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Effect of modality on cardiopulmonary exercise testing in male and female COPD patients

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ABSTRACT

The purpose of this study was to examine the physiological responses to treadmill and cycle cardiopulmonary exercise testing (CPET) in male and female COPD patients. Fifty-five patients [28 males ($FEV_1 = 58.2 \pm 19.5\%$ predicted), and 27 females ($FEV_1 = 65.3 \pm 16.6\%$ predicted)] completed a treadmill and a cycle CPET in random order on two separate days. Respiratory and cardiovascular data were obtained. Compared to the cycle CPET, the treadmill elicited greater peak power output and peak oxygen uptake, while arterial saturation at peak exercise was lower with the treadmill; however, there were no differences between the responses in men and women. No differences were observed in heart rate, ventilation, tidal volume/breathing frequency, inspiratory capacity, or dyspnea responses between modalities or sex. The physiological responses between treadmill and cycle CPET protocols are largely similar for both men and women with COPD, indicating that either modality can be used in mild/moderate COPD patients.

1. Introduction

The relation between sex and the respiratory response to exercise in health and disease has been a topic of much interest. Women have narrower airways and lower lung volumes compared to age-matched men even after correction for body height (Sheel and Guenette, 2008; Sheel et al., 2009), and correspondingly have higher work of breathing during exercise (Guenette et al., 2009, 2007). Further, healthy trained women have decreased ventilatory reserve and develop more expiratory-flow limitation with incremental cycle exercise as compared to men of the same fitness level, potentially because of these underlying anatomical differences within the respiratory system (McClaran et al., 1998). Sex-differences also appear to be evident in lung disease patients with chronic obstructive pulmonary disease (COPD). Women with COPD have greater dyspnea and shorter 6-min walking distance when compared to their male counterparts (de Torres et al., 2005; Martinez et al., 2007), while women with mild COPD also have greater dyspnea at the same absolute cycle workload as compared to male COPD patients matched for age and disease severity (Guenette et al., 2011).

The cardiopulmonary exercise test (CPET) is the standard clinical tool to evaluate dyspnea and exercise tolerance (American Thoracic and American College of Chest, 2003; Stickland et al., 2012; Wasserman et al., 2005). The two most common exercise modalities used for CPET testing are the bicycle ergometer and the treadmill; however, there is currently no consensus as to which exercise mode is preferable to evaluate respiratory patients (American Thoracic and American College of Chest, 2003; Whaley et al., 2006). The cycle ergometer typically provides a more linear increase in work rate; however, the treadmill better replicates daily activities (Wasserman et al., 2005; Whaley et al., 2006). An incremental treadmill protocol has been developed, whereby the corresponding exercise response results in a linear increase in oxygen uptake that is similar to that seen with standard cycle ergometry protocols (Porszasz et al., 2003), allowing for better physiological comparisons between treadmill and cycle responses. Researchers have since compared cycle ergometry to treadmill exercise using this protocol in a small sample of patients with COPD (Hsia et al., 2009)

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and found the cardiorespiratory responses to the linear treadmill and cycle tests to be fairly similar, with the exception of higher peak oxygen uptake ($\dot{V}O_{2peak}$) and greater reduction in SpO_2 on the treadmill.

Cycling results in greater lactate accumulation (Mathur et al., 1995; Palange et al., 2000) and leg fatigue (Marin et al., 1993; Pepin et al., 2005) as compared to treadmill exercise, which would have the effect of potentiating the ventilatory response during cycle CPET testing. Considering that women have a greater propensity for developing ventilatory limitations during exercise (McClaran et al., 1998), and that women with COPD typically have less strength and muscle mass than men with COPD (Verhage et al., 2011; Vermeeren et al., 2006), cycle exercise may result in considerably more dyspnea and hyperinflation in female COPD patients as compared to male COPD patients at the same relative intensity. Examining whether exercise modality has a differential effect on dyspnea and hyperinflation between male and female COPD patients is important with respect to the clinical interpretation of CPET findings. Hyperinflation leads to exaggerated dyspnea and reduced exercise tolerance in COPD (Marin et al., 1993; O'Donnell, 1994; O'Donnell and Laveneziana, 2006). Should female COPD patients develop greater hyperinflation and dyspnea with cycle exercise this would result in greater exercise limitation noted on the cycle as compared to the treadmill. Accordingly, the purpose of this study was to examine the physiological responses to both linear work rate treadmill and cycle ergometer CPETs in a large sample of COPD patients who were naïve to CPET. The increments in work rate during each CPET were carefully matched between modalities, thus permitting direct examination of modality, sex and their interaction on physiological and perceptual responses. We hypothesized that women would experience greater dyspnea and hyperinflation than men during CPET testing, with the greatest response observed during cycle CPET testing.

2. Methods

The study was approved by a University Health Research Ethics Board, and written informed consent was obtained prior to any research procedures. Participants were recruited upon entry into our outpatient pulmonary rehabilitation program. All were referred to the program by a physician with a diagnosis of COPD. Potential participants were excluded if they had a respiratory exacerbation within the past 6 months, unstable cardiac disease, orthopedic limitations, required supplemental oxygen, and/or if they were unable to follow instructions. In total, 65 patients consented to participate; 55 completed the two CPETs and were included in the analysis. None of the participants had previous experience with CPET. Full lung function data were obtained on a day prior to exercise testing, and baseline Medical Research Council (MRC) dyspnea scale (1982) scores were collected on all patients.

2.1. Procedures

All participants were instructed to continue their prescribed medications as normal for both testing days, but were encouraged to avoid caffeine and cigarette smoking 2 h prior to the CPET. The volunteers completed two CPETs (treadmill and cycle) in random order on two different days (mean time between testing = 12.2 ± 9.3 days).

Standardized information was given about the CPET and the data to be obtained. All participants were encouraged to walk/cycle for as long as possible, but were informed that the test would be terminated when workload could no longer be maintained. Once the patient was breathing through the mouthpiece with the nose plugged, baseline blood pressure (BP), breathing discomfort, and leg discomfort data were obtained. Standardized spirometry measures were performed either seated (cycle) or standing (treadmill) in order to position the patients' tidal breathing within the maximal flow volume loop.

The incremental exercise tests were performed on an electromagnetically-braked cycle ergometer (Ergoselect 200P; Ergoline GmbH, Blitz, Germany) and a treadmill (TMX425C by Full Vision Inc., Newton, Kansas, USA). The treadmill (speed and grade) and cycle ergometer (power output) were calibrated for accuracy prior to the study. Spirometry and inspiratory capacity (IC) maneuvers, as well as breath-by-breath measurements of minute ventilation ($\dot{V}_E$), tidal volume (V_T), breathing frequency (BF), oxygen uptake ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), end-tidal oxygen ($P_{ET}O_2$) and end-tidal carbon dioxide ($P_{ET}CO_2$) were collected by a metabolic cart (Vmax Spectra V29 System; SensorMedics, Yorba Linda, CA). The pneumotach and O_2/CO_2-analyzers were calibrated prior to each test. Subjects were monitored by 12-lead electrocardiogram (ECG, Cardiosoft; SensorMedics, Yorba Linda, CA) and pulse oximetry with finger probe (N-595; Nellcor Oximax, Boulder, CO). Blood pressure (BP) was measured by manual blood pressure cuff and barometer.

The incremental protocol was identical for the treadmill and the cycle ergometers. The rate of increase in work rate was determined based on the patient's FEV_1. Increments of 5 W min^{-1} were used in patients with $FEV_1 < 1.0$ L, and increments of 10 W min^{-1} were used in patients with $FEV_1 > 1.0$ L, similar to Hsia et al. (2009). The protocols were changed to 20 W min^{-1} if the researcher anticipated that the test would exceed 8–12 min (Wasserman et al., 2005). Comparative increases in workload on the treadmill were approximated through a constant increase in speed (0.2 mph) and a curvilinear increase in inclination (rounded to closest 0.5%) each minute. The work rate increments were based on the following formula: $W = 0.1634 \times \text{speed} \times (\text{grade}/100) \times \text{body weight (kg)}$ (Cooper and Storer, 2008). Holding on to the treadmill handrails was discouraged; however, some patients required the handrails to maintain their balance. Regardless of performance on the initial CPET, the same work load increments were used for the second test.

Both the ECG and SpO_2 were monitored continuously, while BP was measured at baseline, every 4 min, and at peak exercise. Breath-by-breath measurements of respiratory parameters were collected continuously and reported in 30 s averages. The average of the last 30 sec for each workload was used for analysis, and peak values were recorded as the average of the last 30 s of the last completed workstage. At rest, and every 2 min until peak exercise an IC maneuver was conducted. Assuming that total lung capacity (TLC) did not change with exercise, the changes in IC reflected changes in end-expiratory lung volume (EELV = TLC–IC). Inspiratory reserve volume (IRV) was also calculated and expressed as a percentage of TLC. Patients were asked to rate the intensity of their breathing and leg discomfort by pointing to the modified Borg scale (Borg, 1982). Ratings were performed at baseline, every 2 min, at end exercise, and 2 min into recovery. The IC maneuvers and the exertional symptoms were evaluated at alternating minutes.

2.2. Statistical analysis

For all inferential analyses, the probability of type I error was set at 0.05. To examine the changes in physiological responses, repeated measures ANOVAs were conducted. Sex (men/women) was the between-subjects factor, and modality (treadmill/cycle) and work stage were the within-subject factors. Because the patients had different end stages, the data were grouped and analyzed as relative work stages (baseline, 60%, 80%, and 100% of $\dot{V}O_{2peak}$). Where main effects were found, Tukey post hoc tests were used.