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Basal autonomic balance and during the isometric exercise in young people with different cardiovascular reactivity

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Acronyms
HBP: high blood pressure
HF: high frequency
HR: heart rate
HRV: heart rate variability
LF: low frequency
SD: standard deviation
WBT: dynamic weight-bearing test

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ABSTRACT

Introduction: The autonomic nervous system plays an important role in cardiovascular readjustments to exercise. In cardiovascular hyperreactivity there is a greater sensitivity of the sympathetic system to different stressors.

Objectives: To determine the characteristics of cardiac autonomic control in young adults with different degrees of cardiovascular reactivity under basal conditions and during isometric exercise.

Method: The sample consisted of 97 individuals of both sexes, and was divided into three groups: normoreactive, hyperreactive and with hypertensive response, according to the pressor response to weight-bearing tests. The individuals underwent a complete study of heart rate variability at rest and during isometric test. The frequency domain for the variables was: low, high, low/high resting ratio, and the parameters of Poincaré plots at rest and during exercise (values of standard deviation 1 [SD1], 2 [SD2], and the reason between them).

Results: Under basal conditions, hyperreactive individuals with a hypertensive response had a sympathetic predominance over cardiac function and lower heart rate variability. During the isometric exercise SD1 and SD2 axes values decreased in all groups and SD1/SD2 ratio decreased in normoreactive individuals with hypertensive response; but it was hardly modified in those hyper-reactive.

Conclusions: Individuals with cardiovascular hyperreactivity have a prior autonomic imbalance under basal conditions and a reduction of autonomic vagal modulation during exercise that may favor the development of arterial hypertension.

Keywords: Cardiovascular hyperreactivity, Heart rate, Exercise, Isometric contraction, Dynamic weight-bearing test

Balance autonómico basal y durante el ejercicio isométrico en jóvenes con diferente reactividad cardiovascular

RESUMEN

Introducción: El sistema nervioso autónomo desempeña un papel importante en los reajustes cardiovasculares al ejercicio. En la hiperreactividad cardiovascular existe una mayor sensibilidad del sistema simpático ante diferentes estímulos estresantes.

Objetivo: Determinar las características del control autonómico cardíaco en adultos jóvenes con diferentes grados de reactividad cardiovascular en condiciones

basales y durante el ejercicio isométrico.
Método: La muestra estuvo constituida por 97 individuos de ambos sexos, y se dividió en tres grupos: normorreactivos, hiperreactivos y con respuesta hipertensiva, de acuerdo a la respuesta presora a la prueba del peso sostenido. A todos los individuos se les realizó un estudio de variabilidad de la frecuencia cardíaca en reposo y durante la prueba isométrica. Se estudiaron las variables en el dominio de la frecuencia: baja, alta, relación baja/alta en reposo, y los parámetros del diagrama de Poincaré en reposo y durante el ejercicio (valores de desviación estándar 1 [SD1], 2 [SD2], y la razón entre ambos).
Resultados: En estado basal los individuos hiperreactivos y con respuesta hipertensiva presentaron un predominio simpático sobre la función cardíaca y una menor variabilidad de la frecuencia cardíaca. Durante el ejercicio isométrico disminuyeron los valores de los ejes SD1 y SD2 en todos los grupos y la razón SD1/SD2 decreció en individuos normorreactivos y con respuesta hipertensiva; pero apenas se modificó en los hiperreactivos.
Conclusiones: En los individuos con hiperreactividad cardiovascular ya está presente un desbalance autonómico en estado basal y existe una reducción de la modulación autonómica vagal durante el ejercicio, que puede favorecer el desarrollo de la hipertensión arterial.
Palabras clave: Hiperreactividad cardiovascular, Frecuencia cardíaca, Ejercicio, Contracción isométrica, Prueba del peso sostenido

INTRODUCTION

The recent days have witnessed the recognition of a significant relationship between the autonomic nervous system functioning and cardiovascular mortality. This has spurred efforts for the development of quantitative markers of autonomic balance such as heart rate variability (HRV), which represents one of the most promising. HRV or oscillation in the interval between consecutive heartbeats is an emergent property of interdependent regulatory systems which operates on different time scales to adapt to environmental and psychological challenges[1]. HRV is related to physiological adaptations to internal environment changes and indicates the presence of different diseases[2,3].

There are a number of methods to assess HRV; though today spectral analysis (frequency domain) is most widely accepted. Time domain methods are basically statistical and evaluate variability through averages and standard deviations. They are best known, but seem to have fewer advantages than the spectral methods. Nonlinear methods are also used for HRV assessment, among them Poincaré plot, which unlike frequency-domain measurements is insensitive to changes in R-R intervals on the ECG. Poincaré plot is the simplest technique to describe the nonlinear dynamics of a phenomenon and has good results in clinical/experimental studies and sports physiology[4].

Autonomic imbalance or sympathovagal imbalance links increased sympathetic activity with reduced vagal tone and is involved in the pathophysiology of arrhythmogenesis, sudden cardiac death and high blood pressure (HBP)[2,3]. There are several methods to assess the autonomic activity of an individual[5], among which are HRV at rest and in response to activation of the autonomic nervous system by deep breathing and Valsalva maneuver, the response to active orthostasis and muscle isometric contraction[3,5,6]. These tests are standardized, simple to perform, safe, reproducible and do not involve bloody maneuvers[7-10].

On the other hand, subjects who have an increased response or greater sensitivity to different stressors present a condition called cardiovascular hyperreactivity. Recent research suggests that test for detecting hyperreactive individuals have shown promise for predicting HBP[11,12]. The basis for these studies has been the hypothesis that individuals with greater hyperreactivity are at increased risk of developing hypertension and that this bear no relation to other cardiovascular risk markers.

There are several tests to induce hyperreactivity, among them isometric or isotonic (dynamic) physical exercise, mental stress and cold. The (isometric) weight-bearing test (WBT) is a version of the hand grip test developed by Paz Basanta *et al*[13] in the 90s of the last century, which showed high specificity, sensitivity and predictive value, and was used in primary health care for HBP explorations. However, no further studies were performed to determine the sympathovagal balance characteristics in individuals with cardiovascular hyperreactivity, and whether there are differences with the normoreactive subjects in the autonomic response to the aforementioned test remains unknown. The objective of this research was to determine the characteristics of cardiac autonomic control at rest and during isometric exercise in young adults with different degrees of cardiovascular reactivity.

METHOD

An analytical cross-sectional study was carried out in the Cardiovascular Physiology Laboratory of the Biomedical Research Unit at the Universidad de Ciencias Médicas in Villa Clara. An analytical cross-sectional study of a random sample of 97 students 56 female and 41 male ranging 19.16±1.41 years was carried out.

They had no history of chronic disease except HBP without pharmacological treatment and as a pre-requisite for the test they could not smoke, drink coffee, or perform heavy exercises the previous day.

An initial blood pressure measurement was taken in the right upper limb in the sitting position by the classical auscultatory method with a Kennel brand mercury sphygmomanometer. WBT was then performed sitting upright holding for 2 minutes a 500-gram weight with the left upper limb perpendicular to the body. According to mean arterial pressure the individuals were classified into normoreactive (n= 58), hyperreactive (n=31) and with hypertensive response (n=8) fulfilling the requirements of Paz Basanta *et al*[13].

The pressor response to the WBT was determined in the supine posture shortly afterwards. For this, the individual was placed with the left arm parallel to the floor, perpendicular to the longitudinal axis, with the shoulder outside the bed. Systolic, diastolic and mean blood pressure values were determined in the first and second minute of the test.

The HRV was determined in accordance with the guidelines of the European Society of Cardiology and the American Society for Pacing and Electro physiology[14]. Data were obtained using a PowerLab digital record device and LabChart 8 program, through the standard DII electrocardiographic derivation in the supine decubitus position, at 10-minutes rest and during the isometric exercise. HRV parameters were analyzed in the last 5-minutes rest and when performing the exercise.

HRV was explored in the frequency domain. We calculated every parameter by means of spectral analysis of the tachogram and Lomb periodogram. Power values ms^2/Hz) were expressed as the natural logarithm from the figures obtained.

The measurement of LF, and HF power components were expressed in absolute values of frequency (milliseconds squared) and in the normalized energies values, expressed as a percentage of the different bands with respect to the total spectral power that represents the relative value of each of these components in proportion to the total value of the very low frequency component[15]. Another analysis carried out was the calculation of the relationship between both frequencies (LF/HF), which in controlled conditions represents the sympathovagal balance.

We used a Poincaré plot for our non-linear analysis which was quantitatively performed by fitting an ellipse to the figure formed by plotting each R-R interval against the preceding interval.

From the dots group of the ellipse, the parameters of standard deviation (SD) 1 and 2 that are associated with the transversal and longitudinal diagonals, respectively, were obtained. These parameters correspond to the standard deviations of the ellipse data and describe short and long term variability. SD1/SD2 ratio represents the autonomic balance[16,17].

All measurements of the studied parameters were carried between 08:00 a.m. and 10:00 a.m., in the Cardiovascular Physiology Laboratory of the Biomedical Research Unit.

Statistical analysis

Statistical analysis was performed by using SPSS program version 20.0; results are indicated by mean± standard deviation (χ±SD). A comparison of the study variables between the groups was made through the T test for independent samples, and in the comparison of the basal values with those achieved during the isometric exercise, a T test was used for related samples. Statistical significance was considered for p<0.05.

RESULTS

Table 1 shows means and standard deviations of blood pressure and heart rate (HR) in basal conditions and during isometric exercise. The means were compared in both conditions, and we found that the values of systolic, diastolic and mean arterial pressure showed significant increases in all groups (p<0.05); Moreover, these values increased in relation to the degree of cardiovascular reactivity. On the other hand, HR was also significantly increased in exercise in all groups, although differences were not statistically significant in individuals with hypertensive response (p>0.05).

Table 2 depicts HRV parameters in the resting frequency domain, where we found significant differences in all the variables between normoreactive and hyperreactive (p<0.05); however, no differences were observed in the individuals with hypertensive response with respect to the rest of the groups (p>0.05). Hyperreactives presented the highest LF value (in standardized units: 58.19±14.98) and individuals with hypertensive response had the lowest HF values (in milliseconds squared [23.26±13.02] and in normalized units [40.98±19.76]) and the highest ratio LF/HF 1.93±1.52 (lower HRV), although without significant differences with the normoreactive group.

The Poincaré diagrams revealed that normoreactive individuals presented higher SD1, SD2 and SD1/SD2 axes values than hyperreactive and hypertensive individuals, with statistically significant differences only with the former (p< 0.05).

As no statistical differences were found in the variables of the hypertensive response group, the small size of the sample may have influenced on the greater dispersion of the data.

Table 3 shows the quantitative parameters of the Poincaré during WBT. We confirmed that individuals with a hypertensive response had the lowest SD1 parameter value and SD1/SD2 ratio, although no significant differences were found between the groups (p>0.05).

When comparing the baseline values with those obtained during the isometric test using the Poincaré plot (**Figure 1**), it was observed that in all groups SD1 and SD2 values decreased, with significant differences in normoreactive and hyperreactive (p<0.05). On the other hand, SD1/SD2 ratio was barely modified in the hyperreactive group and decreased in the rest of them, although significantly only in the normoreactives (p <0.05).

Poincaré diagrams represent three types of individuals with different reactivity degrees (**Figure 2**). It can be seen that, under basal conditions, in those with hyperreactivity (B and C) the diameters SD1 and SD2 have values lower than that of the normoreactive (A) and the ellipse is narrower; which indicates less vagal activity and greater sympathetic activity. The shortest HRV in the short and long terms is observed in the individual C with hypertensive response. During the isometric exercise, decrease in the magnitude of both diameters and narrowing of the ellipse is observed in all individuals, which reflects an increase in sympathetic stimulation and vagal inhibition.

Table 1. Hemodynamic parameters under basal conditions and during isometric exercise in normoreactive, hyperreactive individuals with hypertensive response.

Variables	Normoreactive (n=58)			Hyperreactive (n=31)			Hypertensive response (n=8)		
	Basal	WBT	p	Basal	WBT	p	Basal	WBT	p
SBP	111.45±9.81	119.72±8.39	<0.0001	123.42±10.42	131.55±10.6	<0.0001	132.00±12.65	142.00±12.23	0.005
DBP	71.52±8.72	82.65±7.92	<0.0001	78.58±7.38	90.64±5.69	<0.0001	89.00±7.63	98.25±6.27	0.001
MBP	84.81±8.05	95.03±6.95	<0.0001	93.52±6.87	104.26±5.83	<0.0001	103.25±9.06	112.83±7.97	0.001
HR	72.48±9.65	78.72±18.22	<0.0001	75.68±10.20	82.26±11.80	<0.0001	85.62±13.18	93.63±10.78	0.161

The values are expressed as mean ± standard deviation.
Student's T test for related samples, significance p<0.05.
HR, heart rate; DBP, diastolic blood pressure; MBP, mean blood pressure; SBP, systolic blood pressure; WBT, Dynamic weight-bearing test.

Table 2. Heart rate variability parameters under baseline in the study groups.

Variables	Normoreactive (n=58)	Hyperreactive (n=31)	Hypertensive response (n=8)	NR-HR p¤	NR-HTR p¤	HR-HTR p¤
LF (ms^2)	32.70±10.42	32.35±10.30	30.66±10.72	0.882	0.627	0.698
HF (ms^2)	33.38±15.13	24.61±13.56	23.26±13.02	0.008*	0.095	0.812
LF (un)	50.48±14.37	58.19±14.98	56.81±15.38	0.020*	0.300	0.840
HF (un)	48.39±13.41	41.30±14.08	40.98±19.76	0.022*	0.196	0.959
LF/HF	1.27±0.91	1.69±0.95	1.93±1.52	0.040*	0.097	0.599
SD1	45.56±25.27	31.11±12.67	30.00±17.94	0.004*	0.120	0.848
SD2	92.68±31.81	78.68±17.56	77.05±31.19	0.026*	0.223	0.850
SD1/SD2	0.47±0.20	0.40±0.13	0.37±0.88	0.033*	0.090	0.618

The values are expressed as mean ± standard deviation.
¤ T Test for independent variables. Comparison between category means (*p<0.05).
Units: ms^2, milliseconds squared; nu, normalized units.
HF, high frequencies; LF, low frequencies; SD, value of mean ± standard deviation; HR, hyperreactive; NR, Normoreactive; HTR, hypertensive response.

Table 3. Análisis cuantitativo del ploteo de Poincaré durante el ejercicio isométrico en los grupos de estudio.

Variables	Normoreactive (n=58)	Hyperreactive (n=31)	Hypertensive response (n=8)	NR-HR p¤	NR-HTR p¤	HR-HTR p¤
SD1	35.68±25.4	26.80±15.38	24.01±11.95	0.080	0.240	0.657
SD2	76.13±29.62	64.30±23.43	66.47±23.29	0.058	0.410	0.826
SD1/SD2	0.40±0.165	0.40±0.132	0.34±0.08	0.334	0.169	0.287

The values are expressed as mean ± standard deviation (milliseconds).
¤ T Test for independent variables. Comparison between category means.
HR, hyperreactive; HTR, hypertensive response; NR, normoreactive; SD, value of mean ± standard deviation.

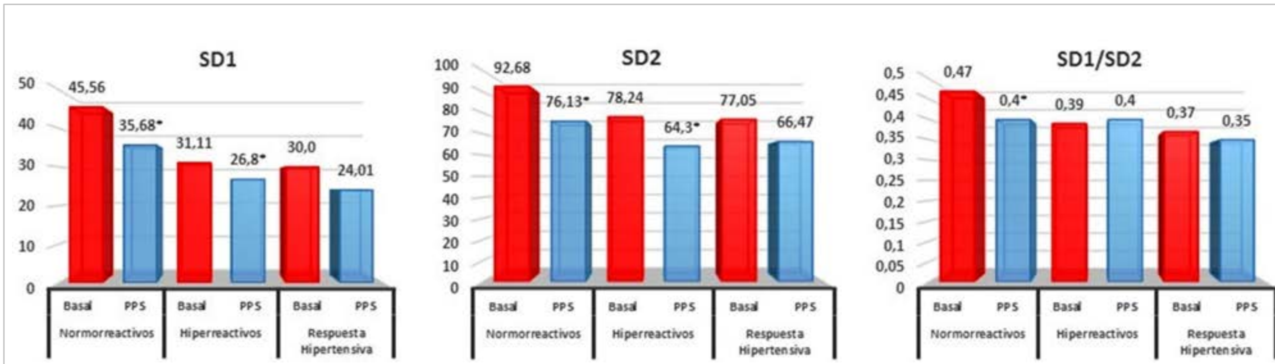

Figure 1. Autonomous basal balance compared to exercise through Poincaré plot. Values are expressed as mean. T Test for comparing related variables (*p<0.05).
WBT: Dynamic weight-bearing test; SD, standard deviation.

DISCUSSION

The study of HRV has been shown to be useful at determining cardiovascular risk and is considered an independent risk marker. Studies on the role of the autonomic nervous system as a modulator of tissue damage progression in diseases such as systemic hypertension and diabetes mellitus are currently gaining renewed interest[4].

Heart Rate Variability is defined as the variation among the intervals between heartbeats and is strongly linked to autonomic modulation. The sympathovagal balance is dependent on the number of internal and external factors acting through retroaction mechanisms that regulate heart rate at different time scales (baroreceptor information, chemoreceptors, atrial and ventricular receptors, changes in respiratory rate, vasomotor system, renin-angiotensin system and thermoregulation mechanisms)[18]. Moreover, it has been suggested that inadequate blood pressure regulation by the autonomic nervous system plays major role in in the genesis of essential hypertension[19]. An increased sympathetic activity is responsible for cardiovascular hyperreactivity and its diagnosis is used as a predictor of high blood pressure[20,21].

The R-R interval variations under resting conditions represent a fine tuning of the beat-to-beat modulating mechanisms. Vagal afferent stimulation leads to reflex excitation of vagal efferent activity and sympathetic efferent inhibition. The opposite reflex effects are mediated by the stimulation of sympathetic afferent activity; on the other hand, vagal and sympathetic efferent activity directed to the sinus node are characterized by synchronous discharge with each cardiac cycle that can be modulated by central oscillations (vasomotor and respiratory centers) and peripheral oscillations (oscillation in arterial pressure and respiratory movements). These oscillators generate rhythmic fluctuations in efferent neural discharge that manifest as long and short oscillation in the cardiac cycle[22,23].

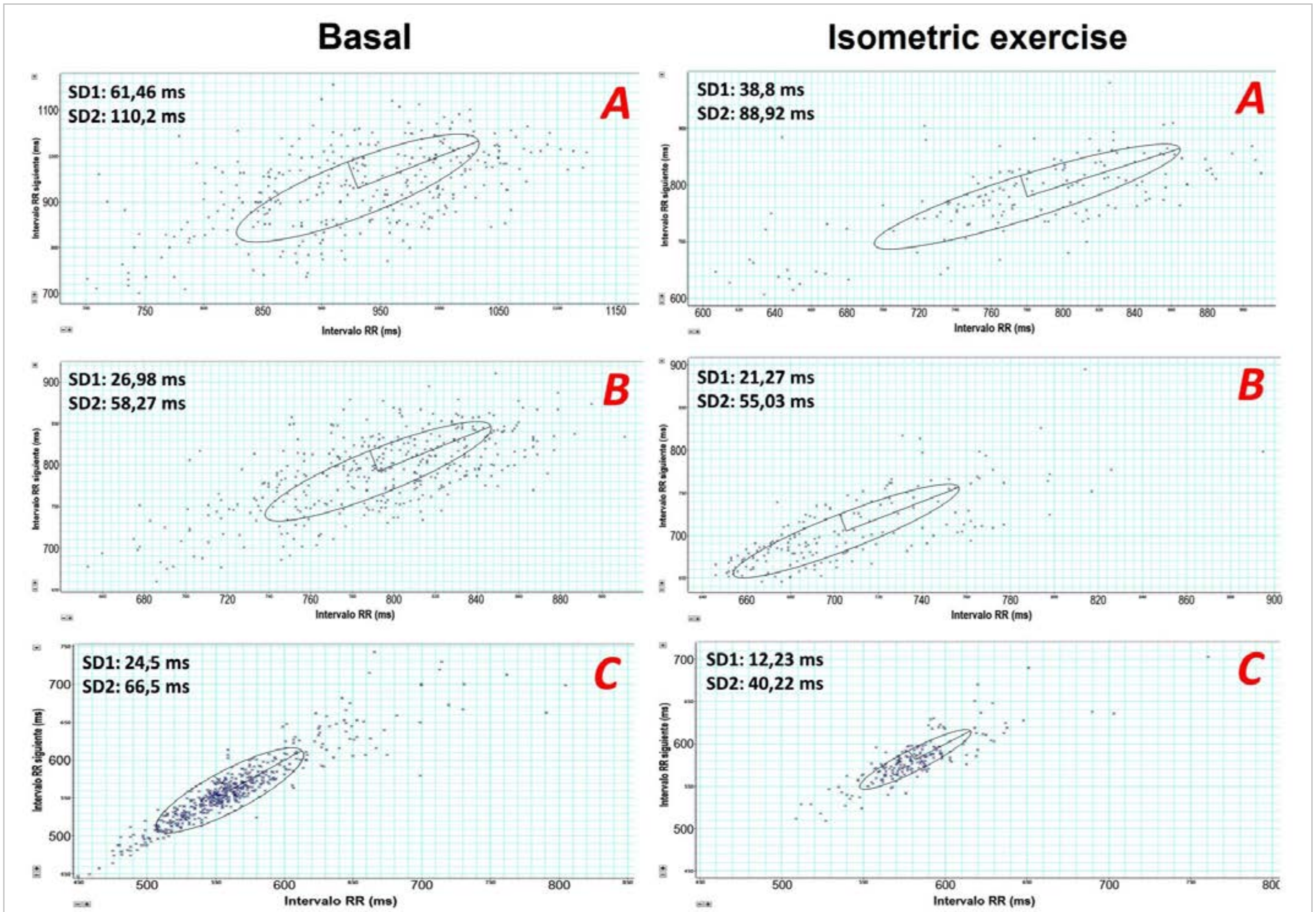

Figure 2. Poincaré diagram in individuals with different degree of cardiovascular reactivity at rest and during exercise. **A:** normoreactive subject. **B:** subject with hyperreactive response. **C:** subject with hypertensive response. SD, standard deviation.

Vagal efferent activity is an important contribution for the HF component (0.15-0.4 Hz) under controlled conditions. Furthermore, it reflects respiratory control and is determined by the frequency generated by respiratory sinus arrhythmia. There is an ongoing debate about the physiological significance of the LF band (0.04 to 0.15 Hz). It is thought to be influenced by sympathetic eference to skeletal muscles and the vascular system or as a measure of sympathetic modulation, when expressed in standardized units (LFun). Other investigations show that it is determined by the baroreceptor reflex feedback mechanisms[1,4]. However, some authors interpret it as indicator of efferent activity from the two branches of the autonomic nervous system; though we must consider that the sympathetic and parasympathetic nervous systems interactions are complex, non-linear, and often not non-reciprocal. Hence, LF/HF index is considered as a reflection of the global autonomic balance[4].

In some conditions associated with sympathetic excitation, as in the case of physical exercise a decrease in the absolute power of the LF component is seen. So it is important to recall that the resulting increased HR is usually accompanied by a reduction in HRV, whereas the opposite occurs with vagal activation. BP elevation reactivates baroreflex sensitivity and cardiac parasympathetic modulation during this context[23].

Our study corroborates that under basal conditions the HF component (in normalized units) is lower in hyperreactive individuals with a hypertensive response, which is reflected in an increased LF/HF ratio in relation to normoreactives. That is, they are less influenced by efferent vagal component in the cardiac activity modulation, which is validated in the lower SD1/SD2 ratio and indicates an increase in sympathetic activity and a decrease in long-term HRV changes.

It is known that there is a predominance of vagal tone over cardiac activity in healthy individuals under resting conditions. However, several authors have reported that in healthy children with hypertensive parents a reduction of autonomic vagal modulation at rest and an impaired response to changes in posture is already present. This may eventually increase blood pressure and risk of cardiometabolic disease[19,24]. Likewise, Almeida *et al*[25] found that in addition to autonomic dysfunction under basal state, children with hypertensive parents have a reduced autonomic modulation during isometric exercise; consistent with our findings on hyperresponsive individuals with a hypertensive response.

According to Sassi *et al*[17], a meta-analysis concluded that the main studies conducted in different types of hypertension point to an influence of the autonomic nervous system characterized by a global decrease in HRV and, particularly, in the parasympathetic component. These authors suggest that hypertension initially promotes an autonomic imbalance that causes difficulties in adapting cardiac function to minimum conditions of physical or mental stress.

In the present study, both blood pressure and HR were increased in all groups during WBT. It is known that during the exercise there are cardiovascular readjustments that guarantee flow distribution to the muscles in activity and metabolites elimination. The hemodynamic changes that occur in response to this isometric test are well established in young adults and include an increase in mean arterial pressure, caused mainly by an increase in total peripheral resistance with a slight increase in cardiac output and in HR[26].

The mechanisms responsible for these responses are central and peripheral, within which there is a central command and a feedback system that operates afferent from receptors located in the skeletal muscles, which are contracted and integrated with the information arriving from the arterial baroreceptors at the brainstem level. The central mechanism activates neuronal pathways in the central nervous system that modify the sympathetic and parasympathetic systems activity and determine cardiovascular responses[27].

There are evidences in electromyographic records demonstrating how the activation of a greater number of motor units in muscle fibers during contraction are related to the neural mechanism of the central command, which determines immediate changes in sympathetic and parasympathetic efferent activity at heart level and the sympathetic nervous system of the blood vessels. Moreover, the reflex mechanism related to the metabolic mechanical activity of the muscle in activity also determines the autonomic response level to the cardiovascular system28. This reflex is mediated by group III afferent fibers that are activated by the mechanical stimulus of muscle tension and length changes, and type IV afferent fibers activated by the metabolic products of muscle contraction[28].

Dos Santos *et al*[27] summarize several studies published over ten years with different protocols and designs on cardiac adjustments to isometric exercise. These authors conclude that cardiac autonomic modulation during exercise is characterized, initially, by a decrease in vagal activity, followed by an increase in sympathetic modulation, which is reversed during the recovery phase. On the other hand, Weippert *et al*[29], when comparing cardiac response to dynamic exercise and static isometric type, reported that the results of the HRV analysis in time and frequency domain indicate an increase in the parasympathetic modulation of HR during isometric exercise. In this sense, Gonzalez-Camarena *et al*[30] found that HRV was reduced in the dynamic exercise and increased during the isometric exercise. These authors suggest an increase in the vagal impulse through the baroreceptors, secondary to sympathetic activation. Michael *et al*[31] consider that the use of standardized parameters in the frequency domain and the LF/HF ratio as indicators of sympathetic autonomic activity and sympathetic-vagal balance during exercise should be questioned due to contradictions found between different studies by the influence of non-neural factors on the HF parameter, mainly on respiration. This was corroborated in our investigation, which was why we decided to use the Poincaré plot.

It is known that traditional methods such as spectral analysis require time intervals of stationary R-R series. During physical exercise this condition is not fulfilled and this may lead to contradictory and inconsistent results[31,32]. In contrast, the Poincaré plot is based on the notion of different temporal effects of the changes in sympathetic and parasympathetic modulation in the HR and in the subsequent R-R intervals, without requiring stationary time intervals[33].

The Poincaré diagram allows to analyze the dynamics of changes in the autonomic nervous system activity on the heart. It shows a morphology that is easily visually analyzed, since SD1 axis measure is proportional to the parasympathetic influence, and that of SD2 axis is inversely proportional to the sympathetic activity. In this way, when observing a narrow graph, parasympathetic activity will be reduced with the consequent sympathetic domain. On the other hand, when the diagram is more dispersed in the transverse direction, there is an increased vagal activity[34,35].

It has been suggested that among the mechanisms underlying isometric exercise response in individuals with cardiovascular hyperreactivity may be an abnormal response of the baroreflex function and pressure reflex. Likewise, it has been shown that they present an intensified activity of muscular sympathetic nerve activity in response to the handgrip test due to the activation of the reflex mechanism related to the metabolic activity of the muscle in action[20].

CONCLUSIONS

Hyperreactive individuals with a hypertensive response have at baseline an autonomic imbalance due to a decrease in vagal tone and an increase in sympathetic activity with a lower variability of heart rate compared with normoreactive ones. During isometric exercise, nervous adjustments are made in the control of cardiac function that guarantee an adequate blood flow to the muscles in activity; However, in individuals with hyperreactivity there is a reduction in autonomic vagal modulation, which is why they have a lower capacity to adapt to stressors, which could favor the development of high blood pressure.

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