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Changes in vitamin D are not associated with changes in cardiorespiratory fitness

Sara M.Gregory[1],Beth A. Parker[1], Jeffrey A. Capizzi[1], Adam S. Grimaldi[1], Priscilla M. Clarkson[2], Stephanie Moeckel-Cole[2], Justin Keadle[2], Stuart Chipkin[2], Linda S. Pescatello[3], Kathleen Simpson[3], C. Michael White[3], Paul D. Thompson[1]

[1]Division of Cardiology, Henry Low Heart Center, Hartford, CT, USA
[2]School of Public Health & HealthSciences, University of Massachusetts, Amherst, MA, USA
[3]NeagSchool of Education, University of Connecticut, Storrs, CT, USA

Email address:

Sara.gregory586@gmail.com (S. Gregory), bparker03@harthosp.org (B. Parker), jac00012@gmail.com (J. Capizzi), agrimaldi@student.uchc.edu (A. Grimaldi), clarkson@kin.umass.edu (P. Clarkson), smcole@kin.umass.edu (S. Moeckel-Cole), jkeadle@gmail.com (J. Keadle), schipkin@kin.umass.edu (S. Chipkin), linda.pescatello@uconn.edu (L. Pescatello), Kathleen.simpson@us.army.mil (K. Simpson), cmwhite@harthosp.org (C. M. White), pthomps@harthosp.org (P. Thompson)

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Abstract: We investigated the relationship between changes in 25-hydroxyvitamin D (25OHD) and changes in aerobic fitness (VO_{2max})over 6 months in healthy adults (n = 213, mean ± SD age 44.8 ±16.4 yr, range 20-76 yr, 109 women). 25OHD status was defined as deficient (DEF: 25OHD <50 nmol·L^{-1}, n = 16), insufficient (INS: 25OHD > 50 nmol·L^{-1} but < 75 nmol·L^{-1}, n = 57), and sufficient (SUF: 25OHD >75 nmol·L^{-1}, n = 140). Tertiles for 25OHD change were computed (lowest: < -17.5 nmol·L^{-1}, n = 67; middle: -17.5 to 9.1 nmol·L^{-1}, n = 75; highest: > 9.1 nmol·L^{-1}, n = 71). Baseline 25OHD level (β = -0.003; p = 0.83) and change in 25OHD level (β = 0.01; p = 0.50) were not significant predictors of changes in $VO_{2max.}$ Changes in VO_{2max}were similar between 25OHD status groups (p = 0.55; DEF = -1.7 ± 2.1, INS = -0.4 ± 3.2; SUF = -0.3 ± 3.1 ml·kg^{-1}·min^{-1}), and 25OHD change tertiles (p = 0.28; lowest = -0.3 ± 2.7, middle = -0.8 ± 3.5, highest = -0.3 ± 2.9 ml·kg^{-1}·min^{-1}). Changes in vitamin D over a 6-month period were not associated with changes in aerobic fitness. Aerobic fitnessis not impacted by temporal variations in 25OHD.

Keywords: Maximal Oxygen Consumption, 25-Hydroxyvitamin D, Aerobic Fitness, Physical Performance

1. Introduction

Cardiorespiratory fitness is a predictor of longevity and incident cardiovascular disease. Greater cardiorespiratory fitness, measured as maximal oxygen consumption (VO_{2max}), is independently associated with reduced all-cause and cardiovascular mortality [1-3], as well as reduced risk for cardiovascular events [4] and incident hypertension [5]. Low vitamin D levels are also associated with incident coronary artery disease [6], myocardial infarction [7], and greater all-cause and cardiovascular mortality [8]. Previously we reported that vitamin D is directly associated with cardiorespiratory fitness [9] and muscle strength [10] in healthy adults. Subsequent reports support that lower serum vitamin D levels are also associated with lower cardiorespiratory fitness in men [11], women [12], and in patients with chronic kidney disease [13].

Vitamin D levels demonstrate seasonal variation, which could translate into impaired cardiorespiratory fitness during months when sunlight exposure is low and vitamin D levels tend to decrease. This relationship would have important performance and health implications. However, to the best of our knowledge the relationships between temporal changes in vitamin D levels and cardiorespiratory fitness have not been established. Therefore, the purpose of this investigation was to examine the impact of changes in vitamin D levels on cardiorespiratory fitness over a 6 month period.

Table 1.*Demographic Variables for Study Variables*

Variable	Baseline	6 Months
Age (years)	44.8 (16.4)	
VO_{2max} (ml/kg/min)	33.3 (10.0)	32.8 (9.0)
Vitamin D (nmol/L)	92.3 (36.2)	87.3 (35.7)
BMI (kg/m2)	26.5 (4.9)	26.4 (5.0)
Activity (counts)	180,733 (97,648)	163,674 (94,990)
Season		
Winter	35 (16)	67 (31)
Spring	64 (31)	48 (23)
Summer	67 (31)	38 (18)
Fall	47 (22)	60 (28)
Race		
Caucasian	197 (92.5)	
African American	9 (4)	
Asian	6 (3)	
Pakistani	1 (.5)	

* Mean (SD) or Frequency (%); Abbreviations: BMI= body mass index; VO_{2max}= maximal oxygen consumption

2. Methods

2.1. Participants

Data were collected from 213 healthy individuals (mean ± standard deviation age 44.8 ±16.4 yr, range 20-76 yr, 109 women; Table 1) assigned to the placebo group in a double-blind clinical trial examining the effects of statin medications on muscular performance (The Effect of Statins on Skeletal Muscle Function, or STOMP, NCT00609063). Participants were free of overt cardiovascular and metabolic disease, and were not taking any medications that might affect blood pressure, muscle metabolism, or blood lipids. This study was approved by the Institutional Review Board at all participating institutions. Participants provided written informed consent prior to participation.

2.2. Study Design

Participants completed three study visits over 2 weeks, including maximal aerobic exercise testing and a fasting blood draw, at baseline and again 6 months later. Seasonal variation in testing sessions was accounted for by recording the date of each study visit. Seasons were defined as winter (December to February), spring (March to May), summer (June to August), and fall (September to November). Participants were instructed to maintain their normal dietary intake and physical activity level between baseline and 6 month testing periods. Participants wore an accelerometer (Actical physical activity monitor, Mini Mitter, a Respironics Inc., Bend, OR, [14]) for 96 hours at baseline and 6 months testing periods. Physical activity level was assessed by the total number of counts from accelerometer recordings averaged over 4 days.

2.1.2. Cardiorespiratory Fitness Testing

Participants completed a graded treadmill exercise test using the Bruce protocol [15] with electrocardiogram monitoring to screen for signs of overt cardiac disease. Several days later, participants underwent a modified Balke protocol treadmill test with simultaneous breath-by-breath analysis of expired gases using a ParvomedicsTrueOne 2400 metabolic cart (ParvoMedics Corp., Sandy, UT) to determine VO_{2max}. Achievement of VO_{2max} was determined when participants met 3 of 4 criteria: plateau of oxygen uptake (defined as < 50 ml·min^{-1} increase with 1% increase in treadmill grade), attainment of heart rate within ± 10 bpm of the participant's age-predicted maximum, volitional exhaustion (rating of perceived exertion ≥ 18), and a calculated respiratory exchange ratio > 1.10 [16]. Participants fasted for 8 to 12 hours prior to testing.

2.1.3. Vitamin D Analyses

Serum 25-hydroxyvitamin D (25OHD) levels, considered the best indicator of vitamin D status [17], were determined from fasted blood samples taken at the first study visit during baseline and 6 month testing. 25OHD was analyzed using a standard enzyme-linked immunosorbent assay method (Clinical Laboratory Partners, Newington, CT).

Baseline 25OHD status was defined according to criteria established by expert consensus [17, 18], as 25OHD deficient (DEF: 25OHD <50 nmol·L^{-1}, n = 16), insufficient (INS: 25OHD > 50 nmol·L^{-1} but < 75 nmol·L^{-1}, n = 57), and sufficient (SUF: 25OHD >75· nmol·L^{-1}, n = 140). We computed tertiles for 25OHD change over 6 months (lowest: < -17.5 nmol·L^{-1}, n = 67; middle: -17.5 to 9.1 nmol·L^{-1}, n = 75; highest: > 9.1 nmol·L^{-1}, n = 71). We further categorized participants based on changes in 25OHD in the following ways: those who increased 25OHD levels (n = 85) vs. those who decreased levels (n = 128); those who moved from insufficient or deficient to sufficient (n = 25) vs. those who moved from sufficient to insufficient or deficient (n = 43) vs. those who did not change vitamin D status (n = 145).

2.1.4. Statistical Analyses

All analyses were performed using SPSS version 14.0 (SPSS, Inc., Chicago, IL). Descriptive statistics (mean ± SD) were computed for all variables. Analysis of Covariance (ANCOVA) was used to compare changes in 25OHD and VO_{2max} over 6 months between 25OHD status and 25OHD change groups, while controlling for statistical and clinical covariates including age, sex, season, activity level, and body mass index (BMI). Two-way interactions between predictors were considered in our ANCOVA models. The dependent variables for ANCOVA models were the change in VO_{2max} over 6 months and change in 25OHD over 6 months determined as the difference between 6-month and baseline values. When significant effects were detected by ANCOVA, post-hoc analyses were performed by pairwise comparisons using the Bonferroni adjustment. Hierarchal linear regression was performed to detect relationships between independent (baseline 25OHD level and change in 25OHD) and dependent variables (change VO_{2max}) while controlling for predictors described above. We accounted for the change in season between baseline and 6 month

measurements by coding a variable indicating the change in season from either spring/winter to fall/summer (moving to higher 25OHD exposure) or fall/summer to spring/winter (moving to lower 25OHD exposure). Change in season and change in activity level were included in ANCOVA and regression analyses as a predictors/covariates.

3. Results

There was a relationship between 25OHD status and change in 25OHD after controlling for age, season, sex, BMI, and activity level ($p < 0.001$). Improvements in 25OHD level over 6 months were greater in DEF when compared to INS ($p = 0.01$) and SUF ($p < 0.001$; Figure 1A).

Neither baseline 25OHD level ($\beta = -0.003$; $p = 0.83$) or change in 25OHD level ($\beta = 0.01$; $p = 0.50$) were significant predictors of changes in VO_{2max} in models including age, sex, baseline season, activity level, and BMI. Including change of season in the model did not alter results.

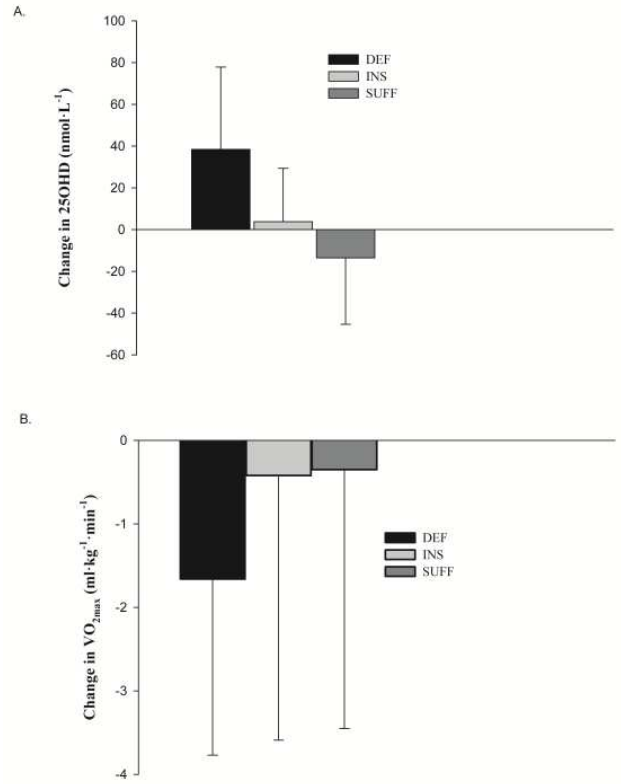

Figure 1.*A) Changes in 25-hydroxyvitamin D (nmol·L^{-1}) over 6 months in groups classified as vitamin D deficient (DEF: 25OHD < 50 nmol·L^{-1}, n = 16), insufficient (INS: 25OHD 50 to 75 nmol·L^{-1}, n = 57), or sufficient (SUFF: 25OHD > 75 nmol·L^{-1}, n = 140) at baseline. B) Changes in maximal oxygen consumption (VO_{2max}; ml·kg^{-1}·min^{-1}) over 6 months in groups classified as vitamin D deficient (DEF: 25OHD < 50 nmol·L^{-1}, n = 16), insufficient (INS: 25OHD 50 to 75 nmol·L^{-1}, n = 57), or sufficient (SUFF: 25OHD > 75 nmol·L^{-1}, n = 140) at baseline. *: Significant difference between groups.*

There were no significant differences in the change in VO_{2max} over 6 months between baseline 25OHD status groups ($p = 0.55$; Figure 1B). Similarly, there were no significant differences in the change in VO_{2max} between 25OHD change tertiles ($p = 0.28$; Figure 2). Changes in VO_{2max} did not differ between those who became sufficient, became deficient, or did not change 25OHD status over 6 months ($p = 0.51$; -0.1 ± 2.5; -0.04 ± 2.6; -0.5 ± 3.2 ml·kg^{-1}·min^{-1}, respectively), or between those who increased versus decreased 25OHD levels over 6 months ($p = 0.55$; -0.4 ± 2.9; -0.4 ± 3.1 ml·kg^{-1}·min^{-1}, respectively). Including change in season as a covariate or factor term did not alter results or indicate any interactions between change in 25OHD and change in season for change in VO_{2max} ($p > 0.05$).

Activity level decreased over 6 months ($p = 0.02$; baseline = 181,698.8 counts, 6 months = 164,148.5 counts). There was no relationship between changes in activity level and changes in VO_{2max} ($p = 0.31$). There were no differences in the change in activity level between 25OHD status groups ($p = 0.61$; DEF = -43,419.1 ± 136,841.4, INS = -13,841.1 ± 89,002.7, SUF = -15,900.9 ± 111,305.3 counts) or 25OHD change tertiles ($p = 0.66$; lowest = -27,927.9 ± 106,365.6, middle = -13,518.5 ± 113,224.6, highest = -12,390.5 ± -104,950.6 counts). Including change in activity level as a covariate did not change the results of any analyses.

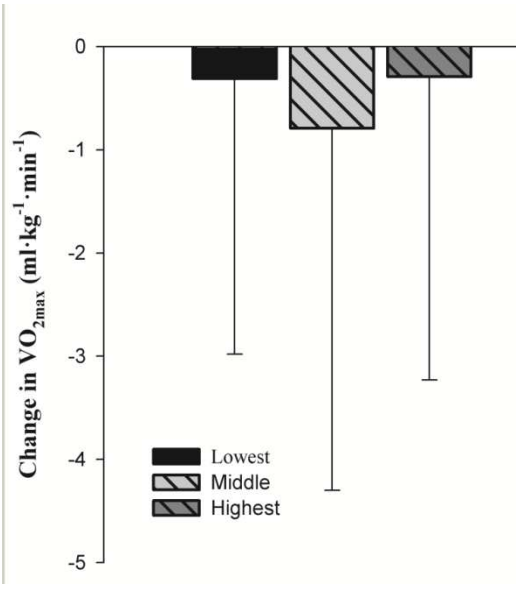

Figure 2.*Changes in maximal oxygen consumption (VO_{2max}; ml·kg^{-1}·min^{-1}) over 6 months in tertile groups for 25OHD change over 6 months (lowest: < -17.5 nmol·L^{-1}, n = 67; middle: -17.5 to 9.1 nmol·L^{-1}, n = 75; highest: > 9.1 nmol·L^{-1}, n = 71).*

4. Discussion

This study is, to our knowledge, the first to investigate the relationship between changes in vitamin D and cardiorespiratoryfitnessover time in a large sample of healthy men and women. The major finding of this investigation was that, despite greater changes in 25OHD in those who were deficient at baseline, neither baseline 25OHD levels or changes in 25OHD levels predicted changes in cardiorespiratory fitness over 6 months.

Moreover, there were no differences between those with the lowest and highest changes in 25OHD levels, between those who increased or decreased 25OHD levels, or between those who transitioned between sufficiency and insufficiency or deficiency, indicating that changes in cardiorespiratory fitness were not related to changes in 25OHD status.

We previously reported a direct relationship between 25OHD and cardiorespiratory fitness [9] and arm and leg strength [10] in the same cohort. Vitamin D may relate to cardiorespiratory fitness due to its role in maintaining normal cardiovascular[19, 20] and musculoskeletal function [21-23], however we did not observe a relationship between changes in 25OHD and cardiorespiratory fitness. Those with baseline vitamin D deficiency experienced the greatest change in 25OHD over 6 months. Twelve out of 16 participants with vitamin D deficiency at baseline had improved to insufficient (n = 7) or sufficient (n = 5) status at 6 months, and 15 out of 16 deficient participants were in the highest tertile for the change in 25OHD. Despite improvements in 25OHD levels, there was no relationship between baseline 25OHD status or changes 25OHD levels over 6 months and changes in cardiorespiratory fitness. Baseline VO_{2max} ranged between 12.9 to 64.9 $ml \cdot kg^{-1} \cdot min^{-1}$ and changes in VO_{2max} ranged between -13.3 to 10.2 $ml \cdot kg^{-1} \cdot min^{-1}$. Therefore our sample included a wide range of cardiorespiratory fitness levels, and there were notable, albeit not consistent, changes in fitness over time.

The lack of an association between changes in 25OHD and cardiorespiratory fitness may be a reflection of the study duration since substantial and uniform changes in 25OHD or VO_{2max} are unlikely to occur over 6 months without a controlled intervention.The improvements in 25OHD seen in baseline deficient individualsmay represent amelioration of transient reductions in 25OHD that do not correspond with changes in fitness in the short-term. The relationship between vitamin D and cardiorespiratory fitness we reported previously, although statistically significant, was weak to moderate strength (r = 0.3) [9]. Therefore, it is not surprising that we failed to find a relationship between changes in 25OHD and fitness over a short time period and in a limited sample of individuals with low vitamin D levels.

25OHD levels reflect vitamin D exposure from sunlight and food sources over the previous 15 days [24], and are influenced by several factors, including dietary intake, sunlight exposure, and health status. Seasonal variations in 25OHD levels may be explained by greater sunlight exposure during warmer months. The relationship between changes in 25OHD and cardiorespiratory fitnessmay be influenced by increased activity levels during warmer months when 25OHD levels are highest. However, controlling for change in activity level or change in season over 6 months did not create a relationship between change in 25OHD and cardiorespiratory fitness, nor did we observe any interactions between 25OHD status and changes in activity level or season. We conclude that seasonal changes in vitamin D levels do not impact cardiorespiratory fitness.

There are limitations to the present report. We didnot record dietary and supplemental intake of vitamin D, but these should be reflected in 25OHD levels, which is the gold standard for assessing 25OHD status. The observational nature of the study limits our ability to make definitive conclusions about patterns of change in 25OHD and cardiorespiratory fitness that may be detected in controlled longitudinal trials with greater and more uniform changes in 25OHD. The assessment of 25OHD and VO_{2max} at two isolated time points, baseline and 6 months later, limits our ability to generalize our findings to relationships between 25OHD and fitness over longer time periods. We assessed changes in activity level by accelerometer counts, which has the advantage of being an objective measure of physical activity but the disadvantage of not being able to account for the intensity and type of activity or to assess long-term patterns of activity level. However, the Actical activity monitor has been validated as an accurate measure of activity level and energy expenditure in adults [25, 26]. Lastly, the majority of our population was Caucasian (93%), and therefore our findings have limited applicability to other racial groups and ethnicities, such as African Americans who have higher rates of vitamin D deficiency.

5. Conclusions

25OHD deficiency was associated with greater improvement in 25OHD levels over 6 months. Despite improvements in 25OHD levels, there was no relationship between baseline 25OHD level, 25OHD status, or changes in 25OHD levels with changes in cardiorespiratory fitness over 6 months. Therefore short-term variations in 25OHD status do not appear to be reflected in changes in cardiorespiratory fitness, which suggests that seasonal deficiencies do not impair aerobic fitness. Rather, the long-term average of 25OHD status is likely to be most closely related to aerobic fitness level, either as the result of similar underlying physiological mechanism or a direct causal relationship.

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Conflicts of Interest: Dr. Paul Thompson is a consultant for Astra Zeneca International, Merck & Company, Inc., Amgen, Sanolfi-Aventis, Regeneron, and Genomas and is a member of the speaker's bureau for Merck & Company, Inc., Pfizer, Inc., Abbott Labs, Astra Zeneca International, and The Schering-Plough Corporation. No other authors report any conflict of interest.

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