MECHANISMS LINKING ORAL HEALTH AND FRAILTY IN OLDER ADULTS: A NARRATIVE REVIEW

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ABSTRACT

Background Frailty is a geriatric syndrome in which multiple systems lose their physiological reserves resulting in increased vulnerability to stressors and risk of adverse health-related outcomes. There is an increasing number of studies discussing the association of oral health with frailty through several pathways.

Objective The aim of this review was to describe the possible mechanisms linking oral health and frailty.

Data Sources A narrative review was performed with literature search in PubMed, Google Scholar and ScienceDirect electronic databases. Reference lists from relevant studies and cited papers were also investigated.

Study Selection The review included full papers of any study design, published in peer-reviewed journals in English until July 2021.

Data Extraction Current literature indicates four possible mechanisms linking oral health and frailty.

Data Synthesis The first mechanism refers to the nutritional pathway. It is reported that poor oral health negatively affects protein and vitamins intake. Malnutrition and decreased energy intake have a dominant role in frailty onset. Inflammation is another mechanism. Periodontal disease causes a systemic increase of pro-inflammatory biomarkers which in turn may lead to muscle strength deterioration. Furthermore, oral health can be related to frailty through neural mechanisms. Specifically, occlusion and proprioception from the periodontal ligament contribute to the control of body balance. Finally, the mechanisms include the psychological pathway, since poor oral health may lead to social isolation and depression which increase the risk of negative general health outcomes. More studies are necessary to clarify the previous associations and reveal any causative effects.

KEYWORDS

Oral Health; Frailty; Malnutrition; Inflammation; Depression.

1. INTRODUCTION

One of the dominant characteristics of the older population is heterogeneity, therefore overall health and function can vary substantially among individuals of the same chronological age. The concept of frailty has come to the forefront of research interest in Geriatric Medicine as a geriatric syndrome characterized by multiple functional impairments trying to explain this diversity among older people [1,2,3]. Frailty is defined as a clinical state of increased vulnerability related to ageing in which multiple systems lose their physiological reserves and the homeostatic balance is disrupted, resulting in an increased risk of adverse health-related outcomes, including functional impairment, dependency, hospital admission, institutionalization, reduced quality of life and mortality, even after exposure to a minor stressor, such as a viral infection or the use of a new drug [2,4]. The most common clinical manifestations of frailty are falls, confusion, functional decline and several non-specific signs and symptoms, such as unintentional weight loss, extreme fatigue and frequent infections. Genetic and environmental factors combined with epigenetic mechanisms are closely associated to the cumulative molecular and cellular damage, and pathophysiology of frailty.

As frailty is considered a dynamic and modifiable condition exercise (aerobic, balance and resistance-based), caloric and protein support, vitamin D intake and reducing polypharmacy seem to be effective strategies in its prevention or even reversion [4]. Prevalence of frailty among community-dwelling older adults and nursing home residents is estimated to be approximately 16.7% [5] and 52.3% respectively [6]. Regarding the assessment of frailty, a total of 67 instruments are available in the literature [7]. The Physical Frailty Phenotype has been identified as the most widely used instrument [7].


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According to this instrument, frailty is diagnosed when at least three of the following components are met: unintentional weight loss, self-reported exhaustion, low physical activity, weak hand grip strength and slow gait speed, while pre-frailty is defined by the presence of one or two of these criteria [8]. Moreover, the Clinical Frailty Scale and the Frailty Index of Accumulative Deficits are among the nine most-referenced frailty instruments [7]. It was developed as a 7-point ordinal scale and has been modified as a 9-point scale from one (very fit) to nine (terminally ill with a life expectancy of less than six months) based on information about health status derived from medical history and clinical examination; a score of 5 or more indicates frailty [9]. The Frailty Index of Accumulative Deficits is based on the multi-dimensional nature of frailty and is expressed as a ratio of various accumulated health deficits [10].

Frailty has come to the forefront of the research interest in the dental field as well. Poor oral health has a high prevalence among older adults and there is an increasing number of studies which demonstrate cross-sectional, as well as longitudinal associations of oral health indicators with frailty or its components through several suggested pathways [11-13]. A systematic review showed a relationship between aspects of oral health, such as number of teeth, need for and use of dental prostheses, and frailty or pre-frailty, and suggested the existence of various mediators of this association which should be further investigated [11]. In a systematic review of longitudinal studies, the number of teeth, oral function, accumulation of oral health problems and number of dry mouth symptoms were identified as predictors of frailty [12]. The evident associations between oral health and frailty status among older people suggest that the integration of frailty assessment into dental treatment planning might be useful in providing the most appropriate dental care and preventive strategies to older adults who are at a state of increasing vulnerability [13]. Moreover, oral health, and particularly occlusal force and mastication, have been associated with sarcopenia [14], a muscle disease characterized by decreased muscle strength and muscle mass, and/or reduced physical performance, which has many mutual clinical features with frailty and may serve as a precursor of frailty [15,16].

Apart from the various individual oral health indicators that have been investigated in relation to frailty, the term “oral frailty” has been introduced by the Japanese Society describing a condition of decreased articulation, slight choking, or spillage while eating and increased number of unchewable foods [17]. A longitudinal study in Japanese community-dwelling older adults, describing oral frailty as the presence of at least three of the following parameters: less than 21 natural teeth, decreased masticatory performance, decreased oral diadochokinesis for the syllable “ta”, decreased tongue pressure, subjective difficulties in eating tough foods and swallowing tea or soup showed that it may predict new onsets of frailty as defined by the Physical Frailty Phenotype and mortality [18].

As an increasing number of studies has shown an association between oral health and frailty, the purpose of the present narrative review was to describe the possible linking mechanisms.

2. METHODOLOGY

A literature search in PubMed, Google Scholar and ScienceDirect electronic databases was performed. The following keywords were used: (oral health OR oral function) AND (frailty) AND (linking mechanisms OR linking pathways). In addition, reference lists from relevant studies and cited papers were investigated. The titles and abstracts of the retrieved articles were screened to decide whether full-text reading was required, and full texts were retrieved for the selected articles. Included studies should have been published in peer-reviewed journals in English language, while no limits were set on the study design and the year of publication. Articles published until July 2021 were included in the present review.

3. RESULTS

Current literature indicates four possible mechanisms through which oral health is associated to frailty: a) nutritional pathway, b) inflammation, c) neural mechanisms and d) psychological pathway (Fig. 1).

![Figure 1. Screening process.](image-url)
3.1. Nutritional pathway

The first linking mechanism refers to the nutritional pathway and there is an interesting discussion on the association between oral health and nutrition. Malnutrition is associated with frailty [19,20]. A meta-analysis revealed that a total of 68% of community-dwelling older adults with malnutrition had frailty [21].

Another meta-analysis demonstrated the substantial association between malnutrition and frailty or sarcopenia, with the co-occurrence of two or all the afore-mentioned conditions in about 50% of the hospitalized older adults [22].

There are indications that energy intake, as well as nutrient quality, have an important role in the onset of frailty and the pathogenesis of sarcopenia [23]. Deficiencies in nutrients have been associated with mitochondrial dysfunction which in turn may cause fatigue and weakness, two elements of Physical Frailty Phenotype [24,25].

Furthermore, a decreased amount of protein intake possibly contributes to the pathogenesis of frailty findings, based on a meta-analysis of observational studies suggesting an association between an increased intake of dietary protein and a lower prevalence of frailty (OR=0.67) [26]. In addition to the quantity of proteins, other parameters, such as protein source and protein distribution across meals, may also have an impact on the development and progression of frailty in older people [18].

Diet quality overall has been associated with a lower incidence of frailty in older adults [27,28]. Regarding the eating patterns in older adults, higher adherence to the Mediterranean Diet, which is characterized by a high intake of plant foods and olive oil and low consumption of red meats, have been inversely correlated to the loss of muscle mass, sarcopenia and frailty [29]; a meta-analysis demonstrated the protective role of the Mediterranean Diet against physical disability (OR=0.75) and frailty (OR=0.42) [30]. It is hypothesized that the Mediterranean Diet has a protective action on skeletal muscle health (myoprotective effect), since it is regarded as a source of bioactive nutrients and has anti-oxidative and anti-inflammatory properties [31]. On the other hand, Westernised dietary patterns, characterized by high consumption of refined cereals, whole dairy products, and processed meat, have a direct relationship with the increased risk of developing several components of physical frailty phenotype, namely weight loss and slow gait speed [32].

Poor dentition, dysphagia and dysgeusia are considered to be among the nine common risk factors (the nine d's) of malnutrition in older adults [33], but more research is necessary to clarify any causative effects and the role of individual contributors.

Edentulism and the presence of less than 21 natural teeth have been associated with the decreased intake of fruits, vegetables and proteins and the increased consumption of carbohydrates [34]. A meta-analysis showed that a lower number of remaining teeth was associated with poorer nutritional status, while edentulism and the presence of a prosthesis were not found to have a statistically significant effect on malnutrition in older adults [35].

However, a systematic review of longitudinal studies has shown that the evidence of a causative effect between tooth loss and nutritional status and nutrient intake was minor [36]. Also, the results of a randomized controlled trial indicated that both removable partial dental prostheses and the shortened dental arch concept generated equal improvement in partially dentate older adults' masticatory performance, but the masticatory performance could not predict nutritional status, due to their weak association [37]. Impaired masticatory performance in older adults is affected by a variety of factors and may lead to alteration of dietary choices and, subsequently, to malnutrition [38]. Better masticatory performance among functionally independent older adults, was independently associated with higher adherence to the Mediterranean Diet, in contrast to other dental indicators such as the number of natural teeth and use of removable prostheses [39], while older Greeks were more adherent to the components of the Mediterranean Diet compared to younger ones disregarding their dental status [40]. The enhancement of the maximum bite force and masticatory performance has been viewed as a prerequisite for a normal nutritional status in older people [41,42]. Nevertheless, the prosthetic rehabilitation of missing teeth does not seem sufficient for the treatment of malnutrition, and should be accompanied by nutritional advice, as this combination has been shown to lead to alterations in the food intake such as fruits and vegetables and to improvement of older adults' nutritional status [41-44].

Regarding dysgeusia, taste alteration leads to a diminution of food enjoyment, which in turn may decrease appetite and result in malnutrition [45]. Dysphagia (swallowing problems), which is highly prevalent in older individuals, can alter the oral intake of foods and liquids and, thus, serves as a risk factor of malnutrition [46-48]. According to a systematic review, chewing and swallowing problems were among the factors which were consistently associated with poor nutrition in nursing home residents [31,49]. Furthermore, high Xerostomia Index scores in older adults have been associated with the selective avoidance of foods including raw carrots, whole apples and nuts, lettuce, corn and grilled or fried meats [50].

In a cross-sectional study, community dwelling older adults with oral frailty (based on the definition proposed by Tanaka et al.) were found to have a greater possibility of more severe malnutrition assessed using the Mini Nutritional Assessment – Short Form (OR=2.17) and the level of serum albumin (OR=1.59) [51].

Also, a two-year longitudinal study demonstrated that oral frailty was associated with an increased risk of deterioration of nutritional status (OR=2.24) [52].
There are indications that oral health status is independently associated with malnutrition [53]. However, the findings of a systematic review of prospective studies regarding dental status and swallowing function as determinants of malnutrition in older adults were inconsistent, while moderate quality evidence proposed that periodontal diseases, oral pain and difficulties in mastication are not determinants of malnutrition [54]. Therefore, mastication seems to explain only part of variance in the intake of food and/or nutrients in independent older adults [41], and more high-quality studies are necessary.

3.2. Inflammation
The term “inflamming” describes an age-related state of low-grade chronic inflammation. It is characterized by both increased levels of proinflammatory cytokines, such as CRP and IL-6 and acute phase proteins, such as CRP, and decreased concentrations of IL-10, which lead to deterioration of immunological homeostasis [55, 56]. Thus, inflamming has been assumed as an underlying mechanism of frailty. Proinflammatory biomarkers, principally interleukin 6 (IL-6) and tumor necrosis factor-alpha (TNF-α) can have an effect on the onset of frailty [57]. The results of a meta-analysis demonstrated a cross-sectional association between higher concentrations of CRP and IL-6, and frailty and pre-frailty, while no statistically significant longitudinal relationship emerged [58]. Another meta-analysis revealed a cross-sectional quantitative relationship between immunological biomarkers and frailty among older adults assessed with Physical Frailty Phenotype, which was stronger for CRP and IL-6 and weaker for TNF-α [56].

In a prospective cohort study, elevated serum levels of IL-6 acted as a predictor of walking speed decline among community-dwelling older adults [59]. Also, the findings of a meta-analysis suggested that higher levels of circulating CRP, IL-6 and TNF-α were significantly associated with lower handgrip strength and knee extension strength, and CRP levels were significantly inversely correlated to skeletal muscle mass [60]. A meta-analysis of cross-sectional studies showed that serum levels of CRP were elevated in people with sarcopenia compared to controls, while no statistically significant associations were found between serum IL-6 levels and TNF-α levels, and sarcopenia [61].

There is evolving evidence of strong associations between periodontitis, low-grade inflammation and systemic health. The accumulation of periodontopathogenic bacteria into the gingival sulcus stimulates a local inflammatory response and pro-inflammatory mediators such as interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α) are produced in periodontal lesions, which may move into the systemic circulation. Also, serum levels of C-reactive protein (CRP), an acute phase reactant produced mainly in the liver in various inflammatory cytokines, are elevated in patients with periodontitis [62].

3.3. Psychological pathway
Late-life depression and frailty have been described as comorbid geriatric syndromes [63]. A meta-analysis supported a reciprocal relationship between depression and frailty in older adults [64]. A systematic review suggested the strong prospective relationship between the presence of depression and greater risk of incident frailty among community-dwelling older adults [65]. Also, a strong correlation between depression and risk of frailty was found in a meta-analysis and this risk was higher for older men compared to older women (OR=4.76 and OR=2.25 respectively) [66]. The findings of another meta-analysis revealed a weak negative correlation between depressive symptomatology and handgrip strength [67]. Furthermore, the results of a longitudinal study demonstrated that both loneliness and social isolation were independently associated with incident frailty [68]. Another prospective cohort study showed a negative association between frequency of laughter and risk of functional disability among older individuals [69].

On the other hand, a longitudinal study showed that high levels of loneliness were associated with increased risk of incident physical frailty, but no relationship was found between loneliness and social isolation, and rate of change in frailty index [70]. Also, the results of a population-based cohort study suggested that depression does not act as a risk factor for the onset of frailty in older people [71]. The bidirectional association between depression and frailty is questioned, but it is indicated that they share some common risk factors in the short and long term [72]. Oral health has an effect on various aspects of older adults’ quality of life among which are appearance and socializing [73]. Poor oral health may have negative consequences on social interaction and self-esteem and may lead to depression, which has an adverse effect on general health and wellbeing [74,75]. Cross-sectional as well as longitudinal associations between oral health related quality of life and loneliness in older adults have been identified [76].

Tooth loss can negatively affect speech and appearance, while denture problems may result in embarrassment due to dislodgement, pain and discomfort [38,77]. Older adults with fewer natural teeth and those who do not use dentures may have a greater possibility of social isolation [78]. In addition, tooth loss and self-reported dry mouth were found to be associated with a higher risk of developing depression among older adults in a longitudinal study [79]. Tooth loss and self-reported oral health problems, such as difficulty in chewing tough foods, may be longitudinally correlated to development or worsening of depression in older adults [80].
Also, a significant association was found between lower GOHAI (Geriatric Oral Health Assessment Index) scores and depression in Greek community-dwelling older adults [81]. A meta-analysis revealed a positive association of edentulism (OR=1.28) and periodontal disease (HR=1.73) with depression in adults and older people [82]. A population-based cross-sectional study indicated a bidirectional association between the number of remaining teeth and the frequency of laughter among community-dwelling older adults [83]. Moreover, the results of a nationwide population-based cohort study demonstrated that periodontitis was associated with the increased risk of subsequent depression [84]. On the other hand, a study in older Greeks has shown that the frequency of eating out was not affected by the dental status, but other biological and social factors played a more significant role indicating the multifactorial nature of human behaviour [85].

3.4. Neural mechanisms
The deterioration of body balance control is one of the most common causes of falls among older people [86]. Evidence has shown the existence of a positive association between postural instability and frailty or pre-frailty [87,88]. In a meta-analysis, an association between falls and frailty (OR=1.80) was found [89]. Moreover, a systematic review and meta-analysis provided a significant association between frailty and the future risk of falls among community-dwelling older adults, greater in males [90]. Another systematic review and meta-analysis with similar findings showed that community-dwelling older adults with frailty and prefrailty were at higher risk for falls and, also, those with frailty were more prone to recurrent falls [91].

Oral health may be related to postural stability through neural mechanisms. The stomatognathic system plays a role in the control of body posture [92]. Dental occlusion, trigeminal afferents and proprioception from the periodontal ligament may contribute to the control of postural stability, therefore tooth loss is a possible risk factor for postural instability [92,93].

A case-control study showed that edentulous older adults had statistically significantly less body balance activity and higher body oscillation compared to those who maintained their dentition, while the use of complete denture(s) was not associated with body balance control [93]. However, in another study, complete dentures were found to have a positive effect on static and dynamic stability among edentulous older individuals [94]. In a longitudinal study, the complete loss of occlusion with natural teeth (Eichner index C) was associated with decreased one-leg standing time with eyes open (OR=4.27) [95]. Furthermore, a prospective study disclosed an independent association of maximum occlusal force with one-leg standing time among men aged 85 and older [96]. The results of a cohort study showed a strong relationship between occlusal status and postural stability [97]. According to a prospective cohort study, older adults with fewer than 20 teeth and those not using dentures were at higher risk for incident falls (OR=2.5) [98].

Also, the presence of teeth (OR=0.59) and dentures (OR=0.66) was significantly associated with decreased risk of falls in older adults with dementia [99]. On the other hand, the findings of a cross-sectional study demonstrated that the use of dentures was correlated to decreased balance in both static and dynamic conditions and the duration of denture use was negatively assoiated with dynamic balance [100].

4. DISCUSSION
Current evidence supports both the cross-sectional and the longitudinal association between oral health and frailty [11-13], but more studies are necessary to confirm the evidence and clarify any causative effects. The majority of studies investigating this relationship were conducted in community dwelling older adults in Japan and the most commonly used frailty assessment instrument was the Physical Frailty Phenotype. This review has also identified four potential pathways which may link oral health and frailty that also need further investigation: the nutritional pathway, inflammation, the psychological pathway and neural mechanisms.

Oral health indicators, such as the number of teeth, masticatory performance, swallowing problems and dysgeusia seem to contribute to the nutritional status in older adults [33-35,38,45-52]. However, robust evidence on the association between oral health and malnutrition is still lacking as various confounding factors are implicated [41,42,54]. Malnutrition and decreased energy intake, in turn, are considered to have a dominant role in the onset of frailty and the pathogenesis of sarcopenia [23-26]. The multifactorial nature of nutritional status and food choices has been acknowledged, therefore, the interdisciplinary collaboration between dental professionals, dietetics practitioners, and primary care providers is necessary for treatment and prevention of malnutrition [42].

Regarding the pathway of inflammation, periodontitis may lead to systemic increase of inflammatory mediators, which may serve as an underlying mechanism of frailty. Nevertheless, the findings regarding the association of periodontitis with frailty are contradictory and evidence which supports inflammation as a linking mechanism between oral health and frailty is weak [12].

There are indications that poor oral health, namely tooth loss, periodontitis and self-assessed oral health status negatively influences older adults’ quality of life and is associated with an increased risk of depression in older adults [78-82,84].
Reciprocal, as well as prospective associations between depressive symptomatology and frailty in older adults have been reported [64,65], while it is suggested that depression and frailty are affected by common causes such as biological, psychosocial, behavioral, and environmental factors [72]. As far as the neural mechanisms are concerned, the literature supports the existence of a relationship between the stomatognathic system and body posture; the loss of proprioception from periodontal ligament may have a negative impact on the head position and contribute to postural instability [92,93]; posture; the loss of proprioception from periodontal ligament may have a negative impact on the head position and contribute to postural instability [92,93]. Deterioration in control of body balance is one of the leading causes of falls in older people [86]. Falls, in turn, are associated with frailty [87-89] and are among the most common clinical manifestations of frailty [90,91]. This narrative review has revealed the need for further research including case-control and randomized controlled trials to thoroughly explore the association between oral health and frailty and also the specific role of oral health as a predictor and marker of frailty. Moreover, more studies are necessary to explore the potential linking mechanisms including nutrition, inflammation, psychological and neural pathways. Studies in community-dwelling older individuals and nursing home residents should also examine the possible protective effect of systematic oral care provision against frailty. Statistically significant results on these parameters may lead to the integration of markers of oral health in the frailty assessment instruments and to the development of appropriate preventive strategies in the context of oral health promotion.

5. CONCLUSIONS

Oral health and frailty may be linked through nutritional, inflammatory, psychological and neural mechanisms. Further studies are necessary to thoroughly elucidate the role of these pathways as mediators of the latter association and, subsequently, to determine the most effective preventive strategies.

AUTHOR CONTRIBUTIONS

KK: protocol, data gathering, data analysis, authoring the draft.
AK: concept, protocol, critically revising the manuscript.

REFERENCES


Mechanisms linking oral health and frailty


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Questions

1. The most widely used instrument to assess frailty is:
   - a. Physical Frailty Phenotype;
   - b. Frailty Index;
   - c. Clinical Frailty Scale;
   - d. Short Physical Performance Battery.

2. Oral health is linked to frailty through:
   - a. Nutrition;
   - b. Inflammation;
   - c. Psychological and neural pathways;
   - d. All of the above are correct.

3. Which of the following sentences is correct?
   - a. Oral health is the dominant determinant of malnutrition;
   - b. Nutritional status and food selection have a multifactorial nature;
   - c. Malnutrition can be reversed solely by prosthodontic rehabilitation;
   - d. Westernized dietary patterns may prevent frailty.

4. Which of the following sentences is correct?
   - a. No prospective associations exist between depression and frailty;
   - b. No reciprocal associations exist between depression and frailty;
   - c. Depression and frailty seem to be affected by common causes;
   - d. None of the above.