

## Sex Differences in Periodontology as a Risk Factor for Cerebrovascular Diseases

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Periodontitis is a chronic inflammatory disease of the tooth supporting apparatus, the main clinical features of which include the loss of clinical attachment and alveolar bone, the formation of periodontal pockets and inflammation of the gingiva; the enlargement and recession of the gingiva, bleeding of the gingiva, increased mobility, migration and tooth loss are often present [1]. Gingival bleeding, as a common symptom of periodontal diseases, reflects reduced collagen density, increased density and fragility of blood vessels and reduced thickness and integrity of the epithelium. Thinned, fragile and interrupted epithelium of the pocket is therefore open door to the systemic circulation [2].

Periodontal medicine is a branch of periodontology focused on the relationship between periodontal health/disease and systemic health/disease, and was firstly mentioned in 1996. The basic concept is that periodontal inflammation and the periodontal bacteria contribute to the overall inflammatory burden at the systemic level and influence on the incidence, as well as progression of numerous chronic inflammatory conditions. Periodontal medicine recognizes the mutual connection that periodontitis affects the systemic health and that systemic health affects periodontitis [3].

It is generally considered that periodontitis is present in 20 - 50 % of the population [4]. At most 10 - 15 % of the population are affected by advanced forms of periodontal disease. NHANES study (3742 adults, age 30 and older) demonstrated that more

than 47 % of subjects have periodontitis - 8.7 % have initial, 30 % moderate and 8.5 % advanced form of the disease. 64 % of people over the age of 65 were diagnosed with moderate or advanced periodontitis. Periodontitis is more often found in men, smokers, people with a lower level of education and economic status [5]. Men more often have periodontitis, more often they ignore their oral health, they have worse oral hygiene habits, visit dentists less often, more often seek therapy for an acute conditions, and less often for disease prevention. Women show more positive attitudes about visits to the dentist, generally have better oral health than men, more regularly attend the check-ups and have greater oral health literacy [6]. Several common risk factors for periodontitis and cerebrovascular disease, such as diabetes mellitus, age and smoking, have been previously demonstrated. In our previous study of intima-media thickness (IMT) values in patients with chronic periodontitis we found significantly higher IMT values in older patients with periodontitis compared with periodontal healthy participants [7,8]. Smoking affects the course of periodontitis by weakening immune and vascular mechanisms. It affects the incidence and progression of periodontitis by 85 % (RR = 1.85). Data from USA shows that 16.7 % of men and 13.6 % of women are smokers [9,10]. The prevalence of moderate to advanced forms of periodontitis was 36.4% in subjects with diabetes mellitus type 2 and 22.7 % in subjects without diabetes. Diabetes mellitus type 2 is significantly associated with moderate to advanced periodontitis in men (OR = 1.47), but the same association was not found in women [11].

Tooth loss and chronic periodontitis are associated with subclinical atherosclerosis in men but not in women [12]. In men, about 10 % difference in carotid artery plaque prevalence and IMT values was found between the lowest and highest tertiles of periodontitis and tooth loss ( $p < 0.05$ ). The influence of sex on the prevalence of carotid artery plaques was evident at the age < 59 years. The difference in the prevalence of carotid artery plaques related to sex was 10%, 15 % and 25 % with regard to the increase in the number

of lost teeth. A significant association between tooth loss and the prevalence of carotid artery plaques was also detected: 0-9 missing teeth in 46 % of carotid plaques, and 10 or more missing teeth in 60 % of carotid plaques [13]. Therefore, tooth loss can serve as a marker of previous periodontal disease and is associated with subclinical atherosclerosis in men.

Periodontitis is strongly associated with atherosclerosis independent of other traditional risk factors. A systematic review examined 925 studies and included 9 observational studies with 7 out of 9 studies confirming the connection between tooth loss and stroke. In one study, the tooth loss was even found to be associated with a 12 % increase on the death from stroke [14].

Although periodontitis is more often found in men, there are certain cerebrovascular diseases that are more common in women, such as multiple sclerosis, migraine, Alzheimer's disease, etc. More than 60 % of patients diagnosed with Alzheimer's disease dementia are women. The risk for Alzheimer's disease is significantly higher in patients with periodontitis (OR = 1.78), especially in more severe forms of periodontitis (OR = 4.89) [15]. Migraine is reported to be 2-3 times more prevalent in women than in men. 68,282 patients with periodontitis were matched with the same number of controls (National Health Insurance Research Database, NHIRD) with a follow-up for 13 years. The incidence of migraine was significantly higher in the group with periodontitis (adjusted HR: 1.21,  $p < 0.001$ ). Women had a 2.69 times higher risk of migraine than men ( $p < 0.001$ ). Also, periodontitis was found to be associated with an increased risk for migraine [16]. Four times as many women have multiple sclerosis as men, and more and more women are developing it [17]. The prevalence of early periodontitis was 25.6 % and 15.4 % for multiple sclerosis and healthy subjects ( $p < 0.001$ ). OR was 1.86 for the diagnosis of periodontitis in patients with multiple sclerosis. Multiple sclerosis patients had higher odds of early periodontitis compared to controls (OR = 2.08); there is an association between periodontitis and multiple sclerosis in women, but not in men [17].

In conclusion, men more often have periodontitis and worse oral hygiene. The direct and indirect influence of periodontitis on systemic health has been proven and periodontitis and cerebrovascular disease share certain risk factors. Additional research is needed to examine the sex specific modifying roles in the association between periodontal diseases, tooth loss and cerebrovascular disease.

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