Journal of
Cardiology & Cardiovascular Therapy
ISSN: 2474-7580

Juniper Publishers
key to the Researchers

Research Article
Volume 14 Issue 5 -September 2019
DOI: 10.19080/JOCCT.2019.14.555898

J Cardiol & Cardiovasc Ther

Association of Habitual Physical Activity with Vascular Endothelial Function in Male Adolescents

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Submission: August 22, 2019; **Published:** September 04, 2019

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Abstract

Introduction: Endothelial dysfunction is an early key event of atherogenesis. To date, there is strong evidence that physical training has a positive impact on endothelial function, however, there are gaps in the Habitual Physical Activity Levels(PALs) that may influence the preservation of endothelium.

Objectives: To correlate the PALs, functional capacity and BMI with the vascular endothelium dilation.

Methods: Cross-sectional study evaluated 51 male adolescents with a mean age(14.6±1.72), data were collected through anthropometry, behavior questionnaire, exercise stress test and flow mediated dilation (FMD).

Results: The mean percentage of FMD(11.5±0.9%), the correlation between the FMD and PALs (r=0.02, p=0.87), FMD and VO2 (r=0.11, p=0.49) and FMD and BMI (r=0.08, p=0.59). The findings related to BP show that 46.3% of the adolescents presented measures above the normal values. Normotensive subjects had lower BMI(-3.5cm^2), SBP(-21mmHg) and DBP(-10mmHg) than those with altered BP(p=0.04); those with a percentile BP>85 had a higher BMI(28.3 vs 24.7) p=0,05.

Conclusions: The mean of FMD is normal. It was observed that subjects with BP changes have higher BMI, SBP and DBP than normotensive, which is problematic for an early intervention on the risk factors for cardiovascular diseases, since these can affect endothelial function in the long term.

Keywords: Physical activity; Endothelial function; Adolescence

Abbreviations: BP: Blood Pressure; BPp: Blood Pressure Percentiles; BMI: Body Mass Index; BMIp: Body Mass Index Percentiles; BR: Brazil; DBP: Diastolic Blood Pressure; EBP: Elevated blood pressure; FMD: Flow mediated Dilation; PALs: Habitual Physical Activity Levels; HTN: Hypertension; LIC: Laboratory of Clinical Investigation of the Institute of Cardiology of Rio Grande do Sul; VO_2: Maximal Oxygen Consumption; NO: Nitric Oxide; PA: Physical Activity; SBP: Sistolic Blood Pressure

Introduction

Physical inactivity has a worldwide prevalence of 80.0% in adolescents between 13-15 years of age, considering the minimum recommendation of 60min/day of Physical Activity (PA) [1]. The National School Health Survey (PeNSE, 2015) classified 60.8% of the ninth year of elementary school as insufficiently active and 4.8% as inactive in the state of Rio Grande do Sul/ Brazil [2]. The Cardiovascular Risk Study in Adolescents (ERICA, 2016) shows the prevalence of physical inactivity in 56% of adolescents in the city of Porto Alegre/ Brazil [1]. Studies [3,4] state that physical inactivity is an important risk factor in the development of chronic noncommunicable diseases, early endothelial dysfunction and later increased chance for coronary artery disease.

Physical inactivity, gender and age are factors that affect the maximal oxygen consumption (VO2), being this variable of great importance when one wants to know the cardiorespiratory condition of the subjects and also because it has a close relationship with health. For males adolescents, the values that rank them as healthy are from 47ml/kg/min [5].

It is also estimated that around 10% of the world pediatric population has a Body Mass Index (BMI) percentile in the level of

overweight and obesity, of which 40% will be obese in adulthood [6], and children obese patients are 2.5 to 3.7 times more likely to have hypertension (HTN) than their non-obese pairs [7] this cardiovascular risk factor itself has an effect on vascular function and its structure [8].

The flow-mediated dilation (FMD) of the brachial artery is a technique with good reproducibility, non-invasive and low cost for the subclinical and early diagnosis of thrombotic and atherosclerotic events that have their genesis in childhood [9]. FMD evaluates the endothelial response to arterial shear stress as a result of reactive hyperemia, which in turn increases the bioavailability of Nitric Oxide (NO) [10]. In this way, possible strategies of vascular evaluation and clinical intervention should be better explored for the most appropriate management of these young people.

In this sense, our objective was to evaluate the correlation coefficient between the level of Habitual Physical activity with the percentage of endothelial dilatation, functional capacity with percentage of endothelial dilation and BMI with percentage of endothelial dilation, besides characterizing the hemodynamic profile of adolescent males.

Methods

A cross-sectional study, which evaluated 51 male adolescents aged 12 to 18 years; recruited randomly in the school network of the city of Porto Alegre/BR. We include public, private and care institutions that serve young people from different regions of the municipality. From telephone contact with the directorates of educational institutions, there was a schedule for project appreciation meetings; two schools did not adhere to the proposal of this study.

Subsequently, lectures were given to expose adolescents to the current scenario of cardiovascular health related to physical activity, after which the interested parties registered the interest for the second phase. In this, the telephone contacts were made to expose the project to the legal responsible for the young volunteers; at this time the exclusion criteria were evaluated. Physically inactive (PA 0 min/week), smokers, congenital heart disease patients, with hypothyroidism, with musculoskeletal limitations, on the use of vasodilator drugs; being eligible the scheduling was performed for the procedures.

The volunteers were received at the LIC (Laboratory of Clinical Investigation of the Institute of Cardiology of Rio Grande do Sul) during the afternoon shift, respecting the 6 hour fast of foods or beverages that contained caffeine or alcohol. In addition to fasting, it was necessary that the volunteers had not performed physical exercise 8 hours prior to the FMD method. The terms of consent and assent were read and signed.

Evaluation of endothelial function

The non-invasive evaluation of endothelial function in the brachial artery was performed at the (LIC) of the Institute of Cardiology of Rio Grande do Sul. The images were captured by a cardiologist with experience in the method using ultrasound by Ecotepler Esaote (MyLab 700X Vision) with a linear transducer of 7-12 MHz. The acquisition of the image was done through the program Ulead Video Studio (EasyCap). The protocol consisted of 1 minute of baseline recording of the arterial flow diameter, followed by 5 minutes of reactive hyperemia (cuff occlusion in the forearm) and then 3 minutes recording after cuff deflation [11]. The exams recorded in MPEG were converted to MP4, edited in the Movie Maker software and later analyzed through the Cardiovascular Suite software.

Evaluation of functional capacity

The tests were performed at the Cardiology Institute of Rio Grande do Sul. Before the exercise test, a snack was provided at least thirty minutes in advance. The stress tests were carried out by a team composed of a doctor with experience in the method, responsible for conducting the test, and assisted by specially trained technical personnel. The environment was adequate for ventilation and had sufficient dimensions for accommodation of the necessary equipment, as well as allowing circulation of at least three persons, with an ambient temperature between 18 and 22° C and relative humidity of about 40 -60% [12].

The electromyographic records obeyed a logical sequence with the following traces: rest during each stage of exercise in Bruce protocol every one or two minutes and recovery for a minimum of 6 minutes [12]. The VO2 values were obtained indirectly.

Assessment of the level of physical activity of adolescents

From an individual interview conducted by a professional in physical education in an air-conditioned room at the LIC, we sought to record in 27 questions, the weekly amount (minutes) that each adolescent performs physical activities. Data were collected in three domains of physical activity: At school, work and daily habits. Using the validated COMPAC research tool "Lifestyle and risk behaviors of young people from Santa Catarina" [13].

Anthropometry

Performed in the LIC in a private environment and conditioned by a professional in physical education, subjects were instructed to wear minimal attire to measure body mass (Kg) and height (cm) using Welmy digital scale model W200 class III. Calibrated by INMETRO n.18.272.682. The calculation of Body Mass Index (BMI) and its percentiles (BMIp) was performed using the Anthro Plus® program. The pBMI ≤ 85 classifies as a eutrophic subject, cut-off points of overweight percentile > 85 <95 and obesity percentile> 95 [14].

Ethics

This study was approved by the research ethics committee of the Institute of Cardiology / University Foundation of Cardiology under registration UP 5173/15, respecting resolution 466/12 of research with human beings.

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Statistical Analysis

The sample was calculated by estimating a bilateral correlation r^2=0.35, considering α=0.05 and β=0.20, the sample was estimated for 49 research subjects. Data were collected from 51 subjects considering possible losses. The data were analyzed by the Statistical Package for the Social Sciences (SPSS), version 24.0. Parametric data are presented on average and the standard deviation and level of correlation between PALs and endothelial function were assessed using the Pearson test. Statistical significance was considered p <0.05 [15].

Results

The distribution of the ages, PALs level, BMIp, functional capacity and BP levels of adolescents are presented as mean and standard deviation in Tables 1 & 2.

Table 1: Baseline characteristics of subjects.

Variables	n	Media ± SD
	51	
Age (years)	51	14.6±1.7
PALs (min/sem)	51	235±24
BMIp (percentiles)	51	76±26
$VO_{2\ máx.}$ (ml/Kg/min.)	48	45±1.5
SBP (mm/Hg)	48	116±2.0
DBP (mm/Hg)	48	77±1.0

PALs physical activity levels; BMIp Body mass index percentiles; VO2máx, Maximum oxygen consumption; SBP Sistolic blood pressure; DBP Diastolic blood pressure

Table 2: Frequencies of blood pressure categories.

BPp	Frequency (n)	Percentage (%)
Normotensive	25	53.7
EBP	16	33.3
HTN Stage 1	5	9.3
HTN Stage 2	2	3.7

BPp Classification of blood pressure percentiles; EBP Elevated blood pressure; normotensive <90; Elevated blood pressure PAS/DBP ≥ p <90 or p <120/80mmHg; Hypertensive I p> 95 and 5mmHg above p 99; Hypertensive 2 for values> stage I.

The PALs shows that 79% of adolescents are below the minimum daily volume (300min/week) recommended by the guidelines [16,17] and the mean maximum oxygen consumption VO2=45.9±10.4ml/kg/min. classifies the cardiovascular condition as good.

Table 3 presents the evaluation of endothelial function. It shows the baseline data measured during 60 seconds of continuous analysis, the remaining data in 180 seconds continuous after release of the cuff. The mean percentage of endothelium-dependent vascular dilation for adolescents, as well as arterial diameters and time to peak (time in seconds to reach maximal diameter of the brachial artery after hyperemia after deflation of the cuff) are normal.

Table 3: Measures of endothelial function.

Variables	n	Media ± SD
FMD (%)	48	11.5±0.9
Basal diameter (mm)	48	3.8±0.6
Peak diameter (mm)	48	4.2±0.7
Diameter to peak (cm)	48	0.4±0.9
Basal shear stress (dynes/s)	48	176±120
Shear Stress (dynes/s)	48	424±192
Baseline flow (mL/min)	48	123±121
Flow to Peak (mL/min)	48	302±166
Time to peak (sec)	48	70±45
Vascular Resistance (Unit)	45	1.8±2.3

FMD Flow mediated dilation; Shear Stress on artery walls; Time to Peak to arterial dilation.

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The correlation found between the PALs and the percentage of endothelial dilation was (r=0.02, p=0.87). When comparing the means of the subjects with less than 300min/week of PALs and those who performed more than 300min, endothelial dilation was 9.9% and 12.1%, respectively (p=0.39). The correlation between the functional capacity and the percentage of endothelial dilation (r=0.11, p=0.49), and the correlation between the percentage of dilation and the BMI (r=0.11, p=0.46).

Our results related to BP showed that 46.3% of the adolescents present altered measures, of which 33.3% for elevated blood pressure, 9.3% for HTN Stage 1 and 3.7% for HTN Stage 2. It was observed that normotensive subjects had lower BMI (-3.5cm2 p=0.04), SBP (-21mmHg) and DBP (-10mmHg) than young subjects with blood pressure change (Table 4). When comparing the averages of adolescents with pBP classified as normotensive versus those with pressure changes, a significant relationship was found with BMI (Figure 1).

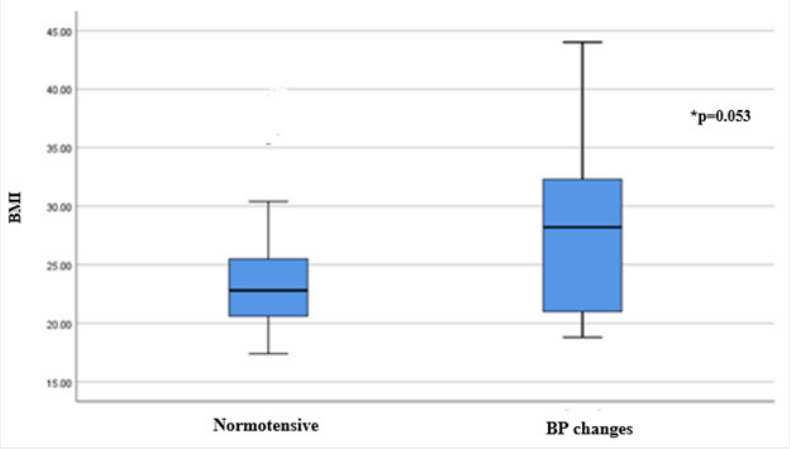

Figure1: Comparison between the means of normotensive subjects and those classified with pressure change according to the blood pressure percentiles with BMI.BMI: Body Mass Index; BP changes, subjects with blood pressure changes; *statistical significance.

Table 4: Comparison between means of normotensive subjects and those with BP changes.

		Media ± SD	p
BMI	normotensive	24.2±5.8	0.04*
	BP changes	27.7±6.6	
pBMI	normotensive	74.3±26.4	0.42
	BP changes	80.2±25.9	
VO_2 (ml/Kg/min)	normotensive	47.7±10.2	0.27
	BP changes	44.2±10.6	
SBP	normotensive	105.5±9.4	0.0001*
	BP changes	126.0±11.9	
DBP	normotensive	72.0±6.7	0.0001*
	BP changes	82.4±4.3	

BMI Body mass index; VO2 Maximum oxygen consumption; SBP Systolic blood pressure; PAD Diastolic blood pressure. BP changes, subjects with blood pressure changes *statistical significance p <0.05.

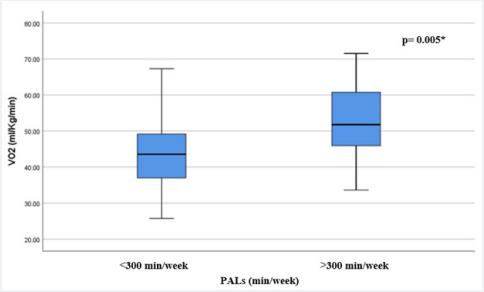

Figure 2: Comparison between the means of the physical activity level (<300 vs. > 300min/week) with functional capacity. PALs physical activity levels; VO2máx, Maximum oxygen consumption; *statistical significance.

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Figure 2 shows a comparison between the averages of adolescents who are below the recommendations of physical activity practice with those who perform > 300min/ week with functional capacity (43.5 vs. 52.2ml/kg/min p=0.005), reinforcing the association between the practice of PALs and cardiovascular health. In the same sense, the correlation between functional capacity and the PALs was statistically significant (Figure 3).

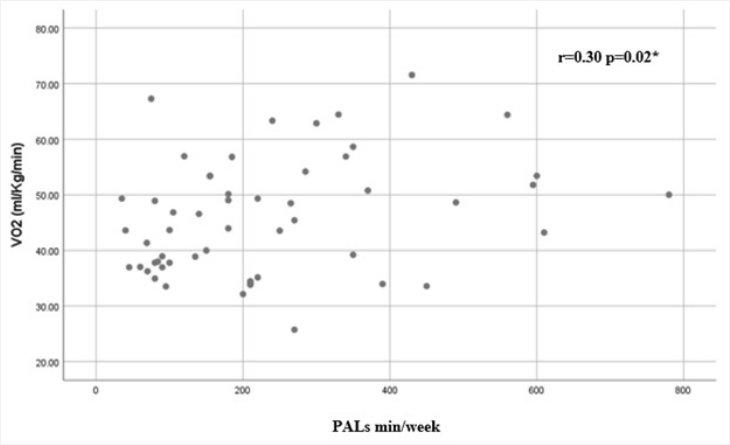

Figure 3: Correlation between functional capacity and physical activity.
PALs physical activity levels; VO2máx, Maximum oxygen consumption; *statistical significance.

Discussion

In this study, we evaluated the correlation coefficient between the PALs level and the percentage of endothelial dilation, functional capacity and percentage of endothelial dilation and BMI with percentage of endothelial dilation, besides characterization of the hemodynamic and vascular profile of adolescents. We included only men, as they presented a higher prevalence of elevated blood pressure (22.3 vs.11.6%) and HTN (15.8 vs. 9.2%), as well as a higher prevalence of obesity (12.4 vs. 9.8%) than in females [18].

The PALs of adolescents is below the minimum daily volume (300min/ week) recommended by the guidelines [16,17], these data are in line with what was observed by Cureau et al. [1] in an epidemiological study in Brazil (n=74.000) in which the prevalence of physical inactivity in schoolchildren (<300min/ week) in the city of Porto Alegre/BR is close to 57%, since it is also corroborated by a review article [19] that shows 56.3% physically inactive; and sociodemographic and behavioral factors associated with physical activity in Brazilian adolescents (n = 109.000), in which only 29% of youngsters are sufficiently active [20].

The mean percentage of endothelium-dependent vascular dilation (11.5±0.9), values for basal diameter (3.8±0.6 mm), diameter up to the peak of dilatation (post-reactive hyperemia) 4.2±0.7mm, and time to peak (time to reach maximal diameter of the brachial artery after reactive hyperemia) 70 ± 45sec; are close to the means of normality [9] for this population.

The correlation between the PALs and the percentage of endothelial dilation may be associated with good functional capacity of the subjects in our sample, as demonstrated in the study conducted by Pahkala et al. [21] concluded that PALs is directly associated with the brachial artery response, evidencing the positive influence on endothelial function in healthy adolescents [21].

As for the correlation between the functional capacity and the percentage of endothelial dilation, according to Hopkins et al. [22] it appears that children with endothelial dysfunction may benefit from high intensity physical activity while there are no relationships between FMD and lower physical activities intensities or between physical activities and FMD in those individuals who have preserved vascular function a priori [22].

Another relevant issue was that we used the functional capacity estimated in exercise electrocardiogram, a relationship that was discussed in a study [23] with non-obese, non-smokers and sedentary healthy male, who only presented correlations between FMD and functional capacity when this was expressed in its absolute value; in fact, no correlation was observed between these variables when VO2 max was normalized to body weight.

The result of the correlation between the percentage of dilation and the BMI can be analyzed through evidence that points to the repletion phase as a mechanism that can lead to a greater accumulation of fat mass without this necessarily representing a risk factor [24], on the other hand there are studies that show an improvement in endothelial function associated with decreased adipose tissue when subjects undergo physical exercise programs alone or combined with dietary intervention [25-27].

Our results related to BP showed that 46.3% of the adolescents present altered measures, of which 33.3% for elevated blood pressure, 9.3% for HTN type I and 3.7% for HTN type II. These data do not classify the research subjects as hypertensive because they would still require a confirmatory phase, however, they are in agreement with the findings of the ERICA study that showed a

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prevalence of elevated BP and HTN of 12.4% and 13.7% between 12-14 years of age, and 33.9% and 18.2% between 15-17 years of age [28].

It is suggested that the percentage of children and adolescents with a diagnosis of HTN has doubled in the last two decades and that the current prevalence of in the pediatric age is around 3% to 5%, whereas that of elevated BP reaches 10-15% [29]. In a meta-analysis that included 122.053 adolescents evaluated in 55 studies from five continents, Moraes et al. [30] observed a reduction in the prevalence of HTN in boys (-3.9%) in the most recent studies, despite the increase in the prevalence of obesity [30].

This transversal study provided the analysis of a moment in which the existence, the degree of relationship between the variables and the force of these variables was verified, that can be explored by another research design by which we will be able to infer possible causes, effects and to diminish the confounding factors. The assumed limitation of this work is the non-use of the Tanner protocol for stratification of sexual maturation of adolescents.

Conclusion

The mean percentage of endothelium-dependent dilation is in the normal range. It was observed that 46% of the subjects had an altered BP measurement and that normotensive patients had a lower BMI, SBP and DBP than those with BP cahnges. These results lead to the need for early intervention on risk factors for cardiovascular diseases, since these may affect endothelial function in the medium and long term.

Funding

This work was supported by the Coordination of Improvement of Higher Education Personnel (CAPES) through the Post-Graduation Support Program for Private Education Institutions (PROSUP) of the Ministry of education, Brazil.

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