

Online Supplement

Age-Dependent Associations Between 25-Hydroxy Vitamin D Levels and COPD Symptoms: Analysis of SPIROMICS

Robert M. Burkes, MD, MSCR¹ David J. Couper, PhD² Igor Z. Barjaktarevic, MD, PhD³
 Christopher B. Cooper, MD⁴ Wassim W. Labaki, MD⁵ Meilan K. Han, MD⁵ Prescott G.
 Woodruff MD, MPH⁶ Stephen C. Lazarus, MD⁶ Trisha M. Parekh, DO⁷ Robert Paine, III, MD⁸
 Alejandro P. Comellas, MD⁹ Russell P. Bowler, MD, PhD¹⁰ Laura R. Loehr, MD, PhD¹¹
 Nirupama Putcha, MD, MHS¹² Robert A. Wise, MD¹² Todd T. Brown, MD, PhD¹³ M. Bradley
 Drummond, MD, MHS¹

Supplementary Tables

Supplementary Table 1. Multivariable associations displaying mean difference in scores per 5 ng/ml increase in vitamin D in total cohort* and stratified by age† with the addition of comorbidity score.						
	Overall		Middle-aged		Older	
	Mean difference (95% CI)	P-Value	Mean difference (95% CI)	P-Value	Mean difference (95% CI)	P-Value
CAT	-0.11 (-0.27 to 0.05)	0.19	-0.39 (-0.70 to -0.07)	0.02	-0.05 (-0.24 to 0.14)	0.59
mMRC	-0.01 (-0.03 to 0.01)	0.32	-0.01 (-0.05 to 0.03)	0.61	-0.01 (-0.04 to 0.01)	0.22
SGQR Total	-0.39 (-0.75 to -0.04)	0.03	-0.99 (-1.70 to -0.29)	0.02	-0.31 (-0.72 to 0.10)	0.14
SGRQ Symptom	-0.31 (-0.80 to 0.18)	0.22	-1.15 (-2.04 to -0.27)	0.01	-0.08 (-0.68 to 0.52)	0.79
SGRQ Impact	-0.40 (-0.76 to -0.04)	0.03	-0.89 (-1.62 to -0.17)	0.02	-0.36 (-0.75 to 0.04)	0.08
SGRQ Activity	-0.45 (-0.91 to -0.0003)	0.05	-1.09 (-1.97 to -0.21)	0.02	-0.37 (-0.90 to 0.16)	0.17
6MWT, m	0.94 (-1.63 to 3.50)	0.47	1.65 (-3.59 to 6.89)	0.53	0.73 (-2.08 to 3.55)	0.47
VSAQ	0.06 (0.003 to 0.11)	0.04	0.09 (-0.01 to 0.19)	0.07	0.05 (-0.01 to 0.11)	0.10

*Adjusted for age, race, sex, current smoking, pack-years smoked, FEV₁, BMI, and comorbidity score
 †Adjusted for race, sex, current smoking, pack-years smoked, FEV₁, BMI, and comorbidity score
 Abbreviations: CAT = COPD Assessment Test; mMRC = Modified Medical Research Council breathlessness test; SGRQ = St. George's Respiratory Questionnaire; 6MWT = Six-minute walk test; VSAQ = Veteran's Specific Activity Questionnaire; m = meters

Supplementary Table 2. Sensitivity analysis* for relationship between vitamin D increase per 5 ng/ml and symptom scores in middle-aged participants								
	Addition of season of blood draw		Addition of vitamin D or multivitamin usage		Addition of average time spent outdoors, hours per day, year prior to admission		Addition of season, vitamin D usage, and outdoor time	
	Unit change, (95% CI)	P-value	Unit Change, (95% CI)	P-value	Unit Change, (95% CI)	P-value	Unit Change	P-value

CAT score	-0.38 (-0.70 to -0.06)	0.02	-0.34 (-0.66 to -0.02)	0.38	-0.47 (-0.81 to -0.14)	0.001	-0.50 (-0.83 to -0.16)	0.004
SGRQ Total	-0.93 (-1.67 to -0.18)	0.01	-0.92 (-1.66 to -0.18)	0.02	-1.21 (-1.96 to -0.45)	0.002	-1.25 (-2.01 to -0.49)	0.001
SGRQ Symptoms	-1.07 (-1.97 to -0.17)	0.02	-1.05 (-1.95 to -0.15)	0.02	-1.33 (-2.26 to -0.39)	0.005	-1.34 (-2.28 to -0.40)	0.005
SGRQ Impact	-0.72 (-1.54 to 0.03)	0.06	-0.81 (-1.58 to -0.04)	0.04	-1.04 (-1.83 to -0.25)	0.01	-1.07 (-1.86 to -0.28)	0.008
SGRQ Activity	-1.14 (-2.04 to -0.25)	0.01	-1.05 (-1.95 to -0.16)	0.02	-1.41 (-2.32 to -0.48)	0.003	-1.48 (-2.40 to -0.56)	0.002

*Multivariable linear regression controlling for race, sex, BMI, FEV₁, current smoking, and pack-years smoked, as well as season of blood draw, reported usage of vitamin D supplementation or a multivitamin, or comorbidity score as indicated. Abbreviations: CAT = COPD Assessment Test; SGRQ = St. George's Respiratory Questionnaire

	Overall	Vitamin D <20 ng/ml	Vitamin D ≥ 20 ng/ml	P-value
N	1621	339	1282	
Age	66 (60-71)	62 (56-68)	67(61-72)	<0.001
Black race	226 (13.9)	97 (28.6)	129 (10.0)	<0.001
Female sex	680 (41.9)	154 (45.4)	526 (41.3)	0.14
BMI, kg/m ²	27.5 (5.3)	27.9 (6.0)	27.5 (5.1)	0.28
Current smoker	532 (33.4)	162 (48.2)	370 (29.4)	<0.001
Pack-years smoked	46 (35-62)	45 (35,60)	48 (36,63)	0.18
FEV ₁ , L	1.64 (1.15-2.28)	1.49 (1.04-2.14)	1.69 (1.18-2.31)	<00.001
FEV ₁ , %predicted	61 (44-78)	56 (40-74)	62 (44-79)	0.001
FVC, L	3.27 (2.55-4.09)	3.10 (2.37-3.95)	3.31 (2.62-4.14)	<0.001
FVC, %predicted	89 (75-102)	85 (72-99)	90 (76-103)	0.002
2+ exacerbations in prior year	225 (14.1)	53 (15.8)	172 (13.6)	0.31
Chronic bronchitis	727 (47.1)	165 (51.9)	562 (45.8)	0.07
Vitamin D supplementation	180 (11.1)	21 (6.19)	159 (12.4)	0.001
Baseline Comorbidities				
Congestive heart failure	47 (2.93)	7 (2.08)	40 (3.15)	0.30
Coronary artery disease	174 (10.9)	22 (6.55)	152 (12.0)	0.004
Diabetes	227 (14.2)	39 (11.6)	188 (14.8)	0.13
History of stroke	70 (4.36)	14 (4.17)	56 (4.41)	0.84
Sleep apnea	403 (25.3)	73 (22.7)	330 (26.2)	0.13
Total Comorbidities	2 (1-4)	2 (1-4)	2 (1-4)	0.34
Average time spent outdoors in year prior, hours per day	3 (2-5.25)	3.13 (2-5.5)	3 (2-5.25)	0.93
Six-minute walk test				
Total distance	392 (127)	387 (137)	394 (125)	0.39
% predicted	79.8 (28.6)	78.4 (31.2)	80.2 (27.8)	0.30
Presence of hypoxia	39 (2.52%)	11 (3.41)	28 (2.28)	0.25
CAT				
Total Score	15 (9,21)	17 (11,23)	14 (9,20)	<0.001
≥ 10	1121 (72.9)	256 (80.5)	871 (70.9)	0.001
mMRC				
Total	1 (1-2)	1 (1-2)	1 (1-2)	<0.001
≥ 2	513 (31.9)	135 (40.5)	378 (29.7)	<0.001
SGRQ				
Total	37.3 (22.1-51.6)	42.9 (28.3-56.8)	34.8 (20.9-49.3)	<0.001

Symptoms	52.5 (34.5-69.7)	58.8 (40.9-75.6)	51.1 (33.1-68.0)	<0.001
Impact	21.7 (9.71-37.1)	27.9 (14.2-43.1)	19.9 (8.70-35.7)	<0.001
Activity	52.3 (32.9-67.7)	58.6 (39.6-79.6)	52.3 (26.7-65.8)	<0.001
VSAQ	4 (3-7)	4 (3-6)	5 (3-7)	<0.001

*Presented as frequency with percentage for count variables or mean (standard deviation) or median (interquartile range) for continuous variables depending on skew.

Abbreviations: BMI = Body mass index; FEV₁ = Forced expiratory volume in 1 second; FVC = Forced vital capacity; FSAD = Functional small airway disease; CAT = COPD Assessment Test; mMRC = Modified Medical Research Council breathlessness test; SGRQ = St. George's Respiratory Questionnaire; VSAQ = Veteran's Specific Activity Questionnaire

Supplementary Table 4. Multivariable associations displaying mean difference in scores between sufficient (≥ 20 ng/ml) and deficient vitamin D in total cohort* and stratified by age†.						
	Overall		Middle-aged		Older	
	Mean difference (95% CI)	P-value	Mean Difference (95% CI)	P-value	Mean Difference (95% CI)	P-value
CAT	-0.10 (-1.13 to -0.92)	0.84	-0.69 (-2.27 to 0.89)	0.39	-0.45 (-1.82 to 0.92)	0.52
mMRC	0.02 (-0.10 to 0.15)	0.72	0.009 (-0.18 to 0.20)	0.92	-0.02 (-0.19 to 0.14)	0.75
SGQR Total	-0.26 (-2.59 to 2.06)	0.82	-0.96 (-4.60 to 2.69)	0.61	-2.24 (-5.54 to 0.70)	0.13
SGRQ Symptom	-0.07 (-3.20 to 3.06)	0.96	-2.69 (-7.11 to 1.71)	0.23	-0.29 (-4.75 to 4.17)	0.90
SGRQ impact	-0.14 (-2.45 to 2.28)	0.91	-0.29 (-4.05 to 3.48)	0.88	-2.64 (-5.63 to 0.34)	0.08
SGRQ Activity	-0.54 (-2.42 to 3.34)	0.71	-1.29 (-5.67 to 3.08)	0.56	-2.70 (-6.64 to 1.23)	0.18
6MWT	6.90 (-8.80 to 22.6)	0.39	0.47 (-24.6 to 25.5)	0.97	12.9 (-7.23 to 33.1)	0.21
VSAQ	-0.06 (-0.40 to 0.27)	0.72	-0.12 (-0.61 to 0.37)	0.62	0.13 (-0.33 to 0.58)	0.59
<p>*Adjusted for age, race, sex, current smoking, pack-years smoked, FEV₁, and BMI †Adjusted for race, sex, current smoking, pack-years smoked, FEV₁, and BMI Abbreviations: CAT = COPD Assessment Test; mMRC = Modified Medical Research Council breathlessness test; SGRQ = St. George's Respiratory Questionnaire; 6MWT = Six-minute walk test; VSAQ = Veteran's Specific Activity Questionnaire</p>						