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Review Article

The Complex Bidirectional Relationship Between Sarcopenia and Tooth Loss: A Concise Review

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Abstract

Sarcopenia, defined as the progressive decline in skeletal muscle mass, strength, and functionality, has garnered considerable attention due to its associations with numerous adverse health outcomes. Emerging research suggests that sarcopenia may adversely affect oral health, particularly by leading to tooth loss, through shared risk factors such as aging, systemic inflammation, nutritional deficiencies, and compromised functional capacity. Sarcopenia may result in diminished chewing function, which can lead to a reduced intake of essential nutrients and an increased vulnerability to periodontal disease, all of which contribute to tooth loss. Conversely, the loss of teeth may exacerbate sarcopenia by limiting dietary diversity and impairing nutrient absorption, thereby accelerating muscle degeneration. Systemic inflammation, hormonal imbalances, and oxidative stress are additional significant factors that influence the interaction between sarcopenia and oral health. A comprehensive understanding of the implications of sarcopenia on tooth loss is essential for developing integrated healthcare strategies that address the interrelated nature of the musculoskeletal system and oral health. Considering the existing proof that indicates a complex bidirectional relationship between sarcopenia and tooth loss, this review seeks to provide a comprehensive, evidence-based summary addressing the definitions and measurement methodologies of sarcopenia, the shared pathophysiological mechanisms connecting sarcopenia and tooth loss, and the implications of these conditions on the overall health status of affected individuals.

Keywords: Sarcopenia; Tooth Loss; Quality of Life

Abbreviations

EWGSOP: European Working Group on Sarcopenia in Older People; SIG: Special Interest Group; ESPEN: European Society of Clinical Nutrition and Metabolism; NHANES: National Health and Nutrition Examination Survey; IWGS: International Sarcopenia Working Group; FNIH: Foundation for the National Institutes of Health; SCWD: Society for Sarcopenia, Cachexia, and Wasting Disorders; SDOC: Sarcopenia Definitions and Outcomes Consortium; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; DXA: Dual-energy X-Ray Absorptiometry; LM: Lean Mass; SMM: Skeletal Muscle Mass; IL-6: Interleukin-6; TNF-α: Tumor Necrosis Factor-Alpha; CRP: C-Reactive Protein; ROS: Reactive Oxygen Species; IGF-1: Insulin-like Growth Factor-1; AMPK: Adenosine Monophosphate-Activated Protein Kinase

Introduction

The aging population is globally experiencing an increasing prevalence of chronic conditions, many of which are interrelated and exert influence upon one another. Among these conditions, sarcopenia—a progressive and generalized decline in skeletal muscle mass, strength, and function—has emerged as a significant health concern for the geriatric population. Sarcopenia, as stated by the European Working Group on Sarcopenia in Older People (EWGSOP), is a significant contributor to physical frailty, disability, and the loss of independence among aging populations [1]. In addition to sarcopenia, tooth loss represents another prevalent concern that has far-reaching effects on quality of life, nutritional status, and overall health [2].

Tooth loss is frequently the end-stage consequence of chronic adverse oral conditions such as periodontitis and dental caries, and it disproportionately impacts older adults. Global estimates reveal that approximately 2.3 billion individuals suffer from untreated dental caries, with nearly 30% of those over the age of 65 being completely edentulous [3]. Tooth loss indicates deteriorating oral health and has been associated with systemic health outcomes, including cardiovascular disease, diabetes, and malnutrition [4]. The noteworthy overlaps in the epidemiology and risk factors of tooth loss and sarcopenia raise significant inquiries regarding their potential bidirectional relationship [5].

Emerging evidence suggests a link between sarcopenia and tooth loss, driven by shared biological and behavioral factors. These factors include nutritional deficiencies, systemic inflammation, and decreased functional capacity. For instance, the weakness and frailty associated with sarcopenia can hinder an individual's ability to maintain proper oral hygiene, which increases the risk of periodontal disease and subsequent tooth loss [6]. On the other hand, tooth loss can significantly affect dietary quality, limiting the intake of protein and essential micronutrients needed for muscle maintenance [7]. This bidirectional interaction creates a vicious cycle, especially in vulnerable populations such as older adults and individuals with severe comorbidities, such as chronic obstructive pulmonary disease, cardiovascular disease, and cancer.

Considering the available evidence suggesting an intricate bidirectional association between sarcopenia and tooth loss, the present review aims to provide an evidence-based summary of the sarcopenia definition and measurement methods, the shared pathophysiological mechanisms between sarcopenia and tooth loss, and their implications for afflicted patients' global health status.

The definition of sarcopenia

The term sarcopenia stems from the Greek sarx, "flesh or muscle," and penia, "poverty or deficiency," namely deficiency of skeletal muscle mass. Sarcopenia is characterized by progressive loss, atrophy, or muscle wastage that can occur due to various systemic illnesses or aging processes [8]. In the early 2010s, new definitions were introduced that broadened the understanding of sarcopenia to include not only the loss of muscle mass (myopenia) but also muscle strength (dynapenia) and athletic performance (kratopenia) [9]. This expanded framework has led to a substantial increase in research endeavors within the field, illustrating that sarcopenia, as defined by these criteria, serves as a significant predictor of clinical outcomes across various medical and surgical disciplines. The EWGSOP researchers established specific criteria for diagnosing sarcopenia in two significant studies [1,9]. The initial research, known as EWGSOP1, was published in 2010 and characterized sarcopenia as a disorder involving progressive and substantial loss of muscle mass (myopenia) and decreased strength (dynapenia). According to this definition, sarcopenia is considered probable when myopenia is present. A definitive diagnosis is made when dynapenia is also identified during clinical assessments. However, the 2019 EWGSOP2 report highlighted that dynapenia is more critical than myopenia for confirming a sarcopenia diagnosis [1]. In the EWGSOP1 guidelines, probable sarcopenia was primarily based on the presence of myopenia. In contrast, the EWGSOP2 criteria have shifted this focus, designating myopenia as a confirmatory criterion rather than the primary criterion for diagnosing sarcopenia. Both reports also accentuated that the presence of kratopenia was indicative of severe sarcopenia, which has more serious clinical consequences than its non-sevre form [1,9].

Various researchers have shaped the definition of sarcopenia over time. For instance, Therakomen., *et al*. [10] stated that sarcopenia is a natural aspect of the aging process. Still, various factors can accelerate its progression, including age-related

inflammation (inflammaging), inactivity, malnutrition, and chronic diseases. In 2010, the Special Interest Group (SIG) of the European Society of Clinical Nutrition and Metabolism (ESPEN) was the inaugural organization to establish a standardized definition of sarcopenia [11]. The committee underscored the necessity of this definition to implement efficient diagnostic and therapeutic approaches for sarcopenia. The SIG defined sarcopenia as a decline in muscle mass and strength following the classifications proposed by Rosenberg and Roubenoff [12,13]. The principal criteria for diagnosing sarcopenia encompassed assessments of muscle mass and walking speed. Specifically, low muscle mass was defined as a measurement that is at least 2 standard deviations below the mean observed in young adults (ages 18–39 years) of the same sex and ethnicity, as identified by the Third National Health and Nutrition Examination Survey (NHANES III) [14].

Cruz-Jentoft., *et al*. defined sarcopenia in 2010 as a progressive and widespread decline in skeletal muscle mass and strength, as outlined by the EWGSOP1 [9]. This group highlighted that muscle strength is not solely contingent upon muscle mass; thus, both low muscle mass and diminished muscle function—referring to either strength or performance—should be considered when diagnosing sarcopenia. In 2011, the International Sarcopenia Working Group (IWGS) and the Sarcopenia, Cachexia and Wasting Disorders Society published a consensus definition of sarcopenia. The IWGS created the definition of sarcopenia because they felt at the time that there was no real consensus on the appropriate criteria for individuals who might be sarcopenic and defined sarcopenia as the age-related loss of skeletal muscle mass and function [15,16]. In 2010, the Society for Sarcopenia, Cachexia, and Wasting Disorders (SCWD) convened to establish a generally agreed definition or collection of definitions that would yield definable outcomes for clinical trials [16]. The group characterized sarcopenia as reducing muscle mass accompanied by restricted movement.

In 2014, the Asian Sarcopenia Working Group (AWGS) released a consensus definition of sarcopenia. To advance research on sarcopenia in Asia, the AWGS included skeletal muscle atrophy alongside reduced muscle strength and decreased athletic performance in its definition. The diagnostic cut-off values for all parameters were carefully evaluated based on existing evidence from Asian countries and standard methodologies similar to those used by the EWGSOP [17]. In the same year, the Foundation for the National Institutes of Health (FNIH) initiated efforts to establish a comprehensive, evidence-based clinical defined as reduced muscle mass and strength [18]. In 2018, the EWGSOP reconvened to update the original definition established in 2010 to incorporate emerging evidence. The revised definition, referred to as EWGSOP2, emphasized muscle strength more due to its reliability as an indicator of muscle function. Nonetheless, it retained three fundamental criteria: muscle strength, muscle quantity or quality, and physical function [1]. According to the EWGSOP2 definition, an individual exhibiting low muscle strength is likely to have sarcopenia; however, the diagnosis is confirmed only when low muscle quantity or quality is also present [1]. In this context, muscle quality was defined to encompass both the micro- and macroscopic aspects of muscle architecture and composition [19]. According to EWGSOP2 criteria, when an individual exhibits low muscle strength, reduced muscle quantity and quality, and diminished physical function, the condition is classified as severe sarcopenia [1]. The EWGSOP2 was the first organization to suggest utilizing a self-report questionnaire called the SARC-F to screen for the risk of sarcopenia. The SARC-F evaluates five components related to the characteristics and consequences of sarcopenia, including muscle power, the ability to walk with support, rising from a chair, climbing stairs, and the incidence of falls [20].

Finally, in 2020, the Sarcopenia Definitions and Outcomes Consortium (SDOC) proposed a new definition of sarcopenia. The consortium aimed to establish evidence-based cutoff points for lean mass and strength to identify individuals at risk for mobility impairment and other negative health outcomes, such as falls and self-reported mobility limitations. Notably, the SDOC defined sarcopenia based on muscle strength and function, making it the first group to exclude muscle mass from its definition. As a result, their approach does not include a measure of skeletal muscle mass, as muscle mass reduction did not show a significant correlation with outcomes [21] (Table 1).

In conclusion, the definition of sarcopenia has evolved over the past 15 years. However, it consistently emphasizes that the condition results in a loss of muscle mass (except for the SDOC definition), strength, and physical function. Different working groups propose varying definitions and thresholds; for instance,

Year	Author	Definition of sarcopenia
1989	Rosenberg., *et al*.	Loss of muscle mass and function
2010	EWSSOP (Cruz-Jentoft., *et al*.)	Loss of muscle mass, strength and function
2010	ESPEN (Muscaritoli., *et al*.)	Loss of muscle mass and strength
2011	SCWD (Morley., *et al*.)	Loss of muscle mass and function
2011	IWGS (Fielding., *et al*.)	Loss of muscle mass and function
2014	FNIH (Studentski., *et al*.)	Loss of muscle mass and strength
2014	AWGS (Chen., *et al*.)	Loss of muscle mass, strength and function
2018	EWSSOP (Cruz-Jentoft., *et al*.)	Loss of muscle mass, strength and function
2020	SDOC (Bhasin., *et al*.)	Loss of muscle strength and function

Table 1: A chronological timeline of evaluation of the definition of sarcopenia [1,9,11,13,15,16,18,21,63].

Abbreviations: EWSSOP; European Working Group on Sarcopenia, ESPEN; The European Society for Clinical Nutrition and Metabolism, SCWD; The Society on Sarcopenia, Cachexia, and Wasting Disorders, IWGS; International Working Group on Sarcopenia, FNIH; The Foundation for the National Institutes of Health, AWGS; Asian Working Group for Sarcopenia, SDOC; The Position Statements of the Sarcopenia Definition and Outcomes Consortium.

the EWGSOP provides a less stringent definition. The methods used to determine the prevalence of sarcopenia also differ, making it more challenging to diagnose and treat affected individuals more reliably. This difficulty largely stems from the lack of consensus on measurement tools for these outcomes (Table 1).

Comprehensive evaluation of sarcopenia

Muscle mass

Magnetic resonance imaging (MRI) and computed tomography (CT) scans are widely regarded as the leading methods for the noninvasive evaluation of muscle mass, recognized for their precision and detailed imaging capabilities [22]. Nevertheless, the utilization of these advanced techniques in primary care settings and research environments is significantly restricted due to several factors. These include limited accessibility in various healthcare facilities, the high costs associated with such scans, the absence of mobile or portable variants, and the need for trained professionals with specialized skills to operate the equipment and interpret the results [23]. In contrast, dual-energy X-ray absorptiometry (DXA) emerges as a more accessible alternative for assessing SMM. While this method is also associated with some costs, it is generally more affordable than MRI and CT scans. Moreover, DXA offers patients the advantage of a low radiation dose, making it a safer option for routine assessments. However, it is essential to acknowledge that while DXA provides valuable information, it may not capture the same level of detail as MRI or CT scans. Sarcopenia is commonly defined by assessing lean soft-tissue mass, widely known as lean mass (LM), utilizing DXA. This measurement is typically adjusted for body composition or height [23]. However, it is crucial to note that different DXA instruments do not yield consistent results, leading to discrepancies in the reported prevalence of sarcopenia [24,25]. Such variations may also result in an underappreciation of the critical role of skeletal muscle in sarcopenia and the associated declines in functional ability and mobility in the aging population [26].

The current methodologies employed for evaluating skeletal muscle mass (SMM), with a particular emphasis on DXA, reveal substantial limitations in their effectiveness and accuracy. DXA is primarily designed to measure lean mass, which includes a variety of tissue components such as muscle, connective tissue, fat-free mass, and water content. However, studies have shown that DXA exhibits weak and inconsistent correlations with important outcomes, such as mobility and the incidence of falls in older adult populations, which are critical indicators of overall health and functional status [27]. Moreover, it is important to note that DXA does not directly measure skeletal muscle mass, as it provides a broader assessment of lean tissue without distinguishing between

its various components [27,28]. This lack of specificity can lead to misinterpretations of an individual's true muscle health. Given these constraints, there is a pressing need to develop and apply innovative tools and methodologies that can accurately quantify skeletal muscle mass. Such advancements would enable more precise assessments, ultimately improving our understanding of muscle health and its implications for aging populations. In this context, recent research has illuminated the fascinating process by which deuterium (D)-labeled creatine, known as D3-creatine (D3-Cr), is taken up by skeletal muscle. Once inside these muscle tissues, D3-Cr undergoes an irreversible biochemical transformation into creatinine, a byproduct that serves as a reliable marker for assessing SMM [27,29]. This ability to indicate SMM makes D3-Cr a powerful tool in clinical settings where monitoring muscle composition is critical. However, the efficacy of D3-Cr as a marker has yet to go beyond conjecture. This introduces an element of uncertainty, meaning that while D3-Cr can provide valuable insights into muscle mass, it should not be regarded as a definitive measurement. Instead, it functions more as a proxy for SMM, suggesting that further research and validation are necessary before it can be classified as a precise and unambiguous measurement technique for evaluating skeletal muscle mass.

Muscle strength

A limited number of validated methods are available for accurately measuring muscle strength. Grip strength is the most commonly utilized tool among these methods. Grip strength testing is straightforward and cost-effective, making it accessible for a wide range of settings [30]. Research has shown that low grip strength is linked to significant clinical outcomes, including increased functional limitations, diminished health-related quality of life, and a greater risk of mortality, encompassing both specific to all-cause mortality rates [31,32]. In addition to grip strength, some experts have proposed the chair stand test as an alternative method for assessing muscle strength, particularly for evaluating leg strength. This test involves measuring the number of times a person can stand up from a seated position within a specific timeframe. However, it's important to emphasize that the EWGSOP2 is the only organization that officially recommends using this assessment tool for muscle strength evaluation [1]. Despite its potential, the chair stand test is not well-validated compared to other methods. Furthermore, its use is often discouraged due to the considerable time it takes to administer and the absence of well-established cutoffs that would enhance its reliability and interpretability in clinical practice [23].

Muscle function

Gait speed is widely recognized as the most effective tool for assessing muscle function and physical performance among individuals. This simple yet powerful measure is practical and dependable, offering a safe evaluation method requiring no specialized equipment [33]. By analyzing a person's gait speed, healthcare professionals can gain valuable insights into potential adverse outcomes, such as increased risk of disability, cognitive decline, institutionalization in care facilities, falls, and even mortality [34]. Throughout various working groups focused on muscle function, gait speed emerged as the dominant metric for assessment. However, it is necessary to note that the FNIH group took a different approach; they explicitly excluded muscle function evaluations from their definition of sarcopenia [18], highlighting a divergence in perspectives on what constitutes this condition. Overall, gait speed remains a crucial indicator of an individual's health and mobility status, helping to guide interventions and support for those at risk.

Pathophysiological mechanisms linking sarcopenia and tooth loss

The connection between sarcopenia and tooth loss involves a range of interrelated biological and behavioral factors, creating a multifaceted relationship. Tooth loss is not merely a result of individual factors; it stems from complex interactions among several risk contributors [35]. Furthermore, demographic variables such as age, gender, household income, and education level play critical roles in the likelihood of experiencing tooth loss. Also, lifestyle factors such as smoking, alcohol consumption, and brushing frequency have been linked to this issue [36]. Whatever the underlying cause, when individuals experience tooth loss, it can significantly impair their ability to chew, which may lead to alterations in dietary habits and negatively impact their overall quality of life—particularly their oral health-related well-being [37,38]. Notably, sarcopenia, a condition characterized by the loss of muscle mass and strength, has been found to correlate with tooth loss in many older adults. This link emphasizes the importance of understanding how these factors intertwine and affect health outcomes in the aging population. Hence, this section will delve

into the main mechanisms that may link these two conditions, focusing on the dynamic interplay of systemic influences, localized effects, and lifestyle choices.

Tooth loss is a significant and objective indicator of an individual's oral health status. Among elderly populations, tooth loss commonly coexists with sarcopenia—a condition characterized by the progressive loss of muscle mass and strength—alongside other risk factors such as diabetes mellitus [38]. While several studies have examined how weight fluctuations impact tooth loss, the relationship between sarcopenia and tooth loss remains mainly unexplored [39]. The adverse effects of low muscle mass can impair chewing efficiency and the overall function of oral muscles. For instance, a compelling study conducted in Japan revealed a noteworthy correlation between occlusal power—the force generated when biting—and measures of physical strength, such as handgrip strength, walking velocity, and total body muscle volume [40]. This suggests that the ability to chew effectively relies on oral health and one's overall muscle condition. Furthermore, a recent longitudinal study demonstrated that a reduction in oral occlusal strength is closely linked to diminishing leg muscle strength [41]. This connection emphasizes that lower muscle mass threatens mobility and is associated with increased tooth loss, highlighting the intricate interplay between oral and physical health in the aging population.

Sarcopenia and periodontal disease are interconnected conditions that both arise from chronic systemic inflammation, which serves as a common underlying factor. In individuals suffering from these conditions, there are typically elevated levels of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP). These inflammatory markers contribute to the pathology of both sarcopenia and periodontal disease [42]. Similarly, periodontitis exhibits almost identical inflammatory mechanisms with sarcopenia. The chronic inflammation associated with periodontitis can lead to tissue destruction, which may intensify inflammatory responses in the body. As such, the overlap in inflammatory pathways suggests a potential bidirectional relationship, where sarcopenia and periodontal disease could exacerbate one another, leading to worsening symptoms and overall health outcomes for affected individuals [43]. In a study, 118 men and 46 women, aged between 61 and 90 years, were categorized into sarcopenia and non-sarcopenia groups based on the AWGS criteria [43]. The researchers compared various factors between these groups, including body composition, walking speed, biochemical indices, levels of IL-6 and IL-10, lifestyle habits, and disease status. The results indicated that sarcopenia presence was directly correlated with increased levels of IL-6 and IL-10, as well as a higher IL-6/IL-10 ratio, while showing an inverse correlation with BMI [43].

One possible mechanism for the relationship between inflammation, muscle mass loss, and periodontitis is the increased catabolism of muscle caused by elevated levels of inflammatory markers [44]. Studies have demonstrated a causal link between inflammatory cytokines and reduced muscle mass *in vivo* (using rodent models) and *in vitro*. For instance, the infusion of TNFα and IL-6 in rats has been shown to lead to proteolysis and atrophy in skeletal muscles [45, 46]. Additionally, negative correlations have been observed between the rate of protein synthesis in skeletal muscles and levels of CRP, IL-6, and TNFα receptor-2 [47]. These findings collectively suggest that low-grade inflammation may play a significant role in the development of sarcopenia and periodontitis.

Periodontal disease is an inflammatory condition that destroys the tissues supporting the teeth, ultimately leading to tooth loss [48]. At the same time, the inflammatory markers associated with this disease circulate throughout the body, contributing to muscle breakdown and exacerbating sarcopenia. Understanding how inflammatory responses are regulated is essential for comprehending the pathogenesis of complex diseases like periodontitis [49]. Systemic inflammation linked to sarcopenia can significantly hinder the body's wound-healing processes and exacerbate damage to periodontal tissues. This deterioration may lead to severe periodontitis and eventual tooth loss, establishing a troubling feedback loop that connects these two conditions [50]. Moreover, the impact of sarcopenia on muscle mass is particularly concerning for older adults, as it often results in notable reductions in the mass of crucial muscles such as the geniohyoid, pterygoid, masseter, tongue, and pharyngeal muscles, which play vital roles in oral function and food intake [51]. In addition, the ability to effectively close the lips is essential for proper feeding; when lip muscle strength diminishes, it can result in food and liquids leaking from the corners of the mouth. This decline in lip strength, attributed to sarcopenia, can lead to complications like dysphagia,

making it difficult for individuals to chew and swallow [52]. It has, therefore, been suggested that decreased lip strength is due to sarcopenia and is associated with difficulties eating and drinking (i.e., dysphagia) [53]. In this vicious cycle, the loss of teeth significantly impacts the ability to chew effectively, reducing overall chewing efficiency. This decrease affects the digestive process and undermines the mechanical stimulation the mouth and jaw muscles rely on for optimal function. When teeth are missing, the forces that stimulate these muscles during chewing are diminished, potentially leading to muscular atrophy and discomfort. This lack of mechanical stimulation can also contribute to additional oral health issues, creating a cascade of problems that affect both function and well-being. Extended periods of unuse of the muscles in the orofacial area can result in significant localized muscle atrophy and weakness. This decline in muscle function can severely hinder various aspects of oral functions. In addition, sarcopenia can further exacerbate this adverse condition by diminishing the strength of the masticatory muscles and the tongue. As a result, individuals may experience a notable reduction in their ability to adequately intake food, leading to nutritional concerns and increasing the risk of periodontal disease and eventual tooth loss due to the compounded effects of weakened muscle function.

The impact of oxidative stress is crucial in understanding the relationship between sarcopenia and tooth loss. Oxidative stress refers to a state in which there is an excessive accumulation of reactive oxygen species (ROS) in the body, overwhelming the capacity of antioxidant defenses. This disruption is significant in two major health issues: sarcopenia, the age-related loss of muscle mass and strength, and periodontal disease, which affects the supporting structures of teeth. In sarcopenia, elevated levels of ROS lead to the breakdown of muscle proteins and impair the function of mitochondria, the energy-producing organelles within cells. This can result in decreased muscle function and overall physical decline [54]. Similarly, ROS plays a destructive role in the context of periodontal disease, contributing to the deterioration of periodontal tissues and facilitating alveolar bone loss in the jaw. This interplay between oxidative stress, muscle deterioration, and dental health underscores the interconnectedness of these conditions and highlights the importance of maintaining a balance between ROS production and antioxidant defenses for overall well-being.

Mitochondria are the main sites for cellular energy production through a process called oxidative phosphorylation. During this process, a small fraction of electrons can leak from the electron transport chain, producing superoxide as a byproduct. Under conditions of mitochondrial dysfunction—such as impaired electron transport chain activity or decreased antioxidant defenses—the production of reactive oxygen species (ROS) by the mitochondria can increase significantly [55]. Oxidative stress occurs when there is an imbalance between the production of ROS and the body's ability to neutralize these reactive species, leading to an accumulation of oxidative damage. This damage can have detrimental effects on multiple cellular components, particularly within skeletal muscle tissue. Proteins are particularly vulnerable to oxidative modification due to their structural and functional importance in cellular processes. Oxidative modifications to proteins can manifest in several ways, including the oxidation of specific amino acid residues, the formation of protein cross-links, and the addition of carbonyl groups to the proteins. These alterations can significantly disrupt normal protein function, impairing enzymatic activity and leading to failures in cellular signaling pathways. Additionally, oxidative damage may promote the degradation of proteins through various cellular pathways, including proteolysis [56]. For example, a study conducted by Bullón., *et al*. observed elevated levels of mitochondrial-derived ROS in peripheral blood mononuclear cells from patients diagnosed with periodontitis [58]. This increase was associated with signs of mitochondrial dysfunction. The implications of such findings are profound; they suggest that conditions like sarcopenia—characterized by the loss of muscle mass and strength—may contribute to systemic issues such as tooth loss, as oxidative stress and subsequent damage can exacerbate periodontal disease. This connection underscores the intricate relationship between muscle health, oxidative stress, and oral health in individuals affected by age-related conditions.

One of the key factors involved in this mechanism is Insulin-like Growth Factor-1 (IGF-1). This growth factor has garnered attention for its wide-ranging effects on cellular growth and development and its considerable therapeutic potential in combating muscle atrophy and frailty that often accompany aging and various diseases [57]. Moreover, IGF-1 is also critical for preserving the health of periodontal tissues, which include the gums and other structures surrounding the teeth. These tissues require robust

repair mechanisms to recover from injury or stress, and insufficient IGF-1 can hinder this process, like in the case of sarcopenia [57]. Low levels of IGF-1 may create a connection between sarcopenia and tooth loss by disrupting the repair processes in both muscle and periodontal tissues. This interplay suggests that inadequate IGF-1 could lead not only to weak muscles and increased frailty but also to compromised oral health, ultimately highlighting the importance of this growth factor in overall bodily function and quality of life.

In adult mammals, IGF-1 is primarily synthesized in the liver, serving as a systemic growth factor. Additionally, IGF-1 is manufactured in extrahepatic tissues, including skeletal muscle, where it fulfills a vital autocrine and paracrine function [58]. The isoform IGF-1Ea plays a crucial role in maintaining the hypertrophic phenotype by promoting the activation of various signaling pathways, notably AMPK (Adenosine Monophosphate-Activated Protein Kinase). AMPK functions as an energy sensor within cells, contributing significantly to the regulation of whole-body energy balance and influencing glucose and lipid metabolism [58]. Furthermore, IGF-1 is recognized for its mitogenic capabilities, which enhance the osteogenic differentiation of periodontal ligament fibroblasts [59]. Research conducted by Raja., *et al*. has demonstrated that IGF-1 improves cell survival in these fibroblasts by up-regulating anti-apoptotic molecules while concurrently down-regulating pro-apoptotic molecules [60]. Available research indicates that localized and controlled release of IGF-1 from Glucan co-gelatin microspheres can enhance periodontal tissue regeneration [61]. In light of this information, a strengthened hypothesis emerges regarding the interrelationship between sarcopenia and periodontal disease. Both conditions exhibit similar underlying mechanisms and appear to trigger one another, potentially increasing tooth loss risk. This relationship underscores the necessity for an integrated approach to understanding and addressing both muscular and oral health simultaneously in affected individuals.

Finally, it has been proposed that sex hormones, in conjunction with behavioral and social factors, contribute to the mechanism of tooth loss associated with sarcopenia [62]. Notably, estrogen deficiency has been shown to accelerate the resorption of alveolar bone and diminish SMM [63]. The research conducted by Sakuma., *et al*. indicates that the decline in levels of sex hormones—such as testosterone, estrogens, and dehydroepiandrosterone sulfate—plays a significant role in the age-related onset of sarcopenia [64]. As the levels of these hormones decrease with aging, the activation of sarcopenia ensues, adversely affecting masticatory muscles and leading to the deterioration of periodontal tissues. In a related study, Su., *et al*. reported that men with low bioavailable testosterone levels, influenced by sex hormone-binding globulin, demonstrated an increased risk of periodontitis [65]. Consequently, it is plausible that the rates of tooth loss may rise with age due to the frailty associated with sarcopenia, compounded by the impact of hormonal changes on periodontal health. Moreover, sarcopenia-related frailty may result in diminished physical activity and decreased social engagement, thereby increasing the likelihood of neglecting oral hygiene and regular dental care. Economic factors, such as limited financial resources, can further exacerbate these conditions by restricting access to nutritious food and essential healthcare services [66]. Additionally, as individuals age and their life circumstances evolve—such as those with lower body weight resorting to frequent sugar intake to mitigate weight loss—the risk of tooth loss due to decay may significantly increase within this demographic [67].

The precise mechanism linking tooth loss and low skeletal muscle mass is still unclear but may involve inflammatory and nutritional pathways. One commonly mentioned factor is that inflammatory cytokines can activate various molecular pathways associated with skeletal muscle loss. This inflammation-induced activation creates an imbalance between protein synthesis and catabolism, resulting in muscle loss. Inflammation can also lead to diseases like periodontitis, which contributes to widespread tooth loss. On the contrary, losing teeth can also negatively impact diet quality and nutrient intake, increasing the risk of sarcopenia and creating a vicious cycle where each condition exacerbates the other, further worsening the overall situation (Figure 1).

Discussion

A comprehensive understanding of the mechanisms through which sarcopenia impacts tooth loss is vital for recognizing the complex interplay between these two health conditions. This relationship underscores the urgent need for integrated healthcare strategies that address not only systemic health but also factors related to nutrition and oral hygiene. By actively pursuing early identification and management of risk factors associated with both

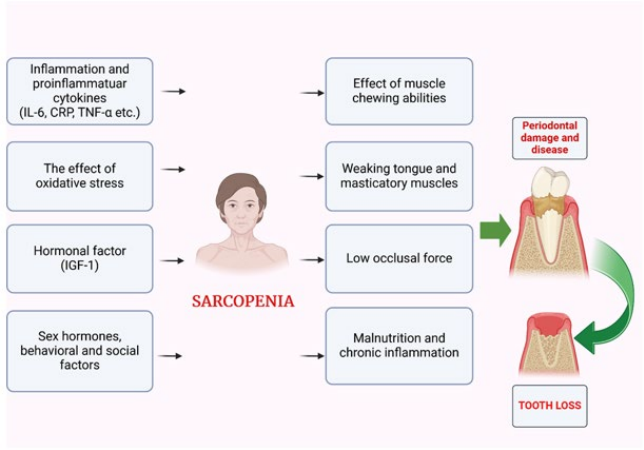

Figure 1: The possible mechanisms linking sarcopenia and tooth loss.

Abbreviations: IL-6; interleukin 6, CRP; C-reactive protein, TNF; Tumor necrosis factor, IGF; insulin-like growth factor.

sarcopenia and tooth loss, healthcare providers can implement effective multidisciplinary interventions that are essential for breaking the cyclical nature of these debilitating conditions. The association between sarcopenia and tooth loss is particularly concerning in older populations, where both conditions are notably prevalent. Sarcopenia, which is defined as the progressive decline in skeletal muscle mass, strength, and overall function, significantly impacts not only musculoskeletal health but also a range of dental outcomes. For instance, the loss of muscle strength can influence an individual's ability to maintain proper oral hygiene practices, leading to an increased risk of dental issues [62]. Furthermore, the nutritional deficits resulting from sarcopenia can adversely affect the health of the gums and supporting structures, contributing to tooth loss.

While researchers and clinicians have a widespread consensus regarding the definition and identification of sarcopenia, no universally accepted standard measurement can be applied consistently across diverse populations and clinical settings. The concept of sarcopenia was first articulated in 2010 when it was defined as a condition characterized by a gradual and systemic loss of skeletal muscle mass, known as myopenia, accompanied by a significant decline in muscle strength referred to as dynapenia [9]. By this definition, the presence of myopenia alone is deemed sufficient to classify an individual as likely having sarcopenia. At the same time, a definitive diagnosis necessitates the identification of dynapenia during thorough clinical evaluations [9]. However, the understanding of sarcopenia has evolved since then. The 2019 report by the EWGSOP2 brought attention to the notion that dynapenia is fundamentally more important than myopenia when confirming diagnoses of sarcopenia [1]. This shift in emphasis suggests that while myopenia serves as an important indicator, it should be viewed as a confirmatory criterion rather than the primary measure in the diagnostic process [1]. Therefore, a comprehensive assessment that prioritizes dynapenia may lead to more accurate diagnoses and, consequently, more effective intervention strategies for individuals at risk of or suffering from sarcopenia. Despite the existence of detailed and comprehensive definitions for sarcopenia, a condition characterized by an age-related decline in muscle mass and strength, the term myopenia is still often utilized as a standalone measure to assess muscle deficiency. The reasons behind this persistent and erroneous use of myopenia are not entirely clear; however, one significant factor may be the straightforwardness and accessibility of radiological data, particularly in clinical practice. To illustrate the situation, in the studies reviewed in the recent meta-analysis conducted by Lin and colleagues [68], the assessment of sarcopenia relied solely on the skeletal muscle index, which was explicitly measured at the lumbar vertebrae L3 or L4 through CT scans. This singular approach to assessing muscle mass mainly centered on the criteria for myopenia, thereby overlooking the broader and more nuanced definitions encompassing sarcopenia and its severe form. Consequently, this narrow focus risks failing to capture the complete clinical picture of muscle weakness and frailty, which can significantly affect individuals' health and quality of life, particularly the aging population. The reliance on a simplified measurement approach may lead to misinterpretations and inadequate management of sarcopenia's implications in clinical settings. In this context, it is crucial to note that the SDOC definition does not consider myopenia in its consensus definition for sarcopenia, as it showed no correlation with outcomes [26]. Considering these facts and potential hazards, Topkan., *et al*. recently drew attention to the fact that defining sarcopenia just via measuring myopenia by evaluating only muscle mass using CT or MRI to measure skeletal muscle index in patients would not meet comprehensive criteria for diagnosing sarcopenia [9,69]. It was

also reported that since muscle strength, rather than muscle mass, can better predict adverse outcomes such as sarcopenia-related hospitalization and death, it would be essential to consider these features simultaneously for an accurate diagnosis. For this reason, it would be helpful to increase the reliability and comparability of the findings by conducting different studies and to reach a common decision encompassing sarcopenia and its severe form. Consequently, this oversimplification might result in an incomplete assessment of the condition, which in turn can hinder healthcare professionals from developing tailored treatment plans that adequately address the complexities of sarcopenia and its impact on patients' overall health and quality of life.

Sarcopenia has been invariably linked to a variety of functional impairments and health conditions. However, its connection to oral health, particularly regarding tooth loss, has only recently begun to receive the attention it deserves in the research community [2]. The mechanisms underlying the link between sarcopenia and oral health involve several shared risk factors. These include age, which is a primary contributor to both muscle deterioration and oral health issues; malnutrition, which can lead to a deficiency in essential nutrients necessary for maintaining both muscle and dental health; and chronic systemic inflammation, a condition negatively impacting various bodily systems [50]. Specifically, muscle atrophy resulting from sarcopenia can impede masticatory efficiency. This impairment can result in diminished oral motor function, making it more challenging for individuals to eat a balanced diet and maintain proper oral hygiene. Consequently, this can indirectly exacerbate the risk of developing oral diseases such as periodontal disease and dental caries, the leading causes of tooth loss [70]. Individuals with sarcopenia may also experience a decline in their physical capability, which can hinder their ability to care for their oral health properly. This decline can lead to neglect in oral hygiene practices, such as regular brushing and flossing, and may reduce their capacity to attend dental appointments. As a result, tooth loss in individuals with sarcopenia may be viewed as a downstream consequence of reduced functional capacity and poor oral care management [70]. Tackling these interconnected issues presents a valuable opportunity to enhance both muscle and oral health in older adults, by which we can significantly improve their overall well-being and quality of life.

The stomatognathic system, which encompasses the complex structures involved in chewing and swallowing, is notably impacted by low muscle mass and diminished muscle strength, primarily due to the condition known as sarcopenia. This gradual decline in muscle function affects overall strength and plays a crucial role in the ability to eat effectively, as mastication and swallowing rely heavily on the performance of facial skeletal muscles [71]. In a significant study by Newton., *et al*. [72], the researchers used advanced CT imaging techniques to investigate the relationship between aging and dental status on the cross-sectional area density of the masseter and medial pterygoid muscles. Their findings revealed that both key masticatory muscles experienced a marked reduction in size as individuals aged, highlighting the physiological changes accompanying the aging process [73]. Moreover, the ability to exert bite force—a critical aspect of masticatory muscle function—can be significantly compromised by tooth loss [74]. The physical strength required to chew effectively is directly tied to the health and integrity of both the teeth and the surrounding musculature, underscoring the interconnected nature of dental health and muscle function in aging. Tooth loss is not simply a result of physiological aging; it is classified as pathological aging and can lead to various complications. One significant consequence of this type of aging is a decrease in bite force, which is commonly observed among older adults [75]. This decline in bite strength may be influenced by sarcopenia, which decreases occlusal force. A recent study aimed to explore the relationship between occlusal force and functional disability among older individuals [76]. This research involved a prospective cohort study with a sample size of 815 community-dwelling adults aged 70 years and older, with a breakdown of 51.7% being female participants. The study's findings revealed a clear link between lower maximum occlusal force and an increased risk of developing functional disabilities in older adults. Importantly, this risk remained elevated even after controlling for various potential confounders, including the number of remaining.

Conclusion

Recent studies show a significant yet complex bidirectional relationship between sarcopenia, which refers to the loss of skeletal muscle mass and strength, and tooth loss. While the precise mechanisms underlying this connection are still not fully understood, it is clear that both conditions can influence each other

in various ways. For instance, the deterioration of muscle strength may impact an individual's ability to maintain proper dental hygiene, potentially leading to tooth loss. Conversely, the loss of teeth can affect nutrition and dietary choices, which may further contribute to muscle decline. This intricate interplay highlights the importance of early intervention and management of either condition. By addressing one issue promptly and effectively, there may be potential to prevent or alleviate the onset or progression of the other, ultimately improving overall health and quality of life. Therefore, further multidisciplinary research into these relationships is essential to better understand how both conditions can be managed simultaneously.

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Conflict of Interest

None.

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