# The role of vitamin D in muscle strength among the elderly

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#### ABSTRACT

Vitamin D deficiency is a common condition among the elderly and it is associated with an increased risk of fractures. The condition is common among elderly at higher latitude locations and very common among the institutionalized. Currently there is also evidence that low levels of vitamin D are associated with multiple disorders such as cardiovascular diseases, inflammation, and infectious diseases, among other things. In addition, clinical studies on the elderly have shown that the low vitamin D levels correlate with reduced muscle strength in the lower limbs and poor physical performance. However, suitable levels for maintaining proper muscle function and strength have not yet been established. **Objective:** To verify recent evidence of the effects of vitamin D on muscle strength in the elderly. **Method:** A survey of studies published between 2010 and 2014 in Pubmed, Medline, and Scopus using the terms "cholecalciferol", "muscle strength," and "elderly." **Results:** Seven studies were selected. The results suggest a positive influence of vitamin D on muscle strength in the elderly. **Conclusion:** This review showed that despite the action of vitamin D on the musculoskeletal system, there is still uncertainty; there tended to be a greater benefit with vitamin D supplementation at higher doses. However, additional studies are needed to define the best therapeutic profile.

Keywords: Cholecalciferol, Muscle Strength, Aged

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#### INTRODUCTION

The lack of vitamin D is a frequent clinical condition among the elderly, and is partly due to a reduced exposure to sunlight, low intake of vitamin D, and decreased ability of the skin to synthesize Vitamin D (25(OH)D).1 Vitamin D insufficiency is defined by the serum levels of 25(OH)D being between 10 ng/mL and 30 ng/mL; levels below 10 ng/mL are considered deficient, while values above 30 ng/mL are the desirable levels.<sup>2</sup>

Currently, there is growing evidence that a low concentration of 25-hvdroxy-vitamin D is also associated with several non-musculoskeletal disorders such as cardiovascular disease, inflammation, and infectious diseases, among other things.<sup>3</sup> Vitamin D deficiency is common among elderly individuals in places of higher latitudes and quite common among the institutionalized.4

The lack of vitamin D is associated with increased risk of fractures, since that leads to increased secretion of parathyroid hormone and bone remodeling, which can result in loss of bone mass, thus causing bone fragility.<sup>2,5,6</sup>

The protective effect of vitamin D against the fractures is attributed to its positive effect on the homeostasis of the calcium metabolism, which suppresses the secretion of PTH, inhibiting the bone remodeling and increasing bone mineral density.1 Studies conducted in recent years have established that the adequate nutritional status of vitamin D suppresses the levels of PTH and, therefore, maintains the homeostasis of calcium in the body.7 However, the levels needed to maintain the muscle function and strength have not been established. Clinical studies with the elderly have shown that the low serum levels of 25(OH)D correlate with reduced muscle strength in lower limbs and diminished physical performance.8-11

A recent review<sup>12</sup> developed four lines to support the role of vitamin D in the health of the muscular system. The first is in muscle manifestations such as proximal muscle weakness, diffuse muscle pain, and a deficient gait; these are well known clinical symptoms of vitamin D deficiency.13-17 Second, the Vitamin D receptor in the muscle tissue has been located.<sup>18</sup> Third, several observational studies suggest a positive relationship between levels of 25(OH)D and muscle function. Fourth, in spite of the arguments outlined above, many researchers have decided to investigate the effects of vitamin D supplements on muscle function, but the results remain controversial.<sup>3</sup>

## OBJECTIVE

Because of the above, this article sought to make an updated review of the effects of vitamin D on muscle strength in elderly individuals.

## METHOD

The strategy of bibliographic search was carried out using the following databases: Pubmed, Medline, and Scopus. The years surveyed were from 2010 - 2014. limited to publications in English. The function "and" was used in basic field and keywords were: Cholecalciferol, Muscle Strength, and Aged. In the initial search 34 articles were selected, 27 of which were excluded upon reading the abstract, because they were not entirely in the English language, because they contained a mixed sample (elderly and non-elderly), for having the outcome being a parameter other than muscle strength, or because they were systematic reviews of another time period.

### RESULTS

Of the seven original articles published between 2010 and 2014 that address the influence of vitamin D in the muscular strength of the elderly used in this literature review, four suggest that vitamin D is related to muscle strength in the elderly, while three do not demonstrate the same relationship (Chart 1).

Mastaglia et al.<sup>1</sup> conducted a study whose objective was to examine the relationship between nutritional status of vitamin D and the muscle function and strength in healthy elderly over 65. They selected 54 elderly women living in Buenos Aires (latitude 34ºS) to perform bone densitometry, body composition, and biochemical markers of bone metabolism (serum calcium, phosphorus, calcium urinary tract, serum creatinine, parathyroid hormone, and vitamin D levels). Nutritional aspects were assessed through questionnaires. Their strength and muscle function were assessed by tests of walking and balance, and measured by manual dynamometry of hip flexors and abductors, and extensors of the knee. The mean age was  $71 \pm 4$  years.

The patients were divided into two groups for analysis of the results. Group 1 had those who presented levels of  $25(OH)D \ge 20$ ng/mL and Group 2, those with levels <20 ng/mL. There was no statistically significant difference between the groups regarding comorbidities, time of exposure to sunlight, or nutritional aspects.

The Group 1 subjects performed better in tests of muscle function and greater strength in the knee extensor and hip adductor. Group 2 subjects took 0.4 seconds longer in the walk test than those in Group 1. In correlating parathyroid hormone (PTH) with muscle function, a negative correlation was shown, however, the same was not observed when correlated with strength. Analyzing the relationship between muscle function, strength, serum levels of 25(OH)D, and PTH revealed that, while the PTH correlates negatively with muscle function, the 25(OH)D does not. Elderly women with levels of 25(OH)D < 20 ng/mL showed less strength of knee extension and hip abductor, but tended to have greater strength in the hip flexors.

The women with serum levels of 25(OH)D above 20 ng/mL had greater strength of limbs and better function than those with lower levels. The analysis of each test of muscular function showed that elderly women with lower levels of vitamin D had worse performance in the speed test. However, there was no statistically significant difference in the balance test. The authors argue and posit that individuals with levels lower than 20 ng/ml of vitamin D tend to walk less, which results in less protective effect on bone mass and a lower risk of fractures.1

In this study presented above,<sup>1</sup> the authors concluded that women over 65 years whose serum levels of 25(OH)D was equal to or greater than 20 ng/mL living in Buenos Aires presented better muscle function and strength.

Janssen et al.<sup>19</sup> also conducted a study assessing whether the levels of 25(OH)D were related to the muscle mass, strength, and muscle function in middle-aged and elderly individuals. This study involved 802 individuals with an average age of  $63.3 \pm 9$  years and mean serum level of 25(0H)D of 56.8 ± 23 nmol/L.

Muscle strength was assessed by testing the grip strength and manual dynamometry of knee extension. Their muscle performance was determined by a test of balance, speed, and sitting rising. After adjusting for co-variables (gender, age, BMI, comorbidities, smoking, alcoholism, and physical activity), each nmol/L of extra 25(OH)D was associated with an increase of 0.025 Kg in grip strength and 0.17 Nm in the strength of the extensor knee. The individuals who had serum 25(OH) D less than 60 nmol/L presented an increase 

Author	Ν	Age (average ± dp)	Gender	Objective	Results
Bird et al <sup>22</sup>	88	69.2 ± 6,5 years	Not described	To assess whether the higher levels of muscle strength are associated with seasonality, levels of vitamin D, or physical activity.	Significant seasonal variation was observed in the strength of dorsiflexores and levels of vitamin D. There was no change in the strength of the quadriceps.
Hirani et al <sup>21</sup>	1659	77 years DP: not informed	Male	To evaluate the association of vitamin D and 1.25D with fragility (weight loss, reduction of muscle strength, slow gait, exhaustion, and low levels of physical activity)	Fragility was present in 9.2% of the sample. Low levels of vitamin D and 1.25D were independently associated with weakness and with four of the five components (except weight loss).
Janssen et al <sup>19</sup>	802	63.3 ± 9,0 years	400 males; 402 females;	To determine the association between vitamin D levels, muscle mass, strength, and physical perfor- mance.	Higher levels of vitamin D were significantly associated with greater lean mass, greater handgrip strength, and better physical performance. Association proved to be more evident with vitamin D levels below 24 ng/mL.
Mastaglia et al <sup>1</sup>	55	71 ± 4 years	Female	To evaluate the relationship between vitamin D, muscle function, and muscle strength in elderly women.	Levels of vitamin D above 20 ng/mL were associated with better muscle function in limbs and strength. 46% had vitamin D greater than 20 ng/mL and had better performance in tests of muscle function, extensor strength of the knee, and hip abduction.
Tellioglu et al⁴	116	75.5 ± 6.1 years	56 females; 60 males;	To evaluate/compare the effects and safety of high doses of intramuscular and oral cholecalciferol serum levels of vitamin D, muscular strength, and physical performance in elderly patients with hypovitaminosis D.	Only 5.2% of the individuals had adequate levels of vitamin D, 37.1% were deficient, and 57.7% were insufficient. After IM and oral supplementation, the average vitamin D levels increased significantly in the 6th and 12th weeks. However, in the 12th week, the IM group presented higher levels. The strength of the quadriceps and the score in the battery of physical performance increased in both groups.
Verschueren et al <sup>23</sup>	113	79.6 ± 5,35 years	Male	Evaluate the effects of 6 months of vibrating platform and/or supplementation of vitamin D on isometric and dynamic strength, muscle mass of limbs, and bone mineral density of the hip.	The dynamic muscular strength, bone mineral density, and vitamin D levels increased. The isometric strength and muscle mass remained unchanged.

#### Chart 1. Studies presented in the literature review

of 0.09 Kg of grip strength for each nmol/L of extra 25(OH)D.

In individuals with levels of 25(OH)D lower than 60 nmol/L, the effect of vitamin D on lean mass was more pronounced. There was an increase of 80 g in lean mass for each nmol/L of extra 25(OH)D. One possible explanation proposed by the authors for this fact is that the lean mass would indicate the anatomical effect of vitamin D deficiency on the muscle tissue, while the strength and physical performance depend on other factors. Therefore, the authors demonstrated that higher levels of vitamin D were associated with greater lean body mass, strength, and performance and that these associations were more pronounced below 60 nmol/L and absent above this value suggesting a possible limit to the effect.

Another study,<sup>20</sup> conducted only on elderly women, sought to evaluate the effects of treatment with vitamin D on the muscular strength and mobility in individuals with insufficiency. The study was developed in Australia, latitude 32°S, randomized, double-blind, with 302 elderly women between 70 and 90 years who walked in the neighborhood and had serum levels of 25(OH)D less than 24 ng/mL. In addition, the participants had to have a history of at least one fall in the last year. They were randomized to one of two groups: the experimental group received 1000 IU of ergocalciferol per day and the control group, an identical placebo. All participants also received 1000 mg/day of calcium citrate for one year.

Their muscular strength and mobility were evaluated in the randomization and 1 year later via the following parameters: strength of dorsiflexion of the ankle, the flexor and extensor of the knee, adductor and abductor of the hip, flexor and extensor of the hip, 3-meter walk test (Timed Up and Go Test). After 12 months, there was a significant increase in the knee flexor strength and all the muscles of the hip, in addition to an improvement of mobility in both groups. 66% of the participants had baseline concentrations of vitamin D less than 20 ng/mL. After 12 months, the vitamin D group had significantly higher levels than the control group, 47% of them reached levels greater than 24 ng/mL.

The present study demonstrated that, in elderly women with low levels of vitamin D who received calcium and supplementation with ergocalciferol, muscle strength and mobility improved in those individuals who were in the lower tertile. The supplementation with ergocalciferol improved the outcome of the walk test by 17.5% in patients with values greater than 12 seconds, which is clinically significant. In addition, the dose used in the study was sufficient for 80% of the people to reach levels above 20 ng/mL.

Another study,<sup>21</sup> also conducted in Australia, examined the association between serum 25(OH)D and  $1.25(OH)_2D$  on fragility and its components in elderly men above 70. The project included 1,659 elderly people in the community who had 3 or more components of fragility: weight loss, reduction in muscle strength/weakness, reduced gait speed, exhaustion, and low levels of physical activity. The majority of the sample (93.4%) did not take vitamin D supplements and the prevalence of fragility was 9.2% when the levels of 25(OH)D were taken into consideration and 8.6% when 1.25(OH)<sub>2</sub>D was used.

The study showed that elderly men with fragility had more chances of having low levels of vitamin D and there was a strong association between fragility and low levels of vitamin D. Both the 25(OH)D and the 1.25(OH)<sub>2</sub>D were associated with fragility and its components. This suggests that the correction of low levels

of vitamin D may influence the incidence and progression of weakness. However, the results are contradictory in the literature researched.

Bird et al.22 assessed the existence of seasonal variations in the strength of the legs and the relationship between muscular strength, the variation of serum 25(OH)D, and the level of physical activity. Eighty-eight independent elderly people in the community were assessed 5 times over the course of one year, at the end of 5 consecutive seasons, at the latitude 41ºS. They evaluated the strength of limbs, serum 25(OH)D, and physical activity, in addition to the diary of falls. Seasonal variations were observed in the strength of ankle dorsiflexors, levels of 25(OH)D, and physical activity, with higher values in summer. The highest level of serum 25(OH)D was seen 4 weeks after the peak of other variables, with no significant difference between the period of ankle strength and that of physical activity. The strength of dorsiflexors showed significant variations over the year, with higher values in the middle of summer. However, neither the strength of dorsiflexors nor of knee extensors were associated with serum levels of 25(OH) D. Reduced dorsiflexor strength was associated with an increased incidence of falls. The magnitude of seasonal variation in the levels of 25(OH)D was 15% with the highest levels presented at the end of the summer. 17% of participants took vitamin D supplements of less than 800 U/day during the study. There was a 13% variation in physical activity during the year, with the participants significantly more active during the summer.

Verschueren et al.<sup>23</sup> assessed the potential benefit of the vibrating platform and supplementation of vitamin D in the improvement of strength, muscle mass, and bone density in postmenopausal women. The controlled and randomized study was conducted on 113 elderly institutionalized women aged over 70 years. The main objective was to assess whether the group that trained on a vibrating platform for six months had greater musculoskeletal benefits than the control group that received the same dose of calcium and vitamin D, but without training on the equipment. The second objective was to compare the effects of a high dose (1600 U) of vitamin D with the conventional supplement dose (880 U). The strength of the knee extensor, muscle mass in the upper limb, bone mineral density of the hip, and serum levels of vitamin D were evaluated at the beginning of the protocol and at the end of six months of training. After six months of treatment, muscle strength and

serum levels of vitamin D were significantly increased, while the isometric strength and muscle mass did not change. Higher doses of vitamin D resulted in greater increases in the levels of vitamin D when compared with the lower dosage. This larger increase in serum levels of vitamin D with use of 1600 U/day did not result in any additional increase in muscular strength when compared with the conventional dose.

Vitamin D supplements at either dosage resulted in circulatory levels of vitamin D above 50 nmol/L in all the elderly women during the study period. The use of the vibrating platform in combination with the vitamin D supplements did not result in any additional musculoskeletal benefit nor did the increased levels of 25(OH)D induced by higher supplement doses increase the muscle mass or the strength.

In a study by Tellioglu et al.<sup>4</sup>, the safety and effects of high oral or intramuscular (IM) doses (600,000 U) of cholecalciferol on serum 25(OH)D, muscular strength, and physical performance were also evaluated on 116 mobile institutionalized elderly above the age of 65 who were selected with insufficient or deficient vitamin D.

After applying the criteria of the study, 66 patients were elected to continue the research. The subjects were randomly assigned to receive vitamin D supplements, with 34 being allocated to receive IM and 32 orally. The serum levels of 25(OH)D increased in the IM group in the sixth and twelfth weeks linearly, while in the oral group it increased in the sixth week and diminished in the twelfth. In the twelfth week, the levels of 25(OH)D were  $\geq$  30 ng/mL in 83% of the oral group and in 100% of the IM group.

The muscular strength of the quadriceps and the total score of the physical performance test increased significantly in both groups; however, the sub-item of balance has improved only in the group IM and only in the twelfth week. There was no statistically significant difference between muscular strength of the quadriceps or the total score on the physical performance test at the end of the twelfth week. Despite the high doses, there was good tolerance and the treatment appears to be safe.

#### DISCUSSION

The current literature has been the focus of several studies about different doses of vitamin D supplements and the impact on functionality. However, there is still a consensus that constitutes the best supplement dosage and its specific impact on the body. Our review showed that the cited authors used different methodologies to replenish vitamin D, as well as in the evaluation of the outcomes presented

Another relevant point is the lack of high-quality studies evaluating only the influence of vitamin D on muscular strength.

Despite the heterogeneity of the studies, it was observed that individuals who have reached levels of vitamin D above 20 ng/mL showed better muscle strength of limbs and function than those with lower levels, as in the studies presented by Mastaglia et al.1, Janssen et al.<sup>19</sup>, and Zhu et al.<sup>20</sup> In addition, another study<sup>24</sup> published prior to the scope of this review article with elderly men between 70 and 79 years already showed that serum levels of 25(OH)D above 20 ng/mL showed improvement in hand grip strength and physical performance. Despite demonstrating the possible positive influence of vitamin D on muscular strength, the studies mentioned above showed significant limitations in their methodology. The negative points, generally, were sample size, study design, and inefficient evaluation instruments.

Another feature that hampers the analysis of the data presented is in regards to the sample. Although our review selected only those articles relating to the elderly, the studies found either had samples of elderly people in general or distinguish the genders. Of the 3 studies performed using only a population of elderly women, 2 articles<sup>1,20</sup> demonstrated some benefit of vitamin D in strength or muscle function.

However, the research developed by Verschueren et al.23 on elderly women showed no additional muscular benefit from the use of higher doses of vitamin D when compared with the conventional dosage. There is only one study that was carried out exclusively with elderly males <sup>21</sup> and that evaluated fragility and its components, so it had no direct outcome as to strength or muscle function.

However, it demonstrated that low levels of 25(OH)D were independently associated with weakness and with 4 of the 5 components of fragility, except for weight loss. The remaining items evaluated the elderly population without distinguishing gender, however one<sup>19</sup> had an age range from 40 to 80 years and another was conducted on institutionalized patients.<sup>4</sup> This diversity of samples makes any comparison between studies practically impossible, even when one takes into account the differentiation by gender, in addition to reducing the external validity of the studies.

Still on the characteristics of the samples, there are only two studies on institutionalized individuals,<sup>4.23</sup> while the rest were on elderly people in the community with no mobility restriction. Studies with institutionalized elderly showed that high doses of vitamin D gave no additional gain in muscle strength. The reasons for this fact may be the previous condition of individuals with very low levels of vitamin D, the high number of comorbidities, and low levels of physical activity. Of the studies<sup>1,19-22</sup> performed on elderly people in the community, only one<sup>22</sup> presented an unfavorable outcome as to associating muscular strength with levels of vitamin D.

The interventional studies with vitamin D supplements showed great variations in relation to the dosage. From the total of three studies<sup>4,16,20,23</sup> that supplemented vitamin D, the following measurements were obtained: 1000 IU of ergocalciferol, 1600 IU of cholecalciferol, 880 IU of cholecalciferol, and 600,000 IU of cholecalciferol. The wide variation of doses, modes of administration, and presentation can justify such diverse results. However, as the studies were not designed to evaluate the pharmacokinetics, any inference about the time or course of decline of 25(OH)D in the groups evaluated becomes infeasible.

Although most studies have demonstrated an improvement in muscle strength or benefit of vitamin D on the musculoskeletal system, we cannot fail to observe the wide variety of instruments or ratings for proof of any determined outcome. There were only 4 articles<sup>1,19,20,22</sup> that had the term "muscle function" or "mobility" in their titles. The of 2.4 m Walk Test was used in half of the studies, 1.19 however to complement the assessment of functionality, one added balance tests and another, a sit-ups test. The other two studies<sup>20.22</sup> used various instruments: Walking Test of 3 m (TUAG) and an evaluation questionnaire for the healthy elderly in the community (CHAMPS). The term "muscle strength" was presented in 4 articles.1,19,20,23

All the studies assessed the strength of the knee extensor, however, the methodology used ranged between isokinetic dynamometry, grip strength, and muscle tension. The differences in answers found may also be due to a combination of different techniques for measuring strength. The only study<sup>23</sup> that used isokinetic dynamometry showed only the strength of the knee extensors, while the others assessed other muscle groups (flexors, extensors, hip adductors and adductors, knee flexors, and grip strength). This was probably a strategy of other authors to minimize the potential risk of measuring with less accurate instruments.

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Despite the different muscle groups measured in the studies, it is known that both the limb and palmar grip strength are correlated with the muscle strength and are therefore good predictors of motor performance.<sup>25</sup>

Two other studies<sup>4.21</sup> did not the above-mentioned terms in their titles, but in their methodologies they also evaluated the strength of knee extensors and grip strength, both by simple dynamometry.

In spite of the methodology for measuring muscle strength presented by articles being validated as good representatives of the overall situation of the individual, the results were varied as to improvements or positive association of strength with the vitamin D *status*. This is likely not due to any error of measurement, but by other characteristics of the studies such as age of the sample, doses of supplementation, serum levels of vitamin D, and the individuals' degree of functionality.

Recently, Wang and DeLuca<sup>26</sup> investigated the presence of vitamin D receptors in the muscle and concluded that they are undetectable in the bones, smooth muscles, and the heart. Therefore, they suggested that the role of vitamin D in the muscles may be indirect (hypocalcemia, hypophosphatemia, and high levels of serum parathyroid hormone) or does not involve any known receptor. This may be an explanation for the conflicting results in different studies.

# CONCLUSION

Recently, there has been growing interest in the role of vitamin D in different sites of the human body. In particular, the influence of vitamin D on the musculoskeletal system can have an impact on the quality of life of the elderly, as that would allow maintenance of mobility and muscle function. However, the results presented above have been controversial. The role of higher doses of vitamin D in the musculoskeletal system remains uncertain, however there was a trend towards greater benefit with the use of supplementation at higher doses, such as greater positive effect on muscular strength when the serum levels of vitamin D were above 20 ng/mL. However, additional studies are necessary to define a better therapeutic profile such as dosage, administration pathway, and duration.

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