Research Article

Associations between vitamin D, adiposity, and respiratory symptoms in chronic spinal cord injury

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Context/Objective: Persons with chronic spinal cord injury (SCI) have an increased risk of respiratory-related morbidity and mortality and chronic respiratory symptoms are clinical markers of future respiratory disease. Therefore, we sought to assess potentially modifiable factors associated with respiratory symptoms, with a focus on circulating vitamin D and measures of body fat.

Design: Cross-sectional study.

Setting: Veterans Affairs Medical Center.

Participants: Three hundred forty-three participants (282 men and 61 women) with chronic SCI participating in an epidemiologic study to assess factors influencing respiratory health recruited from VA Boston and the community.

Methods: Participants provided a blood sample, completed a respiratory health questionnaire, and underwent dual x-ray absorptiometry (DXA) to assess % body fat. Logistic regression was used to assess cross-sectional associations between respiratory symptoms and plasma vitamin D and measures of body fat with adjustment for a number of potential confounders.

Outcome Measures: Chronic cough, chronic phlegm, any wheeze, persistent wheeze.

Results: After adjustment for a number of confounders (including smoking), participants with greater %-android, gynoid, trunk, or total body fat had increased odds ratios for any wheeze and suggestive associations with persistent wheeze, but not with chronic cough or phlegm. Vitamin D levels were not associated with any of the respiratory symptoms.

Conclusion: Increased body fat, but not vitamin D, was associated with wheeze in chronic SCI independent of a number of covariates.

Keywords: Vitamin D, Body fat, Respiratory symptoms, Wheeze, Spinal cord injury

Introduction

Persons with chronic spinal cord injury (SCI) have impaired pulmonary function, resulting in morbidity and mortality attributable to respiratory causes.[1] In persons without SCI, respiratory symptoms, such as chronic cough, chronic phlegm, and wheeze, are associated with future respiratory disease, including asthma, COPD, loss of pulmonary function, and hospitalization due to respiratory illness such as pneumonia.[2–4] We previously demonstrated in SCI that wheeze was associated with future chest illness[5–6] and longitudinal decline in pulmonary function.[7] Cough, phlegm, and wheeze were also associated with future cardiopulmonary hospitalization.[8] Therefore, it is important to identify

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determinants of respiratory symptoms among persons with SCI.

In persons with chronic SCI, there is a high prevalence of vitamin D deficiency,[9–10] possibly due to decreased sunlight exposure, inadequate diet, and effects of obesity, as obesity has been associated with reduced levels of vitamin D.[11–12] While vitamin D's role in calcium homeostasis and bone mineralization is well understood, recent epidemiologic and basic science studies suggest that vitamin D related pathways are involved in maintaining respiratory health, even after adjusting for effects of obesity. Vitamin D deficiency has been associated with reduced pulmonary function,[13–14] chronic bronchitis,[15] upper-respiratory tract infections,[16] airway inflammation,[17] and asthma and wheeze[18] These findings indicate that if lower vitamin D levels were found to be associated with increased respiratory symptoms in SCI, supplementation might be beneficial in maintaining respiratory health.

Additional studies also suggest that greater body fat is associated with respiratory symptoms. There is a greater risk of obesity in SCI that is attributable to an excess visceral fat.[19] In persons without SCI, obesity has been associated with an increased risk of productive cough[20] and wheeze,[21] sometimes independent of asthma.[22] Some studies support an association between obesity and asthma and COPD,[23] while others present contradictory findings.[24–25] In this report we assess associations between chronic respiratory symptoms and measures of body fat determined by DXA scan and plasma vitamin D levels in a community-based cohort with chronic SCI.

Methods

Subjects

Between 8/2009 and 4/2015, we enrolled 360 participants with chronic SCI in a study to assess factors associated with respiratory health. Participants were recruited from persons receiving care at VA Boston, from the greater Boston area through advertisement, and by direct mail to persons who had received care at Spaulding Rehabilitation Hospital, members of the National Spinal Cord Injury Association, and subscribers to New Mobility Magazine. Persons were eligible if they were 22 years of age or older, one or more years after injury, were not ventilator dependent, did not have a tracheostomy, and had no other neuromuscular disease.

Respiratory history

A respiratory health questionnaire based on the American Thoracic Society Questionnaire[26] with supplemental questions was used to obtain a standardized history that included the respiratory symptoms of cough, phlegm, and wheeze. Any wheeze was defined as wheeze or whistling in chest with a cold, occasionally apart from colds, or on most days or nights. Persistent wheeze included reported wheezing with a cold and apart from colds, or wheeze on most days or nights. Chronic cough was defined as cough on most days for 3 consecutive months of the year, and chronic phlegm was defined similarly. We also collected information regarding occupational dust or fume exposure history, cigarette smoking, marijuana smoking, and physician-diagnosed chronic obstructive pulmonary disease (COPD, emphysema or chronic bronchitis), heart disease treated in the last 10 years, diabetes, asthma, or hay fever, and current use of pulmonary medication, including bronchodilators, leukotriene antagonists, and inhaled and oral corticosteroids.

Neurological exam, stature, and weight

Motor level and completeness of injury were assessed based on the American Spinal Injury Association Impairment Scale (AIS) by record review and confirmed by exam.[27] Motor incomplete SCI included AIS C (most key muscles below the neurological level grade $< 3/5$) or AIS D (most muscles below the neurological level grade $\geq 3/5$). For analysis, participants were further grouped into cervical motor complete (AIS A or B) and cervical AIS C, high thoracic (T1-T6) complete (AIS A or B) and AIS C, others with T7 or below motor complete (AIS A or B) or AIS C, and all others (AIS D's). Height was obtained by measuring the body length from top of the head to the heel of the subject in a supine position. Self-reported height was used if severe contracture or bracing hindered measurement ($n=34$). If required, wheelchairs were weighed with and without the participant, and weight was subtracted to determine the participant's weight. Self-reported weight was used for five participants. Body mass index was calculated from height and weight.

Vitamin D analysis

EDTA plasma was drawn and immediately delivered to the core blood research at our facility. Samples were centrifuged for 15 minutes at 2,600 rpm (1459 x g) at 4^0C and stored at -80^0C. Analysis of 25-OH vitamin D was done at the Clinical & Epidemiologic Research Laboratory, Department of Laboratory Medicine at Children's Hospital in Boston by high performance liquid chromatography tandem mass spectrometry (HPLC-MS/MS).[28] The assay is linear up to 100 ng/ml, and sensitive to 1 ng/ml. Day-to-day precision (%

CV) at various levels of 25OHD ranged from 5.6% to 8.5%.

Dual x-ray absorptiometry (DXA) for % body fat

We used a 5th generation GE Healthcare iDXA scanner to assess total and regional body composition using GE Lunar software analyzed by a certified clinical densitometrist (AAL). Daily quality assurance was performed utilizing a phantom. We assessed total % body fat, as well as % trunk fat, % android fat, and % gynoid fat.[29] The cuts that define the trunk region pass through the shoulder joins and as close to the body as possible and through the femoral necks. The lower boundary of the android region is a horizontal cut through the pelvis at the level of the iliac crests. The upper boundary of the android region extends upwards to 20% of the distance between the pelvis and shoulders and laterally to the border of the arms. For the gynoid region, the upper boundary is the iliac crests and the lower boundary extends below the pelvis downward 1.5 times the height of the android region to the outer leg cuts.

Analyses

We excluded persons without a detectable SCI level (n=3), a history of stroke (n=2), with incomplete data collection (n=6), and those where we were unable to obtain blood during the study visit (n=6), leaving a sample size of 343 participants. Since we were unable to obtain DXA data in four subjects due to severe contractures or poor positioning, there were 339 participants for analyses assessing associations with body composition. Logistic regression (PROC LOGISTIC, SAS version 9.4) was used to assess associations with chronic cough and phlegm, any wheeze, and persistent wheeze. Factors significant at an alpha level of 0.10 in univariable models were assessed in multivariable models. We *a priori* included vitamin D and each of the measures of adiposity in multivariable models to evaluate effects adjusted for potential confounders, including age, sex, comorbidities, cigarette smoking, marijuana smoking, and level and completeness of SCI. As respiratory symptoms are known clinical markers for receiving a diagnosis of asthma or COPD, we did not include chronic respiratory disease in assessment of cross-sectional associations with each symptom.

Results

Participant mean age (SD) was 54.2 (14.4) years, mean injury duration was 17.4 (13.3) years, and 282 (82.2%) were men. Most were AIS D (n=146, 42.6%), 82 (23.9%) had cervical motor complete or cervical AIS C SCI, 46 (13.4%) had high thoracic (T1-T7) motor complete or high thoracic AIS C SCI, and 69 (20.1%) had other motor complete & other AIS C SCI. The most common respiratory symptom reported was any wheeze (44.6%), and the overall prevalence of persistent wheeze, phlegm, or cough was 19.0%, 15.2%, and 10.5% respectively and persons with respiratory symptoms were more likely to report pulmonary medication use than persons without symptoms (Table 1). A deficiency of vitamin D (<20 ng/mL) was observed in 93 (27.1%) participants, 164 (47.8%) had insufficient levels (20-<30 ng/mL) and 86 (25.1%) participants had vitamin D levels ≥ 30 ng/mL.[30] Mean (SD) percent fat measured were 42.3% (12.6) for the android region, 40.1% (9.9) for the gynoid region, 39.4% (11.0) for the trunk region, and 36.3% (8.9) for total body. Based on BMI categories, 126 (36.7%) participants were normal or underweight (<25 kg/m^2), 115 (33.5%) were overweight (25-<30 kg/m^2), and 102 (29.7%) were obese (≥30 kg/m^2). A majority of participants were current or former smokers. As expected, persons with obstructive lung disease (asthma or COPD) had a greater prevalence of each respiratory symptom than persons without OLD, and in particular reported more wheeze (Table 1).

In univariable models, vitamin D levels were not statistically significantly associated with any wheeze, persistent wheeze, chronic cough, or chronic phlegm (Supplemental Tables 1 and 2). A greater BMI (if obese) was statistically significantly associated with an increased odds ratio for any wheeze and persistent wheeze (Supplemental Table 1), but was not associated with chronic cough and chronic phlegm (Supplemental Table 2). Persons in the highest quartile of percentage of android, trunk, or total body fat also had a significantly increased odds ratio for any wheeze. Current cigarette smoking and the current use of pulmonary medication were also significantly associated with each respiratory symptom, but marijuana smoking history was not. SCI level and completeness of injury was not associated with respiratory symptoms. In multivariable models (Table 2), vitamin D levels were not associated with any of the respiratory symptoms (P = 0.15–0.98). In these multivariable models, a BMI ≥30 remained significantly associated with any wheeze and persistent wheeze. The association of a BMI ≥30 with any wheeze and persistent wheeze was similar in persons with more severe SCI (motor complete or cervical AIS C, n=197) or with less severe SCI (AIS D, n=146) (Supplemental Table 3).

There was a robust association between any of the measures of greater percent fat and any wheeze or

Table 1 Characteristics of 343 persons with SCI by self-reported respiratory symptoms.

	Chronic Cough		Chronic Phlegm		Any Wheeze		Persistent Wheeze		Total
	Yes n= 36	No n= 307	Yes n= 52	No n= 291	Yes n=153	No n=190	Yes n=65	No n=278	n=343
Age, mean years (SD)	57.9 (13.3)	53.8 (14.5)	56.0 (13.6)	53.9 (14.6)	55.8 (13.1)	52.8 (15.3)	57.7 (12.4)	53.3 (14.8)	54.2 (14.4)
Injury Duration, mean years (SD)	21.5 (15.8)	17.0 (12.9)	17.0 (13.6)	17.5 (13.3)	18.0 (13.1)	17.0 (13.4)	18.3 (14.3)	17.2 (13.1)	17.4 (13.3)
Sex									
Male	29 (80.6%)	253 (82.4%)	48 (92.3%)	234 (80.4%)	125 (81.7%)	157 (82.6%)	54 (83.1%)	228 (82.0%)	282 (82.2%)
Female	7 (19.4%)	54 (17.6%)	4 (7.7%)	57 (19.6%)	28 (18.3%)	33 (17.4%)	11 (16.9%)	50 (18.0%)	61 (17.7%)
Race									
White	33 (91.7%)	263 (85.7%)	48 (92.3%)	248 (85.2%)	135 (88.2%)	161 (84.7%)	56 (86.2%)	240 (86.3%)	296 (86.3%)
Black	2 (5.6%)	27 (8.8%)	3 (5.8%)	26 (8.9%)	12 (7.8%)	17 (9.0%)	5 (7.7%)	24 (8.6%)	29 (8.5%)
Other	1 (2.8%)	17 (5.5%)	1 (1.9%)	17 (5.8%)	6 (3.9%)	12 (6.3%)	4 (6.2%)	14 (5.0%)	18 (5.2%)
Vitamin D, mean ng/mL (SD)	24.1 (11.1)	25.9 (11.6)	26.1 (12.1)	25.7 (11.4)	26.3 (13.0)	25.2 (10.2)	28.1 (16.1)	25.2 (10.1)	25.7 (11.5)
<20	12 (33.3%)	81 (26.4%)	12 (23.1%)	81 (27.8%)	39 (25.5%)	54 (28.4%)	18 (27.7%)	75 (27.0%)	93 (27.1%)
20 - <30	16 (44.4%)	148 (48.2%)	25 (48.1%)	139 (47.8%)	75 (49.0%)	89 (46.8%)	28 (43.1%)	136 (48.9%)	164 (47.8%)
≥30	8 (22.2%)	78 (25.4%)	15 (28.9%)	71 (24.4%)	39 (25.5%)	47 (24.7%)	19 (29.2%)	67 (24.1%)	86 (25.1%)
Diabetes	9 (25.0%)	41 (13.4%)	11 (21.2%)	39 (13.4%)	29 (19.0%)	21 (11.1%)	15 (23.1%)	35 (12.6%)	50 (14.6%)
Heart Disease	5 (13.9%)	34 (11.1%)	6 (11.5%)	33 (11.3%)	23 (15.0%)	16 (8.4%)	15 (23.1%)	24 (8.6%)	39 (11.4%)
COPD	8 (22.2%)	27 (8.8%)	11 (21.2%)	24 (8.25%)	24 (15.7%)	11 (5.8%)	15 (23.1%)	20 (7.2%)	35 (10.2%)
Asthma	7 (19.4%)	38 (12.4%)	6 (11.5%)	39 (13.4%)	32 (20.9%)	13 (6.8%)	15 (23.1%)	30 (10.8%)	45 (13.1%)
Asthma or COPD (obstructive lung disease)	11 (30.6%)	61 (19.9%)	14 (26.9%)	58 (19.9%)	50 (32.7%)	22 (11.6%)	27 (41.6%)	45 (16.2%)	72 (21.0%)
Pulmonary medication (current use)	10 (27.8%)	26 (8.5%)	13 (25.0%)	23 (7.9%)	29 (19.0%)	7 (3.7%)	18 (27.7%)	18 (6.5%)	36 (10.5%)
Hay fever	11 (30.6%)	63 (20.5%)	11 (21.2%)	63 (21.7%)	42 (27.5%)	32 (16.8%)	16 (24.0%)	58 (20.8%)	74 (21.6%)
BMI (kg/m^2)									
≥30 (obese)	12 (33.3%)	90 (29.3%)	18 (34.6%)	84 (28.9%)	58 (37.9%	44 (23.2%)	28 (43.1%)	74 (26.6%)	102 (29.7%)
25-<30 (overweight)	13 (36.1%)	102 (33.2%)	15 (28.9%)	100 (34.4%)	47 (30.7%)	68 (35.8%)	18 (27.7%)	97 (34.9%)	115 (33.5%)
< 25 (normal or underweight, (<18.5, n= 17))	11 (30.6%)	115 (37.5%)	19 (36.5%)	107 (36.8%)	48 (31.4%)	78 (41.1%)	19 (29.2%)	107 (38.5%)	126 (36.7%)
BMI, mean kg/m^2 (SD)	27.3 (6.1)	27.3 (6.1)	27.1 (5.6)	27.3 (6.2)	28.2 (6.6)	26.5 (5.6)	29.3 (7.0)	26.8 (5.8)	27.3 (6.1)
DXA % fat (SD)	*n=35*	*n= 304*	*n=49*	*n=290*	*n=150*	*n=189*	*n= 64*	*n=275*	*n = 339*
android region, %fat	42.2 (13.9)	42.3 (12.5)	40.6 (14.1)	42.6 (12.3)	43.5 (12.3)	41.3 (12.7)	43.4 (13.1)	42.0 (12.5)	42.3 (12.6)
gynoid region, %fat	39.4 (9.4)	40.2 (10.0)	38.2 (9.2)	40.4 (10.0)	40.8 (9.6)	39.6 (10.1)	40.3 (9.2)	40.1 (10.1)	40.1 (9.9)
trunk region, %fat	39.2 (11.8)	39.5 (10.9)	37.8 (12.1)	39.7 (10.8)	40.6 (10.7)	38.5 (11.2)	40.6 (11.2)	39.2 (11.0)	39.4 (11.0)
total body, % fat	36.1 (8.8)	36.3 (9.0)	35.1 (9.1)	36.5 (8.9)	37.3 (8.6)	35.5 (9.1)	37.3 (8.5)	36.1 (9.0)	36.4 (9.0)
Cigarette Use									
Current ≥1/2 pack/day	7 (19.4%)	23 (7.5%)	11 (21.2%)	19 (6.5%)	21 (13.7%)	9 (4.7%)	12 (18.5%)	18 (6.5%)	30 (50.0%)
Current <1/2 pack/day	6 (16.7%)	24 (7.8%)	8 (15.4%)	22 (7.6%)	14 (9.2%)	16 (8.4%)	8 (12.3%)	22 (7.9%)	30 (50.0%)
Former	15 (41.7%)	127 (41.3%)	22 (42.3%)	120 (41.2%)	72 (47.1%)	70 (36.8%)	28 (43.1%)	114 (41.0%)	142 (41.4%)
Never	8 (22.2%)	133 (43.3%)	11 (21.2%)	130 (44.7%)	46 (30.1%)	95 (50.0%)	17 (26.2%)	124 (44.6%)	141 (41.1%)
Quit > 5 years ago	10 (27.8%)	103 (33.6%)	12 (23.1%)	101 (34.7%)	56 (36.6%)	57 (30.0%)	21 (32.3%)	92 (33.1%)	113 (32.9%)
Quit ≤ 5 years ago	5 (13.9%)	24 (7.8%)	10 (19.2%)	19 (6.5%)	16 (10.5%)	13 (6.8%)	7 (10.8%)	22 (7.9%)	29 (8.5%)
Marijuana									
Current	5 (13.9%)	37 (12.1%)	9 (17.3%)	33 (11.3%)	18 (11.8%)	24 (12.6%)	7 (10.8%)	35 (12.6%)	42 (12.2%)
Former	5 (13.9%)	36 (11.7%)	7 (13.5%)	34 (11.7%)	24 (15.7%)	17 (9.0%)	10 (15.4%)	31 (11.2%)	41 (12.0%)
Never	26 (72.2%)	234 (76.2%)	36 (69.2%)	224 (77.0%)	111 (72.6%)	149 (78.4%)	48 (73.9%)	212 (76.3%)	260 (75.8%)
Quit > 5 years ago	4 (11.1%)	29 (9.5%)	4 (7.7%)	29 (10.0%)	19 (12.4%)	14 (7.4%)	7 (10.8%)	26 (9.4%)	33 (9.6%)

Quit ≤ 5 years ago	1 (3.8%)	7 (2.3%)	3 (5.8%)	5 (1.7%)	5 (3.3%)	3 (1.6%)	3 (4.6%)	5 (1.8%)	8 (2.3%)
Occupational dust or fume exposure	23 (63.9%)	177 (57.7%)	37 (71.2%)	163 (56.0%)	91 (59.5%)	109 (57.4%)	39 (60.0%)	161 (57.9%)	200 (58.3%)
SCI classification									
Motor complete cervical & AIS C	6 (16.7%)	76 (24.8%)	13 (25.0%)	69 (23.7%)	42 (27.5%)	40 (21.1%)	10 (15.4%)	72 (25.9%)	82 (23.9%)
Motor complete high thoracic(T1-T6) & AIS C	6 (16.7%)	40 (13.0%)	5 (9.6%)	41 (14.1%)	17 (11.1%)	29 (15.3%)	9 (13.9%)	37 (13.3%)	46 (13.4%)
Other motor complete & AIS C	6 (16.7%)	63 (20.5%)	9 (17.3%)	60 (20.6%)	25 (16.3%)	44 (23.2%)	13 (20.0%)	56 (20.1%)	69 (20.1%)
All AIS D	18 (50.0%)	128 (41.7%)	25 (48.1%)	121 (41.6%)	69 (45.1%)	77 (40.5%)	33 (50.8%)	113 (40.7%)	146 (42.6%)

persistent wheeze in multivariable models (Tables 3). There were statistically significant relationships between greater % android fat, % gynoid fat, % trunk, and % total fat with any wheeze that differed slightly depending on the specific measure of adiposity used. The relationships were of similar magnitude for persistent wheeze, but were not all statistically significant (P = <0.01–0.76). Adding vitamin D to these models did not attenuate the associations with % fat (results not shown). Adjusting for the current use of pulmonary medications did not affect the relationship between obesity or the various measures of fat with any wheeze and persistent wheeze (Supplemental Tables 4 and 5),

Discussion

Our study found that there was an association between obesity and greater percent body fat assessed by DXA scan and wheeze, independent of injury level, vitamin D level, smoking status, hay fever, or heart disease history. BMI and percent body fat were not associated with chronic cough or chronic phlegm. The association with percent body fat was particularly robust and significant for any wheeze and was suggestive for persons who reported wheeze more regularly, defined as persistent wheeze in this study. These results are consistent with previous literature in persons without SCI reporting an association between obesity and wheeze[21–22] including in a large population based study of 85,437 persons reported by Colak *et al.* (2015). As expected, persons with a history of asthma or COPD, and who used pulmonary medications, reported a greater prevalence of respiratory symptoms than persons without either condition.

Based on DXA data from NHANES, mean percent total body fat for Caucasian 55 year olds was 29.8±5.2 for men and 41.7±6.2 for women.[31] In our study (with a mean age of 54.2 years and mostly Caucasian), the values for mean percent total body fat in men was 35.2 ±8.5%, greater than the NHANES values, but for women it was similar, 41.5±9.0%. Normative data for the other regions of fat is sparse and comparable DXA data with our sample could not be found. Stults-Kolehmainen *et a.l* (2013) assessed 432 active Caucasian males, ages 18–30, for body composition and found the mean (SD) percent fat for the android, gynoid, and trunk regions to be 23.3±0.4, 23.8±0.4, and 20.6±0.4 respectively.[32] Our sample of older, predominantly male SCI participants had mean values for android, gynoid, and trunk regions that were much greater, i.e., 42.3±12.6%, 40.1±9.9%, and 39.4±11.0% respectively. There are some studies that have reported DXA data in SCI, but few report

Table 2 Multivariable models of factors associated with respiratory symptoms including vitamin D.

Cough				Phlegm			
Characteristic	Odds Ratio	95% C.I.	p-value	Characteristic	Odds Ratio	95% C.I.	p-value
Injury duration	1.03	1.00, 1.05	0.05	Female (ref: Male)	0.31	0.10, 0.93	0.04
Cigarette Smoking				Cigarette Smoking			
Current ≥1/2 pack/day	5.32	1.72, 16.38	<0.01	Current ≥1/2 pack/day	7.41	2.77, 19.86	<0.01
Current <1/2 pack/day	3.96	1.25, 12.56	0.02	Current <1/2 pack/day	4.19	1.49, 11.75	0.01
Former	2.00	0.82, 4.91	0.13	Former	2.09	0.97, 4.52	0.06
Never	ref			Never	ref		
Vitamin D Level (ng/mL)				Vitamin D Level (ng/mL)			
<20 (deficient)	1.30	0.49, 3.45	0.60	<20 (deficient)	0.52	0.22, 1.26	0.15
≥20 - <30 (insufficient)	1.01	0.41, 2.52	0.98	≥20 - <30 (insufficient)	0.79	0.38, 1.65	0.54
≥ 30 (normal)	ref			≥ 30 (normal)	ref		
Any Wheeze				**Persistent Wheeze**			
Characteristic	Odds Ratio	95% C.I.	p-value	Characteristic	Odds Ratio	95% C.I.	p-value
Hay fever (ref: never)	1.88	1.08, 3.27	0.02	Heart disease last 10 yrs (ref: never)	2.98	1.37, 6.48	<0.01
Cigarette Smoking				Cigarette Smoking			
Current ≥1/2 pack/day	5.95	2.44, 14.51	<0.01	Current ≥1/2 pack/day	5.83	2.29, 14.88	<0.01
Current <1/2 pack/day	2.08	0.92, 4.73	0.08	Current <1/2 pack/day	2.90	1.08, 7.78	0.04
Former	1.97	1.19, 3.26	0.01	Former	1.48	0.74, 2.95	0.27
Never	ref			Never	ref		
BMI (kg/m^2)				BMI (kg/m^2)			
≥30 (obese)	2.48	1.39, 4.41	<.01	≥30 (obese)	2.54	1.24, 5.20	0.01
25-<30 (overweight)	1.15	0.66, 2.01	0.62	25-<30 (overweight)	1.09	0.52, 2.29	0.83
< 25 (normal or underweight)	ref			< 25 (normal or underweight)	ref		
Vitamin D Level (ng/mL)				Vitamin D Level (ng/mL)			
<20 (deficient)	0.75	0.39, 1.42	0.38	<20 (deficient)	0.76	0.34, 1.68	0.50
≥20 - <30 (insufficient)	0.97	0.56, 1.70	0.92	≥20 - <30 (insufficient)	0.76	0.38, 1.54	0.44
≥ 30 (normal)	ref			≥ 30 (normal)	ref		

percent fat specifically. Similar to our results, Cirnigliaro *et a.l* (2015) reported total percent body fat of 35.6 (95% CI = 33.6–37.6) in a slightly younger (mean age 40.0±7.2 years) all male SCI cohort of 63 persons.[19] Also in a younger population (mean age 36.1±11.5 years), Astorino *et al.* (2015) reported lower values than our study for percent fat in total body (31.2±12.9%) and trunk (32.6±14.2%) in 17 men and women with SCI.[33] Taken together, our data is consistent with the accumulation of body fat in persons with SCI and is the largest to date that provides specific estimates using DXA data. However, it is possible that in women with SCI, there is a greater similarity to women in the general population. It is commonly reported that persons with SCI have increased visceral or central fat.[19] However, we saw similar associations between wheeze and all 4 measures of body fat, most likely because of the high correlation between each measure. (r=0.70 for %-android and gynoid fat to r=0.98 for %-trunk fat and android fat, all $P < 0.0001$).

There are two mechanisms relevant to persons with SCI that may explain the positive associations observed between increased body fat and wheeze.[21] It has been suggested that the mechanical effects of obesity and higher neurologic levels of motor complete SCI reduce functional residual capacity and in association with decreased tidal breathing could alter airway smooth muscle contractility and increase airway responsiveness. Another proposed mechanism is that obesity leads to airway inflammation, which then promotes bronchoconstriction and wheeze.[34] Based on animal models, it is possible that obesity results in increased pro-inflammatory cytokines and altered levels of regulatory adipokines.[35] However, this mechanism is much less conclusive in human studies to date.

We did not observe an association between vitamin D levels and respiratory symptoms in this population. These findings are consistent with previous studies that show no statistically significant relationship between vitamin D levels and lung function,[36] COPD, asthma, or wheezing.[37] Nemunaitis *et al.* (2010) reported that 93% of SCI patients admitted to an acute inpatient rehabilitation service in Ohio had vitamin D levels below

Table 3 Multivariable models of factors associated with any wheeze and persistent wheeze including effects of adiposity.

	Any Wheeze											
	Android			Gynoid			Trunk			Total Body		
Characteristic	Odds Ratio	95% C.I.	p-value	Odds Ratio	95% C.I.	p-value	Odds Ratio	95% C.I.	p-value	Odds Ratio	95% C.I.	p-value
Hay fever (ref: never)	2.07	1.19, 3.61	0.01	2.01	1.16, 3.51	0.01	2.05	1.18, 3.56	0.01	1.96	1.13, 3.41	0.02
Cigarette Smoking												
Current ≥1/2 pack/day	7.88	3.08, 20.14	<0.01	7.38	2.88, 18.91	<0.01	7.86	3.05, 20.23	<0.01	7.51	2.92, 19.30	<0.01
Current <1/2 pack/day	2.34	1.01, 5.40	0.05	2.38	1.04, 5.44	0.04	2.33	1.01, 5.33	0.04	2.32	1.01, 5.32	0.05
Former	2.39	1.42, 4.00	<0.01	2.24	1.36, 3.69	<0.01	2.08	1.26, 3.43	0.01	2.05	1.24, 3.38	<0.01
Never	ref			ref			ref			ref		
Region %fat*												
quartile 1 (lowest)	ref			ref			ref			ref		
quartile 2	1.22	0.63, 2.37	0.55	1.94	0.99, 3.80	0.05	1.77	0.92, 3.43	0.09	2.34	1.20, 4.57	0.01
quartile 3	1.25	0.63, 2.47	0.53	2.30	1.19, 4.43	0.01	2.28	1.16, 4.48	0.02	2.49	1.27, 4.89	0.01
quartile 4 (highest)	2.89	1.48, 5.65	<0.01	1.78	0.93, 3.40	0.08	2.62	1.33, 5.16	0.01	2.72	1.38, 5.34	<0.01
Continuous %fat**	1.03	1.01, 1.05	0.01	1.02	1.01 1.05	0.06	1.03	1.01, 1.05	0.01	1.04	1.01, 1.06	<0.01
	Persistent Wheeze											
	Android			Gynoid			Trunk			Total Body		
Characteristic	Odds Ratio	95% C.I.	p-value	Odds Ratio	95% C.I.	p-value	Odds Ratio	95% C.I.	p-value	Odds Ratio	95% C.I.	p-value
Heart disease last 10yrs (ref: never)	3.55	1.64, 7.68	<0.01	3.41	1.57, 7.44	<0.01	3.37	1.56, 7.26	<0.01	3.22	1.49, 6.94	<0.01
Cigarette Smoking												
Current ≥1/2 pack/day	6.99	2.63, 18.56	<0.01	6.58	2.52, 17.17	<0.01	6.68	2.52, 17.67	<0.01	6.51	2.46, 17.18	<0.01
Current <1/2 pack/day	3.15	1.16, 8.56	0.02	3.02	1.11, 8.19	0.03	3.23	1.20, 8.75	0.02	3.09	1.14, 8.36	0.03
Former	1.57	0.78, 3.15	0.21	1.52	0.76, 3.04	0.23	1.39	0.70, 2.76	0.35	1.40	0.71, 2.78	0.33
Never	ref			ref			ref			ref		
Region %fat*												
quartile 1 (lowest)	ref			ref			ref			ref		
quartile 2	0.78	0.33, 1.83	0.57	1.39	0.57, 3.37	0.47	1.15	0.48, 2.74	0.76	1.57	0.65, 3.83	0.32
quartile 3	1.26	0.52, 3.04	0.61	3.21	1.41, 7.29	0.01	2.70	1.15, 6.31	0.02	3.24	1.37, 7.67	<0.01
quartile 4 (highest)	2.16	0.95, 4.90	0.07	1.38	0.57, 3.35	0.48	1.95	0.81, 4.72	0.14	2.06	0.83, 5.09	0.12
Continuous %fat***	1.02	1.00, 1.05	0.10	1.02	0.99, 1.05	0.31	1.03	1.00, 1.05	0.09	1.03	0.99, 1.06	0.11

*Android, % fat quartiles: - ≤ 36,> 36- ≤ 45, >45- ≤ 52, >52%
Gynoid, % fat quartiles: ≤ 34, >34-≤ 40, >40-≤ 47, >47%
Trunk, % fat quartiles: ≤ 34,> 34-≤ 42, >42-≤ 48, >48%
Total body, % fat quartiles: ≤ 31, >31-≤ 38, >38-≤ 43, >43%
**Adjusted for hay fever and cigarette smoking
***Adjusted for heart disease in the last 10 yrs and cigarette smoking

30 ng/mL.[9] Our study is the largest to date in assessing vitamin D levels in persons with SCI, and indicated that 75% (n=257) had vitamin D levels lower than 30 ng/mL assessed in an outpatient setting. In our cohort, living in the Northeast is likely a factor that contributes to vitamin D deficiency.

A limitation of this study is that due to its cross-sectional nature, temporal associations cannot be determined. Additionally, just one vitamin D measurement may not reflect the degree of chronic insufficiency. Strengths of this study include a large cohort of persons with chronic SCI and the ability to assess multiple predictors of respiratory symptoms using a standardized health questionnaire, DXA scan assessed fat, and vitamin D plasma measurements.

Conclusion

Among individuals with chronic SCI, a greater percentage of body fat was associated with symptoms of wheeze, independent of smoking status, hay fever, or heart disease history. Vitamin D levels were not associated with any of the examined respiratory symptoms.

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