Severity of Periodontitis in Patients With Isolated Coronary Artery Ectasia
A Case Control Study

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SUMMARY

The concept that coronary artery ectasia (CAE) is an inflammatory-related disease has been increasingly recognized. Periodontitis induced low-grade chronic systemic inflammation has been shown to be associated with cardiovascular diseases. The aim of the present study was to evaluate the association between periodontitis and CAE.

Thirty-two patients with isolated CAE, and 28 age, sex and smoking status-matched subjects with normal coronary arteries (NCA) underwent full dental examinations. Periodontal disease was evaluated using the following clinical parameters; number of remaining teeth, plaque index (PI), gingival index (GI), bleeding on probing (BOP), and pocket depth (PD).

Cases and controls did not differ according to their baseline characteristics and prevalence of traditional cardiovascular risk factors. Patients with isolated CAE had higher periodontal indices when compared to subjects with NCA (PD: 3.6 ± 1.26 mm versus 2.3 ± 0.79 mm; GI: 2.29 ± 0.86 versus 1.43 ± 1.19; BOP (%): 52.18 ± 20.1 versus 27.8 ± 10.9, P < 0.001, P < 0.05 and P < 0.05, respectively). Moreover, in multivariate analysis higher values for PD were found to be significant predictors for the likelihood of having coronary ectasia.

The results of the present study demonstrate for the first time that there is an association between periodontitis and isolated CAE. (Int Heart J 2014; 55: 296-300)

Key words: Pocket depth

Periodontal disease is defined as a chronic inflammation of gum tissue, including the ligaments and bony structures that hold the tooth in place. Previous studies have suggested an association between periodontal status and cardiovascular disease.1-3 Although the mechanism of this association has not been sufficiently clarified, it has been suggested that periodontitis is an independent risk factor for atherosclerosis and cardiovascular diseases.2-4 Furthermore, in several studies assessing the mechanism underlying this association between periodontal disease and coronary artery disease (CAD), it has been shown that the spread of the bacteria and bacterial products into the circulation may trigger the atherosclerotic process.3-5 In addition, this low grade chronic systemic inflammation, and elevated levels of cytokines, C-reactive protein, and other inflammatory biomarkers can cause platelet aggregation, coronary inflammation, and endothelial dysfunction.5-6

Coronary artery ectasia (CAE) is defined as an inappropriate dilatation of the coronary arteries, exceeding the diameter of normal adjacent segments or vessel by 1.5 times.7 The estimated incidence of CAE varies from 1.2% to 5.3% with a predominance in males, however, isolated CAE compromises a small portion of the total number of CAE cases, with an incidence of 0.1-0.79%.8-9 Although CAE is largely attributed to atherosclerosis, some other chronic inflammatory diseases such as polyarteritis nodosa, Takayasu’s disease, syphilis, scleroderma, Kawasaki disease, and rheumatoid arthritis have been reported to be associated with CAE.8-9 Nonetheless, it has been shown that the presence of coronary ectasia alone is as important as the presence of CAD.7 No studies have investigated the relationship between periodontitis and CAE. The aim of this study was to evaluate the association between isolated CAE and periodontitis as a low grade inflammatory disease.

METHODS

Subjects: The study population was prospectively selected from among the individuals who underwent coronary angiography in our tertiary reference hospital. A total of 32 patients (22 men, 10 women) with isolated CAE as a study group, and 28 (13 men, 15 women) age, sex and smoking status-matched...
subjects with normal coronary arteries (NCA) as a control group were included in the study. The indication for coronary angiography was the suspicion of coronary artery disease based on either the presence of typical angina or high-risk findings on noninvasive testing (stress test, myocardial perfusion scintigraphy) for both groups. All subjects were evaluated for classic risk factors for coronary artery disease. Hypertension was defined as blood pressure ≥ 140/90 mmHg or receiving antihypertensive treatment. The medical treatment received by both groups was investigated. It was the first angiographic procedure for all participants in the study and none of them were receiving statin, acetylsalicylic acid or any anti-inflammatory medication. Thirteen patients in the study group and 9 patients in the control group were receiving antihypertensive treatment. Furthermore, body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters for all participants.

The exclusion criteria were aged over 60 years old, the presence of systemic disease (eg. diabetes mellitus, congestive heart failure, rheumatoid arthritis, valvular heart disease, kidney, liver or lung disease), the presence of any other acute or chronic infections as assessed on clinical examination and routine laboratory testing and systemic antibiotic treatment within the previous 3 months or any other regular medication. Also, patients with fewer than 6 teeth were excluded.

**Laboratory data:** In all subjects, blood samples were collected after overnight fasting and all parameters were measured, using standard laboratory methods.

**Coronary angiography:** Coronary angiography was performed using either the brachial or the femoral approach. Coronary angiograms were evaluated by two experienced angiographers. CAE was defined as the enlargement of the vessel lumen above 1.5 times that of an adjacent normal artery or normal parts of the same vessel (Figures 1 and 2).

**Clinical examination for periodontal disease:** Before discharge, all subjects included in the study underwent a periodontal examination by a trained dentist who was blinded to the coronary angiography results. On periodontal examination, the number of remaining teeth, plaque index (PI), gingival index (GI), bleeding on probing (BOP), and pocket depth (PD) were evaluated in each patient and full dental charting was performed. Gingival plaque was assessed by PI according to Silness and Löe, which includes visual clinical evaluation of each tooth on the mesial, buccal and lingual aspect in terms of 4 categories (0 = no plaque to score and 3 = a lot of plaque on the teeth and along the gingival margin). To evaluate GI which predicts gingival inflammation, the margins of the gingiva for each tooth were scored from 0-3 (0 = free from inflammation, 3 = severe inflammation, strong reddening, a tendency to spontaneous bleeding and ulceration) upon inspective signs of inflamed mucosa and bleeding. PD, which is the distance between the gingival margin and the bottom of the gingival pocket, was measured in millimeters in 6 different teeth using a calibrated periodontal probe. The study was approved by the local ethics committee and all patients gave informed consent before entering the study.

**Statistical analysis:** A complete analysis was performed using SPSS 14 software (SPSS, Chicago, IL). Continuous variables are presented as the mean ± standard deviation (SD) and median [range]. Categorical variables are presented as frequencies (n, %). The chi-square test was used in the comparison of categorical variables for two study groups. Student’s t test and the Mann-Whitney U test were used in the comparison of the distribution of continuous variables between groups after controlling for normality assumptions with the Shapiro-Wilk test. Univariate and multivariate logistic regression analyses (method with Enter) were used to detect the predictors for the likelihood of having ectasia. All statistical analyses were performed according to two-sided hypothesis tests and a P value less than 0.05 was regarded as indicating a statistically significant differ-

**Figure 1.** Coronary angiographic image of a 40 year old male patient with coronary artery ectasia in the right coronary artery (left anterior oblique view with cranial angulation).

**Figure 2.** Coronary angiographic image of a 53 year old male patient with coronary artery ectasia in the left anterior descending artery (left anterior oblique view with caudal angulation).
Results

The mean demographic, clinical, and biochemical parameters for both groups are presented in Table I. The mean age was similar in the two groups (CAE group; 47.59 ± 6.90 years versus control group; 47.21 ± 5.97 years). There were no significant differences between the groups with respect to BMI and the presence of hypertension. In addition, the baseline fasting plasma glucose levels, erythrocyte sedimentation rates, high sensitivity C-reactive protein (hsCRP) levels, leukocyte counts, and lipid parameters were similar in both groups. In the study group, ectasia involved the left anterior descending artery in 26 (81.2%), the left circumflex artery in 10 (31.2%), and the right coronary artery in 20 (62.5%) patients. One-vessel, 2-vessel, and 3-vessel ectasia were found to be present in 11 (34.4%), 13 (40.6), and 8 (25%) patients, respectively (Table I). The periodontal characteristics of the study population (PD, GI, BOP, PI parameters and number of remaining teeth) are given in Table II. The results showed that the PD, GI and BOP values were statistically higher in isolated CAE patients when compared to the subjects with NCA (P < 0.001, P < 0.05 and P < 0.05, respectively). In relation to PI, which indicates poor oral hygiene, no statistically significant difference was observed between the two groups but oral hygiene in the CAE group tended to be worse. In addition, the number of remaining teeth was similar for both groups.

In the multivariate analysis, a higher PD value was found
to be a significant parameter for the likelihood of having CAE (OR = 4.3; 95% confidence interval = 1.66-11.2; P < 0.001). Nonetheless, a modest but statistically not significant odds ratio for GI was found (OR = 1.78; 95% confidence interval = 1.78-0.21; P > 0.05) (Table III).

### Discussion

Several studies have reported that subjects with periodontal disease may have a higher risk for cardiovascular disease. However, no study has evaluated the association between CAE and periodontitis. In our study, we found for the first time that patients with isolated CAE had severe periodontitis irrespective of hsCRP levels. Our study showed that PD, GI values and BOP were significantly higher in isolated CAE patients when compared to the control group. There were no significant differences in PI and the number of remaining teeth between the two groups. Moreover, logistic regression analysis showed a high and significant odds ratio for PD in the CAE group.

It has been shown that periodontitis induces systemic inflammation, as indicated by raised serum levels of various inflammatory markers leading to development of variable systemic complications such as cardiovascular disease, cerebrovascular disease, respiratory diseases, pregnancy complications, altered glycemic control, and renal disease. Two recent studies, however, have demonstrated the association of periodontitis with carotid artery intima-media thickness, arterial stiffness, and carotid shear stress force. In addition, some studies have indicated periodontitis as a risk factor for endothelial dysfunction.

Many etiologies have been reported for CAE, however, the pathogenetic mechanisms that underlie this entity are not well understood. The loss of musculo-elastic arterial wall seems to be a unique characteristic for CAE which results in marked attenuation of the vessel wall and dilatation. It has been shown that CAE is a component of systemic arteriopathy and also is increasingly recognized as an inflammatory-related disease. Although ectasia may occur during the development of coronary atherosclerosis, some authors have suggested that the ectatic process may also be independent from the atherosclerotic process because it can be found isolated in coronary and other vascular systems. Accumulating data have suggested that CAE is associated with an inflammatory response that presented as an increased level of circulating inflammatory markers including pro-inflammatory cytokines, adhesion molecules, acute phase reactant, and inflammatory-related cells. As a result of this destructive chronic inflammatory state, artery walls are weakened potentially resulting in ectasia.

Although significantly higher values for PD, GI and BOP support our hypothesis that local inflammation of periodontal tissue with subsequent low-grade systemic inflammation may influence coronary vasculature and result in CAE, we did not observe an association of hsCRP with periodontal disease. In studies evaluating the association between periodontitis and CAD, it has been reported that patients with severe periodontitis have more elevated levels of hsCRP than controls with healthy periodontal tissues. However, in some studies the relationship between periodontal disease and hsCRP has shown no correlation. One possible explanation for this discrepancy might be poor oral hygiene. A study by Androsz-Kowalska, et al reported no significant correlation was observed between periodontal indices and the inflammatory parameters evaluated (leukocyte counts and and hsCRP levels). In addition, Yakob, et al found that chronic periodontitis is associated with early atherosclerosis irrespective of low hsCRP levels. Moreover, a more detailed analysis of other inflammatory molecules might help to clarify the mechanism of how periodontitis affects/links to CAE in this study.

In order to decrease the potential confounding influence of risk factors for CAE, diabetic patients were excluded in this study. In addition, our study included patients with comparable prevalence of hypertension, smoking status, and BMI values. The prevalence and severity of periodontitis increase with age. On the basis of US National Health and Nutrition Examination Survey 1999-2004 data, the prevalence of moderate to severe periodontitis was 5% among the individuals aged 35 to 49 years, whereas it was 34% among those aged > 65 years. In our study, CAE and the control subjects were in the middle age group. Thus, this design decreased the potential confounding influence of age factor in the final results.

The present study has some limitations. The sample size of our study population was rather small because of the low prevalence of isolated CAE and the patients were derived from a single center. Another limitation of this study was the lack of more detailed analysis of other inflammatory molecules which may help to clarify the link between periodontitis and CAE. Moreover, the data are cross-sectional and no causality may be inferred and many confounders cannot be completely accounted for in this design, such as socioeconomic status. Finally, the lack of determining a periodontal pathogen (e.g., Porphyromonas gingivalis) in subgingival plaque or saliva was also another limitation of this study.

**Conclusion:** The present study demonstrates for the first time that there is an association between periodontitis and isolated CAE. PD was found to be the most powerful predictor for the likelihood of having coronary ectasia in this study. Chronic periodontitis is related to subclinical changes in the coronary arteries. Whether this association might be indicative of future progression of CAE is subject for further large, prospective studies.

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**Table III. Variables Associated With Isolated Coronary Artery Ectasia Identified by Multivariate Logistic Regression Analysis**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (OR)</th>
<th>95% confidence interval</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Pocket depth</td>
<td>4.3</td>
<td>1.66 - 11.2</td>
<td>0.003</td>
</tr>
<tr>
<td>Gingival index</td>
<td>1.78</td>
<td>0.21 - 15.09</td>
<td>0.59</td>
</tr>
<tr>
<td>Plaque index</td>
<td>0.3</td>
<td>0.04 - 2.89</td>
<td>0.33</td>
</tr>
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References


