

Vitamin D and sarcopenia

Introduction

The human body is subjected to considerable changes during the aging process. One important alteration is the progressive loss of muscle mass and function, muscle strength and performance¹ after the fifth decade of life,² known as sarcopenia. The functional limitations and flaws due to sarcopenia decrease quality of life, compromise functional independence during senescence,² and resulting to significant reductions in physical functions, metabolic impairments, and disability.³ Decreased muscle strength has also been related to mortality in older adults.⁴ Although numerous mechanisms have been suggested, the factors leading to sarcopenia are unclear and mostly multifactorial, include of hormonal, neurological, nutritional, environmental, and genetic factors, and their interactions.³ One environmental agent associated with age-related losses in muscle function is vitamin D level. Low levels of vitamin D related to muscle weakness and atrophy of type II fibers.³

Vitamin D is a fat-soluble vitamin, and has an essential role in calcium homeostasis and keeping of normal bone metabolism.⁵ Data suggest that vitamin D status is crucial for the normal function of different organs, such as pancreatic β -cells, vascular endothelial cells, neurons, immune cells, osteoblasts, and myocytes, where vitamin D receptors are expressed.⁵ In addition, vitamin D deficiency is related to loss of skeletal muscle mass and function⁶ and high risk of falls in older adults,⁶ although some researchers have shown conflicting findings.⁷ Vitamin D deficiency is common in elderly population; because of reduced exposure to sun light, low intake of oral vitamin D, intestinal malabsorption, and decreased vitamin D hydroxylase activity in the kidneys.⁸ The prevalence of vitamin D deficiency elevates with age, reaching about 70% in older Caucasians and Asians.⁶ In addition, the effects of low vitamin D levels can be reinforced in older adults, because expression of skeletal muscle vitamin D receptor reduces with age.⁶ Clinical studies about vitamin D deficiency resulted from various causes have demonstrated that beside the (bone) pain, and symptoms related to the deficiency, muscular weakness is commonly found in these patients, with incidences up to 97%.⁸ Low serum 25-hydroxyvitamin D levels were associated with an elevated risk of sarcopenia in older adults, regardless of obesity, in both cross-sectional and prospective studies.^{9,10}

With the recognition of vitamin D receptor in muscle cells and neuronal cells, studies in cell culture and experimental animals proposed that vitamin D impacts on muscle growth, development and contraction.¹¹ A number of observational studies have demonstrated an association between serum 25-hydroxyvitamin D levels and measures of muscle performance¹²⁻¹⁷ and appendicular muscle mass^{12,15} in community-dwelling older adults. Furthermore, several recent randomized controlled trials of vitamin D supplementation show beneficial effects on muscle strength and physical performance in older adults with low vitamin D levels.¹⁸⁻²¹

Vitamin D, muscle strength and body composition

A prospective study in elderly population aged 55-85years, have shown that persons with 25(OH)-D concentration less than 25nmol/L

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and high PTH concentration (4.0+ pmol/Liter) were 2.51times more probable to experience loss of grip strength and 2.38times more probable to experience loss of appendicular skeletal muscle mass, in comparison with persons with a low Parathyroid Hormone (PTH) and a high 25(OH)-D level.²² Kenny et al.,²³ in a randomized trial involving sixty-five healthy older men aged 65-87years, demonstrated that vitamin D₃ 1000 IU plus calcium 500mg daily, compared with the calcium alone, did not elevate muscle strength or ameliorate physical performance over a 6months period.²³ Therefore, these data raise the probability that vitamin D status is more commonly related to muscle performance in women rather than men. Causes for this sex differences are uncertain, but potential explanations may include of differences in baseline lean body mass, muscle strength, physical activity and levels of testosterone, that is an anabolic hormone to muscle.¹¹ The results of the study²⁴ to investigate the association between 25(OH)-D concentration and percentage body fat content in 410 healthy women between 20 and 80years, showed that percentage body fat content is inversely associated with the serum 25(OH)-D levels in healthy women. Evidence has been shown that obesity could be related to lower levels of serum 25(OH)-D²⁵ and higher serum PTH levels.²⁵ Vitamin D status is an important determinant of serum PTH concentrations, and elevated PTH enhances calcium influx into the adipocytes. In these cells, intracellular calcium promotes lipogenesis and thus, PTH surplus may enhance weight gain.²⁵ In a population based-study in older men and women (aged 65 yr and older) have demonstrated that total body fat is inversely related to 25(OH)-D levels and is positively related to PTH levels.²⁵ Another study² assessed the association of serum 25(OH)-D and PTH levels with skeletal muscle mass and strength (handgrip force and isometric knee extension moment), and found no consistent relationship between 25(OH)-D or PTH and any of quantification of muscle mass or strength, in either men or women. The findings of this study are similar to some cross-sectional studies,^{26,27} but not to others.¹²⁻¹⁷

In a randomized controlled trial,¹⁸ 242 healthy ambulatory women and men 70years or older with serum 25(OH)-D level below 78nmol/L were recruited, and administered 1000mg of calcium plus 400 IU of vitamin D or 1000mg of calcium alone, for 12months. Results of this study showed a decrease in the number of persons with first falls, improvement in quadriceps strength of 8%, a reduce in body sway of 28%, and a reduced in time required to perform the TUG (Timed-Up-and-Go) test of 11%. In our study,²⁸ with the aim of investigation the effect of vitamin D supplementation (1000 IU, daily, for 3months) on

muscle strength, muscle function and body composition in healthy vitamin D-deficient middle aged-women (40-55 yr), results of the intervention showed improvement in muscle function (a reduced in time needed to perform the TGUG (Time Get Up and Go) test in vitamin D group compared with the placebo group, and also fat mass content significantly decreased in the vitamin D group at the end of the week 12, but changes did not reach significant compared with the control group. But muscle strength (handgrip strength and knee extension strength) did not differ significantly after 12weeks.

However, methodologies differed widely among these studies, for example one of the important reasons has led to different results when attempting to clarify the relationship between vitamin D and muscle strength includes testing methods. Handgrip strength was one of the most common indicators for muscle strength but different equipment was used on different muscle groups to complete these measurements and probably result to different outcomes. Also, Low levels of vitamin D related to muscle weakness and atrophy of type II fibers;³ type II fibers are fast twitch and contribute to high intensity but short duration activities.²⁹ In addition, there are several vitamin D polymorphisms, which are resulted from variations in DNA sequence of vitamin D receptor gene, that are associated with a variety of biological characteristics including muscle strength.²⁹ Moreover, in these studies, latitude, or other environmental agents that contributed to these differences is unclear.

Furthermore, cross-sectional design could not explain the causality of vitamin D and sarcopenia. It is feasible that sarcopenia results to low vitamin D status. Firstly, sarcopenia has confirmed to be an important predictor of disability and mortality in elderly population.²⁴ Decreased physical activity and less time spent outdoors results to vitamin D insufficiency.²⁸ Secondly, sarcopenia is mainly observed in obese subjects, who reveal significant muscle loss and increased fat mass.³⁰ Promoted body fat mass leads to vitamin D trapping in the adipose tissue, and declines the serum level of vitamin D.²⁴ Third, sarcopenia is related to aging.³⁰ Old age is a major risk factor for vitamin D insufficiency.⁸

Mechanisms of vitamin D activity in muscle

The genomic impact of vitamin D on muscle includes changes in mRNA that will cause de novo protein synthesis that control cell proliferation and induction of terminal differentiation.³¹ In addition, the non-genomic impact of vitamin D on muscle includes the activation of protein kinase C (PKC) and Ca releasing into the cytosol.³¹ Thus, this effect leads to the active transportation of Ca into the sarcoplasmic reticulum by Ca-ATPase elevating the calcium pool which is necessary for muscle contraction. Moreover, the activation of PKC has an impact on protein synthesis in the muscle cells.³¹

On other hand, because inflammation is a potential risk factor for sarcopenia, the anti-inflammatory impacts of vitamin D could lead to the improvements in skeletal muscle composition.⁶

Vitamin D, gait, and balance in elderly population

Few studies have been conducted to investigate the effects of vitamin D on balance and gait performance. In this regard, supplementation with vitamin D plus calcium compared with calcium alone ameliorate body sway by 9% within two months in elderly ambulatory women and similarly, vitamin D plus calcium compared with calcium alone elevated musculoskeletal function by 4-11% in

institutionalized aged women.³² The cellular effect of vitamin D on muscle was shown in one study that three months of treatment with vitamin D enhanced the number and size of type II muscle fibers of aged women.³³

Vitamin D and falls

In the Longitudinal Study Amsterdam, low 25(OH)-D levels (less than 25nmol/L) were related to an increased risk of repeated falling through the following year, particularly in individuals under 75years of age.³⁴ In a randomized, controlled trial, was shown that supplementation with vitamin D₃ and calcium (800 IU and 1200mg per day) for 3months decreased the risk of falls around 49% in comparison to calcium alone.³⁵ Similarly in an Australian study, supplementation with vitamin D₂ (at the beginning 10000 IU per week then 1000 IU per day) plus calcium (600mg per day) for 24months decreased the risk of falls by 30% compared to calcium alone.³⁶ More evidence about the effect of vitamin D supplementation on muscle is found in a meta-analysis of five randomized controlled trials, involving over 1200 ambulatory and institutionalized persons. In this analysis, vitamin D supplementation decreased the risk of falling around 22%.³⁷

The relationship between serum 25(OH)-D level and falls is mediated partially by physical performance.³⁰ This shows that low vitamin D level plays a role in the risk of falling in the aging through an impact on muscle function.³⁰

Conclusion

In conclusion, the prevalence of vitamin D deficiency elevates with age and because the elderly population has had an increasing trend during the last century, and also according to importance of vitamin D for the normal function of different organs and particularly, benefits of vitamin D in this aged group, there is rationality for the supplementation of vitamin D during the aging in order to improvement in muscle mass and performance, public's health status and quality of life.

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Conflict of interest

The author declares no conflict of interest.

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