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REVIEW

THE ROLE OF NUTRITION IN FRAILTY: AN OVERVIEW

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Abstract: Inadequate nutritional intake is an important modifiable risk factor for frailty. Existing evidence supports the importance of adequate dietary quantity and especially quality to ensure sufficient intakes of energy, protein and micronutrients. However, to date no nutritional intervention or supplementation concept has emerged as being effective for the prevention or treatment of frailty. Further research, including specifically the group of frail older persons and those at risk of frailty, and focussing on functional benefits as an outcome, is needed to allow definite recommendations for optimal diet, i.e. food and nutrient intakes, for this population. This article aims to give a short overview on current knowledge concerning the role of nutrition for the prevention and treatment of frailty, while providing readers with references giving an overview for further reading.

Key words: Prevention, aging, diet, supplementation, physical exercise.

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Introduction

While definitions of frailty still vary, it is generally agreed upon that frailty is characterized by decreased reserve and robustness, causing extreme vulnerability to stressors (1) that is mainly observable as diminished physical strength and endurance (2-4). Nutrition is a crucial contributing factor in the complex etiology of frailty and its key component sarcopenia (5), as it provides the energy and essential nutrients needed for the maintenance and performance of all organs and bodily functions, including muscle. However, nutritional intake in general decreases with ageing (among the reasons is the so-called anorexia of ageing; 6-8), and moreover, older individuals with anorexia seem to exhibit altered eating patterns characterized by lower consumption of nutrient-rich foods (9). This may be aggravated by functional problems impairing food access (10) and/or by following restrictive diets (i.e. low-cholesterol, low-salt, diabetes; 11). Monotonous diets result, and it is often challenging for older adults to meet their needs for energy and protein (12-15), but in particular for micronutrients (16–19). A chronic lack of energy, macro- and/or micronutrients, however, not only limits bodily functions, but over time promotes atrophy and subsequent loss of body tissues, including muscle (20-22). Thereby, chronic malnutrition is disturbing metabolic balance, decreasing the reserves of the body and diminishing its abilities to cope with stressors (4, 21), i.e. promoting frailty.

This article aims to give a short overview on current knowledge concerning the role of nutrition for the prevention and treatment of frailty, while providing readers with references giving an overview for further reading.

Observational data

Epidemiological studies examining the association between dietary intake or nutritional status and frailty have indeed supported a putative role for nutrition in the development of frailty (17, 23) and its key components sarcopenia and functional decline (10, 18, 21, 24-26). In these studies, malnutrition, the risk of malnutrition, the presence of weight loss and/or low body weight/body mass index (BMI) were shown to be closely associated with frailty (17, 27, 28). Older adults that were frail (17, 28, 29) (or, in some studies, had less lean/muscle mass and/or worse physical performance, which may be regarded as signs for sarcopenia and frailty; 18, 24, 26, 30-32) were found to have lower intakes of energy, protein and/or of several micronutrients, as well as lower plasma concentrations of various nutrients when compared with non-frail older individuals (or better performing persons, respectively). Semba et al. (33) observed in their study that each additional nutrient deficiency raised the risk of frailty in older women by almost 10%. This emphasises the importance of ensuring a high quality of older persons' diets in addition to sufficient quantity as an essential component in the prevention and treatment of frailty.

Although weight loss often is the most visible sign of chronic malnutrition (and one of the defining characteristics of physical frailty according to Fried et al.; 34), the absence of weight loss as well as a normal or even elevated body weight does not necessarily signify an adequate nutritional intake, especially with regard to micronutrients (35). Moreover, a stable or even increasing body weight may mask an "internal" gradual reduction in lean body mass (skeletal muscle and bone mass) that is accompanied by gains in (visceral) fat mass (20, 36). In recent years, epidemiological research has come to notice that also the presence of obesity (beginning from BMI >

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30 kg/m^2, but certainly at BMI > 35 kg/m^2) and/or of excessive (visceral) fat mass heavily aggravates the risk of mobility limitations and frailty (27, 28, 36–39), especially when it occurs in combination with sarcopenia (sarcopenic obesity; 36). Putting the focus on weight loss or body weight alone may thus inadvertently lead to overlook frailty and/or nutritional deficits in overweight and obese older adults or those with no obvious weight loss.

Intervention studies

Supplementation with Protein or Specific Amino Acids

Given their important role in (muscle) metabolism, the nutrients most extensively studied for the treatment or prevention of frailty, and especially of sarcopenia, are proteins and (essential) amino acids (AA). Current evidence indicates that older persons may have reduced ability to use ingested protein for muscle protein synthesis, and it is suggested to increase the recommendations for protein intake in this age group to at least 1,0-1,2 g/kg body weight/day in order to maintain, or help regain, muscle mass (for an extensive review of these topics see 10, 12–15, 17, 20, 21, 24, 25, 30-32, 40-44). Under debate is also whether the source of ingested protein, specific AA or the timing of protein ingestion are relevant factors affecting the anabolic effect of protein intake in older adults.

To date, reliable evidence from randomized controlled trials (RCTs) including frail older individuals is scarce (28, 45), and most studies in this area focus on sarcopenia and/or include healthy older persons. Moreover, interventional studies using protein supplements (mainly whey/casein protein or mixed/individual AA), and in rare cases protein rich foods such as meat or dairy products (31, 42, 46), mostly focus on the gain of body weight and/or lean/muscle mass or on metabolic outcomes. Studies reporting functional outcomes so far provide heterogeneous results: supplementation has been shown to increase lean mass and to improve (or at least to reduce the decline in) physical function in some studies (13, 14, 28, 41-43, 46-49) and was able to attenuate frailty in one small RCT (50). In other trials, however, such interventions failed to show beneficial effects on strength and performance, although sometimes achieving an increase in body weight and/or lean mass (15, 31, 32, 51, 52).

Supplementation with other Substances

Other nutritional supplements that have been tested in older adults, although again mostly in healthy and not frail persons, and mainly in relation to sarcopenia, are vitamin D, creatine, beta-hydroxy-beta-methylbutyrate (ß-HMB), arginine, beta-alanine and citrulline, omega 3 fatty acids and antioxidants including carotenoids, selenium, vitamin E and C and isoflavones (reviewed in 10, 13, 15, 17, 24, 25, 28, 32, 40-43, 47, 53). However, to date the number of studies is too small and their designs and results are too heterogeneous to draw reliable conclusions regarding relevant effects of supplementation of these substances to help maintain or restore robustness in the older population.

Combination of Nutrition and Exercise Interventions

As described before, based on the currently available evidence it remains unclear if nutritional supplementation of protein and/or any other substance in itself may have sufficient effects to attenuate frailty (28). As in some studies the combination with exercise and/or physical activity was most effective to reinforce lean/muscle mass and physical performance (28, 31, 45-47, 54, 55) and to decrease frailty (50), it is currently recommended to combine both approaches (21, 44).

This is especially important in the case of frail but excessively obese older persons: future treatment strategies for these individuals might need to include the consideration of potential functional benefits of weight loss (39), however, any weight loss (whether intentional or not) in older persons may have potentially harmful effects by promoting sarcopenia, bone loss, nutritional deficiencies, disability and even excess mortality (36, 37, 56, 57). It is therefore of utmost importance for these individuals to achieve a gain (or as a minimal requirement, avoiding a loss) of muscle mass while losing excess fat mass. This implies that it is advisable to judge the benefits of any intervention in such obese (but also in non-obese) frail participants not according to (change of) body weight, but instead to focus on changes in body composition and, most importantly, on functional outcome parameters.

The goal of maintaining muscle is most effectively achieved by adding physical activity and/or exercise components (58). Indeed, in the few studies with older adults conducted in this field, any intervention including nutritional changes with the goal of losing weight provided the best functional results when combined with exercise as a supporting factor (36, 39, 59-61).

However, taking into consideration the "obesity paradox" (several meta-analyses indicate that being overweight up to a BMI of 30 kg/m^2 or even more may protect older persons against mortality and morbidity; 57), and that the harmful effects of obesity only increase at a BMI > 30 kg/m^2 or more, for every frail obese individual the necessity of weight loss has to be really thoroughly reflected (57).

Whole diet approach

A major problem regarding the use of single nutrients in frailty prevention and therapy is that people do not eat single nutrients, but foods and meals containing a whole range of interacting constituents. Therefore it may be more appropriate to consider the influence of the whole diet on frailty, and also on its key components sarcopenia and functional decline (10, 18, 62). Indeed, some epidemiological studies have indicated that high adherence to "healthy" dietary patterns such as the currently best-investigated Mediterranean diet (characterised by high consumption of nutrient-dense foods such as fruits and

vegetables, wholemeal cereals and oily fish, but low intake of saturated fats; (18, 62, 63) in older adults is associated with a lower risk of frailty (17, 28, 64), or with greater muscle strength and/or better functional performance (10, 64, 65). However, research in this field has only started recently (63), and there is still a paucity of data regarding the effects of certain food groups and/or dietary intake patterns on the risk of frailty in older age.

Conclusions

Inadequate nutritional intake is an important modifiable risk factor for frailty. Existing evidence supports the importance of adequate dietary quantity and especially quality to ensure sufficient intakes of energy, protein and micronutrients (21). However, to date no nutritional intervention or supplementation concept has emerged as being effective for the prevention or treatment of frailty (17). Further research, including specifically the group of frail older persons and those at risk of frailty, and focussing on functional benefits as an outcome, is needed to allow definite recommendations for optimal diet, i.e. food and nutrient intakes, for this population.

Consequently, current best practice for frail older persons remains to recommend the intake of high-quality, nutrient-dense foods in order to achieve adequate provision of energy, protein and micronutrients, and to avoid weight loss, together with the promotion of physical activity (21). For severely obese frail older adults, if the benefits of weight loss are clearly established, the most appropriate therapeutic approach might consist of a very moderate energy restriction of 200-500 kcal/day, targeted at a moderate weight loss of 0,5-1 kg/week (or 8-10% of initial body weight after 6 months), while assuring a protein intake of at least 1 g/kg body weight/day and appropriate intake of micronutrients, and always combined with physical activity and/or exercise (36, 57, 59).

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