

VITAMIN D AND MUSCLE STRENGTH

**IS THERE AN ASSOCIATION BETWEEN SERUM 25-HYDROXYVITAMIN D CONCENTRATION AND MUSCLE STRENGTH AMONG OLDER WOMEN? RESULTS FROM BASELINE ASSESSMENT OF THE EPIDOS STUDY**

C. ANNWEILER<sup>1</sup>, O. BEAUCHET<sup>1</sup>, G. BERRUT<sup>2</sup>, B. FANTINO<sup>3</sup>, M. BONNEFOY<sup>4</sup>,  
F.R. HERRMANN<sup>5</sup>, A.M. SCHOTT<sup>6</sup>

1. Department of Geriatrics, Angers University Hospital, France; 2. Department of Geriatrics, Nantes University Hospital, France; 3. Medical health center of Lyon, CNAMTS, France; 4. Department of Geriatrics, Lyon University Hospital, France; 5. Department of Rehabilitation and Geriatrics, Geneva University Hospitals, Switzerland; 6. Department of Medical Information, Lyon University Hospital, France. Correspondence to: Olivier Beauchet, MD, PhD, Department of geriatrics, Angers University Hospital, 49933 Angers Cedex 9, France, E-mail: olbeauchet@chu-angers.fr, Phone: ++33 02 41 35 45 50, Fax: ++33 2 41 35 48 94

**Abstract:** *Objective:* To examine whether low serum 25-hydroxyvitamin D (25OHD) concentration were associated with low muscle strength while taking into account the effects of potential confounders among a cohort of community-dwelling women aged 75 years and older. *Design:* Cross-sectional study corresponding to the baseline assessment of the EPIDOS study. *Setting:* Five French cities including Amiens, Lyon, Montpellier, Paris and Toulouse. *Participants:* Randomized sample of 440 women included in the EPIDOS study. *Measurement:* Maximal isometric voluntary contraction strength of the lower limb and hand with computerized dynamometers, serum 25OHD and parathyroid hormone concentration. Age at baseline evaluation, number of chronic diseases, body mass index (BMI), use of calcium drug, practice of a regular physical activity, serum calcium concentration and clearance of creatinine were used as covariables. Subjects were separated into 3 groups based on serum 25 OHD levels with the following cut-off values: < 15 ng/ml, 15-30 ng/ml and > 30 ng/ml. *Results:* More than 90% of women had a serum 25OHD insufficiency (i.e. < 30ng/ml) and 40.2% had a related secondary hyperparathyroidism. The mean value of muscle strength was not different among the 3 groups of women (174.9±53.2 for serum 25OHD < 15 ng/ml versus 175.9±52.6 for serum 25OHD 15-30 ng/ml versus 173.4±53.1 for serum 25OHD > 30 ng/ml with P=0.946 for quadriceps, and 56.1±13.2 for serum 25OHD < 15 ng/ml versus 57.1±13.5 for serum 25OHD 15-30 ng/ml versus 61.1±12.7 for serum 25OHD > 30 ng/ml with P=0.064 for handgrip). There was no significant association between serum 25OHD concentration and quadriceps strength (crude  $\beta$  = 0.03 with P = 0.891 and adjusted  $\beta$  = -0.04 with P = 0.837). Univariate linear regression showed a significant association between serum 25OHD concentration and handgrip strength (crude  $\beta$  = 0.16 with P = 0.049) but not while using an adjusted model (adjusted  $\beta$  = 0.13 with P = 0.106). *Conclusions:* The findings of this study do not support the hypothesis of a relationship between low serum 25OHD concentration and low muscle strength. Further research is needed to corroborate and explain this finding.

**Key words:** Vitamin D, muscle strength, older adults.

**Introduction**

Muscle is a target site for 25-hydroxyvitamin D (25OHD) and 1,25-dihydroxyvitamin D (1,25 (OH)<sub>2</sub>D) (1-3). These both vitamin D metabolites act on muscle cell via genomic and non-genomic pathway and, thus, may influence muscle function (1, 4). It has been suggested that chronic low serum 25OHD concentration could be associated with muscle weakness defined as the inability to exert strength with ones muscles to the degree that would be expected given the individual's general physical fitness (1-4). However, the relationship between low serum 25OHD concentration and low muscle strength is not fully established among older adults because findings from observational clinical studies are controversial. Some studies have shown that 25OHD insufficiency (i.e. < 30ng/ml) as well 25OHD deficiency (i.e. < 15ng/ml) were associated with muscle weakness (4-8), while others failed to find any relationship (9, 10).

Divergences between studies may result from a lack or an insufficient control of confounders that may modify the

relationship between serum 25OHD concentration and muscle strength. Firstly, it has been shown that secondary hyperparathyroidism associated with low serum 25OHD concentration may directly provoke muscle weakness (11-13). Secondly, a low calcium concentration may also be a modulator of muscle strength by acting on 1,25 (OH)<sub>2</sub>D and on parathyroid hormone (PTH) production (13, 14). Thirdly, age, unhealthy status, malnutrition, level of physical activity are health and life style factors that may also change the relationship between serum 25OHD concentration and muscle strength (15, 16).

Whilst the effects of confounders of the relationship between serum 25OHD concentration and muscle strength are well-identified, few studies have examined their joint effects (4, 15, 16). These studies have highlighted that muscle weakness could be related to confounders and not to low serum 25OHD concentration. Furthermore, Bischoff et al. (10) showed that the relationship was complex and depend on the type of vitamine D metabolites. Although decrease in leg extensor strength in Bischoff 's study was explained by sex, age, body mass index

## JNHA: NUTRITION

(BMI), and serum 1,25 (OH)<sub>2</sub>D but not 25OHD level in older adults, there was a positive correlation between both vitamin D metabolites and lower limb muscle strength while using a univariate model.

Acquiring more information about low serum 25OHD concentration-related changes in muscle strength adjusted for the effects of confounders among older adults could add to our knowledge of low serum vitamin D-related adverse muscle outcomes. Furthermore, in view of previous findings on the interrelated relationships between muscle strength and serum 25OHD, PTH, and calcium concentration, the respective influences of each serum variable on muscle weakness need to be explored. Thus, the objective of the study was to examine whether low serum 25OHD concentration were associated with low muscle strength while taking into account the effects of serum and clinical confounders among women aged 75 years and older using data from the EPIDOS study.

### Methods

#### *Participants*

We studied a randomized sample of 440 subjects included in the EPIDOS study which is a community-dwelling observational prospective cohort study designed to evaluate the risk factors for hip fracture among more than 7500 healthy older women aged 75 years and older. The sampling and data collection procedures have been described elsewhere in detail (17). In summary, from 1992 to 1994, 7598 subjects sampled from electoral lists were recruited in five French cities including Amiens, Lyon, Montpellier, Paris and Toulouse after having given their written informed consent. Exclusion criteria were inability to walk independently, hip fracture or bilateral hip replacement, inability to understand or answer the study questionnaires. Included participants received a full medical examination in each local clinical center by trained nurses which included structured questionnaires, information about chronic diseases, clinical examination and anthropometrics measurements. The study was conducted in accordance with the ethical standards set forth in the Helsinki declaration (1983). The local ethics committee of each city approved the project.

#### *Muscle strength measures*

The procedure consisted of the evaluation of the maximal isometric voluntary contraction (MVC) strength of the lower limb and hand with computerized dynamometers. Before testing for both muscle strength measures, subjects were allowed to practice the isometric movements and a trained evaluator gave standardized verbal instructions regarding the test procedure. Furthermore, subjects were instructed to push against the dynamometers as hard as they could and the maximal peak pressure expressed in Newton per square meter was recorded. The highest value of MVC strength recorded was used in the present data analysis. Quadriceps strength was assessed using a strain gauge system attached to a chair upon which subjects were seated with both hips and knees flexed at

90° angle. The leg to be tested was fixed to the lever arm on an analog strain gauge to measure strength. The seat position was adjusted for the leg length. Three MVC were recorded for the dominant and the non-dominant leg, and analyzed off-line. Secondly, a hydraulic hand dynamometer (Martin Vigorimeter, Medizin Technik, Tutlingen, Germany) was used to measure the handgrip strength. The size of the grip was adjusted so that the subject felt comfortable. The subject stood upright with the arm vertical and the dynamometer close to the body. The test was performed one time on each side.

#### *Serum measures*

Fasting early morning venous blood was collected from resting subjects for the measurement of serum 25OHD, PTH, calcium, creatinine and albumin. Sera were stored at -100°C until analysis. Serum 25OHD concentration was measured by radioimmunoassay (Inctar Corp., Stillwater, MN). With this method, there is no interference of lipids, which is often observed in other non chromatographic assays of 25OHD. The intra- and interassay precisions were respectively 5.2 % and 11.3 %, (range in normal adults aged 20-60 yr, 30-125 ng/ml). Intact PTH (iPTH) was measured by immunochemoluminometric assay (Magic Lite, Ciba Corning Diagnostic, Medfield, MA; normal range for adults 20-60 year of age, 11-55 pg /ml). The intra- and interassay precisions were 5.2-6.8% and 5.0-5.5% respectively. Serum calcium, albumin and creatinine were determined using automated standard laboratory methods. Because of the high prevalence of hypoalbuminemia in older adults, the serum concentration of albumin and calcium were used to correct the calcium value (calcium corrected value = Ca + 0.02 [46-albumin]). The calcium corrected value was used in the subsequent analysis. The clearance of creatinine was calculated from the Cockcroft formula ( $[(140 - \text{age years}) / \text{creatinine mol/l}] \times 1.04$ ). All measurement was performed locally at the University Hospital at Lyon, France.

#### *Clinical covariates*

Age at baseline evaluation, number of chronic diseases, BMI, use of calcium drug and practice a regular physical activity were used as clinical confounders in data analysis. Confounders were obtained from a physical examination and a health status questionnaire to target comorbidities (hypertension, diabetes, dyslipidemia, coronary heart disease, chronic obstructive pulmonary disease, peripheral vascular disease, cancer, stroke, Parkinson's disease and depression). Practice of a regular activity was reported with a self-reported structured questionnaire. Type, frequency and duration of recreational physical activities including walking, gymnastics, cycling, swimming or gardening were recorded. A regular physical activity was considered if the subjects practiced at least one recreational physical activity for at least one hour a week for the past month or more. BMI was calculated as weight (kg)/height<sup>2</sup> (m). Weight was measured with a beam balance scale and height with a height gauge.

VITAMIN D AND MUSCLE STRENGTH

**Statistical analysis**

The subjects' characteristics were summarized using means and standard deviations or frequencies and percentages, as appropriate. The normality in the distribution of variables was verified with skewness and kurtosis tests. Serum 25OHD concentration, clearance and BMI were successfully normalized using a logarithmic transformation, whereas quadriceps muscle strength was successfully normalized by a square root transformation. Subjects were separated into three groups based on serum 25 OHD concentration with the following cut-off values: < 15 ng/ml, 15-30 ng/ml and > 30 ng/ml (18). Firstly, comparisons were performed using the independent samples t-test, the Kruskal-Wallis test, one-way analysis of variance (ANOVA) or Chi-square test, as appropriate. Secondly, univariate and multiple linear regression analyses were performed to specify the relationship between serum 25OHD concentration (independent variable) and MVC strength (dependant variable). Adjustment was performed with subjects' baseline characteristics and the effect of center of recruitment. P-values less than 0.05 were considered as statistically significant. All the statistics were performed using the Stata Statistical Software, release 9.2 (19).

**Results**

The randomised subgroup of EPIDOS cohort was younger (p=0.047) and practiced more regularly physical activity compared to their counterparts (p=0.042) (Table 1). There was no significant difference for the others clinical characteristics. The quadriceps strength did not differ between groups (173.5 ± 66.6 versus 175.1 ± 52.9 Newton per square meter with P=0.540), whereas the mean value of handgrip strength was significantly higher in the randomized subgroup compared to other subjects of the cohort (55.2±12.4 versus 57±13.2 Newton per square meter with P=0.008). More than 90% of subjects had a serum 25OHD insufficiency and 40.2% had a related secondary hyperparathyroidism. In addition, the serum calcium concentration and clearance were normal (respectively, 2.2 ± 0.1 mmol/l and 52.8 ± 15.8 ml/mn).

As shown in Table 2, there was no significant difference for the clinical characteristics and muscle strength between the 3 groups of subjects. The mean values of serum 25OHD differed significantly between groups of subjects (respectively, 10.5±2.6 ng/l, 20.4±4.4 ng/l, and 42.4±9.6 ng/l with P < 0.001). In addition, there was also a significant difference between groups for serum PTH concentration (P < 0.001) but not for calcium and clearance (P = 0.891 and P = 0.597).

**Table 1**  
Characteristics of subjects (n=7598)

	EPIDOS cohort (n=7158)	Randomised subjects (n=440)	P-Value*
<b>Clinical characteristics</b>			
Age, mean ± SD (years)	80.5 ± 3.8	80.1 ± 3.5	0.047
Number of chronic diseases†, mean ± SD	3.4 ± 2.0	3.5 ± 1.8	0.520
Body mass index, mean ± SD (kg/cm2)	25.4 ± 4.2	25.5 ± 4.1	0.701
Regular physical activity ‡, n (%)	3407 (47.6)	231 (52.6)	0.042
<b>Muscle strength¶</b>			
Quadriceps, mean value ± SD	173.5 ± 66.6	175.1 ± 52.9	0.540
Handgrip, mean value ± SD	55.2 ± 12.4	57.0 ± 13.2	0.008
<b>Serum measures</b>			
<b>25ODH (ng/ml)</b>			
Mean ± SD	-	17.4 ± 10.5	
< 30, n (%)	-	397 (90.2)	
<b>PTH (pg/ml)</b>			
Mean ± SD	-	62.5 ± 28.5	
> 65, n (%)	-	177 (40.2)	
Calcium   (mmol/l)	-	2.2 ± 0.1	
Clearance§, mean ± SD (ml/mn)	-	52.8 ± 15.8	

SD: standard deviation; \*: Based on unpaired sample t-test; †: Obtained from physical examination and a health status questionnaire to target comorbid diseases (hypertension, diabetes, dyslipidemia, coronary heart disease, chronic obstructive pulmonary disease, peripheral vascular disease, cancer, stroke, Parkinson's disease and depression); ‡: Considered if subjects practiced at least one recreational physical activity (walking, gymnastics, cycling, swimming or gardening) activity for at least one hour a week for the past month or more; §: Corrected value based on the formula (Ca + 0.02 [46-albumin]); ||: Calculated from the Cockcroft formula ((140-age years) / creatinine mol/l) x 1.04); ¶: Highest value of maximal isometric voluntary contraction strength measured with computerized dynamometers expressed in Newton per square meter; P significant (i.e. < 0.005) indicated in bold

Univariate and multiple regression showed that there was no significant association between serum 25OHD concentration and quadriceps strength (crude β = 0.03 with P = 0.891 and adjusted β = -0.04 with P = 0.837). In contrast, a low quadriceps strength was significantly associated with older age (β = -0.12 with P < 0.001 and β = -0.13 with p < 0.001) and a high number of chronic diseases (β = -0.15 with P < 0.001 and β = -0.14 with P = 0.009). Conversely, a high BMI and a regular practice of physical activity were significantly associated with higher muscle strength (β = 3.14 with P < 0.001 and β = 4.20 with P < 0.001 for BMI; β = 0.56 with P = 0.004 and β = 0.62 with P = 0.002 for physical activity). Furthermore, although univariate model showed that a high clearance was associated with a high muscle strength (β = 0.75 with P = 0.024), the multiple model showed an opposite result (β = -1.28 with p = 0.002) (Table 3a). As shown in Table 3b, univariate linear regression showed a significant association between serum 25OHD concentration and handgrip strength (β = 0.16 with P = 0.049) but not while using an adjusted model (β = 0.13 with P = 0.106). In addition, multiple linear model showed that a high serum PTH concentration (adjusted β = 0.17 with P = 0.044) and a high BMI (adjusted β = 0.78 with P = 0.012) were significantly associated with a high handgrip strength, whereas older age (adjusted β = -0.08 with P < 0.001) and a low clearance (adjusted β = -0.42 with P = 0.020) were associated with a low muscle strength.

JNHA: NUTRITION

**Table 2**

Characteristics and comparison of randomized sample subjects (n=440) separated into three groups based on serum 25OHD concentrations

	Serum 25ODH concentration (ng/ml)			P-Value*
	<15 (n=226)	15-30 (n=171)	> 30 (n=43)	
<b>Clinical measures</b>				
Age, mean ± SD (years)	80.5±3.7	79.9±3.2	79.5±3.0	0.292
Number of chronic diseases†, mean ± SD	3.6±1.9	3.4±1.8	3.0±1.8	0.137
Body mass index, mean ± SD (kg/cm2)	25.6±4.2	25.6±4.1	24.6±3.7	0.232
Regular physical activity ‡, n (%)	110 (48.9)	96 (56.1)	25 (58.1)	0.268
<b>Muscle strength¶</b>				
Quadriceps, Mean value ± SD	174.9±53.2	175.9±52.6	173.4±53.1	0.946
Handgrip, Mean value ± SD	56.1±13.2	57.1±13.5	61.1±12.7	0.064
<b>Serum measures</b>				
25ODH, mean ± SD (ng/ml)	10.5±2.6†	20.4±4.4†	42.4±9.6	<0.001
PTH (pg/ml)				
Mean ± SD	67.2±32.2†	58.5±23.8†	53.9±19.6	0.001
> 65, n (%)	101 (44.7)	62 (36.3)	14 (32.6)	0.132
Calcium   (mmol/l)	2.2±0.1	2.2±0.1	2.2±0.1	0.891
Clearance§, mean ± SD (ml/mn)	52.9±17.0	53.3±14.9	50.4±12.7	0.597

SD: standard deviation; \*: Comparisons based on one-way analysis of variance (ANOVA), Kruskal-Wallis test or Chi-square test, as appropriate; †: Comparison with reference group (i.e. 25OHD >30ng/ml) based on Bonferroni test with p value significant < 0.003; ‡: Obtained from physical examination and a health status questionnaire to target comorbid diseases (hypertension, diabetes, dyslipidemia, coronary heart disease, chronic obstructive pulmonary disease, peripheral vascular disease, cancer, stroke, Parkinson's disease and depression); §: Considered if subjects practiced at least one recreational physical activity (walking, gymnastics, cycling, swimming or gardening) activity for at least one hour a week for the past month or more; ||: Corrected value based on the formula (Ca + 0.02 [46-albumin]); ¶: Calculated from the Cockcroft formula ((140-age years) / creatinine mol/l) x 1.04); #: Highest value of maximal isometric voluntary contraction strength measured with computerized dynamometers expressed in Newton per square meter; P significant (i.e. < 0.05) indicated in bold

**Table 3**

Uni and multivariate linear regression showing the cross-sectional association between maximal isometric voluntary contraction strength (dependant variable) and serum 25OHD concentration (independent variable) adjusted on subjects' baseline characteristics (n=429)

a) Quadriceps strength

	Crude coefficient of regression beta (95% CI)	P-value	Adjusted coefficient of regression beta (95% CI)	P-value*
Serum 25OHD †	0.03 (-0.34;0.39)	0.891	-0.04 (-0.38;0.31)	0.837
High serum PTH concentration ‡	0.04 (-0.36;0.43)	0.852	0.06 (-0.31;0.44)	0.748
Age	-0.12 (-0.17;-0.07)	<0.001	-0.13 (-0.19;-0.07)	<0.001
Number of chronic diseases §	-0.15 (-0.26;-0.05)	0.004	-0.14 (-0.25;-0.04)	0.009
Body mass index †	3.14 (1.97;4.31)	<0.001	4.20 (2.82;5.59)	<0.001
Regular physical activity	0.56 (0.17;0.94)	0.004	0.62 (0.24;0.99)	0.002
Serum calcium concentration ¶	0.93	0.360	0.32	0.743

(mmol/l)	(-1.06;2.92)		(-1.61;2.26)	
Clearance # (ml/mn)	0.75 (0.10;1.40)	0.024	-1.28 (-2.09;-0.48)	0.002

b) Handgrip strength

	Crude (95% CI)	P-value	Adjusted (95% CI)	P-value*
Serum 25OHD †	0.16 (0.00;0.31)	0.049	0.13 (-0.03;0.28)	0.106
High serum PTH concentration ‡	0.10 (-0.07;0.27)	0.264	0.17 (0.00;0.34)	0.044
Age	-0.07 (-0.09;-0.04)	<0.001	-0.08 (-0.11;-0.06)	<0.001
Number of chronic diseases §	-0.03 (-0.78;0.01)	0.151	-0.03 (-0.08;0.01)	0.156
Body mass index †	0.41 (-0.10;0.93)	0.118	0.78 (0.17;1.39)	0.012
Regular physical activity	0.12 (-0.04;0.29)	0.144	0.03 (-0.14;0.20)	0.720
Serum calcium concentration ¶ (mmol/l)	0.01 (-0.85;0.87)	0.984	-0.09 (-0.95;0.77)	0.835
Clearance # (ml/mn)	0.16 (-0.12;0.44)	0.271	-0.42 (-0.78;-0.07)	0.020

SD: standard deviation; PTH: parathyroid hormone; Quadriceps muscle strength was successfully normalized by a square root transformation; β: Coefficient of regression corresponding to an increase of maximal isometric voluntary contraction strength expressed in Newton per square meter; Intercept value (not shown in the table) corresponded to the mean value of a women with an average values for all parameters; \*: Adjusted on effect of center with a significant effect for Amiens (1.13 [0.55;1.72] with P <0.001) and Toulouse (0.92 [0.31;1.53] with P=0.003) for quadriceps strength; and Lyon (0.46 [0.20;0.72] with P=0.001) and Paris (0.27 [0.01;0.52] with P=0.043) for handgrip strength; †: Normalized by taking the logarithmic transformation; ‡: > 65 pg/ml; §: Obtained from physical examination and a health status questionnaire to target comorbid diseases (hypertension, diabetes, dyslipidemia, coronary heart disease, chronic obstructive pulmonary disease, peripheral vascular disease, cancer, stroke, Parkinson's disease and depression); ||: Considered if subjects practiced at least one recreational physical activity (walking, gymnastics, cycling, swimming or gardening) activity for at least one hour a week for the past month or more; ¶: Corrected value based on the formula (Ca + 0.02 [46-albumin]); #: Normalized by taking the logarithmic transformation and calculated from the Cockcroft formula ((140-age years) / creatinine mol/l) x 1.04); Coefficient of regression beta significant indicated in bold

**Discussion**

The prevalence of low serum 25OHD concentration was high in the studied sample of elderly women and calculated at 90.2%, and was poorly associated with low muscle strength. There was no significant association with quadriceps strength, and only handgrip strength was associated with muscle weakness, but this association disappeared while adjusting for confounders. In contrast, our results confirmed that older age, comorbidities and a poor renal function were both related to muscle weakness, whereas a high BMI and the regular practice of physical activity were associated with high muscle strength.

The association between low serum 25OHD concentration and low muscle strength was weak in our study. This finding is in concordance with previous studies which have explored this cross sectional association (9, 10). Whilst studies reported no relationship (9, 10), observational clinical studies showed a positive correlation between low serum 25OHD concentration and low muscle strength (4-8). As an example, in Bischoff's study there was effectively a significant positive correlation between serum 25OHD level and lower limb muscle strength while using an univariate model but, in an ANCOVA including all participants, decrease in leg extensor strength was explained

## VITAMIN D AND MUSCLE STRENGTH

by sex, age, BMI, but not 25OHD concentration anymore (10). Similarly our results highlighted a significant positive correlation between serum 25OHD level and handgrip strength, but this relationship was again no more significant while taking into account the effects of serum and clinical confounders.

This divergence of results has also been found with others surrogate measures for muscle weakness such as fall or performance in mobility during daily activity. Even as most of the studies reported a higher risk of falls in older adults with low serum 25 OHD concentration, few studies found no link (20-22). This discrepancy between findings may be explained by confounders. As an example, Stein et al. (11) showed that low serum 25OHD concentration and high serum PTH concentration were separately associated with a higher frequency of falls, but solely PTH remained significant when the statistical model was adjusted for the two variables. In addition, vitamin D supplementation, examined using randomized controlled trials, also showed the same discrepancy while exploring the vitamin D-related improvement in muscular strength and balance (23-29).

We reported a higher prevalence of vitamin D insufficiency (i.e. < 30 ng/ml) (90.2%) compared to the prevalence reported in community-dwelling older adults which is estimated between 25 and 50% (30-32). The discrepancy may be related to the definition of cut-off value of vitamin D insufficiency. Previous used cut-points for serum 25OHD insufficiency were ranging from 20 to 32 ng/ml. Furthermore, the number of comorbidities of studied subjects may also explain the difference in prevalence. It has been shown that chronic diseases may affect vitamin D metabolism in older adults (15, 16) and, consequently, should be taken into account while evaluating insufficiency. Nevertheless, it is well-recognized that the prevalence of vitamin D insufficiency is frequently underestimated (31-33) and, as a consequence, might be higher in community-dwelling than reported in previous studies.

In our study we showed that low muscle strength is associated with advance in age, low clearance and multiple comorbidities. Firstly, age-related decrease in muscle performance is well-known (34-37). With increasing age, part of the skeletal muscle is lost and the ageing atrophy is accompanied by a reduction in muscle strength (33, 34). Secondly, it is well recognized that exercise performance and leg strength tests are reduced in patients with poor renal function despite maintenance of hemoglobin concentration (35). Thirdly, low muscle strength provoked by comorbidities may be a direct consequence of disease on muscle (38, 39) or the indirect effect of disease related restriction of physical activity (37) leading to decrease in muscle functions and a reduced exposure to UVB rays resulting in low serum 25OHD concentration. In contrast, the practice of regular physical activity and a high BMI are associated to high muscle strength (34-39). Our results are in concordance with this statement.

Our study has some limitations, which could explain the apparent lack of association between hypovitaminosis D and low muscle strength. Firstly, the study cohort was restricted to

women and included relatively healthy subjects. Therefore, the studied sample of subjects might not be representative of community-dwelling older adults. Moreover, participants were probably more motivated and showed greater interest in health issues than the general population of older adults who live in independent senior living facilities. Secondly, the design of the present study which was cross-sectional may be a limitation to explore the relationship between serum 25OHD concentration and low muscle strength compared to prospective cohort design. Thirdly, although we were able to control for many characteristics that may modified the relationship, residual potential confounders might still be present.

In conclusion, this study does not support the hypothesis of a relationship between low serum 25OHD concentration and low muscle strength, but confirms that older age, comorbidities, BMI and the regular practice of physical activity are strongly associated with muscle strength. Further research is needed to corroborate and explain this finding.

*Acknowledgements:* The EPIDOS study participants included coordinator (G Breart, P Dargent-Molina, PJ Meunier, AM Schott, D Hans, and PD Delmas) and principal investigators (C Baudoin and JL Sebert [Amiens], MC Chapuy and AM Schott [Lyon], F Favier and C Marcelli [Montpellier], CJ Menkes, C Cormier, and E Hausherr [Paris], and H Grandjean and C Ribot [Toulouse]).

*Financial disclosure:* None of the authors had any financial interest or support for this paper.

## References

1. Janssen HC, Samson MM, Verhaar HJ. Vitamin D deficiency, muscle function, and falls in elderly people. *Am J Clin Nutr.* 2002;75:611-5
2. Ziambaras K, Dagogo-Jack S. Reversible muscle weakness in patients with vitamin D deficiency. *West J Med.* 1997;167:435-9.
3. Glerup H, Mikkelsen K, Poulsen L, Hass E, Overbeck S, Andersen H, Charles P, Eriksen EF. Hypovitaminosis D myopathy without biochemical signs of osteomalacic bone involvement. *Calcif Tissue Int.* 2000;66:419-24.
4. Campbell PM, Allain TJ. Muscle strength and vitamin D in older people. *Gerontology.* 2006;52:335-8.
5. Houston DK, Cesari M, Ferrucci L, Cherubini A, Maggio D, Bartali B, Johnson MA, Schwartz GG, Kritchevsky SB. Association Between Vitamin D Status and Physical Performance: The InCHIANTI Study. *J Gerontol A Biol Sci Med Sci.* 2007;62:440-6.
6. Bischoff-Ferrari HA, Dietrich T, Orav EJ, Hu FB, Zhang Y, Karlson EW, Dawson-Hughes B. 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;80:752-8.
7. Zamboni M, Zoico E, Tosoni P, Zivelonghi A, Bortolani A, Maggi S, Di Francesco V, Bosello O. Relation between vitamin D, physical performance, and disability in elderly persons. *J Gerontol A Biol Sci Med Sci.* 2002;57:M7-11.
8. Mowe M, Haug E, Bohmer T. Low serum calcidiol concentration in older adults with reduced muscular function. *J Am Geriatr Soc.* 1999;47:220-6.
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;50:912-7.
10. Bischoff HA, Stahelin HB, Urscheler N, Ehlsam R, Vonthein R, Perrig-Chiello P, Tyndall A, Theiler R. Muscle strength in the elderly: its relation to vitamin D metabolites. *Arch Phys Med Rehabil.* 1999;80:54-8.
11. Stein MS, Wark JD, Scherer SC, Walton SL, Chick P, Di Carantonio M, Zajac JD, Flicker L. Falls relate to vitamin D and parathyroid hormone in an Australian nursing home and hostel. *J Am Geriatr Soc.* 1999;47:1195-201.
12. Visser M, Deeg DJ, Lips P; Longitudinal Aging Study Amsterdam. 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;88:5766-72.
13. 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.
14. McCarty MF. Vitamin D status and muscle strength. *Am J Clin Nutr.* 2002;76:1454-5

JNHA: NUTRITION

15. Janssen HC, Samson MM, Verhaar HJ. Vitamin D deficiency, muscle function, and falls in elderly people. *Am J Clin Nutr.* 2002;75:611-5
16. Pfeifer M, Begerow B, Minne HW. Vitamin D and muscle function. *Osteoporos Int.* 2002;13:187-94.
17. Dargent-Molina P, Favier F, Grandjean H, Baudoin C, Schott AM, Hausherr E, Meunier PJ, Breart G. Fall-related factors and risk of hip fracture: the EPIDOS prospective study. *Lancet.* 1996;348:145-9.
18. Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. *Osteoporos Int.* 2005;16:713-6.
19. Stata Statistical Software: Release 9.2 [program]. College Station, Texas, USA: Stata Corporation 2003.
20. Bischoff-Ferrari HA, Dawson-Hughes B, Willet WC, Staehelin HB, Bazemore MG, Zee RY, Wong JB. Effect of vitamin D on falls: A meta analysis. *JAMA* 2004;291:1999-2006.
21. Bischoff-Ferrari HA, Staehelin HB, Dick W, Akos R, Knecht M, Salis C, Nebiker M, Theiler R, Pfeifer M, Begerow B, Lew RA, Conzelmann M. Effect of vitamin D and calcium supplementation on falls: A randomized controlled trial. *J Bone Miner Res* 2003;18:343-51.
22. Dukas L, Bischoff-Ferrari HA, Lindpaintner LS, Schacht E, Birkner-Binder D, Damm TN, Thalman B, Staehelin HB. Alfacalcidol reduces the number of fallers in a community-dwelling elderly population with a minimum calcium intake of more than 500 mg daily. *J Am Geriatr Soc* 2004;52:230-6.
23. Porthouse J, Cockayne S, King C et al. Randomized controlled trial of calcium and supplementation with cholecalciferol (vitamin D3) for prevention of fractures in primary care. *BMJ* 2005;330:1-6.
24. Grant AM, Avenell A, Campbell MK et al. RECORD Trial Group. Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (randomized evaluation of calcium or vitamin D, RECORD): a randomized placebo-control trial. *Lancet* 2005;365:1621-8.
25. Law M, Withers H, Morris J, Anderson F. Vitamin D supplementation and the prevention of fractures and falls: results of a randomised trial in elderly people in residential accommodation. *Age Ageing* 2006;35:482-6.
26. Latham NK, Anderson CS, Reid IR. Effects of vitamin D supplementation on strength, physical performance, and falls in older persons: A systematic review. *J Am Geriatr Soc* 2003;51:1219-26
27. Latham NK, Anderson CS, Lee A, Bennett DA, Moseley A, Cameron ID; Fitness Collaborative Group. 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;51:291-9.
28. Kenny AM, Biskup B, Robbins B, Marcella G, Bureson JA. Effects of vitamin D supplementation on strength, physical function, and health perception in older, community-dwelling men. *J Am Geriatr Soc.* 2003;51:1762-7.
29. Dhesi JK, Jackson SH, Bearne LM, Moniz C, Hurley MV, Swift CG, Allain TJ. Vitamin D supplementation improves neuromuscular function in older people who fall. *Age Ageing.* 2004;33:589-95.
30. Thomas MK, Lloyd-Jones DM, Thadhani RI, Shaw AC, Deraska DJ, Kitch BT, Vamvakas EC, Dick IM, Prince RL, Finkelstein JS. Hypovitaminosis D in medical inpatients. *N Engl J Med.* 1998;338:777-83.
31. Gloth FM 3rd, Gundberg CM, Hollis BW, Haddad JG Jr, Tobin JD. Vitamin D deficiency in homebound elderly persons. *JAMA.* 1995;274:1683-6.
32. Gloth FM 3rd, Tobin JD. Vitamin D deficiency in older people. *J Am Geriatr Soc.* 1995;43:822-8
33. Mosekilde L. Vitamin D and the elderly. *Clin Endocrinol (Oxf).* 2005;62:265-81.
34. Mistic MM, Rosengren KS, Woods JA, Evans EM. Muscle Quality, Aerobic Fitness and Fat Mass Predict Lower-Extremity Physical Function in Community-Dwelling Older Adults. *Gerontology.* 2007;53:260-6
35. Leikis MJ, McKenna MJ, Petersen AC, Kent AB, Murphy KT, Leppik JA, Gong X, McMahon LP. Exercise performance falls over time in patients with chronic kidney disease despite maintenance of hemoglobin concentration. *Clin J Am Soc Nephrol* 2006; 1: 488-95
36. Buchman AS, Wilson RS, Boyle PA, Bienias JL, Bennett DA. Change in motor function and risk of mortality in older persons. *J Am Geriatr Soc.* 2007;55:11-9
37. Marsh AP, Miller ME, Saikin AM, Rejeski WJ, Hu N, Lauretani F, Bandinelli S, Guralnik JM, Ferrucci L. Lower extremity strength and power are associated with 400-meter walk time in older adults: The INCHIANTI study. *J Gerontol A Biol Sci Med Sci.* 2006;61(11):1186-93.
38. Cesari M, Onder G, Russo A, Zamboni V, Barillaro C, Ferrucci L, Pahor M, Bernabei R, Landi F. Comorbidity and physical function: results from the aging and longevity study in the Sirente geographic area (iSIRENTE study). *Gerontology.* 2006;52:24-32.
39. Rantanen T, Volpato S, Ferrucci L, Heikkinen E, Fried LP, Guralnik JM. Handgrip strength and cause-specific and total mortality in older disabled women: exploring the mechanism. *J Am Geriatr Soc.* 2003;51:636-41.