

Evaluation of Heart Rate Variability in Trained and Sedentary Climacteric Women

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Summary

Background: Changes in autonomic cardiac function are frequent during menopause, and various methods have been used to understand and minimize them.

Objective: To study the interference of dynamic aerobic physical activity on heart rate variability (HRV) in climacteric women.

Methods: Cross-sectional study that analyzed HRV in 15 menopausal women (mean age 56.8 ± 4.9 years) who had participated in physical training (one-hour walks, 3 times a week) for at least two years (active group), and 15 menopausal women (mean age 56.5 ± 3.7 years) who were sedentary (sedentary group). None of the volunteers received hormonal replacement therapy. HRV data were compared between the groups by means of the Mann Whitney U Test.

Results: There were significant differences both in the frequency and time domains of the following variables of HRV (in medians) for the active e sedentary groups, respectively: total power (22,626.50 ms² and 4,432.10 ms²), low frequency component (741.20 ms² and 131.70 ms²), high frequency component (668.90 ms² and 131.70 ms²), standard deviations of RR intervals (51.60 ms and 22.50 ms), square root of the sum of squares of differences between the normal RR intervals (35.30ms and 15.90 ms), and percentage of normal adjacent RR intervals greater than 50ms (6.6% and 0.2%).

Conclusion: The study suggests that aerobic training may have afforded a significant improvement in the autonomic cardiac function of the menopausal women in the active group, and may be a useful option for preserving this functional condition without the need for hormonal replacement therapy. (Arq Bras Cardiol 2008; 90(2):74-79)

Key words: Climacteric; women; autonomic nervous system; heart rate.

Introduction

Menopause is a period of physiological decline in ovarian function when there are endocrine, somatic, and psychic changes. Menopause may be defined as the stage of the aging process which marks the transition from the reproductive phase of life to the post-reproductive phase of life.

Although the exact moment of climacteric onset is difficult to determine, it generally begins around 40 years of age and varies considerably from one woman to another, with diverse manifestations. Nonetheless, it is known that hormonal and physical changes are ongoing and that they occur so gradually so as to become almost imperceptible².

As to cardiovascular disease (CVD), women exhibit the same risk factors as men, i.e., systemic arterial hypertension, smoking, diabetes mellitus, obesity, sedentarism, hypercholesterolemia, stress, and familial antecedents of the disease. Nevertheless,

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CVDs have low rates during the reproductive years, primarily due to the maintenance of high levels of HDL (High Density Lipoprotein) cholesterol by estrogen activity. After menopause, this risk increases significantly and progressively approaches the rates seen in men².

Therefore, coronary artery disease has become one of the main causes of death during menopause and is directly related to decreased tissue blood flow caused by an accelerated formation of atheromatous plaques and alterations in vasomotricity regulating mechanisms³ which are responsible for the following problems, respectively: changes in the metabolism of lipoproteins^{4,5}, of carbohydrates, and the production of insulin⁶, all probable facilitators of the onset of obesity⁷ and arterial blood pressure alterations⁸, culminating with a worsening of hypoestrogenism.

Among the various methods used to control the effects of changes in cardiac function resulting from menopause, physical activity has stood out because of its wide success in offering cardiac and multisystem benefits to those who practice it, with insignificant side effects. This differs from hormonal replacement therapy, which despite having progressed in this aspect, still raises concerns because of its association with some types of neoplasms⁹, worsening of uterine myomas, and

reactivation of pelvic endometriosis.

Nevertheless, studies that analyze the benefits of physical activity for this population, and especially the possible positive adaptive modifications of cardiac autonomic functions in response to aerobic training programs, are infrequent.

Even so, as it is a non-invasive and easily accessible tool, Heart Rate Variability (HRV) assessment has been chosen for this type of investigation since in addition its use in revealing cardiac changes linked to physical training programs, it is also used in studies on human aging¹⁰⁻¹⁴, as was proposed in the present investigation.

Thus, the objective of this study was to investigate the interference of low intensity dynamic aerobic physical activity performed frequently by menopausal women in a biological marker linked to the natural aging process represented by tone and modulation of cardiac autonomic function extracted from HRV analysis.

Methods

Sample - Thirty-seven women aged 45 to 65 years who were menopausal, clinically menopausal, and postmenopausal were initially considered for participation in the study. According to inclusion and exclusion criteria, the women were divided into two groups and seven of them were excluded from the study because of irregular findings on their ECG tracings that suggested the presence of pathological conditions. These women were instructed to seek specialized medical care.

The 30 remaining women composed the Active and Sedentary groups, respectively, with 15 women in each group. The 15 active women had an mean age of 56.8 ± 4.9 years and had participated for at least two years in the group for senior women offered by the Secretariat of Social Services of a municipality of the State of São Paulo. The 15 sedentary women chosen had a mean age of 56.5 ± 3.7 years.

Sedentary group inclusion criteria - Women who could participate in this group were those who had clinical proof of being menopausal (amenorrhea for at least one year), were sedentary, had not regularly engaged in any type of physical activity for at least six months, did not perform any type of intensive housework such as cleaning, did not smoke, were not using any type of medication that might interfere in the results, did not receive hormonal replacement therapy, and presented no history of cardiovascular disorders and metabolic diseases.

Active group inclusion criteria - The same prerequisites as above, with the difference that these women had to have been engaged in light to moderate physical activity for at least two years, such as walking three times a week, with 50- to 60-minute sessions, maintaining their heart rates in a zone between 100 and 110 beats a minute (bpm) during the first 3 months, and between 110 and 120 bpm in the subsequent months.

Study exclusion criteria - Women who did not satisfy the inclusion criteria and refused to sign the informed consent form for any reason could not participate in the study.

The research project was approved by a Committee of Ethics in Research Involving Human Participation.

Procedures

The procedures began on the day before data collection, and the subjects were instructed to not exercise, drink alcoholic beverages, coffee, tea, and sodas with stimulants or eat chocolate in the 24 hours prior to the tests and to sleep for at least seven hours the night before evaluations.

Data collection began, always during the morning period, with determinations of body weight and height (Filizolla® scales) and clinical data, as is shown on Table 1.

Next, in order to register heart beats for posterior HRV analysis, all the volunteers were taken to a room with temperature controlled at 23°C, in a quiet environment, and a cardiofrequency meter (S810 Heart Rate Monitor®, Kempele – Finland) was affixed to their chests. The subjects were then placed in supine position in which they remained for 12 minutes, total time of the register. During this procedure, they were instructed to not converse and not move except for closing their eyes in order to relax.

Later, the recorded beats were directed to a computer by means of an IR-Polar® interface for transmission of infrared signals, and Polar Precision Performance® - Finland, and Nevrokard *HRV®* - Slovenia, programs were used to analyze the HRV in the domains of time (TD) and frequency (FD).

Analysis of the HRV in TD refers to the application of certain statistical procedures to successive normal RR intervals (RRi) on the ECG, within a certain period of time¹³. In this way, calculations could be made of the RRi mean and standard deviation of the RRi mean, among other possibilities, each one with a significance representative of autonomic functions reflecting the cardiac vagosympathetic balance at that timepoint.

Analysis in the FD, also called spectral analysis, consists in a study method that allows the decomposition of the HR variation within a certain time period for its fundamental oscillatory components, defining them by frequency and amplitude¹⁵.

For HRV analysis, the first and the last minute of the recording were excluded, and the 10 central minutes were isolated (for greater tracing stability). Additionally, in order to guarantee quality of the signal and elimination of probable

Table 1 - Age, anthropometric, and clinical data of volunteers

Variables	Active Group Mean ± standard deviation	Sedentary Group Mean ± standard deviation	P value
Age (years)	56.8 ± 4.9	56.5 ± 3.7	0.91
Weight (kg)	69.4 ± 10.4	74.2 ± 13.5	0.45
Height (cm)	160.0 ± 0.0	161.0 ± 2.0	1.0
BMI	26.6 ± 3.5	28.2 ± 3.8	0.38
Heart rate (bpm)	64.1 ± 8.6	70.2 ± 8.9	0.08
Systolic arterial pressure (mmHg)	125.0 ± 8.6	125.3 ± 11.2	0.86
Diastolic arterial pressure (mmHg)	82.3 ± 6.7	80.6 ± 9.6	0.39

BMI - body mass index

artifacts, a very strong filter was applied, as a standard part of the programs themselves which provided reports with values of TD and FD variables submitted to statistical analysis.

In order to assess HRV in TD, values of the normal mean RRi, standard deviations (SD) of normal RRi, root mean square of successive differences between adjacent RRi (RMSSD), and the percentage of adjacent RRis with a difference greater than 50ms (pNN50) were analyzed.

In the FD, total power (TP) values were studied which represent the variance of normal RRi on the temporal segment of the record¹³, absolute values of the Low Frequency (BF - more related to sympathetic cardiac activity) and High Frequency (HF - related to parasympathetic cardiac activity) components, and the LF/HF ratio.

Statistical analysis

For comparative analyses of the HRV variables among the groups, the Mann Whitney U test was used and the results are presented in boxplots with highlights for medians, 1st and 3rd quartiles, and extreme values. This test was chosen because this study deals with data that show differences between the two groups (Active and Sedentary), as measurement/evaluation procedures provide knowledge of facts with at least an ordinal level of measurement.

An ordinal level of measurement means that the hierarchy of data is known (by posts), but the intensity and degree of the differences are not completely known or are not perfectly exact. The U Test is a non-parametric test and is, therefore, appropriate since it involves two distinct (independent) samples submitted to the same data collection procedure.

For the same reason, the samples can also be classified as non-paired. Additionally, the Mann Whitney U Test is adequate for evaluating small and average-sized samples, as is the case in this study, allowing good quality judgments. In this way, despite the small number of volunteers (n), the results of the tests applied were at a p \leq 0.01 level among the values of variables, which means that the differences observed in the sample may be extended to the population.

Results

As to ages and anthropometric and clinical evaluations (Table 1), it is clear that the groups are homogenous, with no significant differences between the data compared, and therefore, they do not interfere in the study.

Regarding heart beat records, the analysis of HRV performed in the FD can be visualized in Figures 1, 2 and 3 with the boxplot presentations. There were significant differences (p<0.0001) between the groups, considering the absolute variables TP, LF, and HF. The Active group showed median values for TP, HF, and LF of 22,626.5 ms², 741.2 ms², and 668.9 ms², respectively. The Sedentary group presented median values for TP, HF, and LF of 4,431.1 ms², 131.7 ms², and 119.4 ms², respectively.

These data show that both sympathetic and parasympathetic tone was greater in the group of Active women, and that both bear a significant influence on the Total Power value.

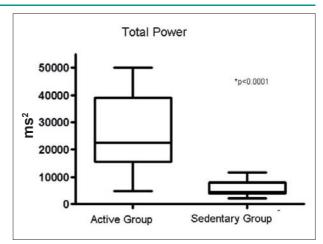


Figure 1 - Total power values obtained in the Active and Sedentary groups by analysis of heart rate variability (HRV) performed in the frequency domain (FD). Data are presented as boxplots that represent median, 1st and 3rd quartiles, and extreme values.

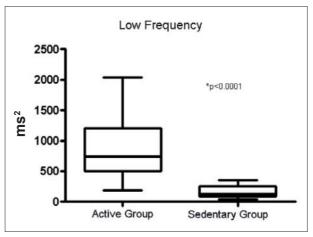


Figure 2 - Low Frequency values obtained in the Active and Sedentary groups by analysis of heart rate variability (HRV) performed in the frequency domain (FD). Data are presented in boxplots that represent medians, 1st and 3rd quartiles, and extreme values.

On the other hand, the LF/HF ratios, since they take into account the values of LF and HF for their calculation in normalized units, were not different between the groups.

Despite the values of mean RR intervals (RRi) not having proved different in the HRV analysis in the TD, Figures 4, 5, and 6 show that there was a significant difference between the median values of the groups for: a) standard deviations of RRi, with 51.6 ms for the Active group and 22.5ms for the Sedentary group; b) RMSSD with 35.3ms and 15.9ms for Active and Sedentary women, respectively, and c) pNN50 with the active women showing 6.6% and sedentary women, 0.2%.

These differences express significant autonomic cardiac differences present in the Active group captured in the analysis performed in TD and FD, which, in general, reflect the greater autonomic sensitivity on the part of this group.

Similarly, we point out that all these positive changes related to autonomic cardiac modulation are linked to respiratory sinus

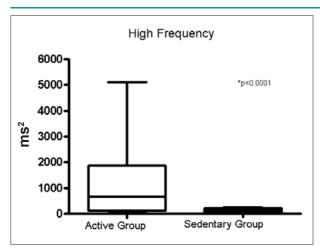


Figure 3 - High Frequency values obtained in the Active and Sedentary groups by analysis of the heart rate variability (HRV) performed in the frequency domain (FD). Data are shown as boxplots that represent medians, 1st and 3rd quartiles, and extreme values.

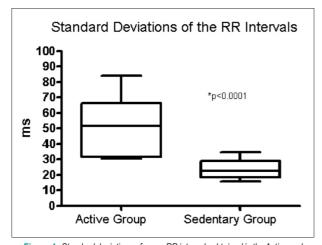


Figure 4 - Standard deviations of mean RR intervals obtained in the Active and Sedentary groups by analysis of heart rate frequency (HRV) performed in the time domain (TD). Data are presented as boxplots that represent medians, 1st and 3rd quartiles, and extreme values.

arrhythmia (RSA)¹⁶ - cyclical changes of heart beats in syntony with respiration - present more often in young adults¹³, athletes¹⁷, and in people with healthy lifestyle habits.

Discussion

Despite a natural tendency towards weight gain in sedentary people¹⁸ and the fact that no diet control was used for the study participants, there was a concern that body weight be similar among the participants in order to avoid its interference in the results. In this way, we noted that the values of this variable and of all the other variables shown on Table 1 express very similar results between the groups, affording greater standardization to the sample in this aspect.

Nevertheless, as to the resting HR, studies have shown a tendency toward reduction of the values of this variable in

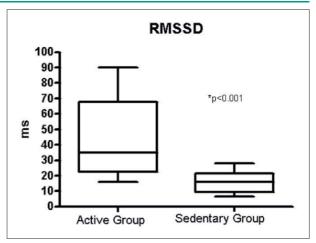


Figure 5 - Root mean square of successive differences between adjacent RRi values (RMSSD) obtained in the Active and Sedentary groups by analysis of the heart rate variability (HRV) performed in the time domain (TD). Data are presented as boxplots that represent medians, 1st and 3rd quartiles, and extreme values.

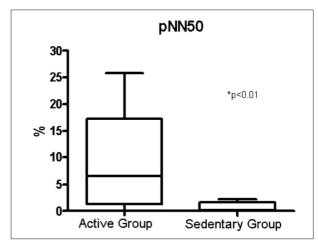


Figure 6 - Values of percentages of adjacent RR intervals greater than 50ms (pNN50) obtained in the Active and Sedentary groups by analysis of heart rate variability (HRV) performed in the time domain (TD). Data are presented as boxplots which represent values of medians, 1st and 3rd percentiles, and extreme values

trained individuals which are different from the values for sedentary participants¹⁹. In this study, however, even though this did not occur, which may be due to the number of volunteers since the value of p was 0.08, which is very close to significance, the values of HR did not influence the analysis of the HRV which showed a significant difference of autonomic modulation between the groups.

We noted that the values of resting HR documented and included in Table 1 were true to the values of the mean RR intervals recorded for 10 minutes which served as basis for the HRV calculation, since the values of these intervals did not differ between the groups during HRV analysis.

As to the other data on Table 1, we point out that this similarity between the groups is due to the fact that the Sedentary group was made up of healthy women, and

therefore the values of the variables fall within parameters of normality.

As to the HRV, it was used to determine likely differences in autonomic cardiac modulation between the women of both groups. This tool was chosen because, under control conditions, it offers extremely sensitive data (fine tuning) of the cardiac adjustment mechanisms, beat by beat, in response to homeostatic and tissue needs^{20,21}, and also because it has already been used in other studies involving climacteric women^{22,23}.

It is known that vagal and efferent activities directed at the sinoatrial node are characterized by a discharge highly synchronized with each cardiac cycle which can be modulated by central (vasomotor and respiratory centers) and peripheral (BP oscillations and respiratory movements) oscillatory components are present in the control conditions used in the present investigation, generating rhythmic fluctuations in the efferent nervous discharges that are manifested in the heart by short and long duration oscillations of the RR intervals, affording a greater or lesser HRV, and therefore, a greater or lesser autonomic cardiac tone¹³.

With age, however, and the decline of estrogenic hormonal production, there is a reduction of the parasympathetic component and, consequently, of the HRV in women after menopause²⁵.

This aspect can be highlighted in the study carried out by Brockbank et al²⁵ who noted a statistically significant reduction in the RR interval (RRi) of postmenopausal women, reinforcing the evidence of a decline of cardiac contractility²⁶, a decline in left ventricular systole²⁷, and changes in baroreceptors in the postmenopausal period.

More relevant than the RRis themselves, the standard deviations (SD) of the mean RRis more adequately reflect vagal modulation of the heart^{11,13}, since the greater the standard deviation of the RRis found, the greater the parasympathetic tone, exactly as was observed in this study, with a significant difference of RRi SDs between the groups, and the greatest values were shown by the active women.

In this way, aerobic exercise is credited with the positive modification of cardiovascular health in this group of women, as had previously been documented in other studies involving individuals of this same age bracket^{11,28-32}.

Myslivecek et al²⁸ presented results similar to ours when they investigated if moderate aerobic training influenced HRV and the spontaneous bar reflexive function in middle-aged women. For this, 32 pre- and post-menopausal sedentary women were selected. After training, the results suggested that even a short aerobic exercise program, when carried out consistently and according to proposed guidelines of physical activity, can increase vagal modulation in middle-aged women.

Additionally, Perini et al²⁹ showed an increase in autonomic cardiac modulation revealed by analyses of HRV made before and after moderate and vigorous aerobic training programs applied to elderly men and women. Moreover, as was documented in this study, these authors reported greater values of the Total Power in the trained group.

In 2004, Jurca et al³³ performed a randomized controlled study with 88 sedentary post-menopausal women divided into two groups. Forty-nine of them participated in an aerobic exercise program carried out for eight weeks, with an average 44 minutes per session, three to four times a week, and an intensity of 50% of the maximum VO₂, while the other 39 formed a control group in which the women continued with their normal lifestyles. The study showed that after the eight weeks, the women who participated in the training program showed a decrease in the resting HR besides an increase in all values of HRV variables in TD and FD, especially RMSSD, LF, HF, and Total Power in absolute units.

As in the present study, the intensity of the exercises applied by Jurca et al³³ was light, and the results of the variable values in the FD, expressed in normalized units, showed no changes after training.

Sometimes the simple analysis of HRV in normalized units (NU) without careful attention can give a false impression that there was no difference between the data analyzed. We point out that the 62.5% (in NU) in the LF for the active women represents, in absolute values, 741.2 ms², while for the sedentary women, the 62.1% of LF represents only 131.7 ms². Similarly, the 37.5% in HF for active women represents, in absolute values, 668.9 ms², while the 37.9% in sedentary women is equivalent to 119.4 ms², with a significant difference between the figures.

Limitations of our study were: number of women evaluated, absence of a control of stress factors which could interfere in the results, and the absence of thyroid function tests - TSH T4, crediting the health of the volunteers only to their clinical parameters.

As to future studies, we believe that there is still much to be investigated on the effects of the different intensities and durations of aerobic exercises. However, there are already strong indications that the important thing is to engage in physical exercise, since studies with light intensity activity and those with moderate intensity activity all showed encouraging results as to the positive modification of HRV.

Conclusions

We concluded that the frequent practice of light-intensity aerobic exercise, with the heart rate controlled between 100 and 120 bpm, performed three times a week for two years by climacteric women with no hormonal replacement, may have been responsible for the improvement in autonomic heart function revealed by HRV analysis, represented by a significant increase in vagal and sympathetic modulation in the domain of frequency (FD) with important reflections on the Total Power result.

Equally, in the domain of time (TD), the analysis of HRV showed a significant improvement of the components that reflect vagal activity, which is considered cardio-protective, in active women, confirming that this analysis may be a very important parameter in this type of investigation.

In this way, frequent aerobic activity, even at a low intensity,

proved to be an excellent option for preservation and/or improvement of autonomic cardiac function in climacteric women who do not tolerate the use of hormone replacement therapy, whether because of discomfort or even the fear of the possibility, still debatable, of this type of treatment being responsible for neoplasms, aggravation of uterine myomas, and reactivation of pelvic endometriosis, besides the risk for development of thromboembolic diseases.

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References

- Copeland JF. Tratado de ginecologia. Rio de Janeiro: Guanabara Koogan; 1996.
- Fernandes CE. Menopausa: diagnóstico e tratamento. São Paulo: Editora Solvay Farma; 2003.
- Satmpfer MJ, Colditz GA. Estrogen replacement therapy and coronary heart disease: a quantitative assessment of the epidemiologic evidence. Prevent Med. 1991: 20: 47-63.
- 4. Henderson BE, Paganini-Hill A, Ross PK. Decreased mortality in users of estrogen replacement therapy. Arch Intern Med. 1991; 151-7.
- Stevenson JC, Crook D, Godsland IF, Collins P, Whitehead MI. Hormone replacement therapy and cardiovascular system nonlipid effects. Drugs. 1994: 47: 35-41.
- Walton C, Godsland IF, Proudler AJ, Wynn V, Stevenson JC. The effects of the menopause on insulin sensitivity, secretion and elimination in non-obese, healthy women. Eur J Clin Invest. 1993; 23: 466-73.
- Haarbo J, Marslew U, Gotfredsen A, Christiansen C. Postmenopausal hormone replacement therapy prevents central distribution of body fat after menopause. Metabolism. 1991; 40: 1323-6.
- 8. Brosnihan KB, Moriguchi A, Nakamoto H, Dean RH, Ganten D, Ferrario CM. Estrogen augments the contribution of nitric oxide to blood pressure regulation in transgenic hypertensive rats expressing the mouse Ren-2 gene. Am J Hypertens. 1994; 7: 576-82.
- 9. Halbe HW. Tratado de ginecologia. 2ª ed, São Paulo: Ed. Roca, 1993.
- Agelink MW. Standardized tests of heart rate variability: normal ranges obtained from 309 heathy humans, and effects of age, gender and heart rate. Clin Auton Res. 2001; (11): 99-108.
- Paschoal MA, Volanti VM, Fernandes FC. Variabilidade da freqüência cardíaca em diferentes faixas etárias. Rev Bras Fisioter. 2006; 10 (4): 4139.
- Silva CS, Marques LS, Moraes FR, Catai AM, Oliveira L, Silva E. Investigação da variabilidade da freqüência cardíaca de mulheres nos períodos manhã e noite. Rev Bras Fisioter. 2001; 5 (2):65-71.
- Heart rate variability: standards of measurement physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation. 1996; 93 (5):1043-65.
- Migliaro ER, Contreras P, Bech S, Etxagibel A, Castro M, Ricca R, et al. Relative influence of age, resting heart rate and sedentary life style in short term analysis of heart rate variability. Braz J Med Biol Res. 2001; 34 (4): 493-500.
- 15. Longo A, Ferreira D, Correia MJ. Variabilidade da frequência cardíaca. Rev Port Cardiol. 1995; 14 (3): 241-62.
- Grossman P, Wilhelm FH, Spoerle M. Respiratory sinus arrhythmia, cardiac vagal control and daily activity. Am J Physiol. 2004; 287: H728-H734.
- Shin K, Minamitani H, Onishi S, Yamazaki H, Lee M. Autonomic differences between athletes and nonathletes: spectral analysis approach. Med Science Sports Exerc. 1997; 29: 1482-90.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any graduation program.

- 18. Smith KR. Exercise can help control body changes during menopause. Health Care Food Nutr Focus. 2005; 22(10):10-2.
- Katona PG, McLean M, Dighton DH, Guz A. Sympathetic and parasympathetic cardiac control in athletes and nonathletes at rest. J Appl Physiol. 1982, 89: 1652-7.
- Akselrod S, Gordon D, Madwed JB, Snidman NC, Shannon DC, Cohen RJ. Hemodynamic regulation: investigation by spectral analysis. Am J Physiol. 1985: 249: H867-H875.
- Saul JP, Rea RF, Eckberg DL, Berger RD, Cohen RJ. Heart rate and muscle sympathetic nerve variability during reflex changes of autonomic activity. Am J Physiol. 1990; 258: H713-H721.
- 22. Sakabe DI, Catai AM, Neves VFC, Oliveira L, Silva de Sá MF, Azevedo GD, et al. Análise da modulação autonômica do coração durante condições de repouso em homens de meia-idade e mulheres pós-menopausa. Rev Bras Fisioter. 2004; 8 (1): 89-95.
- 23. Kimura T, Matsumoto T, Akiyoshi M, Owa Y, Miyasaka N, Aso T, Moritani T. Body fat and body lipids in postmenopausal women are related to resting autonomic nervous system activity. Eur J Appl Physiol. 2006; 97(5):542-7.
- 24. Malliani A, Pagani M, Lombardi F, Cerutti S. Cardiovascular neural regulation explored in the frequency domain. Circulation. 1991; 84: 1482-92.
- 25. Brockbank CL, Chaterjee F, Bruce SA, Woledge RC. Heart rate and its variability change after the menopause. Exp Physiol. 2000; 85 (3): 327-30.
- 26. Pines A, Fisman EZ, Drory Y, Levo Y, Shemesh J, Benari E, et al. Menopause-induced changes in doppler-derived parameters of aortic flow in healthy women. Am J Cardiol. 1992; 69: 1104-6.
- 27. Schillaci G, Verdecchia P, Borgioni C, Ciucci A, Porcellati C. Early cardiac changes after the menopause. Hypertension. 1998; 32: 764-9.
- 28. Myslivecek PR, Broen CA, Wolfe LA. Effects of physical conditioning on cardiac autonomic function in healthy middle-aged women. Can J Appl Physiol. 2002; 27 (1): 1-18.
- Perini E, Fisher N, Veicsteinas A, Pendergast DR. Aerobic training and cardiovascular responses at rest and during exercise in older men and women. Med Sci Sports Exerc. 2002; 34 (4): 700-8.
- Gregoire J, Tuck S, Yamamoto Y, Hughson RL. Heart rate variability at rest and exercise: influence of age, gender and physical training. Can J Appl Physiol. 1996; 21 (6): 455-70.
- Tulppo MP, Timo H, Mäkikallio TH, Seppänen T, Laukkanen RT, Huikuri HV.
 Vagal modulation of heart rate during exercise: effects of age and physical fitness. Am J Physiol. 1998; 274 (Pt 2 2): H424-H429.
- 32. Carels RA, Darby LA, Cacciapaglia HM, Douglass OM. Reducing cardiovascular risk factors in postmenopausal women through a lifestyle change intervention. J Womens Health (Larchmt). 2004; 13 (4): 412-26.
- Jurca R, Church TS, Morss GM, Jordan AN, Earnest CP. Eight weeks of moderate-intensity exercise training increases heart rate variability in sedentary postmenopausal women. Am Heart J. 2004; 147 (5): 8-15.