Low 25-Hydroxyvitamin D Predicts the Onset of Mobility Limitation and Disability in Community-Dwelling Older Adults: The Health ABC Study

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Background. Although low 25-hydroxyvitamin D (25(OH)D) is prevalent among older adults and is associated with poor physical function, longitudinal studies examining vitamin D status and physical function are lacking. We examined the association between 25(OH)D, parathyroid hormone (PTH), and the onset of mobility limitation and disability over 6 years of follow-up in community-dwelling, initially well-functioning older adults participating in the Health, Aging and Body Composition study (n = 2,099).

Methods. Serum 25(OH)D and PTH were measured at the 12-month follow-up visit (1998–1999). Mobility limitation and disability (any/severe difficulty walking 1/4 mile or climbing 10 steps) was assessed semiannually over 6 years of follow-up. The association between 25(OH)D, PTH, and mobility limitation and disability was examined using Cox proportional hazard regression models adjusted for demographics, season, behavioral characteristics, and chronic conditions.

Results. At baseline, 28.9% of the participants had 25(OH)D <50 nmol/L and 36.1% had 25(OH)D of 50 to <75 nmol/L. Participants with 25(OH)D <50 and 50 to <75 nmol/L were at greater risk of developing mobility limitation (HR (95% CI): 1.29 (1.04–1.61) and 1.27 (1.05–1.53), respectively) and mobility disability (HR (95% CI): 1.93 (1.32–2.81) and 1.30 (0.92–1.83), respectively) over 6 years of follow-up compared with participants with 25(OH)D ≥75 nmol/L. Elevated PTH, however, was not significantly associated with developing mobility limitation or disability.

Conclusions. Low 25(OH)D was associated with an increased risk of mobility limitation and disability in community-dwelling, initially well-functioning black and white older adults. Prevention or treatment of low 25(OH)D may provide a pathway for reducing the burden of mobility disability in older adults.

Key Words: 25-hydroxyvitamin D—Mobility limitation—Vitamin D—Parathyroid hormone.

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Limitations in physical function in older adults strongly predict future disability resulting in dependency, institutionalization, greater health care costs and utilization of health care services, poor health outcomes, and mortality (1). With a growing older population, there is an increasing need to identify potentially modifiable risk factors for the onset of limitations in physical function. A growing body of literature suggests that low 25-hydroxyvitamin D (25(OH)D) may accelerate the disablement process through both direct effects on muscular function (2) as well as indirectly through the onset of chronic conditions such as diabetes, hypertension, cardiovascular disease, impaired pulmonary function, and osteoarthritis (3). However, current Institute of Medicine recommendations for vitamin D intake and 25(OH)D concentrations are based only on bone health (4). Several factors put older adults at risk of low 25(OH)D, including low dietary intake, reduced exposure to UVB radiation, and reduced efficiency of cutaneous vitamin D synthesis (5,6). Recent data from the National Health and Nutrition Examination Surveys (NHANES) 2001–2006 show that low 25(OH)D is common in community-dwelling older adults (>70 years) with approximately 31% of older men and 38% of older women having 25(OH)D <50 nmol/L (to convert to ng/mL, divide by 2.496) (7).
In general, observational studies have shown that low 25(OH)D is associated with lower physical performance and strength in older adults (8–14), measures that are predictive of subsequent mobility disability (15). However, the association between low 25(OH)D and change in physical performance and strength over time has been inconsistent (16–21), with some studies showing greater declines in physical performance and others finding no association. Low 25(OH)D has also been associated with prevalent self-reported limitations in mobility among older adults (10,22). We recently showed that low 25(OH)D is associated with incident mobility limitation over 3 years of follow-up among the oldest old (23). However, whether low 25(OH)D is associated with the onset of mobility limitation and disability in younger, initially well-functioning older adults is unknown. Serum 25(OH)D may also indirectly affect physical function via hyperparathyroidism secondary to low 25(OH)D concentrations (5). Previous studies show elevated parathyroid hormone (PTH) is associated with lower physical performance and strength (11,14,24,25).

The primary objective of these analyses was to examine the association between 25(OH)D and incident mobility limitation and disability over 6 years of follow-up using data from the Health, Aging, and Body Composition (Health ABC) study. The role of PTH, both independently and as a contributor to low 25(OH)D, on incident mobility limitation and disability was also examined.

**METHODS**

**Study Population**

Data for this analysis are from the Health ABC study; a prospective cohort study investigating the associations between body composition, weight-related health conditions, and incident functional limitations in older adults. The Health ABC study enrolled 3,075 community-dwelling black and white men and women aged 70–79 between April 1997 and June 1998. Participants were recruited from a random sample of white and all black Medicare eligible residents in the Pittsburgh, PA, and Memphis, TN, metropolitan areas. Participants were eligible if they reported no difficulty walking one fourth of a mile, climbing 10 steps, or performing basic activities of daily living, were free of life-threatening illness, planned to remain in the geographic area for at least three years, and were not enrolled in lifestyle intervention trials. All participants provided written informed consent, and all protocols were approved by the institutional review boards at both study sites.

Participants with Year 2 data (1998–1999), when dietary intake and 25(OH)D and PTH were measured, served as the baseline population for this analysis (n = 2,998). Participants with prevalent mobility limitation at Year 2 (n = 648), those who lacked 25(OH)D (n = 124), and those who were missing pertinent covariates were excluded (n = 127). The final analysis sample included 2,099 participants.

**Assessment of 25(OH)D and PTH**

Fasting blood samples at the Year 2 clinic visit were collected in the morning after a 12-hour fast, centrifuged, and stored at −80°C. Serum 25(OH)D was measured using a two-step radioimmunoassay (25-Hydroxyvitamin D 125I RIA Kit, DiaSorin, Stillwater, MN, USA) in a laboratory meeting the Vitamin D External Quality Assessment Scheme quality criteria. Intact PTH was measured in EDTA plasma with a two-site immunoradiometric assay kit (N-tact PTHSP, DiaSorin, Stillwater, MN, USA). The interassay coefficients of variation for serum 25(OH)D and plasma PTH were 6.8% and 8.6%, respectively. Serum 25(OH)D was categorized as <50 nmol/L, 50 to <75 nmol/L, and ≥75 nmol/L based on recent recommended cutpoints from the Endocrine Society (26). Following analyses from NHANES (27), elevated PTH was defined as ≥70 pg/mL. PTH tertiles of approximately equal numbers in the normal range were created to give four PTH categories: 27 pg/mL, 27 to ≤38 pg/mL, 38 to ≤70 pg/mL, and ≥70 pg/mL.

**Mobility Limitation and Disability**

Occurrence of mobility limitation and disability during follow-up was assessed during annual clinic visits alternating with telephone interviews every 6 months. Persistent mobility limitation was defined as two consecutive reports of having any difficulty walking one fourth of a mile or climbing 10 steps without resting due to a health or a physical problem. Persistent mobility disability was defined as two consecutive reports of having severe difficulty or inability to perform these tasks. Incident cases of mobility limitation and disability were ascertained over 6 years with a median follow-up of 5.3 years.

**Potential Confounders**

Demographic characteristics (age, gender, race, and education), smoking status, alcohol intake, and physical activity were ascertained by an interviewer-administered questionnaire. Physical activity was based on the reported time spent walking for exercise or other walking (e.g., for transportation) over the past 7 days. Body mass index (BMI; kg/m²) was calculated from measured weight and height. The season during which the blood sample was obtained was included to account for seasonal effects on 25(OH)D and PTH. Participants were asked to bring all medications and supplements they were currently taking to their clinic visit. Supplements containing more than three vitamin or mineral ingredients were considered a multivitamin. Vitamin D–containing supplements were defined as supplements containing three or fewer ingredients, one of which was vitamin D. Depressive symptoms were measured using the 20-item Center for Epidemiologic Studies Depression Scale. The Modified Mini-Mental State Examination (3MS) was used as an indicator of general cognitive status.
Glomerular filtration rate (eGFR) was estimated from serum creatinine using the Modification of Diet in Renal Disease formula. Knee pain on most days for at least 1 month in the past year, an indicator of knee osteoarthritis, was assessed by self-report. The prevalence of diabetes, cardiovascular disease (coronary heart disease or stroke), and chronic obstructive pulmonary disease were determined using algorithms based on self-report and medication use. Usual walking speed over 20 m was assessed as an objective measure of physical performance. A walking index score ranging from 0 to 9 (best) was based on self-reported difficulty and ease of walking one fourth mile and, if no difficulty walking one fourth mile, ease of walking 1 mile (28). Education, smoking status, depressive symptoms, cognitive function, and renal function were measured at the baseline clinic visit; all other covariates were measured at the Year 2 clinic visit when 25(OH)D was measured.

**Statistical Analyses**

The association between categories of 25(OH)D and participant characteristics were analyzed using chi-square tests for categorical variables and analysis of variance for continuous variables. The cumulative incidence of mobility limitation and disability were calculated using the Kaplan–Meier method. Cox proportional hazard regression models were used to examine the associations between 25(OH)D and PTH categories and risk of incident mobility limitation and disability. Participants who survived with no evidence of incident mobility limitation or disability, respectively, were censored at their next to the last 6-month contact. Participants who died with no evidence of incident mobility limitation or disability, respectively, were censored at their time of death; and those who were lost to follow-up were censored at their last visit. Tests for linear trends across categories of 25(OH)D and PTH were conducted using the median of each category as a continuous variable in the model. Two-way interactions between gender and 25(OH)D or PTH and race and 25(OH)D or PTH were tested but were not significant; thus, risk of mobility limitation is presented in the total sample. The minimally adjusted models include age, gender, race, field center, education, and season. The fully adjusted models also include smoking status, alcohol intake, physical activity, BMI, kidney function, cognitive function, depressive symptoms, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, knee pain, multivitamin use, and vitamin D supplementation. Additional models included walking speed or self-reported walking index and a model with both 25(OH)D and PTH. The proportional hazards assumption was met for all models. Because mobility limitation and disability were collected every 6 months, we also examined the association between 25(OH)D, PTH, and mobility limitation and disability using an interval-censored model. The results were similar; thus, only the results from the Cox proportional hazards models are shown. All analyses were conducted using SAS version 9.2 (SAS Institute; Cary, NC).

**Results**

The mean age of the study population (n = 2,099) was 74.6 years, 47.9% were women, and 34.9% were black. Participants excluded from the present analysis (n = 251, 10.7%) were not significantly different from those included in the analyses as far as age, gender, race, education, or 25(OH)D. However, those excluded were more likely to be from the Pittsburgh site and have their 25(OH)D measured in the spring (p < .01). The descriptive characteristics of the study population by 25(OH)D category are shown in Table 1. Approximately 35.0% of participants had 25(OH)D ≥75 nmol/L, 36.1% had 25(OH)D of 50 to <75 nmol/L, and 28.9% had 25(OH)D <50 nmol/L. Women, blacks, participants with less than a high school education, current smokers, nondrinkers, participants who did not report walking for physical activity in the past week, and participants with diabetes or chronic obstructive pulmonary disease were more likely to have 25(OH)D less than 50 nmol/L. Participants with 25(OH)D less than 50 nmol/L were also more likely to have had 25(OH)D measured in the winter or spring, have a higher BMI, and PTH, and have lower cognitive function. However, participants who reported taking multivitamins or vitamin D–Containing supplements were more likely to have 25(OH)D ≥75 nmol/L. Observed walking speed as well as self-reported walking ability were both lower among participants with 25(OH)D <50 nmol/L.

Of the 2,099 participants, 738 reported having mobility limitation and 245 reported having mobility disability over 6 years of follow-up for a cumulative incidence of mobility limitation of 36.3% and of mobility disability of 22.0%. The hazard ratios (95% confidence intervals) of incident mobility limitation and mobility disability by 25(OH)D category are shown in Table 2. Participants with 25(OH)D <50 nmol/L and 50 to <75 nmol/L were at significantly increased risk of incident mobility limitation and disability compared with those with 25(OH)D ≥75 nmol/L in the minimally adjusted model. After adjusting for health behaviors and chronic conditions, the association between 25(OH)D and risk of mobility limitation was attenuated but remained significant. For mobility disability, 25(OH)D <50 nmol/L was significantly associated with increased risk of mobility disability after adjusting for health behaviors and chronic conditions. Results were similar after further adjustment for baseline walking speed or self-reported walking ability as well as after adjusting for PTH (data not shown).

Table 3 shows the hazard ratios (95% confidence intervals) of incident mobility limitation and mobility disability by PTH category. Participants with elevated PTH (≥70 pg/mL) were at significantly increased risk of incident mobility limitation and disability compared with those with PTH
Table 2. Incident Mobility Limitation and Disability (HR (95% CI)) by PTH Category: The Health ABC Study.

<table>
<thead>
<tr>
<th>PTH Category</th>
<th>&lt;50 pmol/L</th>
<th>50 to &lt;75 pmol/L</th>
<th>≥75 pmol/L</th>
<th>p Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Model 2</td>
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<td>1.00</td>
<td>1.00</td>
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<tr>
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<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
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<tr>
<td>Model 4</td>
<td>1.00</td>
<td>1.00</td>
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<td>1.00</td>
</tr>
</tbody>
</table>

Note: *Model 1 is adjusted for age, race, gender, education (<high school education vs ≥high school education), site (Memphis vs Pittsburgh), and season (winter, summer, or fall).
Table 3. Incident Mobility Limitation and Disability (HR (95% CI)) by PTH Category: The Health ABC Study.

<table>
<thead>
<tr>
<th>PTH Category</th>
<th>Model 1*</th>
<th>Model 2†</th>
<th>Model 3‡</th>
<th>Model 4§</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;27 pg/mL</td>
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<td>1.10</td>
<td>1.19</td>
<td>1.00</td>
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<tr>
<td>27 to &lt;38 pg/mL</td>
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<td>1.04</td>
<td>1.03</td>
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<tr>
<td>38 to &lt;70 pg/mL</td>
<td>1.00</td>
<td>1.03</td>
<td>0.97</td>
<td>1.00</td>
</tr>
<tr>
<td>≥70 pg/mL</td>
<td>1.00</td>
<td>1.09</td>
<td>0.98</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Note: PTH = parathyroid hormone.
* Model 1 is adjusted for age, race, gender, education (<high school education vs ≥high school education), site (Memphis vs Pittsburgh), and season (winter, spring, summer, or fall).
† Model 2 is adjusted for variables in model 1 plus smoking (current vs never/former smoker), alcohol consumption (none in past year, ≤1 drink/day, or >1 drink/day), physical activity (0 min, 1–149 min, or ≥150 min per wk), body mass index, cognitive function (3MS score), depressive symptoms (Center for Epidemiologic Studies Depression score), kidney function (eGFR), prevalent diabetes, cardiovascular disease, or chronic obstructive pulmonary disease, knee pain, vitamin D-containing supplement use and multivitamin use.
‡ Model 3 is adjusted for variables in Models 1 and 2 plus 20-m walking speed.
§ Model 4 is adjusted for variables in Models 1 and 2 plus self-reported walking index score.

**Discussion**

Low 25(OH)D was associated with greater risk of incident mobility limitation and disability over 6 years of follow-up among initially well-functioning, community-dwelling black and white older adults. After adjusting for demographics, health behaviors and chronic conditions, there was approximately a 30% increased risk of mobility limitation among older adults with 25(OH)D <75 nmol/L and approximately a two-fold increased risk of mobility disability among older adults with 25(OH)D <50 nmol/L. Elevated PTH (≥70 pg/mL) was associated with greater risk of incident mobility limitation and disability in the minimally adjusted model; however, elevated PTH was no longer associated with incident mobility limitation or disability after adjusting for health behaviors and chronic conditions. PTH did not appear to mediate the association between 25(OH)D and mobility limitation or disability.

Longitudinal studies examining the association between baseline 25(OH)D and PTH and change in objectively measured physical performance, predictive of subsequent mobility disability (15), have been inconsistent, showing either greater declines in physical performance among those with low 25(OH)D or elevated PTH (18,20,21) or no association (16,17,19). In the Longitudinal Aging Study Amsterdam, older adults with 25(OH)D <50 nmol/L had a twofold or greater decline in physical performance over 3 years compared with those with 25(OH)D ≥75 nmol/L (18). However, in the InCHIANTI study, 25(OH)D was not associated with change in physical performance over 3 years (19). The discrepancies among these studies may stem from assay-dependent variation in the measurement of 25(OH)D as well as differences in the study population characteristics.

Previous studies have also shown that low 25(OH)D is more prevalent among older adults with mobility limitations (10,22). However, the cross-sectional design of these studies makes it difficult to determine whether low 25(OH)D preceded the onset of mobility limitation or whether individuals had low 25(OH)D because they were limited in mobility and thus, had limited outdoor activity, less exposure to the sun, and consequently reduced endogenous vitamin D synthesis. We recently showed that low 25(OH)D was associated with both prevalent mobility limitation as well as incident mobility limitation over 3 years of follow-up in the CHS All Stars (mean age, 85.2 years) (23). Our results from Health ABC showing an increased risk of mobility limitation and disability over 6 years of follow-up in older adults with low 25(OH)D extend our earlier findings in the CHS All Stars to younger (mean age, 74.6 years), initially well-functioning (mean short physical performance battery score of 10.3 vs 7.5 of the highest possible score of 12) older adults.

The Institute of Medicine has suggested that 25(OH)D concentrations of 50 nmol/L or higher are adequate for bone and overall health (4); however, others have suggested that the optimal 25(OH)D concentration for health conditions other than bone may indeed be higher (26,29,30). In Health ABC, older adults with 25(OH)D <50 nmol/L were at increased risk of mobility limitation and disability and those with 25(OH)D between 50 and 75 nmol/L were at increased risk of mobility limitation compared with those with 25(OH)D ≥75 nmol/L. This suggests that for mobility, higher 25(OH)D concentrations than those suggested by the Institute of Medicine may be optimal.

The strengths of the Health ABC study are that it is a large study of community-dwelling older adults with excellent retention who were extensively characterized providing an unusually rich set of relevant covariates. However, there are important characteristics of Health ABC, which limit the generalization of these findings. Participants were recruited...
to be well-functioning and free of mobility limitation at baseline; thus, these results may not be generalizable to the general older population. Another limitation is the use of self-reported mobility limitation and disability as the primary end points. However, previous studies have shown that self-reported limitations in mobility are valid and have clinical significance (31). Furthermore, the use of two consecutive reports of mobility limitation or disability reduces the influence of transient mobility limitation and disability. Blood samples were collected in 1998–1999 when the vitamin D content of multivitamins was low and the use of individual vitamin D supplements was also low likely resulting in lower 25(OH)D concentrations than would be found currently. Serial measures of 25(OH)D and PTH are not available in Health ABC; thus, we are unable to account for changes in 25(OH)D and PTH over time. Participants with low 25(OH)D concentrations were more likely to have slower walking speed and a lower walking index score at baseline. Although results were similar when those in the bottom 10th percentile of walking speed were excluded from the analyses, we cannot completely rule out the possibility of reverse causality. Low 25(OH)D may result in mobility limitation and disability given vitamin D’s influence on muscle cell metabolism including calcium transport, uptake of inorganic phosphate for the production of energy-rich phosphate compounds, and protein synthesis (2). We cannot, however, rule out the possibility that the association between 25(OH)D and mobility limitation and disability was due, in part, to the effects of low 25(OH)D on interim falls and/or fractures. Lastly, the observational nature of this study does not allow us to evaluate a causal association between 25(OH)D and mobility limitation and disability.

In conclusion, low 25(OH)D was common in this initially well-functioning cohort of older black and white men and women and was associated with both incident mobility limitation and disability. Serum 25(OH)D less than 75 nmol/L was associated with an increased risk of mobility limitation, which is consistent with other health outcomes where 25(OH)D concentrations of 75–80 nmol/L or higher may be optimal (26,29,30). Given that remediation of low 25(OH)D can be done easily and inexpensively with vitamin D supplements, definitive trials of vitamin D supplementation are needed to determine whether increasing 25(OH)D in older adults can improve or prevent further declines in physical function and mobility in particular.

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**References**

VITAMIN D AND MOBILITY DISABILITY


