Vitamin D and Physical Performance in Older Men and Women Visiting the Emergency Department Because of a Fall: Data from the Improving Medication Prescribing to reduce Risk Of FALLs (IMPROVeFALL) Study

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OBJECTIVES: To investigate whether serum 25-hydroxyvitamin D (25(OH)D) is associated with physical performance in men and women.

DESIGN: Cross-sectional.

SETTING: Emergency departments (EDs) of five hospitals.

PARTICIPANTS: Older adults who visited an ED because of a fall (N = 616).

MEASUREMENTS: Physical performance was assessed using the Timed Up and Go Test, the Five Time Sit to Stand Test, handgrip strength, and the tandem stand test. Multivariate linear regression was used to assess the association between physical performance and log-transformed 25(OH)D concentration adjusted for potential confounders.

RESULTS: In men, higher serum 25(OH)D concentration was significantly associated with better handgrip strength (regression coefficient (B) = 3.86, 95% confidence interval (CI) = 2.04–5.69), faster TUG time (B = -2.82, 95% CI = -4.91 to -0.73), and faster FTSS time (B = -3.39, 95% CI = -5.67 to -1.11). In women, higher serum 25(OH)D concentration was significantly associated with faster TUG time (B = -2.68, 95% CI = -4.87 to -0.49).


Key words: older adults; physical performance; vitamin D; falls; muscle strength

Muscle tissue is an important target tissue for vitamin D, and vitamin D deficiency is an important contributor to decline in physical performance and increase in fall incidence, but most studies demonstrating the relationship between serum 25-hydroxyvitamin D3 (25(OH)D) levels and physical performance have been conducted in female-only populations. Studies in men have shown positive or no associations, but most of these studies have been conducted in a population of highly functional, younger men with a low prevalence of vitamin D deficiency. In addition, large studies involving men were population-based, epidemiological studies in randomly selected, nonsymptomatic older persons and have not focused specifically on individuals with possible symptoms of neuromuscular dysfunction, such as falls. A fall is generally considered to be a common symptom of neuromuscular dysfunction and vitamin D deficiency. The current study assessed whether serum 25(OH)D was associated with physical performance in community-dwelling older men and women who visited a hospital emergency department (ED) after experiencing a fall.
METHODS

Data Collection

Baseline data from the Improving Medication Prescribing to reduce Risk Of Falls (IMPROveFALL) study were used, a detailed description of the methods can be found elsewhere. In short, individuals aged 65 and older who visited the ED because of a fall, used one or more fall-risk increasing drugs, had a Mini-Mental State Examination (MMSE) score of at least 21 of 30 points, were able to walk independently, were community dwelling, and provided written informed consent were eligible for enrollment. Enrollment started in October 2008 and was completed in October 2011. The medical ethics committee of the Erasmus MC University Medical Center approved the protocol.

Covariates

A fall was defined as coming to rest unintentionally on the ground or the floor with or without losing consciousness but not induced by an acute medical condition (e.g., stroke) or an exogenous factor such as a traffic accident. A geriatric assessment was performed at baseline. Medical history, prescription medication, supplements, and lifestyle factors (e.g., education, smoking, alcohol intake) were documented. The number of comorbidities (any malignancy, diabetes mellitus, cardiac disease (hypertension, myocardial infarction, cardiomyopathy, congestive heart failure, arrhythmia, valve disease), chronic obstructive pulmonary disease, stroke, neurological disorders (Parkinson’s disease, epilepsy, neuropathy, myopathy, spinal disc herniation, multiple sclerosis), peripheral vascular disease, renal insufficiency, arthritis) was determined. Collected data were verified with records from the participant’s general physician and local pharmacist. Height and weight were measured using standardized equipment and procedure. Body mass index (BMI) was calculated as body weight divided by height squared (kg/m²).

Biochemistry

Nonfasting blood samples were collected at the baseline assessment. Serum 25(OH)D levels were measured using a radioimmunoassay (DiaSorin, Saluggia, Vercelli, Italy). Intra- and interassay coefficients of variation were less than 10%.

Classification of Vitamin D Status

Serum 25(OH)D groups were chosen based on levels of vitamin D deficiency as described in the literature: severe deficiency (<25.0 nmol/L), moderate deficiency (25.0–49.9 nmol/L), sufficient (50.0–74.9 nmol/L), and optimal (≥75.0 nmol/L).

Physical Performance

Physical performance was assessed using handgrip strength measurements, the Timed Up and Go (TUG) Test, the Five Time Sit to Stand (FTSS) Test, and the tandem stand test. Handgrip strength, was measured in kilograms using a digital strain-gauged dynamometer (Takei TKK 5401, Takei Scientific Instruments Co., Ltd., Tokyo, Japan). Participants were asked to stand upright with arms hanging beside their body; grip strength was measured in each hand. In the TUG Test, the time it took for participants to stand up from a sitting position, walk 3 meters along a line, perform a 180º turn, walk back to the chair, and sit down, as fast as safely possible, was measured. In the FTSS Test, the time it took participants to stand up and sit down five consecutive times, as fast as safely possible, was measured. Participants were not permitted to use their hands or the chair’s arm supports during standing up or sitting down. In the tandem stand test, participants stood fully independent for 10 seconds with one foot in front of the other. The test was scored as completed or failed. All tests were performed twice, and the best score was recorded.

Statistical Analysis

All analyses were performed using the SPSS version 17.0 (SPSS, Inc., Chicago, IL). Baseline characteristics were compared using Student t-test analyses for continuous variables and chi-square analyses for dichotomous variables. Linear regression and binary logistic regression models were constructed to adjust for potential confounders. The crude model was solely age adjusted. Potential confounders considered for inclusion in the multivariate model in addition to age were number of comorbidities, degree of urbanization, marital status, level of education, current or past smoker, alcohol units per day, MMSE score, and BMI. Confounders that led to a change in the regression coefficient (B) of 10% or more were retained in the multivariate-adjusted regression model. Participants with incomplete or missing performance test measures were excluded from related analyses (handgrip strength, n = 7; TUG Test, n = 55; FTSS Test, n = 95; tandem stand test, n = 4). Measures were missing mostly because of injuries after the fall (e.g., upper or lower extremity fractures) or preexisting conditions. Because of a right-skewed distribution, serum 25 (OH)D levels were log transformed (natural log) for the regression models, and a general linear model was used to multivariately compare all continuous outcomes and chi-square analyses to compare the tandem stand outcomes. All analyses were stratified according to sex, and P < .05 was considered statistically significant.

RESULTS

Six hundred sixteen participants were enrolled in the IMPROveFALL study. Information on serum 25(OH)D concentration was obtained from 600 participants (230 (38%) men; 370 (62%) women). The sex-specific baseline characteristics are shown in Table 1; the mean age was 76 ± 7. The mean serum 25(OH)D concentration was 59 ± 29 nmol/L. Fifty-five participants (9%) had severe vitamin D deficiency (<25 nmol/L), 209 (35%) had moderate deficiency (25–49.9 nmol/L), 172 (29%) had sufficient vitamin D (50–74.9 nmol/L), and 164 (27%) had optimal 25(OH)D levels (≥75 nmol/L). One hundred two men (44%) and 162 women (44%) had serum 25(OH)D levels of less than 50 nmol/L.
Table 1. Baseline Characteristics According to Sex

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Men, n = 230</th>
<th>Women, n = 370</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>76.4 ± 6.7</td>
<td>76.5 ± 7.0</td>
<td>.82</td>
</tr>
<tr>
<td>Serum vitamin D, mean ± SD</td>
<td>58.9 ± 30.9</td>
<td>58.7 ± 27.8</td>
<td>.94</td>
</tr>
<tr>
<td>Mini-Mental State Examination score, mean ± SD</td>
<td>27.0 ± 2.3</td>
<td>26.9 ± 2.4</td>
<td>.72</td>
</tr>
<tr>
<td>Body mass index, kg/m², mean ± SD</td>
<td>27.1 ± 3.9</td>
<td>27.9 ± 4.9</td>
<td>.03</td>
</tr>
<tr>
<td>Secondary level of education, n (%)</td>
<td>185 (80)</td>
<td>250 (68)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Urban, n (%)</td>
<td>190 (83)</td>
<td>323 (87)</td>
<td>.14</td>
</tr>
<tr>
<td>Recurrent fallers, n (%)</td>
<td>96 (42)</td>
<td>178 (48)</td>
<td>.13</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>28 (12)</td>
<td>40 (11)</td>
<td>.61</td>
</tr>
<tr>
<td>Alcohol units per day, n (%)</td>
<td>152 (66)</td>
<td>122 (33)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Never</td>
<td>76 (33)</td>
<td>245 (66)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of comorbidities, mean ± SD</td>
<td>2.1 ± 1.2</td>
<td>2.1 ± 1.2</td>
<td>.65</td>
</tr>
<tr>
<td>Number of medications, mean ± SD</td>
<td>5.9 ± 2.9</td>
<td>6.5 ± 3.5</td>
<td>.03</td>
</tr>
<tr>
<td>Number of fall–risk increasing drugs, mean ± SD</td>
<td>2.5 ± 1.5</td>
<td>2.7 ± 1.6</td>
<td>.38</td>
</tr>
</tbody>
</table>

SD = standard deviation.

Regression models of physical performance according to log-transformed serum 25(OH)D concentration were constructed (Table 2). In men, in the fully adjusted model, higher serum 25(OH)D concentrations were significantly associated with better handgrip strength (B = 3.86, 95% CI = 2.04–5.69), faster TUG times (B = −2.82, 95% CI = −4.91 to −0.73), and faster FTSS times (B = −3.39, 95% CI = −5.67 to −1.11). In women, higher serum 25(OH)D concentrations were significantly associated with faster TUG times (B = −2.68, 95% CI = −4.87 to −0.49).

A general linear model was used to compare the means of handgrip strength, TUG, and FTSS (Figure 1 A–C) according to sex and vitamin D group. In men, handgrip strength ranged from 30.3 kg (in participants with serum 25(OH)D levels <25 nmol/L) to 36.0 kg (in participants with 25(OH)D levels >75 nmol/L) (21.0 and 21.6 kg, respectively, for women). Results for the TUG Test ranged from 12.1 seconds (serum 25(OH)D <25 nmol/L) to 9.9 seconds (serum 25(OH)D >75 nmol/L) in men; results in women were 18.8 seconds and 12.0 seconds, respectively. Results for the FTSS Test ranged from 20.0 seconds (serum 25(OH)D <25 nmol/L) to 14.6 seconds (serum 25(OH)D >75 nmol/L) in men; results in women were: 23.3 seconds and 17.9 seconds, respectively. The percentage of completed tandem stands according to vitamin D group was 68%, 59%, 64%, and 86%, respectively, in men (P = .009) and 44%, 61%, 66%, and 63%, respectively, in women (P = .15).

Table 2. Results of Regression Analysis of Strength and Physical Performance According to Log-Transformed Serum Vitamin D Concentration and Sex

<table>
<thead>
<tr>
<th>Test</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Handgrip strength (n = 229)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men (n = 230)</td>
<td>4.02 (2.30–5.75) b</td>
<td>3.86 (2.04–5.69) b</td>
</tr>
<tr>
<td>Timed Up and Go (n = 211)</td>
<td>–3.02 (−5.03 to −1.02) b</td>
<td>–2.82 (−4.91 to −0.73) b</td>
</tr>
<tr>
<td>Five Time Sit to Stand (n = 197)</td>
<td>–3.11 (−5.27 to −1.94) b</td>
<td>–3.39 (−5.67 to −1.11) b</td>
</tr>
<tr>
<td>Tandem stand (n = 230)</td>
<td>0.59 (1.05–3.11) b</td>
<td>0.55 (0.93–3.19) b</td>
</tr>
<tr>
<td>Women (n = 370)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handgrip strength (n = 365)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men (n = 370)</td>
<td>0.80 (−0.13–1.72) b</td>
<td>0.67 (−0.26–1.61) b</td>
</tr>
<tr>
<td>Timed Up and Go (n = 334)</td>
<td>–3.19 (−5.34 to −1.04) b</td>
<td>−2.68 (−4.87 to −0.49) b</td>
</tr>
<tr>
<td>Five Time Sit to Stand (n = 308)</td>
<td>–2.69 (−4.90 to −0.49) b</td>
<td>−2.13 (−4.30 to −0.04) b</td>
</tr>
<tr>
<td>Tandem stand (n = 366)</td>
<td>0.15 (0.77–1.76) b</td>
<td>0.04 (0.68–1.59) b</td>
</tr>
</tbody>
</table>

Model 1: adjusted for age. Model 2: adjusted for age, number of comorbidities, smoking, degree of urbanization, body mass index, and Mini-Mental State Examination score. P < .05, b.01, a.001.

DISCUSSION

Serum 25(OH)D levels were significantly associated with physical performance in older fallers who visited a hospital ED after a fall. The population consisted of older men and women with a mean age of 76, many of whom were vitamin D deficient; an average of 44% had 25(OH)D levels less than 50 nmol/L, making it a good population in which to investigate the relationship between vitamin D and physical performance.

In men, an association was found between serum 25(OH)D levels and handgrip strength, TUG time, and FTSS time. In women, there was an association only between serum 25(OH)D level and TUG time.

Various studies have demonstrated a relationship between vitamin D and physical performance. Although most of these studies were conducted in female-only populations, some studies that included men and women reported similar results. In addition, a 3-year follow-up study reported poorer physical performance and a greater decline in physical performance in older vitamin D–deficient men and women, but recent studies investigating men specifically have not found an association between vitamin D levels and physical performance. Lack of an association in the previously mentioned studies may be because of the target population (young, healthy
men) and the low prevalence of vitamin D deficiency. In the current study, older persons were included who visited the hospital after a fall, which can be a sign of possible neuromuscular dysfunction. Variations in baseline functional status and vitamin D status are thought to be important in explaining conflicting results in studies that examine the association between vitamin D and muscle function.22

The different results found for men and women, especially in the FTSS, are not easily explained. It is unclear whether vitamin D deficiency affects men and women differently. There is some evidence, mostly from ex vivo and in vitro studies, that this is the case.23 Sex hormones are known to modulate the vitamin D endocrine system and influence calcium homeostasis. For example, estrogen is known to stimulate vitamin D receptor expression and 1α-hydroxylase activity, and testosterone is reported to stimulate intestinal calcium channel expression.23

The following limitations should be taken into account when interpreting the results of the current study. First, the cross-sectional design of the study limits the ability to infer a causal relationship between serum 25(OH)D levels and physical performance and does not exclude the possibility of reverse causality. Second, serum parathyroid hormone (PTH) levels were not determined. Vitamin D deficiency leads to an increase in serum PTH, which increases bone turnover and bone loss and is related to a decrease in muscle strength.23 Third, the use of a MMSE score of less than 21 as an exclusion criterion could have resulted in the exclusion of the frailest persons. Fourth, information regarding mood or depression was not recorded. Mood disorders might affect vitamin D status and neuromuscular performance. A major strength of this study is the substantial proportion of vitamin D-deficient participants included, which enabled physical performance to be analyzed in vitamin D-deficient and –sufficient men and women.

In addition, it was striking to note how few of the older fallers were prescribed vitamin D supplements, especially the men; although an average of 44% of the men and women were deficient in vitamin D, only 6% of the men and 17% of the women were taking vitamin D supplements. The underprescribing of vitamin D in this age group has been reported,24 but despite evidence that vitamin D supplementation has been shown to increase muscle strength and reduce the risk of falls,25 vitamin D deficiency is common in community-dwelling elderly adults, with a prevalence of 40% to 100% in U.S. and European older men and women.1 Furthermore, although the level for vitamin D sufficiency was set at 50 nmol/L or greater, another opinion is that vitamin D levels should be 75 nmol/L or greater.26 This

![Figure 1. Strength and physical performance according to serum vitamin D group and sex. General linear model analysis of (A) handgrip strength, (B) Timed Up and Go Test, and (C) Five Time Sit to Stand test with mean and standard error. Adjusted for age, number of comorbidities, smoking, degree of urbanization, body mass index, and Mini Mental State Examination score.](https://agsjournals.onlinelibrary.wiley.com/doi/10.1111/jgs.12499)
is interesting to note when considering Figure 1, which indicates that levels closer to 75 nmol/L result in physical performance benefits, especially in men.

In conclusion, higher serum 25(OH)D concentration was associated with better strength and physical performance in older male and female fallers.

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Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

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Author Contributions: Boyé: study design, enrollment of participants, acquisition, analysis and interpretation of data, preparation of manuscript. Oudshoorn: analysis and interpretation of data, preparation of manuscript. Van der Velde: study design, enrollment of participants, analysis and interpretation of data, preparation of manuscript. Van Lieshout, Van Beeck, Patka: study design, interpretation of data, and preparation of manuscript. De Vries, Lips: enrollment of participants, acquisition of data, revision of manuscript. Van der Cammen: study design, enrollment of participants, interpretation of data, revision of manuscript. All authors approved the final version of the manuscript.

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