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SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

Obstructive sleep apnea does not impair cardiorespiratory responses to progressive exercise performed until exhaustion in hypertensive elderly

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Abstract

Background Elderly people have a high prevalence to systemic arterial hypertension (SAH) and obstructive sleep apnea (OSA). Both comorbidities are closely associated and inflict damage on cardiorespiratory capacity.

Methods In order to assess cardiorespiratory responses to the cardiopulmonary exercise test (CPET) among hypertensive elderly with OSA, we enrolled 28 subjects into two different groups: without OSA (No-OSA: apnea/hypopnea index (AHI) < 5 events/h; $n = 15$) and with OSA (OSA: AHI ≥ 15 events/h; $n = 13$). All subjects underwent CPET and polysomnographic assessments. After normality and homogeneity evaluations, independent *t* test and Pearson's correlation were performed. The significance level employed was $p \leq 0.05$.

Results Hypertensive elderly with OSA presented lower heart rate recovery (HRR) in the second minute (HRR_2) in relation to the No-OSA group. A negative correlation between AHI and ventilation (VE) ($r = -0.63$, $p = 0.02$) was found in polysomnography and CPET data comparisons, and oxygen saturation (O_2S) levels significantly correlated with VE/VCO_{2slope} ($r = 0.66$, $p = 0.01$); in addition, No-OSA group presented a positive correlation between oxygen consumption and O_2S ($r = 0.66$, $p = 0.01$), unlike the OSA group.

Conclusions OSA does not affect the CPET variables in hypertensive elderly, but it attenuates the HRR_2. The association between O_2S during sleep with ventilatory responses probably occurs due to the adaptations in the oxygen transport system unleashed via mechanical respiratory feedback; thus, it has been identified that OSA compromises the oxygen supply in hypertensive elderly.

Keywords Obstructive sleep apnea syndrome · Aged · Hypertension · Oxygen consumption · Exercise

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Introduction

Aging is a global trend, and in 2050, it is estimated that 21% of the world's population will be 60 years of age or older [1]. The aging process leads to chronic diseases such as systemic arterial hypertension (SAH) and obstructive sleep apnea (OSA). SAH is an important cause of morbidity and mortality in the elderly due to compromising their cardiorespiratory fitness [2–5].

Despite regular physical exercise contributing to attenuate blood pressure (BP), this response is altered in hypertensive elderly subjects due to deregulation of cardiovascular autonomic balance. Consequently, there is a decline of the maximum and peak oxygen consumption (VO_{2max} and VO_{2peak}, respectively), carbon dioxide

production (VCO_2), maximum and peak heart rate (HR_{max} and HR_{peak}, respectively), and cardiac output [6–9]. Previous studies have found that OSA patients have reduced oxygen consumption and delayed heart rate recovery (HRR), probably due a cardiac dysfunction induced by a chemoreceptors hyperactivity [10–12] and downregulation of beta-adrenergic receptors in response to exaggerated sympathetic activation in OSA patients [13].

Although some studies have shown that SAH and OSA negatively affect the cardiovascular response to exercise, no study to our knowledge has investigated the cardiorespiratory response to exercise in hypertensive elderly with OSA. Therefore, the aim of this study was to evaluate cardiorespiratory response to CPET in hypertensive elderly subjects with OSA. We hypothesized that the association of chronic disease (hypertension plus OSA) will impair cardiorespiratory response to CPET.

Methods

Subjects

Twenty-eight subjects were enrolled in this study (70.0 ± 6.2 years of age, 26.6 ± 2.9 kg/m^2, 5 males and 23 females), diagnosed with stage I or II of systemic hypertension without use of beta-blockers, eutrophics, non-smokers (> 6 months), without diabetes, or any other respiratory or cardiovascular disease and considered irregularly active [14]. The participants were divided into two groups: (1) hypertension without OSA (No-OSA group; AHI < 5 events/h; n = 15) and (2) hypertension with OSA (OSA group: AHI ≥ 15 events/h; n = 13). Participants were informed about all procedures and provided informed consent form before any participation.

Anthropometric, hemodynamics, echocardiographic variables and the medications used by the participants are presented in Table 1. There was no significant difference between hypertensive groups (OSA and No-OSA) for hemodynamics ($p > 0.05$) or echocardiographic ($p > 0.05$) variables, or for the medications used ($p > 0.05$). On the other hand, as expected, elderly hypertensive subjects with OSA presented significantly higher neck (t = 8.23, $p < 0.01$), hip (t = 4.44, $p < 0.01$), and waist (t = 2.67, p = 0.01) circumference values in comparison with elderly hypertensive subjects without OSA. Furthermore, both groups were paired by age and BMI ($p > 0.05$).

This study was approved by the Institutional Review Board of the Federal University of Paraiba (CAAE: 48423815.1.0000.5188) and it was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Table 1 Baseline characteristics of hypertensive elderly with and without obstructive sleep apnea

Variables	OSA (n = 13)	No-OSA (n = 15)
Demographics		
Age, years	70.6 ± 7.4	69.3 ± 5.1
Gender[a], M/F	3/10	2/13
Anthropometrics		
BMI, kg/m^2	26.2 ± 3.2	27.0 ± 2.7
Neck circumference, cm	37.0 ± 1.9*	31.8 ± 1.1
Hip circumference, cm	99.6 ± 2.9*	94.2 ± 3.0
Waist circumference, cm	88.1 ± 3.8*	82.2 ± 6.2
Waist-hip ratio, cm	0.9 ± 0.1	0.9 ± 0.1
Hemodynamics		
SBP_{rest}, mmHg	143.9 ± 14.7	139.7 ± 14.7
DBP_{rest}, mmHg	81.2 ± 7.7	80.7 ± 2.6
HR_{rest}, bpm	76.9 ± 11.7	73.6 ± 13.2
DP_{rest}	11,058 ± 1909	10,515 ± 2602
Echocardiographic		
LV end diastolic diameter, mm	48.2 ± 1.8	46.7 ± 3.2
LV diastolic thickness, mm	8.1 ± 0.9	8.7 ± 0.8
LV mass, g/m^2	135.1 ± 18.8	127.8 ± 10.5
Ejection fraction, %	71.3 ± 4.8	72.5 ± 3.0
Medication[a], n (%)		
Calcium channel blocker	4 (33.3)	5 (38.5)
Diuretic	7 (58.3)	4 (30.8)
Angiotensin antagonist	7 (58.3)	7 (53.8)

Data are presented as mean ± standard deviation

BMI body mass index, SBP_{rest} resting systolic blood pressure, DBP_{rest} resting diastolic blood pressure, HR_{rest} resting heart rate, DP_{rest} resting double product, *LV* left ventricle

*$p < 0.01$;

[a] Chi-squared test

Study design

The sample was randomly recruited from the Lauro Wanderley University Hospital and older people living together centers located in João Pessoa/PB (Brazil). All subjects were submitted to anthropometric assessments (body mass index, neck circumference, hip circumference, and waist circumference), polysomnography, echocardiography, and cardiopulmonary exercise test (CPET). Moreover, they were submitted to a sleep quality questionnaire (Pittsburgh Sleep Quality Index).

Cardiopulmonary exercise test protocol

All subjects performed an incremental cardiopulmonary exercise test (CPET) of maximum exercise tolerance. All procedures were performed in agreement with the guidelines of the American Thoracic Society/American College of Chest

Physicians [15] for cycle ergometer tests. The CPET was performed on an Inbrasport CG-04 cycle ergometer (Inbrasport, Porto Alegre, Rio Grande do Sul, Brazil) with electromagnetic braking. Subjects performed a 5-min warm-up with no resistance (0 W), then the activity rate was increased using a ramp protocol (5–10 W min^{-1}) until maximum exercise tolerance. Verbal encouragements were given during the CPET to ensure maximal effort.

Pulmonary gas exchange variables (VO_2, VCO_2, minute ventilation [VE], oxygen pulse (O_2Pu), respiratory quotient (R), ventilatory efficiency index (VE/VCO_{2slope}), cardiovascular function index ($\Delta HR/\Delta VO_2$), deviation from oxygen consumption efficiency (OUES), metabolic efficiency index ($VO_2/\Delta WR$), blood pressure (BP), heart rate (HR) recovery at first (HRR_1), and second (HRR_2) minutes were measured breath-by-breath with an online gas expiration analysis system (VO2000, MedGraphics, St. Paul, Minnesota, USA). Peak values were established by the highest values achieved during effort.

Polysomnography assessment

All hypertensive subjects were submitted to a polysomnography exam to diagnose OSA. OSA diagnosis was confirmed by the apnea/hypopnea index (AHI) and classified as follows: AHI < 5 events/h, absence of OSA; 5 ≤ AHI ≤ 15 events/h, low OSA; 15 ≤ AHI ≤ 30 events/h, moderate OSA; and AHI > 30 events/h, severe OSA [16].

The assessment was carried out during an entire night of sleep in the participant's residence without the use of sedatives. The variables were monitored by an Embletta portable respiratory monitor (Embla, Embletta® Gold, EUA), previously validated [17] and in agreement with manufacturer's instructions. The Embletta monitor is capable to continuously monitor pulse oximetry, to detect respiratory efforts, to measure the airflow, and to record snoring episodes. Additionally, HR was continually measured by the analysis of pulse waves by oximetry. Finally, brain and muscle activities were monitored by electrodes, and oxygen desaturation (O_2D) was defined as the amount of reduction in O_2S at 4%/h.

Echocardiography

All subjects performed the two-dimensional color Doppler echocardiogram (iE33®—Philips Electronics, Netherlands) before the CPET. Final systolic and diastolic diameters of the left ventricle and the diastolic thickness of the posterior wall of the left ventricle were measured from the short-axis view, and ejection fraction was obtained from these measures. This exam was conducted by an experienced cardiologist, who was blinded to group allocation.

Sleep quality

The subjective sleep quality was assessed by the Pittsburgh Sleep Quality Index, which consists of 19 questions grouped into 7 different components (subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disorders, use of medications, and diurnal dysfunction). The classifications depended upon the scores reached in each question (from 0 to 3): ranging from 0 to 4, good subjective sleep quality; 5–10, bad subjective sleep quality; and 11 or higher, indicates the presence of at least one sleep disorder.

Statistical analysis

Data normality and homogeneity were tested using the Shapiro-Wilk and Levene tests, respectively. Independent sample *t* test was used to evaluate the difference between group means. Chi-squared test was used to compare the proportions of men and women, and medication. Additionally, Pearson's correlation was performed to analyze the association between OSA markers and CPET variables. The alpha level was set as $p \leq 0.05$. SPSS software 21 (IBM, Chicago, IL) was used to run all analyses.

Results

Polysomnography assessment

As shown in Table 2, elderly hypertensive subjects with OSA presented significantly higher values of AHI ($p < 0.01$) and O_2D ($p < 0.01$) in comparison to elderly hypertensive subjects without OSA. There were significant differences in sleep architecture characterized by a significantly higher total sleep time ($t = 2.62$, $p < 0.02$) and sleep efficiency ($t = 2.01$, $p \leq 0.05$) in elderly hypertensive subjects with OSA. No differences were identified in sleep quality by subjective assessments (Pittsburgh Sleep Quality Index) ($p > 0.05$) between the two groups.

Physiological responses to the CPET

The results from the CPET are presented in Table 3. It was observed that elderly hypertensive subjects with and without OSA presented similar peak workloads (OSA group: 85 (47–114) W/min; No-OSA group: 78 (66–96) W/min, $p > 0.05$); peak cardiorespiratory variables did not differ between these groups as well ($p > 0.05$). Elderly hypertensive subjects with OSA had significantly lower HR recovery in the second minute ΔHRR_2 ($t = 2.64$, $p < 0.02$) in comparison to elderly hypertensive subjects without OSA.

Table 2 Polysomnography data in hypertensive elderly with and without obstructive sleep apnea

Variables	OSA (n = 13)	No-OSA (n = 15)
AHI, events/h	24.4 ± 12.6*	2.3 ± 1.5
O_2D, events/h	14.1 ± 11.7*	2.5 ± 1.9
O_2S, %	94.8 ± 1.1	95.4 ± 2.2
Snoring episodes, *n*	33.5 ± 36.9	16.6 ± 19.3
TST, min	257.9 ± 99.3†	176.6 ± 63.2
TST NREM-1, min	3.7 ± 4.3	2.8 ± 2.7
TST NREM-2, min	44.0 ± 56.7	44.9 ± 67.1
TST NREM-3 e 4, min	62.4 ± 49.5	49.4 ± 37.9
TST REM, min	147.9 ± 115.9	79.6 ± 57.6
Sleep latency NREM-1, min	166.4 ± 157.6	109.7 ± 131.3
Sleep latency NREM-2, min	51.1 ± 90.1	70.4 ± 122.7
Sleep latency NREM-3 e 4, min	84.4 ± 94.6	71.1 ± 119.2
Sleep latency REM, min	78.9 ± 90.8	82.6 ± 83.7
Sleep efficiency, %	54.6 ± 21.1#	40.6 ± 15.6
Awakening episodes, *n*	11.0 ± 12.5	7.9 ± 7.4
HR_{mean}, bpm	61.2 ± 8.3	60.1 ± 6.3
SQ, score	8.3 ± 3.2	9.5 ± 3.7

Data are presented as mean ± standard deviation

AHI apnea/hypopnea index, *O_2D* oxygen desaturation, *O_2S* oxygen saturation, *TST* total sleep time, *NREM* non-rapid eye movement, *REM* rapid eye movement, *O_2* oxygen, *HR_{mean}* mean heart rate, *SQ* sleep quality

*$p < 0.01$; † $p < 0.02$; # $p \leq 0.05$

Polysomnography and CPET correlations

The correlation analysis between the OSA markers and physiological responses to the CPET in elderly hypertensive subjects with OSA revealed that significant correlations between AHI and VE ($r = -0.63$, $p = 0.02$), VO_{2peak} and O_2S levels ($r = 0.60$, $p = 0.02$), as well as between the VE/VCO_{2slope} and O_2S ($r = 0.66$, $p = 0.01$). In addition, in the non-OSA group, there are no significant correlations between AHI and VE ($r = 0.42$, $p = 0.134$), VO2peak and O 2 S levels ($r = 0.09$, $p = 0.75$), as well as between VE/VCO2 slope and O2S levels ($r = 0.41$, $p = 0.13$) (Fig. 1).

Discussion

This is the first study to analyze cardiorespiratory responses to the CPET in elderly hypertensive subjects affected by OSA without presence of confounding factors such as obesity and diabetes mellitus. The main findings of the study suggest that in elderly hypertensive subjects paired by age, gender, and BMI: (1) hypertension associated with OSA does not impair cardiorespiratory fitness (CRF), but it attenuates the HRR_2; (2) hypertensive subjects with OSA present a negative linear relation to AHI with VE; and (3) hypertensive subjects with OSA show a positive linear relation between O_2S and VE/VCO_{2slope} as well as between O_2S and VO_2.

Table 3 Cardiopulmonary exercise test parameters in hypertensive elderly with and without obstructive sleep apnea

Variables	OSA (n = 13)	No-OSA (n = 15)
$VO_{2\ peak}$, ml/(kg·min)	17.2 ± 3.7	16.9 ± 3.7
VO_{2at}, ml/(kg·min)	12.0 ± 1.5	12.4 ± 2.8
PuO_2, ml/systole	8.0 ± 2.5	7.6 ± 2.3
VE peak, l/min	37.3 ± 11.5	38.7 ± 12.3
$\Delta VO_2/\Delta WR$, ml/(min W)	9.0 ± 1.7	8.5 ± 24.8
$\Delta HR/\Delta VO_2$, bpm/l	69.6 ± 27.1	79.7 ± 24.8
VE/VCO_{2slope}	36.6 ± 12.2	32.4 ± 5.3
VE/VCO_{2at}	30.7 ± 4.2	30.2 ± 2.6
OUES	1400.3 ± 430.6	1244.0 ± 254.6
R peak	1.0 ± 0.1	1.0 ± 0.1
Work rate peak, W	83.9 ± 36.5	81.2 ± 20.6
HR_{max} predicted, bpm	149.3 ± 7.4	150.7 ± 5.1
HR_{at}, bpm	113.9 ± 14.4	213.4 ± 16.9
HR_{peak}, bpm	144.9 ± 14.4	150.7 ± 9.5
ΔHRR_1, bpm	19.9 ± 5.8	24.4 ± 12.0
ΔHRR_2, bpm	35.5 ± 9.7*	46.5 ± 11.9
SBP_{peak}, mmHg	201.9 ± 15.3	197.3 ± 15.8
SBP_{rec1}, mmHg	179.6 ± 12.3	177.0 ± 13.5
SBP_{rec2}, mmHg	160.8 ± 15.4	160.7 ± 14.3
DP_{peak}	29,124.6 ± 4678.6	28,799.3 ± 4298.9
MET peak, ml/kg/min	4.8 ± 0.9	4.5 ± 1.0

Data are presented as mean ± standard deviation

VO_2 oxygen consumption, *VO_{2at}* oxygen consumption at anaerobic threshold, *PuO_2* oxygen pulse, *VE* maximal ventilation, *$\Delta VO_2/\Delta WR$* metabolic function index, *$\Delta HR/\Delta VO_2$* cardiovascular function index, *VE/VCO_{2slope}* ventilatory function index, *VE/VCO_{2at}* ventilatory function index at anaerobic threshold, *OUES* deviation from oxygen consumption efficiency, *R* respiratory quotient, *HR_{max}* maximum heart rate, *HR_{at}* heart rate at anaerobic threshold, *HRR_1* heart rate recovery at first minute, *HRR_2* heart rate recovery at second minute, *SBP_{max}* maximum systolic blood pressure, *SBP_{rec1}* recovery systolic blood pressure at first minute, *SBP_{rec2}* recovery systolic blood pressure at second minute, *DP_{max}* maximum double product, *METs* metabolic equivalent

*$p < 0.02$

In our study, we showed that maximal cardiovascular responses to CPET are not different in hypertensive subjects with or without OSA. These findings are corroborated by other studies in different populations. Alonso-Fernández et al. [18] showed that normotensive middle-age adults present similar HR_{peak} and HRR responses compared to groups with and without OSA. Moreover, in normotensive adults, Lin et al. [31] observed any abnormality in the HR peak on CPET in subjects with and without OSA. Thus, regarding our results this suggests that the coexistence of hypertension and OSA does not impair maximal cardiovascular responses to CPET.

Previous studies evaluated submaximal responses to exercise [19–21]. Hargens et al. [19] assessed obese adults with

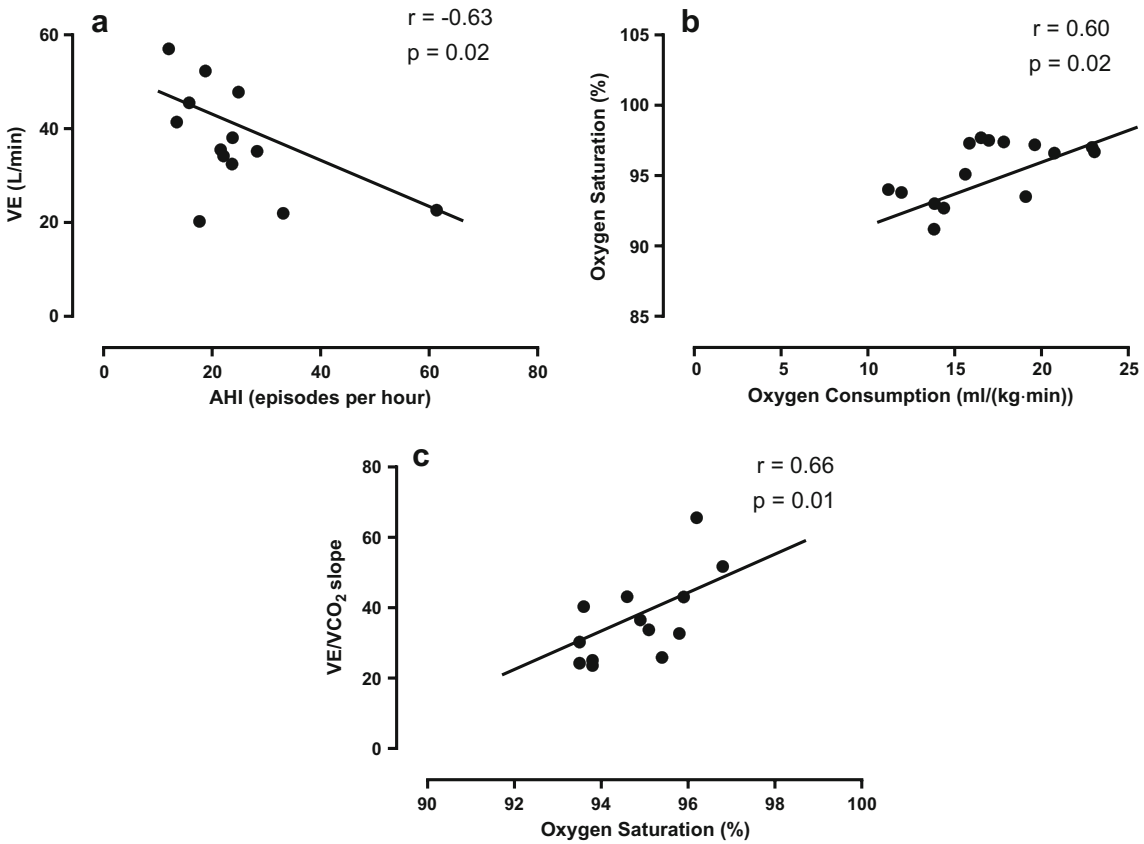

Fig. 1 Correlation analysis between **a** apnea hypopnea index (AHI) and ventilation (VE), **b** oxygen consumption and oxygen saturation, and **c** oxygen saturation and VE/VCO_2 slope in the OSA group

and without OSA and lean control subjects and reported that lean control subjects presented higher VO_2 responses to submaximal exercise compared to both OSA groups, but HR did not differ between among groups. In contrast, Kaleth et al. [20] found an attenuated HR response to submaximal intensities in OSA group compared to control. However, our study demonstrated that submaximal response to cardiopulmonary exercise test in both hypertensive elderly groups (OSA and non-OSA) was similar; these results were corroborated by Alameri et al. [21] who found that OSA patients did not exhibited altered cardiovascular responses to 6-min walk test.

Attenuated HR recovery has been identified as an independent predictor of cardiovascular and all-cause mortality in individuals undergoing diagnostic symptom-limited exercise testing utilizing relatively short recovery periods of 1 to 2 min [22]. Our study showed that hypertensive subjects with OSA had impairment in HRR_2 compared to those without OSA. Similar results were observed by Maeder et al. [23], who showed impairment in HR recovery in hypertensive and obese individuals with OSA for the group with more severe OSA. The mechanisms for attenuated HR recovery in OSA is not clear; however, some studies have shown that patients with OSA presented an exaggerated sympathetic activation at rest [24, 25], and this attenuation in HR recovery response may reflect predominance and/or slower withdrawal of sympathetic influence after exercise [23, 26, 27].

Regarding ventilatory responses to CPET, this study did not find any aggravation due the coexistence of hypertension and OSA in elderly individuals, as indicated by similar values for VE, RER, VE/VCO_{2slope}, and OUES in both study groups. However, we observed a negative correlation between AHI and VE ($r = -0.63$, $p = 0.02$), a finding already described by Lin et al. [31] who verified that individuals with OSA present greater respiratory reserve and lower VE_{max}. In addition, we observed a positive correlation between O_2S and VE/VCO_{2slope} ($r = 0.66$; $p = 0.01$) in the OSA group, which can be explained due to adaptations in the O_2 transport system triggered by respiratory mechanical feedback, thus activating vagal receptors and the chest wall and improving O_2S [28], even at rest and in sleep.

When oxygen consumption and saturation were correlated, significant outcomes were only found in the Non-OSA group ($r = 0.60$, $p = 0.02$), suggesting that OSA compromises the oxygen supply in hypertensive elderly. Some studies have proposed to study ventilatory responses to CPET in individuals with OSA; however, those studies have included adults affected by confounding factors such as obesity which may have limited the observed results [29–31]. Thus, such

delimitations acting as selection bias prevent a deeper discussion about OSA impairments in ventilatory responses to CPET.

This study has evaluated ventilatory responses to CPET in elderly hypertensive patients, and we were not able to verify significant differences between individuals with and without OSA. This is probably due to aging, which is known to promote structural and/or physiological remodeling independent of the adjustments made by OSA. This statement may be partially explained by other studies that have verified ventilatory adjustments to CPET influenced by OSA [30, 31].

As main limitations, the present study had sample size and an unequal amount of men and women, with the latter being minimized by pairing the subjects in groups, thus undermining the influence of gender on the cardiorespiratory variables for the CPET [32–36]. Moreover, the cross-sectional design does not allow us to state causality.

Conclusion

The coexistence between hypertension and OSA does not affect cardiorespiratory responses in elderly subjects. Hypertensive subjects with OSA present attenuated HR recovery, possibly due to autonomic dysregulation. The correlations between AHI-VE and O_2S-VE/VCO_{2slope} can be explained by adaptations in the O_2 transport system triggered via mechanical respiratory feedback. Thus, it has been identified that OSA compromises the oxygen supply in hypertensive elderly.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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