**OSHR - Periodontal Disease and Hypertension**

**Introduction**

Introduction contributed by Dr. Anthony Iacopino, Executive Director, International Centre for Oral Systemic Health, University of Manitoba, Winnipeg.

The vasculature appears to be particularly susceptible to periodontitis-induced alterations that result in atherosclerosis and decreased elasticity/increased stiffness. There appear to be contributions to these negative consequences arising from both periodontitis-induced bacteremia/endotoxemia and a heightened systemic inflammatory state driven by periodontitis-induced serum elevations of pro-inflammatory cytokines (IL-1ß/TNF-α) and lipids (LDL cholesterol/triglycerides).1,2 It is best to specifically limit the discussion of this relationship to vascular dysfunction and hypertension rather than try to make causal linkages to significant downstream adverse clinical events such as myocardial infarction/stroke. The types of clinical studies and interventional trials required to provide the necessary quality of evidence for these endpoints can never be completed due to: 1) length of observation time required; 2) extremely high cost of experimental design; and 3) ethical concerns related to control groups.

It is now generally accepted within the medical community that periodontitis causes vascular dysfunction and this is reversible with periodontal treatment. It is recognized that hypertension is a primary outcome of this vascular dysfunction. The evidence base for this relationship is indisputable. With regard to biological mechanism, atherosclerotic changes to vasculature occur as a result of intimal damage from cross-reactivity of antibodies directed against a periodontal pathogen (*P gingivalis*) combined with elevated serum pro-inflammatory cytokines and lipids induced by periodontitis.3

The term used to describe the autoimmune reaction to *P gingivalis* is molecular mimicry. Damage to vascular endothelial cells is mediated by autoimmune antibodies directed against *P gingivalis* heat shock proteins that cross react with vascular endothelial heat shock proteins. This results in leaky intimal walls and exposes the medial layer. Inflammatory response to this damage along with periodontitis-induced high levels of circulating of serum pro-inflammatory cytokines amplifies intimal/medial damage providing an opportunity for periodontitis-induced high levels of circulating lipids to accumulate. Subsequent recruitment of macrophages and foam cell formation then trigger development of atheromatous plaques (fatty streak formation) and presence of atherosclerosis. These plaques will develop an enlarging core with a fibrous cap over time and may ulcerate and rupture possibly causing myocardial infarction or stroke. Vascular dysfunction and atherosclerotic disease can occur in vascular elements throughout the body although the most relevant are carotid arteries and brain vasculature (cerebrovascular disease) and coronary arteries and heart vasculature (cardiovascular disease).

With regard to hypertension, numerous studies utilizing flow-mediated dilatation and pulseñ wave velocity have documented decreased arterial elasticity/increased stiffness in the presence of periodontitis with improvement of these parameters after standard periodontal intervention.4-8 Vasculature that loses its elasticity and becomes stiffer will result in elevations of systolic and diastolic blood pressure values. This has significant public health implications due to the myriad diseases/conditions linked to hypertension.9-11 Thus, it is important that standard periodontal treatment may reduce morbidity/mortality associated with hypertension as periodontal interventions are relatively non-invasive, cost-effective and readily accessible.

1. Amar S, Gokce N, Morgan S, et al. Periodontal disease is associated with brachial artery endothelial dysfunction and systemic inflammation. *Arterioscler Thromb Vasc Biol* 23:1245-1249, 2003.
2. Choi H, Dey AK, Priyamvara A, et al. Role of Periodontal Infection, Inflammation and Imñnity in Atherosclerosis. *Current Problems in Cardiology* 2020; doi: 10.1016/j.cpcardiol.2020.100638.
3. Miyakawa H, Honma K, Qi M, Kuramitsu HK. Interaction of Porphyromonas gingivalis with low-density lipoproteins: implications for a role for periodontitis in atherosclerosis. *J Periodontal Res* 39:1-9, 2004.
4. D'Aiuto F, Parkar M, Andreou G, et al. Periodontitis and systemic inflammation: control of the local infection is associated with a reduction in serum inflammatory markers. *J Dent* Res 83:156-160, 2004.
5. Tonetti MS, D'Aiuto F, Nibali L, et al. Treatment of periodontitis and endothelial function. *N Engl J Med* 356:911-920, 2007.
6. D'Aiuto F, Nibali L, Parkar M, et al. Short-term effects of intensive periodontal therapy on serum inflammatory markers and cholesterol. *J Dent Res* 84:269-273, 2005.
7. Teeuw WJ, Slot DE, Susanto H, et al. Treatment of periodontitis improves the atherosclerotic profile: a systematic review and meta-analysis. *J Clin Periodontol* 41:70-79, 2014.
8. Orlandi M, Suvan J, Petrie A, et al. Association between periodontal disease and its treatment, flow-mediated dilatation and carotid intima-media thickness: a systematic review and meta-analysis. *Atherosclerosis* 236:39-46, 2014.
9. Leira Y, Rodriguez-Yanez M, Arias S, et al. Periodontitis is associated with systemic inflammation and vascular endothelial dysfunction in patients with lacunar infarct. *J Periodontol* 90:465-474, 2019.
10. Muñoz Aguilera E, Leira Y, Miró Catalina Q, et al. Is Systemic Inflammation a Missing Link Between Periodontitis and Hypertension? Results from Two Large Populations-based Surveys. *J Intern Med* 2020; DOI: 10.1111/joim.13180, 10.1111/joim.13180
11. Lanau N, Mareque J, Zabalza M. Does Periodontal Treatment Help in Arterial Hypertension Control? A Systematic Review of Literature. *Eur J Dent* 2020; doi: 10.1055/s-0040-1718244

Colgate (2023).The Link between Gum Disease and Blood Pressure. At: <https://www.colgate.com/en-us/oral-health/gum-disease/the-link-between-gum-disease-blood-pressure>

Yoon H, Seong JM (2022). The Relationship between Pulse Pressure and Periodontal Disease in Korean Populations with or without Hypertension. At: <https://www.mdpi.com/2076-3417/12/10/4973>Appl. Sci.  12(10), 4973 DOI:  [**https://doi.org/10.3390/app12104973**](https://doi.org/10.3390/app12104973) Abstract: ***Aims*:** This study evaluated the relationship between pulse pressure (PP) and periodontal disease in Korean adults with or without hypertension (classified as HTN and non-HTN, respectively). ***Methods*:** Data on 3496 adults (≥20 years) were obtained from the Korean National Health and Nutrition Examination Survey (2015). We classified those with HTN as SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, or current use of anti-hypertensive medications. ***Results*:** There were a few key findings: when logistic regression analysis was applied for periodontal disease (community periodontal index score ≥ 3), the odds ratios (OR) were significantly higher in the high PP (PP > 60 mmHg) than in the normal PP (PP ≤ 60 mmHg) in the HTN group (OR, 2.131; 95% confidence interval (CI), 1.579–2.876). However, periodontal disease was not associated with high PP in the non-HTN group and was not significant (OR, 0.866; 95% CI, 0.494–1.518). ***Conclusions*:** In Korean adults, periodontal disease was positively associated with PP in the HTN group but not in the non-HTN group. **Keywords:**[**periodontal disease**](https://www.mdpi.com/search?q=periodontal+disease); [**community periodontal index scores**](https://www.mdpi.com/search?q=community+periodontal+index+scores); [**blood pressure**](https://www.mdpi.com/search?q=blood+pressure); [**pulse pressure**](https://www.mdpi.com/search?q=pulse+pressure); [**hypertension**](https://www.mdpi.com/search?q=hypertension)

Surma S, Romańczyk M, Witalińska- Łabuzak J, Czerniuk MR, Łabuzak K, Filipiak JK (2021). Periodontitis, Blood Pressure, and the Risk and Control of Arterial Hypertension: Epidemiological, Clinical, and Pathophysiological Aspects—Review of the Literature and Clinical Trials. At: <https://link.springer.com/article/10.1007/s11906-021-01140-x> **Abstract:** **Purpose of Review:** Arterial hypertension is an important risk factor for cardiovascular disease. In the world, about 45% of people suffer from arterial hypertension, while good blood pressure control is achieved by only approximately 50% of all hypertensive patients treated. The reason for the high prevalence of arterial hypertension and its poor control is low knowledge of hypertensinogenic factors. One such factor is periodontitis, which is a disease of social importance. **Recent Findings:** It has been shown that the occurrence of periodontitis leads to an increase in blood pressure, increasing the risk of arterial hypertension. Periodontitis can also lead to ineffectiveness of antihypertensive treatment. Some interventional studies have shown that treatment of periodontitis reduced blood pressure in patients with arterial hypertension. The pathogenesis of arterial hypertension in periodontitis is complex and concerns mainly the impairment of the vasodilatation properties of the endothelium. **Summary:** Hygiene and periodontitis treatment should be a method of preventing arterial hypertension and a method of increasing the effectiveness of antihypertensive treatment.

# Hypertension Journal Report (2021). People with severe gum disease may be twice as likely to have increased blood pressure. At: <https://newsroom.heart.org/news/people-with-severe-gum-disease-may-be-twice-as-likely-to-have-increased-blood-pressure> Research shows that periodontitis, severe gum disease, is linked to higher blood pressure in otherwise healthy individuals. This study of 500 adults with and without gum disease found that approximately 50% of adults could have undetected hypertension. Promotion of good oral health could help reduce gum disease and the risk of high blood pressure and its complications.

# Aguilera EM, Suvan J, Orlandi M, Cataline QM, Mart J, D’Aiuto F (2021). Association Between Periodontitis and Blood Pressure Highlighted in Systemically Healthy Individuals: Results From a Nested Case-Control Study. *Am Heart Assoc Hypertension.* At: <https://www.ahajournals.org/doi/10.1161/HYPERTENSIONAHA.120.16790> Abstract: Recent evidence suggests hypertension and periodontitis are closely linked but limited data is available on the nature of the association. We aimed to investigate the relationship between periodontitis and mean arterial blood pressure in a sample of otherwise systemically healthy individuals. A case-control study including 250 cases (participants with periodontitis) and 250 controls (without periodontitis) was designed from a register of clinical trials conducted between 2000 and 2018 in a university setting. Cases were age, sex, and body mass index balanced with controls. Linear, logistic regression, and mediation models were planned to test the association between various periodontal measures and arterial blood pressure. We further investigated the role of systemic inflammation assessed by hs-CRP (high-sensitivity C-reactive protein) and white cell counts. Cases presented with 3.36 mm Hg (95% CI, 0.91–5.82, *P*=0.007) higher mean systolic blood pressure and 2.16 mm Hg (95% CI, 0.24–4.08, *P*=0.027) higher diastolic blood pressure than controls. Diagnosis of periodontitis was associated with mean systolic blood pressure (β=3.46±1.25, *P*=0.005) and greater odds of systolic blood pressure ≥140 mm Hg (odds ratio, 2.3 [95% CI, 1.15–4.60], *P*=0.018) independent of common cardiovascular risk factors. Similar findings were observed when continuous measures of periodontal status were modeled against systolic blood pressure. Measures of systemic inflammation although elevated in periodontitis were not found to be mediators of the association between periodontitis and arterial blood pressure values. Periodontitis is linked to higher systolic blood pressure in otherwise healthy individuals. Promotion of periodontal and systemic health strategies in the dental and medical setting could help reduce the burden of hypertension and its complications.

# Landi L, Grassi G, Sforza NM, Ferri C, Italian Working Group on Hypertension and Periodontitis [Hy Per Group] (2021). Hypertension and Periodontitis: An Upcoming Joint Report by the Italian Society of Hypertension (SIIA) and the Italian Society of Periodontology and Implantology (SIdP). *High Blood Press Cardiovasc Prev* 28: 1-3. DOI: [10.1007/s40292-020-00430-w](https://doi.org/10.1007/s40292-020-00430-w) At: <https://pubmed.ncbi.nlm.nih.gov/33400213/>

Muñoz Aguilera E, Leira Y, Miró Catalina Q, Orlandi M, Czesnikiewicz-Guzik M, Guzik TJ, Hingorani AD, Nart J, D’Aiuto F (2020). Is systemic inflammation a missing link between periodontitis and hypertension? Results from two large population-based surveys. *J Intern Med* DOI: [10.1111/joim.13180](https://doi.org/10.1111/joim.13180) At: <https://pubmed.ncbi.nlm.nih.gov/32969093/> Abstract: **Objective:** The primary objective was to investigate the relationship between periodontitis and hypertension in two independent large surveys. The secondary objective was to ascertain whether systemic inflammation had a mediation effect in the association. **Methods:** This cross-sectional study analysed representative samples of the US (n = 3460; NHANES 2009/10) and Korean (n = 4539; 2015 KNHANES VI-3) populations. The association between periodontitis (exposure), hypertension (outcome) and inflammatory markers [C-reactive protein (CRP) and white blood cell counts (WBC)] (mediators) was assessed using multivariate linear and logistic regression models and mediation analysis. **Results:** Participants with periodontitis were more likely to have hypertension (NHANES: OR = 1.3, 95% CI: 1.0-1.6, P = 0.025; KNHANES: OR = 1.2, 95% CI: 1.0-1.4, P = 0.041) and actual systolic blood pressure ≥ 140 mmHg (NHANES: OR = 1.6, 95% CI: 1.1-2.3, P < 0.001; KNHANES: OR = 1.3, 95% CI :1.0-1.6, P < 0.031) than those without the disease. These associations were independent of age, gender, BMI, education level, smoking, alcohol consumption, creatinine, physical activity, presence of other comorbidities and confirmed in participants not taking antihypertensive medications. Diagnosis of periodontitis was directly associated with WBC (in both surveys: NHANES: β ± SE = 0.3 ± 0.1, P < 0.004; KNHANES: β ± SE = 0.3 ± 0.1, P < 0.001) and with CRP levels (in one survey: NHANES: β ± SE = 0.1 ± 0.03, P < 0.007; KNHANES: β ± SE = 0.1 ± 0.04, P > 0.213). Mediation analyses confirmed that CRP acted as a mediator in the association between periodontitis and hypertension in both populations (mediated effect: NHANES: β ± SE = 0.010 ± 0.003, P < 0.001; KNHANES: β ± SE = 0.003 ± 0.001, P = 0.015). WBC acted as a mediator in the KNHANES (mediated effect: β ± SE = 0.004 ± 0.001, P = 0.004) whilst in the NHANES, its effect was dependent of CRP inclusion in the model (mediated effect WBC + CRP: β ± SE = 0.002 ± 0.001, P = 0.001). **Conclusions:** These findings suggest that periodontitis is closely linked to hypertension and systemic inflammation is, in part, a mediator of this association. **Keywords:** CRP; high blood pressure; hypertension; leucocytes; periodontitis; systemic inflammation. © 2020 The Authors. Journal of Internal Medicine published by John Wiley & Sons Ltd on behalf of Association for Publication of *The Journal of Internal Medicine*. [Please also see:

Muñoz-Aguilera E, Suvan J, Buti J, Czesnikiewicz-Guzik M, Ribeiro AB, Orlandi M, Guzik TJ, Hingorani AD, Nart J, D’Aiuto F (2020). Periodontitis is associated with hypertension: a systematic review and meta-analysis*. Cardiovasc Res* 116(1): 28-39. DOI: <https://doi.org/10.1093/cvr/cvz201> At: <https://academic.oup.com/cardiovascres/article/116/1/28/5572510> [Please also note Antipolis S: <https://www.escardio.org/The-ESC/Press-Office/Press-releases/Gum-disease-linked-with-higher-risk-of-hypertension> ]

### Sanz M, Marco de Castillo A, Jepsen S, Guanzalez-Juanatey JR, D’Aiuto F, Bouchard P, Chapple I, Dietrich T, Gotsman I, Gazinani F, Herrera D, Loos B, Madianos P, Michel JP, Michel JP, Perel P, Pieske B, Shapira L, Shechter M, Tonetti M, Vlacopoulos C, Wimmer G (2020). Periodontitis and Cardiovascular Diseases. Consensus Report. *Glob Heart* 15(1): 1 DOI: [10.5334/gh.400](https://doi.org/10.5334%2Fgh.400) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7218770/> **Abstract: Background:** In Europe cardiovascular disease (CVD) is responsible for 3.9 million deaths (45% of deaths), being ischaemic heart disease, stroke, hypertension (leading to heart failure) the major cause of these CVD related deaths. Periodontitis is also a chronic non-communicable disease (NCD) with a high prevalence, being severe periodontitis, affecting 11.2% of the world’s population, the sixth most common human disease. **Material and Methods:** There is now a significant body of evidence to support independent associations between severe periodontitis and several NCDs, in particular CVD. In 2012 a joint workshop was held between the European Federation of Periodontology (EFP) and the American Academy of Periodontology to review the literature relating periodontitis and systemic diseases, including CVD. In the last five years important new scientific information has emerged providing important emerging evidence to support these associations. **Results and Conclusions:** The present review reports the proceedings of the workshop jointly organised by the EFP and the World Heart Federation (WHF), which has updated the existing epidemiological evidence for significant associations between periodontitis and CVD, the mechanistic links and the impact of periodontal therapy on cardiovascular and surrogate outcomes. This review has also focused on the potential risk and complications of periodontal therapy in patients on anti-thrombotic therapy and has made recommendations for dentists, physicians and for patients visiting both the dental and medical practices. **Keywords:**Periodontitis, periodontal therapy, cardiovascular diseases, chronic inflammation, bacteremia, atherosclerosis, antitrombotic therapy

Choi H, Dey AK, Priyamvara A, Aksentijevich M, Bandyopadhyay D, Dey D, Dani S, Guha A, Nambiar P, Nasir K, Jneid H, Mehta NN, Lavie CJ, Amar S (2020). Role of Periodontal Infection, Inflammation and Immunity in Atherosclerosis. *Curr Probl Cardiol* DOI: 10.1016/j.cpcardiol.2020.100638. At: <https://pubmed.ncbi.nlm.nih.gov/32646544/>

Lanau N, Mareque J, Zabalza M (2020). Does Periodontal Treatment Help in Arterial Hypertension Control? A Systematic Review of Literature. *Eur J Dent* doi: 10.1055/s-0040-1718244 At: <https://pubmed.ncbi.nlm.nih.gov/33032337/> Abstract: Arterial hypertension and periodontal diseases are two of the pathologies with more prevalence worldwide. In the last few years, several scientific evidences have demonstrated the relationship between both diseases. Besides the etiopathogenic and causal relationship, some recent publications have pointed out that the therapeutic approach of periodontitis could have positive effects on the control of arterial hypertension. The aim of this systematic review is to determine whether there is a decrease in or better control of blood pressure after performing nonsurgical periodontal treatment in patients with periodontitis. A thorough search in PubMed, Scopus, and ISI Web of Science databases with the keywords "'periodontal disease' OR 'periodontitis' OR 'periodontal' AND 'blood pressure' OR 'hypertension' OR 'arterial hypertension'" was conducted. The quality of the reported information was assessed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for systematic reviews. Eight articles were considered for this systematic review. Five of the studies showed statistically significant reduction in systolic blood pressure (SBP) values. Despite the limitations of the review, nonsurgical treatment of periodontal disease seems to reduce SBP values. Further research with larger and longer-term clinical trials are needed to demonstrate this potential positive effect.

Machado V, Muñoz Aguilera E, Botelho J, Hussain SB, Leira Y, Proenca L, D’Aiuto F, Mendes JJ (2020). Association between Periodontitis and High Blood Pressure: Results from the Study of Periodontal Health in Almada-Seixal (SoPHiAS). J Clin Med 9(5): 1585. DOI: [10.3390/jcm9051585](https://dx.doi.org/10.3390%2Fjcm9051585) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7291060/>

Czesnikiewicz-Guzik M, Osmenda G, Siedlinski M, Nosalski R, Pelka P, Nowakowski D, Wilk G, Mikolajczyk TP, Schramm-Luc A, Furtak A, Matusik P, Koziol J, Drozdz M, Muñoz-Aguilera E, Tomaszewski M, Evangelou E, Caulfield M, Grodzicki T, D’Aiuto F, Guzik TJ (2019). Causal association between periodontitis and hypertension: evidence from Mendelian randomization and a randomized controlled trial of non-surgical periodontal therapy. Eur Heart J 40(42): 3459-3470. DOI: <https://doi.org/10.1093/eurheartj/ehz646> At: <https://academic.oup.com/eurheartj/article/40/42/3459/5556904> Abstract: Aims Inflammation is an important driver of hypertension. Periodontitis is a chronic inflammatory disease, which could provide a mechanism for pro-hypertensive immune activation, but evidence of a causal relationship in humans is scarce. We aimed to investigate the nature of the association between periodontitis and hypertension. Methods and results We performed a two-sample Mendelian randomization analysis in the ∼750 000 UK-Biobank/International Consortium of Blood Pressure-Genome-Wide Association Studies participants using single nucleotide polymorphisms (SNPs) in *SIGLEC5*, *DEFA1A3*, *MTND1P5*, and *LOC107984137* loci GWAS-linked to periodontitis, to ascertain their effect on blood pressure (BP) estimates. This demonstrated a significant relationship between periodontitis-linked SNPs and BP phenotypes. We then performed a randomized intervention trial on the effects of treatment of periodontitis on BP. One hundred and one hypertensive patients with moderate/severe periodontitis were randomized to intensive periodontal treatment (IPT; sub- and supragingival scaling/chlorhexidine; *n* = 50) or control periodontal treatment (CPT; supragingival scaling; *n* = 51) with mean ambulatory 24-h (ABPM) systolic BP (SBP) as primary outcome. Intensive periodontal treatment improved periodontal status at 2 months, compared to CPT. This was accompanied by a substantial reduction in mean SBP in IPT compared to the CPT (mean difference of −11.1 mmHg; 95% CI 6.5–15.8; *P* < 0.001). Systolic BP reduction was correlated to periodontal status improvement. Diastolic BP and endothelial function (flow-mediated dilatation) were also improved by IPT. These cardiovascular changes were accompanied by reductions in circulating IFN-γ and IL-6 as well as activated (CD38+) and immunosenescent (CD57+CD28null) CD8+T cells, previously implicated in hypertension. Conclusion A causal relationship between periodontitis and BP was observed providing proof of concept for development of clinical trial in a large cohort of hypertensive patients. ClinicalTrials.gov: NCT02131922.

Tonetti MS, Graziani F (2019). “The Cardiovascular System and Oral Infections,” Chapter 7, Glick M, Ed. *The Oral-Systemic Health Connection: A Guide to Patient Care*, 2nd Edition (Quintessence, 2019, LCCN 2018044816), pp. 164-179. **Book Level Chapter**

Leira Y, Rodriguez-Yáñez M, Arias S, López-Dequidt I, Campos F, Sobrino T, D’Aiuto F, Castillo J, Blanco J (2019). Periodontitis is associated with systemic inflammation and vascular endothelial dysfunction in patients with lacunar infarct. *J Periodontol* 90:465-474. DOI: 10.1002/JPER.18-0560. At: <https://pubmed.ncbi.nlm.nih.gov/30417380/>

D’Isidoro O, Perrotti V, Hui WL, Piatelli A, Iaculli F, Quaranta A (2019). The impact of non-surgical therapy of periodontal disease on surrogate markers for cardiovascular disease: A literature review. *Am J Dent* 32(4):191-200. At: <https://pubmed.ncbi.nlm.nih.gov/31436940/>

Muñoz Aguilera EM, Suvan J, Buti J, Czesnikiewicz-Guzik M, Ribeiro AB, Orlandi M, Guzik TJ, Hingorani AD, Nart J, D’Aiuto F(2019). Periodontitis is associated with hypertension: a systematic review and meta-analysis. *Cardiovasc Res* DOI: [10.1093/cvr/cvz201](https://doi.org/10.1093/cvr/cvz201) At: <https://pubmed.ncbi.nlm.nih.gov/31549149/>. Recent evidence suggests a link between periodontitis (PD) and hypertension, but the nature of this association remains unclear. The overall aim of this review was to critically appraise the evidence linking these two common disorders. Systematic search was conducted for studies published up to December 2018. Prevalence of hypertension in patients with PD (moderate/severe groups) vs. those without PD (non-PD) was the primary outcome. Additional outcomes included adjusted mean difference in systolic (SBP) and diastolic (DBP) blood pressure (BP) levels in PD vs. non-PD, assessment of biomarkers in PD and hypertension, and BP changes after periodontal therapy. From 81 studies selected, 40 were included in quantitative meta-analyses. Diagnoses of moderate-severe PD [odds ratio (OR) = 1.22; 95% confidence interval (CI): 1.10-1.35] and severe PD (OR = 1.49; 95% CI: 1.09-2.05) were associated with hypertension. Prospective studies confirmed PD diagnosis increased likelihood of hypertension occurrence (OR = 1.68; 95% CI: 0.85-3.35). Patients with PD exhibited higher mean SBP [weighted mean difference (WMD) of 4.49 mmHg; 95% CI: 2.88-6.11] and DBP (2.03 mmHg; 95% CI: 1.25-2.81) when compared with non-PD. Lastly, only 5 out of 12 interventional studies confirmed a reduction in BP following periodontal therapy, ranging from 3 to 12.5 mmHg of SBP and from 0 to 10 mmHg of DBP. PD is associated with increased odds of hypertension (SORT C) and higher SBP/DBP levels. The evidence suggesting that PD therapy could reduce BP is inconclusive. Although additional research is warranted on this association, these results suggest that oral health assessment and management of PD could not only improve oral/overall health and quality of life but also be of relevance in the management of patients with hypertension. **Keywords:** Periodontal therapy; Blood pressure; Hypertension; Inflammation; Oral health; Periodontal diseases; Periodontitis.

Zhao M-J, Qiao Y-X, Wu L, Huang O, Li B-H, Zeng X-T (2019). Periodontal Disease Is Associated With Increased Risk of Hypertension: A Cross-Sectional Study. *Front Physiol* DOI: <https://doi.org/10.3389/fphys.2019.00440> At: <https://www.frontiersin.org/articles/10.3389/fphys.2019.00440/full> Abstract: **Objective:** Published evidence showed that periodontal disease is associated with hypertension. However, relevant findings remain controversial, with few evidences focusing on Chinese population. Therefore, the aim of this study was to investigate the association between periodontal disease and hypertension in Chinese population. **Methods:** A total of 4,930 participants from an available health examination that was carried out in 2017 were selected for this retrospective study. The correlations between periodontal disease and hypertension were investigated using univariate and multiple logistic regression analyses and propensity score adjusted analysis. Interaction and subgroup analyses were also used to detect variable factors. **Results:** Finally, a total of 3,952 participants aged 30–68 years were eligible for this study. The results showed that hypertension risk was statistically significant associated with periodontal disease either in unadjusted (OR = 1.28, 95%CI = 1.14–1.47) or in adjusted (OR = 1.34, 95%CI = 1.14–1.58) model. Result from propensity score adjusted analysis also demonstrated a similar association (OR = 1.23, 95%CI = 1.06–1.42). **Conclusion:** Periodontal disease is significantly and positively correlated with increased risk of hypertension in Chinese population, and exact mechanisms of this association should be explored in future.

*Br. Dent. J.* (2019). New evidence links periodontitis with hypertension. *Br Dent J* 227**,** 546 (2019). <https://doi.org/10.1038/s41415-019-0870-x> At: <https://www.nature.com/articles/s41415-019-0870-x>

Czesnikiewicz-Guzik M, Osmenda G, Siedlinski M, Nosalski R, Pelka P, Nowakowski D, Wilk G, Mikolaiczyk TP, Shramm-Luc A, Furtak A, Maturik P, Koziol J, Drozdz M, Muñoz-Aguilera E, Tomaszekski M, Evangelou E, Calufield M, Grodzicki T, D’Aiuto F, Guzik TJ (2019). Causal association between periodontitis and hypertension: evidence from Mendelian randomization and a randomized controlled trial of non-surgical periodontal therapy. *Eur Heart J* 40(42): 3459-3470. DOI: 10.1093/eurheartj/ehz646 At: <https://www.ncbi.nlm.nih.gov/pubmed/31504461> *AIMS: Inflammation is an important driver of hypertension. Periodontitis is a chronic inflammatory disease, which could provide a mechanism for pro-hypertensive immune activation, but evidence of a causal relationship in humans is scarce. We aimed to investigate the nature of the association between periodontitis and hypertension.*

*CardioSmart News* (2018). Study Confirms the Link Between Gum Disease and High Blood Pressure. At:<https://www.cardiosmart.org/news/2018/10/study-confirms-the-link-between-gum-disease-and-high-blood-pressure>Gum disease may make it more difficult to treat high blood pressure, based on a recent study that links gum disease to higher blood pressure levels. Findings were recently published in the American Heart Association journal Hypertension and help support the association between gum disease and poorer heart health. - The study included more than 11,750 U.S. adults who completed health surveys and underwent dental exams between 2009 and 2014. Participants were part of the National Health and Nutrition Examination Survey, which has studied the health of Americans since the early 1960s. - The goal of the recent analysis was to see if gum disease has any impact on blood pressure control. It’s currently estimated that one in three U.S. adults is living with high blood pressure, yet less than half have their condition under control. - Based results of the health questionnaires, 3,626 of patients reported being on treatment for high blood pressure. Of these, just over half had gum disease based on results of dental exams. Most had moderate gum disease, although a small portion had mild or severe gum disease. - After analysis, researchers found that among participants with high blood pressure, those with gum disease had 2.3-3mmHg higher systolic blood pressure than those with healthy gums. Patients with gum disease were also less likely to have their blood pressure under control with medication than those without good oral health. - Researchers noted that the more severe gum disease was, the more likely it was that treatment for high blood pressure would fail. - What this study suggests, according to authors, is that gum disease may impact outcomes in patients with high blood pressure. Findings show that treatment for high blood pressure may not be as effective in patients with gum disease as it would in patients with good oral health. Therefore, taking care of teeth and gums may be an important way to help promote a healthy blood pressure. - Of course, authors note that this study only looked at data from one period of time and can’t tell us about cause and effect. However, findings add to a body of evidence linking gum disease to poorer heart health. - Gum disease, also referred to as periodontal disease, causes chronic inflammation of the gums. It currently affects nearly half of Americans over 30. Experts believe that that inflammation from gum disease may trigger or worsen inflammation in other parts of the body, including blood vessels and arteries. While we don’t fully understand this association, we know that it’s important to maintain good oral health in addition to taking steps to promote better cardiovascular and overall health.

Pietropaoli D, Del Pinto R, Ferri C, Wright JTJr, Giannoni M, Ortu E, Monaco A (2018). Poor Oral Health and Blood Pressure Control Among US Hypertensive Adults: Results from the National Health and Nutrition Examination Survey 2009 to 2014. *Hypertension* 72:1365–1373. Doi: <https://doi.org/10.1161/HYPERTENSIONAHA.118.115> At: <https://www.ahajournals.org/doi/10.1161/HYPERTENSIONAHA.118.11528> Abstract: Periodontal disease is a chronic inflammatory disorder of the tissues surrounding the teeth, with evidence of systemic effects. Some studies showed the benefit of periodontal therapy on blood pressure (BP), but the impact of periodontitis on BP control is unknown. We retrospectively analyzed cross-sectional, nationally representative data from treated hypertensive adults aged ≥30 years with and without periodontitis. BP was examined as both continuous (mm Hg) and categorical (treatment goal achievement status according to guidelines: at goal and above goal) variable according to the presence or absence of periodontitis and its clinical parameters (probing depth, clinical attachment loss, and disease severity [mild, moderate, and severe]). Systolic BP means and odds ratios for uncontrolled BP according to the presence and severity of periodontitis were calculated using progressively adjusted models. Among treated hypertensive adults, mean systolic BP was about 2.3 to 3 mm Hg higher in the presence of periodontitis (*P*<0.0001). Periodontitis was associated with unsuccessful antihypertensive treatment after multiple adjustments, with higher odds by disease severity. A good periodontal health is associated with better systolic BP profile during antihypertensive therapy by about 2.3 to 3 mm Hg and with lower odds of antihypertensive treatment failure. Dedicated studies are needed to test the impact of periodontal therapy on BP and the long-term effects on cardiovascular outcomes of this complementary approach to systemic health.

Zhou Q-B, Xia W-H, Ren J, Yu B-B, Tong X-Z, Chen Y-B, Chen S, Feng L, Dai J, Tao J, Yang J-Y (2017). Effect of Intensive Periodontal Therapy on Blood Pressure and Endothelial Microparticles in Patients With Prehypertension and Periodontitis: A Randomized Controlled Trial. *J Periodontol* 88(8): 711-722. DOI: [10.1902/jop.2017.160447](https://doi.org/10.1902/jop.2017.160447) At: <https://pubmed.ncbi.nlm.nih.gov/28452620/> Abstract: **Background:** Although some studies show a positive association between periodontitis and blood pressure (BP) elevation, research on the effect of intensive periodontal treatment on decline in BP levels and endothelial microparticles (EMPs) without any antihypertensive management is lacking. Therefore, the present clinical trial explores whether intensive periodontal therapy would lower BP levels and EMPs of patients with prehypertension with periodontitis. **Methods:** From a total 107 patients, 95 underwent randomization (47 assigned to control-treatment [CT] group and 48 assigned to intensive-treatment [IT] group) and completed the trial. Patients received intervention for 4 consecutive weeks and were followed for 6 months. Levels of BP and EMPs were evaluated at baseline and 1, 3, and 6 months after intervention. **Results:** Periodontal conditions were significantly improved (P <0.05) 6 months after intensive periodontal treatment. In parallel, the primary outcomes including systolic and diastolic BP and EMPs were markedly reduced in the IT group compared with the CT group (absolute difference: 12.57 and 9.65 mm Hg and 581.59/μL, respectively; 95% confidence intervals: 10.45 to 14.69, 7.06 to 12.24, and 348.12 to 815.06, respectively; P <0.05). Reduction in BP levels and EMPs was related to improvement in probing depth (r = 0.358, 0.363, and 0.676, respectively, by the Pearson product-moment correlation; P = 0.009, 0.008, and P <0.001, respectively). **Conclusion:** To the best knowledge of the authors, the present study demonstrates for the first time that intensive periodontal intervention without any antihypertensive medication therapy may be an effective means to lower levels of BP and EMPs in patients with prehypertension with periodontitis

Zagaria MAE (2016). Periodontitis: Risk for Atherosclerotic Vascular Disease? *USPharmacist* 2016(2): 9-11. At:<https://www.uspharmacist.com/article/periodontitis-risk-for-atherosclerotic-vascular-disease>

# Kawabata Y, Ekuni D, Miyai H, Katoaka K, Yamane M, Miuitani S, Irie K, Azuma T, Tomofuji T, Iwasaki Y, Morita M (2016). Relationship Between Prehypertension/Hypertension and Periodontal Disease: A Prospective Cohort Study. *Am J Hypertens* 29(3): 388-396. DOI: [10.1093/ajh/hpv117](https://doi.org/10.1093/ajh/hpv117) At: <https://pubmed.ncbi.nlm.nih.gov/26208668/> Abstract: Background: Most cross-sectional studies have found a significant positive relationship between periodontal disease and prehypertension/hypertension. However, these studies had limitations and there are few prospective cohort studies in young adults. The purpose of this prospective cohort study was to investigate whether periodontal disease was related to prehypertension/hypertension in Japanese university students. Methods: Students (n = 2,588), who underwent health examinations before entering university and before graduation, were included in the analysis. The association between periodontal disease such as the percentage of bleeding on probing (BOP) and community periodontal index (CPI) scores, and change in blood pressure status was determined. Results: At the reexamination, the numbers of participants with prehypertension (systolic blood pressure 120-139mm Hg or diastolic blood pressure 80-89mm Hg) and hypertension (≥140/90mm Hg) were 882 (34.1%) and 109 (4.2%), respectively. In a logistic regression model, the risk of hypertension was significantly associated with male (odds ratio (OR): 6.31; 95% confidence interval (CI): 2.63-15.13; P < 0.001), no habitual physical activity at baseline (OR: 2.90; 95% CI: 1.56-5.38; P < 0.01) and periodontal disease defined as the presence of both probing pocket depth (PPD) ≥ 4mm and BOP ≥ 30% at baseline (OR: 2.74; 95% CI: 1.19-6.29; P = 0.02) in participants with prehypertension at baseline. On the other hand, the risk of prehypertension was not associated with presence of periodontal disease (OR: 0.93; 95% CI: 0.51-1.70; P = 0.82). Conclusion: In the short-term prospective cohort study, a significant association between presence of periodontal disease and hypertension was observed in Japanese university students. Keywords: blood pressure; cohort studies; hypertension; periodontal disease; university students.

# Martin-Cabezas R, Seelam N, Petit C, Agossa K, Gaertner S, Tenenbaum H, Davideau J-L, Huck O (2016). Association between periodontitis and arterial hypertension: A systematic review and meta-analysis*. Am Heart J* 180: 98-112. DOI: [10.1016/j.ahj.2016.07.018](https://doi.org/10.1016/j.ahj.2016.07.018) At: <https://pubmed.ncbi.nlm.nih.gov/27659888/> Abstract: ****Background:**** Several studies have shown that periodontal diseases are associated with hypertension (HT). However, heterogeneity among populations, diagnosis criteria, and shared risk factors represent some difficulties in terms of interpretation. Therefore, the aim of this study was to determine the magnitude of the association between periodontal diseases and HT. ****Methods and results:**** A systematic review and meta-analysis, including studies published up to June 2016, have been performed. Sixteen studies assessing the association between periodontal diseases and HT have been included. The meta-analysis considering all included studies (moderate to severe periodontitis) showed that the presence of HT was associated with the presence of periodontal diseases (OR, 1.50; 95% CI, 1.27-1.78). To reduce potential bias, a stratified analysis has been performed illustrating the impact of inclusion criteria and adjustments on the magnitude of the association. Interestingly, when only studies with secure diagnosis of severe periodontitis and HT were considered, an OR=1.64 (95% CI, 1.23-2.19) has been measured. ****Conclusions:**** Periodontal diseases are associated with a higher risk of HT especially for severe periodontitis. However, no conclusions could be made regarding the causative involvement of periodontal diseases mainly due to the reduced number of available prospective studies and remaining questions regarding underlying biological mechanisms.

# Teeuw WJ, Slot DE, Gerdes VEA, Abbas F, D‘Aiuto F, Kastelein JJP, Loos BG (2014). Treatment of periodontitis improves the atherosclerotic profile: a systematic review and meta-analysis. *J Clin Periodontol* 41(1):70-79. DOI: [10.1111/jcpe.12171](https://doi.org/10.1111/jcpe.12171) At: <https://pubmed.ncbi.nlm.nih.gov/24111886/>

# Orlandi M, Suvan J, Petrie A, Donos N, Masi S, Hingorani A, Deanfield J, D’Aiuto (2014). Association between periodontal disease and its treatment, flow-mediated dilatation and carotid intima-media thickness: a systematic review and meta-analysis. *Atherosclerosis* 236(1):39-46. DOI: [10.1016/j.atherosclerosis.2014.06.002](https://doi.org/10.1016/j.atherosclerosis.2014.06.002) At: <https://pubmed.ncbi.nlm.nih.gov/25014033/>

Leong X-F, Ng C-Y, Badiah B, Das S (2014). Association between Hypertension and Periodontitis: Possible Mechanisms, *The Scientific World J*, Vol 2014, ID 768237, 11 pp. DOI: <https://doi.org/10.1155/2014/768237> At: <https://www.hindawi.com/journals/tswj/2014/768237/> Abstract: This review is to examine the current literatures on the relationship between periodontitis and hypertension as well as to explore the possible biological pathways underlying the linkage between these health conditions. Hypertension is one of the major risk factors for cardiovascular diseases. Oxidative stress and endothelial dysfunction are among the critical components in the development of hypertension. Inflammation has received much attention recently and may contribute to a pivotal role in hypertension. Periodontitis, a chronic low-grade inflammation of gingival tissue, has been linked to endothelial dysfunction, with blood pressure elevation and increased mortality risk in hypertensive patients. Inflammatory biomarkers are increased in hypertensive patients with periodontitis. Over the years, various researches have been performed to evaluate the involvement of periodontitis in the initiation and progression of hypertension. Many cross-sectional studies documented an association between hypertension and periodontitis. However, more well-designed prospective population trials need to be carried out to ascertain the role of periodontitis in hypertension.

Paizan MLM, Vilela-Martin JF (2014). Is There an Association between Periodontitis and Hypertension? *Curr Cardiol Rev* 10(4): 355-361. doi: [10.2174/1573403X10666140416094901](https://dx.doi.org/10.2174%2F1573403X10666140416094901) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4101200/> Abstract:Cardiovascular diseases are the leading cause of deaths. Also, cardiovascular risk factors start the atherosclerotic process, which leads to cardiovascular diseases. Nowadays, periodontal disease can also be considered another cardiovascular risk factor. It involves inflammatory, immunological and humoral activities, which induce the production of proinflammatory cytokines and the destruction of the epithelium. This allows the entry of endotoxins and exotoxins in the bloodstream, which may contribute to atherogenesis and thromboembolic events. There is also direct invasion of the vessel wall by oral pathogens, triggering an inflammatory response that produces endothelial dysfunction. In hypertension, changes in microcirculation can cause ischemia in the periodontium, which favors periodontal disease. Moreover, endothelial dysfunction promotes the formation of atherosclerotic plaque and the development of lesions in target organs. Periodontitis has also been associated with insulin resistance and a higher risk for the metabolic syndrome, which is characterized by oxidative stress. This seems to act as a common link to explain the relationship between each component of the metabolic syndrome (including hypertension) and periodontitis. This article will discuss clinical and experimental evidence, as well as possible pathophysiologic mechanisms and links involved in the relationship among periodontal disease, hypertension and cardiovascular disease.

Vidal F, Cordovil I, Figueredo CMS, Fischer RG (2013). Non‐surgical periodontal treatment reduces cardiovascular risk in refractory hypertensive patients: a pilot study. *J Clin Periodontol* 40(7): 681-687. DOI: <https://doi.org/10.1111/jcpe.12110> At: <https://pubmed.ncbi.nlm.nih.gov/23639076/>

Desvarieux M, Demmer RT, Jacobs DRJr, Rundek T, Boden-Albala B, Sacco RL, Papapanou PN (2010). Periodontal bacteria and hypertension: the oral infections and vascular disease epidemiology study (INVEST). *J Hypertens* 28(7): 1413-1421. DOI: 10.1097/HJH.0b013e328338cd36 At: <https://pubmed.ncbi.nlm.nih.gov/20453665/> Abstract: **Objective:** Chronic infections, including periodontal infections, may predispose to cardiovascular disease. We investigated the relationship between periodontal microbiota and hypertension. **Methods and results:** Six hundred and fifty-three dentate men and women with no history of stroke or myocardial infarction were enrolled in INVEST. We collected 4533 subgingival plaque samples (average of seven samples per participant). These were quantitatively assessed for 11 periodontal bacteria using DNA-DNA checkerboard hybridization. Cardiovascular risk factor measurements were obtained. Blood pressure and hypertension (SBP > or =140 mmHg, DBP > or =90 mmHg or taking antihypertensive medication, or self-reported history) were each regressed on the level of bacteria: considered causative of periodontal disease (etiologic bacterial burden); associated with periodontal disease (putative bacterial burden); and associated with periodontal health (health-associated bacterial burden). All analyses were adjusted for age, race/ethnicity, sex, education, BMI, smoking, diabetes, low-density lipoprotein and high-density lipoprotein cholesterol. Etiologic bacterial burden was positively associated with both blood pressure and prevalent hypertension. Comparing the highest and lowest tertiles of etiologic bacterial burden, SBP was 9 mmHg higher, DBP was 5 mmHg higher (P for linear trend was less than 0.001 in each case), and the odds ratio for prevalent hypertension was 3.05 (95% confidence interval 1.60-5.82) after multivariable adjustment. **Conclusion:** Our data provide evidence of a direct relationship between the levels of subgingival periodontal bacteria and both SBP and DBP as well as hypertension prevalence.

Tonetti MS, D’Aiuto F, Nibali L, Donald A, Storry C, Parkar M, Suvan J, Hingorani AD, Vallance P, Deanfield J (2007). Treatment of periodontitis and endothelial function. *New Engl J Med* 356(9): 911-920. DOI: 10.1056/NEJMoa063186 At: <https://pubmed.ncbi.nlm.nih.gov/17329698/>

Hein C, Small D (2006). Combatting Diabetes, Obesity, Periodontal Disease and Interrelated Inflammatory Conditions with a Syndemic Approach. *Grand Rounds in Oral Sys Med* 1(2): 36-47. At: <https://www.caseyhein.com/wp-content/uploads/Combating-Diabetes-Obesity-Periodontal-Disease-and-Interrelated-Inflammatory-Conditions-with-a-Syndemic-Approach-1.pdf> Abstract This article discusses the standard of care-practice gap in diabetes care and makes a compelling case for why dental and medical professionals need to collaborate in integrating oral care in diabetes management. Epidemiologic trends and the etiological rationale for adopting a syndemic orientation to the epidemic of obesity, insulin resistance, diabetes and related inflammatory conditions are presented. The term “syndemic” describes a set of 2 or more linked health problems that interact synergistically to contribute to the excess burden of disease in a population with a specific focus on the forces that bind the problems together. The authors suggest that instead of approaching prevention and treatment of chronic disease states as discrete, individual problems, a syndemic perspective would allow healthcare providers to view chronic inflammatory diseases or conditions such as diabetes, obesity, insulin resistance, hypertension, hyperlipidemia, and infections like periodontal disease as an interrelated cluster of maladies with specific focus on the ties or forces (acquired and environmental risk factors) that bind these conditions together. The article also discusses possibilities for large scale population-based intervention strategies and micro-systems of collaboration targeting obesity, diabetes, and periodontal disease through health promotion in childhood and adolescent populations. Also included are aggressive screening and risk reduction strategies targeting patients with risk factors for diabetes and patients who have undetected diabetes.

Miyakawa H, Honma K, Qi M, Kuramitsu HK (2004). Interaction of *Porphyromonas gingivalis* with low-density lipoproteins: implications for a role for periodontitis in atherosclerosis. *J Periodontal Res* 39(1):1-9. DOI: <https://doi.org/10.1111/j.1600-0765.2004.00697.x> At: <https://pubmed.ncbi.nlm.nih.gov/14687221/>

D'Aiuto F, Parkar M, Andreou G, Suvan J, Brett PM, Ready D, Tonetti MS (2004). Periodontitis and systemic inflammation: control of the local infection is associated with a reduction in serum inflammatory markers. *J Dent* Res 83:156-160, 2004. DOI: [10.1177/154405910408300214](https://doi.org/10.1177/154405910408300214) At: <https://pubmed.ncbi.nlm.nih.gov/14742655/>

The introduction for this bibliographic resource was contributed by Dr. Anthony Iacopino, Executive Director, International Centre for Oral Systemic Health (ICOSH), University of Manitoba, Winnipeg.