Association Between Vitamin D Status and Physical Function in the Severely Obese

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Context: Mortality is 85% higher in severely obese subjects (body mass index [BMI] $>$ 40 kg/m^2) than in subjects with a healthy BMI; poor physical function may be contributory. Hypovitaminosis D is common in obese subjects and is associated with physical dysfunction in the elderly.

Objective: We determined the relationship between vitamin D status and physical function in severely obese subjects.

Design, Setting, and Patients: We conducted a clinic-based, cross-sectional study of severely obese subjects. Participants were stratified into three groups according to the Institute of Medicine (IOM) vitamin D status categorization.

Main Outcome Measures: We compared levels of self-reported activity and times taken to walk 500 m and to ascend and descend a 17-cm step 50 times.

Results: We recruited 252 subjects (age, 43.7 $\pm$ 11.2 y; BMI, 50.7 $\pm$ 9.7 kg/m^2); 25-hydroxyvitamin D (25OHD) concentrations were less than 30 nmol/L in 109 participants. Participants with a 25OHD $>$ 50 nmol/L, compared to those with a 25OHD $<$ 30 nmol/L, had the highest activity levels (3.1 $\pm$ 3.4 h/wk versus 1.5 $\pm$ 2.5 h/wk; $P = .015$) and the shortest 500-m walk times (6.2 $\pm$ 1.1 min versus 7.4 $\pm$ 1.5 min; $P = .003$). Serum 25OHD concentrations had a weakly positive association with activity level ($r = 0.19$; $P = .008$) and a moderately negative association with 500-m walk time ($r = -0.343$; $P < .001$).

Conclusions: Vitamin D status had a significant relationship with physical activity and physical function in this cohort of severely obese subjects. Low activity levels are likely to perpetuate the problem of hypovitaminosis D due to less time spent outdoors. Studies exploring the effects of vitamin D supplementation in this population are warranted. (***J Clin Endocrinol Metab*** **99: E1327–E1331, 2014)**

Severe obesity (body mass index [BMI] $>$ 40 kg/m^2) affects 1.9% of Irish adults (1) and 6.5% of American adults (2), and it confers an 85% increase in mortality (3). Individuals with severe obesity are eight times more likely to have suboptimal physical function than subjects with a healthy BMI (4). Regardless of obesity, subjects with lower physical function scores have reduced quality of life and elevated mortality (5).

Vitamin D is considered to be important for normal muscle function. Approximately 60% of severely obese subjects have a 25-hydroxyvitamin D (25OHD) concentration below 50 nmol/L, and 25OHD concentrations correlate inversely with BMI (6, 7). Sequestration of vitamin D in body fat may explain the high prevalence of hypovitaminosis D among the obese and the lesser response to supplementation (8). Like subjects with severe obesity,

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Abbreviations: BMI, body mass index; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein-cholesterol; 25OHD, 25-hydroxyvitamin D; T2DM, type 2 diabetes mellitus.

subjects with hypovitaminosis D tend to be less active and score lower on tests of physical performance (9). So, it is conceivable that poor vitamin D status adversely affects physical function in obesity. Given the role of reverse causation of obesity on vitamin D status due to poor supply, an iterative paradigm could be envisaged of poor vitamin D status resulting in poor physical function that in turn results in poor sunlight exposure.

Physical function is assessed routinely in subjects attending our hospital-based weight management clinic. Our clinic receives referrals from all over Ireland, and the only criterion for referral acceptance is a BMI greater than 40 kg/m^2. We aimed, therefore, to determine the relationship between vitamin D status with physical activity and with physical function in subjects with severe obesity. We hypothesized that physical activity level and physical function are worse in those with hypovitaminosis D than in their nonaffected counterparts.

Subjects and Methods

Study population

We recruited subjects with severe obesity (BMI $>$ 40 kg/m^2) aged 18 to 75 years during their initial clinic attendance between the months of October 2010 and November 2011 inclusive. We excluded only subjects using mobility aids and those who reported the use of calcium or vitamin D therapy. Based on their serum 25OHD concentration, participants were allocated to one of three groups according to North American Institute of Medicine (IOM) risk categorization (10): 1) at risk of deficiency (25OHD $<$ 30 nmol/L); 2) within range of adequacy (25OHD 30–50 nmol/L); and 3) above adequacy threshold (25OHD $>$ 50 nmol/L) (11). Written informed consent was obtained from all participants, and the study protocol was approved by the St Vincent's Healthcare Group Ethics and Medical Research Committee.

Assessments

Medical and lifestyle information was collected using a standard proforma. Height and weight were measured to the nearest 0.5 cm and 0.1 kg, respectively, while the participant was standing erect and wearing shoes, using an electronic stadiometer and an electronic scale (both from Seca). Physical function was assessed if the participant was willing to undergo this assessment and had no contraindications to exercise. We recorded the time taken to walk around a 500-m mapped-out path and the time taken to ascend and descend a single step that was 17-cm high 50 times. Participants were instructed to exert themselves to a level they found "slightly challenging" or to less than point 6 on a 10-point Borg Rating of Perceived Exertion (12).

Blood was collected before physical function assessment, between the hours of 8 and 11 AM, after an overnight fast lasting at least 12 hours. Serum was isolated within 2 hours of collection and was stored at 4°C or −20°C until analyzed. All laboratory assays were performed within a fortnight of blood collection. Serum 25OHD concentrations were measured using a commercially available competitive RIA kit (Immunodiagnostic Systems Ltd) in the Metabolism Laboratory of St Vincent's University Hospital. The interassay coefficients of variation for this assay, at concentrations of 28.8 and 105.4 nmol/L, were 6.2 and 7.7%, respectively. The intra-assay coefficients of variation for these assays, at concentrations of 28.9 and 73.9 nmol/L, were 3.0 and 2.7%, respectively. To ensure a high standard of analysis, we participate in the Vitamin D External Quality Assessment Scheme (13). Serum calcium, alkaline phosphatase, creatinine, total cholesterol, high-density lipoprotein-cholesterol (HDL-C), and glucose concentrations were measured using standardized and automated Roche assays. Glycated hemoglobin (HbA1c) was determined using a Diabetes Control and Complications Trial calibrated HPLC assay on a Tosoh G7 automated analyzer.

A participant was considered to have a diagnosis of type 2 diabetes mellitus (T2DM) if one of the following criteria was met: 1) fasting plasma glucose concentration greater than 7 mmol/L; 2) HbA1c level greater than 6.5%; or 3) a previous diagnosis of T2DM. A participant was considered to have chronic illness if he/she had a diagnosis of T2DM, obstructive sleep apnea syndrome, and/or cardiovascular disease.

Statistical analysis

All statistical analyses were performed using IBM SPSS for Windows version 20 (IBM). Continuous variables were compared between groups using ANOVA and, to adjust for possible confounding variables, analyses of covariance. Dichotomous variables were compared using the χ^2 test, and multivariable logistic regression analyses were used to adjust for possible confounders. For continuous variables that differed significantly between groups, multiple comparison post hoc analyses were performed using Fisher's least significant differences method. In addition, the relationship of these variables with 25OHD concentrations was determined using Pearson's correlation analyses and using multiple linear regression analyses to adjust for possible confounding variables. Possible confounding variables were identified by multivariable logistic regression analyses including initially those variables with a P value less than .25 on single variable logistic regression analyses and thereafter removing those variables with a Wald statistic greater than 0.25 (see Supplemental Tables 1 and 2). Possible confounding variables were identified also through multiple linear regression analysis including those variables with a P value less than .05 on Pearson's correlation analyses (see Supplemental Tables 3 and 4). The level of statistical significance was set at less than 0.05 for all analyses.

Results

Characteristics of the study population (Table 1)

We recruited 252 subjects with severe obesity into this study. They were aged 43.7 ± 11.2 years, and their BMI was 50.7 ± 9.7 kg/m^2. Just over 40% of the participants were male, and just over 35% had T2DM. Forty-three percent (n = 109) of the cohort had a serum 25OHD concentration less than 30 nmol/L.

Table 1. Participant Characteristics

Parameter	n	At Risk of Deficiency (25OHD < 30 nM)	Within Adequacy Range (25OHD = 30–50 nM)	Above Adequacy Threshold (25OHD > 50 nM)	P^a	P^b	P^c
n		109	96	47			
Age, y	252	42.8 ± 11.4	44.1 ± 10.9	45.2 ± 11.3	.442		
BMI, kg/m^2	251	54.0 ± 11.3	49.2 ± 7.3	46.2 ± 7.4	<.001		
Male, n (%)	252	44 (40.4)	41 (42.7)	16 (34.0)	.609		
Autumn or winter, n (%)[d]	252	70 (64.2)	58 (60.4)	25 (53.2)	.432		
Diabetes, n (%)	249	42 (38.5)	35 (37.2)	11 (23.9)	.196	.190	
Chronic illness, n (%)	242	54 (49.5)	45 (51.7)	15 (32.6)	.087	.111	
Calcium, mmol/L	249	2.34 ± 0.09	2.33 ± 0.10	2.37 ± 0.10	.112	.058	
Serum 25OHD, nmol/L	252	23.1 ± 4.1	37.9 ± 5.5	60.7 ± 10.0	<.001	<.001	<.001
Serum ALP, IU/L	250	94 ± 31	89 ± 25	97 ± 41	.270	.134	.409
eGFR, ml/min/1.73 m^2	250	107 ± 30	103 ± 28	97 ± 24	.123	.617	.992
FPG, mmol/L	246	6.4 ± 2.4	6.1 ± 2.0	5.9 ± 2.7	.487	.543	.635
Plasma HbA1c, %	248	6.4 ± 1.5	6.2 ± 1.2	6.1 ± 1.3	.473	.834	.931
Serum TC/serum HDL-C	238	4.4 ± 1.1	4.3 ± 1.1	4.1 ± 1.0	.358	.461	.497
sBP, mm Hg	241	134 ± 18	133 ± 18	131 ± 16	.514	.935	.918
Activity level, h/wk	184	1.5 ± 2.5	1.4 ± 2.1	3.1 ± 3.4	.004	.008	.015
50 step test completed, n (%)	196	61 (74.4)	67 (83.8)	31 (91.2)	.081	.929	.747
50-step time (s)	159	123 ± 29	112 ± 25	112 ± 23	.036	.083	.143
500-m walk completed, n (%)	240	72 (67.9)	71 (79.8)	32 (71.1)	.171	.230	.347
500-m walk time, min	174	7.4 ± 1.5	6.8 ± 1.1	6.2 ± 1.1	<.001	.015	.003

Abbreviations: eGFR, estimated glomerular filtration rate; ALP, alkaline phosphatase; sBP, systolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol. Data are expressed as mean ± SD or as number (percentage).

[a] *P* values were calculated using ANOVA or χ^2 test.

[b] *P* values were calculated using analyses of covariance or multivariate logistic regression analyses adjusting for age, BMI, and gender.

[c] *P* values were calculated using analyses of covariance or multivariate logistic regression analyses adjusting for age, BMI, gender, chronic illness (including diabetes), and serum calcium concentrations.

[d] If assessment was performed between October and March inclusive.

Relationship of vitamin D status with measured parameters (Table 1)

When the participants were divided into three groups according to their serum 25OHD concentration, the mean BMI was lowest in those with a 25OHD greater than 50 nmol/L. There was no difference in the prevalence of T2DM or chronic illness between the groups. Similarly, there were no associations between vitamin D status with blood pressure, with HbA1c, with total cholesterol to HDL-C ratio, with estimated glomerular filtration rate, or with blood concentrations of calcium, alkaline phosphatase, or glucose. Levels of physical activity were highest and times taken to walk 500 m were shortest among those with a 25OHD greater than 50 nmol/L (Figure 1). Con-

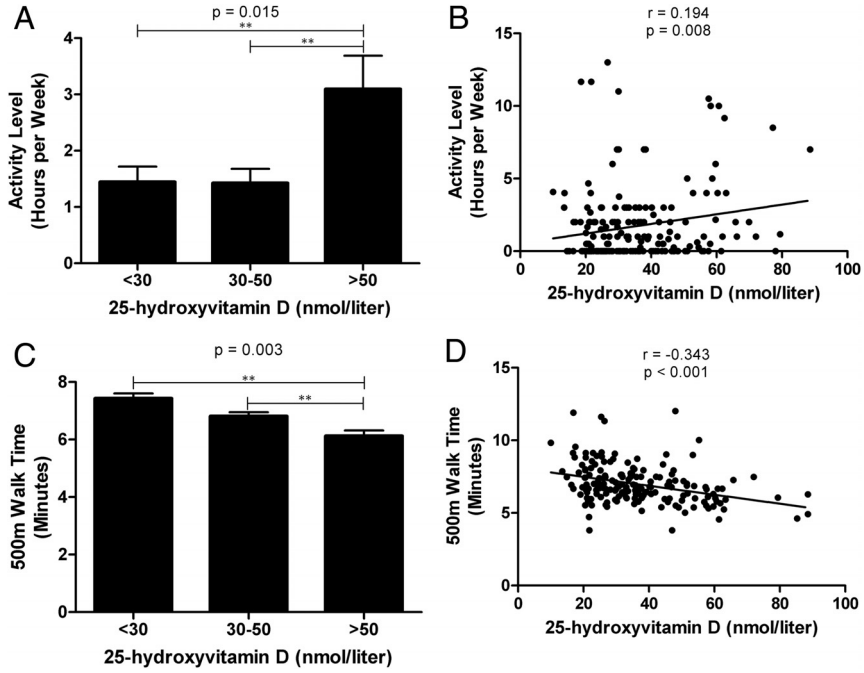

Figure 1. Associations between 25OHD concentrations and self-reported hours of activity level (A and B) and the times taken to walk 500 m at a moderately intense pace (C and D). For between-group comparisons (A and C), data are expressed as means (upper boundary of columns) and SEM (error bars). *P* values for between-group comparisons were determined using analyses of covariance, adjusting for age, BMI, gender, chronic illness, and serum calcium concentration. Family-wide type 1 error rate was controlled using Fisher's least significant differences method. The associations between 25OHD and activity level (B) and 500-m walk (D) were determined by Pearson's correlation analyses. These associations remained significant after using multiple linear regression analyses adjusting for age, BMI, and serum calcium concentration. **, $P < .01$ on post hoc analyses. r, coefficient of correlation.

gruently, 25OHD correlated positively with physical activity levels and negatively with 500-m walk times (Figure 1). These relationships remained significant after adjustment for potential confounders ($\beta = 0.166$, $P = .036$; and $\beta = -0.375$, $P < .001$, respectively; Supplemental Table 3).

Discussion

In this study of 252 severely obese subjects, physical activity levels were highest and physical function was best in the 19% of participants with a 25OHD concentration greater than 50 nmol/L. These participants were able to walk 500 m 15% more quickly, on average, than their counterparts who had a 25OHD concentration less than 50 nmol/L. After adjustment for confounders, serum 25OHD concentrations had significant associations with weekly activity duration and with 500-m walk time. This is the only study designed specifically to determine whether vitamin D status is associated with markers of physical inactivity or of physical dysfunction in subjects with severe obesity.

The limitations of this study include use of submaximal measures of physical function, limited ability to generalize the findings, and the cross-sectional design. We chose to use self-paced step and walking tests because these compare well with physical function and with mortality (5). Self-paced walking tests have been used previously to assess physical function in subjects with severe obesity (14) and in subjects with hypovitaminosis D (9). More than 95% of research participants were white; whether similar results would be found in other ethnic groups remains to be determined. In addition, the study findings may be peculiar to high-risk countries like Ireland where, despite substantial improvements over the past 30 years, poor vitamin D status remains a problem (15–18). The cross-sectional design of the study makes it impossible to exclude the possibility that those who were more active had higher 25OHD due to increased sun exposure.

Our findings are in keeping with those of the existing literature. National Health and Nutrition Examination Survey III studied 4100 ambulatory adults aged greater than 60 years and found that those with higher 25OHD concentrations were able to complete a timed walk test more quickly (9). Similarly, 25OHD concentrations correlate with physical activity levels in subjects with end-stage kidney disease and in postmenopausal women (19, 20). About 60% of subjects with severe obesity seeking bariatric surgery had a 25OHD level less than 50 nmol/L (6, 7).

Our findings suggest that part of the physical inactivity and physical dysfunction associated with severe obesity may be due to poor vitamin D status. Moreover, it may be that vitamin D therapy can improve these parameters in this population. Prospective, interventional studies are required to evaluate this possibility. We conclude that physical inactivity and physical dysfunction are common among subjects with severe obesity and that vitamin D therapy, for those with hypovitaminosis D, is likely to prevent disability in this population.

Acknowledgments

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