

## SLEEP QUALITY, SEDENTARY BEHAVIOR AND CARDIOVASCULAR RISK IN YOUNG ADULTS



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## LIST OF ABBREVIATIONS

AHI - Apnea/hypopnea index
BMI - Body mass index
CV - Cardiovascular
DBP - Diastolic blood pressure
HDL -High-density Lipoprotein
IPAQ - International Physical Activity Questionnaire

LDL - Low-density Lipoprotein MVPA - Moderate to vigorous physical activity OSAS - Obstructive sleep apnea syndrome PSQI - Pittsburgh Sleep Quality Index SAH - Systemic arterial hypertension SBP - Systolic blood pressure SDB - Sleep-disordered Breathing VLDL - Very Low-density Lipoprotein

## ABSTRACT

Sleep is an essential process for maintaining the body's essential biological functions, and disorders associated with it can cause various health problems, including cardiovascular disorders. The practice of physical activity comprises one of the most beneficial habits for a correct sleep regulation, improving its duration and depth. However, the cycle that involves the practice of physical activities, quality of sleep and cardiovascular diseases needs further elucidation, therefore, the objective of this work was to compare and correlate the quality of sleep with the risk of developing Obstructive Sleep Apnea Syndrome (OSAS), and the practice of physical activities, as well as cardiovascular diseases. For this, we carried out a cross-sectional, observational, prospective, epidemiological study, in which volunteers of both sexes, aged between 20 and 50 years, were evaluated regarding anthropometry, questioned using questionnaires on cardiovascular risk, sleep quality (Pittsburgh), presence of OSAS (Berlin) and physical activity practice (IPAQ) and had their lipid profiles evaluated. Comparisons and correlations between variables were established by different statistical analyzes (using p values ≤0.05). Volunteers with poor sleep quality had a higher BMI value, sum of four folds and body fat, less time of vigorous physical activity and lower HDL value, as well as a positive correlation with systolic blood pressure, waist-to-height ratio and risk of developing of SAOS. Volunteers at high risk of developing OSAS had higher values for SBP, DBP, BMI, waist/height ratio, sum of four folds and less time of vigorous physical activity, in addition to a positive correlation with poor sleep quality, total cholesterol and LDL. Thus, we conclude that volunteers classified as having poor sleep guality and high risk for OSAS practice physical activities less frequently and with reduced load, in addition to presenting higher values in the variables of the cardiac, anthropometric and lipid profiles, indicating a greater cardiovascular risk.

Descriptors: Sleep quality; Physical activity; Cardiovascular diseases.

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## INTRODUCTION

Sleep is defined as a natural, reversible and cyclical biological process, with behavioral and physiological manifestations, in which the individual apparently remains asleep, although the brain remains active, extremely important for maintaining essential biological functions of the body, as well as for repairing the human psychosocial balance<sup>(1)</sup>. Because of this, sleep disorders can cause several health damages, ranging from memory deficit to cardiovascular (CV) dysfunctions<sup>(2,3)</sup>.

CV diseases are a class of pathological changes that affect the heart and blood vessels, and currently, comprise the main cause of death in men and women in Brazil. Several factors may increase the risk of developing these diseases, such as sedentary lifestyle, dyslipidemia, smoking, diabetes and sleep quality. The quality of poor sleep, with dysfunctions such as sleep deprivation, somnambulism, insomnia, sleep-disordered breathing (SDB) and the like, generates significant variations in the mechanisms of regulation of cardiovascular function, such as increased activity of the sympathetic nervous system at rest, increased pressure values, venous endothelial dysfunction and others, increasing the CV risk<sup>(1)</sup>.

Among the main SDB that generate direct impacts on cardiovascular health, the Obstructive Sleep Apnea Syndrome (OSAS) stands out, characterized by recurrent obstructions of the upper airways during sleep, interrupting the respiratory flow<sup>(4)</sup>. This relationship is due to hypoxemia and hypercapnia generated by respiratory alteration and increased respiratory effort, which leads to increased blood pressure, heart rate and vascular resistance, and may become chronic and worsen over time<sup>(5,6)</sup>. Oxidative stress and free radicals formed by the repetitive cycle of hypoxemia and reoxygenation resulting from OSAS also function as a factor of elevation of the CV risk<sup>(7)</sup>.

Between the simplest habits for better regulation of sleep, and consequent biological maintenance, is the practice of physical activities. Physical activity, when performed according to the individual capacity of each individual, and far from the usual period of sleep, generate improvements in the duration and depth of sleep<sup>(8,9)</sup>. Some hypotheses that seek to explain this process are based on the metabolic compensation generated during sleep, replacing the energies spent during the activity, and on the increase in body temperature as a sleep trigger<sup>(10)</sup>.

However, this cycle that involves the practice of physical activities, sleep quality and CV diseases still lacks further elucidations, where we aimed to evaluate and relate the practice of physical activities with the quality of sleep and their influence on the predisposition of each patient to develop CV diseases.

## **METHODS**

This is a cross-sectional, observational, prospective, epidemiological study carried out at the Paulista University (UNIP) clinical laboratory. This study was analyzed and approved by the Research Ethics Committee, under number 2,893,644.

A total of 103 volunteers, healthy young adults of both genders, aged between 20 and 50 years, were evaluated, who sought the nutrition service of the Rangel-Santos Campus School of the Paulista University, located at Avenida Ana Costa, 65 - Vila Matias, Santos, during the period from October 2018 to March 2019.

After the consent of the individuals, blood tests were requested and the information pertinent to the lipid profile was duly archived in a spreadsheet. Subsequently, blood pressure was measured and the survey was carried out about the factors of CV risks, physical activity (IPAQ) - short version, sleep quality (PSQI) and presence or risk of developing OSAS (Berlin Questionnaire).

### **Exclusion criteria**

Volunteers with acute diseases, such as infections and inflammatory processes, chronic degenerative diseases, people during the recent postoperative period of fewer than 3 months, besides to anginous volunteers and/or patients with recent acute myocardial infarction were excluded.

The participants were stratified into 2 groups:

**1.** Evaluation of the quality of sleep through the results obtained from the PSQI": when the final score was < 5, classified as good sleep quality; When the final score was > 5, classified as poor sleep quality<sup>(11)</sup>;

**2.** Assessment of the development risk of OSAS through the results obtained from the "Berlin questionnaire": when none or one (1) positive category, classified as low risk for OSAS; when two (2) or more positive categories, classified as high risk for OSAS<sup>(12)</sup>;

# Research on CV risk, the practice of physical activity, sleep quality and OSAS

Questionnaires attached:

A. Questionnaire on CV risk factors;

B. International Physical Activity Questionnaire (IPAQ) - short version;

C. Pittsburgh Questionnaire (PSQI) - research on sleep quality;

D. Berlin Questionnaire - research on OSAS risk;

E. Matrix correlation table.

#### **Body composition**

The information pertinent to body composition was extracted from the medical records of the volunteers participating in the nutrition department, with prior authorization. Bodyweight and height were measured and BMI calculated (weight kg/height m2)<sup>(13)</sup>. The abdominal, arm, waist and hip circumferences were collected using a measuring tape with an accuracy of 1 mm. The waist/hip (waist cm/hip cm) and waist/height (waist cm/height cm) ratios were calculated(14). The percentage of fat and lean mass was evaluated by the sum of four skinfolds obtained using an adipometer: triceps (mm), biceps (mm), subscapular (mm), suprailiac (mm)(15).

#### Collection and testing of blood

The blood was collected by the biomedicine laboratory using a vacuum system in the morning. For lipidogram analysis, the blood was collected in a tube without the presence of anticoagulant (dry), centrifuged and stored at 4°C until the moment of analysis. The biochemical tests are: total cholesterol and fractions (HDL, LDL and VLDL), triglycerides and fasting glucose.

#### Protocol

On the first day, the research participants were clinically evaluated and had their anthropometric data recorded. They were then invited to participate in the study, signed the ICF and had the blood test requested. In the end, their blood pressure was checked and they were questioned through the relevant questionnaires (CV risk, IPAQ, PSQI and Berlin). On the second day, the patients returned for blood collection and subsequent analysis. The CV risk was established utilizing blood pressure measurement, CV risk questionnaire and lipid profile.

#### Statistical analysis

The data were collected from a form prepared in Microsoft® Office Infopath2007 version 12.0 (©Microsoft Corporation, Albuquerque, NM, USA). A descriptive analysis of the data was performed, including frequencies, measures of central tendency and variability through the Microsoft® Office Excel2007 program (version 12.0). Statistical analyses were performed using the GraphpadPrism® version 7 program (GraphPad Software Inc., San Diego, CA, USA). We used the Student's T-Test for parametric results, in the comparative analysis between the groups classified with good and bad sleep quality, and also for those classified with high and low risk of OSAS development, considering the p-value of  $\leq 0.05$ . For analysis of the correlation between variables, we used the Pearson Linear Correlation for parametric results and the Chi-square test, also for parametric results, all considering a p-value of  $\leq 0.05$  and a confidence interval of 95%.

#### RESULTS

The mean age of 103 participants was 34 years ( $\pm$  8.60), with a predominance of females (71.84%). The mean values obtained for systemic arterial pressure remained below 120x80mmHg and the lipid profile is following the reference values of the Brazilian population. Among the anthropometric variables, BMI and body fat percentage were high, indicating an average of volunteers classified as class I obesity, while the other indices were within the normal parameters (Table 1).

According to the result obtained by the PSQI, most volunteers had their sleep quality classified as poor, while the mean obtained through the Berlin Questionnaire indicated that most of the evaluated individuals do not have, or have low risk of developing OSAS. We did not observe significant correlations between the sleep questionnaires and the age of the volunteers (data not demonstrated). Regarding physical activities, it was found that the participants practice activities, on average, only one day a week, for approximately 24 minutes a day (Table 1).

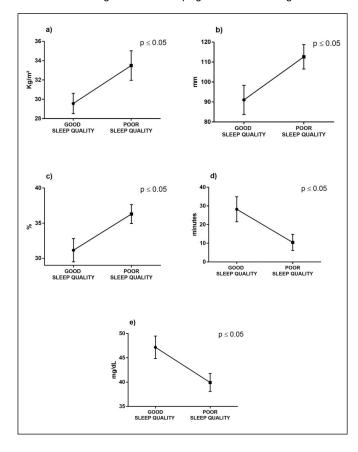
Table 1. Description of the cardiac profile, anthropometric measurements and indices, sleep variables, physical activity and lipidogram.

Participants	N (%) or mean (± DP)	Reference values –	
Sex	-		
Men	29.00 (28,15%)	_	
Women	74.00 (71,84%)	_	
Age	34.20 (± 8,60)	_	
Cardiac Profile			
SBP (mmHg)	119.80 (± 11,90)	< 120.00	
DBP (mmHg)	76.20 (± 12,00)	< 80.00	
Anthropometric measurements and indices			
BMI (kg/m²)	30.90 (± 7,00)	18.50 a 24.90	
Waist/rip ratio (cm)	0.80 (± 0,08)	_	
Men	0.87 (± 0,08)	0.84 a 0.91	
Women	0.78 (± 0,08)	0.72 a 0.78	
Waist/height ratio (cm)	0.50 (±0,09)	≤ 0.40	
Sum of four skinfolds	95.30 (± 33,50)	-	
Body fat percentage (%)	33.40 (± 7,20)	_	

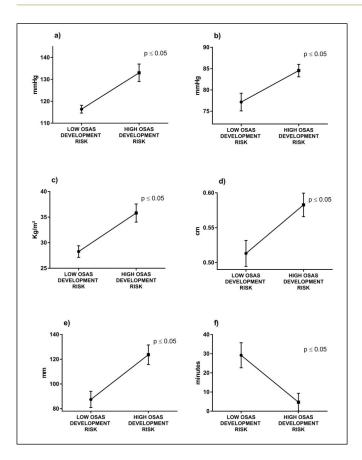
Men	29.20 (±7,50)	10.10 à 20.00%	
Women	34.90 (± 0,70)	15.10 à 25.00%	
Sleep Questionnaires			
PSQI	6.00 (± 3,40)	≤ 4.00	
Berlin Questionnaire	2.00 (± 1,90)	≤ 2.00	
Physical activity level			
Days of vigorous activity per week	1.20 (± 2,00)	≥ 3.00	
Vigorous activity time per day (min)	23.80 (± 45,00)	≥ 20.00	
Lipid Profile			
Total Cholesterol (mg/dL)	150.00 (± 42,50)	< 190.00	
HDL (mg/dL)	44.00 (± 9,20)	> 40.00	
LDL (mg/dL)	85.00 (± 36,10)	< 130.00	
VLDL (mg/dL)	96.20 (± 78,20)	-	
Triglycerides (mg/dL)	121.00 (±13,10)	< 150.00	

Descriptive table with general mean and standard deviation of the variables.

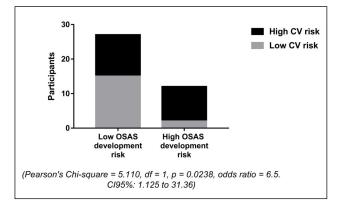
In the comparative analyses, the volunteers with poor sleep quality had higher BMI values, the sum of four skinfolds and body fat percentage, besides lower HDL values concerning those classified as good sleep quality (Graph 1a to 1e). On the other hand, those classified with a high risk of developing OSAS showed higher BMI values, the sum of four skinfolds and waist/height ratio, as well as systolic blood pressure and diastolic blood pressure values higher than those classified with low risk. Regarding physical activity, both groups had lower vigorous physical activity time per day than the volunteers with good sleep quality and low risk for OSAS (Graphs 1 and 2).



**Graph 1: a)** Comparison of BMI among volunteers with good and bad sleep quality. **b)** Comparison of the sum of four skinfolds between volunteers with good and bad sleep quality. **c)** Comparison of the percentage of body fat among volunteers with good and bad sleep quality. **d)** Comparison of vigorous activity time per day among volunteers with good and bad sleep quality. **e)** Comparison of HDL among volunteers with good and bad sleep quality. **e)** Comparison of HDL among volunteers with good and bad sleep quality. Statistical analysis: Student's T-test ( $p \le 0.05$ ).



Volunteers classified as high risk for OSAS development had a significant association with CV risk (Figure 3).



**Graph 3:** Association of the CV risk with OSAS development risk. Statistical analysis: Chi-square ( $p \le 0.05$ ).

In the correlational analyses, the sleep variables presented positive correlations with physical activity, cardiac and lipid profile, except for HDL, which presents a negative correlation with the PSQI (Appendix 1). Sleep quality presented positive correlations with BMI, the sum of four skinfolds, body fat percentage and risk of developing OSAS, as well as a negative correlation with HDL. The risk of developing OSAS showed a positive correlation with systolic blood pressure, BMI and sleep quality (Table 2). **Graph 2: a)** Comparison of systolic blood pressure among volunteers with a low and high risk of developing OSAS. **b)** Comparison of diastolic blood pressures among volunteers with a low and high risk of developing OSAS. **c)** Comparison of BMI among volunteers with a low and high risk of developing OSAS. **d)** Comparison of waist/height ratio between volunteers with a low and high risk of developing OSAS. **e)** Comparison of the sum of four skinfolds between volunteers with a low and high risk of developing OSAS. **f)** Comparison of the vigorous activity time per day between volunteers with a low and high risk of developing OSAS. Statistical analysis: Student's T-test ( $p \le 0.05$ ).

## DISCUSSION

In this study, we observed relationships between the quality of sleep of the volunteers evaluated, cardiac profile, the practice of physical activities and anthropometric data. The average obtained by the PSQI revealed that the sample had the quality of sleep classified as "bad," and the values of vigorous physical activity per week and amount of hours of activity per day were below the recommended. Some anthropometric variables, such as BMI, waist-to-height ratio and body fat percentage, also presented better results than recommended.

The mean blood pressure values did not exceed international reference values<sup>(16)</sup>. In our sample, there was a predominance of females (71.84%) over males (28.15%), but the prevalence of hypertension varies according to the evaluation method. In the instrumental measurement by a sphygmomanometer, the method used in this study, there is the predominance of hypertension in the male population, while the self- reported hypertension is higher in females<sup>(17,18)</sup>. The 34-year-old age group contributed to the blood pressure values being within the tolerable values<sup>(16)</sup>.

In our study, the mean BMI, waist-to-height ratio and body fat percentage were higher than the reference values<sup>(16)</sup>, associated with the low frequency and load of physical activities performed by volunteers, which was below the recommended level<sup>(9)</sup>. There is a consensus that physical activity represents one of the main factors related to body weight control<sup>(19)</sup>, however, there are indications that moderate to vigorous physical activity (MVPA) may be better associated with body composition, because of the energy and caloric expenditure generated by the activity. However, it is not possible to state that it necessarily promotes the reduction of body mass, as well as BMI, since MVPA promotes the increase of fatfree mass and lean mass<sup>(20)</sup>.

VARIABLES	R	R <sup>2</sup>	Confidence Interval	Р
PSQI vs. BMI	0.29	0.08	0.04 to 0.50	0.02*
PSQI vs. Sum of four skinfolds	0.32	0.10	0.06 to 0.54	0.02*
PSQI vs. % Body fat	0.30	0.09	0.02 to 0.53	0.04*
PSQI vs. HDL	-0.38	0.15	-0.67 to ≤0.01	0.05*
PSQI vs. Berlin	0.32	0.10	≤0.01 to 0.58	0.04*
PSQI vs. Systolic blood pressure	0.22	0.05	-0.03 to 0.44	0.08
PSQI vs. Waist/height ratio	0.21	0.04	-0.04 to 0.44	0.10
Berlin vs. BMI	0.45	0.20	0.13 to 0.69	≤0.01*
Berlin vs. PSQI	0.32	0.10	≤0.01 to 0.58	0.04*
Berlin vs. Diastolic blood pressure	0.26	0.07	-0.06 to 0.54	0.11
Berlin vs. Waist/height ratio	0.26	0.07	-0.09 to 0.55	0.14
Berlin vs. Sum of four skinfolds	0.33	0.11	-0.02 to 0.60	0.06
Berlin vs. Total cholesterol	0.49	0.24	-0.20 to 0.86	0.15
Berlin vs. LDL	0.61	0.37	-0.09 to 0.91	0.08

Table 2: Correlation between sleep quality and OSAS development risk and variables.

Correlational analysis performed by Pearso'n Linear Correlation: \*p  $\leq$  0.05.

Our results showed that individuals classified as highly likely to develop OSAS, or who already have the syndrome, presented higher systolic and diastolic blood pressure values. Also, we identified a significant association between CV risk and the development risk of SAOS. The chances of the group with a high risk of OSAS having high CV risk is about 6 times higher when compared to volunteers with low risk of OSAS. The increase in CV risk likely occurs due to a greater compensatory stimulus of the sympathetic autonomic nervous system, leading to an increase in blood pressure, heart rate and peripheral vascular resistance, which may cause chronifications and worsening over time<sup>(5,6)</sup>.

OSAS may also be related to higher CV risk due to the cycle of hypoxemia and reoxygenation that occurs during sleep, responsible for causing oxidative stress and the formation of free radicals, promoting the development of CV diseases<sup>(7)</sup>. Besides, episodes of hypoxia are associated with increased pro-inflammatory cytokines involved in sleep maintenance, such as interleukin 6 and alpha tumor necrosis factor, as well as with changes in the standard peak period of these cytokines. In the physiological context of sleep, cytokines are related to drowsiness and fatigue, reaching a peak during the dawn, between 1:00 and 2:00 hours, stimulating sleep. However, in patients with OSAS, this peak tends to occurs around 6:00 to 7:00 in the morning<sup>(7,21)</sup>.

Among the most important anthropometric variables were BMI, the sum of the four folds and body fat percentage, high values

in individuals classified as poor sleep quality and high risk for OSAS development. Although it is not consensual, evidence points out that the relationship between the increase in anthropometric indices and the quality of sleep is associated with the amount of time in bed for each individual, as much as it is reduced, as well as high<sup>(22)</sup>.

A shorter duration of sleep is related to increased appetite due to reduced leptin and increased ghrelin. Increased sleepiness due to sleep deprivation can also lead to reduced energy expenditure due to the modification of thermoregulatory functions through hypothalamic-pituitary-adrenocortical secretion of growth hormone during slow-wave sleep. On the other hand, the increase in bedtime, associated with an attempt to compensate the individual for poor sleep quality, is related to a reduction in energy expenditure, providing elevations in BMI and body fat<sup>(23)</sup>. Also, the increased consumption of stimulant and caloric foods as a way to compensate for the lack of physical recovery and tiredness generated by poor sleep quality may be associated with an increase in these rates<sup>(22)</sup>.

Concerning OSAS, the increase in BMI and circumference measurements is associated with weight gain, which promotes the alteration of the sleep cycle, contributing to the increase in body fat and favoring the development of syndromes and sleep disorders<sup>(24,25)</sup>. There are significant relationships between anthropometric measurements and the development and/or severity of OSAS, especially the values of the cervical and abdominal

circumference. Friedman<sup>(26)</sup> compared the anthropometric values with the postoperative improvement in the apnea/hypopnea index (AHI) in patients with OSAS, verifying better results in thin patients than in obese patients.

We also observed a higher frequency and load of physical activity on the part of volunteers classified with good sleep quality and lower risk of developing OSAS, indicating that those classified with poor sleep quality and higher probability of developing OSAS have a routine with a load and frequency of vigorous physical activity lower than that recommended by the Pan American Journal of Public Health<sup>(9)</sup>, which guides at least 20 minutes of vigorous activities for 3 or more days a week. Physical activity is recognized by the American Sleep Disorders Association<sup>(6)</sup> as an aid to the quality of sleep.

According to well-accepted hypotheses, the increase in body temperature generated by physical activity stimulates the onset of sleep by activating the processes of heat dissipation and sleep induction by the hypothalamus, facilitating the initial "triggering" of sleep<sup>(10)</sup>. Other hypotheses argue that the activity, by increasing the energy expenditure during wakefulness, increases the need for sleep, generating a positive energy balance that enables a fundamental condition for a new wakefulness cycle(10). However, the intensity of the activities must respect the physical fitness of each individual, because just as it offers benefits when performed properly and healthily, it can generate losses when increased in excess<sup>(27)</sup>.

According to the results obtained, volunteers classified as having good sleep quality and low risk of developing OSAS have higher HDL values, demonstrating a lower risk of developing CV disease. Cintra<sup>(28)</sup> demonstrated that isolated levels of HDL below the reference levels increase the chances of developing OSAS by approximately 3%, and when analyzed together with the diagnosis of SAH, they increase by almost 5%.

On the other hand, LDL and Total Cholesterol correlate positively with the Berlin questionnaire, indicating that the higher the risk of developing the syndrome, the higher the plasma concentration of these molecules. The increase in these levels, together with the decrease in HDL in OSAS, may be related to AHI. An experimental study with mice showed that chronic intermittent hypoxia may be an inducer of atherosclerosis, with a significant increase in total cholesterol and LDL and a decrease in HDL<sup>(29)</sup>.

Positive correlations were found between the sleep questionnaires, PSQI and Berlin, indicating that the quality of poor sleep favors the development of sleep disorders, characterized by changes in sleep patterns. Among these disorders, we can mention insomnia, snoring, bruxism, difficulty in starting or maintaining sleep, among others. SDB, such as OSAS, are also among the main syndromes that afflict the population and interfere in the health of patients. It is estimated that OSAS is present in 5% of the female population, 7% of the male population and approximately 25% of the population over 65 years of age<sup>(30)</sup>.

Among the obstacles encountered during this study is the impossibility of affirming whether the OSAS understands the causal factor of the CV risk or the opposite since it is a cross-sectional study. There is a relative subjectivity of the results obtained through the sleep assessment questionnaires, since the score is obtained according to the answers and considerations of each individual. However, the PSQI and Berlin questionnaires are internationally recognized and widely used in population surveys related to sleep quality.

This project may offer data with significant importance, which helps to corroborate the hypotheses about the influence of quality of sleep on the life aspects of the population, especially about CV disease, which currently represents some of the main causes of mortality worldwide.

## **CONCLUSIONS**

Volunteers classified as having poor sleep quality and high risk for OSAS development practice physical activities less frequently and with reduced load concerning volunteers classified as having good sleep quality and low risk for OSAS development. Besides, these volunteers also presented higher values in the variables of the cardiac, anthropometric and lipidic profiles, indicating higher CV risk.

Good sleep quality is fundamental for the correct maintenance of the organism and consequent reduction of the development risk of CV disease. The frequent practice of physical activities is indicated, especially for the adult population, as it promotes a better quality of sleep and reduces the CV risk.

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