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Spectral and symbolic analysis of the effect of gender and postural change on cardiac autonomic modulation in healthy elderly subjects

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Abstract

The objective of this study was to use linear and non-linear methods to investigate cardiac autonomic modulation in healthy elderly men and women in response to a postural change from the supine to the standing position. Fourteen men (66.1 ± 3.5 years) and 10 women (65.3 ± 3.3 years) were evaluated. Beat-to-beat heart rate was recorded in the supine and standing positions. Heart rate variability was studied by spectral analysis, including both low (LFnu-cardiac sympathetic modulation (CSM) indicator) and high (HFnu-cardiac vagal modulation (CVM) indicator) frequencies in normalized units as well as the low frequency/high frequency (LF/HF) ratio. Symbolic analysis was performed using the following indexes: 0V% (CSM indicator), 1V% (CSM and CVM indicators), 2LV% (predominantly CVM indicator) and 2ULV% (CVM indicator). Shannon entropy was also calculated. Men presented higher LFnu and LF/HF ratio and lower HFnu and 1V% symbolic index (57.56, 4.14, 40.53, 45.96, respectively) than women (24.60, 0.45, 72.47, 52.69, respectively) in the supine position. Shannon entropy was higher among men (3.53) than among women (3.33) in the standing position, and also increased according to postural change in men (3.25; 3.53). During postural change, the LFnu (24.60; 49.85) and LF/HF ratio (0.45; 1.72) increased, with a concomitant decrease in HFnu (72.47; 47.56) and 2LV% (14.10; 6.95) in women. Women presented increased CSM in response to postural change and had higher CVM and lower CSM than men in the supine position. In conclusion, women in the age range studied presented a more appropriate response to a postural change than men, suggesting that cardiac autonomic modulation may be better preserved in women than in men.

Key words: Heart rate variability; Autonomic nervous system; Symbolic analysis; Spectral analysis; Elderly; Gender

Introduction

Heart activity is largely modulated by the autonomic nervous system (1). An important approach to the non-invasive analysis of cardiac autonomic function is heart rate variability (HRV), which refers to oscillations in the intervals between consecutive heartbeats known as RR intervals (RRi) (2). HRV has been widely used as a predictor factor, and its reduction is associated with higher cardiovascular morbidity and mortality rates (3).

Gender is one of the factors that influence HRV. Studies involving models of linear analysis showed that women presented higher HRV in the supine position than men of a similar age, indicating that the female population has a higher cardiac vagal modulation and a lower cardiac sympathetic modulation (4-9). The aging process also interferes with cardiac autonomic modulation, and a decrease in HRV has been observed with aging (3,10-14). However, it has not yet been clearly established if there are any differences in the HRV of elderly subjects due to gender.

Although HRV is commonly analyzed using linear models, the interest in non-linear methods has increased in recent years. This methodology differs from the traditional approach because it considers the qualitative properties

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of the heart rate (HR) time series. The mechanisms that involve cardiovascular regulation are interconnected in a non-linear theory, and therefore non-linear analysis could provide additional information (15-19). A recently used non-linear approach to HRV is the symbolic analysis described by Porta et al. (20). Studies involving pharmacological blockade or autonomic tests showed that the 0V% symbolic index is related to cardiac sympathetic modulation, the 1V% symbolic index corresponds to the simultaneous presence of sympathetic and vagal modulations, and the 2LV% and 2ULV% symbolic indexes are related to cardiac vagal modulation (20-22).

Postural change from the supine to the standing position has also been used for autonomic HR evaluation. This maneuver induces a cardiac sympathetic modulation, which is increased when assessed by a linear methodology, i.e., spectral analysis (23). The same effect is also observed during graded head-up tilt (passive maneuver) by using non-linear methods, i.e., symbolic analysis (22).

Nevertheless, there are no studies in the literature comparing cardiac autonomic modulation between genders in healthy elderly individuals at rest and in response to a postural change (from supine to standing) by using the symbolic analysis of HRV. Moreover, the active standing test does not require a tilt table and can be performed by the bedside (24). It is both more familiar and more functional because it is a daily postural motion performed by everyone, unlike the passive tilt test.

The hypothesis of the present study was that both spectral and symbolic analysis of HRV might be able to detect possible differences in cardiac autonomic modulation responses between genders. Additionally, elderly women were expected to present a lower sympathetic modulation and a higher vagal modulation than elderly men. The postural change from the supine to the standing position was also expected to induce a stimulation of the sympathetic autonomic nervous system, as demonstrated in other age ranges previously studied.

Therefore, the objective of the present study was to investigate HR autonomic modulation in elderly men and women in response to a postural change from the supine to the standing position by using linear and non-linear methods.

Subjects and Methods

Subjects

Thirty-six healthy elderly volunteers (21 men and 15 women) aged 60 to 75 years were selected from places attended by the elderly, such as associations of elderly individuals. Of these, 14 men (66.1 ± 3.5 years) and 10 women (65.3 ± 3.3 years) completed the study. Figure 1 is a flow diagram representing sample loss in this study and details the reasons for this loss.

All subjects were considered to be healthy based on clinical and physical examinations, laboratory tests, standard electrocardiogram (ECG), and a maximum exercise test conducted by a physician. All women were also diagnosed as post-menopausal and none of them was using hormone replacement therapy. None of the subjects presented abnormalities in the cardiovascular or respiratory systems. The ECG results for all volunteers were negative for myocardial ischemia and arrhythmia both at rest and during the maximum exercise test. Smokers, drinkers, users of illicit drugs, subjects with neurological, cardiovascular or respiratory disorders, diabetics and individuals with arterial hypertension were excluded from the study.

Regarding the use of medication, 4 women used calcium replacement drugs, 3 used drugs for controlling thyroid activity (hypothyroidism), and 1 used a drug for controlling dyslipidemia. It is important to emphasize that the hypothyroidism and dyslipidemia presented by the female volunteers were fully controlled by means of regular laboratory tests. Furthermore, studies involving patients with hypothyroidism have shown that an endocrine therapy for restoring euthyroidism normalizes HRV (when analyzed by the time and frequency domains) to values that are similar to those of nondysfunctional subjects (25-28).

Ethical aspects

The study was approved by the Ethics Committee of Universidade Federal de São Carlos, São Carlos, SP, Brazil (protocol #326/2008). All volunteers were informed of the procedures and the noninvasive experiments that would be performed in this study. After agreeing to participate in the study, all subjects signed an informed consent form.

Experimental procedures

All subjects were evaluated in the morning in order to respect the different responses due to circadian influence. The experiments were carried out in a climate-controlled room (21-24°C) with a relative air humidity of 40-60%. Subjects were instructed to avoid both caffeinated and alcoholic beverages as well as any strenuous exercise on the day before the test protocol and until the test application. They were also instructed to have a light meal at least 2 h prior to the test. On the day of the experiment, the subjects were interviewed and examined before the test to determine if they were in good health, if they had slept properly the night before, and that the controlling conditions (HR and systemic blood pressure) were within normal range. Before the experiment, the volunteers were familiarized with the equipment and the experimental procedure in order to reduce anxiety.

Experimental protocol

Subjects remained at rest for 10 min in the supine position and were then instructed to perform the postural change from the supine to the standing position, remaining in that position for 10 min. During this period, the ECG was monitored using a CM5 lead, recorded with a one-channel heart monitor (TC500, ECAFIX, Brazil) and processed with a Lab-PC+ analog-to-digital converter (National Instruments Co., USA), which served as an interface between the heart monitor and a Pentium III PC. Signals were recorded in real time after analog-to-digital conversion at a sampling rate of 500 Hz; the RRi (ms) were calculated on a beat-to-beat basis with specific software (29).

During the recording of the ECG in the supine and standing positions, the respiratory rate was simultaneously recorded on a cardiopulmonary exercise system (CPX/D, Medical Graphics, USA) with a neoprene facemask as an interface. The subjects were instructed to breathe spontaneously throughout the procedure. At the beginning and end of the experiment, the blood pressure of all volunteers was measured by the auscultatory method.

Data analysis

RRi sequences of length N = 250 were selected for the two positions (supine and standing) for each subject. For each position, the length of greatest stability was chosen from the central region of the time series. The initial and final RRi sequences were discarded. The same sequence was used for both the spectral and the symbolic analysis. The mean and variance of RRi were also calculated.

HRV spectral analysis

The HRV frequency domain analysis was performed with an autoregressive model (30,31) on previously selected RRi sequences. Two main spectral components were considered, i.e., low frequency (LF: from 0.04 to 0.15 Hz) and high frequency (HF: from 0.15 to 0.50 Hz) because they best represent the sympathetic and vagal modulations, respectively (2). The respiratory rate was confirmed to assure that it was in the frequency range included in the HF band. All volunteers were within the range, except for one man and one woman who were excluded from the study. The spectral components are reported as normalized units (LFnu and HFnu) and LF/HF ratio. Normalization consisted of dividing the power of a given spectral component (HF or LF) by the total power minus the power below 0.04 Hz, and multiplying the ratio by 100 (30,31).

HRV symbolic analysis

HRV non-linear analysis by symbolic analysis has been described by Porta et al. (20). Briefly, this approach is based on spreading the full range of the RRi sequences on 6 levels (from 0 to 5), transforming them into a sequence of integers (i.e., symbols). Patterns (sequences of 3 symbols) are constructed based on the sequence of symbols.

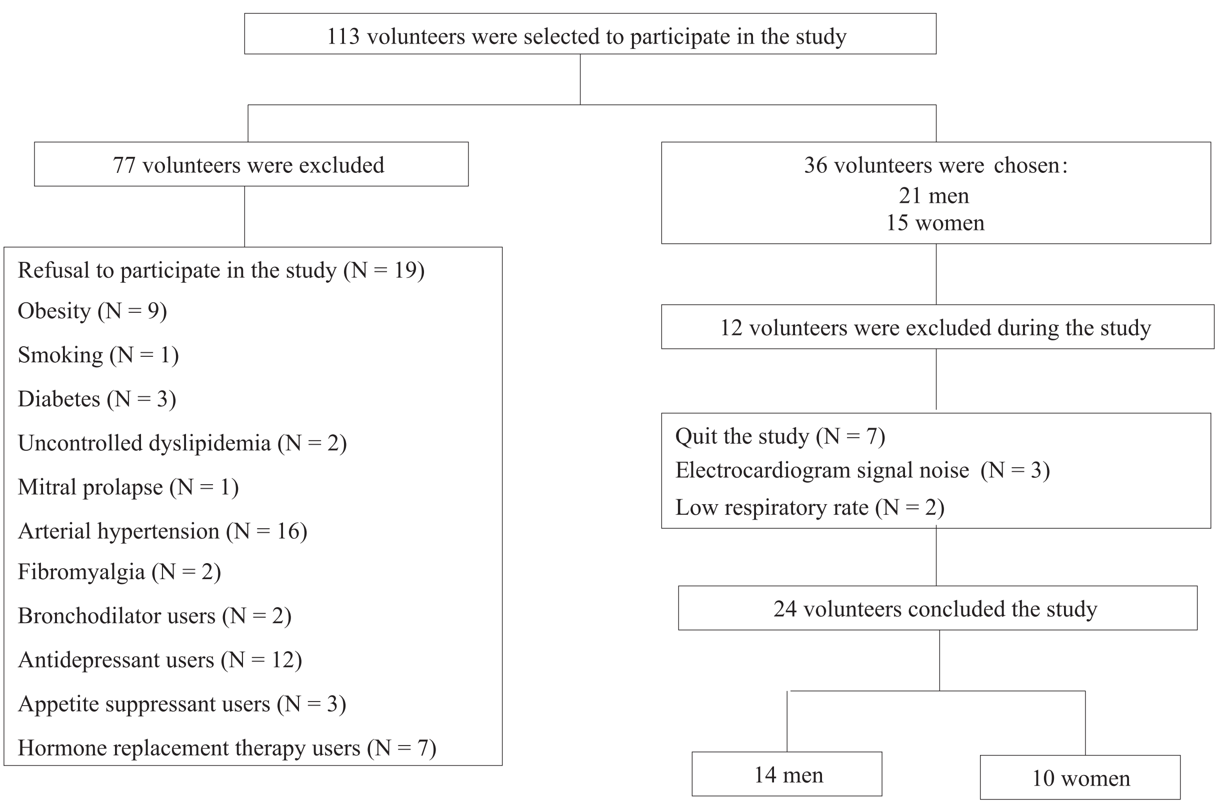

Figure 1. Flow diagram indicating sampling loss in the study.

The number of patterns is reduced by grouping all possible patterns into a small number of families. The pattern families were as follows: 1) 0V: patterns with no variation [3 equal symbols, e.g. (2,2,2) or (4,4,4)], 2) 1V: patterns with one variation [2 consecutive symbols are equal and the remaining symbol is different, e.g. (4,2,2) or (4,4,3)], 3) 2LV: patterns with two like variations [the 3 symbols form an ascending or descending ramp, e.g. (5,4,2) or (1,3,4)], and 4) 2ULV: patterns with two unlike variations [the 3 symbols form a peak or a valley, e.g. (3,5,3) or (4,1,2)]. The rates of occurrence of these families (0V%, 1V%, 2LV%, and 2ULV%) were evaluated in the present study. Previous studies involving pharmacological blockade and autonomic tests (20-22) have indicated that the 0V% index is representative of cardiac sympathetic modulation, the 1V% index corresponds to the simultaneous presence of sympathetic and vagal modulations, and 2LV% and 2ULV% are related to cardiac vagal modulation.

Another variable analyzed was Shannon entropy, which represents the complexity of the pattern distribution (20).

Statistical analysis

The anthropometric characteristics were analyzed by the unpaired *t*-test. The gender effect on the mean and variance of RRi, Shannon entropy, spectral indexes, and symbolic indexes was analyzed by the unpaired *t*-test or the Mann-Whitney rank sum test when appropriate. The position effect on these same variables was analyzed by the paired *t*-test or the Wilcoxon rank sum test when suitable. All data are reported as means ± SD, and the level of significance was set at $P < 0.05$. The statistical analysis was carried out using the Sigma Plot for Windows version 11.0.

Results

Table 1 shows the anthropometric characteristics of the groups evaluated. Men presented significantly greater weight and height than women. Age and body mass index were not significantly different.

Table 2 and Figures 2 and 3 show the results of the HRV spectral and symbolic analysis in response to postural change. There was a gender effect on RRi mean in the supine and standing positions, with men presenting higher values than women. A gender effect was also found on LFnu and the LF/HF ratio in the supine position, which were higher in men than in women. The Shannon entropy analysis in the standing position showed that men presented higher complexity than women. Moreover, women presented higher values of HFnu and of 1V% symbolic index than men in the supine position.

Table 1. Anthropometric characteristics of the volunteer groups.

Characteristics	Men	Women
Age (years)	66.1 ± 3.5	65.3 ± 3.3
Weight (kg)	70.1 ± 7.1	61.4 ± 9.8*
Height (m)	1.67 ± 0.05	1.56 ± 0.05*
BMI (kg/m^2)	25.2 ± 2.0	25.2 ± 3.6

Data are reported as means ± SD. BMI = body mass index. *P < 0.05 women *vs* men (unpaired *t*-test).

Table 2. Heart rate variability determined by spectral and symbolic analysis in the supine and standing positions.

	Men (N = 14)		Women (N = 10)		Gender effect		Position effect	
	Supine	Standing	Supine	Standing	Supine	Standing	Men	Women
RRi mean (ms)	999.50 ± 104.04	925.43 ± 99.84	883.50 ± 83.21	806.40 ± 70.54	0.012	0.004	0.006	0.002
RRi variance (ms)	1.36 ± 1.09	1.02 ± 0.75	0.68 ± 0.47	0.71 ± 0.40	0.169	0.396	0.025	0.879
Spectral analysis								
LFnu	57.56 ± 31.17	54.15 ± 25.70	24.60 ± 19.67	49.85 ± 20.51	0.008	0.666	0.707	0.012
HFnu	40.53 ± 30.60	43.78 ± 26.67	72.47 ± 18.53	47.56 ± 20.14	0.008	0.710	0.706	0.011
LF/HF ratio	4.14 ± 4.81	2.58 ± 3.27	0.45 ± 0.52	1.72 ± 2.12	0.018	0.539	0.310	0.020
Shannon entropy	3.25 ± 0.48	3.53 ± 0.42	3.45 ± 0.44	3.33 ± 0.23	0.318	0.033	0.039	0.464
Symbolic analysis								
0V%	30.03 ± 13.63	25.85 ± 12.52	20.40 ± 12.19	29.24 ± 11.65	0.089	0.508	0.252	0.074
1V%	45.96 ± 5.51	48.48 ± 5.56	52.69 ± 6.21	50.80 ± 5.28	0.010	0.314	0.077	0.463
2LV%	9.04 ± 4.31	9.87 ± 4.85	14.10 ± 10.73	6.95 ± 3.33	0.123	0.114	0.490	0.038
2ULV%	14.97 ± 7.95	15.81 ± 5.42	12.81 ± 3.76	12.13 ± 6.07	0.435	0.133	0.712	0.672

Data are reported as means ± SD. RRi = RR intervals; LFnu = low frequency in normalized units; HFnu = high frequency in normalized units; LF/HF ratio = low frequency/high frequency ratio; 0V = patterns with no variations; 1V = patterns with one variation; 2LV = patterns with two like variations; 2ULV = patterns with two unlike variations. Gender effect: unpaired *t*-test or Mann-Whitney test; position effect: paired *t*-test or Wilcoxon test.

The position effect on HRV can also be seen in Table 2 and Figures 2 and 3. We found a decreased mean RRi for both women and men in the change from the supine to the standing position. RRi variance also decreased in men when they performed the postural maneuver. The opposite occurred with Shannon entropy, which was higher in the men's group while standing than in the supine position. The active standing test induced an increase in LFnu and in the LF/HF ratio in women. However, HFnu and the 2LV% symbolic index were lower in the standing position than in the supine position in the women's group.

Discussion

The major findings of the present study are as follows: 1) men showed no changes in the indexes representing sympathetic modulation when performing the postural change since they had already presented an increased sympathetic modulation in the supine position; 2) women presented an increase in cardiac sympathetic modulation during the postural change; 3) women presented a higher vagal modulation and a lower cardiac sympathetic modulation than men in the supine position; 4) both analyses showed differences between the two groups, but the linear analysis showed more differences than the non-linear analysis in this age range.

Gender effect

With regard to the analysis of cardiac autonomic modulation in the supine and standing positions, we observed a gender effect on HRV. Women presented a higher vagal modulation and a lower sympathetic modulation than men in the supine position, as demonstrated by higher HFnu values and lower LFnu and LF/HF ratio values. There have been few studies involving gender comparison by HRV analysis in response to a postural change, especially in an elderly population such as the one considered in the present study.

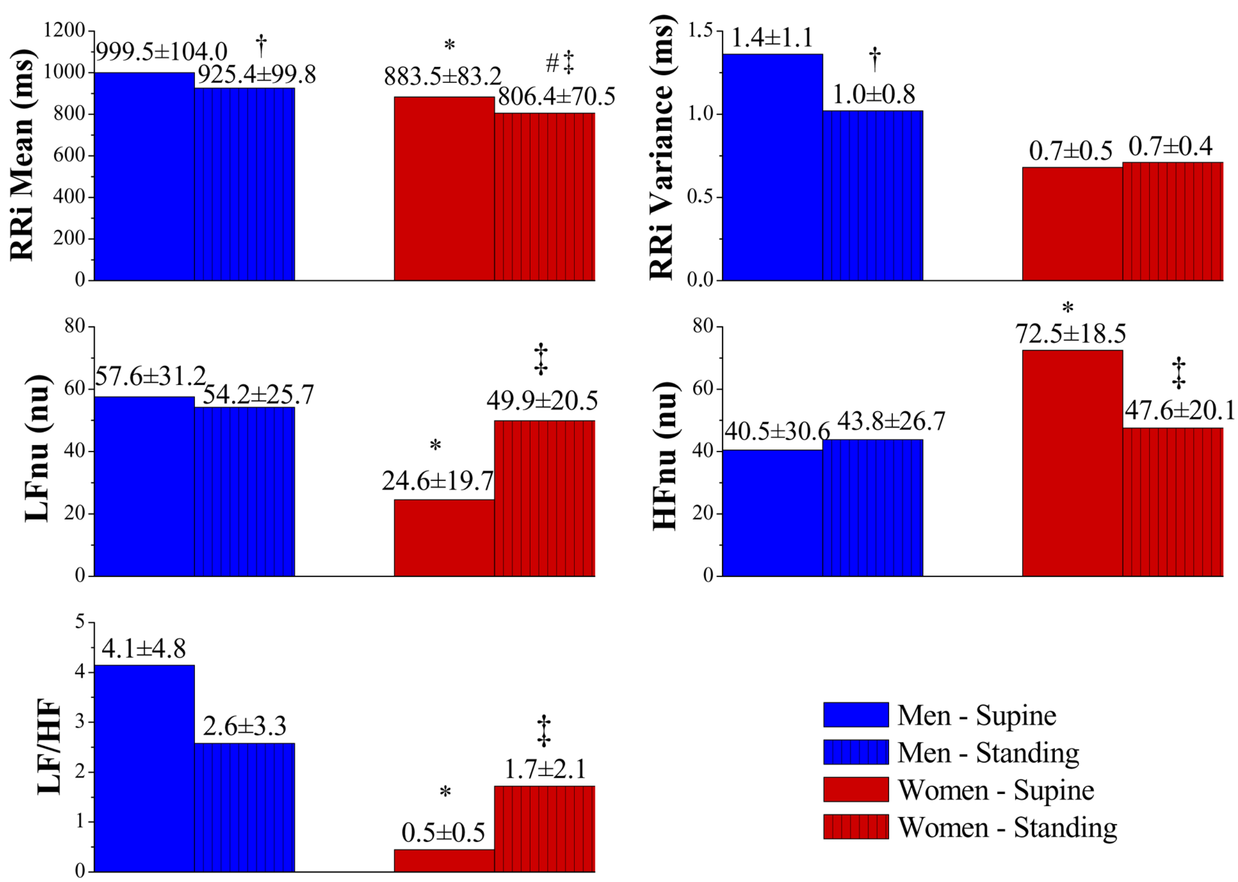

Figure 2. Heart rate variability determined by spectral analysis in the supine and standing positions. Data are reported as means ± SD. RRi = RR intervals; LFnu = low frequency in normalized units; HFnu = high frequency in normalized units; LF/HF = low frequency/high frequency ratio. *P < 0.05 compared to men in the supine position; #P < 0.05 compared to men in the standing position; †P < 0.05 compared to men in the supine position; ‡P < 0.05 compared to women in the supine position. Gender effect: unpaired *t*-test or Mann-Whitney test; position effect: paired *t*-test or Wilcoxon test.

Barantke et al. (23) observed that the LF band components in normalized units were significantly higher in men than in women in both the supine and standing positions, and that there was a shift in the LF/HF ratio toward LF among men, suggesting a more pronounced sympathetic modulation than in women in both positions. However, the HF components in normalized units were statistically higher among women in the supine and standing positions. Therefore, the women should have had a more evident vagal modulation in those postures. The same results were obtained by Fagard et al. (32). However, the cited studies evaluated the cardiac autonomic modulation response to postural change in individuals of both genders from adolescence to approximately 90 years of age.

In the age group evaluated in the present study, only in the supine position were gender differences observed in the HRV indexes. This was due to the fact that the men had a more pronounced sympathetic HR modulation in this position. It is possible that the postural change did not stimulate the sympathetic nervous system modulation significantly. Furthermore, there was a suitable response to the postural change in the women evaluated, causing their HRV indexes to be similar to the men's in the standing position. The women also presented higher 1V% symbolic index values than men in the supine position. Porta et al. (20) showed that this index corresponds to the simultaneous presence of low and high frequency oscillations.

Position effect

Regarding the effect of postural change from the supine to the standing position on HRV, our results showed that RRi mean decreased in both men and women while RRi variance decreased only among men. The HFnu spectral components were higher in the supine position than in

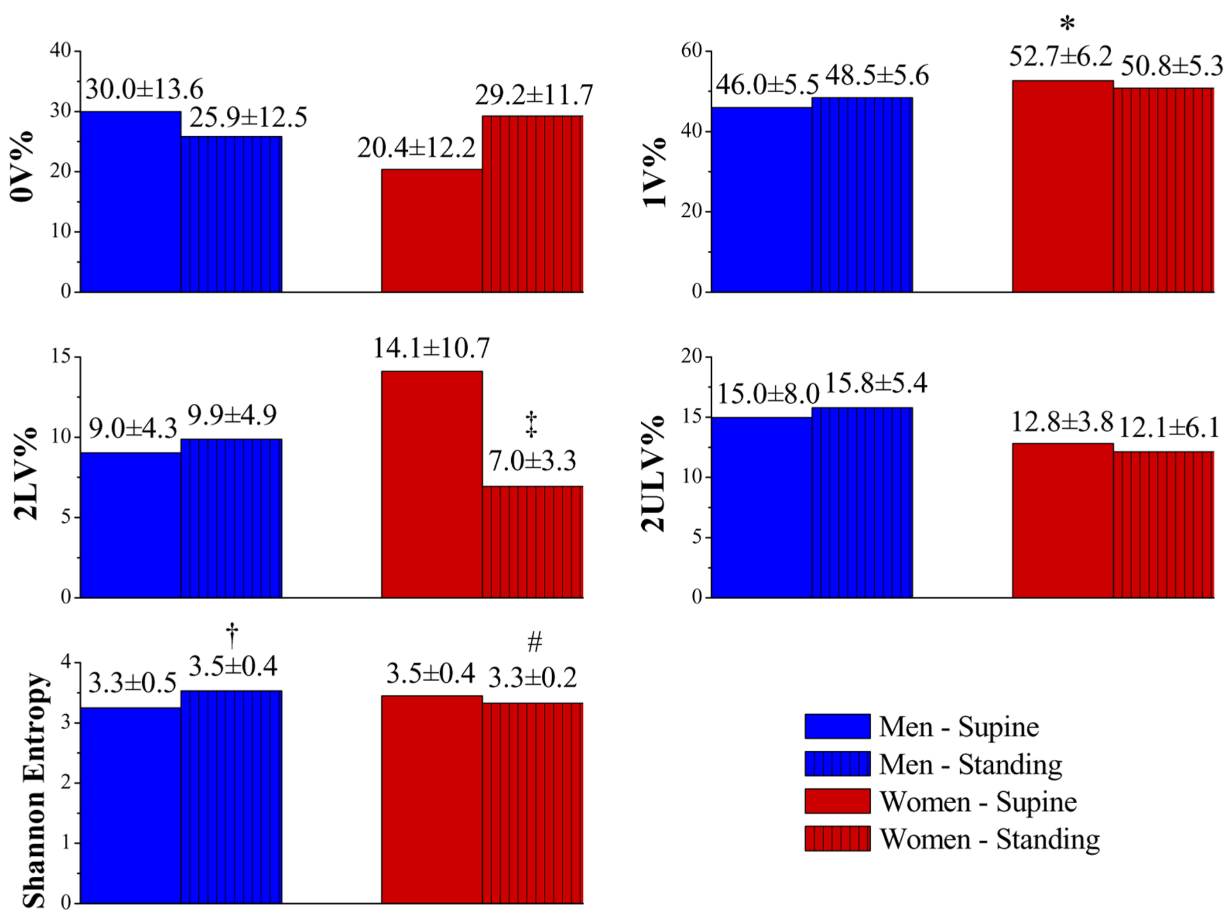

Figure 3. Heart rate variability determined by symbolic analysis in the supine and standing positions. Data are reported as means ± SD. 0V = patterns with no variations; 1V = patterns with one variation; 2LV = patterns with two like variations; 2ULV = patterns with two unlike variations. *P < 0.05 compared to men in the supine position; #P < 0.05 compared to men in the standing position; †P < 0.05 compared to men in the supine position; ‡P < 0.05 compared to women in the supine position. Gender effect: unpaired *t*-test or Mann-Whitney test; position effect: paired *t*-test or Wilcoxon test.

the standing position in the women's group, indicating a reduction of parasympathetic modulation caused by the postural change maneuver in female subjects. Fagard et al. (32) also found a reduction in vagal modulation evident in decreased HF indexes; however, the reduction occurred in both genders and not only in women, as observed in the present study. Nevertheless, these investigators evaluated a wide age range (from 25 to 89 years), which might have been responsible for the differences in results between the two studies.

The women evaluated here demonstrated a more appropriate response to a postural change than the men even though women were postmenopausal, suggesting that autonomic HR modulation is better preserved in the women's group. Another fact that seems to contribute to this hypothesis is that only among women was there an increase in LF spectral components in normalized units due to the postural change, indicating an increased sympathetic modulation in this group in the active standing test. Consequently, there were higher LF/HF ratio values in the standing position than in the supine position. This stimulation of sympathetic nervous system modulation in response to postural change has also been observed in other studies on different populations (22,32,33).

We observed, however, a postural change effect on the 2LV% symbolic index in the women's group, which was reduced with the change from the supine to the standing position, perhaps indicating a decrease in vagal modulation among the female volunteers. That decrease was also evidenced by a reduction in the HFnu spectral index. According to Porta et al. (20,22), the 2LV% index is also related to the components of fast waves that correspond to parasympathetic modulation in the same way that the 2ULV% index corresponds to it.

Regarding the Shannon entropy analysis on short-term HR time series, we found both gender and postural change effects. Men presented higher complexity than women in the standing position. In addition, Shannon entropy increased due to the postural change in the men's group, with greater complexity in the standing position than in the supine one. A possible explanation for these findings would be that the postural change did not induce increased sympathetic modulation, as can be observed by the small alteration of LFnu in men. Although the reduction in this spectral index was not statistically significant, the small change might have affected entropy values, since a reduction of sympathetic modulation could have increased the complexity. It is possible that there are other factors associated with this condition that might have influenced our findings, but we did not consider such factors in this study.

The Shannon entropy analysis showed no position effect in the women's group, demonstrating that the HRV was qualitatively similar in both the supine and standing positions; in other words, there was a similarity in the shape of the pattern distribution. Moreover, we did not observe a significant difference between men and women in the supine position regarding Shannon entropy, which shows that cardiac autonomic modulation was qualitatively similar in both genders, despite the fact that spectral analysis showed quantitative differences.

HRV spectral and symbolic analysis

Regarding the methodologies used for HRV analysis, we observed that both analyses revealed intergroup differences in this age range, but the linear analysis showed more differences than the non-linear analysis.

Porta et al. (22) reported that spectral analysis is strictly based on the definition of the frequency bands, whose upper and lower limits are set by convention and practice. Most importantly, all spectral indexes are helpful only under conditions characterized by reciprocal changes in sympathetic and parasympathetic modulations. Indeed, the LF and HF powers expressed in normalized units (LFnu and HFnu) and LF/HF have been proposed under the hypothesis that an increase in sympathetic modulation corresponds to an equal decrease in vagal modulation. Therefore, Porta et al. (20) proposed a new approach based on symbolic analysis, which has the potential to detect nonreciprocal changes in sympathetic and parasympathetic modulations or reciprocal changes with different magnitudes, since the sum of all symbolic parameters is equal to 100% (0V% + 1V% + 2LV% + 2ULV% = 100%).

Symbolic analysis (non-linear method) of the elderly sample studied here only detected a possible change in parasympathetic modulation, which was reduced by the postural change, as evidenced by the 2LV% index. In addition, we observed that the 1V% index was higher in women in the supine position. Since 1V% corresponds to the simultaneous presence of low frequency oscillations (sympathetic modulation) and high frequency oscillations (parasympathetic modulation), it is possible that there was a predominance of high frequency oscillations, indicative of parasympathetic modulation, which would agree with the responses observed in spectral analysis.

On the other hand, the 0V% and 2ULV% indexes, which are reported to be representative of sympathetic modulation and vagal modulation (20-22), were not significantly changed. Nevertheless, symbolic analysis has proved to be effective for evaluating cardiac autonomic modulation in other studies with different populations, such as healthy subjects, patients with implantable cardioverter-defibrillators, myelopathy patients, and depressed patients. Thus, symbolic analysis, like other non-linear methods, differs from traditional methods in that it considers the qualitative properties of HR time series. The mechanisms that involve cardiovascular regulation are interconnected in non-linear theory, and non-linear analysis methods could provide additional information. Therefore, this study was important for determining the applicability of symbolic analysis in this population. Moreover, according to Voss et al. (34), non-linear parameters in combination with standard linear parameters usually improve the performance of HRV analysis.

Clinical implications

HRV study by linear and non-linear analysis is important for understanding cardiac autonomic modulation in various situations. The fact that older men did not have an adequate response to postural change as well as the fact that they had a lower HRV (lower HF) in the supine position than women of the same age directs our attention to the aging process, which may negatively influence HRV in this population. Since reduced HRV can be associated with higher cardiovascular morbidity and mortality rates (3), it has an important clinical impact on the elderly. This population, therefore, should be encouraged to practice aerobic exercise, which is widely known to improve cardiac autonomic modulation, and thus minimize the effects of aging (13).

Regarding non-linear methods of HRV evaluation, it is important to emphasize that they have been little used for comparison between genders. Specifically, this is the first study that has applied symbolic analysis and Shannon entropy to short-term HR time series in order to qualitatively compare the cardiac autonomic modulation of elderly subjects of both genders. Moreover, according to Voss et al. (34), one parameter alone cannot sufficiently describe complex physiological systems such as HR control. Therefore, multivariate approaches should be considered. Non-linear parameters in combination with standard linear parameters usually improve the performance of HRV analysis.

Our data showed that women presented a more appropriate response to the postural change than men in the age range studied, demonstrating that their cardiac autonomic modulation may be better preserved than men's.

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References

1. Sztajzel J. Heart rate variability: a noninvasive electrocardiographic method to measure the autonomic nervous system. *Swiss Med Wkly* 2004; 134: 514-522.
2. 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: 1043-1065.
3. Bigger JT Jr, Fleiss JL, Steinman RC, Rolnitzky LM, Kleiger RE, Rottman JN. Frequency domain measures of heart period variability and mortality after myocardial infarction. *Circulation* 1992; 85: 164-171.
4. Antelmi I, de Paula RS, Shinzato AR, Peres CA, Mansur AJ, Grupi CJ. Influence of age, gender, body mass index, and functional capacity on heart rate variability in a cohort of subjects without heart disease. *Am J Cardiol* 2004; 93: 381-385.
5. Evans JM, Ziegler MG, Patwardhan AR, Ott JB, Kim CS, Leonelli FM, et al. Gender differences in autonomic cardiovascular regulation: spectral, hormonal, and hemodynamic indexes. *J Appl Physiol* 2001; 91: 2611-2618.
6. Huikuri HV, Pikkujamsa SM, Airaksinen KE, Ikaheimo MJ, Rantala AO, Kauma H, et al. Sex-related differences in autonomic modulation of heart rate in middle-aged subjects. *Circulation* 1996; 94: 122-125.
7. Kuo TB, Lin T, Yang CC, Li CL, Chen CF, Chou P. Effect of aging on gender differences in neural control of heart rate. *Am J Physiol* 1999; 277: H2233-H2239.
8. Neves VFC, Perpétuo NM, Sakabe DI, Catai AM, Gallo L Jr, Silva De Sá MF, et al. Análise dos índices espectrais da variabilidade da freqüência cardíaca em homens de meia idade e mulheres na pós-menopausa. *Rev Bras Fisioter* 2006; 10: 401-406.
9. Pikkujamsa SM, Makikallio TH, Airaksinen KE, Huikuri HV. Determinants and interindividual variation of R-R interval dynamics in healthy middle-aged subjects. *Am J Physiol Heart Circ Physiol* 2001; 280: H1400-H1406.
10. Catai AM, Chacon-Mikahil MP, Martinelli FS, Forti VA, Silva E, Golfetti R, et al. Effects of aerobic exercise training on heart rate variability during wakefulness and sleep and cardiorespiratory responses of young and middle-aged healthy men. *Braz J Med Biol Res* 2002; 35: 741-752.
11. Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part I: aging arteries: a "set up" for vascular disease. *Circulation* 2003; 107: 139-146.
12. Lipsitz LA, Mietus J, Moody GB, Goldberger AL. Spectral characteristics of heart rate variability before and during postural tilt. Relations to aging and risk of syncope. *Circulation* 1990; 81: 1803-1810.
13. Melo RC, Santos MD, Silva E, Quiterio RJ, Moreno MA, Reis MS, et al. Effects of age and physical activity on the autonomic control of heart rate in healthy men. *Braz J Med Biol Res* 2005; 38: 1331-1338.
14. Zhang J. Effect of age and sex on heart rate variability in healthy subjects. *J Manipulative Physiol Ther* 2007; 30: 374-379.
15. Huikuri HV, Makikallio T, Airaksinen KE, Mitrani R, Castellanos A, Myerburg RJ. Measurement of heart rate variability: a clinical tool or a research toy? *J Am Coll Cardiol* 1999; 34: 1878-1883.
16. Makikallio TH, Huikuri HV, Hintze U, Videbaek J, Mitrani RD, Castellanos A, et al. Fractal analysis and time- and frequency-domain measures of heart rate variability as predictors of mortality in patients with heart failure. *Am J Cardiol* 2001; 87: 178-182.
17. Makikallio TH, Tapanainen JM, Tulppo MP, Huikuri HV. Clinical applicability of heart rate variability analysis by methods

based on nonlinear dynamics. *Card Electrophysiol Rev* 2002; 6: 250-255.
18. Huikuri HV, Makikallio TH, Perkiomaki J. Measurement of heart rate variability by methods based on nonlinear dynamics. *J Electrocardiol* 2003; 36 (Suppl): 95-99.
19. Jokinen V, Tapanainen JM, Seppanen T, Huikuri HV. Temporal changes and prognostic significance of measures of heart rate dynamics after acute myocardial infarction in the beta-blocking era. *Am J Cardiol* 2003; 92: 907-912.
20. Porta A, Guzzetti S, Montano N, Furlan R, Pagani M, Malliani A, et al. Entropy, entropy rate, and pattern classification as tools to typify complexity in short heart period variability series. *IEEE Trans Biomed Eng* 2001; 48: 1282-1291.
21. Guzzetti S, Borroni E, Garbelli PE, Ceriani E, Della BP, Montano N, et al. Symbolic dynamics of heart rate variability: a probe to investigate cardiac autonomic modulation. *Circulation* 2005; 112: 465-470.
22. Porta A, Tobaldini E, Guzzetti S, Furlan R, Montano N, Gnecchi-Ruscone T. Assessment of cardiac autonomic modulation during graded head-up tilt by symbolic analysis of heart rate variability. *Am J Physiol Heart Circ Physiol* 2007; 293: H702-H708.
23. Barantke M, Krauss T, Ortak J, Lieb W, Reppel M, Burgdorf C, et al. Effects of gender and aging on differential autonomic responses to orthostatic maneuvers. *J Cardiovasc Electrophysiol* 2008; 19: 1296-1303.
24. Matsushima R, Tanaka H, Tamai H. Comparison of the active standing test and head-up tilt test for diagnosis of syncope in childhood and adolescence. *Clin Auton Res* 2004; 14: 376-384.
25. Cacciatori V, Gemma ML, Bellavere F, Castello R, De Gregori ME, Zoppini G, et al. Power spectral analysis of heart rate in hypothyroidism. *Eur J Endocrinol* 2000; 143: 327-333.
26. Galetta F, Franzoni F, Fallahi P, Tocchini L, Braccini L, Santoro G, et al. Changes in heart rate variability and QT dispersion in patients with overt hypothyroidism. *Eur J Endocrinol* 2008; 158: 85-90.
27. Kahaly GJ. Cardiovascular and atherogenic aspects of subclinical hypothyroidism. *Thyroid* 2000; 10: 665-679.
28. Xing H, Shen Y, Chen H, Wang Y, Shen W. Heart rate variability and its response to thyroxine replacement therapy in patients with hypothyroidism. *Chin Med J* 2001; 114: 906-908.
29. Silva E, Catai AM, Trevelin LC, Guimarães JO, Silva LP Jr, Oliveira L, et al. Design of a computerized system to evaluate the cardiac function during dynamic exercise. *Phys Med Biol* 1994; 33: 409 (Abstract).
30. Malliani A, Pagani M, Lombardi F, Cerutti S. Cardiovascular neural regulation explored in the frequency domain. *Circulation* 1991; 84: 482-492.
31. Pagani M, Lombardi F, Guzzetti S, Rimoldi O, Furlan R, Pizzinelli P, et al. Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. *Circ Res* 1986; 59: 178-193.
32. Fagard RH, Pardaens K, Staessen JA. Influence of demographic, anthropometric and lifestyle characteristics on heart rate and its variability in the population. *J Hypertens* 1999; 17: 1589-1599.
33. Montano N, Ruscone TG, Porta A, Lombardi F, Pagani M, Malliani A. Power spectrum analysis of heart rate variability to assess the changes in sympathovagal balance during graded orthostatic tilt. *Circulation* 1994; 90: 1826-1831.
34. Voss A, Schulz S, Schroeder R, Baumert M, Caminal P. Methods derived from nonlinear dynamics for analysing heart rate variability. *Philos Transact A Math Phys Eng Sci* 2009; 367: 277-296.