No relation between vitamin D status and physical performance in the oldest old: results from the Belfrail study

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Abstract

Background: vitamin D deficiency is a well-known cause of bone loss and fractures but its association, especially among the oldest old, with muscle weakness is less obvious.
Objective: to investigate the relationship between 25-hydroxyvitamin D (25-OHD) and muscle performance in persons aged 80 years and older.
Methods: baseline results of the Belfrail study, a prospective, population-based cohort study were used to study balance, grip strength and gait speed in relation to 25-OHD serum levels in 367 subjects.
Results: a sufficient 25-OHD serum level of 30 ng/ml or more was found in 12.8% of the population. The prevalence of vitamin deficiency (20–29 ng/ml), insufficiency (10–19 ng/ml) and severe insufficiency (<10 ng/ml) was 21.5, 33 and 32.7%, respectively. No significant relation between balance, gait speed and grip strength, and serum 25-OHD was detected neither in bivariate analysis nor after adjustment for age, gender, level of education, institutionalisation, smoking status, body mass index, co-morbidity, level of activity, season, CRP, renal function, serum calcium parathyroid hormone levels, vitamin D intake and use of loop or thiazide diuretics.
Conclusion: in this cohort of octogenarians vitamin D deficiency was highly prevalent. We could not confirm the findings of previous studies showing an association between serum 25-OHD and physical performance in elderly.

Keywords: *older people, physical performance, vitamin D*

Introduction

Low 25-hydroxyvitamin D (25-OHD) levels are very common among elderly and are the result of low exposure to the sun, impaired capacity of vitamin D synthesis and/or decreased vitamin D dietary intake [1]. 25-OHD is metabolised in the kidneys to the active metabolite 1,25-dihydroxy-vitamin D ($1,25(OH)_2D$) and mediates its effects via the vitamin D receptor (VDR). Vitamin D is well known for its role in the regulation of calcium homoeostasis and bone metabolism, but VDRs have been identified in over 30 human tissues including skeletal muscle tissue. In skeletal muscles, two different VDRs in the nucleus and cell membrane have been identified [2]. Binding of $1,25(OH)_2D$ on the nuclear VDR leads to the synthesis of new proteins that affect muscle cell contractility, proliferation and differentiation. The non-genomic pathway of $1,25(OH)_2D$ activity in muscle cells acts by binding the cell membrane VDR also impacting on muscle contraction and possibly muscle cell development [3].

Multiple cross-sectional studies in elderly have demonstrated an association between low 25-OHD and global physical performance mainly using balance or gait tests [4–9]. The association between low serum 25-OHD concentration and physical performance in terms of upper and lower muscle strength in older people, however, is less clear [6, 8–10]. In addition, a few prospective studies have shown that low baseline levels of vitamin D are associated with an increased risk of a decline in physical performance [6, 11–13].

Several meta-analyses have convincingly shown that adequate vitamin D supplementation decreases the risk of falls in older people [14–16]. Studies examining the effects of vitamin D supplementation on physical performance, though, showed controversial results [3, 17]

The very old (>80 years) tend to be under-represented in epidemiological and clinical studies in general and also in the studies investigating the relationship between vitamin D and physical performance specifically. Yet, the relevance of this association for the oldest old in particular is obvious, since the decline of physical performance is a major problem in this population while vitamin D supplementation is an easy, rather inexpensive and well-accepted intervention.

Therefore, the objective of this cross-sectional study is to investigate the relationship between 25-OHD serum level and muscle performance using both measures of global physical performance and muscle strength among persons aged 80 years and older.

Methods

The BF_{C80+} is a prospective, observational, population-based cohort study of Caucasian subjects aged 80 years and older in three well-circumscribed areas in Belgium. The study has been described in detail elsewhere [18]. Briefly, between 2 November 2008 and 15 September 2009, 567 subjects were included by general practitioners (GPs) in three Belgian areas (Wallonia, Brussels and Flanders). Only three exclusion criteria were used: dementia, palliative situation and medical urgency. The study protocol was approved by the Biomedical Ethics Committee of the Medical School of the Université Catholique de Louvain (UCL) of Brussels, Belgium. We present the results of a first cross-sectional data collection.

Functional measures

Physical performance was assessed by means of static balance, gait speed and grip strength. Static balance was assessed by means of the tandem stance test for which the respondent was asked to put the heel of one foot in front of the other and to stand still as long as possible. The test score was dichotomised into a score equal or above and under 10 s. For the walking test, respondents were asked to walk 3 m, turn around, and walk back the 3 m as quickly as possible. Those who could not complete the task were assigned a score of 0. Grip strength was measured in the dominant hand using a JAMAR® Plus digital handheld dynamometer. Three attempts at maximal squeeze were recorded, and the best of the three measurements was used. The test scores were converted into gender-adjusted quartiles and the quartiles were again dichotomised into a score above or in the lowest quartile.

A research assistant questioned about physical activity using the LASA Physical Activity Questionnaire (LAPAQ). The LAPAQ is a face-to-face questionnaire that covers the frequency and duration of walking outside, bicycling, gardening, light household activities, heavy household activities and a maximum of two sport activities during the previous 2 weeks. The LAPAQ test results were converted into gender-adjusted quartiles and these scores were again dichotomised into a score above the lowest quartile and a score in the lowest quartile

Laboratory analyses

The UniCel® DxC 800 Synchron (Beckman-Coulter, Brea, USA) was used to quantify high sensitivity CRP (hCRP) creatinine (IDMS), calcium, and parathyroid hormone (PTH). The 25-OH-vitamin D was measured on the LIAISON® (Diasorin, Saluggia, Italy).

Renal function

The abbreviated modification of diet in renal disease equation was used to estimate the glomerular filtration rate (eGFR): eGFR $(ml/min/1.73\ m^2) = \mathbf{175} \times (S_{cr})^{-1.154} \times (age)^{-0.203} \times (0.742\ \text{if female}) \times (1.212\ \text{if black})$.

Other covariates

Participants were questioned about the level of education and type of living (institutionalised or not) and smoking habits by the GP.

Non-cardiovascular morbidities were defined as a positive response from the GP as to the presence of thyroid problems, anaemia, asthma, COPD, Parkinson's disease, arthritis, osteoarthritis, documented osteoporosis, malignancies and renal insufficiency. Cardiovascular morbidities were defined as a positive response as to the presence of hypertension, diabetes mellitus, hyperlipidaemia, a history of angina pectoris or myocardial infarction, known cardiomyopathy, a history of TIA or CVA, peripheral arterial disease, a history of decompensated heart failure, atrial fibrillation, valvular disease or a history of oedema of the lower extremities. The GP was also asked to report about current vitamin D supplementation and the use of loop and/or thiaide diuretics. The BMI was measured by the clinical research assistant.

Statistical analysis

The baseline characteristics were first compared according to the vitamin D status. Participants were classified based on their 25-OH-vitamin D values using previously published cut-offs: <10 ng/l (=deficiency), 10–19 ng/l (=insufficiency), 20–29 ng/l (=hypo-vitaminosis) and >30 ng/l (=normal).

The continuous variables were compared using ANOVA for variables with a normal distribution and the Kruskal–Wallis test for variables with a skewed distribution. The Chi-square test was used for categorical variables. hCRP serum levels were ln-transformed because of highly skewed distribution.

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Binary logistic regression was used to assess the relationship between the dependent variables (inability to maintain 10 s in tandem stand, gait speed and grip strength in the lowest quartile or above) and the independent variable (vitamin D serum concentration).

Age, gender, level of education, institutionalisation, BMI, smoking status, number of chronic diseases, hCRP, serum calcium, GFR, vitamin D supplementation, season of blood collection (either October–March or April–September), use of loop and/or thiazide diuretics and physical activity were assessed as potential confounders because they have been demonstrated in previous studies to be potential confounders of either the exposures or the outcomes [11, 19]. The statistical analyses were performed using Stata 11.

Results

A quantitative vitamin D analysis was available for 367 participants of whom 133 were men and 234 women. Their mean age was 84.7 (SD ± 3.6) years. The study population was comparable with the total BF_{C80+} cohort with respect to gender, age, living situation (institutionalised or not), level of education, mean 25-OHD serum level and vitamin D supplementation.

A 25-OHD serum level of 30 ng/ml or more was found in 12.8% of the population. The prevalence of vitamin deficiency (20–29 ng/ml), insufficiency (10–19 ng/ml) and severe insufficiency (<10 ng/ml) was 21.5, 32.9 and 32.7%, respectively.

The characteristics of the study population according to their vitamin D status are shown in Table 1. No statistically significant associations between gender, mean age, level of education, smoking status, number of co-morbidities, serum levels of hCRP lapaq score and use of loop and/or thiazide diuretics and vitamin D serum status were found. Persons with sufficient levels of vitamin D or with severe insufficiency were significantly more likely to be institutionalised (Chi-square test, $P = 0.043$). Supplementation with vitamin D was significantly related with higher levels of serum 25-OHD (Chi-square test, $P < 0.0001$), whereas blood sampling in the winter season was significantly associated with lower levels of serum 25-OHD (Chi-square test, $P = 0.001$). There was a significant relationship between serum levels of calcium and PTH, and vitamin D status (Kruskal–Wallis test, $P = 0.0001$, $P = 0.0001$). Persons in the lower vitamin D categories tended to have higher serum levels of PTH and lower levels of calcium. The inability to remain 10 s in tandem stand and gait speed and grip strength measures in the lowest quartile were all not related to vitamin D status (Chi-square test, $P = 0.290$, $P = 0.004$ and $P = 0.023$).

Table 2 shows the association between balance, gait speed and grip strength, and 25-OHD serum level in the unadjusted and adjusted models. Neither in the unadjusted analyses (Model 1) nor after adjustment for age, level of education, institutionalisation gender, co-morbidities, body mass index and smoking habits (Model 2) and after adjustment for the previous variables plus serum calcium level, PTH serum concentration, season of blood-sampling vitamin D supplementation and use of loop and/or thiazide diuretics (Model 3), a significant association between balance, gait speed and grip strength, and 25-OHD could be detected.

Significant independent predictors for a gait speed score in the lowest quartile were higher age and lower serum calcium level. A higher number of co-morbidities and

Table 1. Characteristics of the population in function of vitamin D serum level categories

	Total population (n = 367)		Sufficiency (n = 44)		Deficiency (n = 75)		Insufficiency (n = 119)		Severe insufficiency (n = 129)		P-value
Male	37%	136	31%	15	30.40%	24	43.80%	53	36.70%	44	0.22
Age mean (±SD)	84.7(±3.60)		85.0 (±4.04)		84.2 (±3.00)		84.5 (±3.22)		85.2 (±4.08)		0.185
Institutionalised	10.10%	37	14.90%	7	10.10%	8	4.10%	5	14.20%	17	0.043
Primary school only	39.30%	142	40.40%	19	36.70%	29	42.50%	51	37.40%	43	0.816
BMI mean (±SD)	27.4 (±5.07)		25.3 (±4.89)		26.5 (±4.77)		27.8 (±4.91)		28.4 (±5.20)		0.001
Smoking status	33.2	117	34.80%	16	31.60%	25	35.10%	40	31.90%	36	0.938
Number of morbidities (±SD)	4.9 (±2.5)		5.3 (±2.47)		5.0 (±2.54)		4.9 (±2.68)		4.6 (±2.29)		0.457
lnhCRP (±SD)	−1.6 (1.27)		1.6 (±1.18)		1.8 (±1.21)		1.5 (±1.34)		1.5 (±1.25)		0.413
PTH (IQR)	39.6 (33.35)		26.5 (15.1)		29.5 (+22.0)		43.6 (33.5)		50.4 (38.5)		0.0001
Calcium (IQR)	9.1 (0.57)		9.5 (0.55)		9.2 (0.47)		9.0 (0.43)		9.1 (0.49)		0.0001
GFR (±SD)	62.6 (±22.5)		61.9 (±20.6)		65.2 (±21.1)		57.9 (±21.6)		66.1 (±24.5)		0.0275
Vit D intake	18.90%	69	57.40%	27	31.60%	25	10.80%	13	3.40%	4	<0.0001
Winter season	27.80%	99	6.50%	3	24%	18	28.60%	34	37.90%	44	0.001
Lapacq <p25	29.50%	108	29.80%	14	27.80%	22	23.10%	28	36.90%	44	0.13
Use of loop and/or thiazide diuretics	19.9%	73	17.0%	8	19.0%	15	20.8%	25	20.8%	25	0.937
Handgrip strength <p25	23.20%	81	26.20%	11	23.70%	18	18.90%	22	26.10%	30	0.588
Walking speed <p25	24.60%	86	21.40%	9	28.90%	22	28.40%	33	19.10%	22	0.286
Tandem stance test <10 s	28.9%	101	35.7%	15	22.4%	17	26.7%	31	33.0%	38	0.290

Table 2. Associations between serum 25-OHD concentration and physical performance

Outcome	Odds ratio (95% confidence interval)		
	Unadjusted	Model 1[a]	Model 2[b]
Gait speed in lowest quartile	1.01 (0.99–1.04)	1.02 (1.00–1.05)	1.02 (0.99–1.05)
Grip strength in lowest quartile	1.01 (0.98–1.03)	1.00 (0.98–1.03)	1.02 (0.99–1.06)
Tandem stance test <10 s	1.00 (0.98–1.02)	1.01 (0.98–1.03)	1.00 (0.97–1.03)

[a]Adjusted for age, level of education, institutionalisation gender, co-morbidities, body mass index and smoking habits.
[b]Adjusted for age, level of education, institutionalisation gender, co-morbidities, body mass index and smoking habits, serum calcium level, PTH serum concentration, hCRP serum level, season of blood-sampling, vitamin D supplementation, GFR, physical activity and use of loop and/or thiazide diuretics.

higher age were independently associated with a grip strength in the lowest quartile.

Discussion

This cross-sectional study shows that among the oldest old in Belgium low 25-OHD serum levels are rather the rule than the exception. Eighty-eight and 66% of the population had vitamin D levels <30 and 20 ng/ml, respectively. This study could not demonstrate any association between impaired physical performance and low 25-OHD serum levels.

Previous cross-sectional studies investigating the relation between gait speed or static balance and vitamin D status in older persons have consistently demonstrated a significant positive association between these two parameters [5–8].

In contrast, cross-sectional associations between grip strength and vitamin D status have been contradicting. In two large studies among populations of community-dwelling older adults with a mean age of 74.8 and 77.7 years, respectively, persons with lower levels of vitamin D were significantly more likely to have an impaired grip strength [8, 9]. These findings could, however, not be confirmed in a population of community-dwelling women with a mean age of 80.1 years [10].

It has been shown that the expression of the VDR in human muscle tissue decreases with age [20]. Decreased VDR expression might reduce the functional response of the muscle cells to 1,25(OH)$_2$D. Alternatively, decreased vitamin D levels, as frequently found in older persons may lead to decreased expression of the VDR because of a decrease in stimulation and thus down-regulation of the receptor. The latter hypothesis implies the importance of maintaining a good vitamin D status at younger ages in order to avoid down-regulation of the VDR in muscle tissue and hence

muscle loss. It has also been suggested that restoring the vitamin D levels might increase VDR expression in muscle tissue even in elderly. This is supported by the fact that some randomised clinical trials but not all showed that supplementation with vitamin D or 1a-hydroxylated metabolites can improve muscle function of elderly subjects [3].

The population in the current study is considerably older compared with any population of older populations previously investigated with respect to the relation between vitamin D status and physical performance. The lack of an association between 25-OHD serum level and physical performance might be the result of an age-related decreased expression of the VDR in muscle tissue. Furthermore, VDR polymorphisms may also result in variable susceptibility to age-related decreased muscle performance.

It is possible that part of the divergence of the findings with respect to vitamin D-related physical performance in elderly is the result of 25-OHD being an inadequate proxy measure for the active form of vitamin D (i.e. 1,25-OHD). In a study by Dukas *et al*. [21] among community-dwelling older persons the time for a patient to rise from sitting from a standard arm chair, walk 3 m, turn, walk back to the chair and sit down was significantly associated with serum 1,25-OHD but not with serum 25-OHD levels.

Researchers have not identified yet the circulating 25-OHD concentrations needed to ensure optimal muscle functioning in elder people and use different threshold to define 25-OHD deficiency ranging between 10 and 30 ng/ml. Because of this large range of cut-off values and since vitamin D deficiency causes hyperparathyroidism, it has been hypothesised that elevated PTH levels may be a more accurate marker of a deficient 25-OHD status. In the current study, however, no association was detected between PTH levels and gait speed or grip strength.

This study has several strengths. First, a population-based sample designed to be representative of community-dwelling adults aged 80 and older in Belgium was used. Secondly, validated and standardised measures of physical performance were used. Moreover, the same tests have been used in previous studies of this topic, which made direct comparisons possible. A few limitations must also be considered. First, this was a cross-sectional study, so caution must be exercised when making causal inferences or the lack of it from its results. Secondly, many factors potentially associated with the vitamin D status were considered. However, confounding remains possible, including the possibility that some subjects were taking vitamin D supplements purchased over the counter.

In conclusion, vitamin D deficiency is very common among Belgian persons aged 80 years and older. In contrast to some previous studies in younger populations of old persons no association could be established between physical performance and 25-OHD serum levels. This might be at least partly the consequence of an age-related

down-regulation of the VDR in muscle tissue. Further research is needed to investigate whether vitamin D supplementation can improve physical performance in the oldest old.

Key points

- Vitamin D deficiency is very common in the oldest old.
- No relation between serum vitamin D level and gait speed in the oldest old.
- No relation between serum vitamin D level and grip strength in the oldest old.

Conflicts of interest

None declared.

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