Heart & Lung 43 (2014) 146–151

Contents lists available at ScienceDirect

Heart & Lung

journal homepage: www.heartandlung.org

Comparison of cardiopulmonary exercise testing variables in COPD patients with and without coronary artery disease

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ARTICLE INFO

Article history:
Received 6 September 2013
Received in revised form
26 December 2013
Accepted 26 December 2013

Keywords:
Coronary artery disease
Exercise capacity
Ventilatory efficiency
COPD

ABSTRACT

Background: Coronary artery disease (CAD) is a common concomitant condition and an important cause of morbidity and mortality in patients with chronic obstructive pulmonary disease (COPD). Since COPD and CAD can both independently cause reduced exercise capacity, it is reasonable to hypothesize that the combination of these diseases may compound the abnormalities observed during cardiopulmonary exercise testing (CPET). However, little is known about the impact of CAD on the CPET response in COPD patients. The aim of this study is to compare exercise capacity and gas exchange variables in COPD patients with and without CAD.

Methods: Fifty-four COPD subjects without CAD (COPDnoCAD) were matched to 54 COPD subjects diagnosed with CAD (COPD/CAD) according to age, gender, body mass index and severity of COPD. All subjects underwent resting pulmonary function and symptom-limited CPET.

Results: Comparing COPDnoCAD patients with COPD/CAD patients revealed that exercise capacity, as measured by % peak oxygen consumption (42 ± 16% vs 53 ± 19%, $p = 0.002$) and % peak wattage (23 ± 13% vs 32 ± 16%, $p = 0.001$), was significantly lower in COPD/CAD. Ventilatory response, as measured by VE/VCO_2 nadir (36 ± 9 vs 32 ± 5, $p = 0.001$), was significantly higher in COPD/CAD, with % peak VO_2 and VE/VCO_2 nadir correlating to % FEV_1 and inversely correlating with %DLCO.

Conclusion: COPD patients with CAD have significantly impaired CPET responses with lower exercise capacity and impaired gas exchange compared to COPD patients without CAD. These findings may affect the clinical interpretation of CPET data in COPD patients who have concomitant CAD.

Background

Chronic obstructive pulmonary disease (COPD) is now the third leading cause of death in males and females in the United State of America.[1] In addition, patients with COPD have lower ability to perform daily physical activities, thereby increasing morbidity and mortality rates.[2,3] The cycle of dyspnea, deconditioning, and declining physical activity not only aggravate the problems of COPD but also increase the risk for developing cardiovascular diseases. Coronary artery disease (CAD) is a common concomitant disorder which is present in 27%[4]–30.2%[5] of patients with COPD and is also an important cause of morbidity and mortality.[6] Aging and smoking are shared risk factors in both COPD and CAD that are perhaps linked by systemic inflammation.[7]

Exercise intolerance is an integral component of both COPD and CAD, and is caused by several mechanisms that impact functional capacity. Assessment of the impairment in exercise performance can be quantified by cardiopulmonary exercise testing (CPET). Prior research has shown patients with COPD present with different degrees of impaired aerobic capacity and diminished ventilatory efficiency reflecting the level of disease severity.[8,9] Whereas the primary limiting factor to exercise in COPD may be reduced ventilatory efficiency, the cardiovascular response to exercise in patients with CAD may mimic the normal response, although maximal capacity is often reduced by decreases in maximal stroke volume or heart rate, exercise-limiting symptoms such as angina pectoris or claudication, or deconditioning from inactivity and bed rest.

Author contributions: Dr. Thirapatarapong contributed to original and final manuscript, study concept and design, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content. Dr. Bartels contributed to final manuscript, study concept and design, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content. Ms. Armstrong contributed to final manuscript, statistical analysis and interpretation of data and critical revision of the manuscript for important intellectual content.

Competing interests: The authors declare that they have no competing interests.

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http://dx.doi.org/10.1016/j.hrtlng.2013.12.005

Since COPD and CAD both independently cause reduced exercise capacity, it is plausible to consider that the combination of these diseases may compound the abnormalities observed during CPET. However, little is known about the impact of CAD on CPET responses in patients with COPD. The aim of the present study is to compare CPET variables in COPD patients referred for CPET without CAD to those with CAD. Given the potential independent impact CAD has on the response to aerobic exercise, we hypothesize that individuals with COPD and CAD have a more impaired CPET response compared to subjects exclusively diagnosed with COPD alone.

Methods

Study subjects

We analyzed the records of patients with COPD referred for CPET at the Center for Chest Disease at the New York Presbyterian Hospital, Columbia University Medical Center between January 1998 and June 2010. Patients were referred for exercise tests as part of their standard clinical evaluation for lung transplant, lung volume reduction surgery, pulmonary rehabilitation program, or clinical management. The Institutional Review Board of Columbia University Medical Center approved this study. Selection of patients was based on the following criteria: (1) clinical diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (having a ratio of forced expiratory volume in one second to forced vital capacity (FEV_1/FVC) < 0.7); (2) CPET and PFT performed within 6 months of each other; (3) complete medical history including cardiovascular underlying disease and medical prescription. The sample size was calculated based on having 90% power to detect a difference in peak VO_2 (% predicted) of 10 units between subjects with and without CAD using a two sided hypothesis test and critical level of significance of 0.05. It was assumed that the standard deviation of observations in each group was the same and equal to 15 units. A total sample size of 98 subjects (49 in each group) was required. To allow for an estimated 10% rate of incomplete data, it was necessary to recruit 108 subjects to assure adequate sample size.

In the screened patients, 54 COPD patients without CAD were matched to 54 patients with CAD according to age, gender, body mass index (BMI) and severity of COPD based on FEV_1 (%). The case–control pairing was conducted *a priori* according to the aforementioned baseline characteristics while blinded to all results obtained from clinical assessment. A diagnosis of COPD was defined according to the GOLD criteria. CAD diagnosis was based on a history of previous MI, or previous coronary artery intervention (such as bypass grafting, angioplasty, and stenting). Obesity was defined by BMI $\geq$30 kg/m^2. Smoking status was based on the evidence in the medical record. Never smoker was defined as a subject who has never smoked a cigarette. Former smoker was defined as a subject who has smoked but currently does not smoke and current smoker was defined as a subject who currently smokes cigarettes. Left ventricular ejection fraction (LVEF) dysfunction was defined by LVEF $\leq$40% on echocardiography within 6 month of CPET.

Pulmonary function testing

All pulmonary function tests (PFTs) were performed according to American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines[10] and were performed before and 20–30 min after short acting bronchodilation with albuterol. The values reported include the values of FVC, FEV_1, total lung capacity (TLC), residual volume (RV) and diffusing capacity for carbon monoxide (DLCO). Because there are differences of PFT variables between males and females, we analyzed them by using the appropriate different reference equations. Percent of predicted PFT values were calculated for males and females as described in prior publications.[11–13]

Table 1
Characteristics variables between COPD with and without CAD.

	With CAD	Without CAD	*p*-value
	$N = 54$ (n) %	$N = 54$ (n) %	
Age (years)	63 ± 6	62 ± 5	0.528
Female	32 (30)	32 (30)	1.000
BMI (kg/m^2)	24.9 ± 4.3	25.7 ± 4.5	0.325
Obesity (BMI ≥ 30)	(8) 14.8	(11) 20.3	0.448
Hypertension	(34) 63.0	(20) 37.0	0.007*
Diabetes	(9) 16.7	(4) 7.4	0.139
Dyslipidemia	(26) 48.1	(17) 31.5	0.077
Smoking status			
Never smoker	(5) 9.2	(8) 14.8	0.524
Former smoker	(48) 88.9	(45) 83.3	0.380
Current smoker	(1) 1.9	(1) 1.9	1.000
Medicine			
ACE-inhibitor	(19) 35.2	(6) 11.1	0.003*
ARB	(9) 16.7	(8) 14.8	0.792
Beta blocker	(11) 20.4	(4) 7.4	0.051
CCB	(18) 33.3	(15) 27.8	0.531
Dihydropyridine	(6) 11.1	(2) 3.7	0.135
Nondihydropyridine	(11) 20.4	(13) 24.1	0.643
Diuretic	(14) 25.9	(10) 18.5	0.355
LVEF dysfunction (LVEF ≤ 40%)[a]	(2) 4.0	(5) 9.6	0.235

BMI = body mass index, ACEI = angiotensin converting-enzyme inhibitor, CCB = calcium channel blocker, LVEF = left ventricular ejection fraction.
Continuous data are presented as mean ± SD and categorical data are presented as (no. of patients) percentage.
*Significantly different ($p < 0.05$) between patients with and without CAD.
[a] Four patients with CAD and two patients without CAD did not have LVEF available.

Cardiopulmonary exercise testing

CPET was performed on an electronically braked cycle ergometer (Ergometrics 800, SensorMedics Inc, Yorba Linda, CA) with an Encore metabolic cart from 2005 to 2011; Vmax 229 series workstation before 2005 (SensorMedics Inc., Yorba Linda, CA). Continuous 12-lead telemetry was monitored via CardioSoft electrocardiogram software from 2005 to 2011 (GE/CardioSoft, Houston, TX); Max-1 electrocardiogram before 2005 (Marquette Medical Systems; Milwaukee, WI). Oxygen saturation (SpO_2) was recorded with an N595 pulse oximeter from 2005 to 2011 (Nellcor, Boulder, CO); Sat-Trak Monitor before 2005 (SensorMedics Inc., Yorba Linda, CA). CPETs were performed with 5 min baseline, 3 min unloaded cycling, followed by symptom-limited exercise by 5 or 10 watt-per-minute ramp protocol based on maximal voluntary ventilation (MVV) by National Emphysema Treatment Trial (NETT) criteria.[14] Patients still took their usual medications on the day of the CPET, including short acting bronchodilators within 2 h of the test. They were tested on 30.00 ± 0.20% supplemental oxygen in order to maintain oxygen saturation at ≥88% during rest and exercise for safety reason. Supplemental oxygen was delivered via a closed system and titrated breath-by-breath to maintain the target inspired oxygen level. CPET variables as shown in Table 3 were collected breath-by-breath. Calculations were made of ventilatory equivalents for carbon dioxide (VE/VCO_2). In the majority of the COPD patients studied, the ventilatory threshold (VT) assessed using the combined methods[15] of ventilatory equivalencies, excess CO_2 production, and a modified V-slope could not be identified; therefore values of exercise variables measured at VT are not provided. To estimate ventilatory inefficiency, VE/VCO_2 nadir that defined as the lowest point on the VE/VCO_2 curve was measured.