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Poor Oral Health and Coronary Heart Disease

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Abstract. A few recent studies have shown associations between poor oral health and coronary heart disease (CHD). The objective of this study was to examine the incidence of CHD in relation to number of teeth present and periodontal disease, and to explore potential mediators of this association, in a prospective cohort study. This study is a part of the ongoing Health Professionals Follow-Up Study (HPFS). Participants included a US national sample of 44,119 male health professionals (58% of whom were dentists), from 40 to 75 years of age, who reported no diagnosed CHD, cancer, or diabetes at baseline. We recorded 757 incident cases of CHD, including fatal and non-fatal myocardial infarction and sudden death, in six years of follow-up. Among men who reported pre-existing periodontal disease, those with 10 or fewer teeth were at increased risk of CHD compared with men with 25 or more teeth (relative risk = 1.67; 95% confidence interval, 1.03 to 2.71), after adjustment for standard CHD risk factors. Among men without pre-existing periodontal disease, no relationship was found (relative risk = 1.11; 95% confidence interval, 0.74 to 1.68). The associations were only slightly attenuated after we controlled for dietary factors. No overall associations were found between periodontal disease and coronary heart disease. Tooth loss may be associated with increased risk of CHD, primarily among those with a positive periodontal disease history; diet was only a small mediator of this association.

Key words: coronary heart disease, periodontal disease, edentulousness, diet, infection.

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Introduction

Associations between poor dental health and coronary heart disease (CHD) have been reported recently (Mattila *et al.*, 1989a; DeStefano *et al.*, 1993; Joshipura, 1995; Beck *et al.*, 1996). A third of adults have moderate periodontal disease, a third of the elderly have severe periodontal disease, and nearly 40% of the elderly in the US have no teeth (National Institutes of Health, 1987; Douglass *et al.*, 1993). Due to the high occurrence of dental diseases, their potential association with CHD may have implications for millions of people. This report evaluates the relationship between tooth loss and periodontal disease and CHD in a six-year follow-up study of 52,000 men, and evaluates diet and infection as potential mediators of this association.

A matched case-control study of 200 participants (Mattila *et al.*, 1989a) in Helsinki showed significant positive associations between myocardial infarction (MI) and composite dental indices combining caries, periodontitis, periapical lesions, pericoronitis, and edentulousness. In another study of 88 men, the authors reported a positive dose-response association between coronary atherosclerosis and the composite index (Mattila *et al.*, 1993). The composite dental index was also linked to ischemic events in patients with CHD at entry (Mattila *et al.*, 1995).

In a cohort study (DeStefano *et al.*, 1993) of people initially free of CHD, relative risks (RR) for CHD of 1.25 (95% CI, 1.06 to 1.48) for periodontal disease and 1.23 (95% CI, 1.05 to 1.44) for complete tooth loss were reported, compared with people with no dental disease. Participants included 9760 adults, from 25 to 74 years of age, in a 14-year follow-up of the National Health and Nutrition Epidemiologic Follow-Up Study (NHEFS). A study of 1147 men in the Veterans Administration's Dental Longitudinal study (Beck *et al.*, 1996) reported an association between alveolar bone loss at baseline and the incidence of CHD including angina over 25 years' follow-up (RR of 1.5; 95% CI, 1.04-2.14). A cross-sectional study (Paunio *et al.*, 1993) also showed association between missing teeth and CHD.

Recent reports relating other chronic infections and CHD (Griffiths *et al.*, 1980; Saikku *et al.*, 1988; Mattila, 1989; Valtonen, 1991; Saikku *et al.*, 1992; Mendall *et al.*, 1994) and

Table 1. Description of number of teeth by age, and selected standardized risk factors for CHD at baseline[a]

	Number of Teeth			
	25-32	17-24	11-16	0-10
Number of men	37,079	4,815	950	1,275
Age (years)	52.7	58.2	61.5	63.8
% current smokers	9	15	20	24
Physical activity (MET/wk)[b]	18.5	16.6	14.9	12.8
BMI (kg/m^2)	25.1	25.2	25.5	25.8
History at baseline (%):				
Periodontal disease	13	24	32	30
Hypertension	19	21	22	22
High cholesterol	10	11	9	11
Family history of CHD (%)	12	12	12	12
% users of vitamin E supplements	19	19	19	17
% consuming carrots more than once a month	91	88	88	85
Intake of dietary fiber (g/day)	22.3	21.4	20.5	20.6
Intake of saturated fat (g/day)	24.5	25.1	25.4	26.3
Intake of carotene (IU/day)	10,273	9,203	8,786	9,380
Alcohol intake (g/day)	11.8	12.4	13.2	11.6

[a] Standardized for age to the total cohort (except for age); values are means, unless otherwise specified.
[b] MET-hours = sum of the average time/week spent in each activity x MET value of each activity.

$$\text{MET value} = \frac{\text{caloric need/kg body weight/hour activity}}{\text{caloric need/kg body weight/hour at rest}}$$

inflammatory mediators and CHD (Friedman *et al.*, 1974; Kannel *et al.*, 1987; Yarnell *et al.*, 1991; Ensrud and Grimm, 1992; Lindberg *et al.*, 1992; Ernst, 1993; Heinrich *et al.*, 1995; Tofler and Jadhav, 1996; Mendall *et al.*, 1996) additionally support a role of chronic dental infection in CHD. The association between tooth loss and CHD could possibly be due to antecedent caries or periodontal disease in the extracted teeth, or due to diet. We have reported that tooth loss is associated with increased consumption of saturated fat and cholesterol and decreased consumption of fruits, vegetables, carotene, and fiber (Joshipura *et al.*, 1996a)—factors which may be associated with increased CHD risk (Willett, 1994; Willett and Lenart, 1996). Diet was not examined in the other reports (Mattila *et al.*, 1989a; DeStefano *et al.*, 1993; Beck *et al.*, 1996; Paunio *et al.*, 1993).

In summary, available evidence suggests a possible relationship between dental disease/tooth loss and CHD, perhaps mediated through inflammatory mediators and diet. We therefore prospectively evaluated the relationship between oral health and CHD in the HPFS, and evaluated diet as a potential mediator.

Materials and methods

The study population was comprised of 51,529 health professional men, 58% of whom are dentists, who were from 40 to 75 years of age at baseline (1986). Return of the baseline questionnaire constituted informed consent to a protocol that was reviewed and approved by the Institutional Review Board. We excluded 5604 participants who reported MI, angina, stroke, re-vascularization procedures, or diabetes prior to the follow-up period. Participants missing information on age or number of teeth (457 men) were also excluded. Using *a priori* criteria, we further excluded 1349 participants who reported daily caloric intake outside the plausible range of 800 to 4200 calories or who left 70 or more of the 131 dietary questions blank (Rimm *et al.*, 1992). We followed the 44,119 eligible men for CHD occurrence during the subsequent six years, with biennially mailed questionnaires.

The procedures for follow-up and confirmation of end-points have been described previously (Grobbee *et al.*, 1990). We included as end-points incidence of fatal and non-fatal MI and sudden death. We excluded re-vascularization procedures as endpoints to avoid spurious relationships due to behavioral factors. Physicians reviewing the medical records were unaware of the participants' dental status. The follow-up rate over six years, including deaths, was 94%. We considered non-responders who were not listed on the National Death Index as non-cases.

Number of teeth present was reported as a categorical measure (0, 1-10, 11-16, 17-24, 25+). Self-reported number of teeth is a highly accurate measure in the general population (Douglass *et al.*, 1991). The periodontal disease history was assessed by the question, "Have you had periodontal disease with bone loss?". We assessed the validity of this measure among dentists (Joshipura *et al.*, 1996b). The predictive values' positive and negative are 0.76 and 0.74, respectively, leading to a 30% expected attenuation of the RR. The measure showed validity among non-dentists by confirmation of known associations with age and smoking; however, non-dentists are expected to be less aware of their periodontal status than dentists. Due to concern about the validity of the measure among non-dentists, we repeated the major analyses among only dentists. The conclusions were similar; hence, to utilize the maximum information, we present the analysis for the whole population.

Participants were grouped according to their reported category of tooth loss: Men with 0 teeth and 1 to 10 teeth were combined into one group due to the small numbers. Multiple

Table 2. Relative risk of coronary heart disease, according to number of teeth at baseline.

		Number of Teeth				
		25-32	17-24	11-16	0-10	P-value for Trend
Number of men		37,079	4815	950	1275	
Number of cases (%)		554 (1.49)	117 (2.43)	29 (3.05)	57 (4.47)	
Models adjusted for:						
Age + Smoking	RR[a]	1.0	1.08	1.12	1.40	0.03
	95% CI		0.88-1.33	0.76-1.64	1.04-1.87	
Multivariate[b]	RR	1.0	1.04	1.06	1.32	0.10
	95% CI		0.85-1.28	0.72-1.56	0.98-1.77	
Multivariate + diet[c]	RR	1.0	1.03	1.04	1.29	0.14
	95% CI		0.83-1.27	0.71-1.54	0.96-1.73	

[a] RR denotes the relative risk and CI denotes confidence interval.
[b] The multivariate model includes: age (continuous); body mass index (five categories); exercise (five categories); smoking habits (current smoker [number of cigarettes smoked: 1-14, 15-24, 25+], former smoker, or person who never smoked); alcohol consumption (7 categories); family history of myocardial infarction before 60 years of age; vitamin E (5 categories).
[c] Dietary variables include dietary fiber and carrots (5 categories each).

logistic regression was used to generate odds ratios as an approximation of the RR to compare participants with 10 or fewer, 11 to 16, and 17 to 24 teeth at baseline against those with 25 or more teeth. Due to the high follow-up rate, low CHD prevalence, and use of only one time-point, logistic regression was used. We repeated the primary analyses using Cox regression, and the results were almost identical; hence, only results from the logistic regression are presented. The primary analyses controlled for age and smoking. Additional analyses controlled for baseline values of age, smoking (current = number of cigarettes smoked, 1-14, 15-24, 25+; former = never smoked), alcohol (7 categories), family history of MI before age 60, and 5 categories of obesity, total Vitamin E intake, and exercise. An additional analysis controlled for possible dietary mediators, including dietary fiber and carrots. These factors were chosen based on previous research showing their associations with tooth loss (Joshipura *et al.*, 1996a) and CHD (Rimm *et al.*, 1993, 1996). Trends in CHD risk across number of teeth lost were assessed in the logistic models by use of a single variable, with each participant being assigned a value equal to the mid-point of his tooth category.

Results

We documented 757 CHD end-points: 526 non-fatal MI and 231 fatal coronary events. Table 1 presents a description of the potential CHD risk factors by number of teeth. Baseline number of teeth was negatively related to age (mean age 53 for men with 25 or more teeth *vs.* 64 for men with 0-10 teeth) and smoking (24% of men with 0-10 *vs.* 9% of men with 25 or more teeth were current smokers), and, to a smaller extent, with other coronary risk factors. These associations were similar for men with periodontal disease. Mean age was 58 *vs.* 53, and current smokers were 17% *vs.* 9% among men with and without periodontal disease.

Tooth loss showed a small association with increased CHD risk (Table 2). Men with 0 to 10 teeth, as compared with men with 25 or more teeth, had a RR of 1.40 (95% CI, 1.04 to 1.87), after we adjusted for age and smoking. The p-value for trends across all tooth loss categories was 0.03. The addition of other CHD risk factors moderately attenuated the association (RR, 1.32; 95% CI, 0.98 to 1.77). When we added hypertension and hypercholesterolemia to the model, the RR estimates were almost identical (RR, 1.31; 95% CI, 0.98-1.76; not shown in Tables). Further addition of dietary variables attenuated the RR very slightly. When the analyses were repeated among only dentists, the results were similar.

We did not find any overall association between periodontal disease and CHD in this population (Table 3). In multivariate models, the RR of CHD was 1.04 (0.86, 1.25), when men with and without periodontal disease were compared. We also did not find associations within categories of age and smoking or baseline tooth loss. When the analysis was restricted to dentists, we still did not find any overall association between history of periodontal disease and CHD risk (multivariate RR, 0.97; CI, 0.77, 1.22).

Analyses were carried out separately by periodontal status. The association between tooth loss and CHD was limited to men who reported positive periodontal disease history (Table 4). Among those without a positive periodontal disease history, the RR of CHD was 1.11 (95% CI, 0.74-1.68) when men with 0 to 10 teeth were compared with men who reported 25 or more teeth. However, among the 6619 men with periodontal disease, the multivariate RR was 1.67 (95% CI, 1.03, 2.71) for men with 10 or fewer remaining teeth. The p-value for trend was 0.09. When this analysis was restricted to dentists, the results were similar: no overall association between tooth loss and CHD among men with no periodontal disease; and men with periodontal disease had a RR of 1.71 (95% CI, 0.91 to 3.22) when men with fewer than 10 teeth were compared with men with 25 or more teeth. An interaction term for periodontal disease and tooth loss

Table 3. Relative risk of coronary heart disease, according to periodontal disease at baseline.

		Periodontal Disease	
		No	Yes
Number of men		36,697	6619
Number of cases (%)		582 (1.59)	155 (2.34)
Models adjusted for:			
Age + smoking	RR[a]	1.0	1.04
	95% CI		0.97, 1.25
Multivariate[b]	RR	1.0	1.04
	95% CI		0.86, 1.25

[a] RR denotes the relative risk and CI denotes confidence interval.
[b] The multivariate model includes: age (continuous); body mass index (five categories); exercise (five categories); smoking habits (current smoker [number of cigarettes smoked: 1-14, 15-24, 25+], former smoker, or person who never smoked); alcohol consumption (7 categories); family history of myocardial infarction before 60 years of age; Vitamin E (5 categories).

(comparing 10 or fewer teeth to 25 or more teeth) was added to the multivariate model so that we could evaluate whether the association was higher among men with periodontal disease. The interaction was not statistically significant in the whole population, nor among dentists.

Discussion

Among men with periodontal disease, we found significantly higher incidence of CHD among men with 10 or fewer teeth compared with men with an intact dentition, after controlling for standard CHD risk factors. Potential bias was minimized by the high follow-up rate. No effect of tooth loss was seen among men who reported no periodontal disease. The limitation of the association between tooth loss and CHD to participants with positive periodontal disease suggests that antecedent periodontal infection in the extracted teeth could be a factor.

Three main pathways linking oral infection to secondary disease were suggested (Thoden Van Velzen *et al.*, 1984): (1) metastatic infection, secondary to the oral infection, due to transient bacteremia (presumably resulting primarily in endocarditis); (2) systemic inflammation from immunologic injury caused by oral bacteria; and (3) systemic vascular injury due to oral microbial endotoxins.

Bacterial endotoxin may affect endothelial integrity, plasma lipoprotein metabolism, blood coagulation, platelet function, and prostaglandin synthesis (Syrjanen, 1990). Bacterial endotoxin increases cytokine secretion (Offenbacher *et al.*, 1993; Shapira *et al.*, 1994), which could elevate inflammatory markers (Fey and Fuller, 1987; Fahmy and Young, 1993; Rogers *et al.*, 1994). Participants with periodontal disease showed elevated fibrinogen and white blood cell levels (Kweider *et al.*, 1993), which may be causally related to CHD (Friedman *et al.*, 1974; Kannel *et al.*, 1987; Yarnell *et al.*, 1991; Ensrud and Grimm, 1992; Ernst, 1993; Tofler and Jadhav, 1996). There is also some evidence linking dental infection with Von Willebrand factor (Mattila *et al.*, 1989b), which in turn has been associated with CHD (Thompson *et al.*, 1995).

Tooth loss could lead to changes in diet, which could increase CHD risk. Controlling for dietary factors led to a very small attenuation of the RR, suggesting that diet could explain at most a small part of the association. The effect of diet may be underestimated due to the inherent misclassification in dietary assessment (Willett, 1990). It is

Table 4. Relative risk of CHD according to number of teeth by periodontal status at baseline

		Teeth				P-value
		25-32	17-24	11-16	0-10	for Trend
Men with positive periodontal history						
Number[a]		4489	1284	365	481	
Number of cases (%)		90 (2.00)	28 (2.18)	11 (3.01)	26 (5.40)	
Models adjusted for:						
Multivariate[b]	RR[c]	1.0	0.84	1.09	1.67	0.09
	95% CI		0.54-1.30	0.57-2.09	1.03-2.71	
Men with negative periodontal history						
Number[a]		32,044	3390	542	721	
Number of cases (%)		456 (1.42)	83 (2.45)	16 (2.95)	27 (3.74)	
Models adjusted for:						
Multivariate[b]	RR[c]	1.0	1.10	1.04	1.11	0.47
	95% CI		0.86-1.40	0.62-1.74	0.74-1.68	

[a] Men with missing data on periodontal disease history excluded.
[b] The multivariate model includes age (continuous); body mass index (five categories); exercise (five categories); smoking habits (current smoker [number of cigarettes smoked: 1-14, 15-24, 25+], former smoker, or person who never smoked); alcohol consumption (7 categories); family history of myocardial infarction before 60 years of age; Vitamin E (5 categories).
[c] RR denotes the relative risk and CI denotes confidence interval.

also possible that the effect may be mediated by other unknown and unaccounted dietary factors such as cooking and processing. The effect of diet is likely to be higher in other populations with a socio-economic range wider than that of health professionals.

Tooth loss and CHD can both be reduced by modifications in behavior and habits. Hence, people who take good care of their dentition may be at lower risk for CHD, simply as they practice healthy behaviors. We controlled for confounding from "healthy behavior" by adjusting for smoking, physical activity, and several CHD risk factors. After controlling for age and smoking, we found that additional control of other CHD risk factors had little impact on the RR, suggesting that residual confounding was unlikely. Furthermore, the magnitude of association between tooth loss and CHD among men with periodontal disease was as strong as that of other reported associations for CHD in this population (Grobbee *et al.*, 1990; Rimm *et al.*, 1993, 1996). However, residual confounding cannot be excluded, although our cohort of health professionals with a relatively homogenous high level of health education and awareness and socio-economic status minimizes confounding due to healthy behavior.

We did not find overall associations with periodontal disease, unlike the NHEFS report and VA report (DeStefano *et al.*, 1993; Beck *et al.*, 1996). It is possible that the associations found in the NHEFS and VA studies may reflect confounding, because smoking history was missing for two-thirds of the participants in the NHEFS, and the VA study associated exposures at baseline with CHD incidence over 25 years, and smoking had dropped out in the final stepwise model. Also, periodontal disease could appear to be a risk factor if it is a bigger contributor to tooth loss in the NHEFS and VA than in our study. The stronger effect of tooth loss among periodontal patients in our study supports this possibility. Alternately, tooth loss among participants with periodontal disease may be a marker for severe periodontal disease which was not captured by our periodontal measure. Misclassification of the HPFS measure could have biased the relative risks toward the null: We expect an attenuation of approximately 30% in the RR based on the predictive values; thus, the actual associations may be bigger than what we have documented. The HPFS periodontal measure reflects a cumulative lifetime history of periodontal disease. If there is an effect of periodontal disease with a short incubation period, then this may not be captured by our periodontal measure. Thus, our data do not exclude a small increase in risk associated with periodontal disease.

We did not collect data on dental caries; hence, we cannot know whether caries or extraction of carious teeth increased CHD risk in our study. It is also not possible to know whether caries contributed to the effect of the composite measure in the Helsinki study. Active caries showed no significant relationship with CHD risk in the NHEFS; cumulative caries experience (number of decayed, missing, and filled teeth) was not evaluated. Caries was not evaluated in the VA study.

Overall, our study suggests an association between poor oral health and CHD. Further studies are needed to evaluate the role of periodontal disease, dental caries, and tooth loss in the etiology of CHD. Dental infections may be an important component of CHD risk which is amenable to intervention.

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