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Periodontal Disease and Incidence of Hypertension in the Health Professionals Follow-Up Study

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Abstract

Background—Recent studies suggest a possible association between periodontal disease and hypertension; however, prospective evidence is limited.

Methods—The study population consisted of 31,543 participants of the HPFS prospective cohort who were 40 to 75 years old at baseline, had no prior hypertension history and had complete baseline information on oral health. Information on periodontal disease, hypertension and potential confounders was updated biennially. We used Cox proportional hazards models to study the relation between periodontal disease at baseline, during follow-up, periodontal bone loss severity, baseline number of teeth and tooth loss during follow-up, and the risk of developing hypertension. Multivariate models included age, calendar time, race, comprehensive smoking index, diabetes, alcohol consumption, family history of hypertension, dental profession, BMI, physical activity, fruit and vegetable intake, multivitamin use, calcium, vitamin D and vitamin E intake.

Results—We identified 10,828 cases of incident hypertension over 20 years of follow-up. After adjusting for potential confounders, we did not observe significant associations between incident hypertension and periodontal disease at baseline (RR=1.04; 95% CI: 0.98–1.10), periodontitis during follow-up (RR=1.01; 95% CI: 0.96–1.05), tooth loss during follow-up (RR=1.03; 95% CI: 0.98–1.09), or when comparing men with 0–10 teeth to men with ≥25 teeth at baseline (RR=1.05; 95% CI: 0.91–1.21). Participants reporting severe periodontal bone loss had a relative risk for incident hypertension of 1.02 compared to those without bone loss (95% CI: 0.77–1.35).

Conclusions—We did not observe an association between periodontal disease measures and incident hypertension in this cohort of middle-aged men.

Keywords

periodontal disease; inflammation; hypertension; cohort; blood pressure

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Introduction

Hypertension is a highly prevalent condition; nearly 30% of U.S. adults have high blood pressure.[1] Hypertension is one of the major causes of hospitalization and morbidity worldwide. Hypertension is a strong risk factor for stroke and cardiovascular disease. It is closely associated with endothelial dysfunction,[2] and along with other factors (e.g., smoking, hyperlipidemia) promotes the atherosclerotic process. Over 7 million deaths per year around the world can be attributed to hypertension.[3] Hypertension-related mortality in the U.S. was estimated to reach 54,000 in 2004.[4]

In light of increasing evidence for the role of chronic inflammation in cardiovascular outcomes, emerging evidence from animal and human studies shows a potential inflammatory etiology of hypertension. Several longitudinal studies have demonstrated the relation between circulating levels of inflammatory markers, such as C-reactive protein, and incidence of hypertension.[5–8]

Periodontal disease is a highly-prevalent chronic inflammatory condition associated with an increase in circulating levels of inflammatory biomarkers.[9–13] Several reports,[9,10] including data from Health Professionals' Follow-up Study (HPFS),[10] showed higher serum CRP levels among periodontitis patients when compared to healthy controls, especially in patients with more aggressive[11] and more generalized forms[12] of the disease. Similar results were reported between periodontal disease and plasma levels of IL-6,[12,13] with a clear dose-response relation established between the severity of periodontal attachment loss and circulating IL-6 levels.[13]

The relation between periodontal disease and cardiovascular disease has been evaluated in several prospective studies.[14] However, only one recent prospective cohort[15] and a few cross-sectional studies[16,17] have assessed the relation between periodontal disease and hypertension.

To address this issue further, we prospectively assessed the relation between periodontal disease and incident hypertension while controlling for important potential confounders.

Methods

In this study, we evaluated the relation between self-reported periodontal disease and tooth loss and subsequent incidence of hypertension in a cohort of health professionals.

Study Population

The Health Professionals' Follow-Up Study (HPFS) was initiated in 1986 as a prospective cohort of male health professionals (dentists, pharmacists, optometrists, podiatrists, osteopaths and veterinarians) age 40 to 75. The cohort began with 51,529 men who responded to the initial questionnaire. Throughout the follow-up period, individual data on lifestyle and medical conditions was obtained from cohort participants on a biennial basis. Due to their professional education and high socio-economic status, the cohort participants accurately self-report on health conditions.[18–20] More than 90% of the baseline population has responded to follow-up questionnaires.[21] Deaths of cohort participants were reported in response to biennial questionnaire mailings and matched with the National Death Index.

This study was approved by the Office of Human Research Administration of the Harvard School of Public Health. We excluded a total of 19,986 participants who either indicated they were no longer interested in participating in the study (N=35), reported a hypertension diagnosis (N=12,642) or were taking blood pressure lowering medications (N=1,867) or had

high blood pressure (≥140/90mm Hg) at baseline (N=4,593), had missing information on periodontal disease status (N=649) or number of teeth (N=199) at baseline, or when the baseline questionnaire was received after the date of participant's death (N=1). Our final sample of 31,543 eligible participants contributed 466,514 person-years during 20 years of follow-up, between 1986 and 2006.

Periodontal disease assessment

At baseline, in 1986, participants were asked about history of periodontal disease diagnosis with bone loss. During the follow-up biennial surveys, starting in 1988, the participants responded to the question about new periodontal disease diagnosis. Periodontal disease diagnoses at baseline and during follow-up were used in statistical analyses as binary (yes/no) variables. Participants also reported the severity of their periodontal bone loss in 1996 (none, mild, moderate, severe), which was used to assess potential dose-response.

Self-reported periodontal disease in this population has been shown to be a valid measure for periodontal disease. As demonstrated by Joshipura et al, when compared with radiographic measurements, self-reports of periodontal disease had a positive predictive value of 83% and a negative predictive value of 69% among non-dentist participants.[22] Among dentists, 76% of the reports of periodontal disease diagnosis were confirmed by the presence of bone loss on the radiographs, and 74% of the negative reports had no radiographic bone loss.[23]

Tooth loss assessment

On the 1986 questionnaire, participants were asked about the number of teeth present, grouped as 0, 1–10, 11–16, 17–24, and 25 or more. In the subsequent biennial questionnaires during follow-up, participants reported if they had any tooth loss within the past 2 years. Self-reported number of teeth showed high validity against clinically measured number of teeth in the general population (r= 0.97).[24]

Hypertension assessment

We obtained self-reports of physician-diagnosed hypertension at baseline (1986) and during follow-up. Participants reporting hypertension during the follow-up were assumed to be incident cases. Men who reported hypertension on the questionnaire were also requested to provide information on the year of diagnosis. If the year of diagnosis was not reported, the time of incident hypertension was assumed to be the month prior to the return date of the questionnaire. Self-reported hypertension has been shown to be valid and highly reliable in this cohort of male health professionals. In a validation study among a subset of these men, 100% of those reporting hypertension had their diagnosis confirmed by medical record review, and only 1.8% of those without previous report of hypertension diagnosis by a physician had high blood pressure within 4–13 months after the questionnaire return.[19]

Assessment of covariates and effect modifiers

Participants reported their date of birth, profession, and race in 1986. Family history of hypertension was reported on the 1990 questionnaire. Data on weight, smoking habits, physical activity, multivitamin supplement use, routine check-up visits to a physician and self-reported diabetes diagnosis were collected at baseline and updated on a biennial basis. We calculated body mass index (BMI, in kg/m^2) from the reported weight and height of the participants biennially. Fruit and vegetable, alcohol, calcium, vitamin D and vitamin E intakes were calculated from food frequency questionnaires, administered every 4 years. Information on smoking was summarized in the comprehensive smoking index (CSI), a continuous measure that accounts for intensity, duration and recency of smoking.[25] The

half-life of the effect of smoking on hypertension (τ) was estimated at 6 years by comparing goodness-of-fit (Akaike's information criterion) of models with CSIs calculated with τ within a reasonable range (up to 40 years).[26] Reproducibility and validity of self-reported diabetes, physical activity, weight, alcohol, diet and supplement intake measures in this cohort have been demonstrated previously.[27–31]

Data analyses

We used Cox proportional hazards models with time-dependent covariates to study the relation between self-reported periodontal disease and subsequent incident hypertension with age in months as the time scale variable, stratified by calendar time in two-year intervals. Incidence rate ratios and 95% confidence intervals were reported. In the analysis on severity of periodontal bone loss as assessed in the 1996 questionnaire and subsequent hypertension diagnosis, we compared incidence of hypertension among participants reporting mild, moderate or severe periodontal bone loss to those reporting no periodontal bone loss.

We included the following potential confounders in our multivariate models: family history of hypertension, diabetes diagnosis, alcohol consumption (six categories), CSI, quintiles of leisure-time physical activity (metabolic equivalents of task–hours (METs)/week), BMI (five categories), supplemental multivitamin use (yes/no), and quintiles of vitamins E and D, calcium, and fruit and vegetable intake. We also controlled our analyses for recent and cumulative tooth loss, and periodontal disease diagnosis during the follow-up for the number of teeth at baseline (0–10, 11–16, 17–24, ≥25).

In secondary analyses, we repeated our multivariable models after stratifying by smoking status, profession (dentist, yes/no), family history of hypertension, baseline number of teeth, age, BMI, diabetes status, and also after restricting the population to those who had a screening visit to a physician within the last 2 years, since the association between periodontal disease and hypertension might be modified by these factors. To evaluate potential effect modification by BMI, we created interaction terms between periodontal disease and midpoints of traditional BMI categories (22.5 kg/m^2 for normal and underweight, 27.5 kg/m^2 for overweight, and 32.5 kg/m^2 for obese participants) and compared multivariate models with and without interaction terms using a likelihood ratio test. Effect estimates from strata defined by binary variables were compared by employing a Wald-type test where the squared difference of the log relative risks from the two strata is divided by the sum of their variances, and compared against a χ^2 statistic with 1 degree of freedom. For these analyses, we used cutoffs of 55 years for age, and 24 teeth for baseline number of teeth.

Data on smoking habits was not available for 3.3% of our participants; therefore, we used the missing indicator method and replaced missing smoking index values with the median CSI (zero) in the HPFS population. To evaluate the sensitivity of the assumption on the missing values, we additionally conducted the same analyses while replacing missing smoking index values with the mean CSI value (0.39). Both assumptions led to identical relative risk estimates; therefore, we proceeded with the replacement of missing CSI values with the median value.

We explored the effect of misclassification of periodontal disease measures by adjusting the effect estimates using the method described by Zucker and Spiegelman.[32] Correction for misclassification was performed using the results of previous validation studies of self-reported periodontal disease against radiographic bone loss estimated from pre-existing radiographs.[22,23] All statistical procedures were performed using SAS release 9.1 (SAS Institute, Cary, NC).

Results

Over 20 years of follow-up, we identified 10,828 cases of hypertension. The median follow-up time was 16.3 years. Table 1 summarizes age-adjusted distribution of standard risk factors for hypertension, by baseline periodontal disease status and number of teeth. Participants who reported periodontal disease at baseline (1986) were more likely to be older, dentists, current smokers, have fewer teeth at baseline and report tooth loss during follow-up, compared to those free from periodontal disease. Men with fewer teeth at baseline (0–10 and 11–16) were mostly older, non-dentists, current smokers, and more likely to report periodontal disease. Thirty percent of participants with 25 or more teeth at baseline reported family history of hypertension, compared to 25% of those with 10 teeth or less. Participants with fewer teeth were less physically active at baseline.

Table 2 presents the results of age, calendar year, smoking- and multivariable-adjusted analyses relating periodontal disease and tooth loss with incident hypertension. Baseline number of teeth (RR for 0–10 teeth vs. 25–32 teeth=1.05, 95% CI: 0.91–1.21), recent (RR=1.02, 95% CI: 0.95–1.09) and cumulative (RR=1.03, 95% CI: 0.98–1.09) tooth loss were not significantly associated with hypertension in multivariate models.

After adjusting for risk factors, we did not observe a significant association between periodontal disease diagnosis at baseline and the risk of incident hypertension (RR=1.04; 95% CI: 0.98–1.10). Results were similar for the analysis on periodontal disease during follow-up (RR=1.01; 95% CI: 0.96–1.05). There was no evidence for a dose-response relation between the periodontal bone loss severity level (no, mild, moderate, severe, as reported on the 1996 questionnaire), and hypertension (p-value for trend=0.65); however, we had limited power for this analysis. Compared with men reporting no periodontal bone loss, those with severe periodontal bone loss had a RR of 1.02 for incident hypertension (95% CI: 0.77–1.35).

There was the suggestion of an adverse impact of severe periodontal disease in relation to hypertension risk among those with low BMI (BMI < 25 kg/m^2), and the suggestion of a an inverse association among the obese, with no clear association among the overweight (p-value for interaction with severe periodontal disease=0.01 (p-value for interaction =0.01). However, this finding was not consistent with results for periodontal disease at baseline, and further confirmation is recommended. Although the association between severe periodontitis and hypertension appeared to be stronger among younger participants (RR=1.91, 95% CI: 0.83–4.44), the interaction with age was not significant (p=0.12). The association between periodontal disease and hypertension did not differ between the pre-defined strata of dental profession, baseline number of teeth, smoking, diabetes, and family history of hypertension.

After correcting our effect estimates for misclassification of periodontal disease, the age-, profession- and smoking-adjusted RR for baseline periodontal disease was 0.98 (95% CI: 0.88–1.09), compared with 1.02 (95% CI: 0.97–1.07) from the uncorrected analysis.

Discussion

Recent scientific evidence suggests a possible connection between periodontal disease and systemic inflammation,[9–13] which in turn is associated with an increased risk of hypertension.[33–36] However, in this prospective study among U.S. health professional men, we found no association between periodontal disease and the risk of hypertension during 20 years of follow-up.

The results from this study are similar to the findings from our preliminary work among Puerto Rican elderly, in which there was no significant association between clinically

measured severe periodontal disease and self-report of a hypertension diagnosis (multivariate OR=0.98, 95% CI: 0.38–2.56, adjusted for age, gender, smoking, heavy and binge drinking, diabetes, utilization of preventive dental services, overweight, and dietary factors).

Two other reports showed significant associations between severity of periodontal disease and hypertension. Holmlund et al.[16] conducted a cross-sectional study of 3,352 periodontal patients and 902 population controls in Sweden, using radiographical and clinical measurements to summarize periodontal disease severity. After adjusting for age, gender, number of teeth and current smoking (yes/no), the authors reported a linear trend between severity of periodontal disease (no, minor, moderate, severe), and hypertension (OR for trend=1.32, 95% CI: 1.13–1.54). A recent prospective cohort of Japanese manufacturing company employees by Morita and colleagues[15] demonstrated statistically significant associations between presence of periodontal pockets of at least 4mm at baseline (a clinical measure of moderate-to-severe periodontal disease) and incident hypertension, defined as having ≥130 mm Hg systolic or ≥85 mm Hg diastolic blood pressure during the follow-up visit (RR=1.5, 95% CI: 1.0–2.3, adjusted for age, gender, and binary measures for cigarette smoking, regular exercise, eating between meals and healthy body weight). One of the strengths of both reports was clinical assessment of periodontal disease status. In contrast with reports by Holmlund et al. and Morita et al., our multivariate analyses in the overall population showed no significant association between severe periodontal bone loss and hypertension (RR=1.02, 95% CI: 0.77–1.35; p-value for trend=0.65), possibly due to limited power for this analysis, finer control for confounding and differences in study population characteristics. Our age-adjusted relative risk for severe periodontal bone loss was similar to the results from other studies (RR=1.13, 95% CI: 0.86–1.49); smoking, race and diabetes were the strongest confounders in our analyses. We had detailed information on duration and amount of past and current cigarette smoking, and adjusted for comprehensive smoking index, as well as diabetes, in multivariate analyses. Detailed data collected during the follow-up also allowed thorough adjustment for other potential confounders, such as nutrition and physical activity. Because the Japanese cohort included relatively young participants (20–56 years of age), we restricted our analysis to those 55 years of age and younger. The association between severe periodontitis and hypertension was stronger in this subgroup (multivariate-adjusted RR=1.91, 95% CI: 0.83–4.44), and was more consistent with the findings from the Japanese cohort. The differences in effect estimates for severe periodontitis in younger (RR=1.91, 95% CI: 0.83–4.44) and older (RR=0.94, 95% CI: 0.70–1.26) participants appeared to be large; however, perhaps due to limitations of the available data, this interaction was not statistically significant (p=0.12). This may be worth evaluating in future publications.

Although smoking and diabetes have previously been shown to be effect modifiers of periodontal disease - CVD relationships,[14,37] there was no evidence for modification of the relation between a binary measure of periodontal disease and hypertension by smoking or diabetes. Absence of effect modification by diabetes can be partially explained by residual confounding by severity of diabetes, since poor glycemic control was previously demonstrated to be associated with poorer periodontal health.[38] We observed statistically significant effect modification by obesity in our study. Experimental studies suggest that adiposity impedes the ability of the immune system to appropriately respond to periodontal infection.[39] However, we did not see a consistent trend in the associations between different periodontal measures and hypertension across three BMI groups, with relative risks for hypertension being close to null in all BMI strata; hence, the apparent effect modification could possibly be explained by chance.

One of the limitations of our study is that periodontal disease was self-reported. We hypothesized that misclassification of periodontal disease diagnosis in our population was not associated with hypertensive status of our participants; therefore, it was non-differential and resulted in attenuation of the effect estimates. After correction for misclassification the results were not materially different, possibly because the relative risks were close to null in this population.

In conclusion, after adjusting for important cardiovascular risk factors, we did not observe significant associations between periodontal disease measures and hypertension in the cohort of health professionals, suggesting that periodontal inflammation may not be important in the development of hypertension.

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References

1. Hajjar I, Kotchen JM, Kotchen TA. Hypertension: trends in prevalence, incidence, and control. Annu Rev Public Health. 2006; 27:465–490. [PubMed: 16533126]
2. Felmeden DC, Lip GY. Endothelial function and its assessment. Expert Opin Investig Drugs. 2005; 14(11):1319–1336.
3. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003; 42(6):1206–1252. [PubMed: 14656957]
4. Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y. Heart disease and stroke statistics--2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2007; 115(5):e69–171. [PubMed: 17194875]
5. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. Jama. 2003; 290(22):2945–2951. [PubMed: 14665655]
6. Niskanen L, Laaksonen DE, Nyyssonen K, Punnonen K, Valkonen VP, Fuentes R, Tuomainen TP, Salonen R, Salonen JT. Inflammation, abdominal obesity, and smoking as predictors of hypertension. Hypertension. 2004; 44(6):859–865. [PubMed: 15492131]
7. Wang TJ, Gona P, Larson MG, Levy D, Benjamin EJ, Tofler GH, Jacques PF, Meigs JB, Rifai N, Selhub J, Robins SJ, Newton-Cheh C, Vasan RS. Multiple biomarkers and the risk of incident hypertension. Hypertension. 2007; 49(3):432–438. [PubMed: 17242302]
8. Dauphinot V, Roche F, Kossovsky MP, Schott AM, Pichot V, Gaspoz JM, Gosse P, Barthelemy JC. C-reactive protein implications in new-onset hypertension in a healthy population initially aged 65 years: the Proof study. J Hypertens. 2009; 27 (4):736–743. [PubMed: 19516173]
9. Wu T, Trevisan M, Genco RJ, Falkner KL, Dorn JP, Sempos CT. Examination of the relation between periodontal health status and cardiovascular risk factors: serum total and high density lipoprotein cholesterol, C-reactive protein, and plasma fibrinogen. Am J Epidemiol. 2000; 151(3): 273–282. [PubMed: 10670552]
10. Joshipura KJ, Wand HC, Merchant AT, Rimm EB. Periodontal disease and biomarkers related to cardiovascular disease. J Dent Res. 2004; 83(2):151–155. [PubMed: 14742654]
11. Ebersole JL, Machen RL, Steffen MJ, Willmann DE. Systemic acute-phase reactants, C-reactive protein and haptoglobin, in adult periodontitis. Clin Exp Immunol. 1997; 107(2):347–352. [PubMed: 9030874]

12. Loos BG, Craandijk J, Hoek FJ, Wertheim-van Dillen PM, van der Velden U. Elevation of systemic markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. J Periodontol. 2000; 71(10):1528–1534. [PubMed: 11063384]
13. Mengel R, Bacher M, Flores-De-Jacoby L. Interactions between stress, interleukin-1beta, interleukin-6 and cortisol in periodontally diseased patients. J Clin Periodontol. 2002; 29(11): 1012–1022. [PubMed: 12472994]
14. Joshipura K, Zevallos JC, Ritchie CS. Strength of evidence relating periodontal disease and atherosclerotic disease. Compend Contin Educ Dent. 2009; 30(7):430–439. [PubMed: 19757736]
15. Morita T, Yamazaki Y, Mita A, Takada K, Seto M, Nishinoue N, Sasaki Y, Motohashi M, Maeno M. A cohort study on the association between periodontal disease and the development of metabolic syndrome. J Periodontol. 2010; 81(4):512–519. [PubMed: 20367094]
16. Holmlund A, Holm G, Lind L. Severity of periodontal disease and number of remaining teeth are related to the prevalence of myocardial infarction and hypertension in a study based on 4,254 subjects. J Periodontol. 2006; 77(7):1173–1178. [PubMed: 16805679]
17. D'Aiuto F, Sabbah W, Netuveli G, Donos N, Hingorani AD, Deanfield J, Tsakos G. Association of the metabolic syndrome with severe periodontitis in a large U.S. population-based survey. J Clin Endocrinol Metab. 2008; 93(10):3989–3994. [PubMed: 18682518]
18. Klag MJ, He J, Mead LA, Ford DE, Pearson TA, Levine DM. Validity of physicians' self-reports of cardiovascular disease risk factors. Ann Epidemiol. 1993; 3(4):442–447. [PubMed: 8275223]
19. Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willett WC, Sacks F, Stampfer MJ. A prospective study of nutritional factors and hypertension among US men. Circulation. 1992; 86(5):1475–1484. [PubMed: 1330360]
20. Colditz GA, Martin P, Stampfer MJ, Willett WC, Sampson L, Rosner B, Hennekens CH, Speizer FE. Validation of questionnaire information on risk factors and disease outcomes in a prospective cohort study of women. Am J Epidemiol. 1986; 123(5):894–900. [PubMed: 3962971]
21. Rimm EB, Stampfer MJ, Colditz GA, Giovannucci E, Willett WC. Effectiveness of various mailing strategies among nonrespondents in a prospective cohort study. Am J Epidemiol. 1990; 131(6):1068–1071. [PubMed: 2343859]
22. Joshipura KJ, Pitiphat W, Douglass CW. Validation of self-reported periodontal measures among health professionals. J Public Health Dent. 2002; 62(2):115–121. [PubMed: 11989206]
23. Joshipura KJ, Douglass CW, Garcia RI, Valachovic R, Willett WC. Validity of a self-reported periodontal disease measure. J Public Health Dent. 1996; 56(4):205–212. [PubMed: 8906704]
24. Douglass CW, Berlin J, Tennstedt S. The validity of self-reported oral health status in the elderly. J Public Health Dent. 1991; 51(4):220–222. [PubMed: 1941773]
25. Leffondre K, Abrahamowicz M, Xiao Y, Siemiatycki J. Modelling smoking history using a comprehensive smoking index: application to lung cancer. Stat Med. 2006; 25 (24):4132–4146. [PubMed: 16998807]
26. Dietrich T, Bernimoulin JP, Glynn RJ. The effect of cigarette smoking on gingival bleeding. J Periodontol. 2004; 75(1):16–22. [PubMed: 15025212]
27. Wolf AM, Hunter DJ, Colditz GA, Manson JE, Stampfer MJ, Corsano KA, Rosner B, Kriska A, Willett WC. Reproducibility and validity of a self-administered physical activity questionnaire. Int J Epidemiol. 1994; 23(5):991–999. [PubMed: 7860180]
28. Glovannucci E, Colditz G, Stampfer MJ, Rimm EB, Litin L, Sampson L, Willett WC. The Assessment of Alcohol Consumption by a Simple Self-administered Questionnaire. Am J Epidemiol. 1991; 133(8):810–817. [PubMed: 2021148]
29. Feskanich D, Rimm EB, Giovannucci EL, Colditz GA, Stampfer MJ, Litin LB, Willett WC. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. J Am Diet Assoc. 1993; 93(7):790–796. [PubMed: 8320406]
30. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. Am J Epidemiol. 1992; 135(10):1114–1126. discussion 1127–1136. [PubMed: 1632423]

31. Hu FB, Leitzmann MF, Stampfer MJ, Colditz GA, Willett WC, Rimm EB. Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men. Arch Intern Med. 2001; 161(12):1542–1548. [PubMed: 11427103]
32. Zucker DM, Spiegelman D. Inference for the proportional hazards model with misclassified discrete-valued covariates. Biometrics. 2004; 60(2):324–334. [PubMed: 15180657]
33. Savoia C, Schiffrin EL. Inflammation in hypertension. Curr Opin Nephrol Hypertens. 2006; 15(2): 152–158. [PubMed: 16481882]
34. Boos CJ, Lip GY. Is hypertension an inflammatory process? Curr Pharm Des. 2006; 12 (13):1623–1635. [PubMed: 16729874]
35. Li JJ, Fang CH, Hui RT. Is hypertension an inflammatory disease? Med Hypotheses. 2005; 64(2): 236–240. [PubMed: 15607546]
36. Li JJ. Inflammation in hypertension: primary evidence. Chin Med J (Engl). 2006; 119(14):1215–1221. [PubMed: 16863616]
37. Joshipura KJ, Hung HC, Rimm EB, Willett WC, Ascherio A. Periodontal disease, tooth loss, and incidence of ischemic stroke. Stroke. 2003; 34(1):47–52. [PubMed: 12511749]
38. Taylor GW, Borgnakke WS. Periodontal disease: associations with diabetes, glycemic control and complications. Oral Dis. 2008; 14(3):191–203. [PubMed: 18336370]
39. Amar S, Zhou Q, Shaik-Dasthagirisaheb Y, Leeman S. Diet-induced obesity in mice causes changes in immune responses and bone loss manifested by bacterial challenge. Proc Natl Acad Sci U S A. 2007; 104(51):20466–20471. [PubMed: 18077329]

Table 1

Selected age-standardized risk factors * for hypertension by periodontal diagnosis and number of teeth at baseline

	Periodontal disease at baseline (1986)		Number of teeth at baseline (1986)	
	Yes	**No**	**0–10**	**25–32**
Number of participants	4,641	26,902	732	27,112
Age in 1986 (years)	56	51	62	51
Dental profession (%)	67	57	34	61
Caucasian race (%)	89	91	90	91
BMI (kg/m^2)	25	25	25	25
Alcohol intake (g/d)	13	11	12	11
Physical activity (MET-hours/wk)	21	23	15	23
Current Smoker (%)	13	6	22	6
Family history of hypertension (%)	30	30	25	30
Multivitamin supplement use (%)	40	41	41	41
Periodontal disease (%)				
Baseline	-	-	35	12
Baseline/follow-up	-	-	47	32
Number of teeth (%)				
0–10	5.0	1.8	-	-
11–16	4.8	1.3	-	-
17–24	18	8.5	-	-
25–32	73	88	-	-
Tooth loss during follow-up (%)	39	21	21	22

* Risk factors are assessed at baseline unless otherwise indicated.

Table 2

Relative risks (95% CIs) for incident hypertension according to oral health at baseline and follow-up

	Number of Cases	Age-Adjusted* RR (95% CI)	p-value for test for trend	Age- and Smoking- Adjusted* RR (95% CI)	p-value for test for trend	Multivariate- Adjusted*, † RR (95% CI)	p-value for test for trend
Number of teeth at baseline	10,828						
0–10		1.11 (0.97, 1.28)	0.02	1.06 (0.92, 1.22)	0.15	1.05 (0.91, 1.21)	0.63
11–16		1.11 (0.96, 1.29)		1.08 (0.93, 1.25)		1.02 (0.88, 1.18)	
17–24		1.05 (0.99, 1.13)		1.03 (0.96, 1.10)		0.99 (0.93, 1.06)	
25–32		1.0		1.0		1.0	
Tooth loss during the follow-up‡	10,828	1.10 (1.05, 1.16)§		1.08 (1.03, 1.14)§		1.03 (0.98, 1.09)	
Periodontal disease at baseline	10,828	1.09 (1.04, 1.16)§		1.07 (1.01, 1.13)§		1.04 (0.98, 1.10)	
Severity of periodontal bone loss in 1996	3,912						
severe		1.13 (0.86, 1.49)	0.43	1.08 (0.82, 1.42)	0.79	1.02 (0.77, 1.35)	0.65
moderate		1.03 (0.91, 1.16)		1.01 (0.89, 1.14)		0.97 (0.86, 1.10)	
mild		1.01 (0.94, 1.08)		1.00 (0.93, 1.08)		0.98 (0.91, 1.06)	
no		1.0		1.0		1.0	

* Models are stratified by calendar time (2-year intervals).

† Multivariate model includes age (in months), comprehensive smoking index, family history of hypertension, race (Caucasian, Black, Asian, other), dental profession, diabetes diagnosis, alcohol consumption (6 categories), BMI (5 categories), physical activity (quintiles), fruit and vegetable intake (quintiles), vitamin E, vitamin D and calcium intake (quintiles), and multivitamin supplement use.

‡ Multivariate model additionally includes number of teeth at baseline (0–10, 11–16, 17–24, ≥25).

§ Results are significant at α=0.05 level.

Table 3

Stratified multivariate-adjusted* relative risks (95% CIs) of incident hypertension according to periodontal diagnosis and severity

	Periodontal disease diagnosis at baseline			Severity of periodontal bone loss in 1996		
	Number of cases	RR (95% CI)	p-value for interaction	Number of cases	Severe vs. no bone loss RR (95% CI)	p-value for interaction
Age, years						
Age >55	7,779	1.05 (0.98, 1.11)	0.44	3,227	0.94 (0.70, 1.26)	0.12
Age≤55	3,049	0.99 (0.87, 1.12)		685	1.91 (0.83, 4.44)	
Smoking history						
Never smokers	4,357	0.97 (0.87, 1.09)	0.37	1,690	0.96 (0.48, 1.93)	0.93
Ever smokers	5,597	1.03 (0.96, 1.11)		1,914	0.92 (0.65, 1.30)	
Dental profession						
Yes	6,339	1.04 (0.97, 1.12)	0.81	2,414	0.92 (0.60, 1.41)	0.53
No	4,489	1.03 (0.93, 1.13)		1,498	1.11 (0.74, 1.67)	
Baseline number of teeth						
0–24	1,502	1.11 (0.97, 1.27)	0.38	441	1.01 (0.60, 1.71)	0.94
25–32	9,326	1.04 (0.97, 1.10)		3,471	1.03 (0.71, 1.51)	
BMI at baseline, kg/m^2 †						
Obese (BMI ≥30)	752	1.04 (0.78, 1.37)		364	0.55 (0.15, 2.03)	
Overweight (BMI 25–29.9)	5,016	1.07 (0.98, 1.17)	<0.001	1,913	1.08 (0.70, 1.67)	0.01
Normal or underweight (BMI<25)	4,771	1.03 (0.94, 1.12)		1,635	1.15 (0.75, 1.76)	
Family history of hypertension						
Yes	4,268	1.05 (0.96, 1.16)	0.76	1,482	0.90 (0.50, 1.62)	0.48
No	6,560	1.03 (0.96, 1.11)		2,430	1.15 (0.83, 1.59)	
Diabetes						
Yes	1,561	1.05 (0.89, 1.24)	0.90	436	0.94 (0.35, 2.56)	0.86
No	9,267	1.04 (0.98, 1.10)		3,476	1.03 (0.76, 1.40)	
Screening by a physician within the last 2 years	7,769	1.04 (0.97, 1.11)		3,124	0.97 (0.70, 1.34)	

*Multivariate models are stratified by calendar time (2 year intervals) and include age (in months), comprehensive smoking index, family history of hypertension, race (Caucasian, Black, Asian, other), dental profession, diabetes diagnosis, alcohol consumption (6 categories), BMI (5 categories), physical activity (quintiles), fruit and vegetable intake (quintiles), vitamin E, vitamin D and calcium intake (quintiles), and multivitamin supplement use.

†P-value for effect modification is obtained from test for trend.