FOLIA MEDICA CRACOVIENSIA Vol. LXIV, 1, 2024: 25–37 PL ISSN 0015-5616 eISSN 2957-0557 DOI: 10.24425/fmc.2024.150139

The multifaceted impact of missing teeth on general health: A narrative review

Karolina Kramarczyk¹, Kamil Skowron², Paweł Skowron³, Tomasz Kaczmarzyk¹

¹ Department of Oral Surgery, Jagiellonian University Medical College, Kraków, Poland
 ² Department of Pathophysiology, Jagiellonian University Medical College, Kraków, Poland
 ³ Department of Physiology and Pathophysiology, Wrocław Medical University, Wrocław, Poland

Corresponding author: Karolina Kramarczyk, D.D.S. Department of Oral Surgery, Jagiellonian University Medical College, Kraków, Poland ul. Montelupich 4, 31-155 Kraków, Poland Phone: +48 12 424 54 68; Fax: +12 424 54 99; E-mail: karolina.kramarczyk@uj.edu.pl

Abstract: Tooth loss extends beyond oral health concerns, impacting overall well-being and quality of life. It is a global issue, with approximately 7% of individuals aged 20 years or older affected. Research reveals associations between tooth loss and cardiovascular diseases, including hypertension, atherosclerosis, and peripheral arterial disease, attributed mainly to chronic inflammation and altered dietary habits. However, tooth loss has also been associated with cognitive decline, depression, and certain cancers, including lung, head and neck, pancreatic, and esophageal, suggesting the involvement of complex pathophysiological mechanisms that are increasingly the subject of experimental research. In addition, there are psychosocial consequences, such as self-esteem issues and social discomfort. Therefore, it is indisputable that comprehensive oral care is of utmost importance. Recognizing the importance of oral health for overall well-being highlights the necessity for preventative measures and enhanced dental care. As the global population ages, it is increasingly important to comprehend and address the systemic effects of tooth loss. This review aims to summarize the complex pathomechanisms underlying tooth loss and emphasize the need for a comprehensive approach to address its diverse consequences. It advocates for preventive oral health measures to sustain general health and well-being.

Keywords: tooth loss, cardiovascular disease, cognitive impairment, cancer, edentulous, quality of life.

Submitted: 30-Mar-2024; Accepted in the final form: 10-Jun-2024; Published: 30-Jun-2024.

Introduction

The relationship between missing teeth and overall health extends beyond oral health concerns, encompassing various systemic implications. Tooth loss, defined as the absence of at least one tooth (excluding third molars), affects approximately 7% of individuals aged 20 years or older, as per the latest data from the World Health Organization (WHO) [1]. Also, according to the WHO,



about 30% of people aged 65–74 have no natural teeth. Primary causes include dental caries, periodontal disease, and dental trauma. Dental caries, affecting over 2 billion people globally, predominantly causes tooth loss in younger individuals, while periodontitis becomes the primary reason for tooth loss in older age groups [2]. Globally speaking, there is no significant predilection by sex when it comes to tooth loss. According to Carmen *et al.*, the average count of missing teeth increases by 5% for each year of a patient's age [3]. Various factors influence this trend: age, socioeconomic status, education level, oral hygiene practices, dietary habits, smoking, alcohol consumption, and dental healthcare behaviors. Despite advancements in healthcare, oral health has shown little improvement over the past 25 years, persisting as a significant global public health challenge [4]. The increasing global elderly population, driven by rising life expectancy, has profound implications for societies, healthcare systems, social structures, and economies. Recognizing the impact of missing teeth on overall health is vital, as it significantly affects individuals' ability to prevent other diseases and maintain overall well-being. Thus, addressing dental health through preventive care plays a crucial role in preventing health issues, promoting longer and healthier lives, and sustaining healthcare systems worldwide.

The oral cavity with all its anatomical components, an integral part of the body's digestive system, facilitates essential functions such as chewing, swallowing, speech, taste sensation, and maintaining facial and oral structure. Any structural or functional disruption of its physiological role has a detrimental impact on health. Tooth loss serves as an indicator of poor oral health when an individual has fewer than 20 natural teeth. Beyond oral health, missing teeth can impact cardiovascular health, inflammatory responses, nutritional intake, endocrine functions, cognitive abilities, and psychological well-being. Additionally, the rate of missing teeth greatly influences Oral Health-Related Quality of Life (OHRQoL) [5]. Recognizing the significance of oral health, the WHO considers dental health as one of the top ten indicators of human well-being and a criterion for human health [6, 7]. Moreover, oral conditions contribute more to health deterioration than 35 out of 39 cancer categories [4].

The ongoing process of tooth extraction, resulting in tooth loss, is widely recognized for its significant impact on the digestive system, as extensively supported in current literature. However, its broader implications on various aspects of health have not been thoroughly examined. This undertaking seeks to provide a thorough summary and clarification of these complex connections, actively addressing informational gaps for individuals undergoing the process of tooth extraction. The awareness of these multifaceted connections underscores the importance of addressing missing teeth, not only as a dental issue but as a critical component of overall health. While some impacts of missing teeth on general health are well-documented, others remain underexplored, highlighting the need for further research and clarification.

Missing teeth and cardiovascular health

There is a well-established link between poor oral health, including periodontal disease and tooth loss, and an increased risk of various conditions such as cardiovascular diseases (CVD), pulmonary diseases, diabetes, pregnancy complications, and ultimately all-cause mortality. CVD are a leading cause of morbidity and mortality globally, claiming approximately 17.9 million lives annually [8]. Based on this enormous health burden, recent research has been intensively exploring the intriguing connection between oral health, specifically tooth loss, and cardiovascular health. Since then, numerous studies have illuminated this relationship, offering valuable insights into the potential repercussions of missing teeth on cardiovascular disease. These findings underscore the importance of understanding oral health as a potential factor in the broader landscape of cardiovascular health, especially that both CVD and oral health issues often share common risk factors, such as age, gender, education, smoking, diet, and obesity. Studies consistently show a strong correlation between increased incidence of tooth loss and CVD through both case-control and cross-sectional investigations. Furthermore, tooth loss can alter dietary habits and other behaviors, consequently heightening the risk for CVD [9].

Tooth loss can be linked to CVD due to chronic oral infections like caries/periodontal diseases, and the process of tooth extraction itself may trigger propagation of infection. The advancement of tooth decay leads to the deterioration of healthy periodontal tissues, creating an environment where oral microbes can penetrate deeply into oral tissues, fostering their proliferation. The pathophysiology behind this association is thought to involve mainly inflammatory pathways and the dissemination of bacteria from the oral cavity to systemic circulation. Additionally, tooth loss represents the final stage of periodontal disease and may correlate with elevated levels of C-reactive protein (CRP), a factor implicated in atherosclerosis and consequently in stroke occurrence [6, 10]. This process contributes to the development of cardiovascular disease and subsequently, its complications. The reduced number of teeth itself is associated with an increased risk of atherosclerotic cardiovascular diseases (ACVD). Beukers et al. underscored the multifaceted links between tooth loss due to caries and ACVD [2]. Elevated carbohydrate intake, associated with increased risk of periodontal disease, may lead to obesity, insulin resistance and diabetes, which, together with tooth loss due to periodontitis, is of particular concern through the common element of low-grade systemic inflammation [9]. In particular, daily transient bacteremia associated with periodontitis has been studied in relation to atherosclerosis. This chronic inflammatory stress is believed to exacerbate inflammation around plaques, potentially promoting a pro-inflammatory and pro-thrombotic state, triggering autoimmunity, and inducing dyslipidemia. The progression of atherosclerosis may culminate in ACVD events, such as coronary heart disease (CHD), cerebrovascular accidents, and peripheral arterial disease. Although the exact nature of this relationship is still evolving and requires further research, it does not change the fact that ACVD accounts for about 54% and 45% of deaths in the United States and Europe, respectively [11, 12]. Bokhari et al. conclude that recognizing these potential links underscores the importance of comprehensive health care approaches that consider oral health as an integral component of overall cardiovascular health, fostering a holistic perspective on preventive strategies and wellness [2, 13]. This indicates the importance of addressing oral health issues, particularly tooth loss, in people with cardiovascular risk factors to reduce the overall burden of cardiovascular disease.

The idea that oral health may contribute to cardiovascular risk has been reinforced by studies that show a significant association between tooth loss and hypertension as shown in a metanalysis by Tada *et al.* [14]. Consideration of the etiopathogenesis of this relationship is currently dominated by hypotheses that consider two potential pathways.

Firstly, it's speculated that the progression of periodontitis, a key contributor to tooth loss, may subsequently lead to hypertension, by causing local inflammation [15]. The exact mechanism is intricate and not completely understood, however, it's likely that it primarily involves the spread of inflammation and subsequent damage to the vascular endothelium. Given that periodontal tissue spans a considerable area within the oral cavity, local inflammation from periodontitis could substantially contribute to systemic inflammation mediated by acute-phase proteins like CRP and

key inflammatory cytokines such as tumor necrosis factor alpha, interleukin 1b, and interleukin 6. Furthermore, in patients with periodontitis, a decrease in the abundance of commensal microbiota involved in the nitrate-nitrite-nitric oxide pathway, along with an increase in pathogenic bacterial species, may lead to a reduction in nitric oxide production, potentially resulting in elevated blood pressure [14].

Secondly, tooth loss is associated with deterioration of masticatory function, prompting individuals to change dietary patterns, eating fewer fruits and vegetables while consuming more high-energy foods, which can contribute to obesity. Such dysfunction can lead to a reduction in the intake of key vitamins and fiber which, combined with an increase in cholesterol intake, contributes to an increased risk of hypertension and atherosclerosis [16]. Moreover, reduced chewing might lead to decreased diet-induced thermogenesis and the inactivation of neuronal histamine, potentially leading to obesity [14]. With a similar conclusion, a 2018 meta-analysis by Cheng *et al.* found that likely pathways linking tooth loss to these conditions include chronic systemic inflammation due to periodontal disease, carbohydrate intake and changes in the composition of the oral microbiota, potentially contributing to atherosclerosis and stroke [6]. For every two teeth lost, there is an estimated 3% increase in the risk of coronary heart disease and stroke [6]. Studies have reported a heightened prevalence of metabolic syndrome (MetS) among individuals with periodontitis. Having fewer than 20 teeth may serve as a surrogate marker for the risk of developing MetS. Moreover, evidence suggests that non-surgical periodontal treatment improves both periodontal health and hypertension.

In conclusion, these studies collectively suggest that tooth loss may serve as a marker and/or contributor to cardiovascular diseases and metabolic syndrome urging further exploration of the intricate relationship between oral health and overall cardiovascular well-being.

Cognitive function and mental health

Recent studies have investigated the potential impact of missing teeth on cognitive function and mental health. The research has revealed links between oral health, including tooth loss, and cognitive decline, as well as psychological effects such as reduced self-esteem. The study is significant due to the rising prevalence of dementia, as highlighted by the World Health Organization's Global Burden of Disease Study 2019, which predicts that the prevalence of dementia will double approximately every five years by age 85 in both 2019 and 2050 [17]. Currently, there are no definitive treatments for dementia, and the precise link between cognitive impairment and tooth loss remains uncertain. Therefore, it is crucial to pinpoint modifiable risk factors that aid in preventing dementia, given that even having 7 or more missing teeth significantly increases the risk of dementia as emphasized by Zhang *et al.* [18, 19].

The growing number of elderly individuals has led to a rise in neurological impairments, resulting in a significant increase in disability-adjusted life-years (DALYs) worldwide. These conditions encompass a broad range of disorders affecting the brain, spinal cord, and nerves, often resulting in long-term disabilities and impacting quality of life. Kassebaum *et al.* demonstrated that the loss of an additional tooth was causally associated with a 0.146 percentage point increase in depressive symptoms or a 0.81 percentage point increase in the likelihood of major depression [20]. Depression affects more than 320 million people, or approximately 4.4% of the global population (World Health Organization, 2017), while edentulous individuals represent 2.3% of the global population [4]. Preventing a single average instance of tooth loss, with its anticipated reduction in depression (0.81 percentage points) could potentially benefit approximately 60 million people worldwide [21].

One of the risk factors for developing cognitive impairment is the loss of occlusal support caused by tooth loss, a cause often overlooked in information about the consequences of not replacing a missing tooth. Masticatory muscles clenching has the potential to boost cardiac output. Moreover, functional improvements in the brain have been observed with enhanced dentures in individuals without teeth [22]. This action may stimulate localized blood flow into the brain through jaw clenching [22].

Several potential biological mechanisms underlie the connection between molar loss and cognitive impairment, including reduced sensory input, decreased cerebral blood flow, impaired cholinergic neurotransmission (reduced acetylcholine levels are linked to a decreased pyramidal cell count in the hippocampus), and heightened stress responses. Another proposed pathway involves nutritional imbalance and the absence of potentially protective nutrients against Alzheimer's disease (AD) due to tooth loss. Several dietary elements, including antioxidants, vitamins, and polyphenols, have been associated with a reduced risk of AD [23]. This deficiency in essential nutrients, such as vitamin D and iron, has been linked to an elevated risk of cognitive decline and dementia [24]. Particularly the metabolic, endocrine and immune functions, including -alpha, 25-dihydroxyvitamin D (1,25(OH)2D) are deemed significant contributors to the development of cognitive disorders. Both tooth loss and vitamin D deficiency are associated with common systemic health issues, emphasizing the potential role of low 1,25(OH)2D concentration in linking tooth loss to systemic diseases, including cognitive impairment [24, 25].

Nevertheless, inflammation emerges as a predominant theory in elucidating the impact of tooth loss on cognitive function. The hypothesis suggests that the absence of teeth eliminates a protective barrier, leaving gingival tissue unable to shield the central nervous system (CNS) from continual exposure to pathogenic oral bacteria [26]. This exposure may trigger or exacerbate inflammatory processes, initiating the release of intravascular inflammatory mediators and contributing to neurodegeneration. Periodontitis triggers chronic inflammation in periodontal tissues due to dissemination of oral bacteria, resulting in tissue destruction and tooth loss. This inflammation can extend systemically, inducing a proinflammatory response characterized by elevated serum cytokine levels, potentially compromising the blood-brain barrier's integrity [27]. Consequently, cognitive deficits and dementia may ensue, due to inflammation in the CNS [28]. In a cross-sectional study of periodontitis and cognitive dysfunction published in 2008, Yu et al. found that periodontitis was more common in participants with low cognitive function scores [29]. Additionally, Chen et al. conducted a large retrospective cohort study including 27,963 people over the age of 50 to determine the relationship between periodontitis and AD [30]. Patients who had periodontitis for more than 10 years had more than a 1.7-fold risk of developing AD, indicating the significance of long-term exposure. Support for this inflammation theory comes not only from epidemiological studies showing increased risk and severity of cognitive impairment, but also from clinical observations and corroborating evidence from animal experiments. Notably, excessive levels of nitric oxide (NO) have been linked to heightened cell death and inflammation, reinforcing the inflammatory cascade's role in cognitive decline [19]. Moreover, there is a widespread acknowledgment that periodontitis contributes to the production and buildup of amyloid β , a pathological characteristic observed in the brains of individuals with AD. The pathophysiology of the processes behind this observation remains unclear but has been extensively studied in experimental animal models [31].

Maintaining oral health emerges as a groundbreaking approach to safeguarding cognitive function among seniors. Strategies such as practicing good oral hygiene, managing periodontal issues, and overall oral health care could help preserve optimal brain function. This approach holds promise for advancing our understanding, prevention, and treatment of age-related ailments. Simple, cost-effective, and non-invasive measures, such as regular brushing, flossing, consistent dental check-ups, addressing periodontal concerns, and preserving teeth, have the potential to delay cognitive decline and Alzheimer's disease. As summarized by Galindo-Moreno *et al.*, boosting efforts to prevent tooth loss among adults, a comparatively smaller investment than treating cognitive decline, could significantly reduce overall expenses linked to these conditions. A mere one-year delay in the onset of cognitive impairment might save approximately €375 billion in Europe alone, an amount four times less than the estimated €93 billion budget for dental healthcare in 2020 [32].

Impact on cancer development

The evidence exists suggesting a potential connection between tooth loss and specific cancer types. Poor oral health, encompassing tooth loss, has been linked to an increased risk and heightened susceptibility to lung, gastric, liver, esophageal, pancreatic, and head and neck cancers [33]. In a meta-analytic study, Shi et al. found that for every 10 teeth lost, there was a 9% increase in overall cancer risk. Specifically, this increase was associated with a 14% higher risk of esophageal cancer, a 9% higher risk of gastric cancer, a 31% higher risk of head and neck cancer, a 4% higher risk of colorectal cancer, a 7% higher risk of pancreatic cancer, a 19% higher risk of lung cancer, a 3% higher risk of prostate cancer, a 2% higher risk of bladder cancer, and a 3% higher risk of hematopoietic cancer [7]. The precise mechanisms underlying this association remain not fully understood. Research indicates multiple pathways connecting oral health and cancer development. Firstly, inflammation resulting from oral bacterial infection may initiate malignant transformation through mediators (inflammatory cytokines) released in systemic inflammation [34, 35]. Secondly, nitrosamine, a carcinogen produced by nitrate-reducing oral bacteria, has been identified as a triggering factor in gastrointestinal cancers [36]. Thirdly, chronic inflammation induced by oral bacteria can locally affect surrounding tissues and promote carcinogenesis. Bacteria such as Fusobacterium Nucleatum (second most commonly recovered species in dental plaque biofilms associated with health [37]) and Porphyromonas Gingivalis contribute to oral carcinogenesis by upregulating inflammatory cytokines, affecting DNA integrity, promoting cell proliferation, invasion and metastasis. Furthermore, these bacteria release substances such as volatile sulphur compounds and reactive oxygen species, perpetuating chronic inflammation and potentially paving the way for cancer development [38–40]. In fact, F. nucleatum infection was correlated with unfavorable clinicopathological parameters, including larger tumor size, poor differentiation, lymph node and distant metastases, advanced tumor stage and increased depth of tumor invasion [41]. Beyond this, the transmission of oral microbiota to the biliary tract, pancreas, and colorectal area through saliva ingestion is considered a plausible mechanism contributing to cancer development in these regions [35]. All of these processes are complex interactions between host factors, immune responses and the potential direct effects of the oral microflora on cancer development.

From a different perspective, nutritional status may also play a crucial role in comprehending the connection between inadequate dental health and cancer. Teeth loss significantly affects aspects such as chewing ability, dietary habits, nutritional intake, aesthetics, and food preferences [42, 7]. Even an increased intake of carbohydrates alone, which is a common cause of tooth extraction due to tooth decay, is associated with an increased risk of cancer. Malnutrition or deficiencies in specific nutrients might influence the maintenance of healthy oral mucosa or contribute to the degradation of dental enamel. Further exploring the role of Vitamin D, an increasing body of research strongly suggests that a deficiency in Vitamin D has detrimental effects on oral health, including impaired tooth mineralization and an elevated risk of various cancers [35]. The following is a more detailed discussion of each of these cancers and a summary of them summarized in Table 1.

Tooth loss associated cancer	Tooth loss	Risk of cancer after tooth loss	Possible pathomechanisms
Lung cancer	For every 10 teeth lost	19% [7]	Chronic systemic inflammation triggers onco- genic mutations, generates growth factors, and promotes tumour cell proliferation [44]
Head and neck cancer	1–6 teeth lost	29% [48]	 Chronic inflammation caused by oral bacteria: — elevated level of proinflammatory cyto- kines [38] — invasion of epithelial cells by oral patho- gens [38] — increased production of carcinogenic nitrosamines
	6–15 teeth lost	18% [47] (58% [48])	
	≥11 teeth lost	63% [48]	
	≥15 teeth lost	54% [48] (72% [48)	
	≥20 teeth lost	89% [48]	
Pancreatic cancer	Edentulism	54% [49]	Transmission of oral microbiota to biliary tract and pancreas [35]
Esophageal cancer	For every 10 teeth lost	14% [7]	Migration of oral microorganisms and/or nitrosamines to esophagus [53] Mechanical trauma caused by larger food portions [51]
	Edentulism	30% [53]	

Table 1. Overview of carcinogenesis risk associated with tooth loss and potential causative pathomechanisms.

Lung cancer

Population-based studies examining the association between tooth loss and lung cancer risk are limited, and the potential interaction with smoking remains largely unexplored. Poor oral health conditions, including periodontal disease and tooth cavities, can lead to tooth loss. Oral pathogens associated with these conditions, such as periodontitis and tooth loss, are linked to chronic systemic inflammation [43]. This inflammation may contribute to various forms of carcinogenesis by triggering oncogenic mutations, generating growth factors, and promoting tumor cell proliferation. Interestingly, certain activated cytokines and/or oral bacteria themselves may modify the respiratory epithelium, heightening susceptibility to respiratory infections. All these factors may increase the likelihood of developing lung cancer [44]. The results of the meta-analysis by Yoon *et al.* showed that chronic inflammation associated with tooth loss may potentially contribute to the development of lung cancer by heightening the inflammatory and carcinogenic effects of

smoking [44]. Furthermore, according to a dose-response analysis, each increment of 10 in tooth loss was associated with a 19% rise in the risk of lung cancer [7].

Head and neck cancer including oral cancer

Oral cancer (OC) is a significant public health concern, ranking amongst the top three cancer types in the Indian subcontinent [45]. The meta-analysis by Wang *et al.* on head and neck cancer risk revealed a correlation between tooth loss and an increased likelihood of OC [42]. Furthermore, a 2023 meta-analysis by Gonde *et al.* independently associated tooth loss with a harmful rise in the risk of OC, regardless of conventional factors linked to its development [45, 46]. In the context of head and neck cancer, individuals with moderate tooth (6–15 lost teeth) loss face an 18% elevated risk, while severe tooth loss (+15 lost teeth) is associated with a substantial 54% increase. Additionally, moderate tooth loss correlates with a 45% higher risk of larynx cancer [47]. These findings remain consistent across sensitivity analyses and exhibit no discernible publication bias.

The risk of head and neck cancer shows variations, with a 29% increase for those with 1 to 6 teeth lost, 58% for 6 to 15 teeth lost, 63% for 11 or more teeth lost, 72% for 15 or more teeth lost, and a noteworthy 89% for individuals with 20 or more teeth lost compared to the reference group [48]. These insights underscore the intricate relationship between tooth loss and the heightened risk of head and neck cancers, emphasizing the importance of oral health in assessing cancer susceptibility.

Pancreatic cancer

Tooth loss has been identified as a risk factor for pancreatic cancer (PC), showing a notable 54% increase in the likelihood of developing this form of cancer [49]. PC shares several common risk factors with periodontal disease, as both are associated with prolonged inflammatory conditions. Simultaneously, there is growing evidence connecting oral bacteria to systemic diseases with inflammatory foundations, which could potentially contribute to tumor development.

Esophageal cancer

The 2016 meta-analysis by Chen *et al.* brought to light a notable correlation between tooth loss and the likelihood of developing esophageal cancer (EC), signifying a compelling 30% elevation in risk [30]. Conversely, Shi *et al.* (2018) reported a more conservative increase at 14% risk [7]. Collectively, these findings underscore the importance of tooth loss as a significant factor in the context of EC risk. Furthermore, the association between the frequency of teeth brushing and the risk of esophageal cancer (EC) highlights that individuals with a higher brushing frequency exhibit a lower risk of developing EC [50].

The elevated risk of EC may be elucidated through several potential mechanisms. Firstly, tooth loss could influence dietary patterns, potentially heightening susceptibility to disease. Secondly, it has been hypothesized that tooth loss may lead individuals to swallow large, poorly chewed food boluses, potentially causing mechanical trauma to the esophagus [51]. Thirdly, tooth loss is linked to an oral flora that may facilitate the conversion of nitrate to nitrite. Nitrite can then spontaneously react with amines, forming carcinogenic nitrosamines, some of which may be organ-specific carcinogens in the gastrointestinal system [52, 53]. In summary, these multifaceted factors contribute to our understanding of the intricate relationship between tooth loss and the risk of esophageal cancer [30]. Teeth play a pivotal role in daily life, contributing to essential functions such as eating, speaking, smiling, and expressing emotions. These activities are crucial for fostering positive social interactions. Tooth loss significantly impacts quality of life, as demonstrated in various research. It has been found that individuals with missing teeth reported lower levels of overall well-being and social functioning compared to those with a full set of teeth [54]. Among elderly, the prevalence of tooth loss is notably higher, and primarily linked to the lifelong accumulation of chronic dental conditions like dental caries and periodontal disease [55].

Considering the consistent evidence supporting the positive impact of social participation on the health and well-being of older adults, it becomes imperative to promote mechanisms that encourage increased levels of social engagement. Our findings underscore the importance of older adults retaining a higher number of teeth. This is not only essential for evident advantages in oral functions like mastication and speech but also for cultivating stronger social relationships. Maintaining a greater number of teeth is a pivotal factor in experiencing the associated benefits of enhanced social participation. The absence of teeth can significantly impact the quality of life related to oral health, affecting various aspects such as the ability to chew food properly, speak clearly, maintain facial aesthetics, and have psychological consequences. Individuals who have missing teeth may experience self-esteem issues and social discomfort, which can ultimately affect their overall well-being. Recognizing the multifaceted impact of tooth loss emphasizes the importance of comprehensive oral care for both functional and psychosocial well-being.

Conclusion

In conclusion, the intricate relationship between tooth loss and overall health extends far beyond the confines of oral health concerns. The presented studies discuss selected disease characteristics but often allude to similar underlying mechanisms, highlighting the far-reaching consequences of tooth loss on overall well-being and the urgent need for a holistic approach to understanding its impact (Fig. 1). Cardiovascular health emerges as a prominent area affected by tooth loss, with research indicating associations between tooth loss and increased risks of hypertension, atherosclerosis, peripheral arterial disease, and cardiovascular diseases. The complex connections between poor oral health and cardiovascular conditions involve chronic inflammation leading to endothelial dysfunction and promotion of a pro-thrombotic state, disruption of nitrate-nitrite-nitric oxide pathway, and alterations in dietary habits. Tooth loss has been also found to have intricate connections with cognitive function and mental health. In fact, studies suggest a link between tooth loss and cognitive decline, dementia, and depression. Various biological mechanisms contribute to this association, including reduced sensory input, decreased cerebral blood flow, impaired neurotransmission, nutritional imbalances, and again chronic inflammation. Moreover, a growing body of data points to an association between tooth loss and certain cancers, including lung, head and neck, pancreatic and esophageal cancers, with chronic inflammation, transmission of oral microflora and changes in dietary patterns as potential underlying mechanisms. Finally, tooth loss not only affects physical health but also has a significant impact on quality of life and social interactions.

Teeth play a pivotal role in daily functions such as eating, speaking, smiling, and expressing emotions, which are essential for positive social interactions. Thus, recognizing oral health as

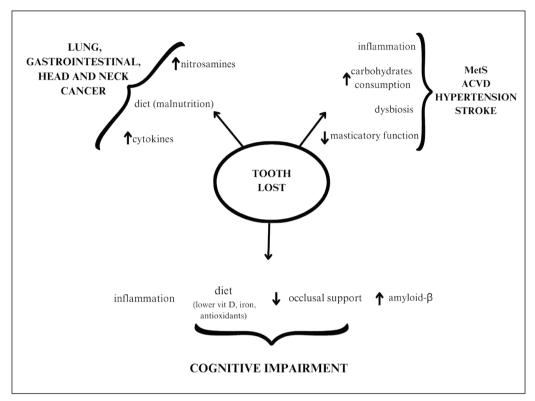


Fig. 1. Schematic overview of mechanisms involved in health complications caused by tooth loss.

an integral component of overall well-being is paramount. The World Health Organization's acknowledgment of dental health as a top indicator of human well-being reflects the growing awareness of its systemic implications. Addressing tooth loss through preventive measures, improved dental care, and public health initiatives is crucial for promoting healthier societies. As the global population ages, understanding and mitigating the impact of tooth loss on general health becomes even more critical. The potential economic benefits of preventing tooth loss, particularly in delaying cognitive decline, underscore the societal importance of investing in oral health. This narrative review argues for a paradigm shift in the perception of oral health, emphasizing its critical role in maintaining overall health and well-being, and suggests prioritizing preventive interventions to reduce the burden on health care systems as well as improve health outcomes in an aging society.

Conflict of interest

None declared.

References

- 1. Global Oral Health Status Report: Towards Universal Health Coverage for Oral Health by 2030. World Health Organization; 2022.
- Beukers N.G.F.M., Su N., Loos B.G., Van Der Heijden G.J.M.G.: Lower Number of Teeth Is Related to Higher Risks for ACVD and Death — Systematic Review and Meta-Analyses of Survival Data. Front Cardiovasc Med. 2021; 8: 621626. doi: 10.3389/fcvm.2021.621626.
- 3. *Fatima Del Carmen A.D., Aída B.Y.S., Javier D.L.F.H.*: Risk Indicators of Tooth Loss Among Mexican Adult Population: A Cross-Sectional Study. Int Dent J. 2021; 71 (5): 414–419. doi:10.1016/j.identj.2020.12.016.
- Kassebaum N.J., Smith A.G.C., Bernabé E., et al.: Global, Regional, and National Prevalence, Incidence, and Disability-Adjusted Life Years for Oral Conditions for 195 Countries, 1990–2015: A Systematic Analysis for the Global Burden of Diseases, Injuries, and Risk Factors. J Dent Res. 2017; 96 (4): 380–387. doi: 10.1177/0022034517693566.
- Gerritsen A.E., Allen P.F., Witter D.J., Bronkhorst E.M., Creugers N.H.J.: Tooth loss and oral health-related quality of life: a systematic review and meta-analysis. Health Qual Life Outcomes. 2010; 8: 126. doi: 10.1186/1477-7525-8-126.
- Cheng F., Zhang M., Wang Q., et al.: Tooth loss and risk of cardiovascular disease and stroke: A dose-response meta analysis of prospective cohort studies. PloS One. 2018; 13 (3): e0194563. doi: 10.1371/ journal.pone.0194563.
- 7. *Shi J., Leng W., Zhao L., et al.*: Tooth loss and cancer risk: a dose-response meta analysis of prospective cohort studies. Oncotarget. 2018; 9 (19): 15090–15100. doi: 10.18632/oncotarget.23850.
- 8. WHO data. https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1.
- 9. Bokhari S.A.H., Khan A.A., Ansari J.A., Alam R.: Tooth loss in institutionalized coronary heart disease patients of Punjab Institute of Cardiology, Lahore, Pakistan. J Epidemiol Glob Health. 2012; 2 (1): 51. doi: 10.1016/j.jegh.2011.11.004.
- You Z., Cushman M., Jenny N.S., Howard G.: Tooth loss, systemic inflammation, and prevalent stroke among participants in the reasons for geographic and racial difference in stroke (REGARDS) study. Atherosclerosis. 2009; 203 (2): 615–619. doi: 10.1016/j.atherosclerosis.2008.07.037.
- Townsend N., Wilson L., Bhatnagar P., Wickramasinghe K., Rayner M., Nichols M.: Cardiovascular disease in Europe: epidemiological update 2016. Eur Heart J. 2016; 37 (42): 3232–3245. doi: 10.1093/eurheartj/ehw334.
- 12. *Mozaffarian D., Benjamin E.J., Go A.S., et al.*: Heart Disease and Stroke Statistics 2016 Update: A Report From the American Heart Association. Circulation. 2016; 133 (4). doi: 10.1161/CIR.0000000000350.
- Gorelick P.B., Scuteri A., Black S.E., et al.: Vascular Contributions to Cognitive Impairment and Dementia: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2011; 42 (9): 2672–2713. doi: 10.1161/STR.0b013e3182299496.
- 14. *Tada A., Tano R., Miura H.*: The relationship between tooth loss and hypertension: a systematic review and meta-analysis. Sci Rep. 2022; 12 (1): 13311. doi: 10.1038/s41598-022-17363-0.
- 15. *Mendes J.J., Viana J., Cruz F., et al.*: Blood Pressure and Tooth Loss: A Large Cross-Sectional Study with Age Mediation Analysis. Int J Environ Res Public Health. 2021; 18 (1): 285. doi: 10.3390/ijerph18010285.
- 16. *Da D., Wang F., Zhang H., et al.*: Association between tooth loss and hypertension among older Chinese adults: a community-based study. BMC Oral Health. 2019; 19 (1): 277. doi: 10.1186/s12903-019-0966-3.
- GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019; 18 (5): 459–480. doi: 10.1016/S1474-4422(18)30499-X.
- 18. Zhang S., Yang F., Wang Z., et al.: Poor oral health conditions and cognitive decline: Studies in humans and rats. PloS One. 2020; 15 (7): e0234659. doi: 10.1371/journal.pone.0234659.
- 19. *Li L., Zhang Q., Yang D., et al.*: Tooth loss and the risk of cognitive decline and dementia: A meta-analysis of cohort studies. Front Neurol. 2023; 14: 1103052. doi: 10.3389/fneur.2023.1103052.

- Kassebaum N.J., Bernabé E., Dahiya M., Bhandari B., Murray C.J.L., Marcenes W.: Global Burden of Severe Tooth Loss: A Systematic Review and Meta-analysis. J Dent Res. 2014; 93 (7 Suppl): 20S–28S. doi: 10.1177/0022034514537828.
- Matsuyama Y., Jürges H., Dewey M., Listl S.: Causal effect of tooth loss on depression: evidence from a population-wide natural experiment in the USA. Epidemiol Psychiatr Sci. 2021; 30: e38. doi: 10.1017/ S2045796021000287.
- Zhang M., Hasegawa Y., Sakagami J., et al.: Effects of unilateral jaw clenching on cerebral/systemic circulation and related autonomic nerve activity. Physiol Behav. 2012; 105 (2): 292–297. doi: 10.1016/j. physbeh.2011.07.028.
- McGrattan A.M., McGuinness B., McKinley M.C., et al.: Diet and Inflammation in Cognitive Ageing and Alzheimer's Disease. Curr Nutr Rep. 2019; 8 (2): 53–65. doi: 10.1007/s13668-019-0271-4.
- 24. *Roy N.M.*: Impact of vitamin D on neurocognitive function in dementia, depression, schizophrenia and ADHD. Front Biosci. 2021; 26 (3): 566–611. doi: 10.2741/4908.
- Gáll Z., Székely O.: Role of Vitamin D in Cognitive Dysfunction: New Molecular Concepts and Discrepancies between Animal and Human Findings. Nutrients. 2021; 13 (11): 3672. doi: 10.3390/nu13113672.
- Gao L., Xu T., Huang G., Jiang S., Gu Y., Chen F.: Oral microbiomes: more and more importance in oral cavity and whole body. Protein Cell. 2018; 9 (5): 488–500. doi: 10.1007/s13238-018-0548-1.
- Wei T., Du Y., Hou T., et al.: Association between adverse oral conditions and cognitive impairment: A literature review. Front Public Health. 2023; 11: 1147026. doi: 10.3389/fpubh.2023.1147026.
- Stein P.S., Desrosiers M., Donegan S.J., Yepes J.F., Kryscio R.J.: Tooth loss, dementia and neuropathology in the Nun study. J Am Dent Assoc 1939. 2007; 138 (10): 1314–1322; quiz 1381–1382. doi: 10.14219/ jada.archive.2007.0046.
- Wang X., Hu J., Jiang Q.: Tooth Loss-Associated Mechanisms That Negatively Affect Cognitive Function: A Systematic Review of Animal Experiments Based on Occlusal Support Loss and Cognitive Impairment. Front Neurosci. 2022; 16: 811335. doi: 10.3389/fnins.2022.811335.
- Chen H., Nie S., Zhu Y., Lu M.: Teeth loss, teeth brushing and esophageal carcinoma: a systematic review and meta-analysis. Sci Rep. 2015; 5 (1): 15203. doi: 10.1038/srep15203.
- Sakakibara Y., Sekiya M., Saito T., Saido T.C., Iijima K.M.: Amyloid-β plaque formation and reactive gliosis are required for induction of cognitive deficits in App knock-in mouse models of Alzheimer's disease. BMC Neurosci. 2019; 20 (1): 13. doi: 10.1186/s12868-019-0496-6.
- 32. Galindo-Moreno P., Lopez-Chaichio L., Padial-Molina M., et al.: The impact of tooth loss on cognitive function. Clin Oral Investig. 2022; 26 (4): 3493–3500. doi: 10.1007/s00784-021-04318-4.
- 33. *Bezamat M., Rothenberger S., Vieira A.R.*: Genetic contribution to cancer risk in patients with tooth loss: a genetic association study. Sci Rep. 2022; 12 (1): 16098. doi: 10.1038/s41598-022-20556-2.
- Hoare A., Soto C., Rojas-Celis V., Bravo D.: Chronic Inflammation as a Link between Periodontitis and Carcinogenesis. Mediators Inflamm. 2019; 2019: 1–14. doi: 10.1155/2019/1029857.
- Kang E.J., Moon S.-J., Lee K., Park I.H., Kim J.S., Choi Y.J.: Associations between missing teeth and the risk of cancer in Korea: a nationwide cohort study. BMC Oral Health. 2023; 23 (1): 418. doi: 10.1186/ s12903-023-02997-x.
- 36. *Chen J., Ren C.J., Wu L., et al.*: Tooth Loss Is Associated With Increased Risk of Dementia and With a Dose-Response Relationship. Front Aging Neurosci. 2018; 10: 415. doi: 10.3389/fnagi.2018.00415.
- Curtis M.A., Diaz P.I., Van Dyke T.E.: The role of the microbiota in periodontal disease. Periodontol 2000. 2020; 83 (1): 14–25. doi: 10.1111/prd.12296.
- Li T.-J., Hao Y.-H., Tang Y.-L., Liang X.-H.: Periodontal Pathogens: A Crucial Link Between Periodontal Diseases and Oral Cancer. Front Microbiol. 2022; 13: 919633. doi: 10.3389/fmicb.2022.919633.
- Chattopadhyay I., Verma M., Panda M.: Role of Oral Microbiome Signatures in Diagnosis and Prognosis of Oral Cancer. Technol Cancer Res Treat. 2019; 18: 153303381986735. doi: 10.1177/1533033819867354.
- Perera M., Al-hebshi N.N., Speicher D.J., Perera I., Johnson N.W.: Emerging role of bacteria in oral carcinogenesis: a review with special reference to perio-pathogenic bacteria. J Oral Microbiol. 2016; 8 (1): 32762. doi: 10.3402/jom.v8.32762.

- 41. *McIlvanna E., Linden G.J., Craig S.G., Lundy F.T., James J.A.*: Fusobacterium nucleatum and oral cancer: a critical review. BMC Cancer. 2021; 21 (1): 1212. doi: 10.1186/s12885-021-08903-4.
- 42. Wang Y., Peng J., Li Y., et al.: Association between tooth loss and risk of oesophageal cancer: a dose response meta-analysis. SpringerPlus. 2016; 5 (1): 1020. doi: 10.1186/s40064-016-2711-6.
- Grivennikov S.I., Greten F.R., Karin M.: Immunity, Inflammation, and Cancer. Cell. 2010; 140 (6): 883– 899. doi: 10.1016/j.cell.2010.01.025.
- 44. *Yoon H.S., Shu X.O., Gao Y.T., et al.*: Tooth Loss and Risk of Lung Cancer among Urban Chinese Adults: A Cohort Study with Meta-Analysis. Cancers. 2022; 14 (10): 2428. doi: 10.3390/cancers14102428.
- Gonde N., Rathod S., Kolte A., Lathiya V., Ughade S.: Association between tooth loss and risk of occurrence of oral cancer — A systematic review and meta-analysis. Dent Res J. 2023; 20: 4.
- Yao Q.W., Zhou D.S., Peng H.J., Ji P., Liu D.S.: Association of periodontal disease with oral cancer: a meta-analysis. Tumor Biol. 2014; 35 (7): 7073–7077. doi: 10.1007/s13277-014-1951-8.
- Wang R.S., Hu X.Y., Gu W.J., Hu Z., Wei B.: Tooth Loss and Risk of Head and Neck Cancer: A Meta-Analysis. PLoS ONE. 2013; 8 (8): e71122. doi: 10.1371/journal.pone.0071122.
- Zeng X.T., Luo W., Huang W., Wang Q., Guo Y., Leng W.D.: Tooth Loss and Head and Neck Cancer: A Meta-Analysis of Observational Studies. PLoS ONE. 2013; 8 (11): e79074. doi: 10.1371/journal. pone.0079074.
- Maisonneuve P., Amar S., Lowenfels A.B.: Periodontal disease, edentulism, and pancreatic cancer: a meta-analysis. Ann Oncol. 2017; 28 (5): 985–995. doi: 10.1093/annonc/mdx019.
- Tsukamoto M., Naito M., Wakai K., et al.: Tooth brushing, tooth loss, and risk of upper aerodigestive tract cancer: a cohort study of Japanese dentisits. Nagoya J Med Sci. 2021 May; 83 (2): 331–341. doi: 10.18999/nagjms.83.2.331.
- Chen X., Yuan Z., Lu M., Zhang Y., Jin L., Ye W.: Poor oral health is associated with an increased risk of esophageal squamous cell carcinoma — a population-based case-control study in China: Oral health and risk of esophageal squamous cell carcinoma. Int J Cancer. 2017; 140 (3): 626–635. doi: 10.1002/ ijc.30484.
- Abnet C.C., Qiao Y.L., Dawsey S.M., Dong Z.W., Taylor P.R., Mark S.D.: Tooth loss is associated with increased risk of total death and death from upper gastrointestinal cancer, heart disease, and stroke in a Chinese population-based cohort. Int J Epidemiol. 2005; 34 (2): 467–474. doi: 10.1093/ije/dyh375.
- Chen Q.L., Zeng X.T., Luo Z.X., Duan X.L., Qin J., Leng W.D.: Tooth loss is associated with increased risk of esophageal cancer: evidence from a meta-analysis with dose-response analysis. Sci Rep. 2016; 6: 18900. doi: 10.1038/srep18900.
- Locker D., Gibson B.: Discrepancies between self-ratings of and satisfaction with oral health in two older adult populations. Community Dent Oral Epidemiol. 2005; 33 (4): 280–288. doi: 10.1111/j.1600-0528.2005.00209.x.
- GBD 2017 Oral Disorders Collaborators, Bernabe E., Marcenes W., et al.: Global, Regional, and National Levels and Trends in Burden of Oral Conditions from 1990 to 2017: A Systematic Analysis for the Global Burden of Disease 2017 Study. J Dent Res. 2020; 99 (4): 362–373. doi: 10.1177/0022034520908533.