Vitamin D status and physical function in older Finnish people: A one-year follow-up study

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Abstract

Objective: The aim was to describe vitamin D status and its association with changes in PF during 12 months in Finnish community-dwelling elderly (≥65 years).

Methods and results: Baseline serum 25-hydroxyvitamin D (25(OH)D) concentration was measured by enzymeimmunoassay, and participants (n=518) were divided according to 25(OH)D to three groups (I ≤50 nmol/l, II 50–74.9 nmol/l, and III ≥75 nmol/l). PF (maximal isometric extension strength of right and left knee, and time in five-repetition sit-to-stand test (5STS) and 10-m walking test) was measured at baseline and after 12 months. 25(OH)D deficiency (≤50 nmol/l) was found in 20.5% of the participants. During a 12-month follow-up, differences in changes in knee extensor strength of right (p=0.044) and left (p=0.010) lower extremity and in 10-m walking test (p=0.040) between the groups were significant. According to further pairwise comparisons these differences were between groups I and III (right knee, p=0.036; left knee, p=0.009; 10-m walk, p=0.044), with the exception of left knee extensor strength in which there were also significant difference between groups I and II (p=0.039). All significant differences in changes were in favour of group II or III. Significant differences in changes in knee extensor strengths maintained after adjustments for group (intervention/control), parathyroid hormone, and baseline level of knee extensor strength.

Conclusions: Prospective analyses showed low 25(OH)D concentrations (≤50 nmol/l) to be associated with deterioration in PF during 12 months compared with high 25(OH)D concentrations (≥75 nmol/l).

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1. Introduction

Vitamin D deficiency is a public health problem worldwide (Mithal et al., 2009). Approximately 50–70% of community-dwelling older people in Europe have vitamin D deficiency, as defined by serum 25-hydroxyvitamin D (25(OH)D) of less than 50 nmol/l (Chan & Woo, 2011). In Finland, vitamin D intake and vitamin D status has been low in all age groups (Lamberg-Allardt, Brustad, Meyer, & Steingrimsdottir, 2013).

There is increasing evidence to show that vitamin D deficiency is an important risk factor for various adverse health outcomes (Holick, 2007; Lamberg-Allardt et al., 2013). Evidence of the role of 25(OH)D in relation to physical function (PF), and especially in relation to changes in PF, is limited. Although many cross-sectional studies have shown that low 25(OH)D concentrations are associated with lower physical performance and muscle strength (Dukas, Staehelin, Schacht, & Bischoff, 2005; Gerdhen, Ringsberg, Obrant, & Akesson, 2005; Wichters et al., 2007; Dam, von Mühlen, & Barrett-Connor, 2009; Shahar, Levi, & Kurtz, 2009; Pramyothin et al., 2009; Dretakis et al., 2010; Houston et al., 2011, 2012; Mastaglia et al., 2011; Michael et al., 2011; Boersma et al., 2011; Menant et al., 2012; Toffanello et al., 2012; Boyé et al., 2013; Gschwind et al., 2014; Janssen, Emmelot-Vonk, Verhaar, & van der Schouw, 2013), others
have found no association \cite{Annweiler2009, Chan2012, Mathieu2013}. The results of few longitudinal studies with 2–4 year follow-ups are inconsistent, some showing low 25OHD levels to be associated with decline in physical performance and muscle strength \cite{Visser2003, Wichters2007, Dam2009, Houston2011} while others show no association \cite{Verreault2002, Michael2011, Chan2012, Houston2012}.

The objective of this study was to describe the cross-sectional associations between 25OHD and PF and associations between 25OHD and changes in PF during 12 months in Finnish community-dwelling people aged 65 and older.

2. Methods

2.1. Participants, settings and study design

The subjects (n = 591) were community-dwelling older persons living in Pori, Finland who participated in a risk-based multifactorial fall prevention trial (ID = NCT00247546). The inclusion criteria were: age 65 years or over, at least one fall during the previous 12 months, sum score in the Mini Mental State Examination test (MMSE) \geq 17, able to walk 10 m independently with or without walking aids, able to live at home or in sheltered housing \cite{Sjosten2007}. The 12-month fall prevention program was based on an individual risk analysis. The intervention consisted of a geriatric assessment, counselling and guidance in fall prevention, home hazards assessment, group physical exercise, home exercise, lectures in groups, and psychosocial groups. The subjects in the control group attended one session of counselling and guidance on specified risk factors of falling at the beginning of the follow-up \cite{Salminen2009a, Salminen2009b, Kivel2009}. Subjects of the intervention study (both those in the intervention group and the control group) with data of 25-hydroxyvitamin D (25OHD) at baseline and measures of PF at baseline and at 12-month follow-up (n = 518) were included in this study. Participants were divided into three groups according to baseline 25OHD level: 1) <50 nmol/l (25OHD deficiency), II 50–74.9 nmol/l, and III \geq 75 nmol/l.

2.2. Laboratory measurements

Fasting blood samples were drawn between 7:45 and 10:00 a.m. Serum samples were stored at \(-20^\circ\)C until analysed. The serum 25OHD concentration was measured by OCTEIA immunoenzymometric assay (IDS, Bolton, UK). Reproducibility was ensured by adhering to the Vitamin D External Quality Assessment Scheme, DEQAS (deqas.kpmd.co.uk). Serum parathyroid hormone (PTH) concentration was measured with an immunoradiometric method \cite{Incsar2002}.

2.3. Outcome measures of physical function

Maximal isometric muscle strength measurements were performed on both sides of the lower extremities in a sitting position with an adjustable dynamometer chair (Good Strength, Mietturi, Jyväskylä, Finland). The tests were carried out by two trained physiotherapists. The dynamometer was calibrated every morning before measurements. Knee extension strengths were measured at knee angle of 60° from full extension with the ankle fastened to a strain-gauge system by a strap. Subjects were allowed to familiarize themselves with the method by doing two submaximal trials. Three to four maximal efforts of three seconds, separated by 30 s of rest, were conducted. During the measurements, the subjects were verbally encouraged to produce their maximum. For each subject, the best performance with the highest value was accepted as a result. The follow-up assessment of muscle strength was non-blinded \cite{Salminen2008}.

Functional lower limb muscle strength was measured with the five-repetition sit-to-stand test (5STS). A straight-backed armless chair with a hard seat was stabilized by placing it against a wall. Seated participants were asked to come forward on the chair seat until the feet were flat on the floor and to fold their upper limbs across the chest. The participants were then instructed to stand up all the way and sit down once without using the upper limbs. For those unable to complete the initial manoeuvre or who required assistance, the test was terminated. If successful on the initial sit-to-stand, the participants were then asked to stand up all the way and sit down landing firmly, as fast as possible, five times without using the arms. Time to perform 5STS was recorded as the participant’s score. Walking ability was measured by a 10-m walking test, which could be carried out with or without walking aids. Walking time in seconds was recorded.

2.4. Other measurements

Education and health habits (the frequency of physical exercises, smoking status, and alcohol consumption) were identified by a questionnaire. Weight and height were measured, and body mass index (BMI), measured as kilograms per square metre, was calculated. Cognitive function was measured with Mini Mental State Examination \cite{Folstein1975}, and nutritional status with Mini Nutritional Assessment (MNA) \cite{Garry1999}. Comorbidity was defined as having three or more diagnosed diseases. The data of diagnosed diseases was gathered from records of Satakunta Central Hospital and the Pori Health Centre. Sunlight exposure was categorized as follows: (1) yes (laboratory measurements carried out between 1st of June and 30th of November) and (2) no (laboratory measurements carried out between 1st of December and 30th of May).

2.5. Ethics

The study was conducted according to the guidelines of the Declaration of Helsinki. The Ethics Committee of the Hospital District of Satakunta approved the study protocol. Participants gave their informed consent.

2.6. Statistical analysis

Categorical variables between the groups were compared with chi-squared or Fisher’s exact tests. One-Way Analysis of Variance with Tukey’s adjustment in pairwise comparisons of Kruskal–Wallis test was used to test the differences in continuous variables between the 25OHD groups. In all analyses, group (intervention/control) was used as a covariate because of the original study design of the fall prevention intervention study. The interactions between group (intervention/control) and 25OHD group were also tested to evaluate the modifying effect of the group on the association of the 25OHD group and the outcome variables. Other possible confounding factors were gender, age, education, body mass index, PTH, cognitive (MMSE) and nutritional (MNA) status, frequency of physical exercises, use of alcohol, smoking status, comorbidity, and sunlight exposure. Only PTH level was associated with outcome variables and had a significant baseline difference between 25OHD groups, and it was used as a covariate in the analyses. Also the baseline levels of measures of PF were used as covariates in the analyses. Changes in PF during a 12-month follow-up between the 25OHD groups were compared using analysis of covariance after adjustment for group (intervention/control), PTH and baseline level of PF. In further pairwise comparisons, p-values were adjusted with Tukey’s method.
All statistical analyses were performed using SAS System for Windows, version 9.4 (SAS Institute Inc., Cary, NC, USA). P-values less than 0.05 were considered statistically significant.

3. Results

A total of 518 participants (79 men and 439 women) were included in the analysis. Excluded participants (with missing data of 25OHD and/or PF) were older, and their physical function was lower than that of included in the study. Also comorbidity was more common among those excluded from the study. Detailed data of drop-out analysis are shown in Table 1.

The baseline data of 518 participants of the study are shown in detail in Table 2. 25OHD deficiency (<50 nmol/l) was found in 20.5% of the participants. There were significant differences between the groups in 5STS and 10-m walking test in favour of those having 25OHD at least 50 nmol/l.

During a 12-month follow-up, differences in changes in knee extensor strength of both lower extremities and in 10-m walking test between the 25OHD groups were significant (Table 3). According to pairwise comparisons, these differences were between those having 25OHD <50 nmol/l and those with 25OHD ≥75 nmol/l, with the exception of left knee extensor strength in which there were also significant difference between participants with 25OHD <50 nmol/l and those with 25OHD 50–74.9 nmol/l. All differences in changes were in favour of subjects with 25OHD 50–74.9 or ≥75 nmol/l. Differences in changes in both right and left knee extensor strength, but not in 10-m walking, maintained after adjustments for group (intervention/control), parathyroid hormone and baseline level (Table 4). No significant differences between the 25OHD groups were found in changes in 5STS. There were no significant interactions between group (intervention/control) and 25OHD group (all p-values >0.119), and therefore, group (intervention/control) was not a significant modifier of the associations of the 25OHD group and the outcome variables.

Table 1
Drop-out analysis.

<table>
<thead>
<tr>
<th></th>
<th>Participants of the study (n = 518)</th>
<th>Excluded from the study (n = 71)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>72.8 (5.7)</td>
<td>78.3 (7.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>25OHD (nmol/l)</td>
<td>65.2 (17.2)</td>
<td>61.5 (18.3)</td>
<td>0.089</td>
</tr>
<tr>
<td>Parathyroid hormone (pmol/l)</td>
<td>50.3 (24.1)</td>
<td>68.0 (53.4)</td>
<td>0.007</td>
</tr>
<tr>
<td>Body mass index</td>
<td>28.8 (4.5)</td>
<td>28.3 (4.5)</td>
<td>0.425</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.0 (26.0–29.0)b</td>
<td>270 (24.0–28.0)b</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MNA</td>
<td>26.4 (1.9)</td>
<td>25.6 (2.8)</td>
<td>0.020</td>
</tr>
<tr>
<td>Extension strength of right knee (Newton)</td>
<td>317.3 (108.4)</td>
<td>268.7 (107.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extension strength of left knee (Newton)</td>
<td>311.8 (105.3)</td>
<td>251.4 (103.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Five-repetition sit-to-stand test (time in s)</td>
<td>11.9 (4.7)</td>
<td>16.1 (9.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10-m walking test (time in s)</td>
<td>7.3 (2.7)</td>
<td>12.7 (14.2)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

|                       | n (%)                               | n (%)                           |          |
| Gender                |                                     |                                 |          |
| Men                   | 79 (15)                             | 5 (21)                          |          |
| Women                 | 439 (85)                            | 58 (79)                         | 0.236    |
| Education             |                                     |                                 |          |
| More than basic       | 143 (28)                            | 16 (22)                         |          |
| Basic                 | 369 (71)                            | 54 (74)                         |          |
| Less than basic       | 6 (1)                               | 3 (4)                           | 0.108    |
| Comorbidity (≥3 diagnosed diseases) | 174 (34)                      | 15 (21)                         |          |
| No                    | 344 (66)                            | 58 (79)                         | 0.031    |
| Sunlight exposure     |                                     |                                 |          |
| Yes                   | 243 (47)                            | 31 (42)                         | 0.532    |
| No                    | 275 (53)                            | 42 (58)                         |          |
| Frequency of alcohol use |                                 |                                 |          |
| None or three times per month | 390 (75)                      | 57 (78)                         |          |
| Almost every day or daily | 128 (25)                      | 16 (22)                         | 0.664    |
| Frequency of exercise |                                     |                                 |          |
| At least several times/week | 401 (77)                      | 32 (44)                         | <0.001   |
| Not at all–2 times/week | 117 (23)                      | 40 (56)                         |          |
| Current smoking       |                                     |                                 |          |
| No                    | 502 (97)                            | 71 (97)                         |          |
| YES                   | 16 (3)                              | 2 (3)                           | 1.000    |

* Chi-squared test or Fisher’s exact test for categorical variables and Student’s T-test or Wilcoxon’s test for continuous variables.

b Values are median and interquartile range.
Table 2
Baseline characteristics of the participants by baseline 25-hydroxyvitamin D level (n = 518).

|                          | I < 50 nmol/l (n = 106) | II 50–74.9 nmol/l (n = 261) | III ≥75 nmol/l (n = 151) | p-value*
|--------------------------|--------------------------|-----------------------------|--------------------------|----------
| Mean (SD)                | Mean (SD)                | Mean (SD)                   |                          |          
| Age, years               | 73.5 (5.8)               | 72.9 (5.7)                  | 72.2 (5.4)               | 0.206    
| Knee extension, right (Newton) | 297.5 (98.6)             | 318.8 (112.2)              | 329.1 (107.1)            | 0.072    
| Knee extension, left (Newton) | 293.7 (101.0)            | 313.1 (108.3)              | 322.5 (101.9)            | 0.096    
| Five-repetition sit-to-stand test (time in s) | 13.8 (5.4)               | 11.7 (4.6)                  | 11.0 (4.0)               | <0.001c  
| 10-m walking test (time in s) | 8.0 (3.0)                | 7.3 (2.9)                   | 6.8 (1.8)                | 0.002c   
| Parathyroid hormone (pmol/l) | 61.7 (25.7)              | 50.3 (25.3)                 | 41.7 (16.1)              | <0.001c  
| Body mass index          | 29.4 (4.7)               | 29.2 (4.4)                  | 27.7 (4.5)               | 0.001    
| MMSE                     | 28.0 (26.0–29.0)d         | 28.0 (26.0–29.0)d           | 28.0 (26.0–29.0)d       | 0.488    
| MNA                      | 26.0 (21.1)              | 26.5 (18.8)                 | 26.4 (2.0)               | 0.068    
| Gender                   | n (%)                    | n (%)                       | n (%)                    |          
| Men                      | 16 (15)                  | 37 (14)                     | 26 (17)                  |          
| Women                    | 90 (85)                  | 224 (86)                    | 125 (83)                 | 0.712    
| Education                | Less than basic          | 2 (2)                       | 3 (1)                    | 1 (1)    
| Basic                    | 71 (67)                  | 191 (73)                    | 107 (71)                 |          
| More than basic          | 33 (31)                  | 67 (26)                     | 43 (29)                  | 0.683    
| Current smoking          | No                       | 101 (95)                    | 253 (97)                 | 148 (98) | 0.497    
|                           | Yes                      | 5 (5)                       | 8 (3)                    | 3 (2)    |          
| Frequency of exercise    | At least several times/week | 73 (69)               | 195 (75)                 | 133 (88) | <0.001d  
|                           | Not at all~2 times/week  | 33 (31)                     | 66 (25)                  | 18 (12)  |          
| Comorbidity              | No                       | 31 (29)                     | 93 (36)                  | 50 (33)  | 0.514    
|                           | Yes                      | 75 (71)                     | 168 (64)                 | 101 (67) |          
| Use of alcohol           | None or three times per month | 95 (90)               | 191 (73)                 | 104 (69) | <0.001b  
|                           | Almost every day or daily | 11 (10)                    | 70 (27)                  | 47 (31)  |          
| Sunlight exposure        | Yes                      | 26 (25)                     | 128 (49)                 | 89 (59)  | <0.001d  
|                           | No                       | 80 (75)                     | 133 (51)                 | 62 (41)  |          

* Chi-squared test or Fisher’s exact test for categorical variables and one-way analysis of variance or Kruskal–Wallis test for continuous variables.
  a Values are median and interquartile range.
  b Tukey-adjusted pairwise analyses between the groups: I vs. II, p < 0.001, I vs. III, p < 0.001.
  c I vs. II, p < 0.001, I vs. III, p < 0.001; II vs. III, p < 0.001.
  d I vs. II, p < 0.001; I vs. III, p < 0.001; II vs. III, p < 0.001.
  e I vs. II, p < 0.005; II vs. III, p < 0.002.
  f I vs. III, p < 0.001; II vs. III, p < 0.001.
  g I vs. II, p < 0.001; I vs. III, p < 0.001.
  h I vs. II, p < 0.001; I vs. III, p < 0.001.

4. Discussion

In our study, one fifth of community-dwelling older adults had 25OHDC deficiency (≤50 nmol/l), and lower 25OHDC concentration were associated with poorer PF in both cross-sectional and prospective analyses. Differences in PF and in changes of PF were most obvious between subjects with 25OHDC <50 nmol/l and those with 25OHDC ≥75 nmol/l.

The results of our study supported strong cross-sectional evidence on the association of 25OHDC deficiency (≤50 nmol/l) and lower PF among older subjects (Dukas et al., 2005; Gerdhen et al., 2005; Wicherts et al., 2007; Dam et al., 2009; Shahar et al., 2009; Pramyothin et al., 2009; Dretakis et al., 2010; Houston et al., 2011; Mastaglia et al., 2011; Michael et al., 2011; Boersma et al., 2012; Menant et al., 2012; Toffanello et al., 2012; Boyé et al., 2013; Gschwind et al., 2014; Janssen, Emmelot-Vonk, Verhaar, & van der Schouw, 2013). Because of the earlier cross-sectional evidence, our

Table 3
Changes in physical performance by baseline vitamin D level during a one-year follow-up (n = 518).

|                          | I < 50 nmol/l (n = 106) | II 50–74.9 nmol/l (n = 261) | III ≥75 nmol/l (n = 151) | p-value*
|--------------------------|--------------------------|-----------------------------|--------------------------|----------
| Mean (SD)                | Mean (SD)                | Mean (SD)                   |                          |          
| Knee extension, right (Newton) | 2.4 (−8.5 to 13.4)       | 14.8 (7.8–21.8)             | 20.5 (11.3–29.8)         | 0.044d   
| Knee extension, left (Newton) | −1.7 (−12.4 to 9.0)      | 14.18 (7.3–21.0)            | 19.36 (10.4–28.4)        | 0.010f   
| Five-repetition sit-to-stand test (time in s) | −2.4 (−3.0 to −18)       | −1.6 (−2.0 to −1.2)         | −1.5 (−2.1 to −1.0)      | 0.082    
| 10-m walking test (time in s) | 0.1 (−0.2 to 0.4)        | −0.3 (−0.5 to −0.1)         | −0.4 (−0.6 to −0.1)      | 0.040d   

* Analysis of covariance; adjusted for group (intervention/control).
  a Tukey-adjusted pairwise analyses between the groups: I vs. III, p = 0.036.
  b I vs. II, p = 0.039; I vs. III, p = 0.009.
  c I vs. III, p = 0.044.
main interest was to describe the association of 25OHD concentration with changes in PF during 12 months. According to the longitudinal analyses of our study, 25OHD deficiency was associated with deterioration in PF, in knee extensor strength of both lower extremities and in 10-m walking test, during the 12-month follow-up. Differences in changes in knee extensor strengths maintained even after adjustments for confounding factors. It was notably, that both baseline differences in PF and changes in PF between the groups were most obvious between those having 25OHD < 50 nmol/l and those with 25OHD > 75 nmol/l, which is consistent with some earlier studies (Wichert et al., 2007; Houston et al., 2011). Some other earlier results showed that subjects with lowest baseline 25OHD concentrations had biggest deterioration in PF over time compared to those with highest baseline 25OHD concentrations (Dam et al., 2009; Visser et al., 2003). On the other hand, in several studies (Verreault et al., 2002; Michael et al., 2011; Chan et al., 2012; Houston et al., 2012), no association between low 25OHD and changes in PF over time were found. The discrepancies among these studies could stem from a variation in the measurement of 25OHD and PF, duration of the follow-up period, as well as from differences in the study population characteristics, such as gender, race, the prevalence of low 25OHD and baseline functional status.

In our knowledge, of the earlier prospective studies, four have been conducted among Caucasian older adults. Among Chinese older men, there were no association between 25OHD and changes in PF during a 4-year follow-up. In these Chinese men, the prevalence of 25OHD deficiency was only 5.9% (Chan et al., 2012). In the Rancho Bernardo Study (RBS), lower 25OHD levels were associated with PF in longitudinal analyses in older community-dwelling women but not in men in southern California. Also in RBS, the prevalence of 25OHD deficiency was very low, and only 14% of participants had 25OHD less than 75 nmol/l (Dam et al., 2009). In the Longitudinal Aging Study Amsterdam (LASA), 99% of participants were Caucasian. In LASA, serum 25OHD levels below 50 nmol/l were associated with greater decline in PF compared with the reference group (25OHD ≥75 nmol/l) among older subjects over a 3-year follow-up (Wichert et al., 2007). Also in another LASA study (Visser et al., 2003), lower 25OHD concentration increased the risk of sarcopenia in a 3-year follow-up. In the LASA study, 25OHD deficiency was higher than that in our study: 47.6% (Wichert et al., 2007) and 9.6% (Visser et al., 2003) of participants had 25OHD less than 25 nmol/l.

The strengths of the current study were the use of cross-sectional and prospective designs, number of potential confounding factors that were investigated and reliable muscle strength and mobility measurements. The one-year follow-up was obviously a short duration to show a large change in PF. Also generalizability is a potential limitation, because most of the participants (85%) in our study were women with rather good physical function at baseline. Because of a limited amount of male participants, statistical analysis was not conducted separately for women and men. Drop-out analysis showed that excluded subjects were older, they had lower 25OHD, they had more diagnosed diseases and their physical function was worse than the PF of those included. Thus, it is possible that the association between low 25OHD and worse PF may have been underestimated.

Subjects of this study consisted of the participants of a 12-month fall prevention study. The subjects of the intervention group got a geriatric assessment, counselling and guidance in fall prevention, home hazards assessment, group physical exercise, home exercise, lectures in groups, and psychosocial groups. The subjects in the control group attended one session of counselling and guidance on specified risk factors of falling at the beginning of the follow-up (Salminen et al., 2009). Because of the original study design of the fall prevention intervention study, group (intervention/control) was used as a covariate in all analyses. From other possible confounding factors, only PTH level was associated with outcome variables and had a significant baseline difference between the 25OHD groups, and was used as a covariate in the analyses. Also the baseline PF values were used as covariates in the analyses.

5. Conclusions

In conclusion, low 25OHD concentrations predicted deterioration in PF during 12 months among community-dwelling older Finnish men and women. The results of this study and some earlier studies (Wichert et al., 2007; Houston et al., 2011) indicated that 25OHD should be at least 75 nmol/l in order to prevent decline in PF among community-dwelling older people.

Conflict of interest

None.

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