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Physical activity and arterial stiffness in chronic obstructive pulmonary disease

Michael K. Stickland[a,b,*], Norah Vogan[c], Stewart R. Petersen[c], Eric Y.L. Wong[a], Mohit Bhutani[a]

[a] Division of Pulmonary Medicine, Department of Medicine, University of Alberta, 3-135 Clinical Sciences Building, Edmonton, Alberta, Canada T6G 2J3
[b] Centre for Lung Health – Covenant Health, 11111 Jasper Avenue, Edmonton, Alberta, Canada T5K 0L4
[c] Faculty of Physical Education and Recreation, University of Alberta, W1-34 Van Vliet Centre, University of Alberta, Edmonton, Alberta, Canada T6G 2H9

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ABSTRACT

Arterial stiffness is predictive of cardiovascular events and is elevated in chronic obstructive pulmonary disease (COPD). As physical inactivity and exercise intolerance are associated with elevated arterial stiffness in health, we hypothesized that lower physical activity would be related to increased arterial stiffness in COPD; and that active COPD patients would have reduced arterial stiffness compared to sedentary counterparts. Arterial stiffness was evaluated using pulse wave velocity (PWV) in 33 COPD patients (FEV_1 = 65% predicted) and 10 controls. $FEV_{1\%pred}$, peak oxygen consumption ($\dot{V}O_{2peak}$), and physical activity data were obtained. The inactive COPD group had higher PWV than controls (9.6 vs. 8.3 m s^{-1}, $p < 0.05$); while there was no difference in PWV between the active COPD group and controls. Within the COPD patients, $\dot{V}O_{2peak}$ ($r = -0.44$, $p = 0.01$) and physical activity ($r = -0.38$, $p = 0.03$) were the best predictors of PWV. Physical inactivity and exercise intolerance appear to be related to arterial stiffness in COPD, and may contribute to increased cardiovascular disease risk in COPD.

1. Introduction

While originally considered primarily a lung disease, chronic obstructive pulmonary disease (COPD) is now recognized to have many systemic consequences which can significantly affect morbidity and mortality. COPD is associated with an elevated risk for cardiovascular morbidity/mortality (Sin and Man, 2003, 2005); however the underlying reasons remain unclear. Arterial pulse wave velocity, which is considered the most clinically relevant measure of arterial stiffness and independently predicts risk of cardiovascular events (Boutouyrie et al., 2002; Mattace-Raso et al., 2006), is elevated in COPD (Maclay et al., 2009; McAllister et al., 2007; Mills et al., 2008; Sabit et al., 2007) as compared to controls matched for age, sex, height, BMI, smoking history, and cardiovascular comorbidities (McAllister et al., 2007; Mills et al., 2008; Sabit et al., 2007). Various associations have been explored to explain the increased PWV in COPD, as compared to controls, including 1 s forced expiratory volume (FEV_1) (McAllister et al., 2007; Sabit et al., 2007), arterial oxygenation (Maclay et al., 2009; McAllister et al., 2007; Sabit et al., 2007), and systemic inflammation (Maclay et al., 2009; McAllister et al., 2007; Mills et al., 2008; Sabit et al., 2007).

Importantly, COPD is associated with substantial physical inactivity (Pitta et al., 2005; Troosters et al., 2010; Watz et al., 2009). Patients with COPD have been shown to be less physically active (as measured by metabolic equivalents, steps and estimated caloric expenditure) than their age-matched counterparts, and when COPD patients do exercise, the duration and intensity are lower (Troosters et al., 2010; Watz et al., 2009). Furthermore, as severity of COPD increases, the amount of daily physical activity decreases (Troosters et al., 2010; Watz et al., 2009).

Regular aerobic exercise has been shown to help reduce the age-related increases in arterial stiffness. Healthy individuals with higher physical activity levels have lower arterial stiffness compared to sedentary counterparts (Sugawara et al., 2006; Tanaka et al., 1998, 2000; Vaitkevicius et al., 1993). Physical activity can increase aerobic fitness (as measured by $\dot{V}O_{2\,max}$), and therefore, not surprisingly, studies have found that healthy subjects with a higher aerobic fitness have lower arterial stiffness than less fit subjects (Boreham et al., 2004; Tanaka et al., 1998; Vaitkevicius et al., 1993). As inactivity is common in COPD, and associated with elevated arterial stiffness in health, the increased PWV in COPD relative to controls may be explained by reduced physical activity. That is, it may be the chronic inactivity associated with COPD,

* Corresponding author at: Division of Pulmonary Medicine, Department of Medicine, 3-135 Clinical Sciences Building, University of Alberta, Edmonton, Alberta, Canada T6G 2J3. Tel.: +1 780 492 3995; fax: +1 780 492 4483.
E-mail addresses: michael.stickland@ualberta.ca (M.K. Stickland), norah.vogan@gmail.com (N. Vogan), stewart.petersen@ualberta.ca (S.R. Petersen), ewong@ualberta.ca (E.Y.L. Wong), mohit.bhutani@ualberta.ca (M. Bhutani).

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Table 1
Subject characteristics.

	Age-matched controls	All COPD	COPD < 5000 steps/day	COPD > 5000 steps/day
Subjects	$N = 10$	$N = 33$	$N = 20$	$N = 13$
Age (years)	68 ± 5	68 ± 10	71 ± 9¥	63 ± 9
Height (cm)	170 ± 10	168 ± 10	168 ± 10	169 ± 9
BMI (kg/m^2)	27 ± 2	25 ± 5	25 ± 5	25 ± 4
Smoking history (pack years)	3 ± 4	41 ± 19*	41 ± 18*	42 ± 21*
FEV_1 (L)	2.81 ± 0.68	1.77 ± 0.71*	1.63 ± 0.7*	1.98 ± 0.67*
FVC (% pred)	105 ± 14	99 ± 23	93 ± 21	106 ± 23
FEV_1/FVC ratio	75 ± 5	61 ± 23	61 ± 22	61 ± 23
TLC (% pred)		122 ± 23	124 ± 21	119 ± 25
FRC (% pred)		140 ± 48	147 ± 49	127 ± 44
RV (% pred)		147 ± 66	161 ± 63	124 ± 63
DLCO (% pred)		68 ± 20	60 ± 22¥	77 ± 15
Respiratory Disturbance Index	5.9 ± 2.4	5.2 ± 3.1	4.7 ± 2.3	5.7 ± 3.7
MRC Dyspnea Scale	1.0 ± 0.0	1.9 ± 0.9*	1.9 ± 0.9*	1.9 ± 0.9*
Time spent >3 METs (min)	276 ± 151	157 ± 104*	126 ± 101*	201 ± 92

Values are mean ± SD. Inactive, <5000 steps/day; active, >5000 steps/day; BMI, body mass index; FEV_1, forced expiratory volume in 1 s; % pred, % predicted; FVC, forced vital capacity; FEV_1/FVC ratio, forced expiratory volume in 1 s to forced vital capacity ratio; TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume; DLCO, diffusing capacity for carbon monoxide; MRC, Medical Research Council.
* Significantly different than age matched control $p < 0.05$.
¥ Significantly different than COPD > 5000 steps per day.

and not the lung disease per se, which may explain the elevation in arterial stiffness (Maclay et al., 2009; McAllister et al., 2007; Mills et al., 2008; Sabit et al., 2007) and corresponding increased cardiovascular morbidity/mortality (Sin and Man, 2003, 2005) observed in COPD relative to age-matched healthy controls. Indeed recent work has shown that arterial stiffness can be reduced in COPD by exercise training (Gale et al., 2011; Vivodtzev et al., 2010), indicating that arterial stiffness is modifiable with exercise training in COPD as well as in health. Accordingly, we examined physical activity, aerobic fitness and arterial stiffness in a sample containing both COPD patients and age-matched healthy controls. Much like what is observed in health, we hypothesized that physical inactivity and exercise intolerance (i.e., low $\dot{V}O_{2peak}$) would be related to increased arterial stiffness independent of underlying lung disease.

2. Methods

The present study was approved by the University of Alberta Health Research Ethics Board (Biomedical Panel). Written informed consent was obtained prior to any research procedures.

2.1. Subjects

Thirty three COPD patients and 10 age-matched controls were recruited (see Table 1). COPD patients were selected using the American Thoracic Society criteria of irreversible post-bronchodilator airflow obstruction (i.e. FEV_1/FVC below the lower limit of normal predicted from height, age, sex) (1987) and a smoking history of greater than 10 pack-years. Each subject was carefully screened to exclude supplemental oxygen therapy, diabetes, cardiovascular disease (including abnormal ECG at rest and during exercise), vasoactive medications, body mass index (BMI) ≥32, severe inflammatory disorders (such as connective tissue disease), and recent participation in pulmonary rehabilitation. No COPD patient had a COPD exacerbation within the previous 6 months. Age-matched controls met the same criteria, except for normal lung function and <10 pack year smoking history. Prior to enrollment, all subjects were screened for sleep apnea, as sleep apnea has been shown to alter basal sympathetic activity (Sin et al., 2003; Spaak et al., 2005). No subject showed evidence of sleep apnea (Respiratory Disturbance Index <15), as evaluated by an overnight home sleep monitor (ApneaLink Plus, ResMed Ltd., Bella Vista, Australia).

2.2. Study protocol

All data for each participant were obtained within a 30 day period. Participants completed a brief medical history and the Medical Research Council (MRC) dyspnea scale (Bestall et al., 1999). All participants performed standardized spirometry (1987), while COPD patients completed a full pulmonary function test. Each subject performed a cardiopulmonary exercise test (CPET). Subjects were given an accelerometer to record physical activity for three consecutive days. Finally, pulse wave velocity was measured on a separate day to evaluate arterial stiffness.

2.3. Procedures and instrumentation

2.3.1. Cardiopulmonary exercise test

The CPET was performed on a treadmill using a modified Balke protocol (ACSM, 2006). Exercise cardiorespiratory data were collected using a V_{max} metabolic testing system (Vmax Spectra V29 System; SensorMedics, Yorba Linda, CA), and data are reported in Table 2. Peak oxygen consumption ($\dot{V}O_{2peak}$) and peak heart rate were defined as the highest values obtained during a 20 s period during the test. Inspiratory capacity maneuvers were conducted at rest and every 2 min up to peak exercise. Breathing reserve was calculated as: (predicted maximum voluntary ventilation ($FEV_1 \times 35$) − peak minute ventilation)/predicted maximum voluntary ventilation × 100.

2.3.2. Quantification of physical activity

To assess physical activity, participants wore a Sensewear biaxial accelerometer (SenseWear Pro3 Armband, Bodymedia; Milan, Italy) for three consecutive days starting from when they awoke. Physical activity data in all groups were collected during the same time of year, thus limiting seasonal variations in physical activity. Participants were asked to wear the armband on one weekend day and two weekdays. Total steps taken, as well as time above 3 METs, which was considered at least moderate intensity exercise (ACSM, 2006), were selected for analysis. To standardize across all participants, the first 10 h of recording for each day was used for analysis, which is similar to previous work (Colbert et al., 2011). Previous research with activity monitors has shown the recording for two or three days is an adequate representation of physical activity for patients with COPD (Pitta et al., 2005; Steele et al., 2000). Our pilot work found that this sampling window differentiated physical activity levels in COPD patients, and total step