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Custódio Rubira, Marcelo; Angelis Rubira, Ana Paula F. de; Silva Soares, Pedro Paulo da; Gusmão Medeiros, Luciana; Alves Neves, Gizele; Consolim-Colombo, Fernanda Marciano

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Cardiovascular risk in eutrophic young subjects: influence of corporal fat and sympathetic activity

Risco cardiovascular em jovens eutróficas: influência da gordura corporal e atividade simpática

Marcelo Custódio Rubira[1]; Ana Paula F. de Angelis Rubira[2]; Pedro Paulo da Silva Soares[3]; Luciana Gusmão Medeiros[4]; Gizele Alves Neves[4]; Fernanda Marciano Consolim-Colombo[3]

[1] Doctor, Physiotherapy Department – São Lucas College, Porto Velho, RO – Brazil.
[2] Master, Physiotherapy Department – São Lucas College, Porto Velho, RO – Brazil.
[3] Doctor, Fluminense Federal University – Physiology and Pharmacology Department. Niterói, RJ – Brazil.
[4] Specialist, Physiotherapist – São Lucas College, Porto Velho, RO – Brazil.
[5] Doctor, InCor (Heart Institute) – Division of hypertension-São Paulo University. São Paulo, SP – Brazil.

Postal address
Marcelo Custódio Rubira
Av. Brasília, 3062, apto 502 – Bairro São Cristóvão
76804-070 – Porto Velho – RO [Brasil]
rubiramc@terra.com.br

Abstract

Introduction: There is a strong relationship between sympathetic activity and obesity to early development cardiovascular diseases. Heart rate variability analyses the balance sheet vague-sympathetic and it is an important prognostic for cardiopathies. **Objective:** The study measured cardiac sympathetic activation in young eutrophic subjects with minor excess fat through the study of heart rate variability. **Methods:** Thirty-eight women were available, 21.1±1.8 years, BMI below 25 kg/m^2, sedentary and divided into two groups: (1) low fat percentile (≤23%) and (2) high (>23%). The electrocardiogram was registered for 10 minutes at rest and stand. Cholesterol and triglycerides fraction was analysed. **Results:** HDL-c was lower in group 2 ($p < 0.019$) and LDL-c higher ($p<0.038$). Group 1 presented higher percentage of LF band in supine ($p<0.13$). LF band in group 2 ($p<0.001$) increased of supine for orthostatic position. **Conclusion:** Low levels of excess fat in young eutrophic women leads an increased the cardiovascular risk.

Key words: Anthropometry; Body mass index; Heart rate; Obesity; Sympathetic Nervous System

Resumo

Introdução: Existe forte relação entre obesidade, atividade simpática e desenvolvimento precoce das doenças cardiovasculares. A variabilidade da frequência cardíaca estuda o balanço vago-simpático, considerado importante fator prognóstico para cardiopatias. Objetivo: Medir ativação simpática cardíaca em jovens eutróficas com menor excesso de gordura pela variabilidade da frequência cardíaca. Método: Trinta e oito mulheres, com 21,1±1,8 anos, IMC abaixo de 25 kg/m^2, sedentárias, divididas em dois grupos: (1) Baixo Percentil de Gordura (≤23%) e (2) Alto (>23%). Realizaram-se eletrocardiograma – registrado por 10 minutos, com as voluntárias em supino e em pé –, análises de colesterol e frações e triglicerídeos. Resultados: HDL-c foi menor no grupo 2 ($p< 0,019$) e LDL-c maior ($p<0,038$). O grupo 1 apresentou maior porcentagem da banda LF em supino ($p<0.13$). Houve aumento significativo da banda LF no grupo 2 ($p<0,001$) de supino para posição em pé. Conclusão: Baixos níveis de excesso de gordura em jovens eutróficas aumentam o risco cardiovascular.

Descritores: Antropometria; Frequência cardíaca; Índice de massa corporal; Obesidade; Sistema Nervoso Simpático.

Introduction

The prevalence of obesity is increasing worldwide, and obesity is currently considered as one of the most important public health problems of modern society. Obesity is considered to be a major risk factor for cardiovascular disorders according to the American Heart Association. In young subjects, the prevalence of obesity more than doubled over the past 15 years[1].

Body composition has fundamental importance in the quality of life and is a powerful predictor of mortality and morbidity in humans[2].

The most common estimate of body composition in populations has been the body mass index, which was actually developed as a measure of weight /height^2 and not as an index of obesity[3]. Its importance is due to values around 30 kg/m^2 (obese subjects) to correlate with high incidence of diseases, mainly arterial hypertension, lipids disorders – high cholesterol, triglyceride and cardiovascular diseases[4].

Identification and monitoring of the amount of body fat have been receiving special attention in aspects related to promotion of the health, not just for its actions in the prevention and in the control of cardiovascular diseases but also for their induction and association with risk factors, especially in the plasmatic lipids levels and arterial pressure[5]. The excess accumulation body fat, in the central part of body and/or total body fat[6], is a sign of abnormal lipids metabolism and is frequently associated with dyslipidaemia and arterial hypertension[7].

The sympathetic nervous system seems to be activated in obesity[8]. However, this increased tonus is not homogenous for all tissues and organs. While the sympathetic activation is demonstrated at the level of the kidneys and skeletal muscles, cardiac sympathetic activity does not seem to be increased[9]. However, cardiac autonomic disturbances such as decreased vagal tonus, with or without sympathetic activation, are documented in obesity[10].

Measurements of heart rate variability (HRV) have been increasingly recognized as important tools to investigate the cardiac autonomic tonus. This is a non-invasive and highly reliable method, which allows the quantification of the autonomic modulation on the frequency of stimulus at the sinoatrial node[11]. It is well documented that reduced HRV is a risk factor for cardiovascular mortality, and it is associated of impaired physiologic cardiovascular modulation[12].

Accordingly, the aims of the study were to measure the cardiac sympathetic activation in young eutrophic subjects with minor excess fat with HRV and changes in the levels of total cholesterol and fractions.

Methods and materials

Characteristics of the sample

Sample consisted of 38 women students, age ranging from 18 to 24 years (21.1±1.8), with body mass index (BMI) within normal ranges (mean, 22.4±1.96). Subjects were sedentary, nonsmoking, and without heart diseases, kidney disorders, respiratory disorders, diabetes, or use of any medications.

This study was approved by the Ethics Committee of São Lucas University, Porto Velho, Rôndonia, Brazil (process nº. 68/2007). Subjects were informed about the study and signed consent forms.

Body composition

Anthropometric measurements included weight, height, and measurements of skinfold. Skinfold were measured using an adipometer (Sanny), with established precision of +/-0.5mm and according to standard procedure.

Based on the assessments subjects were divided into two groups: group 1: less than 23% of body fat (n = 14); group 2: at least 23% of body fat (n = 24).

Lipid profile

Measurements of total cholesterol (Trinder enzymatic method), HDL-cholesterol (Labtest method), triglycerides (enzymatic Trinder method), and VLDL-c (from calculation) were evaluated. Techniques and methods are standardized at the laboratory of Biochemical analyzes.

Electrocardiogram

Electrocardiogram (ECG) was registered in the morning, in a room with pleasant temperature. The subjects were calm and rested for at least 10 minutes, ECG at rest was registered, with patients laying on the orthostatic table, in the supine position (10 minutes register). The table was then inclined and ECG was registered again with subjects at 90 degrees (10 minutes). Equipment was digital and the registers were analyzed using MatLab software.

Spectral analyzes of HRV

HRV was decomposed into the following basic oscillatory bands:

a) High frequency (HF), with variation ranging from 0.15 to 0.4 Hz.
b) Low frequency (LF), ranging from 0.04 to 0.15 Hz.
c) Very low frequency (VLF), ranging from 0.015 to 0.04 Hz.

The ratio between LF/HF reflects the relative and absolute changes in the sympathetic and parasympathetic components of the autonomic nerve system, characterizing the vagal/sympathetic balance at this level[13].

Fast Fourier Transform (FFT) was used in order to obtained an estimate of the spectral analyze of the HRV (frequency domain) during the stationary phases of the experiment (supine and standing), with the aim of allowing comparisons among the results of the studies. Reasons for choosing the method include its relative simplicity and representation of results[14].

Statistical analyzes

Data was entered and analyzed using Software Sigma Stat. Mean and standard deviation of the studied variables were calculated. For comparisons and correlations between the variables, the Student "t" test and Spearman test was used, respectivily. Significance levels of 5% were assumed for all the comparisons.

Results

Anthropometrics characteristics

The sample consisted of 38 women students and was divided into two groups: low proportion of fat and high proportion of fat. These groups showed statistical significance difference into the values of body mass index (BMI), weight and in fat proportion. The anthropometrics characteristics of the groups are showed in the Table 1.

Table 1: Anthropometrics and lipids characteristics and comparison between the groups with low fat and high fat proportion

	Group 1 Low fat proportion	Group 2 High fat proportion	P<0.05
Age (year)	21.14±1.95	21.13±1.72	0.99
Height (cm)	160.28±8.10	159.37±5.70	0.69
Weight (kg)	52.12±6.30	56.93±5.83	0.03
BMI (kg/m^2)	20.24±1.42	22.49±1.95	0.001
Fat (%)	20.63±1.68	29.40±4.04	0.001
Total cholesterol (mg/dL)	158.15±30.13	168.95±31.39	0.33
HDL-c (mg/dL)	57.61±13.58	48.28±8.59	0.019
LDL-c (mg/dL)	87.61±23.23	108.04±28.13	0.036
VLDL -c (mg/dL)	12.58±4.92	12.61±4.75	0.98
Triglycerides (mg/dL)	62.91±24.63	63.09±23.79	0.98

HDL-c – High density lipoprotein, LDL-c – Low density lipoprotein, VLDL-c – Very low density lipoprotein, BMI – Body mass index.

Total cholesterol and fractions

Mean values of total cholesterol and fractions, as well as of triglycerides, were within the normal limits, according to the National Cholesterol Education Program – Adult Treatment Panel[15]. Mean values of high density lipoprotein (HDL-c) were significant lower, while mean values for low density lipoprotein (LDL-c) were significantly higher in group 2 vs. group 1 (Table 1).

Correlation total cholesterol and fractions and heart rate variability

With regard to the values of total cholesterol and fractions and your correlation with the bands of heart rate variability there were no significant correlation in the low fat e high fat groups in the supine and orthostatic positions of the values of HF, LF and VLF and the LF/HF ratio with the total cholesterol, HDL-c, LDL-c and VLDL-c and Triglycerides. The data are expressed in Table 2.

Heart rate variability

Table 3 shows the heart rate variability derived by heart rate spectral analysis, contrasting both groups while in the supine and orthostatic positions. No significant differences were seen for LF while in resting, when comparing both groups, although a numerically higher proportion of LF was seen in group 1 vs. group 2. Non significant increases in the LF and VLF bands and non significant reduction in the HF band were seen when comparing groups in the supine and orthostatic positions.

Table 2: Correlation of the values of total cholesterol and fractions with the bands of heart rate variability between the groups of low fat and high fat proportion in the supine and orthostati

	Total cholesterol		HDL-c		LDL-c		VLDL-c		Triglycerides	
Group 1 Low fat proportion	R	P	R	P	R	P	R	P	R	P
LF SUPINE	0.12	0.69	-0.18	0.56	0.27	0.37	0.12	0.72	0.12	0.72
LF ORTHOSTATIC	0.26	0.39	0.15	0.62	0.29	0.33	-0.11	0.73	-0.11	073
VLF SUPINE	0.23	0.44	0.15	0.63	0.21	0.49	0.09	0.77	0.09	0.77
VLF ORTHOSTATIC	-0.42	0.15	-0.44	0.14	-0.28	0.36	0.01	0.98	0.01	0.98
HF SUPINE	-0.22	0.48	0.04	0.89	-0.31	0.30	-0.14	0.67	-0.14	0.67
HF ORTHOSTATIC	0.18	0.56	0.29	0.34	0.01	0.97	0.11	0.75	0.11	0.75
LF/HF SUPINE	0.00	1.00	-0.29	0.34	0.16	0.60	0.13	0.69	0.13	0.69
LF/HF ORTHOSTATIC	-0.30	0.31	-0.13	0.67	-0.20	0.51	-0.50	0.10	-0.50	0.10
Group 2 High fat proportion	R	P	R	P	R	P	R	P	R	P
LF SUPINE	-0.02	0.94	0.28	0.22	-0.16	0.49	0.32	0.16	0.32	0.16
LF ORTHOSTATIC	0.10	0.68	-0.16	0.48	0.10	0.65	0.32	0.16	0.32	0.16
VLF SUPINE	0.31	0.17	0.19	0.41	0.28	0.21	0.04	0.88	0.04	0.88
VLF ORTHOSTATIC	-0.06	0.80	0.14	0.54	-0.10	0.66	-0.05	0.84	-0.05	0.84
HF SUPINE	-0.31	0.17	-0.34	0.13	-0.21	0.36	-0.20	0.39	-0.20	0.39
HF ORTHOSTATIC	-0.02	0.92	0.04	0.86	0.00	1.00	-0.23	0.31	-0.23	0.31
LF/HF SUPINE	0.26	0.26	0.25	0.30	0.07	0.77	0.31	0.17	0.31	0.17
LF/HF ORTHOSTATIC	0.03	0.90	-0.11	0.64	0.02	0.93	0.26	0.26	0.26	0.26

VLF – Very Low Frequency, LF – Low Frequency, HF – High Frequency
HDL-c – High density lipoprotein, LDL-c - Low density lipoprotein, VLDL-c – Very low density lipoprotein.

Table 3: Comparison of the heart rate variability (supine and orthostatic) in the groups with low fat and high fat proportio

Supine position	Group 1 Low fat proportion	Group 2 high fat proportion	P<0.05
VLF %	22.23±10.69	23.88±13.9	0.41
LF %	37.34±14.17	31.97±6.53	0.13
HF %	42.34±19.87	44.16±13.92	0.74
LF/HF	1.24±0.93	0.85±0.51	0.11
Orthostatic position	**Group 1 Low fat proportion**	**Group 2 high fat proportion**	**P<0.05**
VLF %	35.46±13.95	29.97±13.89	0.25
LF %	47.41±12.49	47.53±15.71	0.98
HF %	22.23±15.99	17.09±14.44	0.33
LF/HF	4.55±2.90	3.59±2.99	0.35

VLF –Very Low Frequency, LF – Low Frequency, HF – High Frequency.

Table 4 compar**es** values of heart rate variability between groups in the two measurements. In group 1, after changing into the orthostatic position, no differences were seen for the LF band, but significant changes were seen for the VLF and HF. In group 2, significant changes were seen for LF and HF.

Table 4: Increase of the heart rate variability during maneuver orthostatic, decubitus change of supine position to the orthostatic position in the groups with low and high proportion

Group 1 Low fat proportion	Supine	Orthostatic	P<0.05
VLF %	22.23±10.69	35.46±13.95	0.003*
LF %	37.34±14.17	47.41±12.49	0.057
HF %	42.34±19.87	22.23±15.99	0.002*
LF/HF	1.24±0.93	4.55±2.90	0.001*
Group 2 High fat proportion	**Supine**	**Orthostatic**	**P<0.05**
VLF %	23.88±13.90	29.97±13.89	0.15
LF %	31.97±6.53	47.53±15.71	0.001*
HF %	44.16±13.92	17.09±14.44	0.001*
LF/HF	0.85±0.51	3.59±2.99	0.001*

VLF – Very Low Frequency, LF – Low Frequency, HF – High Frequency.

Discussion

The importance of conducting studies in young subjects is demonstrated by the increasing prevalence of obesity in this population, and by the fact that minor excess fat developed at young ages imposes even higher vascular risks than onset of obesity at adulthood[16].

The main result of this study is the demonstration that there is a significant group of young women considered "normal" by BMI were already "occult obese" when evaluated by BIA method[17].

An inappropriate body composition can take many disorders in the human organism, for example the obesity and the malnutrition both associated with the development of several diseases[6].

The association of blood pressure with body weight could be due to the increased total body mass or some special underlying relationship between blood pressure and body fat[18].

In the current study, mean values of total and fractions cholesterol and of triglycerides were within normal ranges according to the National Cholesterol Education Program – Adult Treatment Panel[15]. HDL levels were significantly decreased in group 2, when compared to group 1.

A significant number of subjects in this study had elevated fat, while been classified as normal weight by the BMI. Based on the important recognition that excessive adiposity is linked to cardiovascular and metabolic disorders, anthropometric methods are recommended because of their accuracy and simplicity. Anthropometric methods are of utility in several domains including epidemiological vigilance, scientific investigation, individual and social health screenings, and should be particularly recommended for individuals that are not overweight or obese according to the BMI. These methods are supported by the World Health Organization[19].

Obesity (≥30% BMI), excess accumulation of body fat, is a sign of abnormal lipid metabolism, and is a important predictor for hypertension, coronary heart disease, diabetes mellitus, hepato biliary disease[20] and frequently is associated with arterial hypertension and dyslipidaemia (high serum TG and low serum HDL-C rather than high serum TC and LDL-C)[6].

Obesity is not an homogeneous disorder. In a subgroup of obese individuals, the sympathetic tonus is increased to key organs, including the kidney, muscles and peripheric vessels[9]. Evidence for increased sympathetic tonus to the heart is less strong, especially in individuals without hypertension[9]. Sympathetic activation at target organs seems to be of importance in the pathophysiology of insulin-resistance related to obesity and hypertension[21] activation of the renin- angiotensin system[8] and of sudden death[22].

In healthy animals, obesity induced by excessive feeding is associated with sympathetic activation and hypertension. Sympathetic activation is precociously induced by overfeeding, and is reversed by weight loss. Modification in the sympathetic system induced by overfeeding seems to precede alterations in the renin-angiotensin system[8].

Although the pathophysiology of sympathetic activation is not totally known, studies in hypertensive patients demonstrated increased turnover of norepinephrine at the brain, which could explain the increased sympathetic tonus to the heart and kidneys[23]. In studies of norepinephrine turnover, the sympathetic tonus to the heart was normal in non-hypertensive obese individuals, but it was moderately increased in hypertensive obese[24].

Grassi et al. demonstrated that weight loss decreased the neuromuscular sympathetic activity, reduced plasmatic norepinephrine, increased the baroreflex sensibility, as well as improved glucose utilization[9].

Caloric restrictions reduce the weight, improves the sympathetic tonus to the heart during the night, reduces the sympathetic/parasympathetic ratio during the day, without modifying heart frequency at rest[25].

Autonomic modulation of heart frequency is partially responsible by its variability. In healthy individuals, stimulation of the parasympathetic system is associated with reduction in the cardiac frequency and increased heart rate variability[26]. Differentially, sympathetic activation increases heart frequencies and decreases its variability. Frequent oscillations of heart frequency have important diagnostics and therapeutics implications[27]. Decreased heart rate variability is an important prognostic factor for cardiac events in previously health individuals[25].

The LF domain at rest in subjects of group 1 was higher, and different from group 2. This is discrepant to others studies. However, we emphasize that subjects were young and with normal BMI, which is different from other studies. Nagai et al. found a decreased rate of sympathetic activation in the initial phases of obesity in children, suggesting that the autonomic depression is a function of duration of obesity[28].

Postural changes influence heart rate variability. During rest, both the sympathetic and parasympathetic systems are tonic and active, with predominance of the vagal effects. Therefore, studying heart rate variability during rest but at different positions enhances the sensitivity of the method, testing for changes in the sympathetic-vagal balance at the sinusal node[29, 30].

Postural changes from the supine to the orthostatic position, active or passive, trigger vascular adjustments, in response to the hydrostatic shift (from the superior to the inferior extremities), changes in cardiac debit and in the arterial pressure, by the activation of arterial and cardiopulmonary receptors, and by the integration of central and peripheral information[30].

Tilt tests conducted in healthy adolescents and young adults demonstrated important elevations of the LF component, and minor decreases in HF components of the heart rate variability, suggesting that increase in cardiac frequency is mediated both by the decrease in vagal influence and by sympathetic activation[29].

It was observed increased proportions of the VLF and LF components, with decrease in the HF component following the change in the position from supine to orthostatic, although LF changes were not statistically different when comparing both groups. Since the other differences were significant, findings support increased sympathetic activity in group 2.

Conclusion

These findings suggest that eutrophic young subjects with minor increased proportion of fat and normal BMI have sympathetic activation to the heart and also decreased levels of HDL-c and higher levels of LDL-c, both changes are associated with increased risks for cardiovascular and metabolic disorders.

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