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The relationship of oral health with general health and NCDs: a brief review

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Oral health is closely related to systemic health. Periodontitis, a chronic inflammatory disease which is highly prevalent worldwide, interacts with a variety of noncommunicable diseases (NCDs). It is a risk factor in the complex pathogenesis of diabetes mellitus and cardiovascular disease and plays a role in the development of endocarditis and recurrent pneumonia in elderly people. However, the available data may be interpreted in different ways, and more and better-designed studies are still needed to answer relevant questions about the causal role of periodontitis in NCDs. What is clear is that periodontitis contributes to the systemic inflammatory burden. As periodontitis shares many common risk factors with NCDs, close collaboration between physicians and dentists is needed to increase the chance of early detection and improve the prevention and control of these conditions.

Key words: *Ageing, elderly, oral health, systemic health, noncommunicable diseases, NCD, periodontitis, public health*

INTRODUCTION

The links between oral diseases and general health are multifaceted and complex. Systemic diseases influence oral health, either directly via pathological pathways or indirectly via disease- or therapy-related behavioural changes. Changes in oral health also have an impact on systemic health. Tooth loss is closely associated with all-cause mortality, cardiovascular diseases mortality[1,2] and reductions in quality of life[3]. Periodontitis, a chronic inflammatory disease that is highly prevalent worldwide, is the oral health condition with the most prominent links to NCDs. When left untreated, periodontitis may lead to the progressive loss of tooth supporting structures and eventually result in tooth loss. Due to a dysbiosis, the originally physiological biofilm becomes pathogenic, as bacteria start to release virulence factors. The resulting inflammatory reaction leads not only to the destruction of the periodontium, but also creates conditions that help maintain the inflammatory reaction. Components of the pathogenic biofilm may therefore enter the body through the inflamed area, or may be inhaled or ingested, thereby increasing the risk of pneumonia[4] and gastritis[5]. During recent decades, periodontitis has been found to be associated with higher mortality and increased risk of numerous NCDs, such as diabetes mellitus, cardiovascular disease and chronic renal disease[6]. Moreover, the number of lost teeth has been shown to be a predictor of cardiovascular mortality[2,7].

Although these associations are clear and widely accepted, the causal role of periodontitis in the pathogenesis of such diseases is controversial. It is important to keep in mind that the associations between NCDs and periodontitis are risk indicators, meaning that the probability of systemic disease is increased with the presence of periodontitis. However, interventions such as periodontal therapy do not necessarily lead to an improvement in various systemic diseases. If periodontitis is a risk factor for a systemic disease, the probability of a patient developing the systemic disease is increased if they have periodontitis. In such a case, interventions would lead to improvements that would not necessarily be detectable at the individual level, but maybe statistically significant at the cohort level. If periodontitis is a direct cause of systemic disease, successful treatment of periodontitis will lead to

predictable resolution, or at least to predictable improvement, of systemic disease in all cases. This article describes the relationship of periodontitis and NCDs relevant to the elderly. The paper will emphasise the importance of pure associations, theoretical pathogenic pathways that link periodontitis to respective NCDs, the proof of principle (See *Table 1*) and the effect of periodontal treatment on surrogate parameters, and hard endpoints.

BACTEREMIA AND ENDOCARDITIS

Historically, the relationship of periodontitis with systemic health is illustrated by its role as a risk factor for endocarditis. Bacteremia, defined as the entry of bacteria into the blood stream[8], is one precondition for endocarditis. It can be initiated by any mechanical action on the skin or the mucosae. The amount and the frequency of bacteremia originating from the oral cavity depend on both the invasiveness of the mechanical action and the degree of inflammation at the interface between the hard and soft tissues[9,10]. The vast majority of bacteremia do not cause endocarditis, even in patients at high risk. However, in high-risk patients, the more frequently and the more intensely bacteremia occurs, the likelihood of endocarditis will increase.

Periodontal therapy can have a protective effect in people at risk of endocarditis[10–12], and its importance has led to new guidelines for the dental treatment of such patients. The guideline only recommends the preventive use of antibiotics in patients with the highest risk of endocarditis. It advises against antibiotic prophylaxis in those with medium and low risk due to the hazards of such medication[13], and the fact that the preventive fraction of antibiotic prophylaxis, even if taken correctly, is only around 50%[11,14]. The maintenance of a healthy periodontium should therefore be recommended in patients with any increased risk of endocarditis, although the highest degree of evidence is currently with studies using bacteremia as a surrogate marker for the risk of endocarditis.

DIABETES MELLITUS

The relationship between diabetes mellitus and periodontitis has been well known for decades, and periodontitis is regarded as one of the complications of poorly controlled diabetes mellitus[15]. In addition, it has also been known that acute inflammation may lead to poor glycemic control[16]. This is due to the fact that infections reduce the uptake of glucose into cells[17], and endotoxins and inflammatory mediators reduce the efficiency of insulin[18]. Due to these pathogenic pathways, periodontitis has long been regarded as a risk factor for poor blood glucose control in diabetes patients. To test this hypothesis, numerous randomised controlled clinical trials have been performed, all addressing the change in HbA1c after periodontal treatment. Several systematic reviews have condensed these results. Although there is some heterogeneity, the systematic reviews come to the conclusion that mechanical periodontal therapy 'associates with approximately a 0.4% reduction in HbA1c at 3 months, a clinical impact equivalent to adding a second drug to a pharmacological regime for diabetes'. However, it is important to remember that the effect of periodontal therapy on the individual patient's HbA1c levels is not predictable[19]. It may be that only a small fraction of patients contributed to the average reduction of blood glucose values and that for the majority, HbA1c values remained unchanged or even increased after periodontal therapy. The result of such therapy with respect to HbA1c levels may significantly differ from patient to patient. However, a broad awareness of this relationship should be familiar to both professionals and patients. Based on the scientific evidence, the European Federation for Periodontology (EFP)/American Academy of Periodontology (AAP) recommend that patients with diabetes

Table 1 Summary of the evidence on the relationship between periodontitis and NCDs relevant to seniors

Disease	Association	Pathomechanism	Proof of principle	Intervention studies (surrogate parameters)	Intervention studies (hard endpoints)	Pathogenic role of periodontitis
Endocarditis	Yes	Yes	Yes	Yes (+)	No	Strong risk factor
Diabetes mellitus	Yes	Yes	Yes	Yes (+)*	No	Risk factor
Cardiovascular disease	Yes	Yes	Yes	Yes (+)*	No	Risk factor
Chronic kidney disease	Yes	Yes	No	n. a.	Yes (+)	Risk factor
Recurrent pneumonia	Yes	Yes	No	n. a.	Yes (+)	Strong risk factor
COPD	Yes	Yes	No	n. a.	Yes (±)	To be clarified
Gastritis	Yes	Yes	No	n. a.	Yes (+)	To be clarified
Rhematoid arthritis	Yes	Yes	No	No	No	To be clarified
Cancer	Yes	Yes	No	No	No	To be clarified
Dementia	Yes	Yes	No	No	No	To be clarified

Animal studies showing the potential outcome in general.
COPD, chronic obstructive pulmonary disease; n. a., not applicable.
*Heterogeneity on the patient level.

should be monitored carefully and periodontitis, if present, should be treated promptly[20].

CARDIOVASCULAR DISEASE

As early as 1963, Mackenzie and De Millard[21] observed that patients with atherosclerosis had 62% more alveolar bone loss compared to healthy controls. This association was also seen in large cohort studies[22,23], although some of them have been criticised for not correcting for confounding variables such as smoking, which would prevent the associations from becoming statistically significant[17,24,25]. However, a potential pathologic pathway exists as the inflammatory burden contributes to atherosclerosis, and periodontal pathogens are found in atherosclerotic vessel walls[1,26,27]. Moreover, it has been shown in animal models that periodontal pathogens initiate the formation of atherosclerotic plaques[28,29] and *Porphyromonas gingivalis* in particular accelerates the development of atheroma in arterial walls in mice[30]. The 'proof of principle' therefore exists, and Beck *et al.*[22] have published a pathogenic model which hypothesises that there are patients who are susceptible to the side effects of chronic inflammation, and others who are not. To date, we know that there is a broad base of common genetic variants which increase both the risk of cardiovascular disease and the risk of periodontitis[31,32], adding to other common risk factors for both diseases such as increased blood glucose levels, psychosocial stress and smoking.

With this complexity, the potential interaction between cardiovascular disease and periodontitis is therefore both more theoretical and more difficult to prove than that between diabetes mellitus and periodontitis. Moreover, due to financial and ethical issues, no randomised controlled clinical trials on hard endpoints have been performed. Instead, several surrogate parameters have been explored in intervention trials to show the causal role of periodontitis on atherosclerosis. In these studies, it has been shown that periodontitis is associated with endothelial dysfunction of the brachial artery[33,34], which was reversed by periodontal therapy[35]. Most studies have been performed with C-reactive protein (CRP) as a surrogate parameter, showing a statistically significant reduction due to periodontal therapy. Several systematic reviews have, therefore, pointed out that periodontal therapy reduces surrogate parameters for cardiovascular disease[36,37]. However, in a consensus report based on the available evidence, the EFP/AAP conclude that 'while in vitro, animal and clinical studies do support the interaction and biological mechanism, intervention trials to date are not adequate to draw further conclusions'[38]. Similarly to diabetes mellitus[39], the report shows the heterogeneity of systemic inflammatory responses to periodontal therapy with respect to CRP values and points out that despite the overall reduction of CRP values on the patient level, scaling and root planning resulted in largely inconsistent and unsustainable results, without explanation for such heterogeneity. This may again indicate the role of periodontitis as a risk factor, whose clinical relevance is dependent on a complex interplay of various factors ranging from genetics to behaviour.

OVERVIEW OF CURRENT EVIDENCE ON OTHER NCDs

Besides the conditions described above, for which there exists a broad and diverse base of research, there are other NCDs which have been related to periodontitis. These are chronic kidney disease, recurrent pneumonia, chronic obstructive pulmonary disease, gastritis, rheumatoid arthritis, cancer and cognitive impairment. For a limited number of associations, intervention studies with hard endpoints exist that clearly show the benefits of periodontal treatment in such patients. Three separate systematic reviews, for example, have shown that interventions to reduce oral microbial load resulted in reduced risk of nosocomial hospital-acquired pneumonia, an issue of particular relevance for elderly populations[40]. On the other hand, evidence of a causal role of periodontitis and the benefits of therapy on the other systemic diseases are very weak. However, there is interest in these associations, and further research is needed to understand these relationships. The current state of knowledge for all conditions mentioned is summarised in *Table 1*.

CONCLUSION

Periodontitis is a preventable and treatable disease. Its treatment and prevention are therefore an important goal in itself. However, due to its nature as a chronic inflammatory disease and, as a consequence, the long-lasting inflammatory burden on the whole body, an increasing focus on periodontitis' causal role in other NCDs has been seen in the last 25 years. In most cases, associations between periodontitis and NCDs have been shown and pathogenic pathways are plausible, but final proof of a causal role has not yet been demonstrated. This is due to the fact that periodontitis and the NCDs are associated with a broad variety of common risk factors, which range from genetic predisposition to health awareness and preventive behaviour. Some data indicate that, on a patient level, different combinations of risk factors may determine the role that periodontitis and periodontal treatment play in other NCDs, but to date, the exact effect cannot be determined. However, periodontitis seems to qualify as one risk factor in the complex pathogenesis

of diabetes mellitus, cardiovascular disease, kidney disease and recurrent pneumonia in elderly patients. For other diseases, appropriate clinical studies to prove causality are either lacking or have not shown a clear effect.

Therefore, given the lack of data, the benefit of successful periodontal therapy in terms of effectiveness or efficiency, as well as the contribution of oral conditions to the prevention and control of NCDs, remains unclear. Regardless, it is clear that periodontitis contributes to a chronic inflammatory burden, which is of concern. Independent of the extent to which other NCDs are triggered, modified or caused by periodontitis, communication between physicians and dentists is desirable. Ageing is associated with an increase in risk factors for NCDs. Periodontitis is one of these potential risk factors and is modifiable. This opportunity should be seized.

Therefore, the following three suggestions are offered:

- Collaboration between dentists and physicians is required, and obstacles to the communication and exchange of information should be eliminated.
- Early detection of NCDs and oral diseases is essential. Interaction between dentists and physicians is necessary to optimise screening.
- Common risk factors require common/coordinated preventive strategies between dentists and physicians. In particular in tertiary prevention, health promotion measures should be coordinated among oral healthcare providers.

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Conflict of interest

The authors declare that they have no conflict of interest.

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