.10)	1.13 (1.04−1.24)	1.15 (0.95−1.38)
Twice	49,900	1.01 (0.95−1.07)	1.00 (0.92−1.06)	1.02 (0.95−1.11)	1.05 (0.95−1.18)

All models were adjusted for age, gender, household income, smoking status, alcohol consumption, physical activity, diabetes mellitus, hypertension, obesity, hypercholesterolemia, ischemic heart disease, and advanced periodontal treatment except the stratum.
*Reference group: periodontal status [no]
† Reference group: The number of dental visits due to periodontal disease [None]
aHR, adjusted hazard ratio; 95% CI, 95% confidence interval
Bold denotes statistical significance at P < 0.05

To date, there is a lack of research papers utilizing national big data to comprehensively define renal disease. Therefore, it may be challenging to directly compare the results of this study with those of other studies, which could be a limitation. However, given the existence of several cohort studies8,[25,26] and some randomized controlled trials[27,28], it is possible to discuss trends. This allows for a comparison of the periodontal effects in the broader category of renal disease, encompassing both kidney disease and ESRD patients.

Periodontitis triggers the release of endotoxins and pro−inflammatory mediators, leading to systemic inflammation and impacting chronic kidney diseases, with endothelial dysfunction serving as a pivotal mechanism[29,30]. Additionally, a bidirectional association has been identified between periodontal and renal diseases, evident through the presence of inflammatory markers (C−reactive protein, interlukin−6, Tumor necrosis factor−α, etc.) and oxidative stress indicators (plasma carbonyls, isoprostanes) in the inflammatory progression of both conditions[31]. After accumulating evidence suggesting that periodontitis heightens the risk of chronic kidney diseases, the prevailing hypothesis emphasizes that periodontal treatment, by reducing inflammation and bacteria, contributes to enhancing renal function[32].

In our subgroup analysis results, the smoking group exhibited a 1.25-fold higher incidence of renal disease, suggesting that smoking is predicted to be a shared risk factor for both periodontal disease and renal disease, contributing to these observed outcomes. In addition, we observed the finding of a 1.21-fold higher occurrence of renal disease in the group that had never receive advanced periodontal treatment.

In other words, one could infer from these results that the risk of developing renal disease is higher in individuals who do not undergo advanced periodontal treatment (root planning, subgingival curettage, surgery). A study conducted in Taiwan[33], involving a nationwide matched cohort, yielded results similar to those of the present study. Dental scaling was linked to a decreased risks of progression to ESRD, all-cause mortality in patients with CKD. While periodontitis adds to the inflammatory burden and has been linked to diminished kidney function in numerous observational studies[29,34,35], Zhao et al.[36] presented insufficient evidence to draw conclusions about the potential benefits of non-surgical periodontal therapy on renal function in CKD patients with periodontitis. Smoking is anticipated to be a shared risk factor for both periodontal disease and renal disease, explaining the observed outcomes. Therefore, these results suggest the need for further investigation in the future.

This study has several limitations. First, clinical attachment loss was not measured for the diagnosis of periodontal disease, and a review of dental chart records was not feasible. Consequently, there exists a level of uncertainty in the categorization of periodontal disease, contributing to a non-differential misclassification bias. Second, participants who initially displayed a healthy periodontal condition might have developed periodontitis over the 11-year follow-up period, and alterations in the baseline health status of other confounding variables could have occurred. This resulted in a potential misclassification bias among participants initially categorized as non-periodontitis. As a result, the causal association examined in this study may be underestimated.

Nevertheless, these study findings are significant in confirming that individuals with periodontal disease not only have a higher risk of developing renal disease but also that this risk increases progressively with the duration of periodontal diseas.

These results provide significant evidence in clarifying the association between periodontal disease and critical clinical outcomes of renal disease. This confirms that the management of periodontal disease can be a crucial factor in the prevention and reduction of the risk of renal disease occurrence.

Notes

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REFERENCES

1. Kalantar-Zadeh K, Jafar TH, Nitsch D, Neuen BL, Perkovic V. Chronic kidney disease. Lancet 2021;398:786-802. https://doi.org/10.1016/

S0140-6736(21)00519-5.

2. Collaboration. GCKD. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020;395:709-733. https://doi.org/10.1016/S0140-6736(20)30045-3.
3. The Korean Society of nephrology. Chronic Kidney Disease in Korea. Available at: https://ksn.or.kr/bbs/index.php?code=Factsheet. Accessed: 07, 2022.
4. Stengel B, Tarver-Carr ME, Powe NR, Eberhardt MS, Brancati FL. Lifestyle factors, obesity and the risk of chronic kidney disease. Epidemiology 2003;14:479-487. https://doi.org/10.1097/01.EDE.0000071413.55296.c4.
5. Craig RG. Interactions between chronic renal disease and periodontal disease. Oral Dis 2008;14:1-7. https://doi.org/10.1111/j.1601-0825.2007.01430.x.
6. Lertpimonchai A, Rattanasiri S, Tamsailom S, et al. Periodontitis as the risk factor of chronic kidney disease: Mediation analysis. J Clin Periodontol 2019;46:631-639. https://doi.org/10.1111/jcpe.13114.
7. Kshirsagar AV, Moss KL, Elter JR, Beck JD, Offenbacher S, Falk RJ. Periodontal disease is associated with renal insufficiency in the Atherosclerosis Risk In Communities (ARIC) study. Am J Kidney Dis 2005;45:650-657. https://doi.org/10.10 53/j.ajkd.2004.12.009.
8. Iwasaki M, Taylor GW, Nesse W, Vissink A, Yoshihara A, Miyazaki H. Periodontal disease and decreased kidney function in Japanese elderly. Am J Kidney Dis 2012;59:202-209. https://doi.org/10.1053/j.ajkd.2011.08.027.
9. Tai YH, Chen JT, Kuo HC, et al. Periodontal disease and risk of mortality and kidney function decline in advanced chronic kidney disease: a nationwide population-based cohort study. Clin Oral Investig 2021;25:6259-6268. https://doi.org/10.1007/s00784-021-03924-6.
10. França LFC, Vasconcelos A, da Silva FRP, et al. Periodontitis changes renal structures by oxidative stress and lipid peroxidation. J Clin Periodontol 2017;44:568-576. https://doi.org/10.1111/jcpe.12729.
11. Galeno JG, França LFC, da Silva FRP, et al. Renal alterations caused by ligature-induced periodontitis persist after ligature removal in rats. J Periodontal Res 2021;56:306-313. https://doi.org/10.1111/jre.12822.
12. Wyatt RJ, Julian BA. IgA nephropathy. N Engl J Med 2013;368:2402-2414. https://doi.org/10.1056/NEJMra1206793.
13. Pettersson E. IgA nephropathy: 30 years on. J Intern Med 1997;242:349-353. https:// doi.org/10.1046/j.1365-2796.1997.00194.x.
14. Nair R, Walker PD. Is IgA nephropathy the commonest primary glomerulopathy among young adults in the USA? Kidney Int 2006;69:1455-1458. https://doi.org/10. 1038/sj.ki.5000292.
15. The Korean Society of Nephrology. Glomerular disease in Korea. Available at: https://ksn.or.kr/bbs/?code=Factsheet. Accessed: 08.25, 2022.
16. Nagasawa Y, Iio K, Fukuda S, et al. Periodontal disease bacteria specific to tonsil in IgA nephropathy patients predicts the remission by the treatment. PLoS One 2014;9:e81636. https://doi.org/10.1371/journal.pone.0081636.
17. Nagasawa Y, Nomura R, Misaki T, et al. Relationship between IgA Nephropathy and Porphyromonas gingivalis; Red Complex of Periodontopathic Bacterial Species. Int J Mol Sci 2021;22:13022. https://doi.org/10.3390/ijms222313022.

18. Armitage GC. Development of a classification system for periodontal diseases and conditions. Ann Periodontol 1999;4:1-6. https://doi.org/10.1902/annals.1999.4.1.1.
19. Cho HJ, Shin MS, Song Y, Park SK, Park SM, Kim HD. Severe Periodontal Disease Increases Acute Myocardial Infarction and Stroke: A 10-Year Retrospective Follow-up Study. J Dent Res 2021;100:706-713. https://doi.org/10.1177/0022034520986097.
20. Choi YY, Lee KH. Periodontitis as a Risk Factor for Rheumatoid Arthritis: a Matched-Cohort Study. Int Dent J 2021;71:516-521. https://doi.org/10.1016/j.identj. 20 21.01.006.
21. Kim SJ, Kim K, Choi S, et al. Chronic periodontitis and community-acquired pneumonia: a population-based cohort study. BMC Pulm Med 2019;19:268. https://doi.org/10.1186/s12890-019-1017-1.
22. Shin HS, Hong MH, Moon JY, Sim SJ. Periodontal disease could be a potential risk factor for non-alcoholic fatty liver disease: An 11-year retrospective follow-up study. Clin Oral Investig 2022;26:5503-5514. https://doi.org/10.1007/s00784-022-045 18-6.
23. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-163. https://doi.org/10.1016/S0140-6736(03)15268-3.
24. Experet Panel on Detection E, and Treatment of High Blood Cholesterol in Adults,. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001;285:2486-2497. https://doi.org/10.1001/jama.285.19.2486.
25. Grubbs V, Vittinghoff E, Beck JD, et al. Association Between Periodontal Disease and Kidney Function Decline in African Americans: The Jackson Heart Study. J Periodontol 2015;86:1126-1132. https://doi.org/10.1902/jop.2015.150195.
26. Grubbs V, Vittinghoff E, Taylor G, et al. The association of periodontal disease with kidney function decline: a longitudinal retrospective analysis of the MrOS dental study. Nephrol Dial Transplant 2016;31:466-472. https://doi.org/10.1093/ndt/gfv312.
27. Graziani F, Cei S, La Ferla F, Vano M, Gabriele M, Tonetti M. Effects of non-surgical periodontal therapy on the glomerular filtration rate of the kidney: an exploratory trial. J Clin Periodontol 2010;37:638-643. https://doi.org/10.1111/j.1600- 051X.2010.01578.x.
28. Wehmeyer MM, Kshirsagar AV, Barros SP, et al. A randomized controlled trial of intensive periodontal therapy on metabolic and inflammatory markers in patients With ESRD: results of an exploratory study. Am J Kidney Dis 2013;61:450-458. https://doi.org/10.1053/j.ajkd.2012.10.021.
29. Tonetti MS, D'Aiuto F, Nibali L, et al. Treatment of periodontitis and endothelial function. N Engl J Med 2007;356:911-920. https://doi.org/10.1056/NEJMoa063186.
30. Ismail G, Dumitriu HT, Dumitriu AS, Ismail FB. Periodontal disease: a covert source of inflammation in chronic kidney disease patients. Int J Nephrol 2013;2013:515796. https://doi.org/10.1155/2013/515796.
31. Sharma P, Fenton A, Dias IHK, et al. Oxidative stress links periodontal inflammation and renal function. J Clin Periodontol 2021;48:357-367.

https://doi.org/10.1111/jcpe. 13414.

32. Fang F, Wu B, Qu Q, et al. The clinical response and systemic effects of non-surgical periodontal therapy in end-stage renal disease patients: a 6-month randomized controlled clinical trial. J Clin Periodontol 2015;42:537-546. https://doi.org/ 10.1111/jcpe.12411.
33. Chung YH, Kuo HC, Liu HY, et al. Association between Dental Scaling and Reduced Risk of End-Stage Renal Disease: A Nationwide Matched Cohort Study. Int J Environ Res Public Health 2021;18. https://doi.org/10.3390/ijerph18178910.
34. Chambrone L, Foz AM, Guglielmetti MR, et al. Periodontitis and chronic kidney disease: a systematic review of the association of diseases and the effect of periodontal treatment on estimated glomerular filtration rate. J Clin Periodontol 2013;40:443-456. https://doi.org/10.1111/jcpe.12067.
35. Deschamps-Lenhardt S, Martin-Cabezas R, Hannedouche T, Huck O. Association between periodontitis and chronic kidney disease: Systematic review and meta-analysis. Oral Dis 2019;25:385-402. https://doi.org/10.1111/odi.12834.
36. Zhao D, Khawaja AT, Jin L, et al. Effect of non-surgical periodontal therapy on renal function in chronic kidney disease patients with periodontitis: a systematic review and meta-analysis of interventional studies. Clin Oral Investig 2020;24:1607-1618. https://doi.org/10.1007/s00784-019-03066-w.

초록

치주질환과 신장질환 발생과의 연관성: 후향적 코호트 연구

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연구배경: 치주질환 상태와 신장질환과의 연관성에 대한 연구는 아직 명확한 근거가 없는 실정이다. 본 연구에서는 건강보험공단자료를 이용하여 치주질환이 신장질환 발생을 증가시키는지 여부를 후향적 코호트 연구설계로 분석하였다.

연구방법: 국민건강보험공단 표본코호트 데이터를 이용하여 203,538명의 국내 성인을 대상으로 2002년부터 2015년까지의 자료를 활용하였다. 치주질환의 정의는 치과의사에 의해 진단된 치주질환 여부 변수와 치주질환으로 인해 치과를 방문한 횟수(0회, 1회, 2회, 3회 방문)를 주 독립변수로 설정하였다. 신장질환은 국제질병분류 10차 개정판 코드를 사용하여 진단된 급성 신장질환과 유전성 신장질환을 제외한 신장질환을 포함하였다. 연구의 기초조사는 3년(2002년–2004년)으로 설정하였고, 추적조사기간은 11년(2005년–2015년)으로 설정하였다.

연구결과: 11년의 추적기간동안, 전체 203,538명 중 19,868명이 발생하였다. 나이, 성별, 수입, 음주, 흡연, 신체활동, 당뇨병, 고혈압, 비만, 고지혈증, 허혈성 심장질환, 치주치료를 보정한 결과, 치주질환은 신장질환 발생 위험을 1.04배 증가시켰다. (adjusted hazard ratio [aHR] = 1.04, 95% CI = 1.01 to 1.08). 또한 치주질환으로 인한 치과 방문 빈도가 많을수록 신장질환 발생 위험이 증가하는 용량–반응 경향을 보였다 (aHR = 1.02, 95% CI = 1.00 to 1.06 for 1회 방문; aHR = 1.08, 95% CI = 1.04 to 1.13 for 2회 방문; aHR = 1.11, 95% CI = 1.03 to 1.21 for 3회 방문).

결론: 본 후향적 코호트 연구 결과 치주질환은 신장질환의 위험을 발생시킨다는 결과를 보여주었다.

색인어: 코호트 연구: 역학: 치주질환: 역학: 신장질환

ABSTRACT

The Association between Periodontal Disease and Renal Disease Occurrence: A Retrospective Cohort Study

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Background: Research on the association between renal disease and periodontal conditions has yet to yield definitive results. In this study, we analyzed whether periodontal disease increases the risk of developing renal disease using Korean national cohort data over a period of 11 years.

Methods: From 2002 to 2015, a retrospective follow-up investigation was conducted on the 203,538 Korean population using the National Health Insurance Service-National Sample Cohort. Periodontal disease and renal disease were identified through diagnoses using the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) codes. The assessment of periodontal status involved considering the number of dental visits related to periodontal disease during the baseline 3-year period.

Results: During the 11-year follow-up period, renal disease occurred in 19,868 out of the total 203,538 individuals. After adjusting for age, gender, income, smoking, drinking, physical activity, diabetes, hypertension, obesity, hypercholesterolemia, ischemic heart disease, and advanced periodontal treatment, periodontal disease increased the risk of renal disease occurrence by 1.04 times (adjusted hazard ratio [aHR] = 1.04, 95% CI = 1.01 to 1.08). Additionally, a higher frequency of dental visits attributed to periodontal disease was associated with an increased risk of renal disease,exhibiting a dose-response trend (aHR = 1.02, 95% CI = 1.00 to 1.06 for once; aHR = 1.08, 95% CI = 1.04 to 1.13 for two times; aHR = 1.11, 95% CI = 1.03 to 1.21 for three times).

Conclusions: Our data confirmed that periodontal disease is associated witha higher incidence of renal disease.

Keywords: cohort study, epidemiology; periodontal disease; renal disease