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Effect of vitamin D_3 supplementation in winter on physical performance of university students: a one-month randomized controlled trial

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ABSTRACT

Background: There is epidemiological evidence which suggests an association between 25-hydroxyvitamin D [25(OH)D] levels and bone and muscle function; however, it is unclear whether vitamin D supplementation has an added benefit beyond bone health. Here, we investigated the effects of vitamin D_3 supplementation (1 month) on physical performance in Chinese university students in winter.

Methods: One hundred and seventeen eligible subjects with 25(OH)D (19.2 ± 7.8 ng/mL) were randomly assigned to either vitamin D_3 supplement ($N = 56$; 1000 IU/day) or the control ($N = 61$) group for 1 month. Pre- and post-measurements included: 1) serum levels of 25(OH)D; 2) musculoskeletal and pulmonary function [vertical jump height (VJH) and right handgrip strength (RHS), forced vital capacity (FVC), and forced expiratory volume at 1s (FEV_1)]; 3) bone turnover markers [parathyroid hormone (PTH), n-terminal osteocalcin (N-MID), and calcium]; 4) hemoglobin-related parameters [hemoglobin (Hb), hematocrit (HCT), red blood cells (RBC), and red cell distribution width (RDW)]; 5) lipid parameters [total triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C)]; 6) Fatigue-related indicators [serum creatine kinase (CK), lactate dehydrogenase (LDH), and total

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testosterone (T)]. In addition, aerobic capacity was assessed by measuring maximal oxygen uptake (VO_2max) at baseline.
Results: During wintertime, supplementation with 1000 IU/d of vitamin D_3 significantly increased serum 25(OH)D levels (from 18.85 ± 7.04 to 26.98 ± 5.88 ng/mL, $p < 0.05$), accompanied by a decrease of PTH ($p < 0.05$). However, vitamin D_3 supplementation did not significantly impact the physical performance, serum lipid parameters, and bone turnover markers of students. Furthermore, 25(OH)D was found to be positively correlated with VJH and negatively correlated with PTH and TC at the beginning and end of the study ($p < 0.05$). In addition, the multiple linear regression analysis showed that 25(OH)D combined with athletic, gender, height, weight, Hb, and FVC could account for 84.0% of the VO_2max value.
Conclusions: The study demonstrated that one-month of 1000 IU/d of vitamin D3 supplementation during the winter had beneficial effects on 25(OH)D status and PTH. However, vitamin D_3 intervention was not sufficient to improve physical performance. Furthermore, 25(OH)D levels combined with athletic, Hb and FVC could be a predictor of VO_2max.

1. Introduction

Vitamin D_3 is a prohormone that humans obtain primarily by exposure to sunlight and secondarily from diet or dietary supplements [1]. Recent research revealed that low vitamin D levels may lead to a wide range of extra-skeletal health outcomes, including impaired muscular strength [1–3], poor pulmonary function [4], poor cardiorespiratory fitness [5,6], and cardiovacular diseases [7]. Vitamin D deficiency, insufficiency, and sufficiency were defined as a serum 25(OH)D value of <20 ng/mL (50 nmol/L), 21–29 ng/mL (50–75 nmol/L) and >30 ng/mL (75 nmol/L), respectively [8]. The worldwide prevalence of vitamin D deficiency and insufficiency ranges from ~5% to 18% and 24% to 49%, respectively [9]. For Chinese university students, low vitamin D status is prevalent as well [10–12] during the winter months, owing to the lower consumption frequency of vitamin D-rich foods and lower UV exposure [11].

Given that low vitamin D status has become a worldwide problem, a series of vitamin D supplementation studies have been conducted to explore the skeletal and extra-skeletal benefits of vitamin D interventions. Some studies suggest that vitamin D supplementation is beneficial to physical performance and cardiovascular health, partly by atherogenic blood lipids [10,13–16]. For instance, there is growing evidence that vitamin D status may modulate musculoskeletal function [2,17], since 1,25-hydroxyvitamin D_3 ($1,25(OH)_2D_3$), the active form of vitamin D, participates in cell proliferation and differentiation [18,19], regulation of protein synthesis [20] and mitochondrial function [15,21] through activation of various cellular signaling cascades [18,20,22]. In previous studies, it has been demonstrated that vitamin D supplementation appears to be a reasonable strategy for enhancing the vertical jump height among young ballet dancers [23,24]. Furthermore, some studies have reported positive associations between 25(OH)D concentrations and maximal oxygen uptake (VO2max), which is an accurate measure of aerobic capacity and cardiopulmonary health [5,25–27]. And a recent study found that 6,000 IU of vitamin D_3 per day increased VO_2max in rowers[28]. In addition, vitamin

D intervention also showed various benefits for blood lipids for adolescents [29,30]. In contrast, some studies investigated the association between vitamin D supplementation and possible improvements in physical performance in different populations, with conflicting results [31–33]. For instance, vitamin D administration for 12 weeks did not have any effect on changes in lipid parameters in healthy adults [34]. Therefore, the effect of vitamin D intervention on physical performance remains ambiguous due to numerous factors could impact physical performance improvements, including fitness level, physical activity level, type of practiced sport, ethnicity, vitamin D status, and intervention dosages [26]. Nevertheless, there are currently limited data on the effects of vitamin D intake in young healthy adults.

The objectives of this study were to examine the benefits of winter vitamin D_3 supplementation on the serum 25(OH)D levels, physical performance, bone turnover, and serum lipids in university students.

2. Materials and methods

2.1. Participants

Participants were recruited from the campus of the Soochow University. The exclusion criteria included the presence of serious diseases (cardiac diseases, type 1 or 2 diabetes, hepatic disease, chronic renal failure, sickle cell anemia, megaloblastic anemia, and inflammatory diseases), medicines affecting vitamin D metabolism, ongoing treatment with vitamin D, and inability to perform the physical fitness test. The purpose, procedures, and risks of the study were explained to each participant before inclusion, and all of the participants were enrolled with written informed consent. The study was approved by the Ethics Committee of Soochow University. (Reg. No. SUDA20211117A01)

2.2. Study design

We conducted a 1-month, randomized parallel-arm trial to investigate the effect of 1000 IU/d of oral vitamin D_3 versus controls on the physical performance of Chinese undergraduates between November of 2021 and January of 2022.

Eligible participants were randomized by a stratified random sample (based on major specificity) into two groups: 1000 IU/d of oral vitamin D_3 (intervention group) and blank control group. All participants and researchers were blinded to the allocations until completion of the study and subsequent data analysis. Recruitment, the randomization scheme, and final sample distributions group are presented in the consolidated standards of reporting trials (CONSORT) diagram (Figure 1).

2.3. For primary outcomes

The serum concentrations of 25(OH)D, including $25(OH)_2$ and $25(OH)D_3$, were examined with chemiluminescent immunoassay.

Vertical jump height (VJH) (cm) was measured using a calibrated electronic jump mat (Beijing Xindong Huateng Sports Equipment Co. Ltd, Beijing, China). Participants performed three adversarial movement jumps and the best recorded

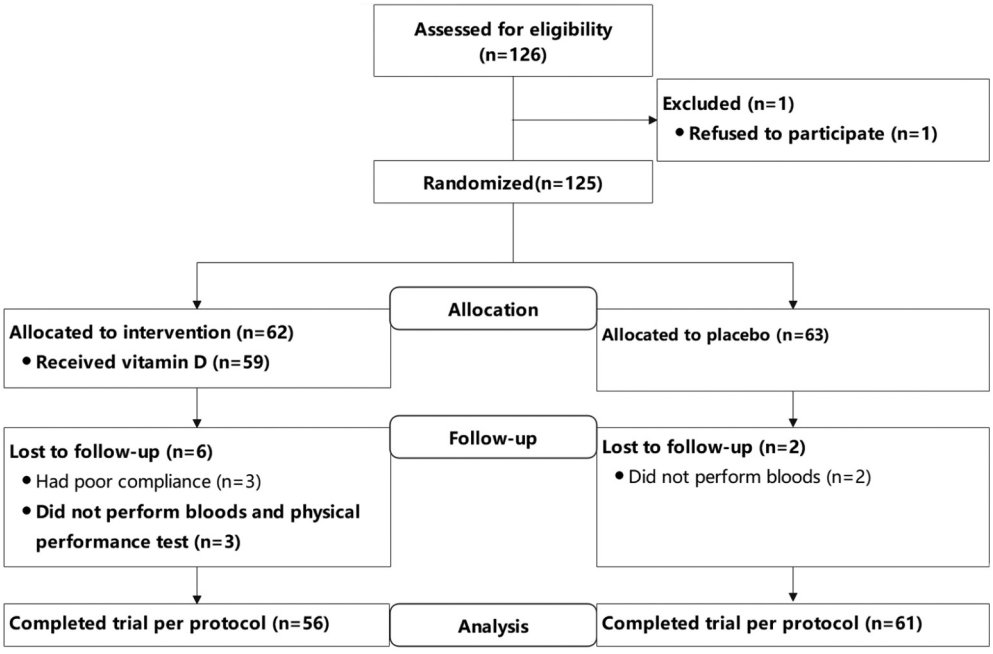

Figure 1. Flow diagram of the study. Among studied participants, 117 (93.6%) completed blood, vertical jump, hand grip, FVC, and FEV_1 analysis (vitamin D group $n = 56$ and control $n = 61$). At baseline, 104 participants completed VO_2max test.

jump height was taken for analysis. Handgrip strength (RHS) (kg) was measured using a hand-held dynamometer (Jamar Plus+, Patterson Medical, Warrenville, IL, China). Participants held the device next to their body and grasped it maximally for a total of three times. The maximum handgrip strength was calculated for the analysis. Lung function was measured using a calibrated Micro Lab portable pulmonary function equipment (Cosmed, Panova di Albano, Rome, Italy) [35]. Forced vital capacity (FVC) and forced expiratory volume at 1s (FEV_1) were quantified by exhaling maximally into a one-way disposable mouthpiece, and a minimum of three repeats was performed in order to derive the best value.

VO_2max testing was performed using a treadmill (MERC-C, WOODWAY GmbH, Germany) [33] and a metabolic cart (Metallizer 3B, CORTEX Biophysik GmbH, Germany) [35]. Participants walked on the treadmill until they reached physical exhaustion. The Bruce protocol treadmill test was used. The test was valid when any three of the four following criteria were reached: a respiratory exchange ratio (RER) >1.15; oxygen consumption remains at a steady state despite a further increase in workload [33]; volitional fatigue, as indicated by the inability to maintain a set rate despite verbal encouragement; and a posttest blood lactate concentration >9 mmol/L in males or >7 mmol/L in females. The posttest blood lactate concentrations were measured using a lactate pro device as per the manufacturers' recommendations (Arkray Inc, Kyoto, Japan). At 1 min, following cessation of the VO_2max test, a capillary blood sample was obtained for blood lactate analysis.

2.4. For secondary outcomes

The blood samples were analyzed using an automatic biochemical analyzer, and these biochemical indicators including: parathyroid hormone (PTH), n-terminal osteocalcin (N-MID), calcium, the level of hemoglobin (Hb), hematocrit (HCT), red blood cells (RBC), red cell distribution width (RDW), glycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), free fatty acids (FFA), creatine kinase (CK), lactate dehydrogenase (LDH), total testosterone (T), total bilirubin (TBIL), serum creatinine (CREA), uric acid (UA), urea (UREA), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and γ-glutamyl transferase (GGT). The intra-assay coefficient of variation (CV) was under 10% for all tests.

Height (cm) was measured by a portable altimeter (seca213, seca Zhong guo, Hangzhou, China), while weight (kg) and body mass index (BMI) were assessed by a performed by electrical impedance analysis (MF-BIA) using the In Body 770 (Bio-space Co., Ltd., Seoul, Korea).

Physical activity was measured using the International Physical Activity Questionnaire (IPAQ) and was completed before intervention [36]. Throughout the study, participants were instructed to maintain their daily physical activity and not to modify their lifestyle.

2.5. Statistical analysis

Randomization was performed by a random computer process. Sample-size calculations were based on the improvement of 25(OH)D levels after vitamin D_3 intervention. A minimum sample size of 49 students per group was necessary in order to provide a statistical power of about 80% for a defect effect size of 0.25. The final sample was at least 62 students in each arm, with a projected dropout rate of 20%.

A repeated measure analysis of variance (ANCOVA) was used to evaluate the interaction effect for group by time. Differences in outcomes over time between groups were measured using the Mann–Whitney U-test. Pearson correlation coefficients were computed to assess relationships of variables. Multiple linear regression was performed to analyze the association between 25(OH)D levels or VO_2max and outcomes. The regression model for estimating VO_2max was evaluated with the coefficients of determination (adjusted R^2) and absolute SE of the estimate (SEE). All data were presented as mean ± SD. The statistical significance level was set at $p < 0.05$.

3. Results

3.1. Baseline characteristics of subjects

One hundred and seventeen subjects (56 interventions and 61 controls) with a mean 25 (OH)D of 19.2 ± 7.8 ng/mL were analyzed in the study (Table 1). There was no significant difference in age, height, weight, BMI, bone turnover indicators, physical performance indicators, hemoglobin-related parameters, fatigue-related indicators, and lipid metabolism-related parameters at baseline ($p > 0.05$).

Table 1. Baseline characteristics of the participants.

Variables	Vitamin D($n = 56$)	Control($n = 61$)
Age, year	19.0(19.0—20.0)	19.0(19.0—20.0)
Male, n (%)	39.0(69.6%)	40.0(65.6%)
Height, cm	173.36 ± 9.19	173.08 ± 9.66
Weight, kg	66.77 ± 14.46	68.53 ± 14.54
BMI, kg/m^2	22.01 ± 3.29	22.64 ± 3.01
Bone turnover		
25(OH)D, ng/ml	18.85 ± 7.04	19.52 ± 8.65
N-MID, ng/ml	33.61 ± 13.96	30.58 ± 10.85
PTH, pg/ml	45.76 ± 18.65	50.92 ± 20.64
Calcium, mmol/L	2.37 ± 0.08	2.38 ± 0.08
Lipid profiles		
TC, mmol/L	4.38 ± 0.74	4.45 ± 0.77
HDL-C, mmol/L	1.38 ± 0.31	1.37 ± 0.32
LDL-C, mmol/L	2.59 ± 0.67	2.58 ± 0.59
TG, mmol/L	0.91 ± 0.46	1.09 ± 0.74
FFA, mmol/L	0.39 ± 0.19	0.38 ± 0.17
Erythrocytes and hemoglobin-related parameters		
Hb, g/L	152.80 ± 15.64	153.95 ± 14.41
HCT, %	46.23 ± 4.10	46.23 ± 3.67
RBC, 10^12/L	5.05 ± 0.46	5.05 ± 0.40
RDW, %	40.98 ± 4.85	41.60 ± 2.27
Fatigue-related indicators		
CK, U/L	276.18 ± 559.42	180.38 ± 121.51
LDH, U/L	187.80 ± 37.77	186.70 ± 30.95
T, ng/ml	4.29 ± 2.66	3.87 ± 2.40
Physical performance		
VJH, cm	39.86 ± 9.84	37.44 ± 11.19
RHS, kg	413.13 ± 114.60	401.15 ± 111.30
FVC, L	4.33 ± 0.92	4.18 ± 1.04
FEV_1, L	3.84 ± 0.77	3.78 ± 0.86
VO_2max, ml/min	3181.86 ± 1139.70[a]	3073.13 ± 1048.32[b]
Physical activity level		
Physical activity level, MET, h/day	1071.07 ± 255.16	1011.43 ± 242.25

Data are presented as mean ± SD or median (IQR) values for continuous variables and n (%) for categorical variables.
[a]$n = 50$. [b]$n = 54$.

3.2. Vitamin D status

As shown in Table 2, after intervention with 1000 IU of vitamin D_3 for 1 month during wintertime, mean serum 25(OH)D levels of students were increased from 18.85 ± 7.04 to 26.98 ± 5.88 ng/mL, and a significant group × time interaction was observed for serum 25 (OH)D concentrations in the intervention group ($p < 0.01$). Correspondingly, vitamin D_3 supplementation resulted in a significant reduction in the incidence of vitamin D deficiency (<20 ng/mL) in the vitamin D group (from 64.3% at the baseline to 8.9% at end point), while no significant difference was observed in the placebo group.

3.3. Effect of vitamin D supplementation on PTH, hemoglobin-related parameters, and physical performance

The baseline and end of study values of PTH, hemoglobin-related parameters, fatigue-related indicators, and athletic performance are shown in Table 2. It was found that vitamin D supplementation could significantly decrease PTH (from 45.76 ± 18.65 to 41.99 ± 20.92 pg/ml) compared with the placebo group ($p < 0.05$), while Hb, HCT, RBC,

Table 2. Changes of between baseline and follow-up in the intervention and the control group.

	Vitamin D					Control						
	Month 0		Month 1		Change[c]	Month 0		Month 1		Change[c]		
Variables	n	Mean ±SD	n	Mean ±SD	Mean ±SD	n	Mean ±SD	n	Mean ±SD	Mean ±SD	*P value*[d]	*P value*[e]
Weight and BMI												
Weight, kg	56	66.77 ± 14.46	56	66.98 ± 14.63	0.21 ± 2.51	61	68.53 ± 14.54	61	68.44 ± 14.76	−0.09 ± 1.48	*NS.*	*NS.*
BMI, kg/m^2	56	22.01 ± 3.29	56	22.09 ± 3.41	0.08 ± 0.78	61	22.64 ± 3.01	61	22.60 ± 3.16	−0.03 ± 0.51	*NS.*	*NS.*
Bone turnover												
25(OH)D, ng/ml	56	18.85 ± 7.04	56	26.98 ± 5.88	8.14 ± 3.85	61	19.52 ± 8.65	61	17.61 ± 8.19	−1.91 ± 2.58	**0.000**	**0.000**
N-MID, ng/ml	56	33.61 ± 13.96	56	32.05 ± 11.60	−1.57 ± 5.57	61	30.58 ± 10.85	61	30.64 ± 10.52	0.06 ± 6.31	*NS.*	*NS.*
PTH, pg/ml	56	45.76 ± 18.65	56	41.99 ± 20.92	−3.77 ± 15.71	61	50.92 ± 20.64	61	49.91 ± 19.52	−1.01 ± 23.20	**0.043**	*NS.*
Calcium, mmol/L	56	2.37 ± 0.08	56	2.37 ± 0.09	0 ± 0.11	61	2.38 ± 0.08	61	2.38 ± 0.08	−0.01 ± 0.1	*NS.*	*NS.*
Erythrocytes and hemoglobin-related parameters												
Hb, g/L	56	152.80 ± 15.64	56	153.88 ± 15.29	1.07 ± 11.73	61	153.95 ± 14.41	61	153.15 ± 16.49	−0.8 ± 11.68	*NS.*	*NS.*
HCT, %	56	46.23 ± 4.10	56	46.56 ± 4.57	0.33 ± 3.25	61	46.23 ± 3.67	61	46.74 ± 4.56	0.51 ± 3.26	*NS.*	*NS.*
RBC,10^12/L	56	5.05 ± 0.46	56	5.12 ± 0.48	0.07 ± 0.30	61	5.05 ± 0.40	61	5.14 ± 0.52	0.09 ± 0.30	*NS.*	*NS.*
RDW, %	56	40.98 ± 4.85	56	40.80 ± 3.48	−0.18 ± 5.42	61	41.60 ± 2.27	61	40.94 ± 3.64	−0.67 ± 3.21	*NS.*	*NS.*
Lipid metabolism												
TC, mmol/L	56	4.38 ± 0.74	56	4.50 ± 0.86	0.13 ± 0.47	61	4.45 ± 0.77	61	4.68 ± 0.79	0.23 ± 0.45	*NS.*	*NS.*
HDL-C, mmol/L	56	1.38 ± 0.31	56	1.37 ± 0.29	−0.01 ± 0.17	61	1.37 ± 0.32	61	1.42 ± 0.31	0.05 ± 0.18	*NS.*	*NS.*
LDL-C, mmol/L	56	2.59 ± 0.67	56	2.71 ± 0.81	0.13 ± 0.43	61	2.58 ± 0.59	61	2.80 ± 0.67	0.22 ± 0.45	*NS.*	*NS.*
TG, mmol/L	56	0.91 ± 0.46	56	0.93 ± 0.39	0.02 ± 0.38	61	1.09 ± 0.74	61	1.03 ± 0.45	−0.06 ± 0.70	*NS.*	*NS.*
FFA, mmol/L	56	0.39 ± 0.19	56	0.44 ± 0.23	0.05 ± 0.26	61	0.38 ± 0.17	61	0.42 ± 0.27	0.05 ± 0.28	*NS.*	*NS.*
Fatigue-related indicators												
CK, U/L	56	276.18 ± 559.42	56	184.05 ± 195.59	−92.13 ± 558.77	61	180.38 ± 121.51	61	154.79 ± 129.25	−25.59 ± 120.76	*NS.*	*NS.*
LDH, U/L	56	187.80 ± 37.77	56	173.91 ± 28.62	−13.89 ± 33.46	61	186.70 ± 30.95	61	171.44 ± 29.29	−15.26 ± 19.16	*NS.*	*NS.*
T, ng/ml	56	4.29 ± 2.66	56	4.26 ± 2.67	−0.03 ± 0.95	61	3.87 ± 2.40	61	3.85 ± 2.49	−0.01 ± 0.87	*NS.*	*NS.*
Physical performance												
VJH, cm	56	39.86 ± 9.84	56	40.71 ± 10.39	0.85 ± 2.96	61	37.44 ± 11.19	61	37.82 ± 11.13	0.38 ± 3.21	*NS.*	*NS.*
RHS, kg	56	413.13 ± 114.60	56	416.07 ± 118.33	2.95 ± 27.99	61	401.15 ± 111.30	61	400.98 ± 114.26	−0.16 ± 29.72	*NS.*	*NS.*
FVC, L	56	4.33 ± 0.92	56	4.35 ± 0.98	0.02 ± 0.26	61	4.18 ± 1.04	61	4.17 ± 1.06	−0.01 ± 0.32	*NS.*	*NS.*
FEV_1, L	56	3.84 ± 0.77	56	3.85 ± 0.81	0.01 ± 0.24	61	3.78 ± 0.86	61	3.77 ± 0.89	−0.01 ± 0.28	*NS.*	*NS.*

Month 0: measurements at baseline; Month 1: measurements after 1 month of intervention.
[c]Change = Month 1 minus Month 0.
[d]A repeated measure analysis of variance (ANCOVA) was used to evaluated the interaction effect for group by time.
[e]Between group differences were compared using the Mann–Whitney U-test.
NS: No significant.

Table 3. Association of subjects' characteristics with 25(OH)D by multiple regression analyses at baseline and after 1 month of intervention ($n = 117$).

	Month 0		Month 1	
Variables	*ß (95% CI)*	*p-value*	*ß (95% CI)*	*p-value*
Bone turnover				
N-MID, ng/ml	−14.238 (−27.436 −1.041)	**0.035**	−0.132 (−0.338 − 0.074)	0.206
PTH, pg/ml	−24.866 (−49.424 −0.308)	**0.047**	−0.580 (−1.041 − 0.118)	**0.014**
Calcium, mmol/L	−0.0360 (−0.137 − 0.065)	0.484	−0.001 (−0.003 − 0.001)	0.271
Erythrocytes and hemoglobin-related parameters				
Hb, g/L	−3.473 (−18.088 − 11.141)	0.639	−0.162 (−0.393 − 0.069)	0.166
HCT, %	−2.028 (−5.656 − 1.601)	0.271	−0.078 (−0.145 − 0.011)	**0.022**
RBC,$10^{\wedge 12}$/L	−0.326 (−0.703 − 0.051)	0.089	−0.009 (−0.016 − 0.002)	**0.016**
RDW, %	−1.906 (−6.504 − 2.692)	0.413	−0.001 (−0.078 − 0.075)	0.977
Lipid profiles				
TC, mmol/L	−0.959 (−1.904 − −0.014)	**0.047**	−0.023 (−0.042 − −0.004)	**0.016**
HDL-C, mmol/L	−0.154 (−0.496 − 0.187)	0.372	−0.005 (−0.010 − 0.001)	0.121
LDL-C, mmol/L	−0.681 (−1.470 − 0.108)	0.090	−0.012 (−0.029 − 0.005)	0.151
TG, mmol/L	−0.27 (−1.040 − 0.500)	0.489	−0.013 (−0.022 − 0.004)	**0.005**
FFA, mmol/L	−0.255 (−0.479 − −0.030)	**0.027**	−0.001 (−0.007 − 0.004)	0.696
Physical performance				
VJH, cm	11.473 (2.979 − 19.966)	**0.009**	0.245 (0.094 − 0.397)	**0.002**
RHS, kg	8.766 (−63.598 − 81.131)	0.811	0.787 (−0.525 − 2.100)	0.237
FVC, L	0.337 (−0.469 − 1.143)	0.410	0.014 (0.000 − 0.029)	0.052
FEV_1, L	0.236 (−0.421 − 0.893)	0.479	0.007 (−0.005 − 0.019)	0.273

Statistically significant variables were adjusted for age, gender, and BMI; ß, unstandardized coefficient; 95%CI, confidence interval.
The 25(OH)D levels at baseline was log transformed for the analysis.

CK, LDH, T, VJH, RHS, FVC, and FEV_1 values were not significantly changed ($p > 0.05$). The same results were obtained after stratifying the analysis by gender (Table S1 and Table S2). At baseline and after 1 month of intervention, serum 25(OH)D levels were found to be negatively correlated with PTH values ($p < 0.05$) and positively correlated with the VJH values adjusted for confounding variables ($p < 0.05$) (Table 3).

3.4. Vitamin D status predicted VO_2max

The relationships between the VO_2max levels and the subjects' characteristics were detailed in Table S4. At baseline, VO_2max level was found to be positively associated with 25(OH)D, height, weight, Hb, RHS, FVC, and FEV_1 values ($p < 0.05$). In order to predict VO_2max, the multiple linear regression analysis was performed (Table 4). The multiple linear regression model 3 showed that 25(OH)D combined with athletic, gender, height, weight, Hb, and FVC could account for 84.0% of the VO_2max (ml/min) value according to the following equation: $VO_2\text{max(ml/min)} = -726.065 \times \text{Athletic} - 638.730 \times \text{Gender} + 28.210 \times \text{Height} + 15.884 \times \text{Weight} + 667.603 \times 25(\text{OH})\text{D} - 9.158 \times \text{Hb} + 405.912 \times \text{FVC}$.

3.5. Effect of vitamin D supplementation on serum lipid profiles

The baseline and end of study values of serum lipid profiles are shown in Table 2. No significant differences were noted for TG, TC, HDL-C or LDL-C levels among groups ($p > 0.05$). The same results were obtained after stratifying the analysis by gender (Table S1 and Table S2). After

Table 4. Multiple linear regression analysis of VO_2max as the dependent variable ($n = 104$).

Prediction models	Coefficients	β	*p-value*	R^2	Adjusted R^2
Model 1				0.818	0.809
Athletic	−796.288	−0.367	.000		
Gender	−386.803	−0.160	.025		
Height, cm	34.228	0.286	.002		
Weight, kg	15.992	0.213	.002		
25(OH)D, ng/ml	678.148	0.099	.041		
Model 2				0.830	0.820
Athletic	−744.219	−0.343	.000		
Gender	−632.902	−0.262	.001		
Height, cm	32.576	0.272	.002		
Weight, kg	17.282	0.230	.001		
25(OH)D, ng/ml	664.428	0.097	.039		
Hb, g/L	−11.065	−0.141	.011		
Model 3				0.840	0.825
Athletic	−726.065	−0.335	.000		
Gender	−638.730	−0.264	.005		
Height, cm	28.210	0.235	.009		
Weight, kg	15.884	0.211	.008		
25(OH)D, ng/ml	667.603	0.097	.036		
Hb, g/L	−9.158	−0.117	.040		
RHS, kg	−0.398	−0.039	.628		
FVC, L	405.912	0.356	.028		
FEV1, L	−355.659	−0.258	.115		

B, unstandardized regression coefficients; β, standardized regression coefficients.
The 25(OH)D levels was log transformed for the analysis.
Athletic (athletes = 1, non-athletes = 2); Gender (Man = 1, Woman = 2).
Model 2: as in model 1 plus Hb.
Model 3: as in model 2 plus RHS、FVC、FEV_1.
VO_2max(ml/min) = −726.065 × Athletic − 638.730 × Gender + 28.210 × Height + 15.884 × Weight + 667.603 × 25(OH)D −9.158 × Hb + 405.912 × FVC.

adjustment for age, gender and BMI, as shown in Table 3, there was no significant relationships between 25(OH)D and TG, HDL-C or LDL-C ($p > 0.05$). However, serum 25(OH)D levels remained negatively correlated with plasma TC values at baseline and after intervention ($p < 0.05$).

4. Discussion

The present data demonstrated that after one-month vitamin D_3 supplementation with 1000 IU/d, 25(OH)D levels were increased by 43%, which was accompanied by a significant decrease in PTH. Even so, short-term vitamin D_3 intervention was not sufficient to improve physical performance, bone turnover, and serum lipids. Furthermore, 25(OH)D levels combined with athletic, FVC, and Hb could be a predictor of VO_2max. To the best of our knowledge, this was the first study to provide a potential model for VO_2max predictor using vitamin D status. These results could provide a hint for vitamin D as an activator of aerobic capacity, and support the evidence for large dose supplementation in winter as a preventative strategy for vitamin D deficiency.

Vitamin D is essential to musculoskeletal health and exercise performance. Evidence from observational studies and meta-analyses of RCTs suggested that deficient or inadequate vitamin D status was associated with adverse muscle function, including muscle weakness [37–39], elevated markers of oxidative stress, and reduced mitochondrial function [39,40]. Additionally, a mechanism by which vitamin D_3 supplementation could enhance muscle function is due to its synergy with testosterone [35]. And some trials

have found that muscle strength has been improved with testosterone supplementation [3,18,41]. In our study, although 25(OH)D level was positively associated with vertical jump height at the baseline and end of the study, supplementation did not significantly increase vertical jump height or right handgrip strength when compared to the control group, which was consistent with findings from a recent RCT conducted in college-age soccer players [33]. One reason might be that vitamin D levels in the intervention group were less than 30 ng/mL at end. Some studies suggested that physically active individuals should maintain a higher vitamin D status, possibly as elevated as 50 ng/mL to achieve an optimal and performance health [42]. Future research will focus on comparing vitamin D and placebo groups for muscle strength changes as they move from deficient or inadequate to adequate vitamin D status in a wider population.

Our study did not observe a positive effect of vitamin D_3 supplementation on FEV_1 or FVC, corroborating findings from a recent RCT in healthy students [33]. Some observational studies have revealed that 25(OH)D levels may be linked to lung function, particularly in individuals with airway disease, contradicting our findings [4,43]. One reason for this may be that the subjects of our survey were healthy individuals. The response to vitamin D_3 supplementation, in terms of benefits on lung function parameters, may vary between healthy individuals and those with disease.

Mechanistic studies support the concept that vitamin D could enhance VO_2max through improving hematological levels [20]. Established primary determinants of VO_2max are cardiac output and oxygen diffusion capacity [44], which is a function in which blood cells and Hb actively participate. An observational study from the United States found that a higher concentration of 25(OH)D was independently associated with better VO_2max in adults [31,45]. It has been demonstrated that tissue oxygenation is improved on a cellar level, where higher 25(OH)D concentrations are present in blood [46]. Nevertheless, no effect of vitamin D supplementation on erythropoiesis and hemoglobin-related parameters was observed in our study. One possible reason was that reported associations between 25(OH)D levels and hematological levels were currently confirmed in subjects with diseases instead of healthy individuals [47,48]. Recently, additional data also revealed that vitamin D supplementation has no effect on VO_2max in healthy individuals [17,32,33,49]. Therefore, the association between vitamin D and VO_2max in collegiate students cannot be concluded based on our limited study.

The present study demonstrated 25(OH)D levels combined with athletic, FVC, and Hb could be a predictor of VO_2max. Traditionally, direct measurement of VO_2max is limited by the expensive and complex equipment, the qualification of the assessor, and the long test time. At the same time, the physical and mental states of the subjects also directly affect the absolute value of VO_2max, making it difficult to promote the use of direct measurement of VO_2max in many situations. Some indirect methods that are relatively safe, effective, and suitable for predicting VO_2max have been proposed [50–53]. Among them, the submaximal model obtains exercise-related data through a specified motion protocol, such as shuttle runs, and constructs an estimation model along with other anthropometric features. Although submaximal models have overcome some of the limitations of cardiopulmonary function testing, they still require trained personnel to perform Submaximal testing [53]. Compared with other indirect measurement methods, our method for VO_2max prediction is simple and easy to implement, and the results are relatively more accurate.

Vitamin D and PTH are two major regulators of mineral metabolism. They play critical roles in maintaining calcium and phosphate homeostasis as well as the development and maintenance of bone [54]. Low vitamin D status can be an independent contribution to high PTH concentrations. The negative association between serum 25(OH)D and PTH has been previously demonstrated, but mostly in elderly, women and/or osteoporotic populations [55,56]. In this study, it was observed that vitamin D_3 supplementation decreased the level of PTH. Our study further validated the relationships between 25(OH)D and PTH in healthy collegiate students.

Previous studies that investigated the association between vitamin D status and serum lipid profiles showed different results. A recent systematic review and meta-analysis found that vitamin D supplementation has a beneficial effect on serum TC, LDL-C, and TG, but not HDL-C [57], whereas others found the serum 25(OH)D concentrations were inversely related to the LDL-C, HDL-C, and TG values in healthy adults [30]. Intriguingly, mechanistic studies support that vitamin D is inextricably linked to cholesterol metabolism with both metabolisms sharing an extensive common biosynthesis pathway [58]. In the present study, we found that TC was negatively correlated with 25(OH)D levels at the begin and end of the study after adjusting for potential confounders, which supports the findings of previous studies [29,59].

Several limitations should also be taken into account in interpreting our results. Firstly, we surmised that receiving vitamin D_3 for a short term (1 month) may obscure its beneficial effects and the mean post-intervention 25(OH)D level (26.98 ng/mL) was not sufficient to improve other outcome variables in our study. Hence, longer intervention durations are needed to explore the effects of vitamin D_3 intervention on bone turnover parameters, physical performance, and lipid parameters. Besides, due to the limitations in testing conditions, we did not complete post-intervention VO_2max measurements for all subjects, but the 25(OH)D levels was identified as a predictor of VO_2max in these young collegiate students highlighting the impact of 25(OH)D on physical performance. Finally, an appropriate placebo was not available in the control group, which would cause research bias. Since individuals in both intervention and control group realized they were being observed, participant reactivity or Hawthorne effect dose still occur. However, it may be hard to determine exactly how participant awareness impacts study results.

5. Conclusion

In summary, we provided data demonstrating a high prevalence of vitamin D insufficiency and deficiency among collegiate students during wintertime. Supplementation with a 1000IU/day vitamin D_3 had beneficial effects on 25(OH)D status and PTH. However, vitamin D_3 intervention, at the dose provided here for 1 month, did not improve physical performance. 25(OH)D levels were found to be positively correlated with vertical jump height and negatively correlated with PTH and total cholesterol. Furthermore, 25(OH)D levels combined with athletic, Hb and FVC could be a potential predictor of VO_2max.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

XLZ, QZ, WJW, and BYL participated in the design, conducted the statistical analyses, interpreted the data, and drafted the manuscript. GMZ, WJW, and BYL supervised the study, assisted in data interpretation, and critically reviewed the manuscript. JFL, XZ, QWG, LJD, HMZ, HMD, and FJ helped in conducting the study and revising the manuscript. YFP and ZLZ helped to manage and analyze the data. All authors read and approved the final manuscript.

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