

Effects of physical activity and sedentary behavior on serum vitamin D in patients with chronic obstructive pulmonary disease

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Advances in Clinical and Experimental Medicine, ISSN 1899–5276 (print), ISSN 2451–2680 (online)

Adv Clin Exp Med. 2024;33(12):1329–1341

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Funding sources

This study was financially supported by the Scientific Research Fund Project of Hebei Provincial Health Commission (grant No. 20231071).

Conflict of interest

None declared

Received on April 23, 2023

Reviewed on April 30, 2023

Accepted on November 24, 2023

Published online on March 20, 2024

Cite as

Wang H, Ge C, Zhang Z, Geng Z, Zhang L. Effects of physical activity and sedentary behavior on serum vitamin D in patients with chronic obstructive pulmonary disease. *Adv Clin Exp Med*. 2024. doi:10.17219/acem/175815

DOI

10.17219/acem/175815

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Abstract

Background. Chronic obstructive pulmonary disease (COPD) is a complex, heterogeneous disease with multiple extrapulmonary manifestations, among which vitamin D deficiency and insufficiency are very common in COPD and are associated with the health status and clinical outcomes of COPD patients.

Objectives. This paper aims to analyze the impact of leisure-time physical activity (LTPA) and daily sitting time (DST) and their interactions on serum vitamin D in patients with COPD.

Materials and methods. Participants aged ≥ 40 years from the National Health and Nutrition Examination Survey (NHANES) in the USA from 2007 to 2012 who had undergone pulmonary function tests and vitamin D tests were selected as the study participants. Participants' LTPA and DST were assessed using the General Practice Assessment Questionnaire (GPAQ). Multivariate logistic regression analysis was used to analyze the relationship between serum vitamin D, LTPA, DST and the combination of the 2 in patients with COPD, and the results were expressed as odds ratio (OR) and 95% confidence interval (95% CI).

Results. This study included 1,448 samples. The mean vitamin D concentration of the samples was (68.27 ± 26.78) nmol/L; 360 participants (24.86%) had vitamin D deficiency and 539 participants (37.22%) had vitamin D insufficiency. Vitamin D and 25(OH)D₃ expression levels differed across the 4 groups (150 min/week and DST > 8 h revealed the highest vitamin D expression levels, while LTPA 8 h showed the lowest. Vitamin D was weakly correlated with FEV₁, FVC, BMI, age, and LTPA ($p < 0.01$), but not with DST. Body mass index (BMI) was weakly positively correlated with DST ($r = 0.142$, $p < 0.01$).

Conclusions. Serum physical activity and DST independently affect vitamin D levels in COPD patients; therefore, increasing physical activity and minimizing DST may help improve vitamin D levels and prevent vitamin D deficiency.

Key words: physical activity, sedentary behavior, vitamin D, chronic obstructive pulmonary disease

Background

Chronic obstructive pulmonary disease (COPD) is a clinical syndrome characterized by chronic respiratory symptoms, abnormal lung structure and impaired lung function.¹ It is a prevalent condition globally and is associated with significant morbidity and mortality. Despite its high incidence, COPD is frequently underdiagnosed, resulting in delayed recognition until the disease has reached an advanced stage. Over the last 2 decades, the treatment options for COPD have expanded considerably, including new oral and inhaled medications and innovative surgical and bronchoscopic procedures.² External environmental factors (such as smoking, exposure to harmful particles, lower respiratory tract infection, and occupational exposure) and internal factors (such as genetic variation, epigenetic factors and population aging) lead to multiple mechanisms involved in the pathogenesis of COPD, which include oxidative stress, protease and antiprotease imbalance, immune inflammation, apoptosis, as well as systemic and lung damage and repair.^{3,4} Owing to the initial oxidative and inflammatory events described above, COPD is linked to several changes in the respiratory airways, in particular the remodeling of alveolar and airways epithelium, mucoid plug formation, increased density of inflammatory cells, smooth muscle hyperplasia, and fibrosis.⁵ These changes are considered to be the part of the tissue regeneration and repair processes that further increase mucus production and lead to emphysematous destruction of the gas-exchanging surface of the lung.⁶ These airway changes manifest as clinical symptoms, including dyspnea and a persistent cough, with or without sputum production. Usually, spirometry is recommended as the subsequent diagnostic test, or a postbronchodilator FEV₁/FVC ratio of less than 0.70 is used for further confirmation.⁷

While COPD is curable and the cure varies from case to case, the dietary and lifestyle changes are also considered indispensable for a quick recovery. While there is a lack of definitive data, the existing scientific evidence suggests that certain foods and nutrients, particularly those with antioxidant and anti-inflammatory properties, as well as when consumed in a balanced dietary pattern, are linked to improved pulmonary function, slower decline in lung function and a decreased risk of COPD. Understanding the impact of diet on COPD can equip healthcare professionals with an evidence-based framework to provide patients with valuable guidance to improve their respiratory wellbeing.⁸ It is also worth noting that nutritional deficiencies need to be assessed and replenished to achieve an effective treatment outcome either via dietary or pharmacological means.

Among several nutritional deficiencies, vitamin D has been extensively reported. Vitamin D deficiency and insufficiency are very common and are associated with the health status and clinical outcomes of patients with COPD.^{9,10} Moreover, vitamin D is a potential modality for

the treatment of COPD due to its anti-inflammatory and antioxidant properties, as well as its ability to modulate the immune response.^{11,12} Although some recent studies suggest that vitamin D supplementation may benefit patients with COPD, the results are inconsistent^{13,14} and the best way to prevent abnormal vitamin D metabolism in patients with COPD has not been determined.

Vitamin D plays a significant role in preventing inflammation and modulating molecular signaling pathways associated with tissue remodeling.¹⁵ Inflammation is a complex immune response involving the activation of various signaling molecules and cellular processes. Vitamin D has been shown to have anti-inflammatory properties by modulating the expression and function of inflammatory mediators, such as cytokines and chemokines.^{16,17} It can inhibit the production of pro-inflammatory cytokines while promoting the synthesis of anti-inflammatory cytokines, thereby helping to maintain a balanced immune response and dampening excessive inflammation. Moreover, vitamin D has been shown to influence molecular signaling pathways involved in tissue remodeling. Tissue remodeling refers to the process of structural changes in tissues that occur in response to injury, repair or chronic diseases. Vitamin D can regulate the expression of genes involved in extracellular matrix synthesis and degradation and cell proliferation and differentiation. It can also influence the activity of enzymes and signaling molecules implicated in tissue remodeling processes, such as matrix metalloproteinases (MMPs) and transforming growth factor-beta (TGF- β).¹⁸ It has also been found to be effective in various lung inflammatory diseases.¹⁹ By exerting anti-inflammatory effects and modulating molecular signaling related to tissue remodeling, vitamin D helps maintain tissue homeostasis and prevent excessive tissue damage. However, it is important to note that the specific mechanisms and effects of vitamin D in these processes are still an area of active research, and further studies are needed to fully understand its role in preventing inflammation and tissue remodeling.

The connection between physical activity, sedentary behavior and serum vitamin D levels in patients with chronic obstructive pulmonary disease (COPD) lies in the impact of lifestyle factors on vitamin D synthesis. Inactivity and prolonged sedentary behavior can contribute to reduced exposure to sunlight, which is essential for the body's production of vitamin D. This deficiency in physical activity and excessive sedentary time may consequently lead to lower serum vitamin D levels in COPD patients.^{20,21} Recent studies have shown that physical activity in patients with COPD is affected by a variety of extrapulmonary factors (such as skeletal muscle dysfunction, depressive symptoms and nutritional status).^{22,23} Regular exercise training and rehabilitation can alleviate the above extrapulmonary complications syndrome²⁴; in the general population, serum vitamin D is related to physical activity, and adequate physical activity is a protective factor for maintaining normal vitamin D levels.^{25,26} However, there is limited epidemiological

evidence on the effects of physical activity and sedentary behavior on serum vitamin D in patients with COPD. Therefore, there is an ongoing scientific effort to explore the role of vitamin D in COPD and reduce the disease burden.

Objectives

This study aims to analyze the impact of leisure-time physical activity (LTPA) and daily sitting time (DST), as well as their interactions, on serum vitamin D in patients with COPD. Additionally, the study suggests ways of preventing abnormal vitamin D metabolism in patients with COPD. The aim of this study is to propose the inclusion of vitamin D status in the diagnosis and treatment of COPD, and to pave the way for further research on need of vitamin D interventions and the development of physical activity standards for routine COPD treatment.

Materials and methods

Study design and setting

This study involves 3 cycles of data retrieved from the National Health and Nutrition Examination Survey (NHANES) conducted between 2007 to 2012 and published by the Centers for Disease Control and Prevention (CDC).

Participants

Among the 48,407 samples in 3 cycles, this study included participants older than 40 years and whose lung function met the diagnostic criteria for COPD,¹⁷ while excluding those lacking data on vitamin D, physical activity time and DST. All NHANES protocols were approved by the National Center for Health Statistics Ethics Review Board. Written informed consent was obtained from all participants. The datasets used contained no personally identifiable information, so they were not subject to ethical review. Demographic data, spirometry, disease information, dietary data, laboratory and questionnaire data associated with disease definitions were collected and merged from different NHANES files.

Variables

According to the current studies, the following variables were chosen as confounding factors measured in the baseline survey. Demographic characteristics included age (40–60, >60), sex (male or female), race/ethnicity (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other race), education level (high school or less, some college and college graduate or higher), family poverty–income ratio (total family income divided by poverty line: <1.3, from 1.3 to <3.5

or ≥3.5); body mass index (BMI; calculated as weight [kg] divided by height [m²] which was separated into 3 groups BMI <25, BMI range from 25.0 to 29.9 or BMI ≥30); lung function test²⁷; smoking status (never, former, current)²⁸; comorbidities included asthma, congestive heart failure, coronary heart disease, diabetes, cancer, and arthritis. Vitamin D intake was assessed based on the intake of vitamin D2 + D3 in the previous month. Then, LTPA (none, from 0 to <150 or ≥150) and DST (<4, 4 to 6, from 6 to 8 or >8) were chosen as categorical variables.

Experimental procedure

Recreational physical activity time, sedentary time and vitamin D determination

The Global Practice Assessment Questionnaire (GPAQ) was used to assess participants' LTPA and DST. The GPAQ is a validated questionnaire developed by the World Health Organization (WHO) to monitor physical activity. This questionnaire was applied in more than 100 countries worldwide via the WHO step-by-step surveillance approach. This questionnaire was used to gather information on daily physical activity, LTPA and sedentary behavior.²⁹ When answering the questionnaire, participants were asked to report their moderate- and high-intensity recreational activities in a week. Leisure-time physical activity is defined as the total time of conducting moderate-intensity recreational activity (min) plus twice the total time of conducting the vigorous-intensity recreational activity [min]. Based on the 2018 Physical Activity Guidelines for Americans, participants were classified as inactive (not participating in any physical activity), insufficiently active (more than 0 min but less than 150 min per week) and adequately active (more than 150 min active). Participants answered the question: "On a typical day, how much time do you usually spend sitting at school, at home, getting to and from places, or with friends, including time spent sitting at a desk, traveling in a car or bus, reading, playing cards, watching television, or using a computer?" to assess the participants' sedentary time. Study participants were divided into 4 groups based on their DST (h/day) (0 to <4, from 4 to <6, from 6 to 8, and ≥8 h/day).^{30,31} Serum 25(OH)D2 and 25(OH)D3 concentrations were determined using standard liquid chromatography-tandem mass spectrometry (LC-MS/MS), following CDC recommendations. Participants' blood was drawn by qualified medical practitioners. Measurement of serum 25(OH)D levels was expressed as nmol/L.³²

Statistical analyses

According to the vitamin D expression level defined by the relevant consensus, the enrolled patients were divided into vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency.³³ Vitamin D, 25(OH)3 and 25(OH)2 expression levels, vitamin D intake, age, BMI,

forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), FEV₁/FVC, LTPA, and DST were used as continuous variables with mean \pm standard deviation (M \pm SD). In this study, we employed a rigorous statistical approach to assess the relationship between vitamin D expression and 2 key lifestyle factors: LTPA and DST. To ensure the robustness of our analysis, we conducted several preliminary tests to examine the underlying assumptions of our chosen statistical methods.

We began by conducting tests of normality and homogeneity of variance on our data, as presented in Supplementary Table 1. The Kruskal-Wallis H test was utilized to assess variations in vitamin D expression based on 2 primary lifestyle factors: LTPA and DST.

Among the nonparametric tests, we used Spearman's rank correlation coefficient to obtain a correlation between vitamin D and its other dependencies. Vitamin D intake number, age (from 40 to 60, >60), BMI (<25, from 25 to 30 and \geq 30), ethnicity, family poverty–income index, education level, smoking history, complications, and LTPA (none, from 0 to <150 and \geq 150) and DST (<4, 4 to 6, from 6 to 8, and >8) as categorical variables. They were expressed as absolute numbers and constituent ratios, and the differences between groups were compared using χ^2 test. Logistic regression of the joint association of DST and with vitamin D was performed using the Wald χ^2 test. Furthermore, we also performed the calculation of odds ratios (ORs) based on control and treatment regimens using MedCalc v. 20.106 (MedCalc Software Ltd., Ostend, Belgium).

Spearman's correlation analysis was used to explore the correlation among vitamin D, FEV₁, FVC, BMI, age, DST, and LTPA. Multivariate logistic regression analysis was used to study the relationship between vitamin D and LTPA, DSA, and the combination of the two. Results were expressed as OR and 95% confidence interval (95% CI). In Model 1, there was no adjustment of confounding factors; in Model 2, age, sex, and race were adjusted as confounding factors; in Model 3, age, sex, race, BMI, family poverty–income index, education level, and smoking history were adjusted as confounding factors; in Model 4, age, sex, race, BMI, household poverty–income index, education

level, smoking history, vitamin D intake, comorbidities, and FEV₁ were adjusted as confounding factors; in Model 5, age, sex, race, BMI, household poverty–income index, education level, smoking history, vitamin D intake, comorbidities, and FVC were adjusted for confounding factors. Data analysis was performed using IBM SPSS 26.0 (IBM Inc., Armonk, USA). A p-value <0.05 represented a statistical difference. GraphPad Prism 8 (GraphPad Software, San Diego, USA) was employed to generate comprehensive visualizations, including scatter plots and box plots (Fig. 2–10).

Results

This study included 1,448 samples for analysis (Fig. 1). Table 1 shows selected demographics and potential confounders according to vitamin D level.

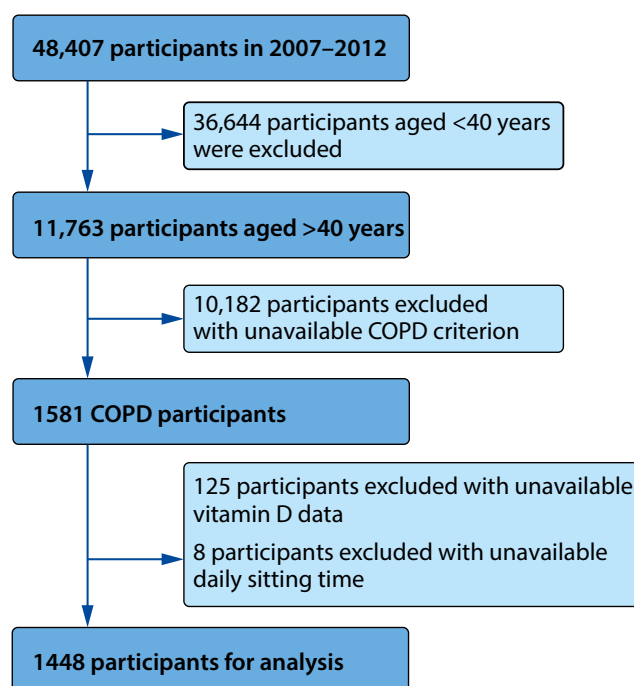


Fig. 1. Flow diagram of the overall procedure. A total of 1,448 samples were included for analysis

COPD – chronic obstructive pulmonary disease.

Table 1. Demographic and clinical characteristics of patients

Characteristic	All (1,448)	Vitamin D deficiency (360)	Vitamin D insufficiency (539)	Vitamin D sufficiency (549)	Statistical value	p-value
Vitamin D [nmol/L], mean \pm SD	68.27 \pm 26.78	35.48 \pm 9.20	63.00 \pm 7.07	94.96 \pm 18.49	1271.28 (K–W)	0.000
25(OH)D3 [nmol/L], mean \pm SD	63.65 \pm 26.30	33.28 \pm 9.37	59.15 \pm 9.53	87.98 \pm 21.47	1087.83 (K–W)	0.000
25(OH)D2 [nmol/L], mean \pm SD	4.62 \pm 11.71	2.19 \pm 3.03	3.84 \pm 6.67	6.96 \pm 17.38	43.47 (K–W)	0.000
Number of patients with vitamin D intake (%)	343 (23.7)	21 (1.5)	115 (7.9)	207 (14.3)	124.81 (χ^2)	0.000
Vitamin D intake [μ g], mean \pm SD	21.49 \pm 134.56	12.38 \pm 5.62	33.91 \pm 232.06	15.51 \pm 11.11	12.81 (K–W)	0.002
Age [years], mean \pm SD	62.06 \pm 10.35	60.93 \pm 9.87	61.68 \pm 10.71	63.19 \pm 10.20	12.72 (K–W)	0.002
40–60, n (%)	598 (41.3)	164 (11.3)	233 (16.1)	201 (13.9)	8.49 (χ^2)	0.014
>60, n (%)	850 (58.7)	196 (13.5)	306 (21.1)	348 (24.0)		

Table 1. Demographic and clinical characteristics of patients – cont.

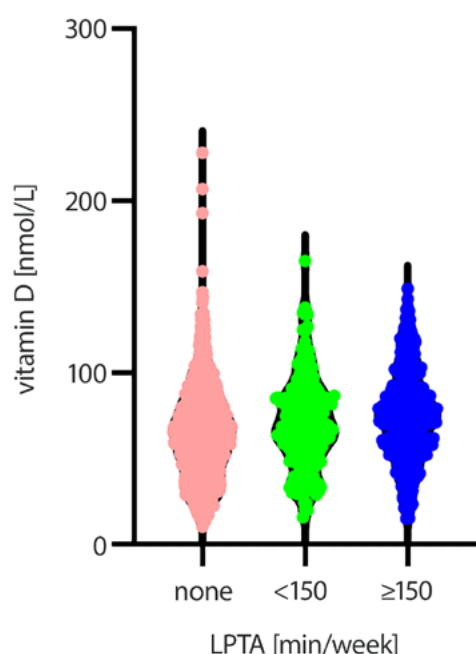
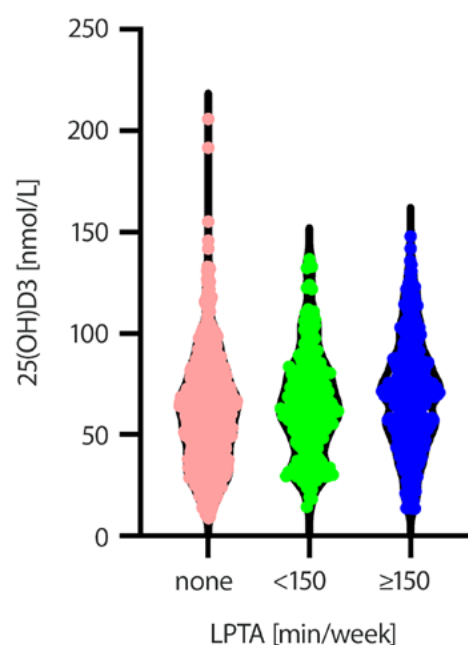
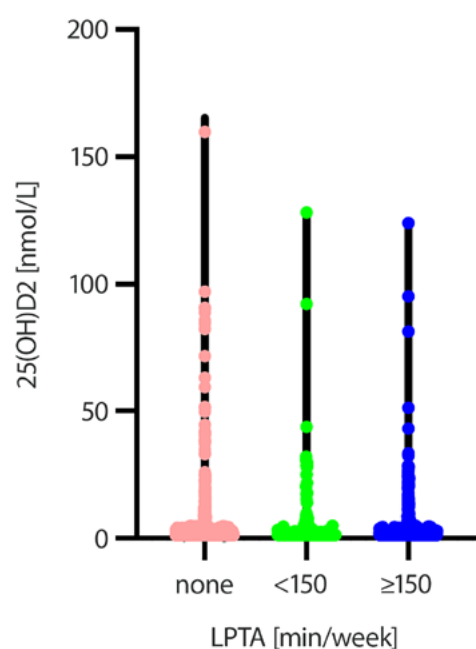
Characteristic		All (1,448)	Vitamin D deficiency (360)	Vitamin D insufficiency (539)	Vitamin D sufficiency (549)	Statistical value	p-value
Sex, n (%)	men	913 (63.1)	222 (15.3)	365 (25.2)	326 (22.5)	8.51 (χ²)	0.014
	women	535 (36.9)	138 (9.5)	174 (12.0)	223 (15.4)		
BMI [kg/m²], mean ±SD		27.85 ±5.97	28.40 ±7.04	28.26 ±5.99	27.08 ±5.06	10.74 (K–W)	0.005
<25, n (%)		502 (34.7)	129 (8.9)	163 (11.3)	210 (14.5)	20.72 (χ²)	<0.001
25–30, n (%)		522 (36.1)	105 (7.3)	211 (14.6)	206 (14.2)		
≥30, n (%)		422 (29.2)	126 (8.7)	163 (11.3)	133 (9.2)		
Race, n (%)							
Mexican American		105 (7.3)	34 (2.3)	50 (3.5)	21 (1.5)	148.79 (χ²)	<0.001
Other Hispanic		23 (1.6)	41 (2.8)	36 (2.5)	100 (6.9)		
Non-Hispanic White		887 (61.3)	148 (10.2)	326 (22.5)	413 (28.5)		
Non-Hispanic Black		277 (19.1)	134 (9.3)	94 (6.5)	49 (3.4)		
Other		79 (5.5)	21 (1.5)	28 (1.9)	30 (2.1)		
Family poverty–income ratio*, n (%)							
<1.3		433 (33.7)	139 (10.8)	152 (11.8)	143 (11.1)	28.33 (χ²)	<0.001
from 1.3 to <3.5		502 (39.1)	116 (9.0)	200 (15.6)	186 (14.5)		
≥3.5		350 (27.2)	59 (4.6)	133 (10.4)	158 (12.3)		
Educational attainment*, n (%)							
High school or less		793 (54.8)	219 (15.1)	302 (20.9)	272 (18.8)	18.82 (χ²)	0.001
Some college		366 (25.3)	90 (6.2)	137 (9.5)	139 (9.6)		
College graduate or higher		288 (19.9)	51 (3.5)	100 (6.9)	137 (9.5)		
Smoking, n (%)							
Never		401 (27.7)	82 (5.7)	157 (10.8)	162 (11.2)	35.59 (χ²)	<0.001
Former		548 (37.8)	109 (7.5)	207 (14.3)	232 (16.0)		
Current		400 (34.5)	169 (11.7)	175 (12.1)	155 (10.7)		
Comorbidities, n (%)							
Asthma		276 (19.1)	79 (5.5)	104 (7.2)	93 (6.4)	3.56 (χ²)	0.169
Congestive heart failure*		69 (4.8)	19 (1.3)	22 (1.5)	28 (2.0)	0.92 (χ²)	0.631
Coronary heart disease*		105 (7.3)	25 (1.7)	47 (3.3)	33 (2.3)	3.04 (χ²)	0.218
Diabetes		229 (15.8)	72 (5.0)	80 (5.5)	77 (5.3)	7.32 (χ²)	0.120
Cancer		244 (16.9)	52 (3.6)	80 (5.5)	112 (7.7)	7.92 (χ²)	0.019
Arthritis		603 (41.6)	135 (9.3)	215 (14.8)	253 (17.5)	7.68 (χ²)	0.021
FEV1 and FVC, mean ±SD							
FEV₁(L)		2.35 ±0.79	2.17 ±0.74	2.40 ±0.81	2.43 ±0.77	22.32 (K–W)	0.000
FVC(L)		3.72 ±1.12	3.48 ±1.06	3.79 ±1.14	3.80 ±1.11	18.58 (K–W)	0.000
FEV₁/FVC		0.63 ±0.07	0.62 ±0.08	0.63 ±0.07	0.64 ±0.07	10.18 (K–W)	0.006
LTPA [min/wk], mean ±SD		137.93 ±299.61	94.63 ±286.90	136.07 ±299.85	168.16 ±304.43	32.93 (K–W)	0.000
None (inactive), n (%)		859 (59.3)	251 (17.3)	325 (22.4)	283 (19.5)	34.78 (χ²)	0.039
From 0 to <150 (insufficiently active), n (%)		231 (16.0)	49 (3.4)	90 (6.2)	92 (6.4)		
≥150 (active), n (%)		358 (24.7)	60 (4.1)	124 (8.6)	174 (12.0)		
DST [h], mean ±SD		5.45 ±3.29	5.84 ±3.45	5.37 ±3.39	5.27 ±3.07	6.47 (K–W)	0.023
<4, n (%)		700 (48.3)	154 (10.6)	270 (18.6)	276 (19.1)	10.252 (χ²)	0.114
4–6, n (%)		317 (21.9)	82 (5.7)	106 (7.3)	129 (8.9)		
6–8, n (%)		204 (14.1)	57 (3.9)	77 (5.3)	70 (4.8)		
>8, n (%)		227 (15.7)	67 (4.6)	86 (5.9)	74 (5.1)		

BMI – body mass index; K–W – Kruskal–Wallis H test; FEV₁ – forced expiratory volume in 1 second; FVC – forced vital capacity; SD – standard deviation; LTPA – leisure-time physical activity; DST – daily sitting time; min/wk – minutes per week; *there was some missing data in these baseline characteristics.

Table 2. The expression of vitamin D according to LTPA

The expression of vitamin D	LTPA			Statistical value	p-value (Kruskal–Wallis H test)
	None (inactive)	from 0 to <150 (insufficiently active)	≥150 (active)		
Vitamin D [nmol/L]	65.11 ±27.02	69.23 ±24.99	74.93 ±26.07	39.51	<0.001
25(OH)D2 [nmol/L]	4.39 ±11.80	5.03 ±12.19	4.89 ±11.16	13.43	0.001
25(OH)D3 [nmol/L]	60.71 ±26.13	64.67 ±24.52	70.05 ±26.70	33.58	<0.001

SD – standard deviation; LTPA – leisure-time physical activity. Values are presented as mean ±SD.

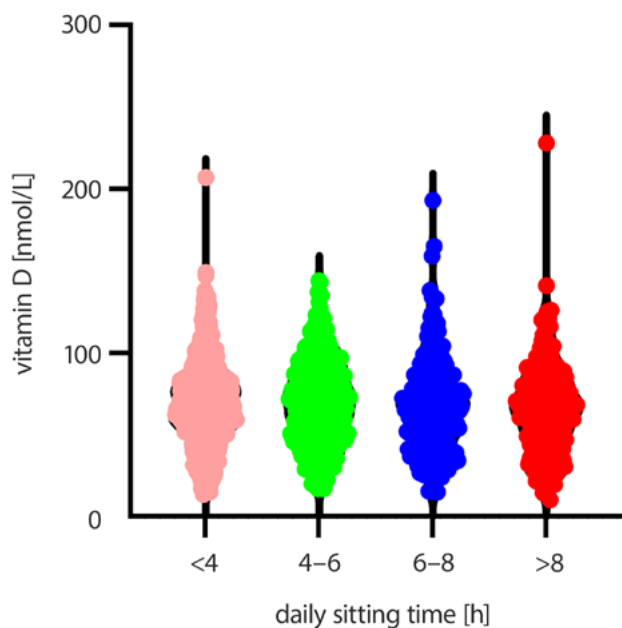
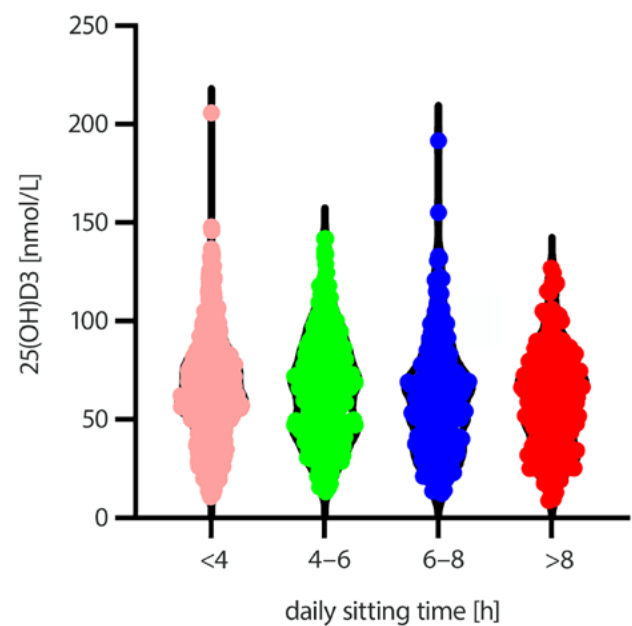
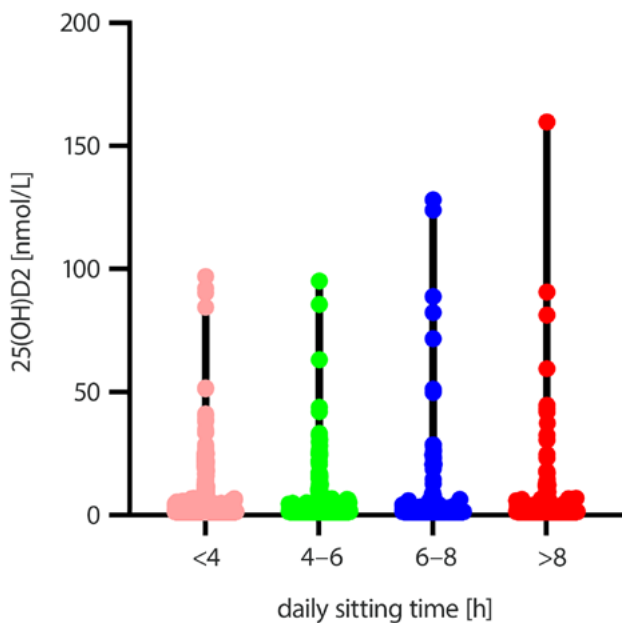
**Fig. 2.** The expression of vitamin D in different leisure-time physical activity (LTPA) levels**Fig. 4.** The expression of 25(OH)D3 in different leisure-time physical activity (LTPA) levels**Fig. 3.** The expression of 25(OH)D2 in different leisure-time physical activity (LTPA) levels

The average concentration of vitamin D in the samples was 68.27 ± 26.78 nmol/L. Of the 1,448 participants, 360 (24.86%) had vitamin D deficiency, with an average concentration of (35.48 ± 9.20) nmol/L, while 539 participants (37.22%) were insufficient in vitamin D, with an average concentration of (63.00 ± 7.07) nmol/L. Participants with vitamin D deficiency were younger, more obese, smokers, had poorer lung function, and had lower education levels and household income. Additionally, these participants were mainly non-Hispanic White men, who were less likely to take vitamin D supplements, and the probability of combining tumors and rheumatic diseases was low. Only 4.1% of the patients in the vitamin D deficiency group conducted sufficient LTPA (≥ 150 min/week), while 17.3% of the participants did not carry out any LTPA, and their activity time was significantly shorter than that of vitamin D insufficient and vitamin D sufficient participants, with a statistical difference ($p < 0.001$). The Kruskal–Wallis H test was utilized to assess variations in vitamin D expression based on 2 primary lifestyle factors: LTPA and DST. Compared to the other 2 groups of participants, the vitamin D deficiency group had a longer sedentary time ($p < 0.05$), and 4.6% of the participants exceeded 8 h of sedentary

Table 3. The expression of vitamin D according with the level of daily sitting time

The expression of vitamin D	Daily sitting time [h]				Statistical value	p-value (Kruskal–Wallis H test)
	<4	4–6	6–8	>8		
Vitamin D [nmol/L]	68.80 ±25.92	69.78 ±26.20	67.51 ±29.19	65.23 ±27.83	6.18	0.103
25(OH)D2 [nmol/L]	4.15 ±9.23	4.37 ±9.92	5.82 ±16.67	5.33 ±15.00	0.07	0.995
25(OH)D3 [nmol/L]	64.66 ±25.89	65.39 ±26.53	61.69 ±28.58	59.89 ±24.76	8.58	0.036

SD – standard deviation. Values are presented as mean ±SD.

**Fig. 5.** The expression of vitamin D in different daily sitting time (DST) levels**Fig. 7.** The expression of 25(OH)D3 in different daily sitting time (DST) levels**Fig. 6.** The expression of 25(OH)D2 in different daily sitting time (DST) levels

time, with no statistical difference ($t = 0.191$, $p = 0.848$) found. The expression levels of vitamin D, 25(OH)D2 and 25(OH)D3 varied between different physical activity

times ($p < 0.05$): the expression level of vitamin D was the highest in the participants with LTPA ≥ 150 min/week, and the lowest in those who did not conduct any physical activity (Table 2, Fig. 2–4); between different sedentary times, only the expression level of 25(OH)D3 showed statistical difference ($p < 0.05$), and there was no statistical difference in the vitamin D and 25(OH)D2 expressions ($p > 0.05$) (Table 3, Fig. 5–7). The combined analysis of physical activity time and sedentary time found that the expression levels of vitamin D 25(OH)D2 and 25(OH)D3 were different among the 4 groups ($p < 0.05$). The participants with LTPA ≥ 150 min/week and sedentary time > 8 h showed the highest vitamin D expression level, while the participants with LTPA < 150 min/week and sedentary time > 8 h had the lowest vitamin D expression level (Table 4, Fig. 8–10).

Table 5 showed the correlations among variables. Vitamin D had a weak correlation with FEV₁, FVC, BMI, age, and LTPA ($p < 0.01$), but had no correlation with sedentary time; BMI and sedentary time were weakly positively correlated ($r = 0.142$; $p < 0.01$); and LTPA was weakly positively correlated with lung function parameters (FEV₁, FVC; $p < 0.01$).

To further analyze the independent effects of physical activity and sedentary time, and their interaction

Table 4. The expression of vitamin D according with the joint associations of total sitting time and leisure-time physical activity (LTPA)

Activity time [h]	<150		≥150		Statistical value	p-value (Kruskal–Wallis H test)
Sedentary time [h]	>8	≤8	>8	≤8		
Vitamin D [nmol/L]	60.94 ±28.05	67.06 ±26.29	78.97 ±22.31	74.22 ±26.66	44.32	<0.001
25(OH)D2 [nmol/L]	5.24 ±15.63	4.39 ±11.04	5.61 ±12.90	4.76 ±10.84	8.21	0.042
25(OH)D3 [nmol/L]	55.6 ±23.70	62.66 ±26.08	73.34 ±23.42	69.4 ±27.24	39.94	<0.001

SD – standard deviation. Values are presented as mean ±SD.

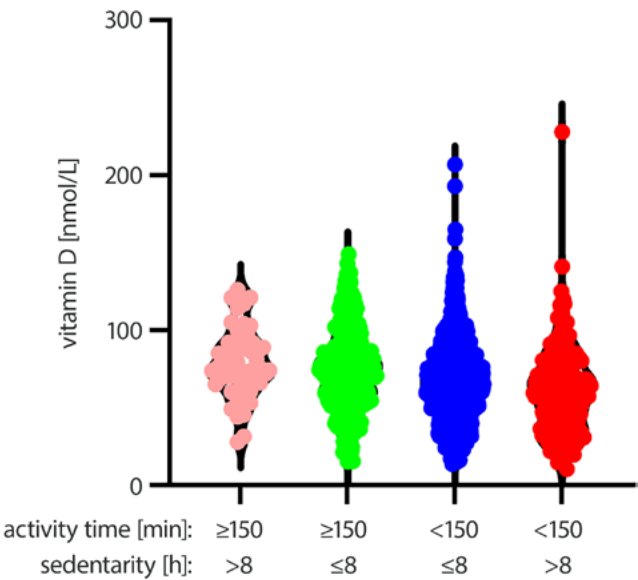


Fig. 8. The expression of vitamin D in combined analysis of physical activity time and daily sitting time (DST)

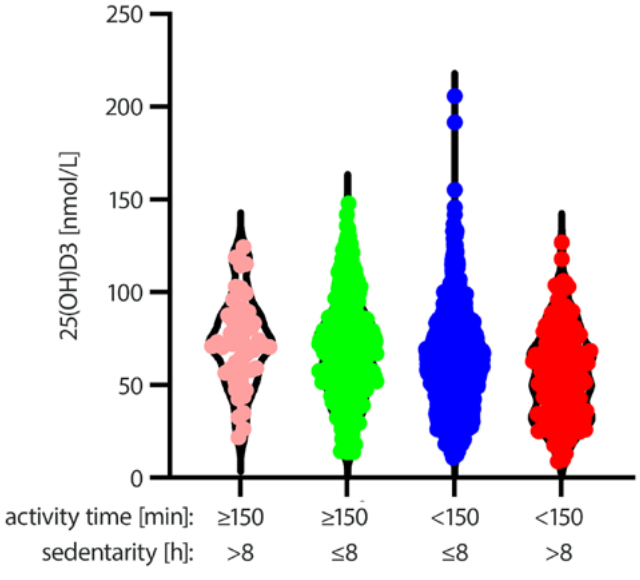


Fig. 10. The expression of 25(OH)D3 in combined analysis of physical activity time and daily sitting time (DST)

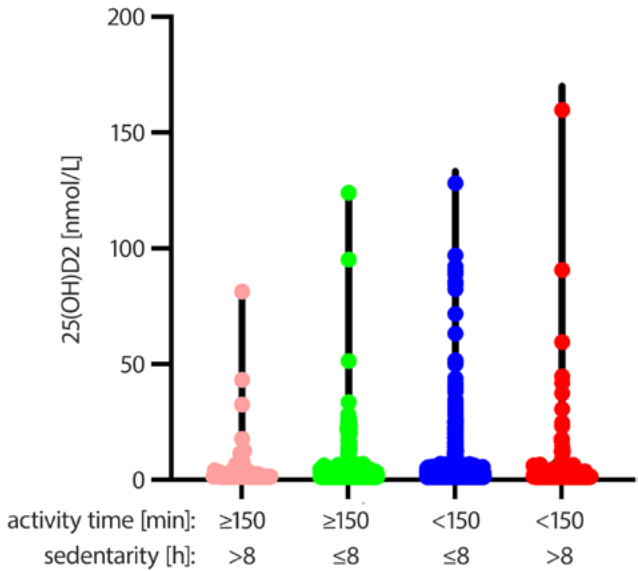


Fig. 9. The expression of 25(OH)D2 in combined analysis of physical activity time and DST

on vitamin D in patients with COPD, vitamin D status (vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency in order) was used as the dependent variable, and an ordinal logistic regression was conducted to provide the estimation and direction of the influence

of physical activity, sedentary time and their interaction on vitamin D sufficiency. Table 6 and Table 7 show that LTPA and sedentary time were related to vitamin D status. Compared with vitamin D deficiency, increased LTPA was a protective factor for vitamin D insufficiency and vitamin D sufficiency (Table 6), while increased sedentary time was a high-risk factor for vitamin D insufficiency and vitamin D sufficiency (Table 7). These associations remained after adjustment for relevant covariates (both p-values for trend <0.05).

Table 8 shows the results of a joint analysis of LTPA and sedentary time on vitamin D status. The combined effect of sedentary time and LTPA still impacted vitamin D status. Compared with the sedentary time of more than 8 h and active time of less than 150 min, when the active time was less than 150 min, sedentary time of less than 8 h was a protective factor for maintaining sufficient vitamin D levels; when the active time was longer than 150 min, no matter how long of sitting time (even more than 8 h) was a protective factor for maintaining normal vitamin D levels, and this relationship remained even after relevant covariates adjustment (both p-values for trend <0.05).

Parallelism test results were analyzed according to ordered logistic regression (Supplementary Table 2–4). We used vitamin D status as a dependent variable to conduct a multi-categorical logistic regression to analyze

Table 5. Relationship between vitamin D and related factors

Variables	Vitamin D [nmol/L]	FEV ₁ [L]	FVC [L]	BMI [kg/m ²]	Age [years]	DST [h]	LTPA [min/week]
Vitamin D [nmol/L]	1	0.095*	0.084*	−0.080*	0.096*	−0.036	0.160*
FEV ₁ [L]	−	1	0.943*	−0.077*	−0.336*	0.002	0.185*
FVC [L]	−	−	1	−0.095*	−0.328*	0.025	0.157*
BMI [kg/m ²]	−	−	−	1	0.054 [#]	0.142*	−0.035
Age [years]	−	−	−	−	1	0.018	−0.025
DST [h]	−	−	−	−	−	1	−0.008
LTPA [min/week]	−	−	−	−	−	−	1

Spearman correlation coefficient was used. * $p < 0.01$; [#] $p < 0.05$; BMI – body mass index; FEV₁ – forced expiratory volume in 1 second; FVC – forced vital capacity; LTPA – leisure-time physical activity; DST – daily sitting time.

Table 6. Ordered logistic regression models investigated the association between LTPA and serum 25(OH)D concentrations in chronic obstructive pulmonary disease (COPD) patients

Models	LTPA [min/week]			Wald χ^2	p-value for tend
	none (745, 59.1%)	from 0 to <150 (204, 16.2%)	≥150 (312, 24.7%)		
Model 1	Ref.	1.42 (1.08, 1.85)	1.97 (1.56, 2.49)	33.92	0.000
Model 2	Ref.	1.32 (1.01, 1.74)	1.89 (1.49, 2.39)	27.71	0.000
Model 3	Ref.	1.20 (0.89, 1.62)	1.67 (1.28, 2.20)	13.69	0.000
Model 4	Ref.	1.17 (0.86, 1.59)	1.49 (1.13, 1.98)	7.84	0.005
Model 5	Ref.	1.18 (0.87, 1.61)	1.51 (1.14, 2.00)	8.27	0.004

Model 1 – LTPA; Model 2 – LTPA, age, sex, race; Model 3 – LTPA, age, sex, race, BMI, family poverty–income ratio, educational attainment, smoking; Model 4 – LTPA, age, sex, race, BMI, family poverty–income ratio, educational attainment, smoking, comorbidities, FEV₁, vitamin D intake; Model 5 – LTPA, age, sex, race, BMI, family poverty–income ratio, educational attainment, smoking, comorbidities, FVC, vitamin D intake. LTPA – leisure-time physical activity; FEV₁ – forced expiratory volume in 1 second; FVC – forced vital capacity; OR – odds ratio; 95% CI – 95% confidence interval. In the logistic regression model, LTPA was treated as the predictor. Values are presented as OR (95% CI).

Table 7. Ordered logistic regression models investigated the association between DST and serum 25(OH)D concentrations in chronic obstructive pulmonary disease (COPD) patients

Models	DST [h]				Wald χ^2	p-value for tend	per 1 h/d increase
	<4	4–6	6–8	>8			
Model 1	Ref.	0.95 (0.75, 1.22)	0.77 (0.58, 1.03)	0.72 (0.54, 0.95)	6.98	0.008	0.97 (0.94, 0.99)
Model 2	Ref.	0.84 (0.65, 1.08)	0.69 (0.52, 0.93)	0.58 (0.44, 0.78)	15.84	0.000	0.94 (0.91, 0.97)
Model 3	Ref.	0.85 (0.65, 1.12)	0.70 (0.51, 0.96)	0.53 (0.38, 0.72)	16.89	0.000	0.93 (0.90, 0.96)
Model 4	Ref.	0.85 (0.64, 1.12)	0.68 (0.49, 0.95)	0.47 (0.34, 0.65)	21.11	0.000	0.92 (0.89, 0.95)
Model 5	Ref.	0.84 (0.63, 1.12)	0.67 (0.48, 0.94)	0.47 (0.34, 0.65)	21.42	0.000	0.92 (0.89, 0.95)

Model 1 – DST; Model 2 – DST, age, sex, race; Model 3 – DST, age, sex, race, BMI, family poverty–income ratio, educational attainment, smoking; Model 4 – DST, age, sex, race, BMI, family poverty–income ratio, educational attainment, smoking, comorbidities, FEV₁, vitamin D intake; Model 5 – DST, age, sex, race, BMI, family poverty–income ratio, educational attainment, smoking, comorbidities, FVC, vitamin D intake. DST – daily sitting time; OR – odds ratio; 95% CI – 95% confidence interval; in the logistic regression model, DST was treated as the predictor. Values are presented as OR (95% CI).

the effects of physical activity, sedentary time, and their interactions on vitamin D. Increased time spent on leisure physical activity after correction for relevant covariates was a protective factor for vitamin D sufficiency compared with vitamin D deficiency (Supplementary Table 5). Increased sitting time was a high factor for vitamin D adequacy (Supplementary Table 6). The joint analysis found that sitting for less than 8 h was a protective factor for maintaining adequate vitamin D levels when compared with sitting for more than 8 h and activity for less than 150 min (Supplementary

Table 7). When the activity time was longer than 150 min, whether the sedentary time was more than 8 h was a protective factor to maintain the normal vitamin D levels.

Discussion

This study found that abnormal vitamin D levels were common in COPD patients, and that there was a significant association between physical activity and sedentary behavior

Table 8. Ordered logistic regression models investigated the joint association of daily sitting time (DST) and leisure-time physical activity (LTPA) with vitamin D levels among chronic obstructive pulmonary disease (COPD) patients

Activity time [h]	<150		≥150		Wald χ^2	p-value for tend
	>8 (173, 11.9%)	≤8 (917, 63.3%)	>8 (54, 3.7%)	≤8 (304, 21.0%)		
Model 1	Ref.	1.57 (1.17, 2.13)	3.36 (1.87, 6.03)	2.57 (1.81, 3.65)	35.98	<0.001
Model 2	Ref.	1.82 (1.33, 2.49)	3.35 (1.85, 6.09)	2.86 (2.00, 4.10)	35.67	<0.001
Model 3	Ref.	2.04 (1.46, 2.87)	3.28 (1.69, 6.34)	2.83 (1.91, 4.19)	25.27	<0.001
Model 4	Ref.	2.13 (1.50, 3.01)	2.74 (1.83, 4.12)	2.32 (1.18, 4.59)	16.89	<0.001
Model 5	Ref.	2.13 (1.50, 3.01)	2.76 (1.84, 4.14)	2.33 (1.18, 4.60)	17.21	<0.001

Model 1 – the joint of daily sitting time and leisure-time physical activity; Model 2 – the joint of daily sitting time and leisure-time physical activity, age, sex, race; Model 3 – the joint of daily sitting time and leisure-time physical activity, age, sex, race, BMI, family poverty–income ratio, educational attainment, smoking; Model 4 – the joint of daily sitting time and leisure-time physical activity, age, sex, race, BMI, family poverty–income ratio, educational attainment, smoking, comorbidities, FEV₁, vitamin D intake; Model 5 – the joint of daily sitting time and leisure-time physical activity, age, sex, race, BMI, family poverty–income ratio, educational attainment, smoking, comorbidities, FVC, vitamin D intake.
eFEV₁ – forced expiratory volume in 1 second; FVC – forced vital capacity; OR – odds ratio; 95% CI – 95% confidence interval; BMI – body mass index. Values are presented as OR (95% CI).

and vitamin D levels in patients with COPD. The lack of sufficient physical activity and exhibiting long-term sedentary behavior are high-risk factors for abnormal expression of vitamin D in patients with COPD. Adequate physical activity and proper control of sedentary behavior can effectively improve vitamin D levels in patients with COPD.

Sedentary behavior and decreased physical activity due to exertional dyspnea are one of the main life characteristics of patients with COPD, and this lifestyle is associated with poor outcomes in patients with COPD³⁴: physical activity level and health status of patients with COPD,³⁵ the symptom burden,^{36–38} prolonged sedentary time, and decreased physical activity levels can all affect the mortality rate and the number of exacerbations³⁹ in patients with COPD. A study with a mean follow-up of 2.7 years found that the number of daily steps in patients with COPD decreased periodically over time, and this change was significantly correlated with the degree of airflow limitation in patients with COPD. Regular physical activity can alleviate the decline in lung function in patients with COPD, reduce the deterioration of health status (symptom burden)^{38,40–42} and limit the risk of hospital admission and mortality in patients with COPD.^{43,44} Although physical activity is also beneficial for COPD extrapulmonary comorbidities, related research is limited.^{22,23} Moreover, these studies did not analyze the effect of serum vitamin D levels in patients with COPD. Sedentary behavior or insufficient physical activity are the risk factors for vitamin D deficiency in the elderly patients.^{45,46} An analysis based on the NHANES data showed that physical activity was associated with serum vitamin D expression levels and was not related to the exercise environment (indoor or outdoor environment).⁴⁷ However, Scragg et al. studied the NHANES III database and found that the association between outdoor exercise and vitamin D was stronger than that of indoor environments.⁴⁸ Ceolin et al. showed that moderate-to-severe physical activity was a protective factor for maintaining normal levels of vitamin D

in the elderly,⁴⁶ and Scragg et al. found out that regular outdoor activities and activity frequency are associated with higher vitamin D levels, and not with activity intensity.⁴⁸ The above findings were based on the general population, and our findings showed that adequate activity time was related to high levels of vitamin D expression in patients with COPD, while prolonged sedentary behavior was related to lower vitamin D levels in patients with COPD. This observation confirmed the independent association of physical activity and sedentary time with serum vitamin D levels in patients with COPD.

Considering that high-intensity physical activity can alleviate the harmful effects of being sedentary, we conducted a joint analysis of the relationship between physical activity time and sedentary time and serum vitamin D levels in patients with COPD. A meta-analysis summarizing evidence from papers involving more than 1 million adults discovered that the risk of death was 59% higher in the least active group (8 h/day of sedentary activity, 2.5 MET h/week of physical activity (about 30 min/week of LTPA)) when compared to the most active group (4 h/day of sedentary activity, physical activity 35.5 MET h/week). The study showed that high levels of physical activity appear to lower the risk of death due to prolonged sitting.⁴⁹ Another study on cancer populations discovered that sedentary behavior was related to an increased risk of death among inactive cancer populations through a combined analysis of sedentary time and active time. Overall mortality (HR: 5.38; 95% CI: 2.99–9.67) and cancer (HR: 4.71; 95% CI: 1.60–13.9) mortality were the highest in inactive cancer patients who sat for more than 8 h/day.³⁰ Our joint analysis revealed that insufficient physical activity, coupled with a sedentary lifestyle of less than 8 h, emerged as a risk factor contributing to the challenge of maintaining optimal vitamin D levels in COPD patients.

Furthermore, to strengthen the statistical significance of the present study, we evaluated several recent studies on vitamin D intervention and analyzed the odds of COPD

occurrence.^{50–52} Based on these papers, we developed a forest plot indicating a strong possibility that vitamin D deficiency and hence its intervention can help in limiting COPD prevalence (Fig. 2).

The impaired ability of the skin to synthesize vitamin D due to the toxic effects of smoking and age. Decreased activity and lack of outdoor exercise contribute to reduced sun exposure. Additionally, intake of glucocorticoids increases the metabolic breakdown of vitamin D. Furthermore, the natural course of COPD involves mechanisms such as inflammatory response, decreased liver potential activation function, decreased gastrointestinal absorption functions, and vitamin D being blocked in adipose tissue, all of which can lead to metabolic disorders of vitamin D in patients with COPD.^{53,54} Physical activity may ameliorate the aforementioned disturbances through various mechanisms. High levels of inflammation in COPD patients, often associated with insufficient physical activity,³⁵ can be mitigated by regular exercise training. This can lead to reductions in immune cell counts and a transformation of the cytokine phenotype from pro-inflammatory to anti-inflammatory.^{55,56} Furthermore, physical activity has the potential to counteract the damage caused by smoking by reducing oxidase activity, promoting antioxidation⁵⁷ and mitigating inflammation.³² Additionally, it worth noting that physical activity can also stimulate the release of vitamin D from adipocytes through fat mobilization, further contributing to its beneficial effects.⁵⁸

Limitations

This study has several limitations. First, we could not make causal inferences in this cross-sectional study, so the association between physical activity and serum vitamin D in patients with COPD needs further confirmation. Second, although our study used a validated physical activity questionnaire, measurement error was inevitable. In addition, non-leisure physical activities (such as work) may have confounded the results of the measurements. Third, we did not analyze whether these activities were carried out outdoors or indoors.

Conclusions

In patients with COPD, serum vitamin D levels are independently associated with physical activity and sedentary behavior, and increasing physical activity time and reducing sedentary time may play an important role in improving vitamin D levels in COPD patients and preventing vitamin D deficiency. Future studies should analyze the effects of activity environment (indoor or outdoor, exposure to sunlight, etc.), frequency and intensity on serum vitamin D concentrations in COPD patients. In addition, the optimal duration of activity and sedentary time needs to be further confirmed.

Supplementary data

The Supplementary materials are available at <https://doi.org/10.5281/zenodo.10124644>. The package includes the following files:

Supplementary Table 1. Test of normality and homogeneity of variance.

Supplementary Table 2. Test of parallel lines of ordered logistic regression models investigate the association between the joint association of DST and LTPA and serum 25 (OH)D concentrations in COPD patients.

Supplementary Table 3. Test of parallel lines of ordered logistic regression models investigate the association between DST and serum 25 (OH)D concentrations in COPD patients.

Supplementary Table 4. Test of parallel lines of ordered logistic regression models were used to investigate the association between the joint association of DST and LTPA and serum 25 (OH)D concentrations in COPD patients.

Supplementary Table 5. Multivariate logistic regression models were used to investigate the association between LTPA and serum 25 (OH)D concentrations in COPD patients.

Supplementary Table 6. Multivariate logistic regression models were used to investigate the association between DST and serum 25 (OH)D concentrations in COPD patients.

Supplementary Table 7. Multivariate logistic regression models were used to investigate the association between association of DST and LTPA and serum 25 (OH)D concentrations in COPD patients.


Availability of data and materials


The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.


Consent for publication


Not applicable.


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References

- Christenson SA, Smith BM, Bafadhel M, Putcha N. Chronic obstructive pulmonary disease. *Lancet*. 2022;399(10342):2227–2242. doi:10.1016/S0140-6736(22)00470-6
- Ferrera MC, Labaki WW, Han MK. Advances in chronic obstructive pulmonary disease. *Annu Rev Med*. 2021;72(1):119–134. doi:10.1146/annurev-med-080919-112707
- Celli BR, Wedzicha JA. Update on clinical aspects of chronic obstructive pulmonary disease. *N Engl J Med*. 2019;381(13):1257–1266. doi:10.1056/NEJMr1900500

4. Higham A, Quinn AM, Cançado JED, Singh D. The pathology of small airways disease in COPD: Historical aspects and future directions. *Respir Res.* 2019;20(1):49. doi:10.1186/s12931-019-1017-y
5. Guo P, Li R, Piao TH, Wang CL, Wu XL, Cai HY. Pathological mechanism and targeted drugs of COPD. *Int J Chron Obstruct Pulmon Dis.* 2022;17:1565–1575. doi:10.2147/COPD.S366126
6. Hogg JC, Timens W. The pathology of chronic obstructive pulmonary disease. *Annu Rev Pathol Mech Dis.* 2009;4(1):435–459. doi:10.1146/annurev.pathol.4.110807.092145
7. O'Reilly S. Chronic obstructive pulmonary disease. *Am J Lifestyle Med.* 2017;11(4):296–302. doi:10.1177/1559827616656593
8. Scoditti E, Massaro M, Garbarino S, Toraldo DM. Role of diet in chronic obstructive pulmonary disease prevention and treatment. *Nutrients.* 2019;11(6):1357. doi:10.3390/nu11061357
9. Mullin MLL, Milne S. Vitamin D deficiency in chronic obstructive pulmonary disease. *Curr Opin Pulm Med.* 2023;29(2):96–103. doi:10.1097/MCP.0000000000000935
10. Minter M, Augustin H, Van Odiijk J, Vanfleteren LEGW. Gender differences in vitamin D status and determinants of vitamin D insufficiency in patients with chronic obstructive pulmonary disease. *Nutrients.* 2023;15(2):426. doi:10.3390/nu15020426
11. Pessoa Mamede LDCG, De Lima RLFC, Silva AS, et al. Effects of a single oral megadose of vitamin D3 on inflammation and oxidative stress markers in overweight and obese women: A randomized, double-blind, placebo-controlled clinical trial. *Diabetes Metab Syndr Obes.* 2021;14:525–534. doi:10.2147/DMSO.S285597
12. Lokesh KS, Chaya SK, Jayaraj BS, et al. Vitamin D deficiency is associated with chronic obstructive pulmonary disease and exacerbation of COPD. *Clin Respir J.* 2021;15(4):389–399. doi:10.1111/crj.13310
13. Rafiq R, Aleva FE, Schrupf JA, et al. Vitamin D supplementation in chronic obstructive pulmonary disease patients with low serum vitamin D: A randomized controlled trial. *Am J Clin Nutr.* 2022;116(2):491–499. doi:10.1093/ajcn/nqac083
14. Martineau AR, James WY, Hooper RL, et al. Vitamin D3 supplementation in patients with chronic obstructive pulmonary disease (ViDiCO): A multicentre, double-blind, randomised controlled trial. *Lancet Respir Med.* 2015;3(2):120–130. doi:10.1016/S2213-2600(14)70255-3
15. Crescioli C. Vitamin D restores skeletal muscle cell remodeling and myogenic program: Potential impact on human health. *Int J Mol Sci.* 2021;22(4):1760. doi:10.3390/ijms22041760
16. Agrawal D, Yin K. Vitamin D and inflammatory diseases. *J Inflamm Res.* 2014;69:69–87. doi:10.2147/JIR.S63898
17. Roffe-Vazquez DN, Huerta-Delgado AS, Castillo EC, et al. Correlation of vitamin D with inflammatory cytokines, atherosclerotic parameters, and lifestyle factors in the setting of heart failure: A 12-month follow-up study. *Int J Mol Sci.* 2019;20(22):5811. doi:10.3390/ijms20225811
18. Halder SK, Osteen KG, Al-Hendy A. Vitamin D3 inhibits expression and activities of matrix metalloproteinase-2 and -9 in human uterine fibroid cells. *Hum Reprod.* 2013;28(9):2407–2416. doi:10.1093/humrep/det265
19. Schapochnik A, Da Silva MR, Leal MP, et al. Vitamin D treatment abrogates the inflammatory response in paraquat-induced lung fibrosis. *Toxicol Appl Pharmacol.* 2018;355:60–67. doi:10.1016/j.taap.2018.06.020
20. Mendoza L, De Oca MM, López Varela MV, et al. Physical activity levels and associated factors in a Latin American COPD population of patients: The LASSYC study. *COPD.* 2021;18(4):393–400. doi:10.1080/15412555.2021.1937090
21. Furlanetto KC, Donária L, Schneider LP, et al. Sedentary behavior is an independent predictor of mortality in subjects with COPD. *Respir Care.* 2017;62(5):579–587. doi:10.4187/respcare.05306
22. Yoshida M, Hiramoto T, Moriwaki A, Osoreda H, Iwanaga T, Inoue H. Impact of extrapulmonary comorbidities on physical activity in chronic obstructive pulmonary disease in Japan: A cross-sectional study. *PLoS One.* 2022;17(7):e0270836. doi:10.1371/journal.pone.0270836
23. Hamakawa Y, Tanabe N, Shima H, et al. Associations of pulmonary and extrapulmonary computed tomographic manifestations with impaired physical activity in symptomatic patients with chronic obstructive pulmonary disease. *Sci Rep.* 2022;12(1):5608. doi:10.1038/s41598-022-09554-6
24. Gloeckl R, Schneeberger T, Jarosch I, Kenn K. Pulmonary rehabilitation and exercise training in chronic obstructive pulmonary disease. *Dtsch Arztebl Int.* 2018;115(18):117–123. doi:10.3238/arztebl.2018.0117
25. Fernandes MR, Barreto Junior WDR. Association between physical activity and vitamin D: A narrative literature review. *Rev Assoc Med Bras.* 2017;63(6):550–556. doi:10.1590/1806-9282.63.06.550
26. Mori B, Barcellos JFM, Lima LER, et al. Relationship between vitamin D and physical activity: Systematic review and meta-analysis. *Braz J Biol.* 2022;82:e263882. doi:10.1590/1519-6984.263882
27. Yang K, Wu Y, Chen D, Liu S, Chen R. The impact of lung function on extra-pulmonary diseases and all-cause mortality in US adult population with and without COPD. *Clin Epidemiol.* 2020;12:997–1005. doi:10.2147/CLEP.S270599
28. Smith L, Sherratt F, Barnett Y, et al. Physical activity, sedentary behaviour and cannabis use in 15,822 US adults: Cross-sectional analyses from NHANES. *Public Health.* 2021;193:76–82. doi:10.1016/j.puhe.2021.01.018
29. Bull FC, Maslin TS, Armstrong T. Global Physical Activity Questionnaire (GPAQ): Nine country reliability and validity study. *J Phys Act Health.* 2009;6(6):790–804. doi:10.1123/jpah.6.6.790
30. Cao C, Friedenreich CM, Yang L. Association of daily sitting time and leisure-time physical activity with survival among US cancer survivors. *JAMA Oncol.* 2022;8(3):395. doi:10.1001/jamaoncol.2021.6590
31. Ussery EN, Fulton JE, Galuska DA, Katzmarzyk PT, Carlson SA. Joint prevalence of sitting time and leisure-time physical activity among US adults, 2015–2016. *JAMA.* 2018;320(19):2036. doi:10.1001/jama.2018.17797
32. Xiao Q, Cai B, Yin A, et al. L-shaped association of serum 25-hydroxyvitamin D concentrations with cardiovascular and all-cause mortality in individuals with osteoarthritis: Results from the NHANES database prospective cohort study. *BMC Med.* 2022;20(1):308. doi:10.1186/s12916-022-02510-1
33. Pludowski P, Takacs I, Boyanov M, et al. Clinical practice in the prevention, diagnosis and treatment of vitamin D deficiency: A Central and Eastern European Expert Consensus Statement. *Nutrients.* 2022;14(7):1483. doi:10.3390/nu14071483
34. Burtin C, Mohan D, Troosters T, et al. Objectively measured physical activity as a COPD clinical trial outcome. *Chest.* 2021;160(6):2080–2100. doi:10.1016/j.chest.2021.06.044
35. Waschki B, Kirsten AM, Holz O, et al. Disease progression and changes in physical activity in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2015;192(3):295–306. doi:10.1164/rccm.201501-0081OC
36. Mihaltan F, Rajnovanu RM, Arghir OC, Alecu S, Postolache PA. High 24-hour respiratory symptoms and low physical activity in the stable COPD Romanian cohort of SPACE study. *COPD.* 2021;16:2533–2544. doi:10.2147/COPD.S321197
37. De Bontridder S, Corhay JL, Haenebalcke C, Fievet F, Etienne I, Vanderhelst E. Correlation of symptoms and physical activity level in chronic obstructive pulmonary disease patients: Results from the observational SPACE study. *Acta Clin Belg.* 2022;77(3):671–678. doi:10.1080/17843286.2021.1950419
38. Oostrik L, Bourbeau J, Doiron D, et al. Physical activity and symptom burden in COPD: The Canadian Obstructive Lung Disease Study. *Chronic Obstr Pulm Dis.* 2023;10(1):89–101. doi:10.15326/jcopdf.2022.0349
39. Hartman JE, Boezen HM, De Greef MH, Ten Hacken NH. Physical and psychosocial factors associated with physical activity in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil.* 2013;94(12):2396–2402.e7. doi:10.1016/j.apmr.2013.06.029
40. Clarenbach CF, Sievi NA, Haile SR, et al. Determinants of annual change in physical activity in COPD. *Respirology.* 2017;22(6):1133–1139. doi:10.1111/resp.13035
41. Demeyer H, Donaire-Gonzalez D, Gimeno-Santos E, et al. Physical activity is associated with attenuated disease progression in chronic obstructive pulmonary disease. *Med Sci Sports Exerc.* 2019;51(5):833–840. doi:10.1249/MSS.0000000000001859
42. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: A population-based cohort study. *Am J Respir Crit Care Med.* 2007;175(5):458–463. doi:10.1164/rccm.200607-896OC

43. Xiang X, Huang L, Fang Y, Cai S, Zhang M. Physical activity and chronic obstructive pulmonary disease: A scoping review. *BMC Pulm Med*. 2022; 22(1):301. doi:10.1186/s12890-022-02099-4
44. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Anto JM. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: A population based cohort study. *Thorax*. 2006;61(9):772–778. doi:10.1136/thx.2006.060145
45. Brock K, Huang WY, Fraser DR, et al. Low vitamin D status is associated with physical inactivity, obesity and low vitamin D intake in a large US sample of healthy middle-aged men and women. *J Steroid Biochem Mol Biol*. 2010;121(1–2):462–466. doi:10.1016/j.jsbmb.2010.03.091
46. Ceolin G, Confortin SC, Da Silva AAM, et al. Association between physical activity and vitamin D is partially mediated by adiposity in older adults: EpiFloripa Aging Cohort Study. *Nutr Res*. 2022;103:11–20. doi:10.1016/j.nutres.2022.03.001
47. Wanner M, Richard A, Martin B, Linseisen J, Rohrmann S. Associations between objective and self-reported physical activity and vitamin D serum levels in the US population. *Cancer Causes Control*. 2015;26(6):881–891. doi:10.1007/s10552-015-0563-y
48. Scragg R, Camargo CA. Frequency of leisure-time physical activity and serum 25-hydroxyvitamin D levels in the US population: Results from the Third National Health and Nutrition Examination Survey. *Am J Epidemiol*. 2008;168(6):577–586. doi:10.1093/aje/kwn163
49. Ekelund U, Steene-Johannessen J, Brown WJ, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *Lancet*. 2016;388(10051):1302–1310. doi:10.1016/S0140-6736(16)30370-1
50. Lehouck A, Mathieu C, Carremans C, et al. High doses of vitamin D to reduce exacerbations in chronic obstructive pulmonary disease: A randomized trial. *Ann Intern Med*. 2012;156(2):105. doi:10.7326/0003-4819-156-2-201201170-00004
51. Rafiq R, Prins H, Boersma W, et al. Effects of daily vitamin D supplementation on respiratory muscle strength and physical performance in vitamin D-deficient COPD patients: A pilot trial. *COPD*. 2017; 12:2583–2592. doi:10.2147/COPD.S132117
52. Zendedel A, Gholami M, Anbari K, Ghanadi K, Bachari EC, Azargon A. Effects of vitamin D intake on FEV₁ and COPD exacerbation: A randomized clinical trial study. *Glob J Health Sci*. 2015;7(4):243–248. doi:10.5539/gjhs.v7n4p243
53. Saleem A, Sharif S, Jarvis S, Madouros N, Koumadoraki E, Khan S. A comprehensive review on vitamin D as a novel therapeutic agent in chronic obstructive pulmonary disease. *Cureus*. 2021;13(2):e13095. doi:10.7759/cureus.13095
54. Janssens W, Mathieu C, Boonen S, Decramer M. Vitamin D deficiency and chronic obstructive pulmonary disease. *Vitam Horm*. 2011;86: 379–399. doi:10.1016/B978-0-12-386960-9.00017-4
55. Watz H, Waschki B, Boehme C, Claussen M, Meyer T, Magnussen H. Extrapulmonary effects of chronic obstructive pulmonary disease on physical activity: A cross-sectional study. *Am J Respir Crit Care Med*. 2008;177(7):743–751. doi:10.1164/rccm.200707-1011OC
56. Nymand SB, Hartmann JP, Rysø CK, et al. Exercise adaptations in COPD: The pulmonary perspective. *Am J Physiol Lung Cell Mol Physiol*. 2022;323(6):L659–L666. doi:10.1152/ajplung.00549.2020
57. Zguira MS, Koubaa A, Fekih S, et al. Physical activity reduces oxidative stress and improves lipid profile made by smoking: Effectiveness of irregular and continuous training programs. *Eur Rev Med Pharmacol Sci*. 2022;26(2):534–543. doi:10.26355/eurrev_202201_27881
58. Hengist A, Perkin O, Gonzalez JT, et al. Mobilising vitamin D from adipose tissue: The potential impact of exercise. *Nutr Bull*. 2019;44(1):25–35. doi:10.1111/mbu.12369