Periodontal Disease, Tooth Loss, and Incidence of Ischemic Stroke

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Background and Purpose—Periodontal and other infections have been suggested as potential risk factors for stroke. This study evaluates periodontal disease and tooth loss as risk factors for ischemic stroke.

Methods—The study population consisted of 41 380 men who were free of cardiovascular disease and diabetes at baseline. Periodontal disease history was assessed by mailed validated questionnaires. During 12 years of follow-up, stroke incidence was assessed and subclassified by use of medical history, medical records, and imaging reports. Hazard ratios (HRs) were adjusted for age, amount smoked, obesity, alcohol, exercise, family history of cardiovascular disease, multivitamin use, vitamin E use, profession, baseline reported hypertension, and hypercholesterolemia. Sex and socioeconomic status were inherently controlled for by restriction. Confounding variables were updated in the analyses for each 2-year follow-up interval.

Results—We documented 349 ischemic stroke cases during the follow-up period. Men who had ≤24 teeth at baseline were at a higher risk of stroke compared to men with ≥25 teeth (HR=1.57; 95% CI, 1.24 to 1.98). There was little evidence of an increased risk with recent tooth loss during follow-up. A modest association was seen between baseline periodontal disease history and ischemic stroke (HR=1.33; 95% CI, 1.03 to 1.70). Addition of dietary factors to the model changed the HR only slightly.

Conclusions—Our results suggest that periodontal disease and fewer teeth may be associated with increased risk of ischemic stroke. **(*Stroke*. 2003;34:47-52.)**

Key Words: cerebrovascular accident ■ infection ■ periodontal diseases ■ stroke ■ tooth loss

Recent reviews have suggested that infections, including respiratory and periodontal infection, may be risk factors for stroke.[1,2] Two case-control studies[3,4] and 4 longitudinal studies[5–8] have evaluated the association between oral conditions (periodontal disease and/or tooth loss) and stroke, and 4 of the 6 have significant positive associations. The definition of stroke varied across total, fatal, nonfatal, and ischemic stroke. Chronic infections have been reported as risk factors for coronary heart disease[9] and ischemic stroke.[3] Ischemic stroke should be evaluated separately because its etiology is more consistent with an infection hypothesis. Because several risk factors are common to oral conditions and stroke, residual confounding from factors related to healthy behavior may possibly explain the association. Hence, additional studies are needed. We therefore examined tooth loss and periodontal disease as risk factors for ischemic stroke in a large cohort of health professional men who are relatively homogenous with respect to socioeconomic status and health awareness, which reduces concern for confounding by factors that are otherwise difficult to control.

Materials and Methods

Study Populations

Data for this analysis were derived from the Health Professionals' Follow-Up Study (HPFS). The population is comprised of 51 529 male health professionals, including dentists, veterinarians, pharmacists, optometrists, osteopaths, and podiatrists, who were 40 to 75 years of age in 1986. Participants have completed mailed questionnaires every 2 years to provide information on medical history, health behaviors, and the occurrence of cardiovascular and other outcomes. This study was approved by the Institutional Review Board for Human Subjects; the response to the questionnaires constituted the participants' informed consent.

Population for Analysis

We excluded 1595 men who reported daily caloric intake outside the plausible range of 800 to 4200 calories or who left ≥70 of the 131 dietary questions blank. We further excluded 8554 participants who

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reported myocardial infarction, angina, stroke, coronary artery bypass grafting, angioplasty, atrial fibrillation, or other heart diseases or those with missing information on age or the exposure variable. We included 41 380 men in the analysis. On average, >90% of the baseline population responded to each follow-up questionnaire.

Assessment of Stroke End Points

Participants (or next of kin for the deceased) who reported an incident stroke on a follow-up questionnaire from 1988 to 1998 were asked for permission to have their medical records reviewed. Using these records, which included imaging results, we subclassified stroke into ischemic (embolic or thrombotic), hemorrhagic (subarachnoid or intracerebral), or unknown type as recommended by the National Survey of Stroke.[10] Cases attributed to infections or malignant processes were not included, nor were cases of indeterminate age discovered on CT or MRI scan without acute symptoms. Physicians reviewing the medical records were unaware of the participants' oral health status. Only fatal and nonfatal strokes confirmed by medical records were included in this analysis. We documented 349 ischemic stroke cases during the follow-up period. Deaths were reported by next of kin or coworkers or were obtained from postal authorities or the National Death Index. We considered nonresponders who were not listed on the National Death Index as noncases.

Assessment of Dental Measures

Tooth Loss

Participants reported baseline number of teeth in 1986 and teeth lost in the past 2 years on biennial questionnaires. We assumed that a missing value on incident tooth loss indicated no tooth loss during follow-up because only ≈10% of participants experienced tooth loss biennially. Self-reported number of teeth has been highly correlated with the actual number of teeth on clinical examination in a general population (correlation coefficient=0.97).[11] We expected self-reported number of teeth and tooth loss during follow-up to be well reported, especially in this population of health professionals.

Periodontal Disease

Self-reported periodontal disease was assessed by validated questions. At baseline, participants responded to the question, "Have you had periodontal disease with bone loss?" The questionnaire measure compared well with radiographs (predictive values, ≈0.75) among both dentists and nondentist health professionals.[12,13]

Dietary Assessment

Diet was assessed in 1986 with an expanded semiquantitative food frequency questionnaire. Participants reported their average intake of a specified portion size for each food item over the past year; 9 responses were possible for each food item, ranging from never or less than once per month to ≥6 times per day. Validity of the dietary data has been documented by comparisons with multiple weighed dietary records.[14] The average daily intakes of individual food items were combined to compute total fruit and vegetable intake.[15] Nutrients were computed by multiplying the frequency of consumption of each food unit by the nutrient content of the specified portion. Dietary patterns were assessed with factor analysis,[16] which generated 2 major eating patterns. The prudent pattern was characterized by a high intake of vegetables, fruits, legumes, whole grains, fish, and poultry. The Western pattern was characterized by a high intake of processed meat, red meat, butter, high-fat dietary products, eggs, and refined grains.

Data Analysis

Person-time for each participant was calculated from the date of return of the 1986 questionnaire to the earlier of the date of first ischemic stroke event, death, or January 31, 1998. Men who reported ischemic stroke events or who were deceased were excluded from subsequent follow-up. Each participant thus contributed only 1 end point, and the cohort at risk for each follow-up period included only those who remained free from stroke at the beginning of each 2-year follow-up period.

We analyzed tooth loss in 3 ways. First, for baseline tooth loss, stroke incidence among men with 0 to 10, 11 to 16, and 17 to 24 teeth at baseline was compared with the incidence among men with 25 to 32 teeth; another analysis combined men with 0 to 24 teeth into 1 group for added power. Second, for incident tooth loss during follow-up, men reporting at least 1 tooth lost during follow-up were compared with all others. Third, for tooth loss during past 2 years, men with tooth loss in past 2 years were compared with those with no tooth loss in the past 2 years. For the analyses of incident tooth loss, we excluded edentulous participants in 1986 because they could not lose teeth. We had incident tooth loss data only from 1988 to 1998. In the multivariate model, we adjusted for major risk factors for cardiovascular disease. The potentially confounding variables were updated for each 2-year follow-up period (maximum of 6 updates) with the biennial questionnaires[15], and we used Cox proportional-hazards models with time-dependent variables in SAS.

Because periodontal disease could be the underlying reason for tooth loss and could affect the association between tooth loss and ischemic stroke, we conducted subgroup analyses for tooth loss among those with and without preexisting history of periodontal diseases. Similarly, we evaluated the association between periodontal disease and ischemic stroke by categories of baseline number of teeth. We additionally controlled for number of teeth in models evaluating periodontal disease and vice versa. Because the validity of reported tooth loss and periodontal disease or factors affecting extraction decisions might differ between dentists and nondentists, we conducted the analyses separately among dentists and nondentists. We performed additional analyses by subgroups to assess whether different factors could modify the association. We used hazard ratio (HR) as an estimate of relative risk. Finally, we evaluated whether dietary factors were mediators by adding dietary variables to the model evaluating the association between number of teeth and ischemic stroke. We assessed dietary factors that were shown to be associated with cardiovascular disease and the intake of which were likely to be affected by tooth loss—specifically fruits and vegetables, dietary fiber, carotene, folate, and potassium—and dietary patterns.

Results

Participants with fewer teeth generally were older, consumed more alcohol, were less physically active, and were more likely to smoke (Table 1). For example, 21% of men with 0 to 10 teeth were current smokers compared with 9% of men with ≥25 teeth. Men with fewer teeth were less likely to report taking vitamin E supplements but were more likely to have diabetes. No consistent trends were seen in history of hypertension, hypercholesterolemia, family history of coronary heart disease, and aspirin use across categories of number of teeth. Periodontal disease history and incident tooth loss were highest among those with 11 to 16 teeth (35% and 37%, respectively).

Table 2 shows the results of the multivariate analysis evaluating oral conditions as risk factors for ischemic stroke. Men with ≤24 teeth at baseline were at higher risk for stroke compared with those with ≥25 teeth (HR=1.57; 95% CI, 1.24 to 1.98), controlling for confounders updated for each 2-year period. When only baseline confounders were controlled for, the results were very similar (HR=1.55). No dose-response relationship was evident; all categories of tooth loss were at elevated risk. When baseline periodontal disease was added to the updated model, having ≤24 teeth was still significantly associated with increased risk of stroke (HR=1.50; 95% CI, 1.18 to 1.91). When we added dietary variables such as fruit and vegetables, carotene, fiber, folate,

TABLE 1. Age-standardized Cardiovascular Risk Factors, History of Periodontal Disease and Tooth Loss, and Standard Deviations, by Number of Teeth at Baseline

	Number of Teeth			
	25–32	17–24	11–16	0–10
Number of participants	34 767	4527	903	1183
No. of cases (ischemic stroke)	230	72	19	28
Age, y	52.5 (9.14)	58.1 (9.48)	61.3 (8.45)	63.5 (8.13)
Alcohol intake, g/d*	11.3 (15.48)	11.7 (15.58)	11.9 (15.50)	12.2 (15.63)
Physical activity (MET/wk)	21.8 (30.34)	19.5 (30.61)	17.9 (30.58)	17.0 (30.68)
BMI, kg/m^2	25.5 (3.41)	25.7 (3.44)	25.8 (3.43)	25.8 (3.45)
% current smokers	8.7 (0.30)	14.4 (0.30)	17.2 (0.30)	21.1 (0.30)
History at baseline, %				
Hypertension	19.3 (0.39)	21.0 (0.40)	20.6 (0.39)	22.1 (0.40)
High cholesterol	10.2 (0.30)	10.0 (0.30)	7.2 (0.30)	8.6 (0.31)
Diabetes	2.3 (0.15)	3.5 (0.15)	3.9 (0.16)	3.7 (0.16)
Family history of CHD, %	11.7 (0.32)	12.0 (0.32)	11.7 (0.32)	11.1 (0.33)
Supplement use, %				
Multivitamin	41.8 (0.50)	41.5 (0.50)	39.9 (0.50)	39.2 (0.50)
Vitamin E	19.0 (0.39)	17.7 (0.39)	17.7 (0.39)	14.6 (0.40)
Regular aspirin (2+ per week)	25.8 (0.45)	28.6 (0.44)	25.6 (0.44)	25.3 (0.44)
Periodontal disease history, %	12.7 (0.35)	25.1 (0.35)	34.6 (0.35)	32.6 (0.35)
Cumulative incident tooth loss, %	17.9 (0.39)	31.4 (0.39)	36.8 (0.39)	17.1 (0.40)

*Means and percentage for all variables (except age) are standardized for age. MET indicates metabolic equivalent hours=sum of the average time per week spent in each activity×MET value of each activity. MET value=(caloric need/kg body weight/hour activity)÷(caloric need/kg body weight/hour at rest). BMI indicates body mass index; CHD, coronary heart disease.

and potassium either singly or together, the HR changed very slightly. The greatest attenuation was seen when folate or potassium was added; the HR changed from 1.57 to 1.55 in the multivariate model comparing ≤24 teeth to ≥25 teeth. We also added the prudent and Western dietary patterns[16], but this did not change the HR appreciably. Additional subanalyses controlling for multiple levels of systolic and diastolic blood pressures did not alter the results appreciably (HR for 0 to 24 teeth remains at 1.57; the HR for periodontal disease changes only slightly from 1.33 to 1.31).

Men with periodontal disease at baseline had a moderately increased risk of ischemic stroke (HR=1.33; 95% CI, 1.03 to 1.70). When baseline number of teeth was added to the model, periodontal disease was no longer significant (HR=1.21; 95% CI, 0.94 to 1.56). The HR for baseline periodontal disease remained essentially unchanged when dietary variables were added to the model. Incident tooth loss during the follow-up over the past 2 years (HR=1.17; 95% CI, 0.84 to 1.62) or any time during the follow-up (HR=1.20; 95% CI, 0.91 to 1.57) showed only a small elevation in risk that was not significant, and the HR was close to null when baseline number of teeth was added to the model.

Table 3 shows the association among different subgroups of the population. The association between baseline periodontal disease and ischemic stroke was higher among ever smokers (1.67 versus 0.61), younger individuals, dentists, diabetics, and men who did not use aspirin regularly. The association between baseline number of teeth and ischemic stroke was higher among diabetics (2.35 versus 1.52), normotensives, never smokers, multivitamin users, and men of normal weight compared with obese men. Small or no differences were seen across other subgroups. The conclusions were similar when we adjusted only for the baseline covariates. The association between baseline number of teeth and ischemic stroke was only slightly higher among people with periodontal disease compared with those without periodontal disease, and the association between periodontal disease was higher among those with 25 to 32 teeth compared with those with ≤24 teeth. When we compared men with 0 to 10 teeth and periodontal disease at baseline with men with ≥25 teeth and no periodontal disease at baseline, the HR was 1.43 (95% CI, 0.74 to 2.73).

Discussion

Our results suggest that baseline periodontal disease and tooth loss may be associated with an increased risk of ischemic stroke. When we assessed periodontal disease as a cumulative history throughout the follow-up period, the risk was similar (HR=1.35 versus 1.33). Because stroke shares several etiologic factors with periodontal disease and tooth loss, it is important to rule out common risk factors as an explanation for the associations. As summarized in 2 review articles,[17,18] major known risk factors for ischemic stroke include older age, smoking, ethnicity, high blood pressure, diabetes, prior cardiovascular disease, heavy alcohol intake, and obesity. Protective factors include exercise, postmenopausal estrogen replacement therapy (among women), moderate alcohol intake, and high intake of fruits and vegetables.[17,18] Our population inherently controls for sex, education, race, and economic status by restriction because the population

TABLE 2. Multivariate Hazard Ratios (HR) and 95% CIs for Ischemic Stroke According to Number of Teeth and Periodontal Disease

	No. of Cases	Age- and Smoking-adjusted HR (95% CI)	HR† (95% CI) Updated Confounders	HR‡ (95% CI) Baseline Confounders
Baseline teeth number*				
25–32	230	1.00	1.00	1.00
17–24	72	1.58 (1.20–2.07)	1.50 (1.14–1.97)	1.49 (1.14–1.96)
11–16	19	1.78 (1.11–2.87)	1.74 (1.08–2.81)	1.68 (1.04–2.70)
0–10	28	1.80 (1.20–2.70)	1.66 (1.10–2.51)	1.62 (1.08–2.45)
25–32	230	1.00	1.00	1.00
0–24	119	1.65 (1.31–2.08)	1.57 (1.24–1.98)	1.55 (1.22–1.96)
Incident tooth loss§				
Incidence in past 2 years		1.26 (0.91–1.75)	1.17 (0.84–1.62)	1.22 (0.88–1.69)
Incidence during follow-up		1.33 (1.02–1.74)	1.20 (0.91–1.57)	1.27 (0.97–1.67)
Periodontal disease history		1.33 (1.04–1.70)	1.33 (1.03–1.70)	1.33 (1.03–1.70)

*41 380 eligible participants and 349 cases in 1986–1998.

†The multivariate model includes: age (5-year categories), smoking (never, former, current, 1–14, 15–24, and ≥25 cigarettes per day), alcohol consumptions (5 categories), body mass index (5 categories), physical activity (quintiles), family history of myocardial infarction, multivitamin supplement use, vitamin E use, history of hypertension, diabetes, hypercholesterolemia, and professions (dentists or nondentists) updated for each 2-year time period.

‡The multivariate model includes baseline covariates only (same covariates as above).

§40 679 eligible participants and 302 cases in 1988–1998; additionally adjusting for baseline teeth number in the model.

consists predominantly of white male health professionals, and we have controlled for the other major potential nondietary confounders in the analyses. The results were essentially similar when we used updated confounders or only baseline confounders; the largest difference between the 2 models was in the subgroup of diabetics—15% higher when only baseline covariates were adjusted—suggesting that updating adjusted for some residual confounding. Because dietary factors, and particularly consumption of fruits and vegetables, are more likely to be mediators rather than confounders of the association between tooth loss and stroke,[19] we have conducted analyses with and without adjusting for these factors. The associations we observed were modest, and residual confounding cannot be excluded as an explanation. Overall, our results support an association between tooth loss and risk of stroke that is mediated only in part by changes in diet.

In a recent report from the National Health and Nutrition Examination Survey, Wu et al[7] found an association between periodontal disease and increased risk of ischemic stroke compared with persons with no periodontitis, gingivitis, or tooth loss (HR=2.11; 95% CI, 1.30 to 3.42); the risk was even higher when limited to fatal stroke (HR=2.90; 95% CI, 1.49 to 5.62). Compared with a reference group without reported periodontitis and ≥11 teeth, we found a smaller association between baseline periodontal disease and ischemic stroke (HR=1.37; 95% CI, 1.06 to 1.78). Only ≈10% of our cases were fatal; hence, we did not have enough fatal cases to evaluate them separately. There is no standard way to assess periodontal disease, and different definitions have been used in the literature. Misclassification in the assessment of periodontal disease is inevitable regardless of measures used but is likely to be greater in our self-reported measures. Our validation studies suggest that health professionals are able to validly report their baseline periodontal status. From our predictive values, we expect a misclassification of 30% compared with a hypothetical perfect measure; a true HR of 2 would translate approximately to an HR of 1.4 with our self-reported measure.[12,20] A study from the Veterans Administration by Beck et al[5] reported that men with periodontal disease were ≈3 times as likely to develop total stroke as men without periodontal disease (HR=2.80; 95% CI, 1.45 to 5.48). Ischemic stroke was not evaluated separately. The analysis controlled only for age, 3 categories of smoking, non–insulin-dependent diabetes mellitus, blood pressure, family history, education, and sex; hence, residual confounding by factors such as amount smoked, exercise, and obesity is likely to explain the higher association. Another prospective study by Morrison et al[6] found a nonsignificant association between periodontal disease and total fatal stroke (HR=1.63; 95% CI, 0.72 to 3.67). The report by Howell et al[8] from the Physicians' Health Study (PHS), on the other hand, showed no associations with history of periodontal disease or tooth loss within the past year assessed at each annual follow-up questionnaire. The PHS and HPFS are similar in design and in restriction to a homogeneous socioeconomic population, but the 2 studies show contradictory results. The HPFS found associations between baseline and recent periodontal disease and baseline number of teeth and the incidence of ischemic stroke, whereas the PHS found no associations. Several explanations are possible. First, the HPFS evaluated baseline and recent tooth loss. The PHS evaluated only recent tooth loss, which may be a marker of good systemic health; people with poor systemic health may be deterred from extracting their teeth because extraction is an elective procedure. Second, the PHS evaluated total nonfatal stroke, whereas HPFS evaluated fatal and nonfatal ischemic stroke. Third, the variation in recent tooth

TABLE 3. Multivariate Hazard Ratios (HR) and 95% CIs for Ischemic Stroke According to Baseline History of Periodontal Disease and Baseline Number of Teeth by Levels of Different Factors

	Baseline History of Periodontal Disease			Baseline Teeth Number 0–24 vs. 25–32		
Stratified Variables	No. of Cases	HR (95% CI) Updated Confounders*	HR (95% CI) Baseline Confounders†	No. of Cases	HR (95% CI)* Updated Confounders	HR (95% CI) Baseline Confounders†
Periodontal diseases						
Yes				89	1.58 (1.01–2.46)	1.53 (0.98–2.39)
No				261	1.48 (1.10–1.98)	1.47 (1.10–1.97)
Multivitamin use						
Yes	148	1.44 (0.99–2.08)	1.41 (0.97–2.05)	148	1.75 (1.23–2.49)	1.67 (1.17–2.23)
No‡	140	1.29 (0.87–1.92)	1.28 (0.86–1.91)	140	1.31 (0.89–1.94)	1.35 (0.91–1.99)
Aspirin use						
Yes	106	1.01 (0.62–1.64)	0.97 (0.60–1.58)	106	1.64 (1.08–2.50)	1.55 (1.01–2.36)
No	243	1.46 (1.09–1.95)	1.47 (1.10–1.96)	243	1.55 (1.17–2.06)	1.56 (1.18–2.08)
Diabetes						
Yes	49	1.68 (0.75–3.74)	1.67 (0.73–3.80)	29	2.35 (1.04–5.31)	2.70 (1.16–6.25)
No	300	1.28 (0.99–1.67)	1.28 (0.98–1.67)	320	1.52 (1.19–1.95)	1.48 (1.15–1.89)
Hypertension						
Yes	194	1.21 (0.83–1.78)	1.19 (0.81–1.74)	156	1.27 (0.89–1.82)	1.27 (0.88–1.81)
No	155	1.39 (1.00–1.94)	1.45 (1.05–2.02)	193	1.83 (1.34–2.51)	1.85 (1.35–2.54)
Dentist						
Yes	190	1.46 (1.07–2.00)	1.49 (1.09–2.04)	190	1.72 (1.24–2.39)	1.68 (1.21–2.34)
No	159	1.13 (0.73–1.72)	1.13 (0.74–1.73)	159	1.45 (1.04–2.03)	1.44 (1.03–2.02)
Age						
≤55	37	2.17 (1.22–3.84)	2.15 (1.21–3.80)	70	1.73 (0.91–3.30)	1.73 (0.91–3.29)
>55	312	1.21 (0.92–1.59)	1.21 (0.92–1.60)	279	1.53 (1.19–1.97)	1.51 (1.17–1.95)
Smoking						
Ever	224	1.67 (1.26–2.23)	1.71 (1.28–2.27)	213	1.45 (1.08–1.94)	1.41 (1.05–1.89)
Never	126	0.61 (0.34–1.12)	0.60 (0.33–1.09)	136	1.78 (1.20–2.64)	1.83 (1.23–2.72)
BMI						
≤25	152	1.55 (1.04–2.30)	1.56 (1.05–2.31)	152	1.87 (1.31–2.65)	1.88 (1.27–2.77)
>25	197	1.20 (0.87–1.66)	1.19 (0.86–1.65)	197	1.36 (0.98–1.87)	1.38 (1.02–1.86)

*The multivariate model includes: age (5-year categories), smoking (never, former, current, 1–14, 15–24, and ≥25 cigarettes per day), alcohol consumptions (5 categories), body mass index (5 categories), physical activity (quintiles), family history of myocardial infarction, multivitamin supplement use, vitamin E use, history of hypertension, diabetes, hypercholesterolemia, and professions (dentists or nondentists) except the stratified variables updated for each 2-year time period.

†The model includes baseline covariates only (same covariates as above).

‡Men who did not consume multivitamins or any other vitamin or mineral supplement.

loss in the PHS is small compared with baseline number of teeth in the HPFS.

Two studies showed significant associations between a composite dental index and nonfatal ischemic stroke[3,4]; however, these studies were not prospective and did not control adequately for confounders. Morrison et al[6] found a nonsignificant association between edentulousness and total fatal stroke (HR=1.63; 95% CI, 0.77 to 3.42), but they did not evaluate ischemic stroke separately. Only 1 other study[7] has evaluated and found an association between edentulousness (compared with no gingivitis or periodontitis) and ischemic stroke (HR=1.41; 95% CI, 0.96 to 2.06), which increased to 2.12 (95% CI, 1.14 to 3.95) for fatal ischemic stroke. Our study found a significant association for edentulousness (HR=1.72; 95% CI, 1.13 to 2.61) comparing men with 0 to 10 teeth with men with ≥25 teeth and no reported periodontal disease. We did not have information on prosthetic replacement of missing teeth. However, questionnaires on a subpopulation from our cohort suggested that this was not an important limitation because all participants with 0 to 10 teeth had prosthetic replacements.

To the best of our knowledge, this is the first study to explore the impact of different timings of tooth loss and periodontal disease on risk of ischemic stroke. Baseline tooth loss was a significant risk factor, whereas recent tooth loss showed little association. A lower consumption of fruits and vegetables is a likely contributor to the increased risk of stroke among men with a small number of teeth at baseline, but only very small changes toward the null were seen between models with and without potential dietary mediators, suggesting that other factors may be important. Baseline tooth loss was significantly associated with ischemic stroke even

among people without periodontal disease (the association was only slightly higher among people with periodontal disease) and was a stronger risk factor than periodontal disease itself, suggesting that factors other than periodontal disease may also play a role. Only 1 small case-control study evaluated dental caries and periapical lesions; periapical lesions were associated with an increased risk of ischemic stroke, whereas no association was found with caries, nonvital teeth, or pericoronitis in 1 small case-control study.

In our study, periodontal disease showed a modest association with increased risk of ischemic stroke; this association was higher among normotensives (1.70 versus 1.12), younger individuals (2.4 versus 1.29), smokers (1.57 versus 0.88), and those who did not use aspirin (1.45 versus 1.11). No association was seen among never smokers. Some residual confounding by smoking could exist in studies on oral health and cardiovascular disease even after controlling for amount smoked. However, our associations are unlikely to be explained by smoking because we found no association between periodontal disease and coronary heart disease,[20] which shows a stronger relation with smoking than ischemic stroke. Additionally, in this study, the association between baseline number of teeth and ischemic stroke was higher among never smokers. The association between baseline number of teeth and ischemic stroke was also higher among normotensives (1.83 versus 1.27) and among diabetics (2.35 versus 1.52). The differences between the subgroups are not consistent across the different studies and need to be corroborated by other studies.

Several potential mechanisms have been proposed for the association between periodontal disease and ischemic stroke. Periodontal microorganisms have been found in atheromas.[22,23] The endotoxin in the microorganisms could damage endothelial cells and induce smooth muscle proliferation.[24] Periodontal disease could increase the production of inflammatory markers and clotting factors such as C-reactive protein[25] and fibrinogen and increase platelet aggregation,[26] thus contributing to atherosclerosis and thrombosis. In addition, infection can reduce glucose tolerance[27] and lead to an atherogenic serum lipid profile.[28] There could also be common genetic factors associated with both periodontal disease and cardiovascular disease.

Further studies are needed to corroborate whether periodontal disease and/or tooth loss is an independent risk factor for ischemic stroke and to elucidate potential mediators. If these associations are confirmed by further studies and shown to be independent of other risk factors including common genetic factors, these findings would have important implications for the prevention of stroke.

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