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Analysis of heart rate variability in submaximal exercise in people with obstructive sleep apnea

Análise da variabilidade da frequência cardíaca no exercício submáximo em pessoas com apneia obstrutiva do sono

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Abstract – Obstructive Sleep Apnea Syndrome (OSAS) is a respiratory disorder characterized by dysfunctions in the autonomic nervous system (ANS). However, the impacts on the exercise performance in heart rate variability (HRV) in these patients remains unclear. It is an observational transversal study, which included patients diagnosed with OSAS, aged over 18 of both sexes. HRV was collected with a Smart Lab HRV heart rate monitor (HMM Group, Heidelberg, Germany) during submaximal exercise testing with 6 minutes step test (6MST), which included 3 stages: pre-exercise, during exercise and post-exercise. Data were analyzed posteriorly in Kubios HRV Scientific Lite software (KUBIOS OY, Finland), in which time and frequency domain data of HRV analyses were obtained for each person. 30 volunteers were recruited, with a mean age of 53.27±13.47 years and 56.6% male. There was statistical difference between pre, during and post exercise values of all frequency domain data (LF Power and HF Power; p= <0,05), except for Ratio LF/HF (p = 0.096) and between pre and exercise and exercise and post exercise for all time domain data (SDNN, RMSSD and TINN). In time domain, there wasn't difference between pre and post exercise values in any variable. In people with OSAS, frequency and time domain values reduced during the exercise phase, which means greater sympathetic activity. There wasn't difference between pre and post exercise phase in time domain variables, which means fast recovery in patients with OSAS.

Key words: Heart rate variability; Heart rate; Obstructive sleep apnea syndrome; Autonomic modulation; Exercise test.

Resumo – *A Síndrome da Apneia Obstrutiva do Sono (SAOS) é um distúrbio respiratório caracterizado por disfunções no sistema nervoso autônomo (SNA). No entanto, os impactos no desempenho do exercício sobre a variabilidade da frequência cardíaca (VFC) nesses pacientes ainda permanecem pouco claros. Trata-se de um estudo observacional transversal, que incluiu pacientes diagnosticados com SAOS, com idade superior a 18 anos, de ambos os sexos. A VFC foi mensurada com um monitor de frequência cardíaca Smart Lab HRV (HMM Group, Heidelberg, Alemanha) durante teste de exercício submáximo com o teste de degrau de 6 minutos (6MST), que incluiu três fases: pré-exercício, durante o exercício e pós-exercício. Os dados foram analisados posteriormente no software Kubios HRV Scientific Lite (KUBIOS OY, Finlândia), no qual foram obtidos dados de domínios do tempo e da frequência da VFC para cada participante. Foram recrutados 30 voluntários, com idade média de 53,27±13,47 anos, sendo 56,6% do sexo masculino. Houve diferença estatisticamente significativa entre os valores pré, durante e pós-exercício para todas as variáveis de domínio da frequência (potência de LF e potência de HF; p < 0,05), exceto para a razão LF/HF (p = 0,096), bem como entre os momentos pré e durante o exercício, e durante e pós-exercício para todas as variáveis de domínio do tempo (SDNN, RMSSD e TINN). No domínio do tempo, não houve diferença entre os valores pré e pós-exercício em nenhuma variável. Em pessoas com SAOS, os valores de domínios da frequência e do tempo reduziram durante a fase de exercício, o que indica maior atividade simpática. Não houve diferença entre as fases pré e pós-exercício nas variáveis de domínio do tempo, o que sugere recuperação rápida em pacientes com SAOS.*

Palavras-chave: *Variabilidade da frequência cardíaca; Frequência cardíaca; Síndrome da apneia obstrutiva do sono; Modulação autonôma; Teste de função física.*

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INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is the most common sleep-related breathing disorder world widely, which affects around 1 billion people[1]. The syndrome is classified according to the occurrence of apneas and hypopneas in asleep condition in three stages: mild, moderate or severe OSAS[2]. If the severity increases, the individuals with OSAS can present frequent episodes of partial or complete collapse of the upper airways during sleep, causing brief and occasional decreases in intrathoracic airflow at nighttime. However, in the face of the respiratory implications of the syndrome in asleep and awake conditions, the impacts of OSAS on autonomic nervous system aren't fully understood yet[3-5].

Heart rate variability (HRV) is a validated method of measuring the quality of the brain-heart interactions[6], encompassing the assessment of sympathetic and parasympathetic modulation of heart rate, in physical activity of different types and/or intensity or in resting conditions[7,8].

In the other hand, the use of submaximal exercise tests has been described as of great importance in the evaluation of cardiopulmonary function, considering they are low-cost, easy to apply and have greater patient acceptance of the test[9-11]. The 6-minute step test (6MST) is a validated tool for OSAS population in this type of assessment, which can produce intense muscle stress and cardiovascular stress, if compared to other submaximal tests and, simultaneously, can provide necessary information to the assessment of the autonomic modulation through HRV[12]. In this view, the objective of this study is to analyze HRV in submaximal exercise in people with obstructive sleep apnea.

METHOD

Study design

This is a quantitative study, which followed the recommendations of the Strengthening of the Reporting of Observational Studies in Epidemiology (STROBE) Statement[13]. It was conducted at the Laboratory for Assessment and Rehabilitation of Cardiac, Oncological and Respiratory Dysfunctions (LACOR) of the University Hospital Complex (UHC) of the Federal University of Pará.

The patients included in this research undergo regular monitoring at the sleep outpatient clinic of the UHC complex. The recruitment of patients happened by phone calls after the contact details were checked by the researchers. The submission of the data to this research team complies with the principles of the General Data Protection Law, 13.709/2013, to conceal the user's health information and protect the dignity of the human person.

Patients who met the inclusion criteria in the approach received information about the procedures to be performed as part of this stud and, subsequently, all the individuals received an invitation to participate in the research by signing the Free and Informed Consent (FIC) Form.

Ethical aspects

This research has approval from the Research Ethics Committee, whose approval number is 6.187.498/2023 and complies with the standards of the

following resolutions: no. 466/2012, no. 510/2016, no. 738/2024, of the Brazilian National Health Council. All the participants signed FIC form.

Inclusion and exclusion criteria

The inclusion criteria were individuals diagnosed with OSAS with type I polysomnography, with defined stratification of the severity level of the disease, over 18 years of age.

The exclusion criteria were: patients with neurological, behavioral or motor dysfunction that prevented them from performing 6MST; patients with decompensated hemodynamic changes, atrial fibrillation, ventricular fibrillation, first-stage atrioventricular block, Wolff-Parkinson-White Syndrome, congestive heart failure grade III or IV and patients with symptoms of angina or ischemia at a stage below the anaerobic threshold.

Assessment procedure

This research obeyed the checklist proposed by Catai et al.[14,15], which established guidelines for management and collection of HRV data. The HRV collection happened in a quiet and calm room, with temperature controlled at 21 °C, humidity at 60%, at the morning period (between 7:00 am and 10:00 am). The patients were advised to avoid physical activity 24 hours prior to the exams, and they all rested for 30 minutes before the start of the collection. For HRV collection, the individual should be in supine position, and it wasn't recommended to vocalize, move actively or fall asleep, unless intercurrences happened. Clinical events, such as dizziness, blurred vision, arrhythmias, sneezing and coughing were recorded in minutes and seconds by the research evaluators. If they occurred, the collection should be interrupted and then rescheduled.

Data recording was performed using a Smart Lab HRV heart rate monitor (HMM Group, Heidelberg, Germany), which was attached directly to the patient's rib cage. The plastic strap with the frequency monitor was humidified and positioned at the patient's xiphoid process, so the frequency monitor would be immediately in front of the sternum[16]. Once positioned, the researcher had to carry a smartphone with the Elite HRV app and, by turning on the Bluetooth tool on his/her device, start connecting the device to the frequency monitor. Once the process starts, the research subject remains for 5 minutes testing the quality of the connection between the frequency monitor and the smartphone, in order to detect oscillations or variations in signal quality. In this context, as soon as the signal test was completed, the Elite HRV application on the Android or iOS device was opened, in which the sensor was located by the parity system between devices and paired after confirmation of the paired function[17].

Submaximal exercise test

The collection during exercise consisted of connecting the heart rate monitor to the Elite HRV application, keeping it in signal quality testing for 5 minutes and, as soon as possible, starting the collection, when, the

participant had to perform the 6MST using a 20 cm step. This 6MST protocol was divided into 3 phases, "pre-exercise phase" (the individual had to remain at rest for 2 minutes in the orthostatic position), "exercise phase" (the execution of 6MST) and the "post-exercise phase" (2 minutes of rest after 6MST) in the orthostatic position, a period also called recovery. In the recovery phase, most studies used a period of 1 to 2 minutes after the exercise, which was used in this research [18]. Also, the time used in this collection was compatible with ultra-short-term (UST) measures of heart rate variability for the "rest" and "post-exercise" phases, which is a technique which period of collection is inferior to 5 minutes, with correction of artefacts and with short-term (ST) heart rate variability, which takes >5 minutes to be done, at "exercise" phase.

The protocol for HRV of this research was derived from Kim et al.[16], which implemented HRV measurements at rest, during exercise, and in the post-exercise recovery period in 30 subjects and then analyzed USF HRV. They used 10s, 30s, 60s, 120, 180s and 240s measures and compared to ST HRV measures. In their results, it was concluded that at least 120 seconds were required to assess viable and reproducible data in post-exercise recovery and exercise conditions to some variables of HRV, considering that USF wasn't suitable for some of them[16].

Once the process was finished, the patient would be disconnected from the elastic strap and the heart rate monitor.

Data analysis

Once the heart rate monitor collection was complete and the data were stored in the Elite HRV application, the data were exported and manually filtered in Microsoft Excel 2013, so the artifacts produced during collection were discarded. From there, the filtered data were analyzed in the Kubios HRV Scientific Lite software (KUBIOS OY, Finland). Time and frequency domain data of HRV analyses were obtained for each person, referring to the collections of each patient at rest, exercise and after exercise.

In the time domain, the following were collected: mean heart rate (bpm), SDNN (ms), Mean Heart Rate, Heart Rate (bpm), RMSSD (ms) and TINN. To indicate the presence of normality or dysfunction in the interpretation of the data (specifically mean RR Intervals, Mean Heart Rate and RMSSD), the software uses the indices obtained from the systematic review by Nunan et al.[19]. In the frequency domains, the following data were collected: LF Peak and LF Power, HF Peak and HF Power and LF/HF ratio, in the Fast Fourier Transform (FFT) spectra, which is considered as a nonparametric method, which aims to point out spectral peaks in different frequency domains and the autoregressive model (AR)[17].

Statistical analysis

The data were stored in Microsoft Excel software and then analyzed in Jamovi software (Jamovi, United States of America). It was adopted Shapiro-Wilk test to analyze normality of the data and descriptive statistics with absolute or relative frequency. Mean and standard deviation was utilized to represent parametric data and median and interquartile range (25.75) to

represent non parametric data. For parametric data, it was utilized two-way repeated measures ANOVA and, for non-parametric data, it was utilized Friedmann test. The sample calculation for the study was performed through the website[20], in which it was necessary to select the option Difference between two Means with Independent Groups, informing the estimated standard deviation, minimum difference to be detected, alpha error and beta error. Considering an alpha error of 5% and a beta error of 20%, a total sample of 30 individuals were obtained.

RESULTS

Seventy-eight patients, who underwent regular treatment in the sleep outpatients, were qualified to participate in this research to be assessed by this research team, as it's possible to see in the flowchart of the sample in Figure 1.

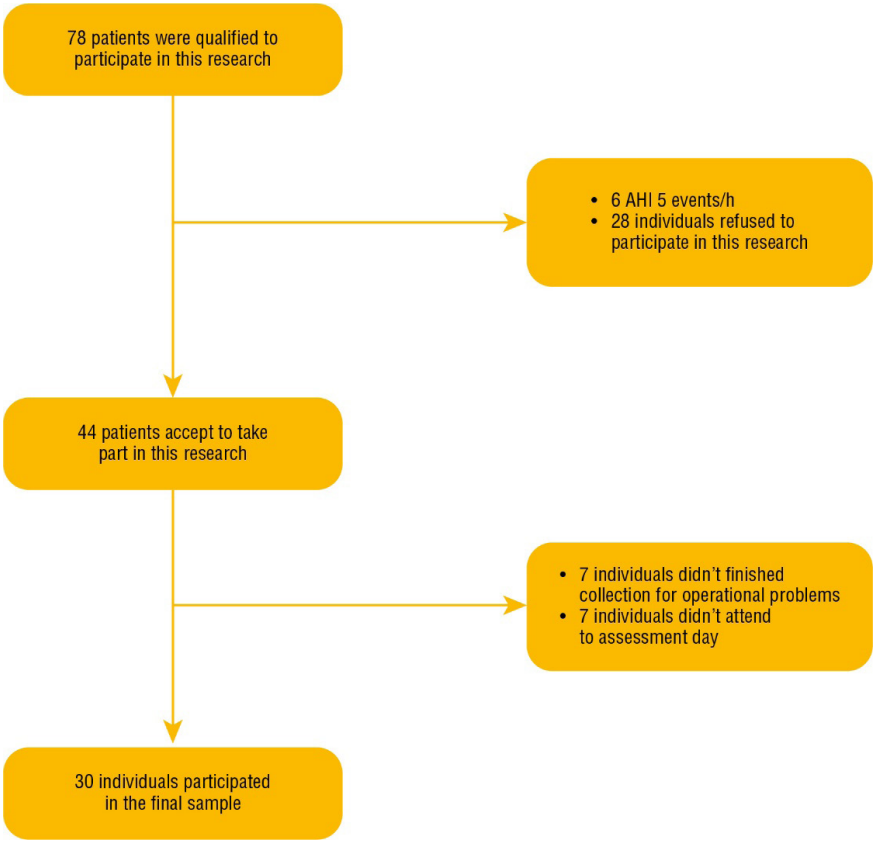

Figure 1. Flowchart of the sample.

The final sample consisted of 30 individuals with OSAS. Table 1 identifies data such as anthropometric and clinical characteristics of the participants, such average age of 53.27 ± 13.47 years, and 60% of this group had severe OSAS. Tables 2 and 3 show the polysomnography data of the patients included in the study and the HRV data pre, during and post exercise phases.

Table 1. Clinical and polysomnographic data of the individuals of the research.

Variables	OSAS (n=30)	p-value
Age (years)	53.27 ± 13.47	
Gender, n (%)		
Male	17 (56.3%)	(0.634)*
Female	13 (43.7%)	
Height (cm)	162 ± 0.09	
Weight (kg)	84.43 ± 14.96	
Body Mass Index (Kg/m2)	31.14 ± 5.40	
Neck circumference (cm)	40.4 ± 3.24	
Waist circumference (cm)	97.2 ± 11.4	
Number of degrees at 6MST	105 ± 25.63	

Note. OSAS = Obstructive sleep apnea syndrome. 6MST = six-minute step test. *Binomial test.

Table 2. Main variables of polysomnography, classification of OSAS severity.

Variables	OSAS (n=30)	p-value
Stage I (%)	39.7 (±18.5)	
Stage II (%)	171 (134 ; 183)	
Stage III (%)	34.8 (22.3 ; 55.1)	
REM sleep (min)	33.3 (13.0 ; 45.0)	
Awake time (min)	80.5 (60.5 ; 111)	
Sleep efficiency (%)		
Apnea-Hypopnea Index (n/h)	34.1 (10.5 ; 62.4)	
Mean SpO2 (%)	95 (93.3 ; 95.0)	
Lowest SpO2 (%)	81 (71.8 ; 86.0)	
Respiratory Distress Index	34.1 (10.5 ; 62.4)	
OSAS severity (n/%)		
Mild	5 (16.6)	
Moderate	7 (23.7)	(0.856)*
Severe	18 (60.0)	

Note. OSAS = Obstructive sleep apnea syndrome. REM sleep = Rapid Eye Movement. SpO_2 = Partial oxygen saturation. *Binomial test

Table 3. Comparison of HRV variables in the pre-exercise, exercise and post-exercise stage.

Variables		X^2 (OSAS=30)	p-value*
SDNN (ms)			
Rest	Exercise	7.77	(<0.001)**
Rest	Post exercise	1.02	(0.311)
Exercise	Post exercise	8.79	(<0.001)**
RMSSD (ms)			
Rest	Exercise	4.10	(<0.001)**
Rest	Post exercise	1.26	(0.213)
Exercise	Post exercise	5.36	(<0.001)**
TINN (ms)			
Rest	Exercise	8.43	(<0.001)**
Rest	Post exercise	1.57	(0.122)
Exercise	Post exercise	6.86	(<0.001)**
LF Power (ms)			
Rest	Exercise	16.31	(<0.001)**
Rest	Post exercise	6.34	(<0.001)**
Exercise	Post exercise	9.97	(<0.001)**
HF Power (ms)			
Rest	Exercise	7.56	(<0.001)**
Rest	Post exercise	2.70	(0.009)**
Exercise	Post exercise	4.86	(<0.001)**
Ratio LF/HF (ms)			
Rest	Exercise	1.041	(0.302)
Rest	Post exercise	1.691	(0.096)
Exercise	Post exercise	0.650	(0.518)

Note. SDNN = standard deviation of NN intervals. RMSSD = root mean square of differences of RR intervals. TINN = Triangular Interpolation of Histogram of NN Intervals. LF = Low Frequency. HF = High Frequency. *Friedmann test. **p-value (<0.05).

DISCUSSION

In this research, the results indicated significant differences in LF and HF power in pre, during e post exercise phases, which are all frequency domain data; also, significant differences in SDNN, RMSSD and TINN values in the comparison of pre and during exercise phases and exercise and post exercise phases. It wasn't possible to assess significant differences between pre and post exercise values of SDNN, RMSSD and TINN, neither difference in Ratio LF/HF in all the stages of exercise test, which means good recovery after submaximal stress.

Exercise decreases HRV variables in time and frequency domains: a reduction of 3-10ms is expected for exercises in which heart rate rises to 160 bpm in SDRR and RMSSD variables. The variations expressed in the RMSSD variables occur more quickly than in SDRR variable and respond according to the intensity and dose of the exercise, and it's also understood that exercise generates changes in LF and HF variables and in LF/HF ratio[21]. HRV decreases even faster in athletes, if compared to regular individuals, which makes HRV an excellent tool for cardiac measurements created by accessible and portable devices[22]. Therefore, in this collection, we could observe this phenomenon in patients of the sample, which indicates expected behavior of HRV for frequency domain.

Dewar et al.[23] mention that exercise causes increase in the sympathetic and a reduction in parasympathetic system. Consequently, at the end of exercise, there's a decrease in heart rate, indicating autonomic recovery with vagal predominance. Therefore, a slower recovery in heart rate indicates autonomic dysfunction, which predicts risk of mortality. Therefore, the data in the table demonstrates that there wasn't significant difference in the SDNN, RMSSD and TINN values if rest and post exercise are compared, which indicates that there's a faster recovery in HRV in these patients. Parasympathetic response influences RMSSD, while SDNN and TINN reflect total power[6]. However, the study by Arêas et al.[24] indicates that HRV can be restored to resting levels in minutes when the duration or intensity of the exercise is shorter, so that longer and more intense exercise represents a longer recovery time.

One point which needs to be highlighted is the use of UST HRV measures. Burma et al.[25] found that, as much as the time increased, the reproducibility and validity of the results did augment as well, directly implying at minimum time for a correct collection; the authors, for example, stated at least 60 seconds of collection for heart rate collection. Parallelly, Shaffer et al.[26] also expressed the further necessity of establishing a minimal time's limit for each variable, according to age and sex and the identification of ST HRV metrics most strongly associated with health and performance outcomes. For this reason, the authors proponed the edition of artifacts of HRV data in USF, which was done in this research, otherwise the data would be considered invalid, only because a false heartbeat can dramatically alter HRV metrics[24]. This was the main reason of the usage of a 120s cut-off in this research, based on Kim et al.[16].

In Orini's research, USF collection of 15s correlated efficiently with standard ST HRV data (RMSSD, SDSD and PHF indices) and could predict increased risk of cardiovascular events (atrial fibrillation, major adverse cardiac events, stroke and mortality) in the large population-representative cohort included on the research[27]. Simultaneously, a 2-minute measure was efficient to predict coronary heart disease and to analyse the incidence of atrial fibrillation. Similar results can be observed in

Arêas et al.[24], which indicated that UST HRV data appears to be a reliable form of standard ST HRV data during resistance exercise in healthy elderly subjects. The demand for correction of artifacts is equally postulated by Canino et al.[18]. In his work, they suggest that individuals' differences in UST HRV depend on physiological state and could predict aerobic fitness in a weak or moderate way, as long as the artifacts be corrected in their data, otherwise it would misrepresent reality.

Regarding the severity of OSAS, according to the apnea-hypopnea index, there was no predominance pattern, although the most severe form of comorbidity was the most frequent in 60% of cases, followed by level II (23.7%), moderate manifestation, and then level I (16.6%), being the mildest form of manifestation. Due to the high number of occurrences of apnea-hypopneas per hour during sleep, there is an increase in sympathetic tone, causing variations in ANS function[28]. Linked to this, there was also no predominance according to stratification by BMI or by cervical and abdominal circumference indices. However, they are risk factors for the severity of OSAS, as observed in the study by Gresova et al.[6] in which the incidence of OSAS is higher in obese patients, since obesity is associated with an increase in cervical circumference and peripheral fat, which can cause compression of upper airways.

The limitation of this study is that was used the SF and USF terms to obtain the HRV data in pre, during and post exercise phases of 6MST, which didn't allow the use of some variables, as VLF.

CONCLUSION

Therefore, in this study, based in USF and ST measures, we can conclude that, in people with OSAS, physical exercise reduced frequency and time domain values during the exercise phase, which means greater sympathetic activity. Concomitantly, it also means fast recovery in post exercise phase, with the values being not different from resting phase, in pre and post exercise comparison in time domain variables.

Compliance with ethical standards

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request. Pre print DOI: 10.22541/au.175420093.31818602/v1

Ethical approval

Ethical approval was obtained from the local Human Research Ethics Committee – Health Sciences Institute of Federal University of Pará, and the

protocol (no. 6.187.498/2023) was written in accordance with the standards set by the Declaration of Helsinki.

Conflict of interest statement

The authors have no conflict of interests to declare.

Author Contributions

Conceived and designed experiments: LBRS, LMTN; Performed experiments: SSF, RHRM, LBRS; Analyzed data: LBRS, LMTN; Contributed with reagents/materials/analysis tools: LMTN; Wrote the paper: SSF, RHRM, LBRS, LMTN.

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