



## Review

## Periodontitis and blood pressure: The concept of dental hypertension

Costas Tsioufis\*, Alexandros Kasiakogias, Costas Thomopoulos, Christodoulos Stefanadis

First Cardiology Clinic, University of Athens, Hippokraton Hospital, Athens, Greece

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## ABSTRACT

Chronic periodontitis is a common inflammatory disorder that is being contemplated as a risk factor for atherosclerotic complications. Current epidemiological evidence also supports its potential association with increases in blood pressure levels and hypertension prevalence. Furthermore, data from cross-sectional studies suggest that in hypertensive subjects periodontitis may enhance the risk and degree of target organ damage. A possible pathogenetic background of an effect of periodontitis on blood pressure should include the systemic generalization of the local oral inflammation, the role of the host immune response, the direct microbial effect on the vascular system and alterations in endothelial function. Inversely, the concept of hypertension unfavorably affecting periodontal tissues cannot be excluded. The two conditions share multiple common risk factors that should be readily controlled for when assessing a possible association. Thoroughly designed prospective and interventional trials are needed in order to determine the impact of periodontitis on blood pressure regulation and incident hypertension and its integration in the clinical approach of both dental and hypertensive patients.

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\* Corresponding author at: 3 Kolokotroni Str., P.Penteli, 15236 Athens, Greece. Tel.: +30 210 6131393; fax: +30 210 7701950.  
 E-mail address: [ktsioufis@hippocratio.gr](mailto:ktsioufis@hippocratio.gr) (C. Tsioufis).

## 1. Introduction

Periodontal disease is a chronic infection that has been documented to insult over 50% of the general population. If left untreated, it leads to deterioration of the supportive tissue of the teeth and eventually to tooth loss [1,2]. Hypertension is also highly prevalent affecting about 30% of adults and is a major cause of cardiovascular morbidity and mortality. Over twenty years ago these two conditions would seem profoundly unrelated and yet research on alternate risk factors for cardiovascular disease has implicated the diseased periodontium in the development of atherosclerotic complications. There is now evidence that supports periodontitis as a risk factor for stroke, coronary heart disease and possibly peripheral arterial disease [3,4]. Such a causal relation has been postulated to be both indirect, i.e. via shared risk factors [5], and direct through adverse systemic ramifications including an inflammatory generalization [1,2]. Impaired vasomotor function has also been consistently reported in periodontitis patients [6]. Since hypertension is a multifactorial disease, the complex sequelae of periodontitis, as reported in current literature, would make an association of the two conditions plausible. In the recent years, data primarily from population studies relating periodontitis to blood pressure (BP) have emerged. This review will therefore focus on running evidence on both an observational level and the possible mechanistic links.

## 2. Periodontitis and blood pressure: epidemiological data

Evidence up to date though restricted has been generally but not globally supportive of an existing association between periodontitis, BP and possibly hypertension [5,7–19]. However, the relevant studies are mostly cross-sectional, often sub-analysis of larger cohorts, and with a varying design and number of participants (Table 1). In some, BP assessment was not included in the primary scope [5,8–10], while others have focused on potential periodontitis surrogates such as tooth loss and oral hygiene [20–25] (Table 2). Considering these limitations, data may sometimes need to be derived with caution or even indirectly.

BP check in two time points one year apart was performed in a study of 364 apparently healthy and predominantly male young individuals, that applied a case definition of periodontitis [11]. Affected subjects compared to controls exhibited higher diastolic and at least a trend for higher systolic BP at the two visits, though hypertension prevalence did not differ. In a large Swedish population study a thorough periodontal examination including an X-ray was performed in a total of over 4200 adult participants of a wide age range [12]. An association of periodontitis severity and number of diseased periodontal pockets, but not of number of teeth, with hypertension prevalence was documented. Age stratification revealed that the finding remained significant in subjects over 60 years of age.

An analysis derived from data of 653 patients of The Oral Infections and Vascular Disease Epidemiology Study (INVEST) on a multiethnic cohort focused on direct assessment of the subgingival periodontal bacterial burden and its relation to BP, thus restricting the bias of clinical periodontal assessment [16]. Still, increasing percentage of sites per mouth with a 3 mm or more probing depth was associated with higher diastolic BP. After adjusting for common cardiovascular risk factors, inflammatory markers and non-causative bacteria, the highest compared to lowest tertile of etiologic bacterial burden was associated with an almost four-fold risk of hypertension, with the association being twice as large for men than women. Interestingly, putative and health-associated bacteria exhibited an inverse and absent association with hypertension respectively. Although the cumulative bacterial burden was also positively associated with BP and hypertension, this finding

suggests that diverse mixtures of periodontal bacteria may have a different impact on BP.

A recent large study was performed on data derived from the 3rd National Health and Nutrition Examination Survey (NHANES III) on almost 12,000 adult dentate participants to examine associations between periodontal disease measures and BP levels, by applying an extensive adjustment process [17]. Mean systolic BP was reported higher among participants with moderate or severe periodontitis compared to mild disease, in almost all age groups. A positive linear relationship between systolic BP and increased severity of periodontitis was further identified in middle-aged subjects. After adjusting for age, sex and ethnicity, a 10% rise in extent of gingival bleeding, attachment loss and pocket depth were associated with a 0.7, 0.2 and 0.6 mmHg elevation in systolic BP respectively. Quite unexpectedly, the fully adjusted model of the study revealed a consistent association of systolic BP and hypertension only with gingival bleeding, a marker of acute periodontal inflammation. Moreover, only in men was there a clear linear trend between periodontitis severity and hypertension risk.

Periodontal disease is a major cause of tooth extraction in adults and tooth loss, the ill-favored outcome of untreated periodontitis, could be construed at least partially as a surrogate for this condition. A study on Japanese relatively healthy nonsmoking postmenopausal women demonstrated that subjects with missing teeth had higher diastolic BP and a greater risk of high BP compared to controls [21]. Yet, in a study on a population derived from the Study of Health In Pomerania (SHIP), that is at a high risk for both tooth loss and hypertension, only in men was there a positive association of fewer teeth with greater systolic BP and hypertension [22]. This finding was even stronger in patients not taking antihypertensive medication. The same working group investigated the relation of echocardiographically assessed left ventricular dimensions to teeth count in middle-aged and older people. They reported an inverse relation of left ventricular mass and hypertrophy to teeth number after adjusting for confounders such as lifestyle and BP data, but this time in women and not in men [23]. The sex-related differences can be attributed to various factors including osteoporosis and bone turnover rate, or even a different susceptibility to infectious causes of hypertension such as periodontitis.

Teeth brushing by removing the dental plaque, is a simple measure of oral health and can be considered as a proxy of periodontal disease. In a very large cross-sectional population study in Japan, individuals that hardly ever brushed their teeth exhibited a higher risk for hypertension, as well as diabetes and hypertriglyceridemia compared to those that brushed after every meal [24]. In a recent British study, decreasing brushing frequency was associated with an increasing prevalence of hypertension and higher values of CRP and fibrinogen [25].

Preeclampsia originates from an abnormal inflammatory and vascular response to placentation that leads to endothelial dysfunction and maternal hypertension, while periodontitis may represent a vascular stressor for the pregnant woman. Though studies involving preeclampsia and periodontitis have not provided consistent results, in a recent systematic review periodontal disease during pregnancy was associated with a 76% higher risk of preeclampsia [26], while specific subgingival microbiota have been accused for a higher preeclamptic risk [27].

## 3. Hypertension and periodontitis: potential pathophysiologic links

Alterations in BP regulatory components such as the central and peripheral nervous system, the circulating and tissue renin–angiotensin–aldosterone-system, the kidney and complex feedback loops have been investigated as the substrate for the

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