저작자표시-비영리-변경금지 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.

다음과 같은 조건을 따라야 합니다:

저작자표시. 귀하는 원저작자를 표시하여야 합니다.

비영리. 귀하는 이 저작물을 영리목적으로 이용할 수 없습니다.

변경금지. 귀하는 이 저작물을 개작, 변형 또는 가공할 수 없습니다.

- 귀하는 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 이용허락규약(Legal Code)을 이해하기 쉽게 요약한 것입니다.

Disclaimer
Association between periodontitis and cognitive impairment among Korean elders

-한국 노인에서 치주질환과 인지장애와의 연관성-

2016년 2월

서울대학교 대학원
치의과학과 예방 및 사회치의학 전공
신혜선
Association between periodontitis and cognitive impairment among Korean elders
-한국 노인에서 치주질환과 인지장애와의 연관성-

지도교수  김 현 탁

이 논문을 치의학박사 학위논문으로 제출함
2015년 10월

서울대학교 대학원
치의과학과 예방 및 사회치의학 전공
신 혜 선

신혜선의 치의학박사 학위논문을 인준함
2015년 12월

위원장 ______________________ (인)
부위원장 ______________________ (인)
위원 ______________________ (인)
위원 ______________________ (인)
위원 ______________________ (인)
Abstract

Association between periodontitis and cognitive impairment among Korean elders

Hye-Sun Shin, RDH, BA
Department of Preventive and Social Dentistry
Seoul National University School of Dentistry
(Directed by Professor Hyun-Duck Kim, DDS, PhD)

Objectives: The association between cognitive impairment and periodontitis remains controversial. No study has yet reported on the link between periodontitis and cognitive functioning in Korean elderly population. Hence, this study aims to investigate the association between periodontitis and cognitive impairment among Korean elders.

Methods: This study was set in the Yangpyeong cardiovascular cohort (YCC), a part of the Korean Genome Epidemiologic Study (KoGES), Yangpyeong, South Korea. This study is a cross-sectional study with age and sex matched case-control selection. From the YCC, 65 cognitive impairment cases and 124 normal controls (aged 60 or more) participated in this study. Alveolar bone loss was assessed on dental panoramic radiographs to categorize the cumulative history of periodontitis (HOP). HOP was dichotomized as non severe versus severe
periodontitis (≥2 interproximal sites with RABL ≥6mm) and categorized into three groups according to severity of periodontitis: normal, moderate periodontitis (≥2 interproximal sites with RABL ≥4mm) and severe periodontitis (≥2 interproximal sites with RABL≥6mm). Mini–Mental State Examination (MMSE) test was used to categorize the participants as either normal or cognitively impaired. For analysis, age–and sex–matched conditional logistic regression models were used. Confounders considered in the analysis include: age, sex, drinking, smoking, exercise, total cholesterol, total protein, body mass index defined obesity, fasting plasma glucose, intima–media thickness, hypertension medication and depression.

Results: Participants with HOP were more likely to have cognitive impairment (odds ratio [OR] = 2.14, 95% confidence interval [CI] =1.04–4.41) than those without HOP. Interaction effect of smoking and exercise on periodontitis highlighted the link.

Conclusion: Periodontitis was independently associated with cognitive impairment after controlling for various confounders. Further longitudinal research is needed to determine whether periodontitis plays a role in cognitive decline among older adults.

keywords : MMSE; cognitive impairment; periodontitis; epidemiology; inflammation
Student Number : 2007–23384
# Contents

1. Introduction  

2. Methods  
   2.1. Sample size estimation  
   2.2. Study population  
   2.3. Assessment of cognitive impairment  
   2.4. Assessment of history of periodontitis  
   2.5. Assessment of confounders  
   2.6. Statistical analysis  

3. Results  

4. Discussion  

5. Conclusion  

References  

Supplement  

Korean Abstract  

1  

3  

3  

4  

5  

6  

8  

10  

16  

20  

21  

27  

30
Table list

[Table 1] Distribution of confounding and main explanatory variables according to cognitive impairment 12

[Table 2] Adjusted association between periodontitis and cognitive impairment using a conditional logistic regression model 14

[Table 3] Effect of interaction terms between periodontitis and confounders on the association between periodontitis and cognitive impairment 15
1. Introduction

Cognitive impairment is a growing global health problem. In Asia, the number of people with dementia is expected to nearly double every 20 years hereafter\(^1\). In Korea, in particular, the speed of population aging is reported to be one of the fastest in the world, and the prevalence of dementia and mild cognitive impairment is estimated to be as high as 8.1% and 24.1%, respectively, in elderly Koreans\(^2\). Thus prevention of and screening for cognitive impairment before the development of dementia is an important issue in Korea. The Mini-Mental State Examination (MMSE), which has been adopted as a Korean national survey of cognitive impairment\(^2\), is the most widely used screening tool for dementia\(^3\).

Periodontitis is a chronic inflammatory disease that is associated with bacterial infection that results in the destruction of tissues that surround and support teeth. Periodontitis is also associated with systemic diseases. The host defense response against periodontal bacteria may result in high levels of such systemic inflammatory mediators as IL-1\(\beta\), IL-6, and TNF-\(\alpha\)\(^4\). Chronic inflammation as measured according to blood inflammatory markers is, in turn, associated with greater risk of mild cognitive impairment\(^5,6\) and dementia\(^7,8\). Although the
molecular mechanisms involved in the etiology and pathogenesis of cognitive impairment have not been completely elucidated. Inflammation within the central nervous system is thought to play a pivotal role. This central role of inflammation in cognitive impairment yields the hypothesis that peripheral infection and inflammation might alter the inflammatory state of the brain\textsuperscript{9).}

An association between cognitive impairment and periodontitis has been found in some but not all epidemiological studies\textsuperscript{10-14). Most of the studies were not fully adjusted for current confounders such as blood test results and systemic health status, and no study has addressed the association between periodontitis and cognitive impairment in elderly Koreans. Hence, this study aims to assess the relationship between periodontitis and cognitive impairment, measured using the MMSE, elderly Koreans, taking into account possible confounders such as age, sex, drinking, smoking, exercise, total cholesterol, total protein, body mass index defined obesity, fasting plasma glucose (FPG), intima-media thickness (IMT), hypertension medication, and depression.
2. Materials and Methods

The institutional review board for human subjects at the Seoul National University School of Dentistry approved this cross-sectional study with age- and sex-matched case-control selection (S-D20100006), and all participants provided written informed consent for voluntary participation. Health professionals associated with the project assessed oral health status and other systemic status.

2.1. Sample size estimation

Sample size was estimated using the group sequential test for two proportions. Alpha and beta error were 0.05 and 0.2, respectively. In the pilot study, the prevalence of periodontitis among those with cognitive impairment and normal was 0.41 in individuals with cognitive impairment and 0.20 in those who were cognitively normal. The ratio between cases and controls was 1:2, and the estimated sample size was 186 (62 cases and 124 controls).

2.2. Study population

The Korean Genome Epidemiologic Study (KoGES), supporte
d by the Korea Centers for Disease Control and Prevention (KCDC), was launched in 2007 to examine the etiology of cardiovascular diseases by focusing on gene–environment and gene–gene interaction in the Korean population. Seven hundred eighty-three residents of Yangpyeong (located 45 km east of Seoul) completed the health assessment and questionnaires during the period of August 2010 to January 2011, which marked the first year of the third phase of KoGES. Cognitive function tests using the MMSE were conducted on 503 participants aged 60 years or older, whom did not complete the test and were excluded from the analysis. Among 447 participants, 220 with fewer than 12 teeth or removable partial denture or complete denture wearers were excluded from the analysis. Study participants consisted of 227 dentate elderly adults. Of these, 71 had cognitive impairment, 59 of whom were matched with controls in a 1:2 ratio and six of whom were matched with controls in a 1:1 ratio for age±3 years and sex. Ultimately, 189 participants were included in the final case–control analysis models: 98 men and 91 women aged between 60 to 86 (Table1).

2.3. Assessment of cognitive impairment

The MMSE is a widely used screening tool for cognitive
The Korean version (MMSE-KC) was developed as a part of the Korean version of the Consortium to Establish a Registry for Alzheimer’s disease Assessment Packet\(^{15}\). The MMSE-KC contains 19 items adding up to 30 points (10 points for orientation, 6 points for verbal memory, 5 points for concentration and calculation, 5 points for language, 3 points for praxis, 1 point for visuospatial construction), with higher scores indicating better cognitive performance. Because of the high prevalence of illiteracy in elderly Koreans, two items focusing on judgment ability replaced the reading and writing items of the original version of MMSE in the MMSE-KC. The MMSE-KC showed adequate diagnostic accuracy for moderate dementia, with an area under the receiver operating characteristic curve of approximately 0.9\(^{16}\). Trained neuropsychopathologists administered the MMSE-KC.

Because MMSE score can be different according to age, sex, and education, the standard cut-off criteria for MMSE-KC scores were determined according to age (60–69, 70–74, 75–79, 80–90), sex (male and female) and education level (0–3, 4–6, and ≥7 years) in elderly Koreans\(^{17}\). Finally, MMSE-KC scores were classified as cognitively normal (0) or cognitively impaired (1).

2.4. Assessment of history of periodontitis

Dental digital panoramic radiographs were used to evaluate
the history of periodontitis (HOP). Panoramic radiography was performed with dimensions of 1,150 mm wide, 1,150 mm deep, and 2,200 mm high (Pax-Primo Model, Vatech, Gyeonggi-do, Korea). The voltage setting varied between 50 and 80 kV at 2 to 10 mA. Radiographs were processed in an automatic processor with a developing time of 9.7 seconds. A dental radiology specialist performed all radiographic interpretation. Radiographic alveolar bone loss (RABL), defined as the distance from the cemento-enamel junction (CEJ) to the level of the alveolar bone crest, was evaluated as the indicator of cumulative periodontitis history. In subjects with crowns or implants, the CEJ of the adjacent teeth was measured. Twenty-eight teeth, excluding the wisdom teeth, were measured on the mesial and distal aspects. HOP was dichotomized as nonsevere versus severe periodontitis (≥2 interproximal sites with RABL ≥6 mm) and categorized into three groups according to severity of periodontitis: normal, moderate periodontitis (≥2 interproximal sites with RABL ≥4 mm) and severe periodontitis (≥2 interproximal sites with RABL ≥6 mm)\textsuperscript{18}).

2.5. Assessment of confounders

To obtain information regarding sociodemobehavioral confounders, subjects were interviewed in person. Interviewers were
recruited from the survey area and trained before the main survey using structured questionnaires. Demographic factors included age and sex, and alcohol drinking, smoking, and exercise were considered as health-related behavioral confounders.

Physicians performed a general health-condition assessment and physical examination, and blood samples were obtained at the field survey center. Blood samples were collected in the morning after 8 hours of fasting, and all biochemical markers were analyzed on the same day. Total cholesterol, total protein, and fasting plasma glucose (FPG) were measured (ADVIA1650 Automatic Analyzer, Bayer, Stillwater, MN). Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m$^2$), and obesity was defined as a BMI of 25.0 kg/m$^2$ and normal weight as a BMI less than 25.0 kg/m$^2$. Current hypertension medication was noted.

Carotid IMT was measured as an indicator of subclinical atherosclerosis. IMT of the common carotid artery was assessed with the subject in a supine position using high-resolution B-mode ultrasound (SonoAce-9900, Medison Company Ltd., Seoul, South Korea) equipped with a 7.5-MHz linear-array transducer. The maximal value of the IMT in a region free of plaque was measured in both carotid arteries from the longitudinal view of the carotid bifurcation at a point 10 mm proximal to the common carotid artery. End-diastolic images were captured and
saved as files for offline analysis by five sonographers at the three centers. A single trained reader at the reading center in the Department of Preventive Medicine at Chonnam National University analyzed the still images (Sigma ScanPro 5.0, Systat Software Inc., San Jose, CA)\textsuperscript{19}. History of coronary heart disease and cerebrovascular disease and depression status were assessed using a self-reported questionnaire. The questionnaire for depression was based on the Center for Epidemiologic Studies Depression Scale (CES-D)\textsuperscript{20}.

2.6. Statistical analysis

Baseline differences in characteristics between participants in the cognitively normal and the cognitively impaired groups were compared using bivariate analyses (Table 1). Characteristics were described using frequency distributions for categorical variables and mean values with standard deviations for continuous variables. Chi-square and Fisher exact tests were used to compare differences in categorical variables, T-tests for normally distributed continuous variables, and Mann–Whitney test for non-normally distributed continuous variables.

Multivariable conditional logistic regression analysis was used to evaluate the association between periodontitis and cognitive impairment after controlling for various confounders. A pair-ID
variable was created by giving a different number to each of 65 pairs and used in the conditional logistic analysis. Periodontitis was an explanatory variable, and cognitive impairment was an outcome. Cognitive impairment was dichotomized (no and yes). For evaluating the main association, we used dichotomized periodontitis variable (no vs yes). The severity-of-periodontitis variable with ordinal three groups (normal, moderate and severe) was used to evaluate a dose–effect response. Drinking, smoking, exercise, cholesterol, total protein, obesity, fasting plasma glucose, IMT, hypertension medication, and CES–D were included in the model for adjustment. Next, interaction terms between periodontitis and five confounders (drinking, smoking, exercise, obesity, hypertension medication) were added to the models. In multivariable analysis, history of coronary heart disease (n = 9) and cerebrovascular disease (n = 3) were not included in the model, because their frequencies were too low. All analyses were performed using SPSS version 19.0 (SPSS, Inc., Chicago, IL).
3. Results

Subjects with cognitive impairment were more likely to have HOP, high IMT, and history of cerebrovascular disease and not to exercise, than controls (Table 1). There was no significant difference between individuals with and without cognitive impairment in terms of age, sex, drinking, smoking, cholesterol, total protein, obesity, FPG, hypertension medication, history of coronary heart disease, CES-D, and severity of periodontitis.

Participants with HOP were 2.1 times as likely to have cognitive impairment as those without (odds ratio (OR) = 2.14, 95% confidence interval (CI) = 1.04–4.41) after controlling for drinking, smoking, exercise, cholesterol, total protein, obesity, FPG, IMT, hypertension medication, and CES-D (Table 2), although there was no significant dose–response effect on the association between cognitive impairment and severity of periodontitis (normal, moderate, severe) (OR = 1.02, 95% CI = 0.42–2.45 for moderate periodontitis; OR = 2.16, 95% CI = 0.86–5.44 for severe periodontitis). The interaction effect of periodontitis with smoking and exercise terms increased the likelihood that individuals with HOP would have cognitive impairment from 2.14 times as great as those without HOP to 2.40 times (OR = 2.40, 95% CI = 1.08–5.30) and 2.47 times
(OR = 2.47, 95% CI = 1.07-5.72) as great, respectively (Table 3), although the effects on cognitive impairment of the interaction terms between periodontitis and drinking, smoking, exercise, obesity, and hypertension medication were not significant.
Table 1. Distribution of Confounding and Main Explanatory Variables According to Cognitive Impairment (n=189)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cognitively Impaired, n=65</th>
<th>Cognitively Normal, n=124</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD</td>
<td>69.7±6.4</td>
<td>68.7±4.9</td>
<td>0.151a</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>0.829b</td>
</tr>
<tr>
<td>Male</td>
<td>33 (50.8)</td>
<td>65 (52.4)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>32 (49.2)</td>
<td>59 (47.6)</td>
<td></td>
</tr>
<tr>
<td>Drinking, n (%)</td>
<td></td>
<td></td>
<td>0.215b</td>
</tr>
<tr>
<td>No</td>
<td>35 (53.8)</td>
<td>55 (44.4)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>30 (46.2)</td>
<td>69 (55.6)</td>
<td></td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td></td>
<td></td>
<td>0.888b</td>
</tr>
<tr>
<td>No</td>
<td>54 (83.1)</td>
<td>102 (82.3)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11 (16.9)</td>
<td>22 (17.7)</td>
<td></td>
</tr>
<tr>
<td>Exercise, n (%)</td>
<td></td>
<td></td>
<td>0.034b</td>
</tr>
<tr>
<td>No</td>
<td>53 (81.5)</td>
<td>83 (66.9)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 (22.6)</td>
<td>41 (33.1)</td>
<td></td>
</tr>
<tr>
<td>Cholesterol (mg/dL), mean±SD</td>
<td>190.4±35.6</td>
<td>197.5±34.6</td>
<td>0.788a</td>
</tr>
<tr>
<td>Total protein (mg/dL), mean±SD</td>
<td>7.4±0.5</td>
<td>7.4±0.4</td>
<td>0.159c</td>
</tr>
<tr>
<td>Obesity (body mass index≥ 25 kg/m2), n (%)</td>
<td></td>
<td></td>
<td>0.323b</td>
</tr>
<tr>
<td>No</td>
<td>40 (61.5)</td>
<td>67 (54.0)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25 (38.5)</td>
<td>57 (46.0)</td>
<td></td>
</tr>
<tr>
<td>Fasting plasma glucose (mg/dL), mean±SD</td>
<td>106.8±22.4</td>
<td>105.4±19.8</td>
<td>0.943c</td>
</tr>
<tr>
<td>Intima media thickness (mm), mean±SD</td>
<td><strong>0.767±0.185</strong></td>
<td><strong>0.742±0.139</strong></td>
<td><strong>0.025</strong></td>
</tr>
<tr>
<td>Hypertension medication</td>
<td></td>
<td></td>
<td>0.748b</td>
</tr>
<tr>
<td>No</td>
<td>33 (50.8)</td>
<td>66 (53.2)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>32 (49.2)</td>
<td>58 (46.8)</td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td></td>
<td></td>
<td>0.279d</td>
</tr>
<tr>
<td>No</td>
<td>60 (92.3)</td>
<td>120 (96.8)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5 (7.7)</td>
<td>4 (3.2)</td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td></td>
<td></td>
<td>0.039d</td>
</tr>
<tr>
<td>No</td>
<td><strong>62 (95.4)</strong></td>
<td><strong>124 (100)</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (4.6)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Center for Epidemiologic Studies</td>
<td>14.56±7.20</td>
<td>13.92±7.32</td>
<td>0.446c</td>
</tr>
<tr>
<td>Depression Scale score, mean±SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Periodontitis, n (%)</td>
<td></td>
<td></td>
<td>0.049b</td>
</tr>
<tr>
<td>No</td>
<td>41 (63.1)</td>
<td>95 (76.6)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>24 (36.9)</td>
<td>29 (23.4)</td>
<td></td>
</tr>
</tbody>
</table>
Periodontitis severity, n (%)  
<table>
<thead>
<tr>
<th>Severity</th>
<th>Obs1</th>
<th>Obs2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>15 (23.1)</td>
<td>40 (32.3)</td>
</tr>
<tr>
<td>Moderate</td>
<td>26 (40.0)</td>
<td>55 (44.4)</td>
</tr>
<tr>
<td>Severe</td>
<td>24 (36.9)</td>
<td>29 (23.4)</td>
</tr>
</tbody>
</table>

Obtained using \(^a\)T-test, \(^b\)chi-square test, \(^c\)Mann-Whitney test, \(^d\)Fisher exact test, \(^e\)linear-by-linear association test.

\(^f\) Periodontitis defined as ≥2 sites with radiographic alveolar bone loss (RABL) ≥ 6 mm.

\(^g\) Severe periodontitis ≥2 sites with RABL ≥ 6 mm, moderate periodontitis ≥2 sites with RABL ≥ 4 mm, all else normal.

SD = standard deviation.
Table 2. Adjusted Association between Periodontitis and Cognitive Impairment Using a Conditional Logistic Regression Model (N=189)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>N</th>
<th>Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontitis(^a)</td>
<td>No</td>
<td>136</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>53</td>
<td>2.14 (1.04–4.41)</td>
</tr>
<tr>
<td>Drinking</td>
<td>No</td>
<td>90</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>99</td>
<td>0.69 (0.33–1.44)</td>
</tr>
<tr>
<td>Smoking</td>
<td>No</td>
<td>156</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>33</td>
<td>0.87 (0.29–2.62)</td>
</tr>
<tr>
<td>Exercise</td>
<td>No</td>
<td>136</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>53</td>
<td>0.45 (0.19–1.02)</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td></td>
<td>189</td>
<td>0.99 (0.98–1.00)</td>
</tr>
<tr>
<td>Total protein (mg/dL)</td>
<td></td>
<td>189</td>
<td>1.32 (0.54–3.20)</td>
</tr>
<tr>
<td>Obesity(^b)</td>
<td>No</td>
<td>107</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>82</td>
<td>0.60 (0.28–1.27)</td>
</tr>
<tr>
<td>Fasting plasma glucose (mg/dL)</td>
<td></td>
<td>189</td>
<td>1.02 (1.00–1.03)</td>
</tr>
<tr>
<td>Intima media thickness (mm)</td>
<td></td>
<td>189</td>
<td>4.17 (0.49–35.47)</td>
</tr>
<tr>
<td>Hypertension medication</td>
<td>No</td>
<td>99</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>90</td>
<td>0.85 (0.41–1.74)</td>
</tr>
<tr>
<td>CES–D(^c)</td>
<td></td>
<td>189</td>
<td>1.01 (0.97–1.06)</td>
</tr>
</tbody>
</table>

\(^a\) Periodontitis defined as \(\geq 2\) sites with radiographic alveolar bone loss \(\geq 6\) mm.

\(^b\) Obesity defined as body mass index \(\geq 25\) kg/m\(^2\).

\(^c\) Center for Epidemiologic Studies Depression Scale score,
Table 3. Effect of Interaction Terms between Periodontitis and Confounders on the Association Between Periodontitis and Cognitive Impairment

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontitis</td>
<td>1.69</td>
<td>2.40*</td>
<td>2.47*</td>
<td>4.83</td>
<td>1.53</td>
</tr>
<tr>
<td></td>
<td>(0.59–4.83)</td>
<td>(1.08–5.30)</td>
<td>(1.07–5.72)</td>
<td>(0.45–52.08)</td>
<td>(0.19–12.32)</td>
</tr>
<tr>
<td>Periodontitis by Drinking</td>
<td>1.56</td>
<td>0.54</td>
<td>0.53</td>
<td>0.58</td>
<td>1.26</td>
</tr>
<tr>
<td></td>
<td>(0.36–6.72)</td>
<td>(0.10–3.02)</td>
<td>(0.09–3.19)</td>
<td>(0.13–2.63)</td>
<td>(0.33–4.83)</td>
</tr>
</tbody>
</table>

Periodontitis defined as ≥2 sites with radiographic alveolar bone loss ≥6 mm.

Model 1: conditional logistic regression model, conditional on age and sex, adjusted for drinking, smoking, exercise, cholesterol, total protein, obesity, fasting plasma glucose, intima media thickness, hypertension medication, and Center for Epidemiologic Studies Depression Scale plus the interaction term between periodontitis and drinking.

Model 2: Model 1 plus the interaction term between periodontitis and smoking.

Model 3: Model 1 plus the interaction term between periodontitis and exercise.

Model 4: Model 1 plus the interaction term between periodontitis and obesity.

Model 5: Model 1 plus the interaction term between periodontitis and hypertension medication.

*P < .05
4. Discussion

This cross-sectional study with age- and sex-matched case-control selection showed that HOP was associated with cognitive impairment in elderly Koreans. A recent study showed that individuals with cognitive impairment had higher levels of several inflammatory mediators, including tumor necrosis factor alpha and IL-1b, than cognitively normal groups\textsuperscript{21}. It has also been suggested that high C-reactive protein and IL-6 levels increase the risk of cognitive decline and Alzheimer’s disease\textsuperscript{22}. A previous study provided initial data that demonstrated high levels of antibodies to periodontal pathogens and suggested that periodontal disease could contribute to the risk of Alzheimer’s disease onset and progression\textsuperscript{23}. The current study confirmed results of previous studies that periodontitis is associated with cognitive impairment\textsuperscript{12,22}. To the best of the knowledge of the authors of the current study, the results are the first evidence of the association between periodontitis and cognitive impairment in elderly Koreans.

This study has five major strengths. First, participants were sampled from the general population. Second, a dentist evaluated RABL using dental panoramic radiograph. The reliability and validity of panorama radiographic data for the evaluation of HOP
was previously assessed in the Yangpyeong cohort and at the Seoul National University Dental Hospital. Panoramic radiographic calibration was more reliable for the assessment of history of periodontitis than using a periodontal probe and can be used as an evaluation tool for the assessment of alveolar bone loss\(^{24}\).

Third, a medical professional evaluated cognitive impairment using the MMSE, which is the most widely used cognitive impairment screening tool in clinical practice and research. Fourth, an age- and sex-matched case-control design was used to control for important effect modifiers. Finally, the association was adjusted for well-known potential confounders, including demographic, behavioral, and systemic health factors.

Although the data showed that HOP was associated with cognitive impairment, the severity of periodontitis was not associated with cognitive impairment. The likelihood of moderate periodontitis was only slightly larger than that of no periodontitis (OR = 1.03), whereas the likelihood of severe periodontitis was more than twice as large (OR = 2.15), although neither was statistically significant. This indicates that, until periodontitis reaches a moderate degree of severity, the effect of periodontal inflammation on cognitive impairment is not sufficient to have a positive association, although the effect increases as periodontal inflammation progresses. There could be a threshold level of periodontal inflammation at which cognitive impairment is
affected. The inconsistency in previous data between periodontitis and cognitive impairment could be due to the definition (criteria) of periodontitis. For example, a study using clinical attachment loss (CAL) as the criterion for periodontitis reported that periodontal disease progression independently increased the likelihood of low cognitive test scores\(^1\)\(^2\), but another study using CAL and active periodontal inflammation as the criteria for periodontitis did not find a statistically significant effect of periodontitis on cognitive test scores\(^2\)\(^5\). Hence, it is thought that some period of time is necessary for periodontal inflammation to affect cognitive impairment.

In terms of interaction effect, the interdependent interaction between periodontitis, smoking, and exercise increased the likelihood that subjects with periodontitis would have cognitive impairment. Smoking is a well-known risk factor for periodontitis\(^2\)\(^6\), and it is also associated with cognitive impairment\(^2\)\(^7\). Smoking could increase the risk of cardiovascular disease, which is associated with periodontitis and cognitive impairment. Exercise has been associated with better cognitive ability in elderly adults\(^2\)\(^8\)\(^,2\)\(^9\), and it is considered to be an important preventive factor against cardiovascular disease. Although smoking and exercise may affect brain and periodontal health through the cardiovascular circulatory system, future studies are indicated to clarify these mechanisms. It was hypothesized that
the systemic influence of periodontal inflammation could explain the link between periodontitis and cognitive impairment. An inflammatory model has been suggested in which periodontal disease induces systemic inflammatory products, which stimulate the production of beta amyloid and tau protein in brain tissue, leading to Alzheimer’s neuropathology. A similar model was suggested to show that periodontal infection might contribute to or exacerbate Alzheimer’s disease through inflammatory mechanisms.

Further studies are indicated for clarification of the causality and biological mechanism and further valid estimation with the least bias. A prospective study will clarify the direction of causality in the link between periodontitis and cognitive impairment. Studies including biomarker information and social desirability will further clarify the biological mechanism and social influence of the link between periodontitis and cognitive impairment. Future studies with larger sample sizes and that are more representative of the general population will reduce selection bias and allow stratified analysis for detecting factors that modify the effect of periodontitis on cognitive impairment. Notwithstanding some limitations, the results of the current study are sufficiently valid to evaluate the association between periodontitis and cognitive impairment in elderly Koreans.
4. Conclusion

Overall, these results show that periodontitis is independently associated with cognitive impairment after controlling for various confounders such as age, sex, drinking, smoking, exercise, cholesterol, total protein, obesity, IMT, hypertension medication, and depression. Thus, the data suggest that medical and dental health professionals should pay attention to the link between periodontal and cognitive health.
References


among subjects aged 75 years or older. Gerodontology 2012;29:36–42.


22. Holmes C, Cunningham C, Zotova E, Woolford J, Dean C, Kerr S, Culliford D, Perry VH. Systemic inflammation and


부록. 간이정신상태검사 (MMSE-KC)

실 시 요령

- 문항 중 [이탤릭체]로 쓰여진 부분은 검사의 시행 지침이다.
- 문항 중 곱은 글씨로 쓰여진 글은 피검자에게 읽어 주는 부분이다.
- 문항 중 밑줄 친 부분은 질문의 정답이다.
- 피검자의 응답을 ‘틀림’, ‘맞음’, ‘평가 안 됨’으로 평가하여 문항 오른쪽에 있는 0, 1, 9에 0 표를 한다.
- 일부 문항의 채점은 뒤편에 제시한 기준을 참조한다.
- 총점은 9로 평가된 항목을 제외한 나머지 점수의 합계이다.

검사자는 “지금부터 000님의 기억력과 집중력을 알아보기 위해 몇 가지 질문을 드리겠습니다. 질문 중 몇 가지는 쉽지만 몇 가지는 어려울 수도 있습니다.”라는 말로 검사를 시작한다.

질문 틀림 맞음 평가

<table>
<thead>
<tr>
<th>문항</th>
<th>틀림 맞음</th>
<th>평가</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 올해는 몇 년도입니까?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>2. 지금은 무슨 계절입니까?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3. 오늘은 몇일입니까?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4. 오늘은 무슨 요일입니까?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>5. 지금은 몇 월입니까? [피검자가 음력을 사용하면 음력으로 묻는다.]</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>6. 우리가 있는 이곳은 무슨 도/ 특별시/ 광역시입니까?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>7. 여기는 무슨 시/ 군/ 구입니까?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>8. 여기는 무슨 병/ 동입니까?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>9. 우리는 지금 이 건물의 몇층에 있습니다?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>10. 이 장소의 이름은 무엇입니까?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>11. 지금부터 제가 세 가지 물건의 이름을 말씀드리겠습니다. 끝까지 다 들으신 다음에 세 가지 물건의 이름을 모두 말씀해 보십시오. 그리고 몇 분 후에는 그 세 가지 물건의 이름들을 다시 물어 볼 것이니 들으신 물건의 이름들을 잘 기억하고 계십시오.</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

나무, 자동차, 모자

이제 0 0 0 넘겨서 받금 들으신 세 가지 물건 이름을 모두 말씀해 보세요.

문항 11은 첫 응답으로만 평가한다. 첫 응답에서 물건의 이름을 모두 말하지 못하는 경우는 문항 13의 지연 회복을 정확하게 검사하기 위해 ‘물건 이름을 불러주고 기억하도록 하는 과정’을 3회까지 반복할 수 있다.
12. 지금부터 제가 0 0 0 남겨 다섯 글자로 된 단어 하나를 말씀해드릴 것이니 따라 해 보십시오.

‘삼천리강산’

[피검자가 글자를 순서대로 바르게 말할 수 있도록 필요하다면 이 단어를 몇 차례 반복하여 말해 줄 수 있다.]

잘 하셨습니다. 이번에는 이 단어를 뒤 글자부터 거꾸로 말해 보십시오.

□ □ □ □ □ □ [□□점]

[피검자의 답을 위의 네모칸에 기록한다. 점수는 위의 제시한 기준에 따라 계산하여 우측 네모칸에 기록한다.]

13. 조금 전에 제가 기억하라고 말씀드렸던 세 가지 물건의 이름이 무엇인지 말씀하여 주십시오.

나 무 자동차 모 자

14. [열쇠를 보여주며] 이것을 무엇이라고 할니까?

[도장을 보여주며] 이것을 무엇이라고 할니까?

[절제 열쇠와 도장을 보여준다.]

15. 제가 하는 말을 끝까지 듣고 따라 해 보십시오. 한 번만 말씀드릴 것이라 잘 듣고 따라 하십시오.

간 장 공 장 공 장 장

[한 번만 말해주고 반복하지 않는다.]

16. 지금부터 제가 말씀드리는 대로 해 보십시오. 한 번만 말씀드릴 것이니 잘 듣시고 그대로 해 보십시오. 제가 종이를 한 장 드릴 것입니다. 그러면 그 종이를 오른손으로 받아, 반으로 점은 다음, 무릎 위에 올리 놓으십시오.

[지시를 끝낸 후에 종이를 건네준다. 지시를 반복하거나 옆에서 도와주면 안 된다.]

오른손으로 받는다.
반으로 접는다.
무릎 위에 놓는다.
17. [별지의 오각형 그림을 가리키며] 여기에 오각형이 겹쳐져 있는 그림이 있습니다. 이 그림을 아래 빈 곳에 그대로 그려보세요.

18. 옷은 왜 빨아서 입습니까?

19. 다른 사람의 주민등록증을 주웠을 때 어떻게 하면 쉽게 주인에게 돌려 줄 수 있습니까?
국문초록

한국 노인에서 치주질환과 인지장애와의 연관성

서울대학교 대학원 치의과학과 예방 및 사회치의학 전공

(지도교수 : 김 현덕)

신 혜 선

1. 목 적

기존의 연구결과, 치주질환과 인지장애와의 연관성은 아직 확증되지 않았고, 특히 한국인을 대상으로 한 연구 결과는 보고되지 않았다. 따라 서, 본 연구의 목적은 한국 노인에서 치주질환과 인지장애와의 연관성을 조사하는 것이다.

2. 방 법

본 연구는 한국 유전체 역학 조사연구의 양평 심혈관질환호호트에 기반한 단면조사연구로, 연구대상자는 60세이상 인지장애로 분류된 65 명의 환자군과 환자군의 나이와 성별을 짝짓기한 124명의 대조군을 포 함한 총 189명이었다. 인지장애군과 정상군은 한국판 간이정신상태검사 (Mini-Mental State Examination) 를 사용하여 분류하였다. 치주질환 은 파노라마 방사선사진으로 평가한 치조골소실을 미국치주학회의 기준 에 따라 정상, 중등도, 심도로 분류한 다음, 심도치주질환 유무로 재분 류하였다. 혼란변수는 나이, 성별, 음주, 흡연, 운동, 총콜레스테롤, 총단

- 30 -
백질 체질량지수, 공복혈당, 경동맥 내중막 두께, 고혈압약 복용여부, 그리고 우울증 등이었다. 통계분석은 조건부 로지스틱 회귀분석 (conditional logistic regression models)을 사용하였다.

3. 결과
치주질환 이환자에서 인지장애에 걸릴 가능성이 치주질환 비이환자보다 2.14배 (odds ratio=2.14, 95% confidence interval =1.04-4.41) 높았다. 치주질환과 주요 혼란변수인 흡연, 운동 간에는 교호작용효과 (interaction effect)가 있었다.

4. 결론
치주질환은 다양한 혼란변수를 보정한 후 인지장애와 독립적인 연관성이 있었다. 따라서 치과의사와 의사들은 이 연관성에 관심을 가져야한다. 추후 연구에서 치주질환이 인지기능 감소에 기여한 역할에 대한 기전 (mechanism)을 확인할 필요가 있으며, 치주질환의 예방 및 치료가 인지기능의 변화가 있는지에 대한 임상연구가 필요할 것으로 사료되었다.

주요어: 간이정신상태검사, 인지장애, 치주질환, 역학, 염증
학번: 2007-23384