Osteoporos Int
DOI 10.1007/s00198-012-2124-5

ORIGINAL ARTICLE

Vitamin D status is associated with physical performance: the results of three independent cohorts

E. Sohl · R. T. de Jongh · A. C. Heijboer · K. M. A. Swart · E. M. Brouwer-Brolsma · A. W. Enneman · C. P. G. M. de Groot · N. van der Velde · R. A. M. Dhonukshe-Rutten · P. Lips · N. M. van Schoor

Received: 20 July 2012 / Accepted: 9 August 2012

Abstract
Summary This study, on the association between vitamin D status and physical performance and its decline, shows that vitamin D status is associated with physical performance in several older age groups. However, vitamin D status does not predict a decline in physical performance in individuals aged 55–65 years.
Introduction Previous research in the Longitudinal Aging Study Amsterdam (LASA) showed an association of vitamin D status with physical performance and its decline in persons aged 65 years and older. The current study aims to determine these associations in younger individuals and to replicate previous research of LASA.
Methods Data from three independent cohorts were used: two cohorts of LASA (LASA-II with measurements in 2002 (n=707) and 2009 (n=491), LASA-I-2009 (n=355)) and the baseline measurement of the B-Vitamins for the Prevention of Osteoporotic Fractures (B-PROOF) study (n=2,813). Participants performed three tests (walking test, chair stands, and tandem stand; range total score 0–12), except in LASA-II-2002 (only walking and chair stands tests; range total score 0–8). Multiple linear and logistic regression were used to assess whether vitamin D status was associated with total physical performance and its decline, respectively.
Results The mean age of the participants was 60.0 (SD 3.0), 65.9 (2.9), 78.4 (5.3), and 74.4 (6.8) years for LASA-II-2002, LASA-II-2009, LASA-I-2009, and B-PROOF, respectively. Vitamin D status was not predictive of a clinical decline in total physical performance score in the LASA-II-2002 cohort (aged 55–65 years). After adjustment for confounding, participants with serum 25(OH)D<50 nmol/L scored 0.8 (95 % confidence interval 0.4–1.2), 0.9 (0.3–1.5), 1.5 (0.8–2.3), and 0.6 (0.3–0.9) points lower on total physical performance than participants with serum 25(OH)D≥75 nmol/L.
Conclusion Our study confirmed that serum 25(OH)D is associated with physical performance. However, vitamin D status did not predict a clinical decline in physical performance in individuals aged 55–65 years.

Keywords Decline in physical performance · Older individuals · Physical performance · Vitamin D deficiency

Clinical trial registration number for B-PROOF: Netherlands trial: NTR 1333, ClinicalTrials.gov: NCT00696514.

E. Sohl · K. M. A. Swart · N. M. van Schoor (✉)
Department of Epidemiology and Biostatistics,
EMGO Institute for Health and Care Research,
VU University Medical Center,
Amsterdam, The Netherlands
e-mail: nm.vanschoor@vumc.nl

R. T. de Jongh · P. Lips
Department of Internal Medicine and Endocrinology,
VU University Medical Center,
Amsterdam, The Netherlands

A. C. Heijboer
Department of Clinical Chemistry, VU University Medical Center,
Amsterdam, The Netherlands

E. M. Brouwer-Brolsma · C. P. G. M. de Groot · R. A. M. Dhonukshe-Rutten
Division of Human Nutrition, Wageningen University,
Wageningen, The Netherlands

A. W. Enneman · N. van der Velde
Department of Internal Medicine-Section Geriatric Medicine,
Erasmus MC, University Medical Centre Rotterdam,
Rotterdam, The Netherlands

Introduction

Vitamin D deficiency is highly prevalent in the older population. The prevalence in Western countries ranges from 0 to

Published online: 08 September 2012

90 %, depending on country, age, lifestyle, used definition of deficiency, and method used for vitamin D determination [1, 2]. The classical function of vitamin D is to increase calcium absorption from the gut to stimulate the mineralization of bone. Lately, however, vitamin D has been proposed to play a role in the function of many other tissues, for instance, in muscle tissue, and its function is related to physical performance [3]. Nevertheless, epidemiologic studies addressing the potential relationship between vitamin D status and physical performance in older individuals have shown contradictory results [4–13].

Previous analyses of data from the Longitudinal Aging Study Amsterdam (LASA), an ongoing cohort study in a representative sample of the aging Dutch population, demonstrated an association between serum 25-hydroxyvitamin D (25(OH)D) and physical performance and its decline in 3 years in persons aged 65 years and older [12]. Most other studies which found a positive association, focussed on individuals of 65 years and older as well. Only few studies focussed on the younger old, and in these studies, no association was found [4, 5]. Since a positive association was mainly found in older age groups, potentially, the association is age dependent. The previous LASA study suggests that younger persons may have more skills to compensate for a low vitamin D-induced decline in physical performance and that, therefore, an association may not be found in younger individuals [12]. Accordingly, it is of interest to examine the relationship between vitamin D status and physical performance in younger individuals and to determine whether vitamin D status predicts a decline in physical performance.

This study had two different aims. The first aim was to determine the association between vitamin D status and physical performance and its decline in persons aged 55–65 years. Second, we aimed to replicate previous LASA findings on the cross-sectional association between vitamin D status and physical performance in older individuals in two different cohorts aged 65–98 and 70–98 years, respectively. The cross-sectional analyses were performed in the two independent cohorts of LASA and in the baseline measurement of the B-PROOF (B-Vitamins for the Prevention of Osteoporotic Fractures) study. The longitudinal analyses were performed in the second cohort of LASA.

Methods

Study participants

Data for this study were collected in LASA and the B-PROOF study for the Prevention of Osteoporotic Fractures (B-PROOF), which is a randomized double-blind placebo-controlled trial on the effects of B vitamins on the prevention of osteoporotic fractures. The sampling, data collection procedures, and nonresponse data of LASA are described elsewhere in detail [14, 15]. Briefly, a random age- and sex-stratified sample was drawn from population registers of 11 municipalities in three different regions in the Netherlands. At the start in 1992, 3,107 participants, aged 55–85 years, were interviewed. An additional cohort, which consisted of 1,002 participants (aged 55–65 years), was started in 2002. The study was approved by the Medical Ethics Committee of the VU University Medical Center, and all participants gave informed consent. Figure 1 shows the recruitment and exclusion of participants of the first cohort of LASA (LASA-I). The recruitment and exclusion of participants of the second cohort (LASA-II) is shown in Fig. 2. Both LASA-II-2002 and LASA-II-2009 are based on this second cohort of LASA.

The sampling and data collection details of the B-PROOF study are described elsewhere [16]. Briefly, the participants (aged 65 years and older) were recruited mainly via population registries. Participants were screened for plasma homocysteine and only included if they had homocysteine concentrations ≥12 μmol/L. In total, 2,919 participants were included for baseline measurements and randomization, which started at the end of 2008. All participants gave written informed consent before the start of the study. For the present study, only baseline data were used. Serum 25 (OH)D was measured in 2,879 participants and after exclusion due to missing values for potential confounders or physical performance (n=66), the study sample consisted of 2,813 individuals.

To answer the first research question, i.e., to determine the association between vitamin D status and physical performance and its decline in individuals aged 55–65 years, LASA-II-2002 and the two following measurement cycles were used. LASA-II-2002 consisted of 707 individuals. Three and 6 years later, respectively, 639 and 561 of these 707 participants finished the performance tests. The second question, the replication of the previous study, was answered by using LASA-II-2009 (n=491, not shown in Fig. 2. Vitamin D was not measured in all participants of LASA-II-2009 and therefore, this study sample consisted of less participants than the 6-years follow-up sample), the baseline measurement of B-PROOF (n=2,813) and LASA-I-2009 (n=355).

Physical performance tests

Total physical performance score was calculated by the sum of the scores of three individual tests and ranged from 0 to 12 points. The three performance tests were the following: time taken to walk 3 m, turn 180°, and walk back 3 m as fast as possible (walking test); time taken to rise five times from a chair without using the hands as fast as possible (chair stand test); and the ability to perform the tandem stand for

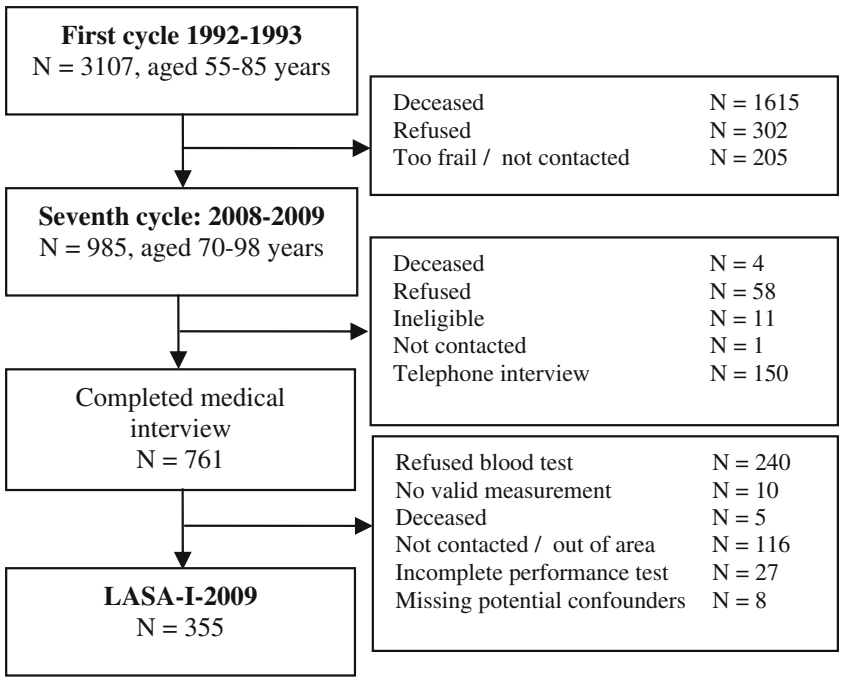

Fig. 1 Recruitment and exclusion of the participants of the first cohort of LASA (LASA-I-2009)

10 s (with one foot behind the other and the heel of the first foot directly touching the toes of the other foot) (tandem stand test). The different study samples were divided into quartiles to score the walking and chair stand tests (1 to 4 points according to quartile number, based on baseline scores of all cohorts separately). The fastest quartile received score 4, and

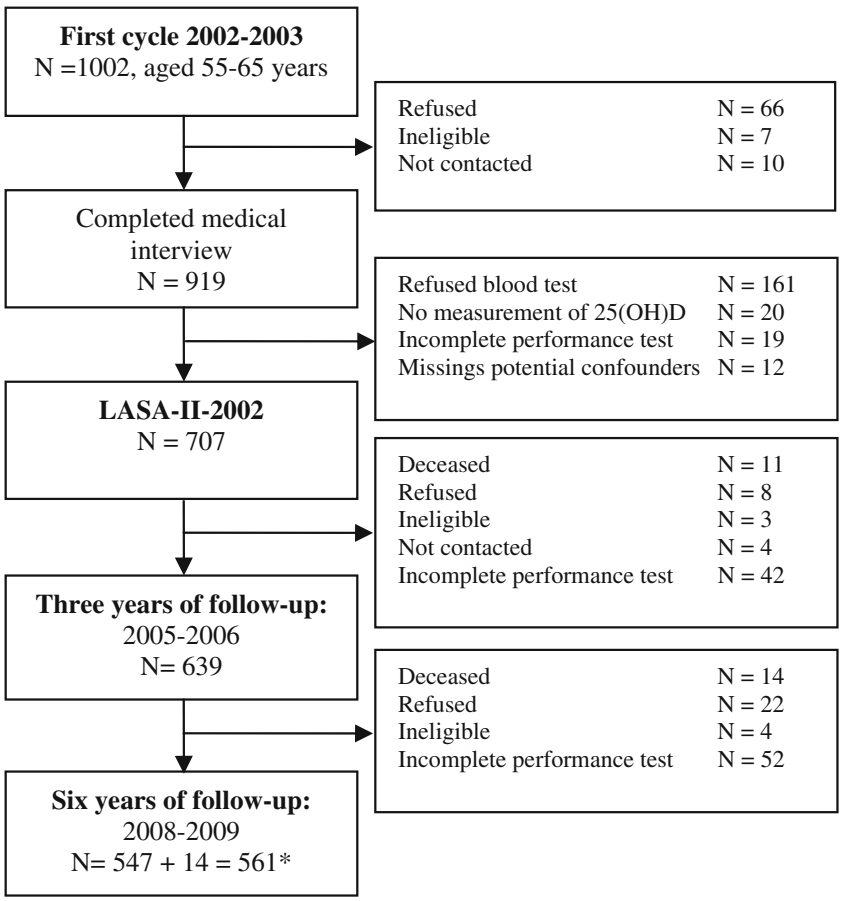

Fig. 2 Recruitment and exclusion of the participants of the second cohort of LASA (LASA-II-2002 and follow-up). *Asterisk* (*): 14 participants, who did not have complete measurements at 3-years follow-up, were included in the 6-years follow-up

the participants who could not finish the test received score 0. The scores for the tandem stand were distributed as follows: unable (score 0), able to hold position for 4–9 s (score 2), and able to hold position for at least 10 s (score 4). Unfortunately, the tandem stand was not assessed in LASA-II-2002. At that time point, we composed a total physical performance score based on two tests, the walking and the chair stand tests, and the maximum score ranged from 0 to 8 points.

Decline in physical performance

The Edwards–Nunnally index (EN index), which accounts for regression to the mean, was used to determine whether a decrease in physical performance score during 3- and-6 years follow-up was a clinically significant decline [17, 18]. Confidence intervals were created and these were used to classify the change as improved, stable, or declined. Afterwards, a dichotomization into decline or no decline was made. The following formula was used for the EN index: $X_2 < \text{or} > ((\alpha \times (X_1 - M) + M \times (\pm 1.96 \times SE)))$, with the following parameters: X_1=the physical performance score at baseline, X_2=score at follow-up, M=mean score of the group at baseline, and $\text{SE} = \left(\text{SD} \times \sqrt{(1-\alpha)}\right)$ [18].

Measurement of serum 25(OH)D

Morning blood samples were drawn in LASA-II-2002. Participants were only allowed to take tea and toast, but no dairy products. In LASA-I-2009 and LASA-II-2009, fasting blood samples were obtained. Participants were not allowed to take any food or drinks except water from midnight. The samples were centrifuged and stored at −20 °C until determination in 2010/2011. Morning blood samples of the B-PROOF participants were drawn; participants were fasting or had a light breakfast. Samples were stored at −80 °C until determination in 2011/2012. Serum 25(OH)D was measured in the LASA-samples by a competitive protein binding assay (DiaSorin, Stillwater, MN, USA). The interassay coefficient of variation was 10 % at the level of 30 nmol/L and 65 nmol/mL. Serum 25(OH)D was measured in the B-PROOF study by isotope dilution–online solid-phase extraction liquid chromatography–tandem mass spectrometry (ID-XLC-MS/MS) [2]. In short, 25(OH)D was released from its binding protein(s) and a deuterated internal standard (25(OH)D_3-d6), was added. Samples were extracted and analyzed by XLC-MS/MS (a Symbiosis online SPE system (Spark Holland, Emmen, the Netherlands) coupled to a Quattro Premier XE tandem mass spectrometer (Waters Corp., Milford, MA, USA)). The interassay coefficient of variation was 9 % at the level of 25 nmol/L and 6 % at the level of 63 nmol/L. All analyses were performed in the Endocrine Laboratory of the VU University Medical Center.

Potential effect modifiers

Potential effect modifiers were age, gender, and physical activity. Vitamin D deficiency is more common in older individuals [1] and physical activity may associate with physical performance [19]. Therefore, vitamin D may have less influence on physical performance in active individuals than in inactive individuals.

Potential confounders

Potential confounders were age, gender, level of education, degree of urbanization, body mass index (BMI), alcohol use, smoking, chronic diseases, physical activity, season of blood collection, and serum creatinine. Data on age and sex were derived from population registries. Education level was converted into years of education, and subsequently divided into three categories: low (≤9 years), intermediate (10–12 years), and high level (>12 years). Degree of urbanization was assessed by the division of Statistics Netherlands, which recodes the postal codes into five categories, based on the number of addresses per square kilometer [20]. BMI was calculated as weight in kilograms divided by height in square meters. Smoking (never, former, and current smoker) and alcohol consumption (none, light, moderate, and (very) excessive drinker) were based on self-report. Classification of alcohol use was based on the number of days per week alcohol was consumed and the number of drinks per time [21]. The number of chronic diseases was obtained by self-report, using questions on seven major diseases: chronic obstructive pulmonary disease, cardiac disease, peripheral arterial disease, diabetes mellitus, stroke, cancer, and rheumatoid arthritis/osteoarthritis. The number of chronic diseases was less extensively assessed in B-PROOF; only kidney disease, cardiac disease, diabetes mellitus, and transient ischemic attack/stroke were available for 1,864 individuals. Physical activity was assessed using the LASA Physical Activity Questionnaire, which is a validated questionnaire about the duration and frequency of activities during the past 2 weeks [22]. Season of blood collection was dichotomized into summer (April–September) and winter (October–March). Creatinine level was measured in LASA using the Jaffe alkaline picrate reaction with a Hitachi 747 analyzer (Roche Diagnostics, the Netherlands) and in B-PROOF using the enzymatic colorimetric Roche CREA plus assay.

Statistical analysis

Serum 25(OH)D was divided into three categories: <50, 50–75, and ≥75 nmol/L, the latter serving as the reference group for all analyses. In the Netherlands, the advised minimum level of serum 25(OH)D for older persons is 50 nmol/L and this is also according to the guidelines of the Institute of Medicine [23]. The level of

75 nmol/L is the required level according to the guidelines of the Endocrine Society [24]. For the cross-sectional analyses, which aimed to determine whether vitamin D status is associated with physical performance, multiple linear regression analyses were used. Assumptions of linear regression analysis were tested by normal probability plots and histograms. To determine whether a decline in physical performance could be predicted by serum 25(OH)D, multiple logistic regression analyses were used. Ordinal logistic regression analyses were used to assess which of the physical performance tests was most strongly associated with vitamin D status. Assumptions of ordinal logistic regression were tested by the test of parallel lines. To succeed this test, the scores 0 and 1 (or scores 0 and 2 in case of the tandem stand) were combined in one group. To test whether the tandem stand was associated with serum 25(OH)D, multiple logistic regression was used. All continuous variables were tested on linearity. Only BMI had a nonlinear relationship with physical performance, and we divided BMI into three categories: low weight (BMI <20 kg/m^2), normal weight (20 kg/m^2≤BMI <25 kg/m^2), overweight (25 kg/m^2≤ BMI <30 kg/m^2), and obese (≥30 kg/m^2). For all cohorts, the potential confounders were added one by one to the univariable model. Parameters, which gave a change in the regression coefficient of more than 10 %, were added to the models. The confounders which were identified in the cross-sectional analyses, were also included in the longitudinal analyses. To test for interaction, age and physical activity were dichotomized around the median, and a P value <0.1 was considered statistically significant. For all other analyses, a P value <0.05 was considered significant. Two sensitivity analyses were performed. First, because information on over-the-counter vitamin D use was not available for all participants, the use of vitamin D supplements was only added to the fully adjusted models for LASA-I-2009 and LASA-II-2009. In B-PROOF, the number of chronic diseases was only added to the fully adjusted models because data were only available for part of the participants. All analyses were performed using SPSS version 15.0.

Finally, we used restricted cubic spline plots to estimate an optimal cutoff point for serum 25(OH)D in the relationship with physical performance. Cubic splines are piecewise polynomial functions that are constrained to join smoothly at points called knots. These spline functions provide better insight into dose–response relationships compared with analyses using categorized variables. Restricted cubic spline functions use all data points to estimate the risk at each level of exposure, as opposed to step functions using categorical variables, which assume a constant risk within categories. Cubic spline functions were tested in regression models at three knots using spline plots and likelihood ratio tests. All spline regression analyses were performed using R version 2.15.0 [25].

Results

The baseline characteristics of the different cohorts are shown in Table 1. A decline in physical performance, defined using the EN index, was observed in 4.1 % of the participants who were included in the 3-year follow-up and in 7.3 % in the 6-year follow-up of the LASA-II-2002.

Table 2 shows the results of multiple linear regression analyses of the association between serum 25 (OH)D and physical performance. In all cohorts, participants with serum 25(OH)D <50 nmol/L had a significantly lower physical performance compared with the reference group, which consisted of participants with serum 25(OH)D ≥75 nmol/L. In LASA-II-2002, serum 25(OH)D between 50 and 75 nmol/L was also associated with a significantly lower physical performance score compared to the highest category, in the fully adjusted model. In B-PROOF, age was a significant effect modifier (aged 65–73.4 years versus >73.4 years). In both subgroups, the lowest vitamin D category (<50 nmol/L) was associated with a lower physical performance score. However, the effect was stronger in the oldest group (−0.8 (95 % confidence interval −1.3, −0.4)) compared to the youngest group (−0.3 (−0.6,−0.0)). Table 2 shows the results for the total group. Figure 3 shows the multivariable cross-sectional relationship between serum 25(OH)D and physical performance in B-PROOF. Up to serum 25(OH)D levels of approximately 65 nmol/L, physical performance score increased with increasing serum 25(OH)D. A similar pattern was observed in the LASA cohorts (data not shown).

Multiple logistic regression analyses of serum 25(OH)D, as a predictor of clinical decline in physical performance over 3- and 6-year periods in LASA-II-2002 and follow-up, did not show significant results (Table 3). The odds ratios (OR) for a decline in physical performance in 3 and 6 years, respectively, were 3.4 (95 % confidence interval 0.7–16.0) and 1.4 (0.5–3.7) in the fully adjusted models for serum 25 (OH)D <50 nmol/L versus serum 25(OH)D ≥75 nmol/L.

The results of ordinal logistic regression showed that vitamin D status is associated with all separate tests (except the tandem stand in LASA-II-2009 and LASA-I-2009) (data not completely shown). Vitamin D was most strongly associated with the walking test. The cumulative ORs were 2.0 (1.2–3.2), 2.9 (1.6–5.1), and 1.2 (1.0–1.5), indicating that participants with serum 25(OH)D<50 nmol/L have 2.0, 2.9, or 1.2 times higher odds for scoring one point lower on the

Table 1 Baseline characteristics of the study samples

	LASA-II-2002	LASA-II-2009	LASA-I-2009	B-PROOF
N	707 (100)	491 (100)	355 (100)	2,813 (100)
Gender				
Men	328 (46.4)	246 (50.1)	158 (44.5)	1,417 (50.4)
Women	379 (53.6)	245 (49.9)	197 (55.5)	1,396 (49.6)
Age (years)	60.0±3.0	65.9±2.9	78.5±5.3	74.4±6.8
Serum 25(OH)D (nmol/L)	56.7±20.3	69.6±21.6	59.3±20.5	55.7±24.6
<50	287 (40.6)	96 (19.2)	129 (36.3)	1,250 (44.4)
50–75	296 (41.9)	199 (40.5)	150 (42.3)	952 (33.8)
≥75	124 (17.5)	196 (39.9)	76 (21.4)	611 (21.7)
Body mass index (kg/m^2)				
<20	12 (1.7)	9 (1.8)	1 (0.3)	44 (1.6)
20–25	205 (29.0)	137 (27.9)	94 (26.5)	781 (27.8)
25–30	333 (47.1)	225 (45.8)	171 (48.2)	1,430 (50.8)
≥30	157 (22.2)	120 (24.4)	89 (25.1)	558 (19.8)
Smoking status				
Never	170 (24.0)	136 (27.7)	120 (33.8)	950 (33.8)
Former	340 (48.1)	268 (54.6)	210 (59.2)	1,589 (56.5)
Current	197 (27.9)	87 (17.7)	25 (7.0)	274 (9.7)
Alcohol consumption				
Nondrinker	57 (8.1)	41 (8.4)	55 (15.5)	375 (13.3)
Light drinker	321 (45.4)	252 (51.3)	210 (59.2)	1,510 (53.7)
Moderate drinker	252 (35.6)	162 (33.0)	79 (22.3)	820 (29.2)
(Very) excessive drinker	77 (10.9)	36 (7.3)	11 (3.1)	108 (3.8)
Number of chronic diseases	1 (0–1)[a]	1 (0–2)[a]	1 (1–2)[a]	0 (0–1)[b]
Physical activity (min/day)	147 (90–226)	152 (101–216)	131 (79–197)	129 (84–193)
Degree of urbanization (no. of addresses/km^2)				
Rural (<500)	121 (17.1)	109 (22.2)	80 (22.5)	136 (4.8)
Low (500–1,000)	224 (31.7)	102 (20.8)	77 (21.7)	447 (15.9)
Moderate (1,000–1,500)	89 (12.6)	82 (16.7)	55 (15.5)	582 (20.7)
High (1,500–2,500)	144 (20.4)	103 (21.0)	84 (23.7)	1,075 (38.2)
Very high (>2,500)	129 (18.2)	95 (19.3)	59 (16.6)	573 (20.4)
Level of education				
Low (≤9 years)	312 (44.1)	189 (38.5)	187 (52.7)	1,490 (53.0)
Moderate (10–12 years)	253 (35.8)	178 (36.3)	113 (31.8)	592 (21.0)
High (>12 years)	142 (20.1)	124 (25.3)	55 (15.5)	731 (26.0)
Season of blood collection				
Winter	623 (88.1)	64 (13.0)	72 (20.3)	1,372 (48.8)
Summer	84 (11.9)	427 (87.0)	283 (79.7)	1,441 (51.2)
Creatinine (μmol/L)	90.5±20.8	80.5±16.6	87.1±27.3	84.0±18.2
Physical performance (0–12)	–	8.6±2.4	7.5±3.1	8.0±3.2
Physical performance (0–8)	4.8±2.1	–	–	–

Values are means ± SD, number (percentage), or median (interquartile range)

[a] Chronic diseases from seven majors: chronic obstructive pulmonary disease, cardiac disease, peripheral arterial disease, stroke, diabetes mellitus, rheumatoid arthritis/osteoarthritis, and cancer

[b] Chronic disease from four diseases: kidney disease, diabetes mellitus, cardiac disease, and transient ischemic attack/stroke, *N*=1,864

walking test than participants of the highest serum 25(OH)D category. None of the results changed materially in the sensitivity analyses, after adding vitamin D use in LASA and chronic diseases in B-PROOF (data not shown).

Table 2 Results of multiple linear regression analyses of serum 25(OH)D as a predictor of physical performance

Serum 25(OH)D category	LASA-II-2002[a]		LASA-II-2009[b]		LASA-I-2009[b]		B-PROOF[b]	
	Aged 55–65 years		Aged 60–71 years		Aged 70–98 years		Aged 65–98 years	
	N=707		*N*=491		*N*=355		*N*=2,813	
	Model 1[c]	Model 2[d]	Model 1[c]	Model 2[d]	Model 1[c]	Model 2[d]	Model 1[c]	Model 2[e]
<50 nmol/L	−0.9 (−1.3, −0.5)***	−0.8 (−1.2, −0.4)***	−1.2 (−1.8, −0.6)***	−0.9 (−1.5, −0.3)**	−1.8 (−2.6, −1.0)***	−1.5 (−2.3, −0.8)***	−0.7 (−1.0, −0.4)***	−0.6 (−0.9, −0.3)***
50–75 nmol/L	−0.5 (−0.9, 0.0)*	−0.5 (−0.9, −0.1)*	−0.4 (−0.8, 0.1)	−0.3 (−0.7, 0.2)	−0.4 (−1.2, 0.3)	−0.4 (−1.0, 0.3)	−0.2 (−0.5, 0.1)	−0.2 (−0.4, 0.1)
≥75 nmol/L[f]	0	0	0	0	0	0	0	0

Difference in physical performance score of different vitamin D categories as compared to the reference group. Data are expressed as B (95 % confidence intervals)

[a] Maximum total physical performance score: 8 points

[b] Maximum total physical performance score: 12 points

[c] Adjusted for age and gender

[d] Adjusted for age, gender, BMI, chronic diseases, degree of urbanization, and level of education

[e] Adjusted for age, gender, BMI, degree of urbanization, and level of education

[f] Reference group

*** $P<0.001$; ** $P<0.01$; * $P<0.05$

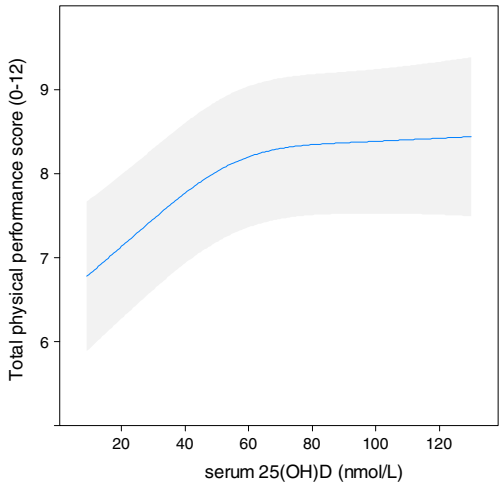

Fig. 3 Physical performance in 2,813 individuals of B-PROOF in relation to serum 25(OH)D. Adjusted for age, gender, BMI, degree of urbanization, and level of education

Discussion

This study showed that serum 25(OH)D <50 nmol/L was strongly associated with lower physical performance in individuals aged 55–65 years. However, vitamin D status did not significantly predict a decline in physical performance in this age group in contrast with previous findings in an older cohort aged 65 years and older [12]. In addition, it confirmed that vitamin D status was associated with physical performance in older (aged 65 years and older) and very old (aged 70–98 years) population and that the physical performance score increased with increasing serum 25 (OH)D until levels of 65 nmol/L. Furthermore, vitamin D status was positively associated with all three performance tests, i.e., the walking test, chair stands, and tandem stand, but it was most strongly associated with the walking test.

The first aim of the current study was to evaluate the association between vitamin D status and physical performance and its decline in individuals aged 55–65 years. The authors of the previous LASA study stated that their results might also apply to younger individuals [12]. In the current study, it was shown that vitamin D status was indeed also associated with physical performance, cross-sectionally, in younger persons aged 55–65 years. In addition, the previous study within LASA showed that vitamin D status predicted a decline in physical performance over 3 years in individuals aged 65 years and older [12]. This is in line with one study on the Rancho Bernardo cohort, which found that low serum 25(OH)D independently predicted a decline in two individual performance tests in older women (mean age 74.7 years) [26]. Other studies, however, were not able to demonstrate a significant association between vitamin D status and a decline in physical performance in older persons [8, 11, 27, 28]. To the best of our knowledge,

Table 3 Results of logistic regression analyses: odds ratios for decline in physical performance after 3- and 6-years follow-up (LASA-II-2002 and follow-up)

Serum 25(OH)D category	3-years follow-up		6-years follow-up	
	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
<50 nmol/L	3.3 (0.7–14.8)	3.4 (0.7–16.0)	1.4 (0.5–3.8)	1.4 (0.5–3.7)
50–75 nmol/L	1.8 (0.4–8.7)	2.1 (0.4–10.2)	1.3 (0.5–3.4)	1.3 (0.5–3.6)
≥75 nmol/L[c]	1.0	1.0	1.0	1.0

Data are expressed as odds ratios (95 % CI)

[a] Adjusted for age and gender

[b] Adjusted for age, gender, BMI, chronic diseases, degree of urbanization, and level of education

[c] Reference group

the present study is the first study which examined the predictive value of vitamin D status in individuals younger than 65 years. Our study confirmed the hypothesis [12] that vitamin D status does not predict a decline in physical performance in younger individuals. However, the physical performance score was calculated by summing up the scores of only two tests, and the maximum physical performance score was 8 instead of 12 points. A lower maximal score, without balance data measured by the tandem stand, may be less sensitive to score a decline in the total score and only 4.1 % and 7.3 % of the participants were classified as declining. In addition, there was a substantial increase in mean serum 25(OH)D (57 nmol/L in 2002 versus 70 nmol/L in 2009. These values cannot be compared directly because of different assays being used). Also, there was an increase in the proportion of participants of whom blood was taken in the summer. Therefore, it is possible that the observed low proportion of participants with a decline in physical performance is related to the fact that they were tested at a time when vitamin D status had generally improved.

The information on the predictive value of vitamin D status is of interest because it is known that physical performance predicts mortality, nursing home admission, and fractures [29–32]. Therefore, potential prevention programs supplementing vitamin D to prevent a decline in physical performance may be considered. Based on the results of the current and previous studies [12, 26], prevention strategies should be aimed at individuals of 65 years and older. There is much evidence for a role of vitamin D in muscle health [33]. However, the effect of prevention strategies is still questionable because the results of several trials on the effect of vitamin D supplements on physical performance are contradicting and two systematic reviews on this topic were not conclusive [34, 35]. Since these first systematic reviews, the number of studies on this topic has increased and a recent meta-analysis showed a beneficial effect of vitamin D supplementation on balance and muscle strength, but not on gait [36]. This discrepancy may be explained by the fact that the studies that evaluated gait were of lower quality and used lower doses of vitamin D than studies on muscle strength and balance [36]. Therefore, further studies with, for example, higher doses, are necessary to draw a definite conclusion regarding the effect of vitamin D supplements in preventing a decline in physical performance. However, future trials should proceed with caution because a high annual dose of vitamin D has been shown to increase the risk of falls and fractures in older women [37].

The second aim of our study was to replicate previous results of LASA, in which a significant relationship between vitamin D status and physical performance in individuals of 65 years and older was observed [12] and we confirmed these findings. The results of LASA-II-2009 (aged 62–72 years) and B-PROOF (aged 65 years and older) showed that a lower vitamin D status was associated with lower physical performance. This is largely in line with the literature, since up till now most studies have observed a significant relationship between vitamin D status and physical performance [6–9, 13]. However, this was not the case for all studies [4, 5, 11]. These contradictory results may be partly explained by the differences in used tests and in sample characteristics. For instance, the studies with negative results included participants with a wide age range (30–79 years [5] and 24–77 years [4]), or were Moroccan [4], or only disabled women [11]. In addition to this age group, the results of LASA-I-2009 demonstrated a similar relationship for older individuals aged 70–98 years.

The differences in physical performance score between participants with serum 25(OH)D <50 nmol/L and with serum 25(OH)D ≥75 nmol/L were 0.8, 0.9, 1.5, and 0.6 points, respectively, in LASA-II-2002, LASA-II-2009, LASA-I-2009, and B-PROOF. Studies on determining the meaningful change in physical performance measures stated that the smallest meaningful change is approximately 0.5 points on a 12-point scale and 1 point indicates substantial change [38, 39]. Although this meaningful change is based on an individual change over time, and not on differences between groups, this could be used as an example of the clinical relevance of our findings. Therefore, we may conclude that the observed differences in our study are of clinical interest.

The current study has several limitations and strengths. The main limitation is that the relationships might be underestimated because the cohorts were relative healthy, partly because in LASA, most participants had to visit the hospital for blood collection. Furthermore, in LASA-II-2002, we were not able to compute the physical performance score based on three tests because the tandem test was not assessed in LASA-II-2002. However, the results of the logistic regression analysis showed that vitamin D status was not significantly associated with the tandem test in LASA-II-2009, and therefore, this should not be considered as a major problem. In addition, the results of the different cohorts cannot be compared directly because of different assays used for the determination of serum 25(OH)D. Finally, we had no information on the use of vitamin D supplements and diet of all participants at all measurement cycles. However, sensitivity analyses in LASA-I-2009 and LASA-II-2009 showed no difference in results after adding the use of vitamin D supplements to the models. The main strengths of the current study are the large independent study samples and the several age groups that were analyzed. In addition, the study consists of two population-based samples and has a prospective design. Moreover, the EN index, which accounted for regression to the mean, was used to test for a decline in physical performance rather than raw scores.

In conclusion, serum 25(OH)D lower than 50 nmol/L is associated with lower physical performance both in persons aged 55–65 years and in older age groups. A decline in physical performance could not be predicted by vitamin D status in individuals aged 55–65 years in contrast to previous findings in individuals aged 65 years and older. Therefore, prevention strategies, such as vitamin D supplementation, may be considered in individuals above the age of 65 years.

Acknowledgments This study was partly funded by ZonMw (the Netherlands Organization for Health Research and Development). LASA is largely supported by a grant from the Netherlands Ministry of Health, Welfare, and Sports, Directorate of Long-Term Care. The B-PROOF study is funded by ZonMw, NZO (Dutch Dairy Association), Orthica, NCHA (Netherlands Consortium Healthy Ageing), and Ministry of Economic Affairs, Agriculture, and Innovation. The serum 25(OH)D measurements in LASA were partly funded by Merck & Co. We would like to thank the research team and participants of LASA and B-PROOF.

Conflicts of interest An unconditional grant was received from Merck & Co. for part of the 25-hydroxyvitamin D measurements. All authors have nothing to disclose.

References

1. Lips P (2001) Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev 22:477–501
2. Heijboer AC, Blankenstein MA, Kema IP, Buijs MM (2012) Accuracy of 6 routine 25-hydroxyvitamin D assays: influence of vitamin D binding protein concentration. Clin Chem 58:543–548
3. Bischoff-Ferrari H (2010) Health effects of vitamin D. Dermatol Ther 23:23–30
4. Allali F, El Aichaoui S, Khazani H, Benyahia B, Saoud B, El Kabbaj S, Bahiri R, Abouqal R, Hajjaj-Hassouni N (2009) High prevalence of hypovitaminosis D in Morocco: relationship to lifestyle, physical performance, bone markers, and bone mineral density. Semin Arthritis Rheum 38:444–451
5. Ceglia L, Chiu GR, Harris SS, Araujo AB (2011) Serum 25-hydroxyvitamin D concentration and physical function in adult men. Clin Endocrinol (Oxf) 74:370–376
6. Dhesi JK, Bearne LM, Moniz C, Hurley MV, Jackson SHD, Swift CG, Allain TJ (2002) Neuromuscular and psychomotor function in elderly subjects who fall and the relationship with vitamin D status. J Bone Miner Res 17:891–897
7. Gerdhem P, Ringsberg KAM, Obrant KJ, Akesson K (2005) 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 16:1425–1431
8. Houston DK, Tooze JA, Hausman DB, Johnson MA, Nicklas BJ, Miller ME, Neiberg RH, Marsh AP, Newman AB, Blair SN, Kritchevsky SB (2011) Change in 25-hydroxyvitamin D and physical performance in older adults. J Gerontol A Biol Sci Med Sci 66:430–436
9. Kenny AM, Biskup B, Robbins B, Marcella G, Burleson JA (2003) Effects of vitamin D supplementation on strength, physical function, and health perception in older, community-dwelling men. J Am Geriatr Soc 51:1762–1767
10. Scott D, Blizzard L, Fell J, Ding C, Winzenberg T, Jones G (2010) A prospective study of the associations between 25-hydroxyvitamin D, sarcopenia progression and physical activity in older adults. Clin Endocrinol (Oxf) 73:581–587
11. Verreault R, Semba RD, Volpato S, Ferrucci L, Fried LP, Guralnik JM (2002) Low serum vitamin d does not predict new disability or loss of muscle strength in older women. J Am Geriatr Soc 50:912–917
12. Wicherts IS, van Schoor NM, Boeke AJ, Visser M, Deeg DJH, Smit J, Knol DL, Lips P (2007) Vitamin D status predicts physical performance and its decline in older persons. J Clin Endocrinol Metab 92:2058–2065
13. Zamboni M, Zoico E, Tosoni P, Zivelonghi A, Bortolani A, Maggi S, Di Francesco V, Bosello O (2002) Relation between vitamin D, physical performance, and disability in elderly persons. J Gerontol A Biol Sci Med Sci 57:M7–M11
14. Deeg DJH, van Tilburg T, Smit JH, de Leeuw ED (2002) Attrition in the longitudinal aging study Amsterdam. The effect of differential inclusion in side studies. J Clin Epidemiol 55:319–328
15. Huisman M, Poppelaars J, van der Horst M, Beekman ATF, Brug J, van Tilburg TG, Deeg DJH (2011) Cohort profile: the longitudinal aging study Amsterdam. Int J Epidemiol 40:868–876
16. van Wijngaarden J, Dhonukshe-Rutten R, van Schoor N, van der Velde N, Swart K, Enneman A, van Dijk S, Brouwer-Brolsma E, Zillikens M, van Meurs J, Brug J, Uitterlinden A, Lips P, de Groot L (2011) Rationale and design of the B-PROOF study, a randomized controlled trial on the effect of supplemental intake of vitamin B12 and folic acid on fracture incidence. BMC Geriatr 11:80
17. Speer DC (1992) Clinically significant change: Jacobson and Truax (1991) revisited. J Consult Clin Psychol 60:402–408
18. Speer DC, Greenbaum PE (1995) Five methods for computing significant individual client change and improvement rates: support for an individual growth curve approach. J Consult Clin Psychol 63:1044–1048
19. Visser M, Pluijm SMF, Stel VS, Bosscher RJ, Deeg DJH (2002) Physical activity as a determinant of change in mobility performance: the longitudinal aging study Amsterdam. J Am Geriatr Soc 50:1774–1781
20. Den Dulk CJ, Van De Stadt H, Vliegen JM (1992) Een nieuwe maatstaaf voor stedelijkheid: de omgevingsadressendichtheid (A new measure for degree of urbanization: the address density of the surrounding area). Maandstat Bevolking 40:14–27

21. Garretsen HFL (1983) Probleemdrinken, prevalentiebepaling, beinvloedende factoren en preventiemogelijkheden, Theoretische overwegingen en onderzoek in Rotterdam (dissertation in Dutch).
22. Stel VS, Smit JH, Pluijm SMF, Visser M, Deeg DJH, Lips P (2004) Comparison of the LASA physical activity questionnaire with a 7-day diary and pedometer. J Clin Epidemiol 57:252–258
23. IOM (Institute of Medicine) (2011) Dietary reference intakes for calcium and vitamin D. The National Academies Press, Washington
24. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM (2011) Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 96:1911–1930
25. Steenland K, Deddens JA (2004) A practical guide to dose–response analyses and risk assessment in occupational epidemiology. Epidemiology 15:63–70
26. Dam T-TL, von Muhlen D, Barrett-Connor EL (2009) Sex-specific association of serum vitamin D levels with physical function in older adults. Osteoporos Int 20:751–760
27. Bartali B, Frongillo EA, Guralnik JM, Stipanuk MH, Allore HG, Cherubini A, Bandinelli S, Ferrucci L, Gill TM (2008) Serum micronutrient concentrations and decline in physical function among older persons. JAMA 299:308–315
28. Faulkner KA, Cauley JA, Zmuda JM, Landsittel DP, Newman AB, Studenski SA, Redfern MS, Ensrud KE, Fink HA, Lane NE, Nevitt MC (2006) Higher 1,25-dihydroxyvitamin D3 concentrations associated with lower fall rates in older community-dwelling women. Osteoporos Int 17:1318–1328
29. Cawthon PM, Fullman RL, Marshall L, Mackey DC, Fink HA, Cauley JA, Cummings SR, Orwoll ES, Ensrud KE (2008) Physical performance and risk of hip fractures in older men. J Bone Miner Res 23:1037–1044
30. Corsonello A, Lattanzio F, Pedone C, Garasto S, Laino I, Bustacchini S, Pranno L, Mazzei B, Passarino G, Incalzi, On behalf of the PharmacosurVeillance in the elderly Care (PVC) Study (2012) Prognostic significance of the short physical performance battery in older patients discharged from acute care hospitals. Rejuvenation Res 15:41–48
31. Gill TM (2010) Assessment of function and disability in longitudinal studies. J Am Geriatr Soc 58(Suppl 2):S308–S312
32. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, Scherr PA, Wallace RB (1994) A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 49:M85–M94
33. Bischoff-Ferrari HA (2012) Relevance of vitamin D in muscle health. Rev Endocr Metab Disord 13:71–77
34. Annweiler C, Schott AM, Berrut G, Fantino B, Beauchet O (2009) Vitamin D-related changes in physical performance: a systematic review. J Nutr Health Aging 13:893–898
35. Latham NK, Anderson CS, Reid IR (2003) Effects of vitamin D supplementation on strength, physical performance, and falls in older persons: a systematic review. J Am Geriatr Soc 51:1219–1226
36. Muir SW, Montero-Odasso M (2011) Effect of vitamin D supplementation on muscle strength, gait and balance in older adults: a systematic review and meta-analysis. J Am Geriatr Soc 59:2291–2300
37. Sanders KM, Stuart AL, Williamson EJ, Simpson JA, Kotowicz MA, Young D, Nicholson GC (2010) Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial. JAMA 303:1815–1822
38. Kwon S, Perera S, Pahor M, Katula JA, King AC, Groessl EJ, Studenski SA (2009) What is a meaningful change in physical performance? Findings from a clinical trial in older adults (the LIFE-P study). J Nutr Health Aging 13:538–544
39. Perera S, Mody SH, Woodman RC, Studenski SA (2006) Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc 54:743–749