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Association of Clinical Measures of Periodontal Disease with Blood Pressure and Hypertension among Postmenopausal Women

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Abstract

Background—Hypertension and periodontal disease are common conditions among postmenopausal women. Periodontal disease has been found associated with hypertension in previous studies, but data in postmenopausal women is limited.

Methods—We assessed the cross-sectional associations of clinically measured periodontal disease with prevalent hypertension and measured systolic blood pressure (SBP) among 1,341 postmenopausal women enrolled in the Buffalo Osteoporosis and Periodontal Disease (OsteoPerio) study, an ancillary study of the Women's Health Initiative-Observational Study.

Results—Clinical attachment level (CAL) and number of teeth missing were positively associated with SBP among those not taking antihypertensive medication in crude and multivariable adjusted linear regression models (both $P < 0.05$). Alveolar crestal height (ACH) and gingival bleeding on probing were associated with higher SBP in crude but not multivariable adjusted models. Neither probing pocket depth (PPD) nor severity categories of periodontitis were associated with SBP. Number of teeth missing was significantly associated with prevalent hypertension in crude and multivariable adjusted models (OR=1.14, per 5 teeth; $P=0.04$). ACH was associated with prevalent hypertension in crude but not adjusted models. CAL, PPD, gingival

bleeding, and severity of periodontitis were not significantly associated with prevalent hypertension.

Conclusion—These results suggest that measures of oral health including CAL and number of teeth missing are associated with blood pressure in postmenopausal women. Prospective studies are needed to further investigate these associations and the potential underlying mechanisms for these relationships.

Keywords

Hypertension; Blood Pressure; Periodontitis; Tooth Loss; Cross-Sectional Studies; Postmenopause

INTRODUCTION

There is a growing body of evidence that supports a role of inflammation and the immune system in the dysregulation of blood pressure control and in developing hypertension^{1–6}. Periodontal disease is a common disease associated with chronic low-grade inflammation and an altered host immune response, as represented by elevated levels of inflammatory cytokines among individuals with clinically measured periodontitis.^{7,8} Periodontal disease commonly leads to tooth loss⁹ and has been associated with systemic inflammatory diseases, including type 2 diabetes¹⁰ and atherosclerotic vascular disease¹¹. Prevention of periodontal disease and its progression is possible and treatment of periodontal disease is associated with improvement in inflammatory cytokine profile¹².

Impaired arterial blood pressure regulation and clinical hypertension are systemic conditions that also are associated with inflammation and immune function¹³. Epidemiologic studies examining the relationship between periodontal disease and hypertension have ranged in sample size and quality of data collection¹⁴; some studies utilize clinical measures of periodontal disease and blood pressure¹⁵ while others rely on self-reported periodontal disease and hypertension¹⁶. The majority of studies support a positive association^{15,17–20} between these conditions, while others did not observe this association^{16,21}. There are limited data on the associations between hypertension and clinical measures of periodontal disease specifically in postmenopausal women¹⁴. This association is particularly important to study because periodontal disease²² and hypertension²³ each have high prevalence among postmenopausal women. The prevalence of hypertension in the United States is 55.5% among women aged 55–64, 65.8% among women 65–74 and 81.2% among women 75 years of age²³. According to NHANES 2009–2010 and 2011–2012 prevalence of periodontal disease was 68% among US adults age 65 years²². Furthermore, hypertension is a major modifiable risk factor for cardiovascular disease and stroke, which are leading causes of death in postmenopausal women²³. Hypertension is associated with cardiovascular disease and mortality in a log-linear relationship such that starting at 115 mmHg systolic blood pressure until 180 mmHg, each 20 mmHg of blood pressure is associated with approximately 2 fold increase in risk of mortality from stroke, heart disease, or other vascular disease. A small cross-sectional study evaluated the association between oral health and hypertension specifically in postmenopausal women and found a significant positive association between prevalent hypertension and having missing teeth²⁴; however, this study did not assess clinical measures of periodontal disease. As such, the present study provides

further assessment of a potential association for blood pressure and hypertension prevalence with clinical measures of periodontal disease in a sample of postmenopausal women where clinical periodontal measures and hypertension status are well-characterized.

METHODS

Study Design and Study Population

Our study consists of postmenopausal women who were enrolled in the Buffalo Osteoporosis and Periodontal Disease (OsteoPerio) Study, which is ancillary to the Women's Health Initiative Observational Study (WHI-OS). OsteoPerio consists of 1,341 women who completed clinical periodontal disease examinations at a baseline visit between 1997–2001. OsteoPerio was designed to assess the association between systemic bone density and oral health, including oral bone loss, in postmenopausal women. Women were excluded from the OsteoPerio study if they had < 6 teeth remaining in their mouths, history of bone disease other than osteoporosis, had bilateral hip replacement, had cancer diagnosed in the past 10 years, or reported other serious illness²⁵.

Measurement of Study Variables

Participants completed questionnaires, medication inventory, physical examination, and oral examination at an in-clinic study visit. Systolic and diastolic blood pressure was measured via auscultation using a conventional sphygmomanometer after participants rested quietly for 5 minutes in a clinic room without excessive noise. The first and fifth Korotkoff sounds were used to define systolic and diastolic blood pressures, respectively. The average of two measures taken at least 30 seconds apart was recorded. Previous diagnosis and/or treatment of hypertension or high blood pressure by a physician was assessed via questionnaire as follows: "Have you been diagnosed and/or treated by a physician for any of the following (*check all that apply*) and also fill in the age when you were first diagnosed and/or treated. Hypertension/High blood pressure" Current anti-hypertension medication use was assessed via medication inventory. We created a composite definition of hypertension (yes/no) based on questionnaire-reported hypertension, presence of anti-hypertension medication in their current medication inventory, systolic blood pressure ≥ 140 , and/or diastolic blood pressure ≥ 90 . As a clinical diagnosis typically requires ≥ 2 office visits with measured blood pressure $\geq 140/90$, a sensitivity analysis was conducted assessing the impact of using a more stringent cutoff of systolic blood pressure ≥ 160 and/or diastolic blood pressure ≥ 100 .

Standardized whole-mouth examinations were conducted by nine trained calibrated dental hygienists and dentists. Gingival bleeding on probing was assessed by manual periodontal probe, with bleeding presence or absence recorded at three sites per tooth and expressed as whole-mouth percentage of sites bleeding. Probing Pocket depth (PPD; millimeters) was measured using a constant force (20 g) electronic probe[¶] on six surfaces per tooth in all teeth present with the mean value of all teeth measures used here. Clinical Attachment Level (CAL; millimeters) was measured using a manual periodontal probe[#] probe on 6 surfaces

[¶]The Florida Probe System, Florida Probe, Gainesville, FL.

[#]Michigan O periodontal probe, Hu-Friedy, Chicago, IL.

per tooth, with whole mouth mean used in the analysis. Number of teeth missing was assessed by dental examination and recorded for all teeth except third molars. A total of 11 standardized intra-oral radiographs were taken to determine alveolar crestal height (ACH) of oral bone surrounding the teeth, a measure of longer-term cumulative exposure to periodontal disease and breakdown of the periodontium and surrounding bone. These assessments have been shown to be reliable and with acceptable measurement error²⁶. Quality and projection geometry of the radiographs was assisted by use of extra-oral fixation with ear rods, a medical x-ray unit **, laser positioning and a lateral cephalostat head holder and set exposure times with ACH heights determined using the Hausmann method²⁷. Mean coefficient of variation and intraclass correlation for within-examiner reliability of PPD were 6% and 0.91 across duplicate measures performed in random quadrants of 724 of the study participants; for ACH, mean coefficient of variation and intraclass correlation were 5.1% and 0.98 across duplicate random quadrants of 885 participants²⁸. Reproducibility of PPD, CAL, and ACH also has been demonstrated by intra- and inter-examiner mean differences <0.75 mm (<0.45 mm SD) in a randomly selected set of postmenopausal women assessed in duplicate by study examiners²⁹. Twenty postmenopausal women were randomly selected from a parallel study with the same examiners as the present study to assess inter-examiner reliability; intraclass correlations for examiners were 0.97 for ACH and 0.86 for CAL³⁰. We utilized a case definition of periodontitis based on CAL and PPD as proposed by the Centers for Disease Control (CDC) and the American Academy of Periodontology (AAP)³¹. This approach defines severe periodontitis as 2 interproximal sites with CAL ≥ 6 mm (not on the same tooth) and 1 interproximal site with PPD ≥ 5 mm and moderate periodontitis as interproximal sites with CAL ≥ 4 mm (not on the same tooth) or 2 interproximal sites with PD ≥ 5 mm (not on the same tooth); no or mild periodontitis constitutes those who do not fit into the moderate or severe categories³¹. We also utilized a categorization of ACH which defined severe as mean ACH ≥ 3 mm, 2 sites with ACH ≥ 5 mm, or any tooth loss due to periodontal disease based on self-report. Mild/moderate was defined as mean ACH ≥ 2 mm to <3 mm or at least 1 site with ACH ≥ 4 mm but no reported tooth loss due to periodontal disease; a value of none constitutes those who do not fit into the previous categories based on ACH or self-reported tooth loss due to periodontal disease²⁵.

Additional study covariates were collected via questionnaire including smoking history (current status: never, former current; total pack years), alcohol intake, physical activity (total energy expended from recreational physical activity including walking, mild, moderate, and strenuous physical activity), highest level of education, race/ethnicity, hormone therapy use, and prevalent comorbidities^{25,29,32-34}. Some of these were recorded as part of the parent WHI-OS, whereas others were collected as part of the OsteoPerio study. Healthy Eating Index-2005 (HEI), a composite dietary score based on 12 food categories, and sodium intake were calculated based on information obtained from a self-administered food frequency questionnaire developed for use in the WHI program³⁵. Neighborhood socioeconomic status (NSES) was determined at the level of census tract based on the following 6 variables collected in the 2000 census: percent of adults age > 25 years with less than high school education, percent of males unemployed, percent of households with

** Bennett HFQ 300, Bennett X-Ray, Copiague, NY.

income below the poverty line, percent of households receiving public assistance, percent of households receiving public assistance, percent of households with children headed by a woman, and median household income as described previously³⁶. Measurements of height and weight²⁵ were taken at the clinical exam, and body mass index (BMI) was calculated as kg/m². Medication for hypertension, diabetes mellitus, and high cholesterol were recorded via medication inventory³⁷. In our analyses, individuals were considered to have prevalent diabetes if they reported history of diabetes diagnosis or were currently taking medication for diabetes.

Statistical Analyses

Participant characteristics were assessed across categories of hypertension diagnosis as defined previously, as well as dichotomous categories of measured SBP (≥ 140 vs <140 mmHg). For all statistical tests, p values less than 0.05 were considered statistically significant. Differences in distribution across categories for categorical variables were assessed using χ^2 test and continuous variables were assessed using non-parametric Wilcoxon rank-sum test. Binary logistic regression was used to test crude, age-adjusted, and multivariable-adjusted associations between periodontal disease measures and prevalent hypertension. Linear regression was used to assess crude, age-adjusted, and multivariable-adjusted relationships between periodontal disease measures and measured systolic blood pressure, modeled as a continuous variable, in groups based on hypertension medication. Multivariable models were adjusted for age, smoking status (never, former, current), BMI (kg/m²), HEI, sodium intake, alcohol intake, neighborhood socioeconomic status, and total recreational physical activity (metabolic equivalent [MET] hours per week; MET-hr/wk). Sensitivity analyses were conducted using a more stringent blood pressure cutoff for hypertension ($\geq 160/100$ mmHg) in logistic models. Data analysis was conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Characteristics of study participants by hypertension and blood pressure categories are presented in Table 1. The mean (SD) age of our study sample was 66.7 (7.0) years. The majority were never-smokers (53%), with only 3% reported being current smokers. Participants were predominantly white (97%) and highly educated, with 78.8% having attended college or graduate school. Fifty-two women (4%) had diabetes mellitus, 137 (10%) had heart disease, and 218 (16%) took cholesterol-lowering medication. Four hundred and twenty-four (32%) women reported ever having hypertension diagnosis and/or treatment by a physician and 465 (35%) were currently taking antihypertensive medications on the date of the study visit. Overall the mean (SD) systolic and diastolic measured blood pressures were 122.0 (18.4) and 70.6 (9.1) mmHg, respectively.

The number of missing teeth was significantly greater in both those with hypertension ($P<0.0001$) and those with elevated blood pressure ($P=0.0002$). Categories of none, mild/moderate, and severe periodontal disease, defined by ACH measures, were significantly different according to blood pressure categories, with those having SBP ≥ 140 demonstrating presence of more severe disease ($P=0.04$). Other periodontal measures were not significantly

different in those with hypertension or elevated blood pressure compared with women who did not have hypertension or elevated blood pressure (Table 2).

Periodontal Measures and Prevalent Hypertension

In logistic regression analyses, number of teeth missing was significantly associated with prevalent hypertension in crude, age-adjusted, and multivariable-adjusted models (Table 3). After multivariable adjustment, a 1.0 standard deviation higher number of teeth missing, equivalent to 5.3 teeth, was associated with a 15% higher odds of prevalent hypertension (OR, 95% CI: 1.15, 1.01 to 1.30). ACH was significantly associated with hypertension in crude models (OR, 95% CI: 1.16, 1.01 to 1.33); this association was attenuated towards the null after age adjustment (OR, 95% CI: 1.02, 0.88 to 1.18). No other associations between measures of periodontal disease and prevalent hypertension were statistically significant. Gingival bleeding showed a non-significant positive association with hypertension in crude and age-adjusted models that was attenuated with multivariable adjustment. CAL, PPD, and categorical severity of periodontitis (CDC/AAP definition) trended toward positive associations with hypertension prevalence in crude and adjusted models but were not statistically significant. The category of severe periodontal disease based on ACH compared to the 'none' category trended toward a positive association with hypertension in crude models; however, in age- and multivariable-adjusted models the mild/moderate and severe categories of ACH were associated with lower odds of hypertension compared to the 'none' category, however this was not significant.

Periodontal Measures and Continuous Blood Pressure Measurement

Among those not taking antihypertensive medication, CAL and number of teeth missing were significantly positively associated with SBP in crude, age adjusted, and multivariable adjusted linear regression models (Table 4a). Based on regression models after multivariable adjustment, 5.3 higher teeth missing or 0.4 mm higher mean CAL were each associated with a 1 mmHg higher systolic blood pressure (CAL $\beta = 2.39$ mmHg/mean mm, $P=0.01$; Number of Teeth Missing $\beta = 1.55$ mmHg/5 teeth missing, $P = 0.01$). ACH was positively associated with SBP in crude models both when assessed continuously and categorically (Severe vs. None). However, this association was greatly attenuated and lost statistical significance with age- and multivariable-adjustments. No other measures had significant associations with systolic blood pressure among those not taking antihypertensive medication.

Among those taking antihypertensive medication, severity of periodontitis based on CDC/AAP definition and categorization of alveolar crestal height were significantly associated with systolic blood pressure in crude models, but were attenuated and no longer significant in age and multivariable adjusted models, although there remained a trend toward an association between CDC/AAP definition of periodontitis and systolic blood pressure after adjustment. Percentage of sites with gingival bleeding trended towards an association with hypertension in crude and adjusted models.

Sensitivity Analysis

Overall, results were similar when considering more stringent criteria for hypertension (systolic blood pressure ≥ 160 and diastolic blood pressure ≥ 100), however with this criteria, the multivariable adjusted association between number of teeth missing and prevalent hypertension was attenuated and no longer significant (OR 95%CI per 5 teeth missing = 1.07, 0.94 to 1.21; $P=0.30$), suggesting that individuals deemed hypertensive based on blood pressures between 140–159 and 90–99 make a notable contribution to the observed significant association between teeth missing and hypertension using the lower cutoff.

DISCUSSION

This study is the one of the first to assess the association between a series of clinical measures of periodontal disease and both prevalent hypertension and measured blood pressure in a large sample of postmenopausal women. The OsteoPerio study represents a well-characterized cohort, which allows for the consideration of numerous potential confounders of this association. Clinical measures of periodontal disease in our study are among the most comprehensive in studies of this type, which allows for the comparison of measures representing various aspects of periodontal disease in relation to hypertension and blood pressure status. Several variables show expected association with self-reported hypertension (e.g., age, physical activity, BMI, history of diagnosed and treated diabetes and cardiovascular disease), providing some level of confidence the outcome variable reflects its underlying construct (Table 1).

The finding that number of teeth missing was associated with both prevalent hypertension and increased blood pressure among those not treated for hypertension is consistent with the finding of Taguchi and colleagues, who studied non-smoking postmenopausal women without diabetes not using medication for blood pressure²⁴. Comparing age-matched women missing any number of teeth to those missing no teeth, they found that the odds of having SBP ≥ 140 or DBP ≥ 90 were higher in those with missing teeth (OR, 95% CI; 3.59, 1.10 to 11.7), after adjustment for BMI, total cholesterol, HDL cholesterol, Triglycerides, and LDL cholesterol. The sparsity of other published studies of the kind in older women limits further comparison of results beyond the findings of Taguchi et al.

Relationships similar to those in the present study were assessed among 6617 men and 7377 women who received dental exams as part of NHANES III¹⁵. In this investigation, gingival bleeding was associated with measured systolic blood pressure and with increased odds of hypertension after multivariable adjustments, while severity of periodontitis (defined by CDC/AAP criteria) as well as measures of CAL and PPD were significantly positively associated with blood pressure in crude analyses but were attenuated and lost significance after adjustment. Of note, a partial mouth oral examination was used to characterize periodontal disease status in NHANES III, whereas the present study conducted full-mouth exams which has been shown to increase accuracy and precision of periodontal disease assessment. Furthermore, the NHANES III examination only included measures for CAL, PPD, and gingival bleeding, whereas the present analysis also includes radiographic assessment of ACH, a measure with greater inter-examiner reliability than CAL and PPD²⁹, as well as number of teeth missing.

We found consistent associations between number of teeth missing and both prevalent hypertension and systolic blood pressure among those not treated with antihypertensive medication. Number of missing teeth may serve as a proxy for poor oral health in the past, likely including caries and periodontal disease. Thus, those having higher number of missing teeth could have had more severe periodontal disease, caries, or other oral health problems in the past which contributed to increasing blood pressure. Although age is included as a covariate in multivariable models, it is possible that there is residual confounding by age that could partially explain the observed association.

We also saw significant positive associations between systolic blood pressure and CAL among those not treated for hypertension. This is a soft tissue measure that may capture accumulated periodontal disease³⁸. It is possible that this measure may best capture aspects of a cumulative history of periodontal disease associated with hypertension. We also a trend toward associations of systolic blood pressure with gingival bleeding on probing, which might capture the influence of ongoing disease and inflammatory processes. Positive associations of CAL with elevated blood pressure could be consistent with pathways linking the number of teeth missing and hypertension. CAL may represent severity of cumulative periodontal disease, which could increase the likelihood of both tooth loss and blood pressure dysregulation. Since calcium channel blockers used in treating hypertension are associated with gingival overgrowth and thus may influence measures of oral health³⁹, we assessed associations between periodontal measures and blood pressure based on categories of treatment with antihypertensive medication. The absence of an association between gingival bleeding and blood pressure in the non-treated group suggests that the trend towards an association in the treated group may be related to antihypertensive medication.

We did not see significant associations after adjustment with PPD, ACH, or categorical measures of periodontal disease presence and severity defined using two different case criteria (CDC/AAP, and ACH). PPD may capture conflicting information, as it may be influenced by both moderate periodontal disease as well as acute gingival inflammation. ACH may represent longer term periodontal disease, but a lack of association after adjustment may suggest that processes influencing this measure may be less associated with systolic blood pressure. The lack of associations with categorical measures (ACH and CDC/AAP) after adjustment may suggest that these measures do not adequately differentiate individuals based on likelihood of hypertension; however, alternatively it is possible that sample size and statistical power were insufficient for precise estimation of the true direction and magnitude of association, particularly with regard to these categorical analyses

Several potential mechanisms may be involved in the observed positive association of number of teeth missing with elevated blood pressure and prevalent hypertension. Higher numbers of teeth missing may be indicative of more severe periodontal disease or other oral disease in the past. Immune system activation associated with periodontal infection may lead to higher levels of oxidative stress, sympathetic nervous system activation, autoimmune reactivity, and elevated levels of inflammatory cytokines, which may all contribute to downstream elevation of blood pressure¹⁴. Possible pathways include stimulation of hormones in the renin-angiotensin-aldosterone system, modulation of kidney function, and endothelial dysfunction. Additionally, oral microbes fulfil a crucial role in the production of

vasodilator nitric oxide (NO). After absorption, dietary nitrates are concentrated in saliva, and subsequently reduced to nitrite by oral bacteria. Nitrite is reabsorbed in the gut and converted to NO peripherally. Thus changes to the oral microbiota associated with periodontal disease may impact the nitrate-nitrite-NO pathway, which could negatively impact vascular function⁴⁰.

An important limitation of the present study is the cross-sectional nature precludes our ability to assess temporality of the association between periodontal disease and hypertension. Prospective studies are indicated that may better evaluate this relationship. Another limitation is the possibility of residual confounding. Although we have controlled for multiple potential confounders, it is a possibility that these or other factors were not adequately controlled for. For example, our dietary data is based on a food frequency questionnaire, which may not necessarily represent participants' diets throughout the lifetime. We utilized blood pressure measured at a single time point, so we cannot exclude the possibility that certain individuals may have "white-coat" or masked hypertension, which could have yielded misclassification of our case definition of prevalent hypertension. Further research utilizing 24-hour ambulatory blood pressure monitoring would help resolve this issue. Also, our study consisted of predominantly healthy Caucasian women, thus it may be that adequate variability involved in some of these associations was not captured. Future studies should aim to expand our results to additional socioeconomic and racial/ethnic groups. The strengths of the present study include well-characterized oral health based on multiple clinical measures of periodontal disease. Hypertension was also well characterized, based on measured blood pressure and medication inventory as well as self-report of physician diagnosis of hypertension. Additionally, we have data on multiple covariates that has allowed us to control for numerous potentially confounding factors.

New research should focus efforts to further investigate mechanisms linking periodontal disease and hypertension. The oral microbiome and systemic inflammation are two such potential mechanisms. This association may have profound public health implications, as it would imply that preventing periodontal disease could in turn reduce hypertension risk. Further understanding of this potential relationship could eventually lead to public health interventions that could reduce the burden of morbidity and mortality attributed to hypertension.

CONCLUSIONS

In this cross-sectional study of postmenopausal women number of teeth missing were associated with prevalent hypertension. Additionally, CAL and number of teeth missing were associated with systolic blood pressure among women not taking antihypertension medication. Other measures of periodontal disease were not associated with number of teeth missing. These results suggest that measures representing cumulative burden of oral disease may be associated with blood pressure control. Although we controlled for multiple potential sources of confounding, possibility of residual confounding could persist due to several factors related to both periodontal disease and hypertension.

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Bibliography

1. Wang L, Manson JE, Gaziano JM, et al. Circulating inflammatory and endothelial markers and risk of hypertension in white and black postmenopausal women. *Clin Chem*. 2011; 57:729–36. [PubMed: 21398601]
2. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. *JAMA*. 2003; 290:2945–51. [PubMed: 14665655]
3. Wenzel P, Knorr M, Kossmann S, et al. Lysozyme M-positive monocytes mediate angiotensin II-induced arterial hypertension and vascular dysfunction. *Circulation*. 2011; 124:1370–81. [PubMed: 21875910]
4. Guzik TJ, Hoch NE, Brown KA, et al. Role of the T cell in the genesis of angiotensin II induced hypertension and vascular dysfunction. *J Exp Med*. 2007; 204:2449–60. [PubMed: 17875676]
5. Madhur MS, Lob HE, McCann LA, et al. Interleukin 17 promotes angiotensin II-induced hypertension and vascular dysfunction. *Hypertension*. 2010; 55:500–7. [PubMed: 20038749]
6. Barhoumi T, Kasal DA, Li MW, et al. T regulatory lymphocytes prevent angiotensin II-induced hypertension and vascular injury. *Hypertension*. 2011; 57:469–76. [PubMed: 21263125]
7. Noack B, Genco RJ, Trevisan M, Grossi S, Zambon JJ, De Nardin E. Periodontal infections contribute to elevated systemic C-reactive protein level. *J Periodontol*. 2001; 72:1221–7. [PubMed: 11577954]
8. Glurich I, Grossi S, Albin B, et al. Systemic inflammation in cardiovascular and periodontal disease: comparative study. *Clin Diagn Lab Immunol*. 2002; 9:425–32. [PubMed: 11874889]
9. Hull PS, Worthington HV, Clerehugh V, Tsirba R, Davies RM, Clarkson JE. The reasons for tooth extractions in adults and their validation. *J Dent*. 1997; 25:233–7. [PubMed: 9175351]
10. Taylor GW, Borgnakke WS. Periodontal disease: Associations with diabetes, glycemic control and complications. *Oral Dis*. 2008; 14:191–203. [PubMed: 18336370]
11. Lockhart PB, Bolger AF, Papapanou PN, et al. Periodontal disease and atherosclerotic vascular disease: Does the evidence support an independent association?: A scientific statement from the American heart association. *Circulation*. 2012; 125:2520–44. [PubMed: 22514251]
12. Teeuw WJ, Slot DE, Susanto H, et al. Treatment of periodontitis improves the atherosclerotic profile: a systemic review and meta-analysis. *J Clin Periodontol*. 2014; 41:70–9. [PubMed: 24111886]
13. Rodríguez-Iturbe B, Pons H, Quiroz Y, Johnson RJ. The Immunological Basis of Hypertension. *Am J Hypertens*. 2014; 27:1327–37. [PubMed: 25150828]

14. Tsioufis C, Kasiakogias A, Thomopoulos C, Stefanadis C. Periodontitis and blood pressure: the concept of dental hypertension. *Atherosclerosis*. 2011; 219:1–9. [PubMed: 21640351]
15. Tsakos G, Sabbah W, Hingorani AD, et al. Is periodontal inflammation associated with raised blood pressure? Evidence from a National US survey. *J Hypertens*. 2010; 28:2386–93. [PubMed: 20706132]
16. Rivas-Tumanyan S, Spiegelman D, Curhan GC, Forman JP, Joshipura KJ. Periodontal disease and incidence of hypertension in the health professionals follow-up study. *Am J Hypertens*. 2012; 25:770–6. [PubMed: 22476024]
17. Morita T, Yamazaki Y, Mita A, et al. A cohort study on the association between periodontal disease and the development of metabolic syndrome. *J Periodontol*. 2010; 81:512–9. [PubMed: 20367094]
18. 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; 77:1173–8. [PubMed: 16805679]
19. D’Aiuto F, Sabbah W, Netuveli G, et al. Association of the metabolic syndrome with severe periodontitis in a large U.S. population-based survey. *J Clin Endocrinol Metab*. 2008; 93:3989–94. [PubMed: 18682518]
20. Iwashima Y, Kokubo Y, Ono T, et al. Additive interaction of oral health disorders on risk of hypertension in a Japanese urban population: the Suita Study. *Am J Hypertens*. 2014; 27:710–9. [PubMed: 24343779]
21. Nesse W, Dijkstra PU, Abbas F, et al. Increased prevalence of cardiovascular and autoimmune diseases in periodontitis patients: a cross-sectional study. *J Periodontol*. 2010; 81:1622–8. [PubMed: 20583916]
22. Eke PI, Dye BA, Wei L, et al. Update on Prevalence of Periodontitis in Adults in the United States: NHANES 2009 – 2012. *J Periodontol*. 2015; 86:611–22. [PubMed: 25688694]
23. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics’2017 update: A report from the American Heart Association. *Circulation*. 2017; 135:146–603.
24. Taguchi A, Sanada M, Sueti Y, et al. Tooth loss is associated with an increased risk of hypertension in postmenopausal women. *Hypertension*. 2004; 43:1297–300. [PubMed: 15117916]
25. Wactawski-Wende J, Hausmann E, Hovey K, Trevisan M, Grossi S, Genco RJ. The association between osteoporosis and alveolar crestal height in postmenopausal women. *J Periodontol*. 2005; 76:2116–24.
26. Hausmann E, Allen K, Dunford R, Christersson L. A reliable computerized method to determine the level of the radiographic alveolar crest. *J Periodontal Res*. 1989; 24:368–9. [PubMed: 2531791]
27. Hausmann E, Allen K, Carpio L, Christersson La, Clerehugh V. Computerized methodology for detection of alveolar crestal bone loss from serial intraoral radiographs. *J Periodontol*. 1992; 63:657–62. [PubMed: 1507045]
28. LaMonte MJ, Williams AM, Genco RJ, et al. Association between metabolic syndrome and periodontal disease measures in postmenopausal women: The Buffalo OsteoPerio Study. *J Periodontol*. 2014; 26:1–15.
29. Tezal M, Wactawski-Wende J, Grossi SG, Dmochowski J, Genco RJ. Periodontal disease and the incidence of tooth loss in postmenopausal women. *Journal of Periodontology*. 2005; 76:1123–8. [PubMed: 16018755]
30. Tezal M, Wactawski-Wende J, Grossi SG, Ho AW, Dunford R, Genco RJ. The relationship between bone mineral density and periodontitis in postmenopausal women. *J Periodontol*. 2000; 71:1492–8. [PubMed: 11022780]
31. Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. *J Periodontol*. 2007; 78:1387–99.
32. Bole C, Wactawski-Wende J, Hovey KM, Genco RJ, Hausmann E. Clinical and community risk models of incident tooth loss in postmenopausal women from the Buffalo Osteo Perio Study. *Community Dent Oral Epidemiol*. 2010; 38:487–97. [PubMed: 20636416]
33. Meyer A-M, Evenson KR, Morimoto L, Siscovick D, White E. Test-retest reliability of the Women’s Health Initiative physical activity questionnaire. *Med Sci Sports Exerc*. 2009; 41:530–8. [PubMed: 19204598]

34. Patterson RE, Kristal AR, Tinker LF, Carter RA, Bolton MP, Agurs-Collins T. Measurement characteristics of the Women's Health Initiative food frequency questionnaire. *Ann Epidemiol.* 1999; 9(98):178–87. [PubMed: 10192650]
35. Guenther PM, Krebs-Smith SM, Reedy J. , et al. Center for Nutrition Policy and Promotion. Alexandria, VA: 2006. Healthy Eating Index – 2005. revised 2008. CNPP Fact Sheet No. 1.
36. Dubowitz T, Ghosh-Dastidar M, Eibner C, et al. The Women's Health Initiative: The food environment, neighborhood socioeconomic status, BMI, and blood pressure. *Obesity.* 2012; 20:862–71. [PubMed: 21660076]
37. Meng JE, Hovey KM, Wactawski-Wende J, et al. Intraindividual variation in plasma 25-hydroxyvitamin D measures 5 years apart among postmenopausal women. *Cancer Epidemiol Biomarkers Prev.* 2012; 21:916–24. [PubMed: 22523182]
38. Goodson JM. Diagnosis of periodontitis by physical measurement: interpretation from episodic disease hypothesis. *J Periodontol.* 1992; 63:373–82.
39. Ellis JS, Seymour RA, Steele JG, Robertson P, Butler TJ, Thomason JM. Prevalence of gingival overgrowth induced by calcium channel blockers. *J Periodontol.* 1999; 70:63–7. [PubMed: 10052772]
40. Bondonno CP, Liu AH, Croft KD, et al. Antibacterial mouthwash blunts oral nitrate reduction and increases blood pressure in treated hypertensive men and women. *Am J Hypertens.* 2015; 28:572–5. [PubMed: 25359409]

Key findings

Clinical attachment level was associated with systolic blood pressure and number of teeth missing was associated with systolic blood pressure and hypertension; probing pocket depth, alveolar crestal height, gingival bleeding, and periodontal disease severity were not associated with systolic blood pressure or hypertension among postmenopausal women.

Characteristics of participants by hypertension* prevalence status and measured systolic blood pressure at baseline in the Buffalo OsteoPerio Study (N=1,341)

Table 1

Characteristics:	Hypertension*		p [†]	Systolic Blood Pressure*		p [‡]
	No (N=814)	Yes (N=527)		<140 (N=1051)	140 (N=235)	
	Mean (±SD)			Mean (±SD)		
Age (years)	65.5±6.7	68.1±7.1	<0001	66.1±6.9	69.6±6.9	<0001
Neighborhood Socioeconomic Status	76.4±6.8	75.8±7.1	0.06	76.2±6.8	75.5±7.3	0.11
Pack-years cigarettes	10.3±18.5	9.8±17.5	0.85	10.4±18.6	8.4±15.5	0.18
Alcohol (oz/day)	0.5±0.7	0.4±0.7	<0001	0.5±0.7	0.4±0.7	0.06
Healthy Eating Index [‡]	69.7±10.1	69.8±10.4	0.53	69.6±10.2	70.7±10.2	0.07
Sodium intake (mg)	2549±946	2637.7±1044.7	0.18	2601±1006	2548±896	0.73
Total physical activity (MET-hrs/wk)	15.6±14.4	12.7±13.9	<0001	14.5±14.3	13.4±14.2	0.33
BMI (kg/m ²)	25.7±4.5	27.8±5.7	<0001	26.6±5.2	26.6±4.8	0.57
SBP (mmHg)	113.2±12.2	132.6±19.1	<0001	115.7±12.4	150.6±13.1	<0001
DBP (mmHg)	68.2±7.5	73.5±10.0	<0001	68.6±7.8	79.5±9.3	<0001
	N (%)		p [†]	N (%)		p [‡]
Smoking status			0.96			0.26
Never	386 (52.4)	321 (53.1)		547 (52.0)	132 (56.4)	
Former	326 (44.3)	263 (43.5)		469 (44.6)	98 (41.9)	
Current	24 (3.3)	20 (3.3)		35 (3.3)	4 (1.7)	
Education (Highest level)			0.20			0.27
High School	143 (19.8)	137 (22.9)		213 (20.6)	56 (24.0)	
College or some college	318 (44.0)	270 (45.2)		465 (45.0)	92 (39.5)	
Post-graduate	261 (36.1)	191 (31.9)		356 (34.4)	85 (36.5)	
Race/ethnicity			0.17			0.30
White	719 (97.7)	586 (96.9)		1026 (97.6)	227 (96.6)	
Black or African American	8 (1.1)	14 (2.3)		13 (1.2)	6 (2.6)	
Other	9 (1.2)	5 (0.8)		12 (1.1)	2 (0.9)	

Characteristics:	Hypertension*		p [†]	Systolic Blood Pressure*		p [‡]
	No (N=814)	Yes (N=527)		<140 (N=1051)	140 (N=235)	
	Mean (±SD)			Mean (±SD)		
BMI (Categories)			<.0001			0.63
< 25 (kg/m ²)	375 (51.0)	214 (35.4)		472 (44.9)	98 (41.7)	
25 – 29.9 (kg/m ²)	253 (34.4)	213 (35.2)		359 (34.2)	87 (37.0)	
30 (kg/m ²)	108 (14.7)	178 (29.4)		220 (20.9)	50 (21.3)	
Anti-cholesterol agent status			<.0001			0.57
Never	633 (86.7)	433 (72.2)		838 (80.4)	185 (79.1)	
Former	18 (2.5)	20 (3.3)		27 (2.6)	9 (3.8)	
Current	79 (10.8)	147 (24.5)		177 (17.0)	40 (17.1)	
Diabetes mellitus (Meds at OP visit or WHI self-report)			<.0001			0.87
No	727 (98.8)	562 (92.9)		1013 (96.4)	226 (96.2)	
Yes	9 (1.2)	43 (7.1)		38 (3.6)	9 (3.8)	
Cardiovascular disease history (WHI self-report)			<.0001			0.33
No	708 (96.2)	496 (82.0)		948 (90.2)	207 (88.1)	
Yes	28 (3.8)	109 (18.0)		103 (9.8)	28 (11.9)	

* Hypertension defined as taking self-reported physician diagnosis or treatment for hypertension, blood pressure-lowering medication on medication inventory, having systolic blood pressure 140, or diastolic blood pressure 90

[†] p-values based on χ^2 test for categorical variables, and Wilcoxon Rank-Sum test for continuous variables

[‡] HEI is a composite diet score based on intake of 12 categories of foods including fruit, vegetable, whole grains, milk, meat and beans, oils, and sodium.

Measures of periodontal disease by hypertension* prevalence status and measured systolic blood pressure at baseline in the Buffalo OsteoPerio Study (N=1,341)

Table 2

Periodontal Measures:	Hypertension*		p [†]	Systolic Blood Pressure		p [†]
	No (N=814)	Yes (N=527)		<140 (N=1051)	140 (N=235)	
	Mean (±SD)			Mean (±SD)		
Clinical Attachment Level (mean mm)	2.4±0.7	2.43±0.7	0.09	2.4±0.7	2.4±0.7	0.22
Probing Pocket Depth (mean mm)	2.2±0.4	2.18±0.4	0.84	2.2±0.4	2.2±0.4	0.43
Alveolar Crestal Height (mean mm)	2.4±0.7	2.5±0.8	0.11	2.4±0.7	2.5±0.9	0.10
Number of Teeth missing	4.2±4.9	5.6±5.7	<.0001	4.5±5.1	5.7±5.6	0.0002
Percentage of sites with gingival bleeding on probing	0.3±0.2	0.4±0.2	0.27	0.3±0.2	0.4±0.2	0.21
	N (%)		p [†]	N (%)		p [†]
Periodontitis (CDC/AAP Definition) ³¹			0.91			0.20
None or mild	199 (27.2)	155 (26.2)		288 (27.7)	51 (22.1)	
Moderate	417 (57.0)	341 (57.6)		586 (56.3)	143 (61.9)	
Severe	115 (15.7)	96 (16.2)		166 (16.0)	37 (16.0)	
Alveolar Crestal Height (categorical) ²⁵			0.36			0.04
None	178 (24.2)	140 (23.1)		269 (25.6)	42 (17.9)	
Mild/Moderate	373 (50.7)	292 (48.3)		510 (48.5)	125 (53.2)	
Severe	185 (25.1)	173 (28.6)		272 (25.9)	68 (28.9)	

*Hypertension defined as taking self-reported physician diagnosis or treatment for hypertension, blood pressure-lowering medication on medication inventory, having systolic blood pressure 140, or diastolic blood pressure 90

[†]p-values based on X² test for categorical variables, and Wilcoxon Rank-Sum test for continuous variables

Table 3 Logistic regression on the association between periodontal measures and prevalent hypertension* at baseline. Buffalo OsteoPerio Study (N=1,341, N cases=527)

Periodontal Measures:	Crude			Age Adjusted			Multivariable Adjusted [†]		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Clinical Attachment Level (per mean mm)	1.17	1.00 – 1.37	0.06	1.11	0.94 – 1.31	0.21	1.18	0.98 – 1.41	0.08
Probing Pocket Depth (per mean mm)	0.99	0.75 – 1.40	0.94	1.12	0.85 – 1.48	0.43	1.09	0.80 – 1.48	0.57
Alveolar Crestal Height (per mean mm)	1.16	1.01 – 1.33	0.04	1.02	0.88 – 1.18	0.79	1.06	0.90 – 1.26	0.48
# Teeth Missing	1.05	1.03 – 1.08	<0001	1.04	1.02 – 1.06	0.0005	1.03	1.00 – 1.05	0.03
#Teeth Missing per SD (5 teeth) of Teeth Missing	1.32	1.18 – 1.47	<0001	1.22	1.09 – 1.37	0.0005	1.15	1.01 – 1.30	0.03
Percentage of Sites with Gingival Bleeding (per 1%)	1.33	0.84 – 2.13	0.23	1.28	0.80 – 2.06	0.31	0.93	0.55 – 1.55	0.77
Periodontitis (Compared to 'None/Mild'; N=354, N cases=155)³¹									
Moderate (N=758, N cases=341)	1.05	0.81 – 1.35	0.71	0.97	0.75 – 1.25	0.80	1.06	0.80 – 1.40	0.68
Severe (N=211, N cases=96)	1.07	0.76 – 1.51	0.69	0.99	0.70 – 1.40	0.95	1.03	0.71 – 1.50	0.88
Alveolar Crestal Height (Compared to 'None'; N=318, N cases=140)²⁵									
Mild/Moderate (N=665, N cases=292)	1.00	0.76 – 1.30	0.97	0.82	0.62 – 1.08	0.16	0.82	0.60 – 1.11	0.19
Severe (N=358, N cases=173)	1.19	0.88 – 1.61	0.26	0.90	0.66 – 1.24	0.53	0.92	0.65 – 1.31	0.64

* Hypertension defined as taking self-reported physician diagnosis or treatment for hypertension, blood pressure-lowering medication on medication inventory, having systolic blood pressure 140, or diastolic blood pressure 90

[†] Adjusted for age, smoking status, BMI, healthy eating index, sodium intake, alcohol intake, neighborhood socioeconomic status, physical activity.

Linear regression between measured systolic blood pressure and periodontal measures at baseline among postmenopausal women not taking antihypertensive medication. Buffalo OsteoPerio Study (N=876).

Table 4a

Periodontal Measures	Crude			Age Adjusted			Multivariable Adjusted*		
	β	SE	p	β	SE	p	β	SE	p
Clinical Attachment Level (per mean mm)	2.66	0.88	0.003	2.08	0.85	0.01	2.39	0.87	0.01
Probing Pocket Depth (per mean mm)	-0.30	1.49	0.84	1.48	1.45	0.31	1.12	1.47	0.45
Alveolar Crestal Height (per mean mm)	2.21	0.77	0.04	0.77	0.77	0.32	1.23	0.82	0.14
# Teeth Missing	0.52	0.11	<0.0001	0.35	0.11	0.002	0.31	0.12	0.01
Percentage of Sites with Gingival Bleeding (per 1%)	4.39	2.66	0.10	3.97	2.57	0.12	2.39	2.60	0.36
Periodontitis (Compared to 'None/Mild'; N=240)³¹									
Moderate (N=496)	1.78	1.00	0.14	-1.23	1.33	0.35	-0.59	1.33	0.66
Severe (N=134)	2.13	1.63	0.19	-0.66	1.81	0.72	-0.07	1.85	0.97
Alveolar Crestal Height (Compared to 'None'; N=210)²⁵									
Mild/Moderate (N=440)	2.03	1.46	0.16	-0.35	1.44	0.81	0.18	1.47	0.90
Severe (N=226)	3.41	1.67	0.04	0.26	1.66	0.88	0.70	1.74	0.69

* Adjusted for age, smoking status, BMI, healthy eating index, sodium intake, alcohol intake, neighborhood socioeconomic status, physical activity.

Linear regression between measured systolic blood pressure and periodontal measures at baseline among postmenopausal women taking antihypertensive medication. Buffalo OsteoPerio Study (N=465).

Table 4b

Periodontal Measures	Crude			Age Adjusted			Multivariable Adjusted*		
	β	SE	P	β	SE	P	β	SE	P
Clinical Attachment Level (per mean mm)	1.55	1.33	0.24	0.87	1.28	0.49	0.86	1.35	0.53
Probing Pocket Depth (per mean mm)	-0.41	2.24	0.86	0.80	2.16	0.71	0.67	2.26	0.77
Alveolar Crestal Height (per mean mm)	2.01	1.14	0.08	0.08	1.14	0.94	-0.28	1.25	0.82
# Teeth Missing	0.26	0.16	0.10	0.01	0.16	0.96	-0.002	0.17	0.99
Percentage of Sites with Gingival Bleeding (per 1%)	7.2	3.7	0.05	6.21	3.56	0.08	7.00	3.79	0.07
Periodontitis (Compared to 'None/Mild'; N=114)³¹									
Moderate (N=262)	5.36	2.13	0.01	3.85	2.06	0.06	3.85	2.17	0.08
Severe (N=77)	5.97	2.81	0.03	3.92	2.73	0.15	3.88	2.86	0.18
Alveolar Crestal Height (Compared to 'None'; N=108)²⁵									
Mild/Moderate (N=225)	4.52	2.2	0.04	1.66	2.17	0.45	0.81	2.30	0.73
Severe (N=132)	5.94	2.46	0.02	2.15	2.45	0.38	1.41	2.63	0.59

* Adjusted for age, smoking status, BMI, healthy eating index, sodium intake, alcohol intake, neighborhood socioeconomic status, physical activity.