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# Is there an association between periodontitis and arterial hypertension?

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## KEYWORDS

Blood pressure, Arterial hypertension, Oxidative stress, Endothelial function, Peripheral arterial disease, Myocardial infarction, Stroke, Sudden death, Heart failure, Kidney failure, Bacteria, Microbiota, Microbiome, Gingival disease, Periodontitis, Inflammation, Cytokines.

## ABSTRACT

*Aim: Periodontitis is estimated to affect more than 50% of the world population and, in its severe form, is the sixth most common human disease. Clinical evidence supports that periodontitis affects systemic endothelial function and this could have an impact on hypertension; some reports suggest possible direct effects of microbiota-related oral bacteraemia also in the vascular dysfunction. The aim of the present paper is to understand the pathogenesis of hypertension and its association with periodontitis as well as the possible common mechanisms involved.*

*Methods: A review of the literature was performed, by querying MEDLINE, in order to analyze recent data supporting that patients with periodontitis have an increased likelihood to have arterial hypertension. The conceptual framework supporting this hypothesis is discussed.*

*Results: The data support that, in the presence of moderate periodontitis, the probability of having high blood pressure is 22% and this probability increases to 49% for severe forms. This condition can potentially contribute to pro-hypertensive immunity in a number of ways; moreover, it could be associated with permanent endothelial dysfunction. Thus, it has become evident that inflammation and immune system have a causal role in pathogenesis of hypertension, though this mechanism is still unclear.*

*Conclusion: From our analysis we can conclude that there is an association between periodontitis and hypertension and, therefore, periodontal therapy can be considered as a tool in the prevention and treatment of hypertension. The challenge is still open for research directed at understanding the pathogenesis of hypertension.*

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## Introduction

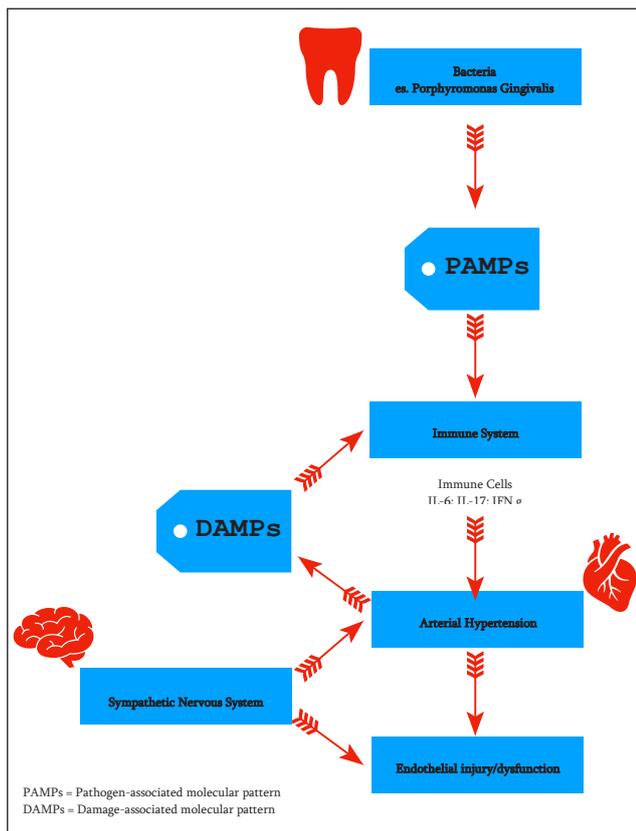
Arterial hypertension, defined as having values of  $\geq 140$  mmHg systolic blood pressure and/or  $\geq 90$  mmHg diastolic blood pressure (1), affects 30-45% of adult population and is closely associated with adverse cardiovascular events such as stroke, myocardial infarction, sudden death, heart failure, peripheral arterial disease and kidney failure. On the other hand, periodontitis affects over 50% of the world's population, with an even higher incidence in low and middle income countries (2).

Several studies have analyzed the relationship between periodontal diseases and arterial hypertension. By retrieving MedLine [Arterial Hypertension+Periodontitis, and/or periodontal disease; April 2020], we found about 680 matching records, among them, only 10 are clinical trials on

humans and 12 are systematic reviews of the last 5 years.

Among systematic reviews, a recent meta-analysis of all available studies (3) supports a significant "overlapping" between these two conditions: among the subjects suffering from severe gingival disease, hypertensives would represent 49%. In fact, the mean arterial pressure was found to be higher by 4.5 mmHg for PAs and 2 mmHg for Pad in patients affected with periodontitis than in those who were not; these data are commensurate with evidence that supports a 25% increase in the risk of death from heart attack or stroke due to an increase in PAs of 5 mmHg (4).

Arterial hypertension is considered a complex, multifactorial mechanism that includes endothelial dysfunction, oxidative stress, inflammation and immune response; indeed, all these factors are



**Figure 1** The possible connection between chronic inflammation and hypertension and pro-hypertensive immune activation

capable of altering neurohumoral blood pressure control (5). However, understanding the pathogenesis of hypertension, is still incomplete. On the other hand, periodontitis is a chronic multifactorial inflammatory disease caused by invasive pathogens that alter oral microbiota and microbiome, leading to a progressive destruction of the supporting tissues of the tooth with instability/loss of teeth and a negative impact on the quality of life of the patient (6).

The aim of this paper is to analyze the evidence linking periodontitis and hypertension in humans and the possible mechanism of this association.

### Disruption of microbial homeostasis

Periodontal inflammation initiates a systemic inflammation and monitoring inflammatory markers like C-reactive protein or fibrinogen levels could be useful for its detection (7). The interaction between the bacteria and the host is the most plausible biological mechanism that connects periodontitis to a series of chronic systemic diseases such as respiratory conditions, as chronic obstructive pulmonary diseases, and coronary heart diseases as

well as coronary heart diseases-related events, such as angina and infarction, atherosclerosis, stroke, diabetes mellitus, preterm labor and low-birth-weight delivery (8).

Microbiota is an aggregate of microorganism that colonize and reside on or within human tissues and biofluids; microbiome, on the other hand, indicates the totality of the genetic heritage owned by the microbiota. It is therefore evident that the microbiome refers to all gene expression.

The possible link between chronic inflammation and hypertension and pro-hypertensive immune activation is explained in figure 1.

### Hypertension and periodontitis

The cause of hypertension is a question unsolved. To address this question, analysis has taken two roads: the first examined genetic interferences and the second benefited from randomized clinical trial results. Recent large-scale genome-wide association studies identified four polymorphisms that have been associated with periodontitis. Mendelian randomization were used and this method identified horizontal pleiotropic variants and showed significant influence of periodontitis on all blood pressure values, systolic, diastolic and average. To confirm the association between periodontal disease and hypertension, a randomized controlled trial was performed on the effects of periodontal therapy on hypertension; it was observed that 24 h systolic and diastolic ambulatory pressure monitoring in patients treated with intensive periodontal treatment resulted in a significant systolic and diastolic blood pressure decrease. Furthermore, systemic inflammation measured by the level of circulating cytokines (IFN-g, IL-17A, TNF- $\alpha$ , IL-6) significantly decreased in patients undergoing intensive periodontal therapy (9).

We know that in periodontal disease pathogenesis, cytokines produced by cells of the innate immune response, including TNF- $\alpha$ , IL-1b and IL-6, are the first to be secreted after microbial recognition (10). Bacteria and inflammatory mediators can enter the blood and spread systemically with a measurable impact on systemic inflammation (11). Using DNA amplification techniques periodontal bacterial DNA has been detected in carotid atheroma (12). Periodontal disease is not universally expressed in subjects with poor oral hygiene, the expression of the disease also requires a sensitive host (13).

### Conclusion

Periodontitis is estimated to affect more than 50% of the world's population and, in its severe form, is the sixth most common human disease. As stated above, clinical evidence supports the notion that periodontitis affects systemic endothelial function and this could

have an impact on hypertension; some reports suggest possible direct effects of microbiota-related oral bacteraemia also in the vascular dysfunction.

The postulated association between periodontitis and hypertension has been verified as statistically significant, therefore, a possible indication is that periodontal therapy can be instrumental in the prevention and treatment of hypertension.

In conclusion, a change of paradigm is needed and we should start considering oral health as a global priority. The challenge for research in this area consists, therefore, in understanding the pathogenetic mechanisms that shape these relationships and, in the field of personalized medicine, informing patients with periodontal disease on the risk of having/developing high blood pressure and providing oral health advice in people already affected. In patients unaware of having high blood pressure, a simple way could be measuring blood pressure before the dental visit.

## Perspective

The association between periodontitis and the risk of developing cardiovascular disease remains a topic of extreme interest. Thinking that an intensive periodontal treatment might contribute to a significant reduction of cardiovascular hard endpoints may be a historic breakthrough.

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