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Association Between Vitamin D Status and Physical Performance: The InCHIANTI Study

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Abstract

Background—Vitamin D status has been hypothesized to play a role in musculoskeletal function. Using data from the InCHIANTI study, we examined the association between vitamin D status and physical performance.

Methods—A representative sample of 976 persons aged 65 years or older at study baseline were included. Physical performance was assessed using a short physical performance battery (SPPB) and handgrip strength. Multiple linear regression was used to examine the association between vitamin D (serum 25OHD), parathyroid hormone (PTH), and physical performance adjusting for sociodemographic variables, behavioral characteristics, body mass index, season, cognition, health conditions, creatinine, hemoglobin, and albumin.

Results—Approximately 28.8% of women and 13.6% of men had vitamin D levels indicative of deficiency (serum 25OHD < 25.0 nmol/L) and 74.9% of women and 51.0% of men had vitamin D levels indicative of vitamin D insufficiency (serum 25OHD < 50.0 nmol/L). Vitamin D levels were significantly associated with SPPB score in men (β coefficient [standard error (SE)]: 0.38 [0.18], $p = .04$) and handgrip strength in men (2.44 [0.84], $p = .004$) and women (1.33 [0.53], $p = .01$). Men and women with serum 25OHD < 25.0 nmol/L had significantly lower SPPB scores whereas those with serum 25OHD < 50 nmol/L had significantly lower handgrip strength than those with serum 25OHD ≥ 25 and ≥ 50 nmol/L, respectively ($p < .05$). PTH was significantly associated with handgrip strength only ($p = .01$).

Conclusions—Vitamin D status was inversely associated with poor physical performance. Given the high prevalence of vitamin D deficiency in older populations, additional studies examining the association between vitamin D status and physical function are needed.

With a growing older population, there is an increasing need to identify potentially modifiable risk factors for the onset of disability. In the past two decades, it has become evident that the role of vitamin D extends beyond calcium homeostasis and includes modulation of skeletal and cardiac muscle function, immune cell function, and anticancer activity (1). Within the muscle cell, vitamin D plays an important role in the regulation of calcium transport and protein synthesis (2,3). In older adults, low serum vitamin D (serum 25OHD) levels have been associated with muscle weakness, poor physical performance, balance problems, and falls,

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although findings from different studies are somewhat inconsistent (4–11). Thus, vitamin D deficiency may not only affect the onset of chronic conditions, which are frequent causes of disability, but may also directly affect functional status through vitamin D's role in muscle function.

Consensus to define a cut-point for vitamin D insufficiency based on serum 25OHD levels is lacking. Various cut-points have been proposed based on population-based reference limits or biological indices, such as parathyroid hormone (PTH), calcium absorption, or bone mineral density, with cut-points for serum 25OHD insufficiency ranging from 50 to 80 nmol/L (12–14). Regardless, low levels of serum 25OHD are common in older populations with wide variability in prevalence depending on geographic location, season, and the cut-points used to define insufficiency and/or deficiency (15–19). Older adults are at risk for low serum 25OHD because of reduced exposure to ultraviolet B (UVB) radiation and reduced efficiency of previtamin D synthesis in the skin (20). Dietary intake of vitamin D is also often inadequate, as there are few natural food sources of vitamin D (16).

Low serum 25OHD may also indirectly affect muscle function via hyperparathyroidism secondary to vitamin D deficiency (17). Primary hyperparathyroidism is characterized by muscle weakness that is improved by treatment (21,22). It has been demonstrated that administration of PTH negatively affects skeletal muscle function in animal models (2,3,17). PTH has also been shown to induce the production of serum interleukin-6 (IL-6) (23). Observational studies have shown that elevated IL-6 levels are associated with lower muscle strength and poor physical performance (24,25). However, few studies have examined the joint effect of vitamin D and PTH on physical performance (9,10).

The objective of this study was to examine the associations between vitamin D status and physical performance using data from the InCHIANTI study. Comparisons between different serum 25OHD cut-points and physical performance were examined. Additionally, the association between PTH and physical performance and the role of PTH as a potential mediator in the association between serum 25OHD and physical performance was examined.

Methods

Study Population

Data for this analysis are from the InCHIANTI study, a prospective population-based study of the factors contributing to the decline of mobility in late life. The study population included 1155 participants aged 65–102 years who were randomly selected using a multistage stratified sampling method from two towns in the Chianti geographic area of Italy (Greve in Chianti and Bagno a Ripoli, Tuscany, Italy). Data were collected from September 1998 through March 2000. The sampling procedures and data collection methods have been described elsewhere (26). The Italian National Research Council of Aging Ethical Committee approved the study protocol, and participants provided written informed consent.

Physical Performance Measures

A short physical performance battery (SPPB) based on the lower-extremity performance tests used in the Established Populations for the Epidemiologic Studies of the Elderly (EPESE) (27) was used to summarize physical performance. The SPPB consisted of walking speed, ability to stand from a chair, and ability to maintain balance in progressively more challenging positions. Walking speed was defined as the best performance (time in seconds) of two 4 m walks at usual pace along a corridor. Participants were allowed to use canes or walkers. To test the ability to stand from a chair, participants were asked to stand up and sit down as quickly as possible in a chair five times with their hands folded across their chest; time (in seconds) to

complete the test was recorded. For the standing balance test, participants were asked to stand in three progressively more difficult positions for 10 seconds each: a side-by-side position, a semitandem position, and a full-tandem position. Each physical performance measure was categorized into a five-level score, with 0 representing inability to do the test and 4 representing the highest level of performance. The three measures were then added to create a summary physical performance measure ranging from 0 (worst) to 12 (best).

Handgrip strength was measured using a handheld dynamometer (hydraulic hand “BASELINE”; Smith & Nephew, Agrate Brianza, Milan, Italy). Participants were asked to perform the task twice with each hand. The average of the best result obtained with each hand was used for these analyses.

Serum Vitamin D and PTH

Fasting blood samples were collected in the morning after a 12-hour fast, centrifuged, and stored at -80°C . Serum levels of vitamin D (25OHD) were measured by radioimmunoassay (RIA kit; DiaSorin, Stillwater, MN). The intraassay and interassay coefficients of variation for vitamin D were 8.1% and 10.2%, respectively. Serum intact PTH levels were measured with a two-site immunoradiometric assay kit (N-tact PTHSP; DiaSorin). The intraassay and interassay coefficients of variation for PTH were $< 3.0\%$ and 5.5% , respectively.

Covariates

Covariates included sociodemographic variables (age, study site, education [years]), smoking status (never/former vs current), body mass index (BMI; computed as weight in kg/height in meters squared), physical activity (physically active defined as moderate-intensity to high-intensity exercise performed for at least 1–2 hours per week or light intensity exercise performed for more than 4 hours per week), total energy intake (EPIC questionnaire; kcal/d), and cognition (Mini-Mental State Examination score). Season of the year (November–February vs March–October) was included to account for seasonal effects on vitamin D and PTH levels. Adjudicated disease diagnoses were based on self-reported history, clinical documentation, and medication use and included the following conditions: coronary heart disease, congestive heart failure, cerebrovascular disease, peripheral artery disease, hypertension, diabetes, chronic obstructive pulmonary disease, and osteoarthritis.

Biological parameters were also examined in the modeling of vitamin D status and physical performance. Serum creatinine (a marker of kidney function) was measured by a standard creatinine Jaffe method (Roche Diagnostics, Mannheim, Germany). Hemoglobin was measured using the hematology automated Autoanalyzer DASIT SE 9000 (Sysmex Corporation, Kobe, Japan). Albumin was measured using an agarose electrophoretic technique [Hydrigel Protein(E) 15/30; Sebia, Issy-les-Moulineaux, France].

Exclusions

Participants who did not undergo blood tests ($n = 100$), who were missing values for serum 25OHD ($n = 50$), or who lacked both of the physical performance measures of interest (the SPPB and handgrip strength; $n = 29$) were excluded, resulting in an analysis sample of 976 participants. An additional 16 participants were missing the SPPB and 149 were missing handgrip strength; these participants were excluded only from analyses specific to that physical performance measure.

Statistical Analyses

Cross-sectional analyses of baseline data were conducted using SAS statistical software (version 8.2; SAS Institute, Cary, NC). Vitamin D and PTH were examined both as a continuous

(normalized by transformation using the natural logarithm) and categorical variable. Vitamin D status was categorized as follows: serum 25OHD < 25 nmol/L, 25 to < 50 nmol/L, and ≥ 50 nmol/L (reference group) based on established deficiency (< 25 nmol/L) and insufficiency (< 50 nmol/L) cut-points (12). PTH was categorized into tertiles (≤ 17.70 ng/L [reference group], 17.80–28.00 ng/L, and ≥ 28.10 ng/L). Differences in the frequencies and means of covariates by categories of vitamin D status were examined using age-adjusted analysis of variance (ANOVA). Multiple linear regression models were used to examine the effect of vitamin D and PTH status on physical performance measures after adjustment for potential confounding variables (those covariates known to be associated with vitamin D and physical performance or that showed a significant association ($p \leq .10$) with vitamin D status in age-adjusted models), and least-squares means were reported. There was a significant Gender \times Vitamin D interaction for handgrip strength ($p < 0.05$), thus, all analyses were stratified by gender.

Results

The mean age of the study population was 74.8 years. Participants who were excluded from the analysis were older (78.9 vs 74.8 years, $p < .001$) and were more likely to be women (63.7% vs 55.4%, $p = .04$). The mean serum 25OHD level was 57.92 (standard deviation [SD] 35.35) nmol/L in men and 43.30 (SD 34.91) nmol/L in women. Approximately one quarter of the women and half of the men had vitamin D levels in the sufficient range (serum 25OHD ≥ 50 nmol/L). However, 28.8% of women and 13.6% of men had vitamin D levels indicative of deficiency (serum 25OHD < 25 nmol/L). Tables 1 and 2 show the age-adjusted participant characteristics for key covariates by categories of vitamin D status in men and women, respectively. Vitamin D levels were lower in older age and in participants who had been evaluated in the winter compared to in the spring, summer, or fall but higher in those who reported higher physical activity. Vitamin D and PTH levels were inversely correlated (Pearson $r = -0.45$, $p < .0001$).

Vitamin D levels were significantly and positively associated with SPPB score [β coefficient (standard error [SE]) per unit of the natural logarithm of serum 25OHD: 0.38 (0.18), $p = .04$] in men and handgrip strength in men (2.44 [0.84], $p = .004$) and women (1.33 [0.53], $p = .01$) after adjustment for sociodemographic variables, physical activity, BMI, energy intake, season, cognition, health conditions, and levels of creatinine, hemoglobin, and albumin. Tables 3 and 4 show the mean physical performance measures by categories of vitamin D status in men and women, respectively. SPPB scores were significantly lower among men and women with serum 25OHD < 25.0 nmol/L compared to those with serum 25OHD ≥ 25.0 nmol/L ($p < .05$). Men and women with serum 25OHD < 50.0 nmol/L had significantly lower handgrip strength compared to those with serum 25OHD ≥ 50 nmol/L ($p < .05$). Additional analyses examined the association between vitamin D status and handgrip strength using a proposed higher cut-point of serum 25OHD ≥ 75 nmol/L (23% of men and 12% of women met this definition) (14). Men, but not women, with serum 25OHD ≥ 75 nmol/L had significantly higher handgrip strength compared to those with serum 25OHD < 75 nmol/L ($p < .05$).

Vitamin D may play a role in physical performance through its actions on PTH. Further adjustment for PTH levels attenuated the associations between vitamin D status and physical performance measures; however, associations remained between vitamin D status and SPPB score (β coefficient [SE]: 0.36 [0.19], $p = .06$) in men and handgrip strength in men (1.90 [0.90], $p = .03$) and women (1.02 [0.55], $p = .06$).

The associations between PTH levels and physical performance measures were also examined. Significant associations between PTH levels and physical performance measures were found for handgrip strength only (β coefficient [SE] per unit of the natural logarithm of serum PTH: -2.50 [0.98] and -1.70 [0.67], in men and women, respectively; $p = .01$). When the associations

between physical performance and PTH were examined using PTH tertiles (Table 5), men in the highest PTH tertile (≥ 28.10 ng/L) had significantly lower handgrip strength than did those in the lower two tertiles ($p = .0003$). Although there was a trend towards lower handgrip strength among women across PTH tertiles ($p = .08$; Table 6), there were no significant differences in handgrip strength. SPPB scores were not significantly associated with PTH levels (continuous or by tertiles).

In additional analyses, we examined the association between physical performance and combined categories of vitamin D status and PTH levels. Men and women with insufficient vitamin D status (serum 25OHD < 50 nmol/L) and high PTH levels (≥ 28.10 ng/L) had handgrip strengths that were $\geq 10\%$ lower than those who had sufficient vitamin D (serum 25OHD ≥ 50.0 nmol/L) and low PTH (≤ 17.70 ng/L; $p < .05$). This difference was greater than that observed in comparing handgrip strength by vitamin D status or PTH levels alone.

Discussion

The results from this cross-sectional study suggest that vitamin D status is associated with physical performance among older men and women. Serum 25OHD levels < 25.0 nmol/L were significantly associated with lower SPPB scores, whereas serum 25OHD levels < 50.0 nmol/L were significantly associated with handgrip strength after adjusting for sociodemographic variables, behavioral characteristics, and season. These associations remained after adjusting for cognition, health conditions, renal function, and serum markers of health status.

Cross-sectional associations between vitamin D and muscle strength and physical performance have been inconsistent (4–8,11). Among older adults in the National Health and Nutrition Examination Survey (NHANES) III study, serum 25OHD levels < 40 nmol/L were associated with poor physical performance on an 8-foot walk test and sit-to-stand test compared to serum 25OHD levels ≥ 40 nmol/L (7). To our knowledge, only two prospective studies have examined the association between vitamin D and muscle strength and physical performance (9,10). Elderly men and women with low serum 25OHD in the Longitudinal Study of Aging Amsterdam were significantly more likely to lose handgrip strength and appendicular skeletal muscle mass over 3 years of follow-up (10). In contrast, there was no association between serum 25OHD and subsequent loss in muscle strength or physical performance over 3 years of follow-up in the Women's Health and Aging Study (WHAS) (9). However, the assay used in WHAS has been shown to be less reliable than more recent methods and insensitive to the vitamin D₂ form, which may have resulted in misclassification of vitamin D status (28–30). In addition, participants in WHAS already had moderate to severe disability leading the authors to speculate that it was possible that most of the women were already below a baseline threshold of strength where vitamin D deficiency may not have had any additional impact.

Randomized controlled trials have shown that vitamin D supplementation can significantly improve muscle function and physical performance among older adults at high risk for vitamin D deficiency, institutionalized elderly women (31) and patients attending a falls clinic (32). Others have also shown that supplemental vitamin D may improve balance and reduce the incidence of falls (31,33–36). However, other vitamin D supplementation studies have found no effect on physical function or falls (37,38). The discrepancies among these studies may be the result of the study population characteristics, inadequate dose of vitamin D, low calcium intake or lack of a calcium supplement in combination with vitamin D supplementation, and baseline vitamin D status.

Vitamin D plays an important role in muscle function through its regulation of calcium transport, uptake of inorganic phosphate for the production of energy-rich phosphate compounds, and protein synthesis in the muscle (2,3). In addition, the association between

vitamin D and physical performance may be mediated by PTH. Vitamin D deficiency is a recognized cause of secondary hyperparathyroidism. In animal models, administration of PTH has been shown to increase protein catabolism and decrease the number of type 2 muscle fibers, intracellular energy-rich phosphate compounds, and mitochondrial oxygen uptake (2,3,17). PTH also induces the production of IL-6 (23). Previous studies have linked elevated IL-6 levels with lower muscle strength (24) and poor physical performance (25). In the current study, PTH was associated with handgrip strength but not SPPB scores. When examining the joint effect of vitamin D and PTH, the associations between vitamin D and physical performance were attenuated slightly after adjusting for PTH, suggesting that the association between low vitamin D and poor physical performance may be independent of PTH.

The cross-sectional design of our study does not allow us to evaluate a causal association between vitamin D status and physical performance. Although it is biologically plausible that low vitamin D levels may result in low muscle strength and poor physical performance, it is also possible that participants with poor physical performance had less exposure to UVB rays, resulting in low vitamin D levels. Results from both cross-sectional and prospective studies examining the role of vitamin D status on physical performance measures have been inconsistent. Substantial variation in the measurement of serum 25OHD, because of different assay methodology, laboratory experience, and differences between assays to recognize the vitamin D₃ and D₂ form equally (28–30), may confound the ability to detect an association between vitamin D status and physical function in some studies. These discrepancies between the assays used to measure serum 25OHD also make it difficult to make comparisons across studies. Randomized controlled trials of vitamin D supplementation, however, have shown improvement in muscle function and physical performance (31,32). Further investigation aimed at assessing the predictive value of vitamin D status on physical performance is needed.

Conclusion

Low vitamin D status was associated with poor physical performance among elderly men and women in a cross-sectional population study. There is a growing awareness that the prevalence of low vitamin D levels is common among the elderly population. In this population of community-dwelling older adults residing in Italy, there was a high prevalence of vitamin D deficiency (serum 25OHD < 25 nmol/L) and vitamin D insufficiency (serum 25OHD < 50 nmol/L), particularly among women. Recent findings showing the importance of vitamin D status on multiple health outcomes (1,18) underscore the need for more research on the effects of low vitamin D status in elderly populations.

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References

1. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. *Am J Clin Nutr* 2004;80(6 suppl):1678S–1688S. [PubMed: 15585788]
2. Pfeifer M, Begerow B, Minne HW. Vitamin D and muscle function. *Osteoporos Int* 2002;13:187–194. [PubMed: 11991436]
3. Mosekilde L. Vitamin D and the elderly. *Clin Endocrinol (Oxf)* 2005;62:265–281. [PubMed: 15730407]
4. Pfeifer M, Begerow B, Minne HW, et al. Vitamin D status, trunk muscle strength, body sway, falls, and fractures among 237 postmenopausal women with osteoporosis. *Exp Clin Endocrinol Diabetes* 2001;109:87–92. [PubMed: 11341304]

5. Dhese JK, Bearne LM, Moniz C, et al. Neuromuscular and psychomotor function in elderly subjects who fall and the relationship with vitamin D status. *J Bone Miner Res* 2002;17:891–897. [PubMed: 12009020]
6. Mowe M, Haug E, Bohmer T. Low serum calcidiol concentration in older adults with reduced muscular function. *J Am Geriatr Soc* 1999;47:220–226. [PubMed: 9988294]
7. Bischoff-Ferrari HA, Dietrich T, Orav EJ, et al. Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged > or =60 y. *Am J Clin Nutr* 2004;80:752–758. [PubMed: 15321818]
8. Zamboni M, Zoico E, Tosoni P, et al. Relation between vitamin D, physical performance, and disability in elderly persons. *J Gerontol Med Sci* 2002;57:M7–M11.
9. Verreault R, Semba RD, Volpato S, Ferrucci L, Fried LP, Guralnik JM. Low serum vitamin D does not predict new disability or loss of muscle strength in older women. *J Am Geriatr Soc* 2002;50:912–917. [PubMed: 12028180]
10. Visser M, Deeg DJ, Lips P. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): the Longitudinal Aging Study Amsterdam. *J Clin Endocrinol Metab* 2003;88:5766–5772. [PubMed: 14671166]
11. Gerdhem P, Ringsberg KA, Obrant KJ, Akesson K. Association between 25-hydroxy vitamin D levels, physical activity, muscle strength and fractures in the prospective population-based OPRA Study of Elderly Women. *Osteoporos Int* 2005;16:1425–1431. [PubMed: 15744449]
12. Lips P. Which circulating level of 25-hydroxyvitamin D is appropriate? *J Steroid Biochem Mol Biol* 2004;89–90:611–614.
13. Heaney RP. Functional indices of vitamin D status and ramifications of vitamin D deficiency. *Am J Clin Nutr* 2004;80(6 suppl):1706S–1709S. [PubMed: 15585791]
14. Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. *Osteoporos Int* 2005;16:713–716. [PubMed: 15776217]
15. van der Wielen RP, Lowik MR, van den Berg H, et al. Serum vitamin D concentrations among elderly people in Europe. *Lancet* 1995;346:207–210. [PubMed: 7616799]
16. Ovesen L, Andersen R, Jakobsen J. Geographical differences in vitamin D status, with particular reference to European countries. *Proc Nutr Soc* 2003;62:813–821. [PubMed: 15018480]
17. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocr Rev* 2001;22:477–501. [PubMed: 11493580]
18. Holick MF. Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. *Am J Clin Nutr* 2004;79:362–371. [PubMed: 14985208]
19. Maggio D, Cherubini A, Lauretani F, et al. 25(OH)D Serum levels decline with age earlier in women than in men and less efficiently prevent compensatory hyperparathyroidism in older adults. *J Gerontol Biol Sci Med Sci* 2005;60A:1414–1419.
20. Holick MF. Vitamin D requirements for humans of all ages: new increased requirements for women and men 50 years and older. *Osteoporos Int* 1998;8(suppl 2):S24–S29. [PubMed: 10197179]
21. Joborn C, Joborn H, Rastad J, Akerstrom G, Ljunghall S. Maximal isokinetic muscle strength in patients with primary hyperparathyroidism before and after parathyroid surgery. *Br J Surg* 1988;75:77–80. [PubMed: 3337959]
22. Kristoffersson A, Bostrom A, Soderberg T. Muscle strength is improved after parathyroidectomy in patients with primary hyperparathyroidism. *Br J Surg* 1992;79:165–168. [PubMed: 1555067]
23. McCarty MF. Secondary hyperparathyroidism promotes the acute phase response—a rationale for supplemental vitamin D in prevention of vascular events in the elderly. *Med Hypotheses* 2005;64:1022–1026. [PubMed: 15780504]
24. Visser M, Pahor M, Taaffe DR, et al. Relationship of interleukin-6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly men and women: the Health ABC Study. *J Gerontol Med Sci* 2002;57:M326–M332.
25. Cesari M, Penninx BW, Pahor M, et al. Inflammatory markers and physical performance in older persons: the InCHIANTI study. *J Gerontol Biol Sci Med Sci* 2004;59A:242–248.

26. Ferrucci L, Bandinelli S, Benvenuti E, et al. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. *J Am Geriatr Soc* 2000;48:1618–1625. [PubMed: 11129752]
27. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994;49:M85–M94. [PubMed: 8126356]
28. Carter GD, Carter R, Jones J, Berry J. How accurate are assays for 25-hydroxyvitamin D? Data from the international vitamin D external quality assessment scheme. *Clin Chem* 2004;50:2195–2197. [PubMed: 15375018]
29. Hollis BW. The determination of circulating 25-hydroxyvitamin D: no easy task. *J Clin Endocrinol Metab* 2004;89:3149–3151. [PubMed: 15240585]
30. Binkley N, Krueger D, Cowgill CS, et al. Assay variation confounds the diagnosis of hypovitaminosis D: a call for standardization. *J Clin Endocrinol Metab* 2004;89:3152–3157. [PubMed: 15240586]
31. Bischoff HA, Stahelin HB, Dick W, et al. Effects of vitamin D and calcium supplementation on falls: a randomized controlled trial. *J Bone Miner Res* 2003;18:343–351. [PubMed: 12568412]
32. Dhese JK, Jackson SH, Bearne LM, et al. Vitamin D supplementation improves neuromuscular function in older people who fall. *Age Ageing* 2004;33:589–595. [PubMed: 15501836]
33. Pfeifer M, Begerow B, Minne HW, Abrams C, Nachtigall D, Hansen C. Effects of a short-term vitamin D and calcium supplementation on body sway and secondary hyperparathyroidism in elderly women. *J Bone Miner Res* 2000;15:1113–1118. [PubMed: 10841179]
34. Harwood RH, Sahota O, Gaynor K, Masud T, Hosking DJ. A randomised, controlled comparison of different calcium and vitamin D supplementation regimens in elderly women after hip fracture: The Nottingham Neck of Femur (NONOF) Study. *Age Ageing* 2004;33:45–51. [PubMed: 14695863]
35. Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, et al. Effect of vitamin D on falls: a meta-analysis. *JAMA* 2004;291:1999–2006. [PubMed: 15113819]
36. Bischoff-Ferrari HA, Orav EJ, Dawson-Hughes B. Effect of cholecalciferol plus calcium on falling in ambulatory older men and women: a 3-year randomized controlled trial. *Arch Intern Med* 2006;166:424–430. [PubMed: 16505262]
37. Latham NK, Anderson CS, Lee A, Bennett DA, Moseley A, Cameron ID. A randomized, controlled trial of quadriceps resistance exercise and vitamin D in frail older people: the Frailty Interventions Trial in Elderly Subjects (FITNESS). *J Am Geriatr Soc* 2003;51:291–299. [PubMed: 12588571]
38. Kenny AM, Biskup B, Robbins B, Marcella G, Burleson JA. Effects of vitamin D supplementation on strength, physical function, and health perception in older, community-dwelling men. *J Am Geriatr Soc* 2003;51:1762–1767. [PubMed: 14687355]

Table 1
Selected Participant Characteristics by Vitamin D Status in Men: The InCHIANTI Study

Characteristics	Serum 25OHD (nmol/L)			<i>p</i> for Trend
	< 25	25 to <50	≥50	
<i>N</i> (%)	59 (13.6)	163 (37.5)	213 (49.0)	
Age, y	79.8 (0.8)	74.5 (0.5)	72.2 (0.4)	<.0001
Education, y	6.0 (0.5)	6.0 (0.3)	6.3 (0.2)	.37
Current smoker, %	15.7	21.7	21.8	.56
Physically active, % [*]	38.3	51.4	56.2	.05
BMI, kg/m ²	27.1 (0.5)	27.1 (0.2)	27.0 (0.2)	.81
Total energy intake, kcal/d	1995.9 (71.3)	2174.6 (40.9)	2218.2 (36.5)	.04
Season (Nov–Feb), %	69.4	54.5	33.9	<.0001
Cognition, MMSE score	23.6 (0.5)	25.6 (0.3)	25.2 (0.3)	.37
Chronic conditions				
Coronary heart disease, %	11.6	11.4	10.6	.77
Congestive heart failure, %	12.6	6.0	4.1	.06
Cerebrovascular disease, %	12.6	7.8	5.1	.08
Peripheral artery disease, %	9.8	8.4	7.7	.66
Hypertension, %	39.2	24.0	29.0	.83
Diabetes, %	21.2	11.2	11.8	.34
COPD, %	25.5	18.3	13.2	.04
Osteoarthritis, %	3.9	7.2	4.7	.60
Parathyroid hormone, ng/L	40.5 (3.2)	27.7 (1.8)	20.6 (1.6)	<.0001
Creatinine, mg/dL	1.03 (0.03)	1.03 (0.02)	1.01 (0.01)	.30
Hemoglobin, g/dL	14.4 (0.2)	14.4 (0.1)	14.4 (0.1)	.90
Albumin, g/dL	4.23 (0.04)	4.22 (0.02)	4.23 (0.02)	.72

Notes: Means (standard error [SE]) or frequencies with age-adjusted analysis of variance (ANOVA) were used to evaluate the distribution.

* Physically active: participants who reported moderate- to high-intensity exercise performed for at least 1–2 hours per week or light intensity exercise performed for more than 4 hours per week.

BMI = body mass index; COPD = chronic obstructive pulmonary disease; MMSE = Mini-Mental State Examination.

Table 2
Selected Participant Characteristics by Vitamin D Status in Women: The InCHIANTI Study

Characteristics	Serum 25OHD (nmol/L)			<i>p</i> for Trend
	< 25	25 to < 50	≥50	
<i>N</i> (%)	156 (28.8)	249 (46.0)	136 (25.1)	
Age, y	78.3 (0.6)	75.1 (0.4)	72.5 (0.6)	<.0001
Education, y	4.8 (0.2)	4.4 (0.2)	5.3 (0.2)	.04
Current smoker, %	9.9	5.9	8.8	.99
Physically active, % [*]	21.7	24.1	30.6	.06
BMI, kg/m ²	27.6 (0.4)	28.2 (0.3)	27.0 (0.4)	.09
Total energy intake, kcal/d	1726.4 (37.8)	1704.1 (29.4)	1724.7 (40.5)	.93
Season (Nov–Feb), %	55.9	38.3	22.4	<.0001
Cognition, MMSE score	23.9 (0.3)	24.0 (0.2)	25.0 (0.3)	.01
Chronic conditions				
Coronary heart disease, %	8.1	4.0	4.6	.33
Congestive heart failure, %	8.0	6.1	1.0	.007
Cerebrovascular disease, %	5.5	3.2	1.0	.05
Peripheral artery disease, %	3.9	3.3	6.3	.24
Hypertension, %	40.4	38.8	43.7	.48
Diabetes, %	11.3	9.7	9.7	.73
COPD, %	3.0	0.5	2.3	.95
Arthritis, %	15.1	15.4	17.9	.49
Parathyroid hormone, ng/L	34.5 (1.3)	26.7 (1.0)	21.3 (1.4)	<.0001
Creatinine, mg/dL	0.85 (0.02)	0.87 (0.01)	0.84 (0.02)	.56
Hemoglobin, g/dL	13.2 (0.1)	13.2 (0.1)	13.0 (0.1)	.08
Albumin, g/dL	4.14 (0.02)	4.15 (0.02)	4.20 (0.02)	.10

Notes: Means (standard error [SE]) or frequencies with age-adjusted analysis of variance (ANOVA) were used to evaluate the distribution.

* Physically active: participants who reported moderate-intensity to high-intensity exercise performed for at least 1–2 hours per week or light intensity exercise performed for more than 4 hours per week.

BMI = body mass index; COPD = chronic obstructive pulmonary disease; MMSE = Mini-Mental State Examination.

Table 3
Adjusted Physical Performance Measures [Mean (SE)] by Vitamin D Status in Men: The InCHIANTI Study

Physical Performance Measure	Serum 25OHD (nmol/L)				<i>p</i> Value < 25 vs ≥25	<i>p</i> Value < 50 vs ≥50	<i>p</i> for Trend
	< 25	25 to < 50	≥50	<i>N</i>			
SPPB score							
<i>N</i>	59	157	209				
Age adjusted	8.69 (0.34)	10.57 (0.20)	10.75 (0.17)		<.0001	.02	.0004
Model 1	10.16 (0.31)	10.71 (0.16)	10.95 (0.14)		.05	.11	.05
Model 2	10.15 (0.29)	10.73 (0.15)	10.94 (0.14)		.03	.10	.04
Handgrip strength, kg							
<i>N</i>	40	136	188				
Age adjusted	35.19 (1.46)	36.90 (0.76)	38.08 (0.66)		.13	.11	.07
Model 1	36.46 (1.41)	36.31 (0.73)	38.88 (0.63)		.49	.007	.01
Model 2	36.28 (1.40)	36.37 (0.71)	38.80 (0.62)		.42	.009	.01

Notes: Model 1 was adjusted for sociodemographic variables (age, site, education), smoking status, physical activity, body mass index, total energy intake, and season. Model 2 was adjusted for variables in Model 1 plus cognition, congestive heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, and levels of creatinine, hemoglobin, and albumin.

SE = standard error; *SPPB* = short physical performance battery.

Table 4
Adjusted Physical Performance Measures [Mean (SE)] by Vitamin D Status in Women: The InCHIANTI Study

Physical Performance Measure	Serum 25OHD (nmol/L)			p Value < 25 vs ≥25	p Value < 50 vs ≥50	p for Trend
	< 25	25 to < 50	≥50			
SPPB score						
N	155	245	135			
Age adjusted	8.58 (0.22)	9.49 (0.17)	9.45 (0.23)	.0005	.31	.03
Model 1	9.12 (0.20)	9.85 (0.15)	9.68 (0.21)	.005	.76	.18
Model 2	9.29 (0.19)	9.85 (0.14)	9.59 (0.20)	.03	.74	.58
Handgrip strength, kg						
N	110	225	128			
Age adjusted	20.65 (0.66)	21.96 (0.45)	21.88 (0.61)	.09	.66	.33
Model 1	20.46 (0.61)	21.53 (0.42)	22.94 (0.58)	.03	.01	.005
Model 2	20.58 (0.60)	21.52 (0.41)	22.83 (0.57)	.06	.02	.009

Notes: Model 1 was adjusted for sociodemographic variables (age, site, education), smoking status, physical activity, body mass index, total energy intake, and season. Model 2 was adjusted for variables in Model 1 plus cognition, congestive heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, and levels of creatinine, hemoglobin, and albumin.

SE = standard error; SPPB = short physical performance battery.

Table 5
Adjusted Physical Performance Measures [Mean (SE)] by PTH Status in Men: The InCHIANTI Study

Physical Performance Measure	PTH Status (ng/L)*			p Value 1st Tertile vs 2nd and 3rd Tertiles	p Value 1st and 2nd Tertiles vs 3rd Tertile	p for Trend
	1st Tertile	2nd Tertile	3rd Tertile			
SPPB score						
<i>N</i>	155	151	119			
Age adjusted	10.56 (0.21)	10.51 (0.21)	10.03 (0.24)	.36	.08	.09
Model 1	10.81 (0.17)	10.75 (0.17)	10.75 (0.20)	.83	.92	.83
Model 2	10.79 (0.16)	10.76 (0.16)	10.75 (0.19)	.86	.89	.86
Handgrip strength, kg						
<i>N</i>	145	132	87			
Age adjusted	38.22 (0.74)	38.39 (0.76)	34.20 (0.96)	.17	.0002	.001
Model 1	38.24 (0.69)	38.72 (0.72)	35.05 (0.91)	.38	.001	.006
Model 2	38.31 (0.68)	38.73 (0.71)	34.75 (0.90)	.28	.0003	.002

Notes: Model 1 was adjusted for sociodemographic variables (age, site, education), smoking status, physical activity, body mass index, total energy intake, and season. Model 2 was adjusted for variables in Model 1 plus cognitive status, congestive heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, and levels of creatinine, hemoglobin, and albumin.

* PTH tertiles: 1st ≤ 17.70 ng/L; 2nd 17.80–28.00 ng/L; 3rd ≥ 28.10 ng/L.

SE = standard error; SPPB = short physical performance battery; PTH = parathyroid hormone.

Table 6
Adjusted Physical Performance Measures [Mean (SE)] by PTH Status in Women: The InCHIANTI Study

Physical Performance Measure	PTH Status (ng/L)*			p Value 1st and 2nd Tertiles vs 3rd Tertile	p Value 1st and 2nd Tertiles vs 3rd Tertile	p for Trend
	1st Tertile	2nd Tertile	3rd Tertile			
SPPB score						
<i>N</i>	167	161	207			
Age adjusted	9.15 (0.21)	9.38 (0.21)	9.14 (0.19)	.70	.58	.60
Model 1	9.57 (0.19)	9.70 (0.19)	9.57 (0.17)	.81	.76	.70
Model 2	9.58 (0.18)	9.73 (0.18)	9.60 (0.16)	.69	.82	.44
Handgrip strength, kg						
<i>N</i>	158	150	155			
Age adjusted	21.62 (0.54)	22.47 (0.55)	20.81 (0.55)	.96	.07	.19
Model 1	22.31 (0.51)	21.72 (0.52)	20.95 (0.51)	.14	.10	.07
Model 2	22.29 (0.51)	21.69 (0.52)	21.00 (0.51)	.14	.12	.08

Notes: Model 1 was adjusted for sociodemographic variables (age, site, education), smoking status, physical activity, body mass index, total energy intake, and season. Model 2 was adjusted for variables in Model 1 plus cognitive status, congestive heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, and levels of creatinine, hemoglobin, and albumin.

* PTH tertiles: 1st ≤ 17.70 ng/L; 2nd 17.80–28.00 ng/L; 3rd ≥ 28.10 ng/L.

SE = standard error; SPPB = short physical performance battery; PTH = parathyroid hormone.