

Original Article

Cardiorespiratory response to exercise in men and women with obstructive sleep apnea

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Abstract

Background: OSA severity has been associated with self-reported lack of exercise. Most of the research has been done with men recruited from sleep clinics. There is limited data on the exercise performance of women with OSA. Therefore, the aim of this study was to assess exercise performance in a prospective, consecutive sample of men and women with OSA to compare their cardio respiratory parameters, arterial blood pressure and heart rate responses during and after exercise.

Methods: Sixty-two subjects (32 men) completed the protocol. Men had a higher peak VO_2 , percent predicted peak VO_2 , VCO_2 , heart rate, systolic BP, and oxygen pulse than women.

Results: There were no differences between men and women for peak oxygen saturation, peak Borg scales for dyspnea and leg fatigue and diastolic BP. A significant negative correlation was found between severity of OSA as measured by AHI, and peak VO_2 ($r = -0.4$) in women, but not in men.

Conclusion: Men with OSA have higher peak VO_2 and higher peak exercise heart rate than women with OSA; they also have higher end-exercise systolic BP than women and higher SBP during recovery from exercise; although this difference is not significant when adjusted for peak systolic BP. In men with OSA, there is no correlation between peak VO_2 and AHI, but there is a significant correlation between these variables in women. Heart rate and blood pressure behaved similarly during exercise in both groups.

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Keywords: Blood pressure; Heart rate; Oxygen consumption; Obstructive sleep apnea; Exercise performance; Cardiovascular response

1. Introduction

Obstructive sleep apnea (OSA) is a common condition caused by an intermittent collapse of the upper airway during sleep that results in repetitive hypoxemia and nighttime arousals, poor sleep quality, and excessive daytime somnolence. OSA has been named a risk factor for a number of cardiovascular conditions, such as arterial hypertension [1,2], congestive heart failure [3], and stroke [4], and has been associated with increased cardiovascular mortality [5]. Physical exercise poses signif-

icant stress for the cardiovascular and pulmonary system and often leads to early diagnosis of cardiovascular (CV) abnormalities, such as coronary artery disease or cardiac arrhythmias [6–8].

OSA severity has been associated with self-reported lack of exercise, independent of body habitus, after adjusting for body mass index (BMI) [9]. OSA subjects are frequently overweight and often complain of fatigue and exercise intolerance, yet it is not clear whether OSA impairs exercise performance. A significant decrease in peak oxygen consumption was noted in patients with moderate to severe OSA in some studies [10–12], while, in others, the exercise performance of OSA subjects was normal [13,14]. Most of the research has been done with

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men recruited from sleep clinics. There are limited data on the exercise performance of women with OSA or on cardiovascular response to exercise for men and women with OSA.

The aim of this study was to assess exercise performance in a prospective, consecutive sample of men and women with OSA to compare cardiorespiratory parameters, blood pressure, and heart rate responses during and after exercise.

2. Methods

2.1. Subjects

Patients eligible were those subjected to polysomnography at the Sleep Institute Universidade Federal de São Paulo (UNIFESP) due to clinical suspicion of OSA with an apnea hypopnea index (AHI) > 5. A total of 108 patients with AHI > 5 were consecutively selected in March and April 2006, and 68 of them agreed to participate. Subjects were included if they were over 18 years old, sedentary, capable of performing a treadmill test, and reported no recent hospitalization or change in medication. Exclusion criteria included BMI > 40, chronic pulmonary disease based on the spirometric classification defined as FEV₁/FVC under 0.7, history of bronchial asthma, smoking, New York Heart Association class III or IV heart failure, unstable angina, valvular heart disease, life-threatening arrhythmia, atrial fibrillation, left bundle branch block, uncontrolled hypertension, renal disease, and neuromuscular conditions.

All subjects were asked to abstain from caffeinated beverages and to come to the Sleep Clinic at 8:00 AM for a physical examination by a staff cardiologist prior to assessment from the following: the Epworth sleepiness scale (ESS), a 12-lead ECG, spirometry, a symptom-limited maximum cardiorespiratory exercise study (CPET) on a treadmill, and an echocardiogram. The study was approved by UNIFESP's Ethics Committee, and all subjects signed an informed consent form.

2.2. Polysomnography

Overnight polysomnography was performed using an EMBLA digital system[®] (17 channels, Medicare Medical Devices). The following variables were monitored: electroencephalogram (EEG) (four channels: C3-A2, C4-A1, O1-A2, and O2-A1), electrooculogram (two channels: LOC-A2 and ROC-A1), electromyogram (two channels: submental and anterior tibialis muscles), electrocardiogram (one channel), snoring, and body position. Airflow was monitored using a thermocouple and pressure transducer. Chest and abdominal piezosensors monitored respiratory effort. Arterial oxygen saturation (SaO₂) and pulse were recorded with a pulse

oximeter (Nonin[®], model 9500, Plymouth, USA). All polysomnograms were performed and scored by an experienced sleep technician following guidelines for sleep studies [15] and reviewed by a sleep medicine physician. Arousals were defined using criteria from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association [16], and respiratory events were rated using the American Academy of Sleep Medicine Task Force criteria [17]. An apnea was defined as a decrease in airflow of at least 80% for 10 s or more, and hypopnea was defined as a decrease in airflow of at least 50% for 10 s or more. An apnea-hypopnea index (AHI) > 5 was considered diagnostic for OSA.

2.3. Spirometry

Lung function testing was performed with a computerized spirometer, i.e., a KoKo spirometer[®] (Pulmonary Data Service Instrumentation, Inc., Louisville, KY, USA), following the procedures recommended by the American Thoracic Society [18] to exclude pulmonary disease. The lung function system was calibrated with a 3 L syringe at different flow rates at least once daily. All spirometric measurements were performed in a sitting position. Forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), and FEV₁/FVC ratio were measured in each subject, recorded in absolute values and percent predicted. All measurements were performed by technicians experienced in lung function testing. Bronchodilators were not administered during the spirometry.

2.4. Cardiopulmonary exercise test

All patients fasted for two hours before the cardiopulmonary exercise test (CPET). Subjects underwent a maximum, symptom-limited CPET on a treadmill (ErgoPC13, Micromed[®], Brasilia, Brazil) in a quiet air-conditioned room with an average temperature of 21 °C and full resuscitation facilities. During the tests, subjects were monitored with a 12-lead ECG by pulse oximetry (Nonin[®], model 9500, Plymouth, USA), a non-invasive brachial artery blood pressure sphygmomanometer and breath-by-breath measurement of respiratory parameters: oxygen consumption (VO₂), carbon dioxide production (VCO₂), minute ventilation (VE), respiratory rate (RR), and tidal volume (V_T) through a mask (Vista CPX[®], Vacumed, Ventura, CA, USA). After calibration, CPET was performed on a treadmill with a ramp protocol taking into account age and sex of the subject [19]. Each test was supervised by an experienced cardiologist, nurse, and physiotherapist.

Arterial blood pressure was measured at baseline, every 3 min during exercise and at 1, 2, 4, and 6 min during recovery. Modified Borg scales were obtained at rest and at peak exercise for dyspnea and leg fatigue [20].

Continuous ECG recording was performed during the test and continued for 6 min of recovery. The CPET was stopped by the attending physician if diastolic blood pressure (BP) became greater than 120 mmHg in normotensive subjects, if diastolic BP became greater than 140 mmHg in hypertensive subjects, if systolic BP became greater than 260 mmHg, if there was a sustained decrease in systolic BP, if clinical symptoms of chest pain, syncope or near-syncope occurred, or if ECG changes consistent with ischemia, complex ventricular arrhythmia, sustained atrial arrhythmia, or 2nd or 3rd degree AV block occurred.

2.5. Echocardiography

All subjects underwent conventional echocardiography (iE33[®], Philips Electronics, The Netherlands) before the CPET. End-diastolic and end-systolic diameters were measured from the short-axis views at the level of the tips of the mitral valve leaflets, and ejection fraction was derived from these measurements. All echocardiograms were analyzed by an experienced cardiologist staff member blinded to the exercise data.

2.6. Statistical analysis

Subject characteristics are presented as means and standard deviations. Shapiro–Wilk normality tests were performed for all baseline demographic characteristics. Peak exercise and recovery data were compared using ANOVA. Correlation analysis was performed using Pearson correlation coefficients. *p* Values of 0.05 or less were considered significant. The statistical analysis was performed using Statistics 8.0 software.

3. Results

Sixty-two subjects (32 men) completed the protocol. Six subjects were excluded: four because of poorly controlled hypertension, one because of musculoskeletal disease, and one because of morbid obesity. Their baseline characteristics are presented in Table 1. There were no differences between men and women in age, BMI, ESS, AHI, and resting systolic and diastolic BP. Spirometry variables [FEV₁ (L) and FVC (L)] differed in men and women, but not from the predicted percentage as expected. The ejection fraction of the left ventricle and the pulmonary artery pressure were normal (<35 mmHg) in all subjects. No cardiac arrhythmia or ischemia during the CPET was observed.

Peak exercise variables are presented in Table 2. Men had a higher peak VO₂, percent predicted peak VO₂, VCO₂, heart rate, systolic BP, and oxygen pulse than women. There were no differences between men and women for peak oxygen saturation, for peak Borg scales for dyspnea and leg fatigue, or for diastolic BP. A signif-

Table 1

Baseline characteristics of sample, showing means and standard deviations

Variable	Men (N = 32)	Women (N = 30)	<i>p</i>
Age (years)	57.2 ± 10.9	60.5 ± 7.4	NS
BMI (kg/m ²)	27.8 ± 4.2	28.4 ± 6.3	NS
AHI	32.5 ± 23.6	33.9 ± 27.6	NS
ESS	10.3 ± 4.8	8.7 ± 6.0	NS
Systolic BP (mmHg)	126.0 ± 14.8	121.7 ± 14.6	NS
Diastolic BP (mmHg)	79.4 ± 10.1	78.8 ± 9.4	NS
Hypertension (%)	46.9	66.7	NS
Diabetes (%)	12.5	10.0	NS
Ejection fraction (%)	70.2 ± 4.9	70.1 ± 5.6	NS
FEV ₁ (L)	3.1 ± 0.8	2.5 ± 0.6	<i>p</i> = 0.008
FEV ₁ (%)	98.8 ± 22.4	110.0 ± 25.3	NS
FVC (L)	4.11 ± 0.9	3.42 ± 1.2	<i>p</i> = 0.02
FVC (%)	101.5 ± 18.8	110.2 ± 18.3	NS

ANOVA.

NS, non-significant.

Table 2

Subjects' peak exercise data showing mean values and standard deviations

	Men (N = 32)	Women (N = 30)	<i>p</i>
Peak VO ₂ (L/min)	2.60 ± 0.8	1.65 ± 0.7	<0.0001
Peak VO ₂ (ml/kg/min) (%)	33.3 ± 10.2	23.3 ± 7.0	<0.0001, predicted)
	(116.6 ± 27.7)	(91.3 ± 28.7)	<0.0001
Peak VCO ₂ (L/min)	34.3 ± 12.3	22.6 ± 5.5	<0.0001
Peak SaO ₂ (%)	94.0 ± 3.0	95.1 ± 2.4	NS
Peak heart rate (bpm)	157 ± 23	141 ± 20	0.007
(% predicted)			
Peak systolic BP (mmHg)	193.8 ± 22.4	173.2 ± 22.8	<0.0001
Peak diastolic BP (mmHg)	80.8 ± 10.3	81.3 ± 14.6	NS
O ₂ pulse (ml min ⁻¹ beat ⁻¹)	16.5 ± 4.3	11.0 ± 3.1	<0.0001
Resting Borg dyspnea	0.2 ± 0.6	0.6 ± 1.52	NS
Resting Borg leg fatigue	0.2 ± 0.9	0.9 ± 1.5	NS
Peak Borg dyspnea	4.3 ± 2.6	5.3 ± 2.7	NS
Peak Borg leg fatigue	4.5 ± 2.6	5.1 ± 3.1	NS

ANOVA.

NS, non-significant.

icant negative correlation was found between severity of OSA as measured by AHI and peak VO₂ (*r* = -0.4) in women but not in men, (Fig. 1). We also found differences between men and women in systolic BP after 1, 2, and 4 min of recovery, but this did not reach significance when correction was made for systolic BP at maximum exercise. Diastolic BP and heart rate (Fig. 2) did not change significantly during recovery when corrected for peak exercise values (Table 3).

4. Discussion

We analyzed cardiopulmonary exercise behavior in men and women with OSA. The main finding of this study was an association between exercise performance and AHI in women but not in men in the absence of heart or lung disease. This finding suggests a gender difference in exercise performance in patients with OSA.

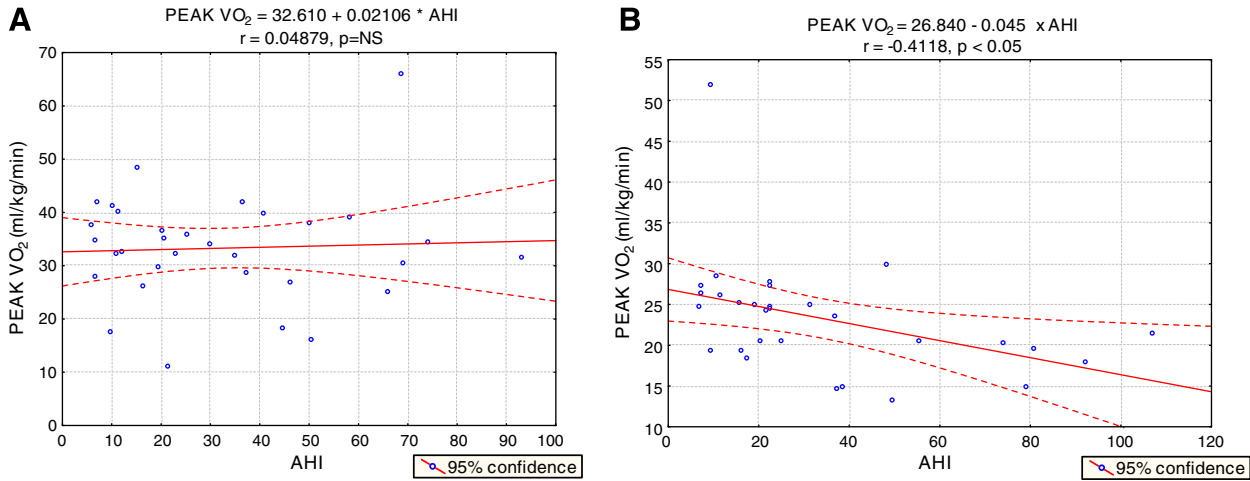


Fig. 1. Correlation between Peak VO₂ and AHI in males (A) and females (B).

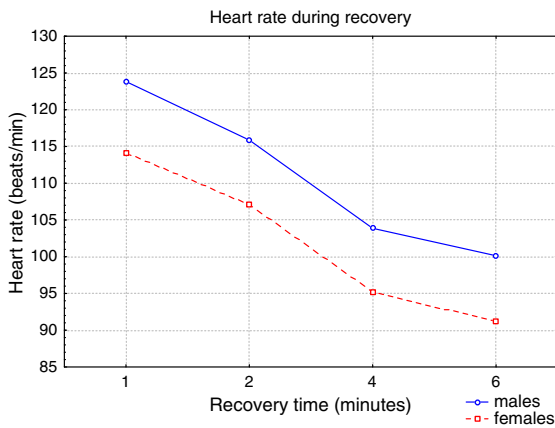


Fig. 2. Heart rate during recovery in men and women with OSA.

OSA is a recognized risk factor for certain cardiovascular disorders, such as arterial hypertension [2,1], heart failure [21], cardiac arrhythmias [22,23], metabolic syndrome [24], and stroke [25]. Therefore, the relationship between OSA and exercise performance has been of interest in recent years. Results from clinical studies suggest that subjects with OSA have a lower VO₂ peak, VO₂ peak/kg, and work peak than control groups and that they show abnormal CPET results [11]. Furthermore,

OSA patients with normal resting left ventricular systolic function and no hypertension had worse cardiac response to exercise than healthy subjects [26]. Duchna et al. [14], however, examined ventilatory efficiency in OSA patients during exercise, before and after treatment with CPAP, and found that OSA was not associated with disturbed ventilatory efficiency during exercise and that long-term CPAP therapy did not change ventilatory efficiency. In contrast, Przybylowski et al. [13] demonstrated that OSA patients were not limited when exercising. It is important to note that the majority of subjects selected for these studies were male, probably due to the high male prevalence of OSA.

Gender differences in exercise performance are likely multifactorial: previous studies have demonstrated lower muscle mass and lower maximum aerobic power in women, and gender differences in pulmonary structure and in ventilatory responses to exercise. Jordan et al. [27] demonstrated that men have a more positive pharyngeal critical closing pressure and that they experience more severe OSA than women matched for body mass index. Pillar et al. [28] concluded that normal men are more vulnerable to load-induced hypoventilation than women due to increased upper airway collapse, which could not be explained by differences in dilator muscle

Table 3
Cardiovascular parameters during recovery in men and women with OSA

Recovery time (min)	Men			Women		
	SBP (mmHg)	DBP (mmHg)	HR (bpm)	SBP (mmHg)	DBP (mmHg)	HR (bpm)
Peak exercise	193.8 ± 22.4	80.8 ± 10.3	157 ± 23	173.2 ± 22.8	81.3 ± 14.6	142 ± 20
1	181.3 ± 21.5	78.6 ± 9.7	123 ± 24	161.3 ± 24.3	79.0 ± 11.0	114 ± 17
2	162.3 ± 21.9	78.1 ± 9.3	116 ± 19	144.3 ± 24.0	77.0 ± 10.2	107 ± 16
4	141.7 ± 20.6	77.2 ± 8.1	104 ± 18	127.0 ± 21.2	76.7 ± 10.0	95 ± 15
6	128.0 ± 18.8	76.6 ± 7.9	100 ± 19	119.8 ± 18.4	75.7 ± 10.4	91 ± 16

ANCOVA.

Peak exercise values as covariate.

All non-significant.

activation. These findings imply that there is a fundamental cross-gender difference in the upper airway anatomy and/or tissue characteristics, which may suggest a possible anatomic factor to explain our finding. In fact, it has been demonstrated that an exercise-mediated adaptation is related to the recruitment of the upper airway stabilizer muscles [29], and an upper airway obstruction had a marked influence on maximum exercise capacity due to hypoventilation [30]. In upper airway obstruction, however, the relationship between the degree of obstruction and exercise limitation indices is not well established.

In addition, gender differences in fat metabolism during exercise have also been demonstrated [31]. Finally, though it is possible that the differences in exercise performance may be related to fatigue and deconditioning, our subjects were all sedentary. Sheperdycky et al. [32] showed differences in the clinical presentation of patients diagnosed with obstructive sleep apnea syndrome; women were more likely than men with the same degree of OSA to be treated for depression, have insomnia, and have hypothyroidism. There is still considerable controversy about the exact role each of these factors plays in the gender difference in exercise performance. Our study did not attempt to elucidate the exact mechanism of this difference. Future studies should evaluate the role of different levels of daily physical activity and other potential factors that may account for the gender difference.

In the present study, men with OSA demonstrated higher peak exercise heart rates than women with OSA. They also demonstrated higher end-exercise systolic BP and higher recovery from exercise systolic BP; although this difference was not significant when adjusted for peak systolic BP.

Despite the fact that sedentarism was part of inclusion criteria, the difference in daily physical activity between men and women was not assessed in the present study and should be considered a limitation since the cardiorespiratory parameters could be made similar if both groups were trained to the same level. The absence of a control group and the use of VO_2 (a non-specific cardiorespiratory parameter) to assess exercise performance should be considered as additional limitations for which future studies may correct.

In conclusion, heart rate and blood pressure behaved similarly during exercise in both groups. No correlation was found between peak VO_2 and AHI in men with OSA, but a significant correlation was found between these variables in women, suggesting that OSA causes a greater impact in women than men. More studies are needed to elucidate the mechanisms involved in these differences.

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