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# Periodontitis is associated with angiographically verified coronary artery disease

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***Abstract***

**Introduction:** We investigated the association of periodontitis and severity of coronary artery disease (CAD) as verified using coronary angiography.

**Material and Methods:** Participants were recruited among those attending coronary angiography at Helsinki University Central Hospital, Finland, in 2007 and 2008. Detailed clinical periodontal examination [number of teeth, bleeding on probing, periodontal probing depth (PPD)] and oral panoramic radiographs [alveolar bone loss (ABL), angular bone defects] were performed.

**Results:** Of 506 patients, 123 (24.3%) had no significant CAD, whereas 184 (36.4%) had stable CAD and 169 (33.4%) acute coronary syndrome (ACS). Both stable CAD and ACS were associated with 8–17 missing teeth with ORs 4.33 (1.61–11.7, $p = 0.020$) and 5.24 (1.90–14.5, $p = 0.014$), and more than seven teeth with PPD $\geq 6$ mm with ORs 2.44 (1.01–6.07, $p = 0.049$) and 2.75 (1.16–6.53, $p = 0.022$) respectively. Severe ABL was associated with ACS with an OR 5.39 (1.23–23.6, $p = 0.025$). Number of stenosed arteries was linearly associated with ABL ($p$ for trend <0.001), number of missing teeth ($p < 0.001$), and pockets with probing depth $\geq 6$ mm ($p = 0.033$).

**Conclusions:** Compared with patients with no significant stenosis, poor periodontal health including missing teeth, periodontal inflammation, and bone loss is associated with angiographically verified coronary artery narrowing in patients with stable CAD or ACS.

Key words: coronary angiography; coronary heart disease; infection; inflammation; periodontitis

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Periodontal diseases are common in Finland; a population-based study revealed that deepened periodontal pockets are found in 64% and signs of more severe forms of the disease in 21% of adults (Suominen-Taipale et al. 2008). Periodontitis is associated with an increased risk for coronary artery disease (CAD) and other cardiovascular diseases (CVD) (Mattila et al. 1989, 1993, 1995). These two inflammatory diseases share similar behavioural and risk patterns, such as low socioeconomic status, smoking, and diabetes, which again are strongly linked to hypertension, obesity, and dyslipidaemia. The definitions of both CAD and periodontitis, as well as the exposure and the outcomes, differ between studies. This may explain why some of them show a relationship whereas the others do not.

In the intensive research of periodontitis as a risk factor for atherosclerosis, CAD has usually been diagnosed by its acute manifestations, hospital files or discharge registers, or by self-reported questionnaires. The inconsistency in the diagnosis has probably resulted in some contradictory results. Up to date, one of the most reliable techniques to examine the degree of stenosis in the coronary

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arteries is the angiography (Gani et al. 2007). Only a few researchers, however, have investigated the association between angiographically defined CAD and periodontal disease (Mattila et al. 1993, Malthaner et al. 2002, Briggs et al. 2006, Amabile et al. 2008). Due to the disadvantages of being not only time-consuming and costly but also well-indicated as an invasive method, the study populations have been relatively small or lacked an angiographically examined reference group without significant CAD. Thus, the aim of this study was to determine the association between signs of periodontitis and CAD in a relatively large sample of symptomatic patients. Signs of periodontal diseases, such as number of missing teeth, gingival bleeding, probing pocket depth and marginal bone level were registered in clinical and radiographic examinations, and severity and degree of CAD were registered in coronary angiography.

## Methods

### Patients and recruitments

The large COROGENE study is based on 5788 consecutive patients, who underwent a coronary angiography of any reason in Helsinki University Central Hospital, Finland, between June 2006 and March 2008 (Vaara et al. 2011). As 351 refused to give informed consent and 140 were excluded, 93.8% of the designed patients ($n = 5297$) were included in the COROGENE study. The inclusion criteria were that the patient was assigned to a coronary angiogram and was of Finnish origin for the follow-up reasons. The exclusion criteria comprised: non-Finnish origin, previous heart transplantation and low haemoglobin or previous blood transfusion during the same hospitalization (Ripatti et al. 2010). All subjects enrolled into the study gave an informed consent and the research plan was approved by the local ethics committee.

The population comprised patients with acute coronary syndrome (ACS) ($n = 2104$) or stable CAD ($n = 1850$), patients without significant CAD ($n = 1143$), and ACS-like patients with no significant CAD ($n = 200$). The study data collection included all information available of the patients as gathered from the patient records and a two-page patient questionnaire. We collected information on previous medical conditions, cardiovascular risk factors, medications, ECG, echocardiography and coronary angiogram results. The COROGENE study aims to identify coronary disease risk factors and genetics behind it.

The present Parogene study is a subsample of the COROGENE sample**.** Ten percentage of the COROGENE-patients were planned to be invited in an extensive oral examination. A random sample of 567 patients were reached by telephone and interviewed by an advanced practice nurse. Subjects willing to participate in the Parogene study were invited to visit the dental clinic, if the clinical and the radiographic oral examinations could be done for at least 6 weeks, but no later than 5 months after the angiography. Of 567 subjects, 506 (89%) were eventually examined due to no-shows. The mean (SD, range) time between these two examinations was 113 (30, 37–224) days. No selection concerning the cardiac condition could be done at this stage; the only information came from the subjects themselves. The goal was to include about 30% women, which is their proportion in the whole COROGENE study as well. All subjects enrolled into the study gave an informed consent and the research plan was approved by the local ethics committee.

Immediately before oral examination, a dental assistant helped the patients to fill in a questionnaire concerning their general health, especially targeting diabetes and current medications, smoking habits, possible antimicrobial medications, previous visits to a dentist, and existing dental/gingival/mucosal problems.

### Coronary angiography, CAD diagnosis, and CAD risk factors

In the coronary angiography, 123 (24.3%) patients had no significant CAD (<50% stenosis), 184 (36.4%) stable CAD ($\geq 50\%$ stenosis), and 169 (33.4%) ACS. Thirty-two patients with the diagnosis "ACS-like, but no significant CAD" were excluded from the present statistical analyses due to their low number. Patients were defined to have ACS if he/she had an episode of typical chest pain for ischaemia, and $\geq 50\%$ stenosis in at least one coronary artery (Korhonen et al. 1996). In addition, for unstable angina and for non-ST-elevation myocardial infarction, in an ECG at least 1 mm transient ST-depression, and for ST-elevation myocardial infarction, at least 1 mm ST-elevation, in two leads were needed. For ST-elevation and non-ST-elevation infarctions, elevated levels of a cardiac biomarker of necrosis was needed. Typically, the angiogram was done for "no significant CAD"-patients due to chest pain diagnosis, valve problems, or cardiomyopathy. Patient was defined to have 1- to 3-vessel disease according to the number of main coronary vessels with $\geq 50\%$ stenosis. Left main disease was defined as if left anterior descending and left circumflex vessels were diseased (two-vessel disease). No or mild stenosis, <50%, were grouped together.

### Diabetes, dyslipidemia, hypertension, and medications

Patients were considered as having hypertension, dyslipidaemia, or diabetes (insulin-dependent and non-insulin-dependent combined), if they (i) had medication for them, or (ii) were told by a doctor that they have these conditions, but refused to use medication prescribed. Information on rheumatoid arthritis and renal dysfunction was received from the patient records. Medications were registered after the coronary angiography and before entering the oral examination. Height and weight were recorded when entering the hospital for the angiography.

### Oral examinations

Before starting the project, detailed instructions and information with regard to the categorization of results were agreed by the investigators (PM, SP, and KB). Oral examinations were carried out by two periodontal specialists (KB, PM). For inter-individual calibration purposes, six patients were examined jointly the same day. The probing pressures between the two specialists were similar according to the probing depth (difference ±0.8 mm). The

complete clinical oral examination included palpation of lymph nodes, masticatory muscles and temporomandibular joints, examination of oral mucosa, and type and condition of removable dentures. In addition, dental charting with periodontal probing depths (PPD) was registered from six sites on each tooth, and bleeding from the bottom of the periodontal pocket (bleeding on probing, BOP) and suppuration (pus from periodontal pocket) from four sites on each tooth. Furcation lesions of multirooted teeth, caries lesions, fractured fillings, filling overhangs and tooth mobility were registered from all clinical teeth/implants. A manual periodontal probe was used for periodontal registrations. From edentulous subjects, the clinical oral examination was identical excluding the dental status.

Digital panoramic radiographs were taken from both dentate and edentulous subjects at the Department of Oral Radiology, Institute of Dentistry, University of Helsinki using ProOne unit (Planmeca Co., Helsinki, Finland). All radiographs were evaluated by one experienced oral radiologist (JSP). The radiologist was blinded regarding the patients coronary heart diagnosis. The evaluation of the radiographs was performed using Romexis (Planmeca Co.) digital imaging programme and a monitor of a good quality in a darkened room.

Alveolar bone loss (ABL) per patient was calculated from radiographs by choosing from each dentate sextant, the tooth with the most severe bone loss and categorized into: 0 (no bone loss), 1 (ABL in cervical third of the root), 2 (ABL in mid third of the root), 3 (ABL in apical third of the root) and 4 (total bone support lost) (modified from Hugoson & Jordan 1982). Furthermore, the mean value of these six measurements was calculated for each subject.

The periodontal inflammatory burden index (PIBI) described by Lindy et al. (2008) takes into account the enlargement of inflamed subgingival surface area in the deeper periodontal pockets. It was calculated for each study subject by adding the number of periodontal sites indicating moderate periodontitis (periodontal pockets with probing depths 4–5 mm) to the weighted number of periodontal sites indicating advanced periodontitis (number of periodontal pockets with probing depths $\geq$6 mm multiplied by two).

### Statistics

The statistical differences of the characteristics between the three groups were analysed using chi-squared or Kruskal–Wallis test. In the analyses of oral status and CAD risk stratification, the patients with "no significant CAD" were used as the reference group. The parameters with skewed distributions (PIBI) were ln-transformed before statistical analyses or given as median and interquartile ranges (IQR) (number of teeth). The classifications of oral parameters were done into tertiles (BOP, PIBI) or according to the clinical practice (ABL, angular bone defects). Possible effect modification of periodontal health was tested by adding the interaction terms between age, gender, smoking, diabetes, hypertension, and BMI one-by-one in the fully adjusted regression models for CAD diagnosis. The associations between each of the seven oral status parameters (number of missing teeth, BOP, PPD 4–5 mm, PPD $\geq$6 mm, angular bone defects, ABL, and use of dentures) as well as the two parameters calculated from those (edentulousness and PIBI) separately and the CAD diagnosis were evaluated using logistic regression analyses adjusted by age (continuous variable) (data not shown), and further by gender, smoking status (never/former/current), hypertension (no/yes), dyslipidaemia (no/yes), BMI (continuous variable), and diabetes (no/yes). Hypertension and dyslipidaemia were used as binary variables instead of measurements or serum determinations due to the high number of antihypertensive and lipid lowering medication users. The analyses were performed separately for those with stable CAD or ACS with the no significant CAD as the reference group. The linear trends across the subgroups of no CAD and 1- to 3-vessel disease were analysed using ANOVA polynomial linear contrasts assuming equal variances. The statistics was done with the SPSS version 15 (SPSS Inc., Chicago, IL, USA).

### Results

The mean age (SD) of the whole population was 64.0 (9.0) years and 319 (67.0%) were male. When divided according to the main diagnosis and the results from the coronary angiography, 123 (24.3%) had minimal or no significant CAD (<50% stenosis), 184 (36.4%) had stable symptomatic CAD ($\geq$50% stenosis), and 169 (33.4%) had ACS. The established CAD risk factors and medications according to these groups are summarized in Table 1. The distributions or mean levels were significantly different for age and gender, as well as for the prevalence of dyslipidemia and the medications registered.

Using the same CAD classifications as above, the oral findings of the patients are characterized in Table 2 with *p*-values for differences between patients with and without significant CAD. From the whole population, 31 (6.5%) patients were edentulous and they were evenly distributed across the CAD classes. The number of teeth, however, was highly significantly different across the classes: stable CAD and ACS were associated with 8–17 missing teeth. The median (IQR) number of teeth in the groups were 25 (21–28), 22 (13–26), and 22 (12–26) for no CAD, stable CAD ($p < 0.001$), and ACS ($p = 0.006$) respectively. The patients with stable CAD ($p = 0.105$) or ACS ($p = 0.032$) had more bleeding sites on probing, and teeth with deepened periodontal pockets with PPD $\geq$6 mm ($p = 0.025$ and 0.013) compared with those with no significant CAD. As analysed in the panoramic radiographs, the patients with stable CAD ($p = 0.041$) or ACS ($p = 0.045$) had more often moderate to total ABL, than those with no significant CAD.

The risk stratification of oral findings in CAD with *p*-values for trends across the categories is presented in Table 3 adjusted for age, gender and CVD risk factors. In the main findings, there were no notable differences between the risk estimates obtained after adjusting for age only (data not shown) and those additionally adjusting for other confounders. In multivariate analyses, both stable CAD and ACS were associated with 8–17 missing teeth with ORs of 4.33

*Table 1.* Characteristics of the subjects

| | *N* (%) | | | *p*-value* |
|---|---|---|---|---|
| | No significant CAD *n* = 123 | Stable CAD *n* = 184 | ACS *n* = 169 | |
| Gender (men) | 61 (49.6) | 136 (73.9) | 122 (72.2) | <0.001 |
| Diabetes | 24 (19.7) | 55 (30.4) | 37 (21.9) | 0.063 |
| Smoking | | | | |
| Never | 66 (53.7) | 84 (45.9) | 72 (42.6) | 0.191 |
| Former | 40 (32.5) | 78 (42.6) | 79 (46.7) | |
| Current | 17 (13.8) | 21 (11.5) | 18 (10.7) | |
| Hypertension | 71 (57.7) | 129 (70.5) | 107 (63.3) | 0.066 |
| Dyslipidaemia | 90 (73.2) | 172 (94.0) | 123 (74.0) | <0.001 |
| Rheumatoid arthritis | 4 (3.3) | 11 (6.0) | 11 (6.5) | 0.444 |
| Renal dysfunction | 4 (3.3) | 7 (3.8) | 3 (1.8) | 0.511 |
| Coronary angiography, stenosed vessels† | | | | |
| 0–mild | 123 (100) | 0 (0) | 0 (0) | <0.001 |
| 1 | 0 (0) | 49 (26.6) | 79 (46.7) | |
| 2 | 0 (0) | 57 (31.0) | 44 (26.0) | |
| 3 | 0 (0) | 78 (42.4) | 46 (27.2) | |
| Medications | | | | |
| Beta blockers | 94 (79.0) | 161 (88.5) | 153 (90.5) | 0.012 |
| Calcium blockers | 15 (12.5) | 46 (25.3) | 22 (13.3) | 0.003 |
| ACE/ATII blockers | 74 (61.7) | 127 (70.2) | 132 (79.0) | 0.005 |
| Diuretics | 47 (39.5) | 52 (28.7) | 35 (21.1) | 0.003 |
| Statins | 85 (70.8) | 172 (94.5) | 162 (95.9) | <0.001 |
| Acetylsalicylic acid | 66 (55.0) | 156 (86.2) | 157 (92.9) | <0.001 |
| Clopidogrel | 3 (2.5) | 56 (30.8) | 143 (84.6) | <0.001 |
| Marevan | 28 (23.9) | 22 (12.2) | 11 (6.7) | <0.001 |
| Nitrates | 11 (9.2) | 84 (46.2) | 30 (18.1) | <0.001 |
| | | Mean (SD) | | *p*-value‡ |
| Age (years) | 61.7 (9.0) | 65.5 (8.2) | 62.9 (9.6) | <0.001 |
| Smoking (pack years) | 9.0 (14.4) | 12.5 (19.2) | 13.6 (21.9) | 0.148 |
| BMI (kg/m$^2$) | 27.6 (5.3) | 27.8 (4.7) | 28.2 (5.3) | 0.084 |

*Chi-squared test.
†0 = no or mild stenosis (<50%); 1 = stenosis ($\geq$50%) in one artery, 2 = stenosis ($\geq$50%) in two arteries, 3 = stenosis ($\geq$50%) in three arteries.
‡Kruskal–Wallis test.

(1.61–11.7, $p = 0.020$) and 5.24 (1.90–14.5, $p = 0.014$), and more than seven teeth with probing pocket depth $\geq$6 mm with ORs of 2.44 (1.01–6.07, $p = 0.049$) and 2.75 (1.16–6.53, $p = 0.022$) respectively. Moderate and high periodontal inflammation burden index (PIBI) were associated with stable CAD with ORs of 1.90 (0.99–3.66, $p = 0.050$) and 2.02 (1.11–3.80, $p = 0.039$) respectively. In addition, ACS was associated with a high percentage of bleeding sites with an OR of 1.90 (1.10–3.50, $p = 0.040$). The radiographic measurements revealed that severe to total mean ABL was associated with ACS with an OR of 5.39 (1.23–23.6, $p = 0.025$). When the interaction terms between age, gender, smoking, diabetes, hypertension, and BMI were examined in the fully adjusted regression models for CAD diagnosis, no effect modification of periodontal health was found.

According to the findings in coronary angiography, the patients were further divided into those with no or mild stenosis ($n = 123$), and to those with a "1- ($n = 128$), 2- ($n = 101$), or 3-artery ($n = 124$) disease" (Table 1, Fig. 1a–c). Among the oral parameters, ABL ($p = 0.019$), number of missing teeth (<0.001), and probing pocket depth $\geq$6 mm ($p = 0.008$) were found to be significantly different between these groups. The trends of association were linear between these parameters and the severity of the disease with *p*-values of <0.001, <0.001, 0.001 and 0.033 respectively.

## Discussion

Our results show in a relatively large population with coronary angiography results that poor periodontal health is associated with an increased risk for CAD. The oral parameters that significantly related to coronary stenosing included missing teeth, signs of ongoing periodontal inflammation with periodontal pocket formation and bleeding, and reduced alveolar bone level. These associations were independent of age and main established CVD risk factors, gender, dyslipidaemia, smoking, hypertension, diabetes, and obesity. Furthermore, the CAD severity was linearly associated with the number of missing teeth and pathological periodontal pockets, as well as ABL.

The main result is in accordance with previous reports with smaller populations or non-investigated reference groups (Mattila et al. 1995, Briggs et al. 2006, Amabile et al. 2008). However, it differs from that of an American study, where no

*Table 2*. Oral status of the patients

| Oral parameter | Classes | *N* (%) | | *p*-value* | *N* (%) | *p*-value* |
|---|---|---|---|---|---|---|
| | | No significant CAD *n*=123 | Stable CAD *n* = 184 | | ACS *n* = 169 | |
| Number of missing teeth | 28 | 7 (5.3) | 12 (6.5) | **< 0.001** | 12 (7.1) | **0.006** |
| | 18–27 | 13 (10.6) | 26 (14.1) | | 28 (16.6) | |
| | 8–17 | 7 (5.7) | 45 (24.5) | | 29 (17.2) | |
| | 3–7 | 38 (20.9) | 42 (22.8) | | 47 (27.8) | |
| | 0–2 | 58 (47.2) | 59 (32.1) | | 53 (31.4) | |
| Bleeding on probing (% of sites) | 0–26† | 45 (38.8) | 64 (37.2) | 0.105 | 44 (27.3) | **0.032** |
| | 27–44 | 43 (37.1) | 48 (27.9) | | 57 (35.4) | |
| | 45–91 | 28 (24.1) | 60 (34.9) | | 60 (37.3) | |
| Teeth with probing pocket depth 4–5 mm | 0 | 13 (10.9) | 13 (7.4) | 0.371 | 28 (17.3) | 0.089 |
| | 1–6 | 40 (33.6) | 51 (29.1) | | 34 (21.0) | |
| | 7–16 | 33 (27.7) | 64 (36.6) | | 49 (30.2) | |
| | 17– | 33 (27.7) | 47 (26.9) | | 51 (31.5) | |
| Teeth with probing pocket depth $\geq$6 mm | 0 | 73 (61.3) | 89 (50.9) | **0.025** | 86 (53.1) | **0.013** |
| | 1–3 | 29 (24.4) | 44 (25.1) | | 27 (16.7) | |
| | 4–6 | 8 (6.7) | 16 (9.1) | | 18 (11.1) | |
| | 7– | 9 (7.6) | 26 (14.9) | | 31 (19.1) | |
| Edentulous | Dentate | 116 (94.3) | 172 (93.5) | 0.088 | 157 (92.9) | 0.630 |
| | Edentulous | 7 (5.7) | 12 (6.5) | | 12 (7.1) | |
| Dentures | None | 97 (78.9) | 122 (66.3) | **0.045** | 115 (68.0) | 0.102 |
| | Partial | 19 (15.4) | 50 (27.2) | | 43 (25.4) | |
| | Whole | 7 (5.7) | 12 (6.5) | | 11 (6.5) | |
| Alveolar bone loss‡ | None | 36 (31.0) | 30 (17.4) | **0.041** | 36 (22.8) | **0.045** |
| | Mild | 52 (44.8) | 84 (48.8) | | 63 (39.9) | |
| | Moderate | 25 (21.6) | 49 (28.5) | | 44 (27.8) | |
| | Severe or total | 3 (2.6) | 9 (5.2) | | 15 (9.5) | |
| Angular bone defects | 0 | 71 (60.7) | 93 (54.1) | 0.265 | 94 (59.5) | 0.843 |
| | $\geq$1 | 46 (39.3) | 79 (45.9) | | 64 (40.5) | |
| PIBI§ | 0–5† | 45 (37.8) | 43 (24.6) | **0.043** | 52 (32.1) | 0.320 |
| | 6–19 | 40 (33.6) | 72 (41.1) | | 50 (30.9) | |
| | 20–158 | 34 (28.6) | 60 (34.3) | | 60 (37.0) | |

*Chi-squared test compared to group of "No significant CAD".
†Tertiles.
‡None, mild = cervical third of the root, moderate = middle third, severe = apical third, total.
§Periodontal inflammatory burden index.
The statistically significant values are in bold face ($p < 0.05$).

association between periodontitis and chronic CAD was found after adjusting for risk factors, especially smoking and age (Malthaner et al. 2002). Therefore, our study is the first one to describe a significant direct association between periodontitis and CAD status verified with coronary angiography in such a large population of symptomatic patients, which allowed us to divide them into those with no significant stenosis, and those with stable CAD or ACS. The group of present patients with no significant CAD were typically examined due to chest pain, valve problems, or cardiomyopathy, forming an exceptional reference group in our investigation. For that reason, the group cannot be referred to as healthy or general population, but those with other cardiac problems than significant CAD.

As expected, those with stable CAD were older than the ones with ACS or no significant CAD. Also, the other established CVD risk factors, diabetes, hypertension and dyslipidaemia, were more frequently found among patients with stable CAD or ACS. In our study, however, the multiple regression model showed a significant relationship between CAD and periodontal breakdown, even after basic adjustments. Some symptoms measured, i.e. bleeding on probing, may be partially attributed to medications (Schrodi et al. 2002). Only a few of the periodontal parameters, i.e. number of teeth and periodontal inflammation burden index, had a significant linear association with the cardiac findings as seen in the *p* for trend values. Clearly, the notable risk estimations for CAD were among those with the worst oral status and actually on a higher level than frequently published; i.e. OR of 1.2–1.7 (Scannapieco et al. 2003). The reason for the higher odds observed in the current study compared with those frequently published in the past studies may be related to the well-defined CAD diagnosis available in the study.

Patients with stable CAD or ACS had more radiographic signs of periodontitis, such as ABL. No differences regarding the angular bone defects between the groups were, however, found. Although this suggests that the most affected teeth had already been extracted, no significant relation with the use of dentures was shown either. On the other hand, the association between 8 and 17 missing teeth and CAD was fivefold. Even though reasons for

*Table 3.* Risk stratification of oral findings on CAD

| Oral parameter | Classes | Multi adjusted* | |
|---|---|---|---|
| | | Stable CAD | ACS |
| Number of missing teeth | 28 | 0.98 (0.30–3.25) | 2.06 (0.67–6.32) |
| | 18–27 | 1.36 (0.55–3.36) | 2.14 (0.90–5.08) |
| | 8–17 | 4.33 (1.61–11.7) | 5.24 (1.90–14.5) |
| | 3–7 | 0.77 (0.38–1.56) | 1.27 (0.67–2.41) |
| | 0–2 | 1.00 | 1.00 |
| | *p* for trend | 0.014 | 0.021 |
| Bleeding on probing (% of sites) | 0–26† | 1.00 | 1.00 |
| | 27–44 | 0.63 (0.33–1.21) | 1.23 (0.67–2.25) |
| | 45–91 | 1.20 (0.51–2.04) | 1.90 (1.10–3.50) |
| | *p* for trend | 0.280 | 0.044 |
| Teeth with probing pocket depth 4–5 mm | 0 | 1.00 | 1.00 |
| | 1–6 | 1.93 (0.71–5.24) | 0.28 (0.12–0.67) |
| | 7–16 | 2.12 (0.79–5.73) | 0.59 (0.25–1.36) |
| | 17– | 1.97 (0.69–5.65) | 0.69 (0.27–1.31) |
| | *p* for trend | 0.516 | 0.224 |
| Teeth with probing pocket depth $\geq$6 mm | 0 | 1.00 | 1.00 |
| | 1–3 | 1.06 (0.55–2.04) | 0.83 (0.44–1.58) |
| | 4–6 | 1.47 (0.52–4.21) | 1.89 (0.72–4.93) |
| | 7– | 2.44 (1.01–6.07) | 2.75 (1.16–6.53) |
| | *p* for trend | 0.279 | 0.048 |
| Edentulous | Dentate | 1.00 | 1.00 |
| | Edentulous | 0.76 (0.26–2.25) | 1.20 (0.43–3.31) |
| | *p*-value | 0.619 | 0.732 |
| Dentures | None | 1.00 | 1.00 |
| | Partial | 1.50 (0.77–2.94) | 1.71 (0.89–3.30) |
| | Whole | 0.87 (0.29–2.62) | 1.24 (0.43–3.55) |
| | *p* for trend | 0.442 | 0.273 |
| Alveolar bone loss‡ | None | 1.00 | 1.00 |
| | Mild | 1.21 (0.58–2.51) | 1.12 (0.58–2.17) |
| | Moderate | 1.35 (0.57–3.15) | 1.52 (0.68–3.39) |
| | Severe-total | 2.64 (0.47–14.7) | 5.39 (1.23–23.6) |
| | *p* for trend | 0.715 | 0.135 |
| Angular bone defects | 0 | 1.00 | 1.00 |
| | $\geq$1 | 1.10 (0.63–1.92) | 0.98 (0.58–1.66) |
| | *p*-value | 0.737 | 0.939 |
| PIBI§ | 0–5† | 1.00 | 1.00 |
| | 6–19 | 1.90 (0.99–3.66) | 1.16 (0.64–2.12) |
| | 20–158 | 2.02 (1.11–3.80) | 1.47 (0.78–2.75) |
| | *p* for trend | 0.016 | 0.491 |

*Adjusted for age, sex, hypertension, dyslipidaemia, DM, smoking, and BMI.
†Tertiles.
‡None, mild = cervical third of the root, moderate = middle third, severe = apical third, total.
§Periodontal inflammatory burden index.

extractions were asked in the dental questionnaire, only a few patients with missing teeth were aware of them. In several earlier reports, missing teeth or edentulousness have been regarded as signs of past periodontal disease or the final stage of it, an opinion that our findings also suggest (Desvarieux et al. 2003, Holmlund et al. 2006).

The patients were classified into three groups, as pathophysiology of ACS is different from that of stable CAD. Recently, it was suggested that clinical coronary events may arise by the effect of acute infections and obstructing lesions by a chronic inflammatory stimulus (Pesonen et al. 2009); serum antibody response against a common periodontal pathogen, *Aggregatibacter actinomycetemcomitans*, and chlamydial and human heat shock protein 60 were associated with stenosing lesions in a study, where 211 coronary angiograms were performed on ACS patients. From the present study, no such conclusions can be drawn, as the bleeding from periodontal pockets, a sign of present inflammation, and the ABL, a sign of experienced periodontal infection, were both associated with ACS.

There are several possible mechanisms connecting periodontal diseases to CAD. On one hand, they may include the spread of bacteria and their products into the circulation (Pussinen et al. 2005, Sakurai et al. 2007). On the other hand, the release of host-derived inflammatory mediators and cytokines from the chronically inflamed periodontal tissues may predispose individuals to atherogenesis (Buhlin et al. 2003, 2009a,b, Tonetti et al. 2007, Hansson 2009). Anyhow, it is not known if infection in periodontal tissues can trigger atherogenesis in the vessels or

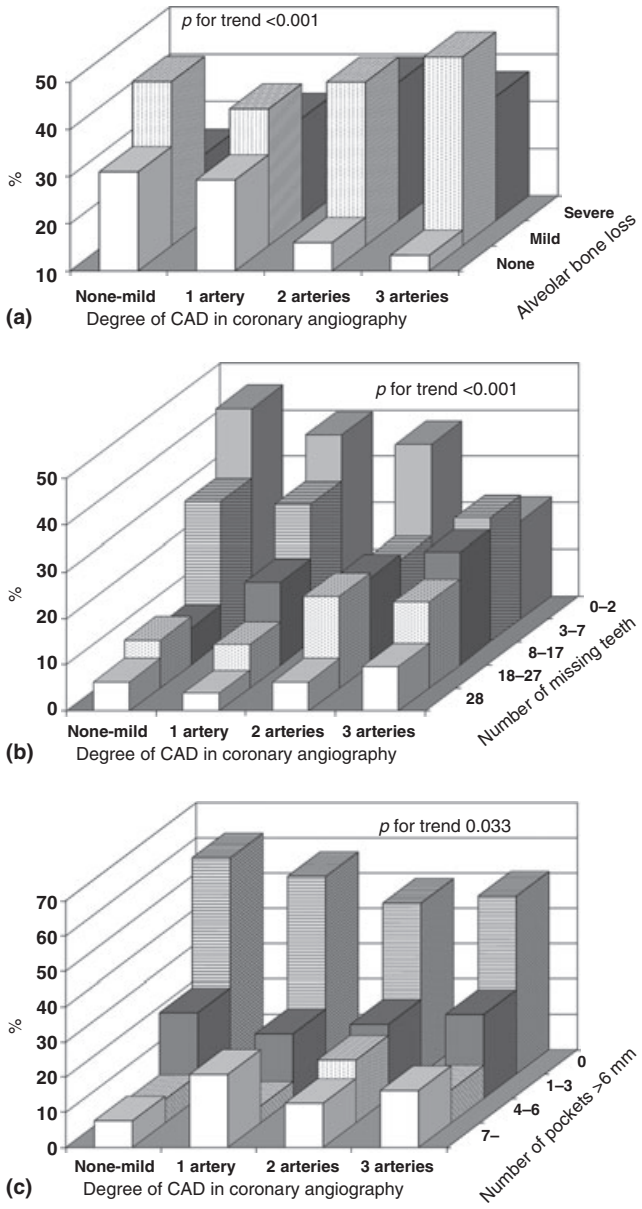


*Fig. 1*. According to the findings in coronary angiography, the 476 patients were further divided into those with no or mild CAD ($n$ = 123), and to those with a 1 ($n$ = 128), 2 ($n$ = 101), or 3 narrowed arteries ($n$ = 124). Their frequencies were categorized according to the alveolar bone loss (a), number of missing teeth (b), and teeth with probing pocket depths $\geq$6 mm (c). The $p$-values for trend across the categories as analysed using the ANOVA polynomial linear contrasts are shown.

if it maintains the process initiated by another trauma. The atherosclerotic process is slow and accumulates overtime, which is another feature in common between the two diseases. Therefore, the chronic low-grade inflammation and continuous spread of bacterial-derived antigens and endotoxins may be of importance (Pussinen et al. 2004, 2007). Overall, our findings are consistent with the idea that chronic inflammation can promote atherogenesis (Ross 1999, Hansson 2009).

Limitations of the study include the cross-sectional design and possible selection of the population. As mentioned, we did not have any opportunity to choose the patients based on the cardiological diagnosis beforehand. This may have caused a bias away from a population with multiple diseases or those in an institutional care. CAD, however, was treated as well as possible in all patients thus not producing limitations to enter the dental clinics. No-shows and several times cancelled appointments may also have caused a small bias in the cardiac status, but probably towards smaller differences between the groups than those observed. In addition, the results are at the moment based on clinical examinations and some case records; no knowledge about e.g. the systemic inflammatory markers is yet available. The age and gender differences between the subgroups cannot be regarded as a limitation, as they follow those generally found in Finland. One limitation of the study is, however, that information on socioeconomics or education levels were not collected.

The study indicates that missing teeth and poor periodontal health with periodontal inflammation and bone loss are associated with angiographically verified coronary artery narrowing in patients with stable symptomatic CAD or ACS.

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**Clinical Relevance**

*Scientific rationale for the study:* There are contradictory results concerning an association between coronary artery disease (CAD) and periodontitis. We investigated the oral health of 506 patients with the CAD degree verified by coronary angiography.

*Principal findings:* Severe CAD was associated with deteriorated oral health compared with those with no significant CAD. Severity of CAD was linearly associated with alveolar bone loss, number of missing teeth, and deepened pockets.

*Practical implications:* These findings support the proposition that these diseases have an association. Additional studies are needed to determine if there is a causal relationship between periodontal disease and coronary artery disease.