



Is subclinical cardiovascular disease linked with periodontal disease in diabetic and non-diabetic subjects?

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ARTICLE INFO

Keywords

Cardiovascular diseases
Periodontitis
Vascular stiffness
Carotid intima-media thickness
Diabetes mellitus
Inflammation

ABSTRACT

Periodontal disease leads to a systemic hyper-inflammatory state that might impair other co-morbidities including cardiovascular disease. Evidence-based findings showed that periodontitis may be linked with sub-clinical signs of cardiovascular diseases such as arterial stiffness. Nevertheless, some contrasting results have been reported over the years. A cross-sectional study regarding the relationship between periodontal disease and subclinical cardiovascular diseases, in non-diabetic and diabetic individuals, has been recently published. Therefore, the aim of this commentary is to give an in-depth on this topic.

The article by Bailey et al. investigated the association between periodontal disease severity and subclinical markers of cardiovascular diseases (CVD), in 144 diabetic (Type 1 diabetes) and 148 non-diabetic patients.¹ The authors found that, compared to healthy subjects, diabetic patients had higher mean probing depth, higher mean attachment loss, lower brachial artery distensibility (brachD) (mean 5.8 vs. 6.4 mmHg; $p < 0.01$), higher carotid intima-media thickness (c-IMT) (mean 0.68 vs. 0.64 mm; $p < 0.01$), and higher pulse wave velocity (PWV) (mean 8.3 vs. 7.8 m/s; $p < 0.01$). However, no significant associations between periodontitis and CVD parameters were found, after adjusting for age, gender, race/ethnicity, lipid measures, blood pressure, smoking, and medication use.¹

Since it might be detected before the occurrence of clinically apparent CVD, arterial stiffness is considered as a marker of arteriosclerosis and a predisposing factor for the future development of CVD. Definitely, increased arterial stiffness is associated with modifications in nitric oxide production, impaired endothelial function, and reduced vasodilation.² Past literature highlights that an intensive periodontal treatment may result in acute, short-term systemic inflammation^{3,4} and endothelial dysfunction.⁵

Related to this topic, a previous cross-sectional study among 121 patients with Type 2 diabetes and either periodontal health, gingivitis or periodontitis, observed that periodontal inflammation was associated with c-IMT and blood pressure but not with PWV.⁶ A systematic review and meta-analysis reported that subjects affected by metabolic

syndrome (MetS) are about twice as likely to have periodontitis than the rest of the population (OR: 2.09; 95 % CI: 1.28 to 3.44).⁷ Another cross-sectional study investigated the systemic impact of periodontitis in 103 patients with MetS, by assessing measures of sub-clinical atherosclerosis, and showed that patients with severe periodontitis had increased average ventricular relative wall thickness (RWT) (that is related to concentric left ventricular remodeling, a predictive index of cardiovascular events), whereas no associations between periodontitis and c-IMT, PWV, and left ventricular mass index (LVM) were detected after adjusted analyses.⁸ Overall, despite some studies which did not find any correlation between periodontitis and the abovementioned subclinical CVD parameters, several systematic reviews reported that periodontal disease is associated with arterial dysfunction measured as increased c-IMT and flow-mediated dilation (FMD)⁹ and increased PWV.^{10,11}

In contrast to Bailey and co-workers, proceedings of the workshop jointly organised by the European Federation of Periodontology (EFP) and the World Heart Federation (WHF) reported that there is evidence from epidemiological studies that periodontitis patients have a higher prevalence of subclinical CVD, exhibiting significant endothelial dysfunction.¹² In particular, an imaging study associated high levels of antibodies against periodontal pathogens and a lower extent of positive atheromatous plaque remodeling.¹³ Besides, some authors interestingly observed that atherogenic dyslipidemia and elevated circulating Heat-shock protein 60 kDa (Hsp60) tended to be linked and associated to periodontal disease.¹⁴ In fact, 22 untreated patients with mild

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<https://doi.org/10.1016/j.jdiacomp.2023.108580>

Received 16 July 2023; Accepted 29 July 2023

Available online 5 August 2023

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periodontitis presented increased small, dense low-density lipoproteins (LDL) and serum Hsp60 concentrations, when compared to 22 age- and BMI-matched controls, and both parameters showed a strong positive correlation; in addition, elevated levels of circulating Hsp60 significantly correlated with the severity of periodontitis and might be considered as another potential predictor of risk for CVD.¹⁴

Despite Bailey and his team corroborated previous findings regarding the association between periodontitis and subclinical CVD (e. g., arterial stiffness), they did not find any significant interactions between periodontal parameters and Type 1 diabetes on cardiovascular outcomes. This was probably due to several limitations of the trial such as the study design, the limited number of participants with periodontitis and the age of the included subjects (mean age was early 50s).¹ In light of the existing literature^{15,16}, this is quite controversial and urges further investigation. Thus, larger methodologically robust clinical trials with longer follow-ups are needed in order to draw stronger conclusions.

Declaration of competing interest

None.

References

- Bailey RJ, Sarkar A, Snell-Bergeon JK, et al. Periodontitis and cardiovascular risk factors in subjects with and without type 1 diabetes: a cross sectional analysis. *J Diabetes Complicat.* 2023;37:108494. <https://doi.org/10.1016/j.jdiacomp.2023.108494> (Jul).
- Laurent S, Cockcroft J, Van Bortel L, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J.* 2006;27:2588–2605. <https://doi.org/10.1093/eurheartj/ehl254> (Nov).
- Graziani F, Cei S, Tonetti M, et al. Systemic inflammation following non-surgical and surgical periodontal therapy. *J Clin Periodontol.* 2010;37:848–854. <https://doi.org/10.1111/j.1600-051X.2010.01585.x> (Sep).
- Mainas G, Ide M, Rizzo M, Magan-Fernandez A, Mesa F, Nibali L. Managing the systemic impact of periodontitis. *Medicina (Kaunas).* 2022;58. <https://doi.org/10.3390/medicina58050621> (Apr 29).
- Tonetti MS, D'Aiuto F, Nibali L, et al. Treatment of periodontitis and endothelial function. *N Engl J Med.* 2007;356:911–920. <https://doi.org/10.1056/NEJMoa063186> (Mar 1).
- Franek E, Januszkiewicz-Caulier J, Blach A, et al. Intima-media thickness and other markers of atherosclerosis in patients with type 2 diabetes and periodontal disease. *Kardiol Pol.* 2012;70:7–13.
- Nibali L, Tatarakis N, Needleman I, et al. Clinical review: association between metabolic syndrome and periodontitis: a systematic review and meta-analysis. *J Clin Endocrinol Metab.* 2013;98:913–920. <https://doi.org/10.1210/jc.2012-3552> (Mar).
- Nibali L, Donos N, Terranova V, et al. Left ventricular geometry and periodontitis in patients with the metabolic syndrome. *Clin Oral Investig.* 2019;23:2695–2703. <https://doi.org/10.1007/s00784-018-2667-8> (Jun).
- 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.* 2014;236:39–46. <https://doi.org/10.1016/j.atherosclerosis.2014.06.002> (Sep).
- Schmitt A, Carra MC, Boutouyrie P, Bouchard P. Periodontitis and arterial stiffness: a systematic review and meta-analysis. *J Clin Periodontol.* 2015;42:977–987. <https://doi.org/10.1111/jcpe.12467> (Nov).
- Darnaud C, Courtet A, Schmitt A, Boutouyrie P, Bouchard P, Carra MC. Association between periodontitis and pulse wave velocity: a systematic review and meta-analysis. *Clin Oral Investig.* 2021;25:393–405. <https://doi.org/10.1007/s00784-020-03718-2> (Feb).
- Sanz M, Marco del Castillo A, Jepsen S, et al. Periodontitis and cardiovascular diseases: consensus report. *J Clin Periodontol.* 2020;47:268–288.
- de Boer SP, Cheng JM, Rangé H, et al. Antibodies to periodontal pathogens are associated with coronary plaque remodeling but not with vulnerability or burden. *Atherosclerosis.* 2014;237:84–91. <https://doi.org/10.1016/j.atherosclerosis.2014.08.050> (Nov).
- Rizzo M, Cappello F, Marfil R, et al. Heat-shock protein 60 kDa and atherogenic dyslipidemia in patients with untreated mild periodontitis: a pilot study. *Cell Stress Chaperones.* 2012;17:399–407. <https://doi.org/10.1007/s12192-011-0315-1> (May).
- Sanz M, Cieriello A, Buyschaert M, et al. Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International Diabetes Federation and the European Federation of Periodontology. *J Clin Periodontol.* 2018;45(2):138–149. <https://doi.org/10.1111/jcpe.12808>.
- Paunica I, Giurgiu M, Dumitriu AS, et al. The Bidirectional Relationship between Periodontal Disease and Diabetes Mellitus-A Review. *Diagnostics (Basel).* 2023;13(4). <https://doi.org/10.3390/diagnostics13040681>. Feb 11.