Periodontitis Increases the Risk of a First Myocardial Infarction

A Report From the PAROKRANK Study

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Background—The relationship between periodontitis (PD) and cardiovascular disease is debated. PD is common in patients with cardiovascular disease. It has been postulated that PD could be causally related to the risk for cardiovascular disease, a hypothesis tested in the Periodontitis and Its Relation to Coronary Artery Disease (PAROKRANK) study.

Methods and Results—Eight hundred five patients (<75 years of age) with a first myocardial infarction (MI) and 805 age- (mean 62±8), sex- (male 81%), and area-matched controls without MI underwent standardized dental examination including panoramic x-ray. The periodontal status was defined as healthy (≥80% remaining bone) or as mild-moderate (from 79% to 66%) or severe PD (<66%). Great efforts were made to collect information on possibly related confounders (≈100 variables). Statistical comparisons included the Student pairwise *t* test and the McNemar test in 2×2 contingency tables. Contingency tables exceeding 2×2 with ranked alternatives were tested by Wilcoxon signed rank test. Odds ratios (95% confidence intervals) were calculated by conditional logistic regression. PD was more common (43%) in patients than in controls (33%; $P<0.001$). There was an increased risk for MI among those with PD (odds ratio, 1.49; 95% confidence interval, 1.21–1.83), which remained significant (odds ratio, 1.28; 95% confidence interval, 1.03–1.60) after adjusting for variables that differed between patients and controls (smoking habits, diabetes mellitus, years of education, and marital status).

Conclusions—In this large case–control study of PD, verified by radiographic bone loss and with a careful consideration of potential confounders, the risk of a first MI was significantly increased in patients with PD even after adjustment for confounding factors. These findings strengthen the possibility of an independent relationship between PD and MI. **(*Circulation*. 2016;133:576-583. DOI: 10.1161/CIRCULATIONAHA.115.020324.)**

Key words: case-control study ■ causality ■ myocardial infarction ■ periodontitis ■ radiography, panoramic ■ risk factors

Cardiovascular disease is a leading mortality cause, which, despite a recent decline, still contributes to 4 million deaths per year, that is, almost half of all deaths in Europe, whereof ≈30% occurred at <65 years of age.[1] It contributes to 22% of all disability-adjusted life-years lost in the European Union and a hospital discharge rate of 2400/100 000 inhabitants.[2] Although traditional risk factors are behind a substantial proportion of cardiovascular disease, other factors are important.[3] Chronic inflammation accelerates the progress of atherosclerosis, and inflammatory activation increases the risk for plaque rupture leading to acute coronary syndromes.[4,5]

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Periodontal diseases are inflammatory conditions ranging from gingivitis to severe periodontitis, the latter with a prevalence of 9% in the western European population.[6] The prevalence is age dependent as exemplified by a survey from the United States where it increased from 11% in the age group 50 to 65 years to 20% among those >75 years.[7] The disease, which is diagnosed by clinical and radiographic examination,[8] is a chronic tissue-destructive inflammatory state, predominantly induced by Gram-negative bacteria colonizing the gingival crevice.[9]

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There is an association between periodontitis and cardiovascular disease.[10,11] The character of this association is under debate. An obvious possibility is that the diseases are promoted by shared risk factors, but it has also been postulated, although not confirmed, that periodontitis in itself may cause cardiovascular disease. In support of a causal relationship, it has been claimed that periodontal treatment lowers C-reactive protein and low-density lipoproteins and improves endothelial function.[12–15] Such findings, addressing surrogate end points and not cardiovascular events, must be interpreted with caution, leaving an uncertainty regarding the true nature of the association between periodontal and cardiovascular disease. This knowledge gap was recently recognized by the American Heart Association in the following way …"statements that imply a causative association between periodontal disease and specific atherosclerotic vascular disease events or claim that therapeutic interventions may be useful on the basis of that assumption are unwarranted."[16]

The hypothesis behind the present investigation, Periodontitis and Its Relation to Coronary Artery Disease (PAROKRANK), was that there could be an independent relationship between periodontitis and the development of a first myocardial infarction.

Methods

PAROKRANK is a multicenter case–control study, recruiting patients May 2010 through February 2014 at 17 Swedish hospitals. The study centers all had a coronary care unit linked to the Swedish National quality registry SWEDEHEART[17] and a dental care unit at the hospital or in its close proximity. The study was coordinated from the Cardiology Unit, Department of Medicine at Karolinska Institutet, Stockholm.

Patients <75 years of age hospitalized for a first myocardial infarction according to international criteria[18,19] were included following informed consent. Exclusion criteria were previous myocardial infarction, previous heart valve replacement, and any other condition that, according to the judgment of the investigator, could limit the ability to cope with the protocol.

Controls from the same postal code area as the corresponding patient were randomly selected from the national population registry. They were of the same sex and age (±3 months). A list of candidates was generated from which contact was started with the person closest in age. A research nurse at the PAROKRANK coordinating center approached this person by telephone providing study information and collecting information on the relevant medical history. To be selected as a control, the contacted person had to be willing to participate and free from previous myocardial infarction and heart valve replacement. The next person on the list was approached if the first contacted person could not be reached, refused, or did not fit the criteria. Contact information to the selected control persons was subsequently sent to the local study center where written informed consent to participate was obtained. The number of persons approached to recruit 1 control was ≈4.

Study Protocol

Patients were recruited during their hospital stay and scheduled for outpatient visits 6 to 10 weeks later at the local departments of cardiology and dental medicine. To perform the investigations during the same season, the matched control persons were contacted usually within 10 days after the outpatient visit of their corresponding patients.

Study participants, patients and controls, fasted 12 hours, including no smoking, before the visit at the cardiology department where a physical examination including heart rate, blood pressure following 5 minutes of rest in a sitting position, height, body weight, and waist circumference was performed. Venous blood was sampled for the following analyses performed at the local laboratory: complete blood count, P-lipids (total and high-density lipoprotein cholesterol and triglycerides), P-creatinine, P-fibrinogen, P-glucose, and glycohemoglobin A1c. Study participants without known diabetes mellitus underwent an oral glucose tolerance test (75 g glucose in 200 mL water) with venous P-glucose measured in the fasting state and 2 hours after glucose intake. The point-of-care HemoCue 201 System (HemoCue AB, Ängelholm, Sweden) was used for the P-glucose analysis. High-sensitivity C-reactive protein was analyzed at a central laboratory (redhot diagnostics, Södertälje, Sweden) by means of an enzyme-linked immunosorbent assay method (MP Biomedicals, New York, NY) intended for quantitative determination of C-reactive protein, with the functional sensitivity of 0.1 mg/L. In addition, whole blood (4 mL) and plasma (6 mL) were collected and stored at –70°C in a central bio bank at Karolinska Institutet. A set of questionnaires including information on family and medical history, risk, and health-preserving factors were completed together with the Montgomery Åsberg Depression Rating Scale[20].

The national quality registry SWEDEHEART (www.swedeheart.se) was used to amass medical information from the patients at the time of their initial hospitalization (Swedish Register of Information and Knowledge about Swedish Heart Intensive Care Admissions [RIKS-HIA]) and at the secondary prevention follow-up (Secondary Prevention after Heart Intensive Care Admission [SEPHIA]) 6 to 10 weeks after the myocardial infarction.[17] The registry was modified to comply with the study needs. Equivalent information was collected for the control population with data entered into a separate database. Smoking habits were defined as current, previous (stopped >1 month ago), or never, and are for patients, as ongoing pharmacological treatment, presented both at the time for hospital admission and follow-up.

Definitions

Myocardial infarction was diagnosed by the physician in charge according to international criteria on an acute ST or non–ST-segment–elevation myocardial infarction as issued during the study period.[18,19]

The presence of a family history of cardiovascular disease (close relative with cardiovascular disease at <60 years of age) and the presence of peripheral artery, rheumatic, pulmonary, and kidney disease, and cancer and depression, as well, was based on self-reported information in standardized questionnaires. The diagnoses of hypertension, diabetes mellitus, and stroke were based on a medical history obtained by the study personnel.

Dental Examinations

The dental examination followed a standardized protocol. The maximum number of teeth was 28 because the third molars were excluded. Dentures, complete, partial, and a complete implant bridge, in either jaw, were classified as removable dentures. Analogue or digital panoramic radiographs were taken from both dentate and edentulous subjects at the local centers for central analysis at the Department of Dental Medicine, Karolinska Institutet Huddinge, by means of a computer program, ImageJ (Image Tool 3.0 software program, Department of Dental Diagnostics Science, University of Texas Health Science Center, San Antonio, TX). Measurements were performed with a high-resolution computer monitor in a darkened room. Each tooth was measured at the site with the most pronounced bone loss. Measurements were, as delineated in the Figure, made from the marginal bone crest to the tooth apex (total bone height) and from the cementoenamel junction to the tooth apex (total root length) mesially and distally.[21] The arithmetic mean, calculated from the total root length and bone height, was used as a measure of the proportion of remaining bone height supporting each tooth. Measurements were made of all teeth with visible cementoenamel junctions and visible apices. Dental implants were not examined. Participants were subsequently, based on the mean value of all teeth, allocated to the following groups: healthy (≥80% remaining bone), mild to moderate periodontitis (from 79% to 66%), and severe periodontitis (<66%). The radiographic examinations were performed by 3 dentists blinded to whether the panoramic radiograph came from a patient or a control and trained in the use of the equipment. For interindividual calibration purposes, 42 randomly selected panoramic radiographs were

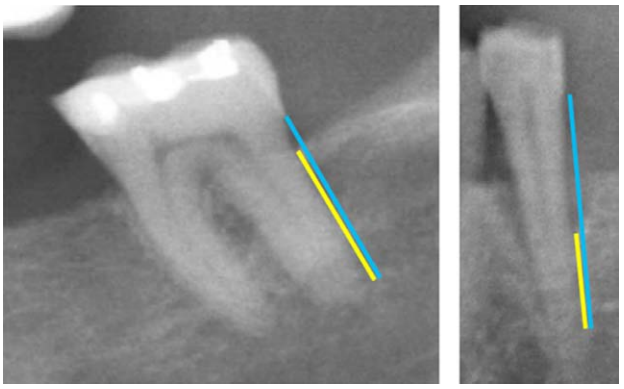

Figure. Radiographic measurements were made from the marginal alveolar bone to the tooth apex (yellow line) and from the cementoenamel junction to the tooth apex (blue line). The examples show the left normal bone height and the right alveolar bone loss.

examined. These dental x-rays were graded by 3 dentists, ie, in 126 separate observations. The 3 graders were in complete agreement in 121 of these observations (96%). The correlation between dentist 1 and 2 was 0.95, the correlation between 1 and 3 was 0.90, and the correlation between 2 and 3 was 0.90 (κ value, 0.82).

Ethical Approval

The PAROKRANK study was approved by the Regional Ethics Committee at Stockholm (Dnr:2008/152-31/2) before the study, and all patients provided written informed consent. PAROKRANK was conducted according to the principles outlined in the Helsinki Declaration.

Statistical Considerations

Calculations based on an assumed prevalence of severe periodontitis in the Swedish population[22] supported by an analysis of the first 120 patients and 120 controls in PAROKRANK revealed that, to detect an increased risk of myocardial infarction (odds ratio, 1.4) among subjects with periodontitis with a power of 80%, there was a need for 800 patients and a similar number of matched controls.

Statistical comparisons to test differences between the 2 groups were made by use of the Student *t* test for matched pairs, and, to evaluate hypotheses of variables in 2×2 contingency tables for matched pairs, the McNemar test was used. Contingency tables larger than 2×2 with ranked ordered alternatives were tested by the use of the Wilcoxon signed rank test. Odds ratios, crude and adjusted for confounders, and corresponding 95% confidence intervals were calculated by the use of conditional logistic regression. In addition, descriptive statistics were used to characterize the data. All analyses were performed by the use of the SAS system (The SAS system for Windows 9.4, SAS Institute Inc, Cary, NC), and the 5% level of significance was considered. In the case of a statistically significant result, the *P* value has been given.

Results

When first asked, 922 patients accepted participation, but 117 (13%) withdrew their consent before follow-up, leaving 805 fully investigated patients and 805 controls according to the protocol. Their mean age was 62±8 years and 81% were men.

Clinical characteristics are presented in Table 1. Several variables, eg, a history of hypertension, diabetes mellitus, kidney disease, and rheumatic disease did not differ between the 2 groups. A family history of cardiovascular disorders was more common in patients than controls. In comparison with the control population, smoking was more frequent among patients at admission. Pulmonary diseases (chronic obstructive pulmonary disease, emphysema, and asthma) did not differ between the groups. Of the components, chronic obstructive pulmonary disease was more common among patients than controls (4.4 versus 1.9%; P=0.005). The oral glucose tolerance test disclosed that 74 patients (9.3%) and 42 controls (5.2%; P<0.003) had previously undetected diabetes mellitus. When added to the participants with already known diabetes mellitus (see Table 1), the total number of patients and controls with diabetes mellitus was 153 (19.1%) and 107 (13.3%; P<0.002). The use of cardiovascular treatment (aspirin, β-blockade, renin-angiotensin inhibitors, and statins) did not differ significantly in comparison between the patients at the time for admission and controls. The use of these drugs was, at the time of follow-up, significantly more common among patients than controls, which resulted in a lower blood pressure and lipids among patients than controls (Table 1). Factors expressing socioeconomic status (Table 2) showed a higher number with low education (66% versus 62%) and a higher rate of divorce among patients (15% versus 10%).

The number of remaining teeth was 24±6 in patients and 25±5 (P<0.001) in controls. Dental x-rays were available in 797 (99%) of the patients and 796 (99%) of the controls. Mild to moderate or severe periodontitis was present in 43% of the patients and 33% of the controls (P<0.001). The distribution on the 2 groups is presented in Table 3. The risk for myocardial infarction was significantly increased among subjects with periodontitis with a crude odds ratio of 1.49 (95% confidence interval [CI], 1.21–1.83). When edentulous participants (patients, 12; controls, 4) were excluded from the analysis of periodontal status, the corresponding prevalence was 41% versus 33% and the odds ratio (OR) for myocardial infarction risk was 1.46 (95% CI, 1.19–1.80). Following statistical adjustments for confounders (diabetes mellitus, smoking habits, years of education, and marital status) and including edentulous participants, there was still a positive association between periodontitis and the risk of myocardial infarction with an OR of 1.28 (95% CI, 1.03–1.60).

Discussion

In this large study of the relation between periodontal disease and a first myocardial infarction, the risk was significantly increased in patients with moderate to severe periodontitis, objectively verified by radiographic bone loss and with a careful consideration of potential confounders. This finding strengthens the possibility of an independent relationship between periodontitis and cardiovascular disease manifestations.

Several cross-sectional and case–control investigations have reported on a relation between periodontitis and cardiovascular disease. In an extensive meta-analysis by Blaizot et al,[10] the pooled odds ratio from 22 case–control and cross-sectional studies was 2.35 (95% CI, 1.87–2.96) and somewhat less in 7 cohort studies (OR, 1.35; 95% CI, 1.27–1.42). There was, however, a considerable heterogeneity in reported odds ratios from insignificant (OR, 1.08; 95% CI, 0.77–1.51) to rather strong (OR, 5.14; 95% CI, 1.37–19.27) risk associations in other studies.[23,24] This discrepancy is reasonably explained by 2 factors. The first relates to methodological issues such as too-small study populations, less strict definitions of

Table 1. Clinical Characteristics

Variables	Patients n=805	Controls n=805	*P* Value
Age, y	62±8	62±8	*
Male sex	654 (81)	654 (81)	*
Known family history of cardiovascular disease	302 (38)	183 (23)	<0.001
Medical history			
Hypertension	285 (36)	268 (34)	0.38
Peripheral artery disease	20 (3)	10 (1)	0.099
Stroke	22 (3)	18 (2)	0.64
Diabetes mellitus	79 (10)	65 (8)	0.25
Rheumatic disease	164 (21)	136 (17)	0.056
Pulmonary disease	106 (14)	85 (11)	0.11
Kidney disease	33 (4)	32 (4)	1.00
Cancer	66 (8)	58 (7)	0.51
Depression	76 (9)	71 (9)	0.73
Smoking habits (patients at admission)			
Current	206 (26)	96 (12)	
Previous	286 (36)	361 (45)	<0.001
Never	297 (38)	348 (43)	
Smoking habits (patients at follow-up)			
Current	70 (9)	96 (12)	
Previous	440 (55)	361 (45)	0.22
Never	283 (36)	348 (43)	
Waist circumference, cm	99±11	98±12	0.12
Body mass index, kg/m^2	27±4	27±4	0.24
Blood pressure, mm Hg			
Systolic	129±17	137±17	<0.001
Diastolic	77±10	84±10	<0.001
Laboratory			
Cholesterol, mmol/L	3.9±0.8	5.5±1.1	<0.001
Triglycerides, mmol/L	1.3±0.9	1.5±1.3	0.009
HDL-cholesterol, mmol/L	1.2±0.3	1.5±0.4	<0.001
HbA1c, mmol/mol	41±8	39±8	<0.001
Fibrinogen, g/L	3.4±0.8	3.2±0.7	<0.001
High-sensitivity CRP, mg/L	2.3±2.6	2.2±2.5	0.48
White blood cell count, ×10^9/L	6.6±4.8	5.7±3.0	<0.001
Questionnaire (total score)			
MADRS	6.0±6.2	4.4±5.1	<0.001
Pharmacological treatment (patients at admission)			
Renin-angiotensin inhibitors	194 (24)	213 (27)	0.29
Aspirin	90 (11)	82 (10)	0.53
β-Blockers	116 (15)	106 (13)	0.49
Statins	119 (15)	134 (17)	0.37
Anti-inflammatory agents (NSAIDs)	15 (2)	32 (4)	0.019
Corticosteroids	26 (3)	30 (4)	0.89
Pharmacological treatment (patients at follow-up)			
Renin-angiotensin inhibitors	687 (86)	213 (27)	<0.001
Aspirin	776 (97)	82 (10)	<0.001
β-Blockers	735 (92)	106 (13)	<0.001
Statins	775 (97)	134 (17)	<0.001
Anti-inflammatory agents (NSAIDs)	13 (2)	32 (4)	0.007
Corticosteroids	24 (3)	30 (4)	0.39

Data are presented as mean±SD or number (%). If not otherwise stated, patient data were retrieved at the follow-up visit. CRP indicates C-reactive protein; HbA1c, glycohemoglobin A1c; HDL, high-density lipoproteins; MADRS, Montgomery Åsberg Depression Rating Scale; and NSAID, nonsteroidal anti-inflammatory drug.

*Matching variable, not tested

Table 2. Socioeconomic Factors

Variables	Patients n=805	Controls n=805	*P* Value
Education			
1–12 y	533 (67)	494 (62)	0.052
University	269 (34)	307 (38)	
Occupation			
Working	420 (52)	395 (49)	
Retired	353 (44)	370 (46)	0.051
Sick leave	10 (1)	4 (1)	
Other	21 (3)	36 (4)	
Annual income (household; SEK/y)			
<180 000	100 (13)	90 (11)	
180 000–300 000	226 (28)	192 (24)	0.048
>300 000	468 (59)	516 (65)	
Marital status			
Single	86 (11)	83 (10)	
Married	597 (74)	642 (80)	0.046
Divorced/widowed	121 (15)	79 (10)	

Data are presented as number (%). SEK indicates Swedish krona.

periodontitis, and information based on data retrieved from registries or questionnaires rather than examinations.[25] The second is a suboptimal gathering of risk factors such as diet, smoking, overweight, diabetes mellitus, and stress, important for the development of cardiovascular and periodontal disease, as well.[26] Incomplete adjustment for confounders may spuriously reinforce associations suggesting causality.[11,16,27] Thus, previous data are, as underlined by the American Heart Association,[16] inconclusive regarding whether the relationship between periodontitis and cardiovascular disease is causal or coincidental and, therefore, in need of further evaluation.

The ideal study design to provide proof for the assumption that periodontics is causally related to cardiovascular disease is a prospective trial randomly assigning people with periodontitis who are free from cardiovascular disease to dental treatment or to be left untouched and with a composite of cardiovascular death and nonfatal myocardial infarction and stroke as the primary end point. Such a study does not exist[28] and would be very difficult if at all possible to conduct. The major obstacles are the demands of a very large sample size of screen-detected subjects with periodontitis followed for a long time, probably in the magnitude of decades.[29] Moreover, it may be considered unethical to deny people with established dental disease treatment. A study design that could provide useful information on associations between various risk markers and myocardial infarction would be a carefully conducted case–control study as, for example, demonstrated over the years by the Stockholm Heart Epidemiology Program (SHEEP) a population-based case-referent study of causes of a first myocardial infarction.[30–32] Experiences gained from SHEEP were used in the PAROKRANK protocol.

Several design features support the strength of the observed outcome in PAROKRANK, to the best of our knowledge the largest study of its kind. The study population was recruited from a large geographical area with the intention to cover the broadest possible distribution of participants representing a variety of educational and socioeconomic conditions. The cardiovascular disease manifestation was a first myocardial infarction, covering the 2 expressions of cardiovascular disease possibly influenced by periodontal disease, progressive atherosclerosis, and plaque rupture.[4,5] An upper age limit of 75 years was instituted to avoid a multiplicity of concomitant disorders in people with more advanced cardiovascular disease. Great emphasis was put on careful characterization of patients and controls, ruling out, so far, less-well-studied confounders, eg, glucometabolic state, socioeconomic factors, stress, and mental health, and by defining periodontitis with an objective, radiographic method, evaluated at a core center. To balance basic disturbing factors, age, sex, and geographic location, we matched 1 control to each patient. In this respect, we got 2 well-balanced groups (Table 1). Accounting for previous observations on the importance of diabetes mellitus, not only for myocardial infarction, but also periodontal disease,[33–35] the presence of diabetes mellitus was extensively covered by including participants with previously undetected diabetes mellitus. The method used for grading the periodontal disease, digital panoramic radiographs, has good agreement with other radiographic methods[36,37] and good compatibility with other measures of periodontal disease and diagnostic methods.[38–40]

The primary goal of the study was to assess the relative risks for first-time myocardial infarction based on calculations of odds ratios using patients with myocardial infarction and their controls. When checking for clinically relevant confounders in the univariate and multivariate analyses, only factors unaffected by treatment administered to the patients were included. Based on the opinion that the presence of periodontitis in patients and controls are independent of each other, we used methods for independent measures when testing our primary hypothesis. Diabetes mellitus, smoking habits, years of education, and marital status were considered as relevant confounders and therefore included in the adjusted statistical model. Other factors that possibly could be mediators between periodontal and cardiovascular disease, ie, reflecting reversed causality such as markers of inflammatory activation, were not included and, by similar reason, the Montgomery Åsberg Depression Rating Scale was omitted.

The decision to investigate the patients 6 to 10 weeks after the index infarction was based on several reasons. First, periodontitis usually starts by the age of 35 to 40 years and progression to the in PAROKRANK as moderate to severe defined states takes many years.[11] Accordingly, a potential difference between patients and controls can be considered independent of this delay. Another and important reason was

Table 3. Periodontal Status According to Panoramic X-Rays*

Periodontal Status	Patients n=796	Controls n=797	*P* Value
Healthy	458 (58)	530 (67)	
Mild-moderate periodontitis	261 (33)	231 (29)	<0.001
Severe periodontitis	78 (10)	35 (4)	

Data presented as number (%).
*X-rays not available in 9 patients and 8 controls.

to avoid the influence of the acute infarction on inflammatory activation and glucose metabolism. Finally, an earlier investigation had to be balanced against the increased risk for bleeding with dental examinations in the immediate postinfarction period. Information gained from questionnaires, the medical history, and the use of pharmacological treatment at admission should reflect the period during which the periodontal disease may provoke atherosclerosis and the development of myocardial infarction. As demonstrated in Table 1, it seems as if such cardiovascular risk factors as hypertension, dyslipidemia, and (known) diabetes mellitus had been detected and treated in similar proportions of patients and controls, thereby limiting their confounding influence in this fairly homogeneous population, apart from smoking habits, diabetes mellitus, and family history.

PAROKRANK showed a positive association between periodontitis and a first myocardial infarction, which remained following adjustment for the differences in clinical characteristics between patients and controls. This strengthens the possibility of an independent relationship between periodontitis and the risk for cardiovascular disease presently expressed as myocardial infarction. There are several possible reasons for a potential causal relationship. Chewing, tooth brushing, and dental treatments transfer microorganisms from dental pockets into the blood stream causing bacteremia and systemic inflammation.[11] This may provoke accelerated atherosclerotic vascular damage, aggregation of platelets, and the development of thrombotic material, all of which are important for the development of acute myocardial infarction.[41] DNA from oral microorganisms has indeed been identified in atherosclerotic plaques.[42,43] The outcome of PAROKRANK makes further and more detailed analyses of the character of the association of great interest. Such studies, including a close look at the importance of diabetes mellitus and other forms of dysglycemia and of various inflammatory markers, are underway in an attempt to find the pathophysiological mechanisms behind the connection between the 2 diseases.

The ongoing long-term follow-up of PAROKRANK, looking both at risk for recurrent cardiovascular events among cases and risks for cardiovascular events among patients and controls with and without periodontitis, as well, will be of considerable interest in the light of the present findings. A positive relationship between the severity of periodontal disease and subsequent cardiovascular events would further strengthen a potential causal character of the relation between periodontitis and cardiovascular disease.

Strength and Limitations

The careful case–control design with patients and controls recruited from a representative sample of Swedish hospitals and with a large number of important variables covered is the major strength of the present study. Another strength is the use of bone loss as an objective indication of the severity of the periodontal disease. Moreover, and to avoid interpretation bias, trained and blinded dentists examined all radiographs centrally according to predefined definitions. Clinical evaluation of periodontitis was also performed, but not used as a criterion in this study because of the difficulties in controlling the representativity of this type of classification, which depends on the investigator to a considerable extent. The major limitation is that PAROKRANK is an observational study, which can support but not prove the concept of a causal relationship. This limitation will, at least in part, be overcome by the ongoing follow-up for which Sweden offers excellent possibilities through the nationwide registries of hospital admissions, myocardial infarctions, and coronary interventions. Thus, a follow-up may continue over a considerable period of time, which may be necessary because the contemporary prognosis after a first myocardial infarction is fairly benign.[15]

In conclusion, PAROKRANK makes it likely that periodontitis could be looked on as a risk factor of first-time myocardial infarction, which seemingly is independent of a multitude of other risk factors. This observation should increase the interest in preventing and treating periodontal disease with the intention to improve both dental and cardiovascular health in the population.

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Disclosures

None.

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CLINICAL PERSPECTIVE

PAROKRANK, a Swedish case–control study recruiting 805 patients with a first myocardial infarction and the same number of controls matched for age, sex, and geographical area, explored whether the relation between periodontitis and cardiovascular disease is related to shared risk factors or if there may be a causal relationship. The presence of periodontitis was significantly higher among patients than controls, and the risk to develop myocardial infarction was significantly higher in the presence of moderate to severe periodontal disease even after adjustment for potential confounders, of which smoking and dysglycemia were the most important. These findings strengthen the concept that the relation between periodontal and cardiovascular disease may be causal, thereby opening the way for further exploration of pathophysiological mechanisms. In clinical practice, these findings confirm that periodontal disease should be searched for and treated, not only to improve dental health, but also to improve cardiovascular health, as well.