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Relation of Vitamin D Level to Maximal Oxygen Uptake in Adults

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Abstract

Both low cardiorespiratory fitness and low serum vitamin D levels are associated with increased cardiovascular and all-cause mortality, but whether low vitamin D is independently associated with cardiorespiratory fitness in healthy adults is not known. We examined vitamin D levels and fitness in 200 healthy adults, participating in a double-blind clinical trial investigating statins and muscle performance (the STOMP study). Maximal aerobic exercise capacity (VO₂max) was measured using metabolic gas analysis during graded treadmill exercise to exhaustion. Vitamin D [25(OH)D] was measured using enzyme-linked immunosorbent assay (ELISA). Daily physical activity was assessed using the Paffenbarger Physical Activity Questionnaire. Serum 25(OH)D concentration was positively related to VO₂max ($r = 0.29$, $p = 0.0001$), even after adjusting for relevant predictors (e.g., age, gender and body mass index) ($p = 0.0004$). There was also a significant interaction between 25(OH)D level and self-reported hours of moderate to vigorous physical activity (MVPA) ($p < 0.02$). With each standard deviation increase in vitamin D, VO₂max increased by 2.6 ml/kg/min ($p = 0.0001$) when MVPA was low (16 hr/wk), 1.6 ml/kg/min ($p = 0.0004$) when MVPA was moderate (35 hr/wk), but only 0.07 ml/kg/min ($p = 0.9$) when MVPA was high (64 hr/wk). In conclusion, serum vitamin D levels predict VO₂max in adults; the effect is greatest among those with low levels of physical activity.

Keywords

Vitamin D level; VO₂max

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Vitamin D deficiency is present in approximately 50% of US adults¹² and is associated with increased cardiovascular (CV) events and overall mortality.³⁴⁵ Vitamin D deficiency may affect CV morbidity and mortality via its effect on cardiovascular risk factors, such as elevated blood pressure and the incidence of Type II diabetes.⁶⁷⁸ Poor cardiorespiratory fitness is an additional independent risk factor for CV morbidity and mortality,⁹¹⁰ and cardiorespiratory fitness, measured as maximal oxygen consumption or VO_2max , has recently been shown to be directly related to serum vitamin D in 59 healthy young women.¹¹ The present study examined the relationship of vitamin D levels to cardiorespiratory fitness in a larger cohort of men and women.

Methods

Baseline data were collected on 200 adults free of overt cardiovascular and metabolic disease, who were participating in a double-blind, clinical trial investigating the effect of statins on skeletal muscle performance (STOMP study).¹² Subjects were not taking medications known to affect serum lipids, blood pressure or muscle metabolism. Prior to statin or placebo treatment, subjects completed three study visits over a period of 2 weeks. Participants underwent a modified Balke treadmill test to determine VO_2max .¹³ VO_2max and ventilatory threshold were determined using breath-by-breath analysis of expired gases with a Parvomedics TrueOne 2400 metabolic cart (ParvoMedics Corp., Sandy, UT). Subjects fasted for 8–12 hours before the test. Attainment of VO_2max was affirmed when subjects met 3 of 4 criteria: plateau of oxygen uptake (defined as $< 50 \text{ mL/min}$ increase with a 1% increase in treadmill grade), attainment $\pm 10 \text{ bpm}$ of age-predicted maximal heart rate, volitional exhaustion (defined as a rating of perceived exertion ≥ 18) and calculated respiratory exchange ratio > 1.10 .¹⁴

Subjects' daily physical activity levels at baseline were documented using the Paffenbarger Physical Activity Questionnaire (PPAQ).¹⁵ Subjects reported their average hours of physical activity over the course of the week to identify hours of sedentary, light, moderate and vigorous activities (Question #8, PPAQ). Vigorous activities were defined as any strenuous sports, jogging, aerobic exercise, bicycling on hills and similar activities. Moderate activities were defined as lighter sports, regular walking, golf, house and yard work. Total hours of moderate to vigorous physical activity per week (MVPA) were used to examine the relationship between vitamin D, cardiorespiratory fitness and daily physical activity. Body weight was measured using a calibrated balance beam scale. Height was determined using a wall mounted tape measure. Serum 25(OH)D, which measures combined serum vitamin D2 and D3, was determined using blood collected at the first study visit, using a standard ELISA immunoassay protocol (Clinical Laboratory Partners, Newington, Connecticut). The seasons in which the vitamin D level was measured were recorded to account for potential seasonal variation in vitamin D levels. The seasons were defined as: winter (December–February); spring (March–May); summer (June–August); and fall (September–November).

The response variable of interest was cardiorespiratory fitness (VO_2max). The independent variables included age, MVPA, 25(OH)D, body mass index, gender, cigarette smoking, and season. Means and standard deviations were calculated for all continuous variables;

frequencies and percentages were reported for all categorical variables. Bivariable associations were assessed using simple linear regression and t-tests. Analysis of covariance (ANCOVA) was used to evaluate the relationship between VO_2max and serum vitamin D level after controlling for clinically and statistically significant predictors. Two-way interactions between the predictors were considered in our ANCOVA models. All analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, North Carolina).

Results

Data from 200 healthy adults were analyzed, of whom 108 (54%) were women and 22 (11%) were chronic smokers (Table 1). Vitamin D levels were directly related to VO_2max ($r=0.29$, $p<0.0001$) (Figure 1). VO_2max was also significantly correlated with age ($r=-0.58$, $p<0.0001$) and body mass index ($r=-0.24$, $p=0.0005$). We also compared the mean VO_2max levels among vitamin D deficient ($25(\text{OH})\text{D}<20$ ng/ml, $n=29$, 15%), insufficient ($25(\text{OH})\text{D}=20-30$ ng/ml, $n=52$, 26%) or sufficient ($25(\text{OH})\text{D}>30$ ng/ml, $n=119$, 59%) groups and documented higher VO_2max values in the sufficient group (Figure 2).⁷⁸ The relationship between vitamin D level and VO_2max remained statistically significant even after adjusting for gender ($p=0.001$), age ($p=0.0001$), BMI ($p=0.0001$) and MVPA ($p=0.05$). Seasonal variation ($p=0.7$) and tobacco use ($p=0.2$) were not significantly associated with VO_2max . There was also a statistically significant interaction between vitamin D level and MVPA ($p<0.02$), indicating that the effect of vitamin D level on VO_2max is modified by the hours of MVPA. Consequently, we reanalyzed the effect of vitamin D on VO_2max by percentiles of physical activity. The mean hours of MVPA at the 25th (<23 hr/wk, $n=49$), 25–75th ($23-48$ hr/wk, $n=103$) and 75th (>48 hr/wk, $n=48$) percentiles were 16, 35 and 64 hr/wk, respectively. Including these mean values in the model showed that for each standard deviation (SD) (13 units) increase in vitamin D, VO_2max increased by 2.6 ml/kg/min ($p<0.0001$) when MVPA was low, 1.6 ml/kg/min ($p<0.0004$) when MVPA was moderate and only 0.01 ml/kg/min ($p=0.9$) when MVPA was high (Figure 3).

Discussion

This study is to our knowledge the first large cross sectional study of the relationship between vitamin D levels and aerobic cardiorespiratory fitness. We documented that vitamin D is positively associated with cardiorespiratory fitness in healthy adults independent of their age, gender and body mass index. Moreover, this relationship of vitamin D levels and aerobic exercise performance was more prominent among those subjects who did not engage in substantial amounts of moderate to vigorous physical activity.

There has been little published on the relationship between cardiorespiratory fitness and serum 25 (OH) D levels. Mowry et al. examined the association of baseline cardiorespiratory fitness (VO_2max) with 25[OH]D in 59 young healthy women, aged 16 to 24 years.¹¹ There was a positive association between VO_2max and serum 25(OH)D ($r=0.36$ $p<0.05$). The present study confirms a direct relationship between vitamin D levels and VO_2max ($r=0.29$, $p<0.0001$), in both men and women over a broad age range of age (20 to 73 years) and serum 25(OH)D levels (10 to 82 ng/ml). The positive relationship between vitamin D levels and VO_2max persisted after adjustment for age, gender, body mass index,

and MVPA, especially among individuals with low levels of physical activity. This suggests that Vitamin D contributes to cardiorespiratory fitness.

An alternative explanation is that cardiorespiratory fitness is simply a surrogate for an individual's daily physical activity, which could be related to light exposure and therefore to vitamin D. To explore this hypothesis, we examined the interaction of MVPA and seasonal variation to the relationship between vitamin D and VO₂max. Despite the higher daily physical activity and serum 25(OH)D level observed during the warmer months, seasonal variations in vitamin D did not affect VO₂max or the VO₂ max – vitamin D relationship.

We did find an interaction of 25(OH)D level with the amount of physical activity such that individuals with the lowest level of MVPA demonstrated the strongest relationship between vitamin D and VO₂max. For example, each SD increase in 25(OH)D level increased VO₂max by 8% (with percent change calculated relative to the group average) among those with the lowest level of MVPA. Notably, this effect size is comparable to the change in VO₂max observed with mild to moderate intensity exercise training.¹⁶ One SD increase in serum 25(OH)D also increased VO₂max by 5% among those with moderate level of MVPA, but only by 0.2% among those with high level of MVPA (Figure 3).

The mechanism for the interactive effect of vitamin D and MVPA on cardiorespiratory fitness is not clear. VO₂max is limited by cardiac output, arterial oxygen content, shunting of blood to active muscle and the extraction of oxygen by these muscles. Low serum 25(OH)D levels can cause myocardial hypertrophy, elevated blood pressure and endothelial dysfunction via vitamin D receptors.⁷⁸¹⁷¹⁸¹⁹ Consequently, low vitamin D levels may decrease cardiac output and increase peripheral vessel resistance reducing VO₂ max. Physical activity is also known to increase VO₂max through increased cardiac output.¹⁶²⁰²¹ Results from a large healthy adult cohort study suggest that the greatest benefits of physical activity on cardiac remodeling occur at the lowest levels of reported physical activity.²² Therefore, vitamin D could potentially have a greater benefit on cardiac remodeling and VO₂max among individuals with low levels of physical activity than among those who already engage in high levels of activity. There is also evidence that both physical inactivity²³²⁴ and vitamin D deficiency²⁵²⁶²⁷ can cause muscle atrophy and shift muscle fiber type from IIa to IIb. Therefore, it is possible that individuals with the lowest level of physical activity receive a greater aerobic benefit from increasing vitamin D levels via changes in muscle mass and fiber type than those who already engage in high levels of physical activity. Alternatively, less active subjects in our study had a higher BMI (p<0.007) and waist circumference (p<0.02). This could indicate a clustering of other cardiovascular risk factors such as insulin resistance, high blood pressure and arterial stiffness, which could augment the negative effect of low vitamin D on VO₂max among sedentary individuals.²⁸

There are several limitations to this study. We did not record the amount of vitamin D taken by supplemental or dietary means. However, serum 25(OH)D level is reflective of all vitamin D sources and is the benchmark for determining vitamin D status. In addition, other biomarkers related to vitamin D, such as serum parathyroid hormone, calcium and phosphorus levels were not analyzed and could contribute to the relationship between exercise performance and vitamin D. Furthermore, physical activity was measured by self

report and subject to recall bias, although The Paffenbarger Questionnaire has been well validated.²⁹

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Figure 1.

The simple linear regression equation and 95% prediction bands for the regression of serum 25(OH)D with maximal oxygen uptake (VO₂max) (N=200, crude $r=0.29$, $p<0.0001$).

Figure 2.

Comparison of mean VO_{2max} (shown within bar graphs with the corresponding standard error) among vitamin D deficient (25(OH)D <20 ng/ml), insufficient (25(OH)D, 20–30 ng/ml) and sufficient (25(OH)D >30 ng/ml) subjects.

Figure 3.

The relationship between 25 (OH) vitamin D [25 (OH) D] and maximal oxygen uptake (VO2 max) by percentiles and mean hours of moderate to vigorous physical activity (MVPA) for the low (25th, 16 hrs/wk), moderate (25th–75th, 35 hrs/wk) and high (75th, 64 hrs/wk) groups.

Table 1

Subject (N=200) Baseline Characteristics

Variable	Total Mean $\pm$ SD	Male (n=92) Mean $\pm$ SD	Female (n=108) Mean $\pm$ SD	p-value
VO ₂ max (ml/kg/min)	34 $\pm$ 10.3	40 $\pm$ 9.1	30 $\pm$ 8.5	< 0.01
Age (years)	40 $\pm$ 14.4	39 $\pm$ 15.2	42 $\pm$ 13.9	0.12
25(OH) D (ng/ml)	34 $\pm$ 13.3	33 $\pm$ 11.3	35 $\pm$ 14.6	0.44
Waist circumference(cm)	85 $\pm$ 13.7	92 $\pm$ 12.2	80 $\pm$ 11.9	< 0.01
BMI (kg/m ²)	26 $\pm$ 5.1	27 $\pm$ 4.5	26 $\pm$ 5.3	0.01
MVPA (hrs/wk)	37 $\pm$ 19	36 $\pm$ 17.0	38 $\pm$ 20.0	0.56
Season [25(OH)D measurement]				
Spring	71 (35%)	31(34%)	40(37%)	0.7
Summer	53 (26%)	27(29%)	26(24%)	
Fall	30 (15%)	15(16%)	15(14%)	
Winter	46 (23%)	19(21%)	27(25%)	

25(OH) D = Serum 25-hydroxy vitamin D, BMI = body mass index, MVPA = hours of moderate to vigorous physical activity per week, SD = Standard Deviation, VO₂max = Maximal oxygen uptake. P-value for gender difference.