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The relationship among periodontal condition, serum lipid, and electrocardiographic abnormalities in the elderly: A prospective cohort study

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ABSTRACT

Periodontal disease is recognized as a risk factor for cardiovascular disease (CVD). Some studies have suggested that serum lipids might play a role in the association between periodontal disease and CVD. However, this hypothesis remains unproven. Present study evaluated the association between periodontal disease and CVD-related parameters including electrocardiographic (ECG) parameters and serum lipid levels in the elderly. This study was a prospective cohort study. A total of 107 subjects (57 males and 50 females) from Niigata City's community-dwelling elderly (all aged 75 years old) who possessed at least 20 teeth and did not exhibit ECG abnormalities at the baseline underwent annual examinations for 5 years. Logistic regression analysis was used to assess the relationship between periodontal condition and the presence of ECG abnormalities, after adjusting for confounding factors including serum lipid levels. Logistic regression analysis showed that the subjects who exhibited a poor periodontal condition at the baseline had a 2.97 times greater risk of suffering from ECG abnormalities than the subjects who displayed a good periodontal condition at the baseline (p = 0.019). Furthermore, the subjects who displayed a poor periodontal condition and an unfavorable serum lipid profile at the baseline showed a significantly higher frequency of ECG abnormalities (63.6%) than those who exhibited a healthy periodontal condition and a favorable serum lipid profile (21.6%, p = 0.008) as well as those who displayed a healthy periodontal condition and an unfavorable serum lipid profile (21.4%, p = 0.010). As a conclusion, periodontal condition could be a marker of CVD, even in the healthy elderly.

Keywords: Periodontal Condition; Serum Lipid; Cardiovascular Disease; Elderly People

1. INTRODUCTION

It has been determined that poor oral health can have a profound effect on general health, and several oral diseases are known to be associated with chronic diseases [1]. Besides the fact that periodontal disease is one of two major dental diseases that display high prevalence rates worldwide [2], the World Health Organization (WHO) has also found that periodontal disease shares some common risk factors with systemic diseases such as cardiovascular disease (CVD) [3].

Previous studies have suggested that serum lipids might play a role in the association between periodontal disease and CVD, particularly in elderly patients. While a reduced high-density lipoprotein cholesterol (HDL-C) level is a well-recognized risk factor for CVD and ischemic stroke [4,5]. Izumi *et al*. [6] found that a higher total cholesterol (TC) level is associated with a lower prevalence of periodontitis in non-smoking elderly people. Moreover, two cross-sectional studies have been conducted in Japan to assess the associations between blood chemical parameters and periodontal status, and both studies indicated that elevated HDL-C levels are correlated with a reduced incidence of periodontal disease [7,8].

On the other hand, other studies failed to identify any

association between periodontal disease and CVD. Holm-Pedersen *et al*. [9] investigated the correlations among dental caries, periodontal disease, and cardiac arrhythmia in community-dwelling elderly individuals who were aged 80 or older and showed that there was no association between periodontal disease and arrhythmia. In line with this result, a case-control study by Sridhar *et al*. [10] found that coronary heart disease did not exacerbate the destruction of periodontal tissue.

The inconsistencies between these studies might have been due to differences in study design, the adjustments made for confounding variables, and other methodological details. Some previous studies used a case-control design, which is known to introduce various types of bias [11], while other studies employed a cross-sectional design, which made it impossible to assess the direction of the relationship between the assumed cause and effect [12]. Furthermore, some previous studies might have inadequately controlled for confounding factors such as gender, age, smoking status/history, and body mass index (BMI).

Therefore, the purpose of this study was to evaluate the association between periodontal disease and CVD-related parameters including electrocardiographic (ECG) parameters and serum lipid levels in the elderly using a prospective cohort study design. The result of this study was considered to be important in giving more insights for the elucidation of the correlation between oral and general health.

2. MATERIALS AND METHODS

2.1. Subjects

The subjects for this study was drawn from the Niigata Elderly Study, which was a community-based prospective study that aimed to assess the relationship between oral health and general health in the elderly. Invitations were sent to all residents (n = 4542) who were born in 1927 based on the Niigata City's resident registry. The invitations also informed the recipients of the purpose of the study. As a result, 81.4% (n = 3695) of the invitees agreed to participate in the study. Considering the availability of resources, appointments for examinations could only be arranged for 600 individuals. The final study subjects (n = 600) were randomly selected so that they included approximately equal numbers of men (306) and women (294). We assessed the general condition of the subjects using the Tokyo Metropolitan Institute of Gerontology Index (TMIG-Index) of Competence subscale questionnaires. All of the subjects were Japanese, in good general health, and did not require special care for their daily activities. The subjects' mean score on the TMIG-Index subscales was 11.9 ± 1.4, and the results of this assessment were indicative of a high level of competence among the study participants. The 600 subjects were invited for annual examinations including oral and general physical examinations from 1998 to 2008. All of the subjects agreed and signed informed consent forms regarding the examination protocols. Of the 600 subjects, 312 participated in all of the annual examinations from 2003 to 2008. An age of 75 years in 2003 was set as the baseline for the present study since a recent review showed that approximately 50% of patients with dysrhythmia, especially atrial fibrillation, were aged 75 years or older [13]. One hundred and seven (57 males and 50 females) of the 312 subjects were selected for the present study because they had at least 20 teeth and did not display any atherosclerosis-related ECG abnormalities at the baseline which was considered as the inclusion criteria for this study. All of the subjects were examined at local community centers in Niigata City. The ethics committee of the Niigata University School of Dentistry approved this study and protected the subjects' rights.

2.2. Oral Examinations

The periodontal examinations were carried out by four trained dentists under sufficient illumination with artificial light. Periodontal conditions was assessed using dental mirrors and a specially designed constant-pressure periodontal probe (Vivacare TPS Probe®; Schaan, Liechtenstein), which was applied at a probing force of 20 g. The probing depth (PD) and clinical attachment level (CAL) at six sites (mesiobuccal, mid-buccal, distobuccal, mesiolingual/palatal, mid-lingual/palatal, and distolingual/palatal) were recorded for all teeth, including the third molars, and rounded to the nearest millimeter. The examiners were calibrated before and during the survey, and inter-examiner reliability was assessed. According to replicated examinations of 10 patients, the percentage agreement (within ± 1 mm) ranged from 87.5% to 100.0% for PD and 83.3% to 100.0% for CAL. In addition, the Kappa value ranged from 0.8 to 1.0 for PD and 0.7 to 1.0 for CAL. The National Health and Nutrition Examination Survey (NHANES) III [14] found that about 30.0% of 70- to 80-year-old subjects had moderate to advanced periodontitis. Accordingly, we used the 30th percentile to indicate a poor periodontal condition. Therefore, each subject's periodontal condition was classified according to whether their mean PD was ≥ 1.8 mm or < 1.8 mm and whether their mean CAL was ≥ 2.5 mm or < 2.5 mm [15]. Subjects with a mean PD of ≥ 1.8 mm and a mean CAL of ≥ 2.5 mm were considered to exhibit a poor periodontal condition. The mean PD was 2.05 mm, and the mean CAL was 2.98 mm. The number of teeth present was also investigated.

2.3. General Examinations

2.3.1. Electrocardiography

A resting 12-lead ECG recording was taken using a standard ECG machine (CardioStar FCP-7411; Fukuda ME Kogyo Co., Tokyo, Japan) equipped with an automated analysis system whilst the subject was in the supine position, in accordance with standard recommendations [16]. The criteria established by Takata *et al*. [17] were used to diagnose atherosclerosis-related ECG abnormalities. Atrial fibrillation was defined as a markedly irregular R-R interval and the absence of P-waves, with disorganized electrical activity being seen in their place. VPC (Ventricular premature contractions) were defined as an antecedent R-R interval of ≤ 0.8 × the mean R-R interval, a subsequent R-R interval of ≥ 1.05 × the mean R-R interval, and an abnormal QRS complex. SVPC (Supraventricular premature contractions) were defined as an antecedent R-R interval of ≤ 0.8 × the mean R-R interval, a subsequent R-R interval of ≥ 1.05 × the mean R-R interval, a normal QRS complex, and no evidence of atrial fibrillation or sinus dysrhythmia. Sinus dysrhythmia was defined as an irregular R-R interval with no other dysrhythmia. Sinus tachycardia was defined as a P-wave rate of greater than 100 beats/min, with no other dysrhythmia. Sinus bradycardia was defined as a P-wave rate of less than 60 beats/min, with no other dysrhythmia. LVH (left ventricular hypertrophy) and ST-segment depression as defined by the Minnesota Code were also evaluated [18]. All of the abovementioned conditions were considered to be abnormal ECG findings. The subjects who displayed any of these ECG abnormalities during a follow-up examination were categorized as "positive", and those that did not were categorized as "negative".

2.3.2. Blood Pressure, Gender, Smoking History, BMI, and Blood Measurements

The blood pressure (BP) measurement and blood sampling were performed with the subjects in the supine position. The patients' TC, HDL-C, and low-density lipoprotein cholesterol (LDL-C) levels were determined by a commercial laboratory (BML, Inc., Tokyo, Japan) under non-fasting conditions. Based on the threshold for people in the intermediate-risk group for CVD (possessing 1 - 2 major risk factors for CVD other than LDL-C; age ≥ 45 for males and ≥ 55 for females is a major risk factor) suggested by the Japan Atherosclerosis Society [19], subjects with serum LDL-C levels of < 140 mg/dL, serum HDL-C levels of ≥ 40 mg/dL, and serum TC levels of < 220 mg/dL were considered to display favorable serum lipid profiles, while the subjects that exhibited the opposite findings were considered to display unfavorable serum lipid profiles. Personal interviews were conducted to obtain information regarding the subjects' smoking habits and sex. Anthropometric evaluations including measurements of weight and height were performed to allow BMI calculations to be performed.

2.4. Statistical Analysis

Initially, the subjects' characteristics were compared between the subjects with and without ECG abnormalities using the *t*-test for quantitative data and the *chi-square* test for categorical variables. During this analysis, baseline data regarding the number of remaining teeth; HDL-C, LDL-C, and TC levels; and mean PD and CAL were compared.

Furthermore, to analyze the effects of periodontal condition and the serum lipid profile on the presence/absence of ECG abnormalities during the study period, the *chi-square* test was used to compare the following four groups: the subjects who exhibited a healthy periodontal condition and a favorable serum lipid profile (n = 37); a healthy periodontal condition and an unfavorable serum lipid profile (n = 28); a poor periodontal condition and a favorable serum lipid profile (n = 31); and a poor periodontal condition and an unfavorable serum lipid profile (n = 11).

Finally, logistic regression analysis was performed to examine the independent effect of periodontal condition on the presence/absence of ECG abnormalities during the study period. The presence of ECG abnormalities during the study period was used as the dependent variable, while the independent variables were periodontal condition at the baseline and other parameters that were found to be significantly associated with ECG abnormalities in the initial analysis. All calculations and statistical analyses were performed using SPSS version 17. Statistical significance was set at $\alpha = 0.05$.

3. RESULTS

Table 1 shows the means and distributions of the study variables according to the presence or absence of ECG abnormalities during the study period. The subjects with ECG abnormalities had significantly higher BMI values at the baseline than those without (23.9 ± 2.8 vs 22.6 ± 2.8 kg/m^2, $p = 0.030$). Furthermore, ECG abnormalities were significantly associated with lower LDL and TC levels at the baseline. While only 29.2% of the subjects who did not exhibit ECG abnormalities displayed a poor periodontal condition, 60.0% of the subjects with ECG abnormalities displayed a poor periodontal condition ($p = 0.002$).

As shown in **Figure 1**, a significantly higher percentage of the subjects who displayed a poor periodontal condition and an unfavorable serum lipid profile at the baseline suffered from ECG abnormalities (63.6%)

Table 1. Background characteristics of the subjects according to their ECG status.

Subjects' characteristics	ECG abnormalities		
	Negative	Positive	
	n = 72	n = 35	
	Mean ± SD		*p*-value[a]
Present teeth at the baseline	25.1 ± 2.9	25.4 ± 3.0	0.641
BMI at the baseline (kg/m²)	22.6 ± 2.8	23.9 ± 2.8	**0.030**
Mean BMI over 5 years (kg/m^2)	22.1 ± 2.7	23.2 ± 2.9	0.060
Systolic BP at the baseline (mmHg)	129.9 ± 15.3	133.8 ± 17.4	0.231
Mean systolic BP over 5 years (mmHg)	132.5 ± 10.1	134.9 ± 12.2	0.259
Diastolic BP at the baseline (mmHg)	70.3 ± 9.3	71.8 ± 9.7	0.433
Mean diastolic BP over 5 years (mmHg)	71.8 ± 6.5	72.4 ± 8.7	0.734
Mean PD at the baseline (mm)	2.0 ± 0.4	2.1 ± 0.3	0.287
Mean CAL at the baseline (mm)	2.9 ± 0.7	3.1 ± 0.7	0.138
HDL level at the baseline (mg/dL)	60.3 ± 15.6	59.8 ± 21.5	0.893
LDL level at the baseline (mg/dL)	119.7 ± 25.6	104.1 ± 26.8	**0.005**
TC level at the baseline (mg/dL)	206.2 ± 28.8	194.1 ± 28.5	**0.044**
	N (%)		*p*-value[b]
Gender			
Male	36 (50.0)	21 (60.0)	0.331
Female	36 (50.0)	14 (40.0)	
Periodontal condition at the baseline			
Healthy	51 (70.8)	14 (40.0)	**0.002**
Poor condition[c]	21 (29.2)	21 (60.0)	
Lipid condition at the baseline			
Favorable	46 (63.9)	22 (62.9)	0.917
Unfavorable[d]	26 (36.1)	13 (37.1)	
Smoking status[e]			
Non-smoker	64 (88.9)	30 (85.7)	0.921
Smoker	8 (11.1)	4 (11.4)	

BMI; Body mass index, BP; Blood pressure, PD; Probing depth, CAL; Clinical attachment level, HDL; High density lipoprotein, LDL; Low density lipoprotein, TC; Total cholesterol; [a]*t*-test; [b]*Chi-square* test; [c]Mean PD ≥ 2 mm and mean CAL ≥ 2.5 mm; [d]Serum LDL-C level ≥ 140 mg/dL and/or serum HDL-C level < 40 mg/dL and/or serum TC ≥ 220 mg/dL; [e]Data was missing for 1 subject.

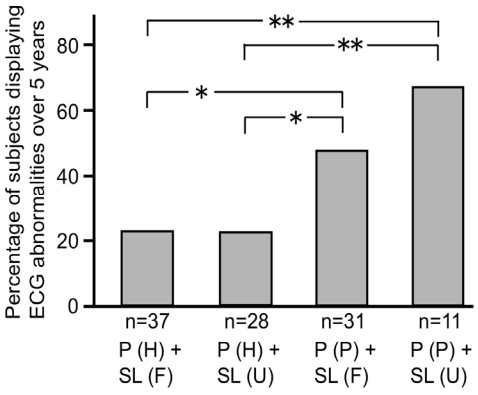

Figure 1. Percentage of subjects that displayed ECG abnormalities over 5 years in four groups according to their periodontal condition and serum lipid level [P (H); Healthy periodontal condition, P (P); Poor periodontal condition, SL (F); Favorable serum lipid profile, SL (U); Unfavorable serum lipid profile]. *$p < 0.05$, **$p < 0.01$.

compared with the subjects who exhibited a healthy periodontal condition and a favorable serum lipid profile (21.6%, $p = 0.008$), or a healthy periodontal condition and an unfavorable serum lipid profile, at the baseline (21.4%, $p = 0.010$). Furthermore, the frequency of ECG abnormalities was significantly lower in the latter two groups than in the other two groups (21.5% vs 50.0%, $p = 0.002$).

The results of the multivariate logistic regression analysis are shown in **Table 2**. The subjects who displayed a poor periodontal condition at the baseline were found to be at a 2.97 times higher risk of exhibiting ECG abnormalities than the subjects who displayed a healthy periodontal condition at the baseline ($p = 0.019$). Moreover, BMI at the baseline was positively associated with the presence of ECG abnormalities (OR = 1.22, $p = 0.019$) while the LDL-C level at the baseline had a significant negative effect on the risk of ECG abnormalities (OR = 0.96, $p = 0.019$).

Table 2. Binary logistic regression analysis of the effects of the explanatory variables including periodontal condition on the presence of ECG abnormalities.

Independent variable	Dependent variable: Presence of ECG abnormalities over 5 years				
	Coefficient	SE	*p*-value	OR	95% CI
Periodontal condition (0: healthy/1: poor)	1.09	0.47	**0.019**	**2.97**	1.19 - 7.38
TC at the baseline	0.02	0.02	0.227	1.02	0.99 - 1.05
LDL at the baseline	−0.04	0.02	**0.019**	**0.96**	0.92 - 0.99
BMI at the baseline	0.20	0.09	**0.019**	**1.22**	1.03 - 1.45

TC; Total cholesterol, LDL; Low density lipoprotein, BMI; Body mass index, SE; Standard error, OR; Odds ratio, CI; Confidence interval.

4. DISCUSSION

An association between periodontal condition and the presence of ECG abnormalities was detected in this study. It has been suggested that dental caries and periodontal disease are related to myocardial infarction [20], dysrhythmia [21], coronary heart disease [4], and abnormal ECG findings in octogenarians [17]. Furthermore, some studies have reported that periodontitis results in higher systemic levels of C-reactive protein and interleukin-6 and increased numbers of neutrophils, suggesting that elevated levels of these inflammatory substances cause inflammatory changes in atherosclerotic lesions, increasing the risk of cardiac or cerebrovascular disease events [22,23]. Other recent studies have suggested that *S. mutans* migrates to cardiovascular endothelial tissue [24] and binds to extracellular matrix molecules and fibrinogen [25]. Moreover, DNA from periodontal pathogens was highly prevalent in coronary artery atherosclerosis samples taken from patients with coronary artery disease [26]. These findings support the view that infection with oral bacterial species could be a risk factor for coronary heart disease.

A negative association between the serum LDL-C level and the presence of ECG abnormalities during the study period was found in this study. One possible explanation for this inverse association is the effect of selective survival; *i.e*., those who are susceptible to the biological effects of high cholesterol levels tend to die before reaching an advanced age [27,28]. Thus, the individuals who lived longer would form an unintentionally selected group with lower cholesterol levels and a genetic background (or other factors) that protects them from the effects of higher cholesterol concentrations [29]. This explanation agrees with the fact that the subjects in the present study were relatively healthy and did not require special assistance for their daily activities. Another study stated that in the very elderly, changes in the vessel wall might lower their susceptibility to cholesterol [28].

This finding might also explain our study results. The subjects who exhibited a poor periodontal condition and unfavorable serum lipid levels at the baseline displayed the highest frequency of ECG abnormalities during the study period. The difference in the frequency of ECG abnormalities was greatest between the subjects who did and did not display a healthy periodontal condition, regardless of their baseline serum lipid levels. Moreover, no significant difference in the frequency of ECG abnormalities was found between the subjects with and without favorable serum lipid levels who displayed the same periodontal condition. Therefore, periodontal condition was more closely associated with ECG abnormalities than serum lipid levels at the baseline. One possible explanation for this is that the subjects were relatively healthy and independent community-dwelling elderly individuals who had few problems with their general health, particularly with their serum lipid profiles. Another possible explanation is that we did not include serum triglycerides when assessing serum lipid condition since non-fasting blood samples were collected. Since serum triglycerides might influence a patient's lipid profile, this should be considered as one of the limitations of our study. Another possible limitation of our study was the fact that we did not possess information about the medication being taken by the subjects, which might have also had an influence on the presence/absence of ECG abnormalities, nor did we have any information about the other medical conditions suffered by the subjects, such as their blood glucose levels, which could have affected their systemic condition.

5. CONCLUSION

Our results suggest that in the elderly periodontal condition has a significantly positive effect on the risk of ECG abnormalities, while the LDL-C level has the opposite effect. These findings indicate that periodontal condition could be used as a marker of coronary heart disease, even in the healthy elderly. Therefore, it is important to recognize periodontitis as a possible marker for coronary heart disease with an inverse association of serum lipid condition in the elderly.

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