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Nutritional determinants of mobility

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Abstract

Purpose of review—In many countries, persons over 65 is one of the fastest growing segment of the population. Mobility disability is one of the major risk factors for morbidity and mortality in this age group. There is increasing evidence that improved nutrition can reduce the risk of developing disability in older age. This review summarizes the recent literature showing the associations between different nutrients and mobility-related outcomes in older adults.

Recent findings—Recent studies suggested an association between low intake and low serum concentrations of micronutrients, such as antioxidants and vitamins, with measures of physical performance, muscle strength and disability in older adults.

Summary—The role of low micronutrients as cross-sectional and longitudinal correlates of mobility disability is consistent with a growing number of studies showing that a diet rich in fruits and vegetables, such as the Mediterranean diet, has a beneficial role in healthy aging.

Keywords

Mobility; aging; nutrition; antioxidants; vitamins; AGEs

Introduction

Mobility underlies the ability to perform basic activities of daily living (ADLs) necessary for independence and is a core indicator of health and function in aging. Mobility difficulties are highly predictive of more severe disablement, which affect older people's independence and quality of life, and impose considerable burden on caregivers and health care system [1]. Measures of physical performance have been shown to predict adverse health events, such as nursing home admission, disability and death among older adults [2–4*]. Thus, mobility disability is a marker of a high risk group for whom interventions may well be beneficial in preventing further decline in function. Understanding the determinants of mobility decline is crucial in order to identify interventions that may prevent functional decline and delay the onset of disability. In recent years, several epidemiological studies suggested an association between low intake and serum concentrations of different nutrients and poor mobility outcomes. Among older persons, different factors can lead to a decline in food intake such

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as eating-difficulties, alterations of stomach-fundus compliance, activity of cholecystokin, depression and inflammatory process. Decline in overall food consumption increases the risk of inadequate intake of essential nutrients [5,6]. The purpose of this review is to highlight recent research examining the association of different nutrients and bioactive compounds with mobility-related outcomes.

Dietary intake

Protein consumption is essential for maintenance of muscle mass and strength particularly in the elderly. In community-dwelling older people from the Health, Aging and Body Composition Study (Health-ABC), low protein intake was associated with loss of muscle mass (as measured by DEXA) during 3-year follow-up [7]. These findings are consistent with the observation of low protein intake was associated higher prevalence of frailty, a syndrome characterized by low muscle strength and poor physical performance, in InCHIANTI study participants older than 65 years of age [8]. Frailty is associated with higher risk of accelerated physical and functional decline, disability and death in older persons, therefore reducing the risk for frailty is critical [9]. There is no consensus on the degree to which dietary protein needs change with advancing age. Studies aimed at prevent muscle/strength loss in older persons via protein-energy supplementation have obtained conflicting results, in particular, protein supplementation trials involving frail patients have been unsuccessful [10**]. A definitive answer to the question of whether protein supplementation may prevent or delay physical disability in older adults requires randomized clinical trials on large samples, long follow-up and multiple outcomes. However, the administration of large quantities of proteins in older individuals raises some concerns. Protein supplementation increases satiety inducing a compensatory decrease of voluntary food ingestion [11]. Moreover, it appears [12] that aging may be associated with reduced anabolic efficiency in response to carbohydrate coingestion. Finally, there is evidence that that a higher protein intake may accelerate greater decline in renal function in those with modest renal insufficiency [11].

Consumption of specific micronutrients have also been associated with mobility-related outcomes. In the InCHIANTI study, higher dietary intake of vitamin-C was significantly correlated with measures of knee extension and lower extremity performance as assessed by SPPB (Short Physical Performance Battery) [13]. Similarly, Bartali et al. [8] reported an association between low intake of vitamin D, E C with prevalence of frailty.

Nutrient Biomarkers

Nutrient biomarkers have been extensively studied in association with physical function. Plasma concentrations of α - and γ -tocopherol (vitamin-E) were positively correlated with physical performance and strength. Ble et al. [14] confirmed an association between low circulating levels of vit-E and the presence of frailty in the InCHIANTI sample. In a longitudinal analysis [15], participants in the lowest quartile of serum α -tocopherol were more likely to develop lower extremity physical decline (loss of at least 1 point in SPPB) during a 3-year follow-up. Similar findings were obtained by the Women's Health and Aging Study (WHAS). At baseline, frail women had significantly lower serum concentrations of vitamin D, E and B₆ and carotenoids, as compared to their non-frail peers [16,17]. Moreover, non frail women in the lowest quartiles of serum α -tocopherol, 25-hydroxyvitamin-D [25(OH)D] and carotenoids had an increased risk of becoming frail during the follow-up [16]. Furthermore, women in the lowest quartile of serum concentrations of vitamin B₆, B₁₂ and selenium had significantly higher risk of developing disability in ADLs during a 3-year follow-up compared with women in the upper quartiles [18].

The six major dietary carotenoids (α -carotene, β -carotene, β -cryptoxanthin, lutein, zeaxanthin, and lycopene) comprise an important component of the antioxidant defense system in humans, and are considered a good indicator of fruit and vegetable intake [19]. Among older women in WHAS, low serum carotenoids were associated with poor grip, hip, and knee muscle strength after adjustment for age, race, smoking, cardiovascular disease, arthritis, and IL-6 [20]. Further investigation showed that among women without severe walking disability (inability to walk or walking speed <0.4 m/sec) at baseline, women in the lowest quartile of serum carotenoids were at higher risk of developing severe walking disability over 36 months of follow-up [21]. More recently, it has been reported that serum carotenoids were associated with mean walking speed over three years of follow-up and with rate of change of walking speed adjusting for age, BMI and chronic disease [22**]. From the InCHIANTI Study, Lauretani et al. [23] reported that participants in the lowest quartile of plasma carotenoids had higher decline in hip flexion and knee extension power and hand-grip strength than those in the upper three quartiles at six-year follow-up. Moreover, higher total plasma carotenoids were associated with a significantly lower risk of developing severe walking disability and a less steep decline in 4-meter walking speed over six years of follow-up, and lower incidence rates of being unable to successfully complete the 400-meter walking test at the 6-year follow-up visit [24].

Selenium is a trace element that exerts antioxidative functions in myocytes and other tissues after integration into proteins. In the InCHIANTI study populations, more than 30% of older adults in the InCHIANTI Study had a plasma selenium concentration <0.88 $\mu\text{mol/L}$, the concentration below which selenium may be limiting the synthesis of selenoproteins [25]. At baseline, participants in the lowest versus the highest quartile of plasma selenium were at higher risk of poor hip, knee and grip strength after adjustment for age, sex education, total energy intake BMI, and chronic disease [25]. Similarly, among disabled women in the WHAS, after adjusting for age, race, BMI, MMSE, current smoking, hypertension, congestive heart failure and depression, higher serum selenium was associated with higher grip strength [26].

Antioxidants play an important role in counterbalancing the age-dependent increase in oxidative stress. With aging, increased oxidative damage to DNA, protein and lipids has been described in skeletal muscle with associated atrophy and loss of muscle fibers [27]. Analyses conducted on the WHAS sample have shown that serum protein carbonyls, markers of oxidative damage to proteins, were associated with poor grip strength [28], incident severe walking disability [29] and mortality [30]. Antioxidants may play a preventive role in muscle damage by reducing oxidative injury through the quenching of hydroxyl radicals and reduction in lipid peroxidation [31]. By reducing free radical concentrations, antioxidants may modulate redox balance and activation of nuclear factor κB , a major transcriptional factor involved in the expression of proinflammatory cytokines [32], which are associated with loss of muscle strength, reduced physical function and disability [33,34]. Walston et al [35] reported that WHAS participants with the highest serum levels of carotenoids and selenium were significantly less likely to be in the highest tertile of serum IL-6 at baseline; those with the lowest levels of carotenoids were significantly more likely to have increasing IL-6 levels over a period of 2 years, and those with the lowest selenium levels had a significantly higher risk of total mortality over a period of 5 years.

Vitamin D

Vitamin D insufficiency in older persons is highly prevalent worldwide [36]. While more than 90% of the vit-D requirement comes from exposure to sunlight, a smaller part comes from food intake. Nutritional sources of vit-D are mostly limited to oily fish (salmon, mackerel, and sardines) which are not regularly consumed [36]. Vit-D nutritherapy through

dietary supplements and consumption of enriched foods has been proposed as a strategy to prevent sarcopenia (the progressive reduction in muscle mass and strength prevalent in late-life) [37*].

Studies testing the relationship between Vit-D and physical performance yielded mixed results. Among participants aged ≥ 65 years in the Longitudinal Aging Study Amsterdam (LASA) [38], those with lower serum 25(OH)D, as compared to those with higher levels, had poorer physical performance at baseline and higher odds ratios of 3-year decline in physical performance after adjusting for age, gender, chronic diseases, degree of urbanization, BMI, and alcohol consumption. From the InCHIANTI Study, Shardell et al. [39**] reported that in older men, lower serum 25(OH)D was associated with frailty. In a recent analysis (Semba et al., unpublished observations) among InCHIANTI participants, those in the highest quartile of serum 25(OH)D at baseline had higher walking speed at baseline, and at 3- a 6-year follow-up compared to those in the lowest quartile. A systematic review by Annweiler et al. [40**] examined publications about the effects of low serum Vit-D concentration and Vit-D supplementation on physical performance among people aged ≥ 65 years. Authors identified eight observational and eight interventional studies. Among the observational studies, five showed a significant positive association between physical performance and serum 25(OH)D, whereas three studies showed no significant association. Among the interventional studies, four of the five studies and two of the three studies testing the vit-D supplementation effect on balance and gait respectively found no significant effect. Four studies showed a significant effect on muscle strength while three studies did not. A recent meta-analysis by Bischoff-Ferrari et al. [41**] based on eight double-blind randomized controlled trials (RCTs) examined the benefit of supplementation on fall prevention. High dose (700–1000 IU per day) supplemental vit-D and achieved serum 25(OH)D ≥ 60 nmol/L resulted in a reduction of falls of, respectively, 19% and 23%. Low dose supplementation or achieved serum 25(OH)D < 60 nmol/L did not reduced fall risk. In two RCTs, the active form of vitamin D (1 α -hydroxyvitamin D and 1,25-dihydroxyvitamin D) reduced fall risk by 22%

Vit-D may influence mobility-related outcomes through different mechanisms. Vit-D receptors are present in human muscle tissue [42]; binding of vit-D to its nuclear receptor in muscle tissue may lead to de novo protein synthesis [43]. Positive effect of Vit-D on global physical performance may be due to its action on the nervous system, improving balance and neuromuscular control and coordination [40**].

The relationship between vit-D and mobility requires further investigation. Some studies found a significant association between low serum vit-D concentration and physical performance or vit-D-related improvement in physical performance, while others failed to show any association or effect of supplementation [40**,41**]. This discrepancy between studies is probably attributable to methodological issues such as variability in the results obtained by different assays, different threshold values used to define deficiency, insufficient control of confounders, high comorbidity in older subjects, type of vit-D supplemented, heterogeneity of dosage and association with other compounds [37*,40**,41**].

Advanced glycation end products

Advanced glycation end products (AGEs), are bioactive compounds found in foods and generated endogenously in the body by nonenzymatic glycation of proteins, lipids and DNA. Diet is a major source of exogenous AGEs, especially Western diets where foods are processed under elevated temperatures (broiling, roasting, deep frying, oven frying, or grilling) [44].

Recently, it has been hypothesized that AGEs could play a role in the pathogenesis of sarcopenia [45] and cross-sectional studies found evidence of a relationship between carboxymethyl-lysine (CML), a dominant AGE in serum and tissue, and sarcopenia-related outcomes. Among older disabled women in the WHAS [46**], those with elevated serum CML were at higher risk of poor grip strength adjusting for age, race, BMI, cognitive dysfunction depression and diabetes. From the InCHIANTI Study, Semba et al. [47**] reported that participants in the highest quartile of plasma CML were at higher risk of slow walking speed after adjustment for age, education, cognitive function, smoking and chronic diseases and after the exclusions of participants with diabetes. AGEs may play a role in sarcopenia through inflammation and endothelial dysfunction in the microcirculation of skeletal muscle [45] and through cross-linking of intramuscular connective tissue [48,49]. Prospective studies are needed to determine whether elevated serum AGEs predict decline in mobility measures.

Conclusion

Recent studies suggesting an association between different nutrients and mobility in older adults were revised. Attempts to translate the results from observational studies to dietary intervention trials may result in disappointing outcomes. There are various considerations when implementing diet interventions. First observation studies examine exposure to specific nutrients over an extended period of time while intervention studies usually have shorter exposure periods. Second, there is an inherent disconnection between observation trial of nutrients from the diet versus provided intervention based on supplementation of a single or multiple nutrients. For example, the role of protein requires further investigation based on longer-term trials with better defined clinical endpoints; moreover, interventions via protein-energy supplementation in older persons have raised several concerns [10**,37*]. Observational and clinical trials testing the relationship between vit-D and physical performance provided mixed results [40**,41**]. Achievement of an adequate vit-D status through increasing nutritional intakes is difficult: less than 10% of the Vit-D requirement for most people comes from nutritional sources, very few foods naturally contain vit-D and fortification of foods policies varies widely across the world [36]. Finally, supplementation interventions require further clinical trials addressing important methodological issues such as type of Vit-D supplemented, dosage and association with other compounds. Further prospective studies are needed to confirm the relationship between AGEs and mobility-related outcomes [46**,47**]. AGEs are potentially an important modifiable risk factor, since diet is a major source of exogenous AGEs.

In the last few years epidemiological studies in older persons suggested that micronutrients with antioxidative capacity contained in fruit and vegetable, such as vitamins, carotenoids and selenium, are protective against physical function impairment and disability [8,9,13–26].

There is increasing efforts to examine dietary patterns rather than single nutrients. Intervention that aims at improving overall diet quality may prove to have better success than single nutrient intervention. For example, among older adults in the Atherosclerosis Risk in Communities study, fruit and vegetable intake was inversely correlated with functional limitations and disability [49]. There is growing scientific evidence that the type of diet rich in fruits and vegetables, such as the Mediterranean diet, has a beneficial role in preventing cardiovascular diseases, cancer, and neurodegenerative disorders, and promoting quality of life and overall survival [50]. Recent trials showed that nutritional interventions based on Mediterranean-style diet significantly reduced the levels of inflammatory markers such as IL-6 and CRP [51,52], which are part of the hypothesized pathway that leads to loss of muscle strength, reduced physical function and disability. Epidemiological studies are

needed to confirm whether a Mediterranean-style diet may reduce functional decline and the onset of disability in older persons. This could provide strong rationale and justification for dietary interventions studies aimed at reducing mobility impairment among older adults.

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