ORIGINAL ARTICLE

https://doi.org/10.1590/1806-9282.20220219

Do heart rate variability indices present potential to predict late postmenopausal? A retrospective study

Tatiana Dias de Carvalho[1*], Alex Rey Norberto[1], Fernando Rocha Oliveira[2], Laercio da Silva Paiva[3], Edmund Chada Baracat[1], José Maria Soares Júnior[1], Luiz Carlos Marques Vanderlei[4], Isabel Cristina Esposito Sorpreso[1]

SUMMARY

OBJECTIVES: This study aimed to compare heart rate variability indices in early and late postmenopausal women and assess their correlation and prognostic value to predict late postmenopausal.

METHODS: An observational and retrospective study was performed with the medical records of patients from Hospital das Clínicas, Faculdade de Medicina da Universidade de Sao Paulo between 2018 and 2019. We selected medical records of women with menopause, over 40 years old, which were divided into two groups, according to postmenopausal time, i.e., early and late postmenopausal.

RESULTS: We analyzed data from 123 women (55 in the early and 68 in the late postmenopausal group). RRtri (triangular index) was lower in the late postmenopausal group (8.68 vs. 7.15, p=0.040). There was a significant weak negative correlation in SDNN, RRtri, and SD2 and postmenopausal time. RRtri presented the potential to predict late postmenopausal.

CONCLUSION: The increase in postmenopausal time decreases global heart rate variability indices. The geometric index RRtri was significantly lower in late postmenopausal women and presented the potential to predict late postmenopausal.

KEYWORDS: Autonomic nervous system. Climacteric. Postmenopause. Heart rate determination. Gynecology. ROC curve.

INTRODUCTION

The postmenopausal period can be divided into early and late postmenopausal. Early postmenopausal is defined as the period of up to 6 years after menopause, in which follicle-stimulating hormone (FSH) levels remain high; there is a progressive reduction in estradiol and greater acceleration of bone loss. The late phase starts from the 6th year after menopause and goes until senectivity[1,2]. In general, it is characterized by menopausal symptoms and changes in different systems, including cardiac autonomic modulation[2,3].

Apparently, hypoestrogenism changes the autonomic control of heart rate (HR), inducing alterations in sympathetic and vagal regulation. Previous studies[1-4] have observed that cardiac parasympathetic function is reduced in postmenopausal women, due to aging and hormone level, when compared with pre- or transition to menopause. Other studies indicate that certain interventions, such as physical exercise, could increase the heart rate variability (HRV)[4], the parasympathetic modulation[5], and the system complexity[3] in postmenopausal women.

Indeed, HRV as a measure of the autonomic nervous system function has been used in several conditions, including in menopause[1-3,5]. However, these studies do not divide their population into early and postmenopausal groups. In general, the menopausal group consists of women with different years without a menstrual cycle, and the authors generalized their conclusions, regardless of the possible influence that the postmenopause time could have on cardiac regulation.

In this sense, considering that previous studies[6-9] show that some linear and nonlinear HRV indices have good diagnostic accuracy in certain populations, and with the intention of distinguishing the postmenopause stages, our objectives were to compare HRV indices in early and late postmenopausal women and to assess their correlation and prognostic value to predict late postmenopausal.

METHODS

Study design and ethical considerations

This observational and retrospective study was performed using the medical records of patients seen at Climacteric Sector,

[1]Universidade de São Paulo, Faculdade de Medicina, Departamento de Obstetrícia e Ginecologia, Disciplina de Ginecologia – São Paulo (SP), Brazil.
[2]Universidade de São Paulo, Faculdade de Saúde Pública, Departamento de Epidemiologia – São Paulo (SP), Brazil.
[3]Centro Universitário FMABC – Santo André (SP), Brazil.
[4]Universidade Estadual Paulista "Júlio de Mesquita Filho", School of Technology and Sciences – São Paulo (SP), Brazil.
*Corresponding author: carvalho.td1@gmail.com
Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
Received on February 15, 2022. Accepted on February 16, 2022.

Gynecology Division, Hospital das Clínicas, Faculdade de Medicina da Universidade de Sao Paulo (FMUSP) between 2018 and 2019.

This study was approved by the Research Ethics Committee of the same institution (number 1.977.216). The written informed consent was obtained from the participants, and their anonymity was guaranteed, according to the Helsinki Declaration and the 466/2012 resolution of the Brazilian National Health Council.

Population and eligibility criteria

As inclusion criteria, we selected medical records of women with a clinical (absence of menstruation for a period longer than 12 months) or laboratory (FSH > 30 IU/L) diagnosis of postmenopause, composing a non-probabilistic sampling of convenience.

Exclusion criteria were primary or premature ovarian failure; active gynecological neoplasia; thromboembolic disorders; active parathyroid and thyroid endocrine disorders without treatment; malabsorption syndrome; endometrial thickening (suspected endometrial cancer); abuse of alcohol or illicit drugs and psychiatric illness in treatment, use of beta-blockers, acute cardiovascular disease, and arrhythmias in pregnancy; morbid obesity (body mass index [BMI] ≥40 kg/m^2); insulin-dependent diabetes mellitus; and current diagnosis of neoplasms and/or under treatment. All these information were obtained from medical records. For this reason, we also excluded records with incomplete information.

Then we divided them into two groups, according to postmenopause time[2], i.e., early (≤6 years) and late (>6 years) postmenopausal. From this, we have excluded those HRV data with an error greater than 5% in the RR intervals (RRis). Both the sample composition process and the analyses were carried out by an independent researcher. Figure 1 shows the sample selection process.

Sociodemographic and clinical characteristics

For characterization of volunteers, we recollected information about age (years), postmenopausal time (years), last menstruation age (years), menarche age (years), reproductive cycle time (years), BMI, race/ethnicity (i.e., white, mixed race, and black), marital status (stable union and unstable union), exercise (yes or no), and smoking (yes or no).

Heart rate variability analysis

For the HRV analysis, we have used the methodologies proposed by Catai et al.[10] and Vanderlei et al.[11]. Initially, the RRis were recorded by a validated HR receiver (acquisition rate 1000 Hz) validated equipment for HR capturing beat by beat, during 20 min in rest supine, individually in a quiet environment with the minimum circulation of people[10]. To standardize circadian influences, all HR records were performed at the same time of the day (8:00 to 12:00 a.m.) in a room with a temperature between 22°C and 25°C[10,11].

The data series was first digitally filtered, in which only series with more than 95% sinus rhythm beats were included. Then, it was manually complemented, and the visual inspection of the time series on the computer showed the absence of artifacts. Finally, 1000 consecutive RRis were selected for data analysis[10,11]. We used Kubios HRV Analysis software (v.1.1, Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Finland) for the HRV analysis in linear (time and frequency domains) and nonlinear methods[10,11].

Linear and nonlinear heart rate variability indices

We have performed a linear (time and frequency domains) and nonlinear analysis of HRV. In the time domain, we have analyzed statistics and geometric indices. The statistics indices were as follows: MEANRR (median of RRis/ms), SDNN (mean standard deviation of all normal RRis/ms), and RMSSD (square root of the mean of squared differences between successive beat intervals/ms)[10,11].

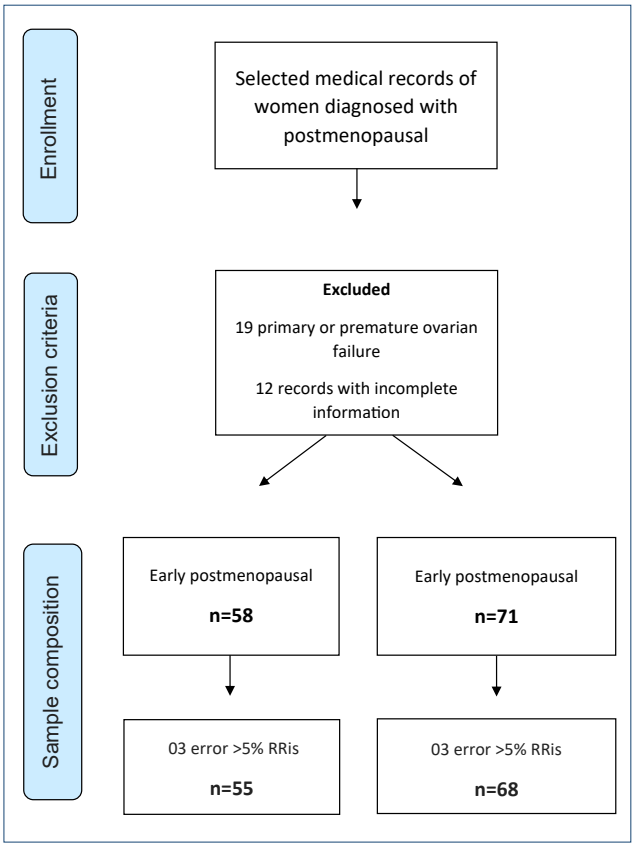

Figure 1. Sample selection process.

The geometric indices were as follows: SD1 (standard deviation of the instantaneous variability in continuous RRis, determined by the width of the ellipse formed by the Poincare plot), SD2 (standard deviation of long-term continuous RRis, which determines the length of the plot), SD1/SD2 (ratio between short and long variations of the intervals), RRtri [triangular index, calculated from the construction of the histogram density of normal RRis and obtained by integral division of the histogram (RRis total number) by the maximum density distribution (RRi modal frequency), obtained with a sampling frequency of 128 Hz] and TINN (RRi triangular interpolation, distribution baseline width measured as a triangular base, approximating the distribution of all RRi)[4,11].

In the frequency domain, we studied the spectral indices obtained by Fourier Transform mathematical algorithm. The indices were obtained from the frequency bands, in which high-frequency (HF) fluctuations ranging from 0.15 to 0.4 Hz, low-frequency (LF) fluctuations ranging from 0.04 to 0.15 Hz, and LF/HF ratio. These indices were presented in normalized units (nu) and ms[2,10,11].

In the nonlinear methods, we have analyzed the fractals proprieties and entropy for evaluating the system complexity. The fractal analysis was performed by indexes ALPHA1 (short-term fractal scaling exponent, which corresponds to a period of 4–11 beats), ALPHA2 (long-term fractal scaling exponent that is longer than 11 beats), and ALPHA1/ALPHA2 (short-term fractal scaling exponent/long-term fractal scaling exponent ratio). Entropy is an approach used to quantify the regularity (complexity) of the RRi series fluctuations. As some entropy measurements require relatively short recordings, we have evaluated the sample entropy (SAMPEN), which needs <200 points[11].

Statistical analyses

Data normality was initially determined by the Shapiro-Wilk test. To describe the variables, the median and the standard deviation values were used for quantitative variables, and absolute and relative frequency for qualitative variables. Comparisons between early postmenopausal and late postmenopausal women were performed using the Mann-Whitney test and chi-square test. In addition, Spearman's correlation test was used to compare the HRV and time since menopause.

The definition of the cutoff points for the HRV indices was obtained by the receiver-operating characteristic (ROC) curve. In addition, sensitivity, specificity, positive predictive values, and negative predictive values for the occurrence of the late postmenopausal phase were obtained. The cutoff point was determined by the Youden index[12]. The area under the curve was considered significant when values ≥0.650 were obtained[8]. For all analyses, a 95% confidence level was used. The program used was Stata version 13.0.

RESULTS

We analyzed data from 160 women, of which 37 were excluded. Sociodemographic and clinical profiles and comparison between HRV indices of the women evaluated are shown in Table 1.

Table 2 presents the correlation between HRV indices and postmenopausal time. There was a significant weak negative correlation in SDNN, RRtri, and SD2.

Table 3 shows sensitivity, specificity, ROC curve, and positive and negative predictive values of HRV indices to predict late postmenopausal. The geometric index RRtri presented the potential to predict late postmenopausal.

DISCUSSION

The main results of this study are that there was a significant weak negative correlation in global HRV indices and postmenopausal time, and the RRtri presented potential to predict late postmenopausal. In addition, except for the RRtri, there were no differences in autonomic modulation between women with early or late postmenopause.

Regarding sociodemographic and clinical characteristics, because of groups characteristics, differences were already expected. Also, we have observed no differences in their BMI, smoking, and exercise habits, which are factors that can influence cardiac autonomic modulation[3,13]. Overweight has been reported in other studies, and it is a comorbidity associated with menopausal status and increased cardiovascular risk in this population[3,13]. About exercises, many studies evaluated the effects of different physical exercise programs on autonomous regulation and found an increase in HRV[3-5], parasympathetic modulation[5], and system complexity[3] in postmenopausal women.

In the analysis of linear and nonlinear HRV indices, only RRtri was significantly lower in postmenopausal women, indicating reduced global HRV in this group. Interestingly, other global HRV indices (i.e., SDNN and SD2) also tended to decrease. As for the others, they were not different between groups. Most studies[1-3] on cardiac autonomic modulation in postmenopausal women do not divide the subjects by the postmenopausal time. In general, they carry out evaluations considering the period before and after menopause, and their results suggest decreased parasympathetic regulation of HR in the postmenopause in general. To the best of our knowledge, only one study[14] divided its sample according to the stages of

Table 1. Sociodemographic and clinical characteristics and heart rate variability indices of the postmenopausal women (Sao Paulo, Brazil).

Variables	Early (n=55)	Late (n=68)	p[a]
	Mean (SD)		
Age (years)	54.01 (3.69)	63.07 (7.28)	<0.001[a]
Age of last menstruation (years)	50.60 (3.73)	47.61 (4.45)	<0.001[a]
Postmenopausal time (years)	3.41 (1.68)	15.45 (7.24)	<0.001[a]
Menarche age (years)	12.92 (1.75)	12.52 (1.85)	0.136
Reproductive cycle time (years)	37.67 (4.29)	35.08 (5.11)	0.009[a]
BMI	27.67 (4.11)	27.19 (3.95)	0.566
	n (%)		p[b]
Race/ethnicity			
White	21 (39.62)	42 (62.69)	0.030[a]
Mixed race	24 (45.28)	21 (31.34)	
Black	8 (15.09)	4 (5.97)	
Marital status			
Stable union	25 (45.45)	35 (52.24)	0.904
Unstable union	30 (54.54)	33 (47.76)	
Exercise			
Yes	25 (54.55)	31 (53.73)	0.928
No	30 (45.45)	36 (46.27)	
Smoking			
Yes	8 (84.91)	5 (91.94)	0.235
No	45 (15.09)	57 (8.06)	
HRV indices	**Early (n=55)**	**Late (n=68)**	**p[c]**
	Mean (SD)		
MEANRR	880.70 (135.39)	909.68 (119.82)	0.153
SDNN	33.71 (26.07)	25.55 (10.17)	0.059
RMSSD	24.43 (13.81)	21.66 (10.08)	0.388
RRtri	8.68 (4.21)	7.15 (2.56)	0.040[c]
TINN	153.89 (118.14)	126.76 (51.18)	0.115
LF, ms²	378.34 (409.27)	254.80 (258.67)	0.230
LF, nu	59.26 (18.63)	58.24 (18.47)	0.678
HF, ms²	265.18 (270.44)	180.26 (181.15)	0.123
HF, nu	40.82 (18.31)	41.63 (18.44)	0.708
LF/HF	2.06 (1.59)	2.21 (2.28)	0.695
SD1	18.86 (14.38)	15.33 (7.14)	0.259
SD2	43.42 (36.77)	31.96 (14.32)	0.056
SD1/SD2	1.25 (0.86)	1.28 (0.80)	0.929
SAMPEN	1.58 (0.35)	1.62 (0.36)	0.407
ALFA1	1.08 (0.27)	1.04 (0.28)	0.389
ALFA2	0.62 (0.33)	0.59 (0.29)	0.963
ALFA1/ALFA2	2.13 (0.96)	2.03 (0.75)	0.530

[a]Mann-Whitney U test. [b]Chi-square test. [c]p<0.05, Mann-Whitney U test. SD: standard deviation; BMI: body mass index. SD: standard deviation; MEANRR: median of RR intervals/ms; SDNN: mean standard deviation of all normal RRis/ms; RMSSD: square root of the mean of squared differences between successive beat intervals/ms; HF: high frequency; LF: low frequency; LF/HF: low-frequency/high-frequency ratio; SD1: standard deviation of the RRis; SD2: standard deviation of long-term continuous RRis; SD1/SD2: ratio between short and long variations of the intervals; RRtri: triangular index; TINN: RRi triangular interpolation; SAMPEN: sample entropy; ALPHA1: short-term fractal scaling exponent; ALPHA2: long-term fractal scaling exponent; ALPHA1/ALPHA2: short-term fractal scaling exponent/long-term fractal scaling exponent ratio.

Table 2. Correlation between heart rate variability indices and postmenopausal time (Sao Paulo, Brazil).

Variables	Rho	p
MEANRR	0.037	0.678
SDNN	-0.193	0.032[a]
RMSSD	-0.093	0.303
RRtri	-0.188	0.036[a]
TINN	-0.087	0.335
LF, ms²	-0.121	0.181
LF, nu	-0.003	0.969
HF, ms²	-0.139	0.125
HF, nu	-0.0001	0.999
LF/HF	-0.001	0.987
SD1	-0.104	0.249
SD2	-0.198	0.027[a]
SD1 SD2	0.087	0.334
SAMPEN	0.050	0.580
ALFA1	-0.012	0.891
ALFA2	-0.035	0.697
ALFA1/ALFA2	0.058	0.518

Rho: Spearman's correlation test. [a]p<0.05. MEANRR: median of RR intervals/ms; SDNN: mean standard deviation of all normal RRis/ms; RMSSD: square root of the mean of squared differences between successive beat intervals/ms; HF: high frequency; LF: low frequency: LF/HF: low-frequency/high-frequency ratio; SD1: standard deviation of the RRis; SD2: standard deviation of long-term continuous RRis; SD1/SD2: ratio between short and long variations of the intervals; RRtri: triangular index; TINN: RRi triangular interpolation; SAMPEN: sample entropy; ALPHA1: short-term fractal scaling exponent; ALPHA2: long-term fractal scaling exponent; ALPHA1/ALPHA2: short-term fractal scaling exponent/long-term fractal scaling exponent ratio.

menopause, but the authors did not discuss the differences within the postmenopause group.

Regarding the correlation between HRV indices and groups, there was a significant weak negative correlation in SDNN, RRtri, and SD2. These indices express global HRV[10,11], which could indicate that with the increase in postmenopausal time there would be a reduction in the global variability. Global variability can be reduced mainly for two physiological mechanisms: (1) either decreased parasympathetic activity alone or both sympathetic and parasympathetic systems, and (2) or even by an increase in the sympathetic branch that leads to an imbalance in the autonomous function. In our study, we believe that the justification for these results may be the reduction in the parasympathetic system. Therefore, the discrimination of late menopause may be related to indexes that are influenced by cardiac vagal control. When compared to pre- or transition to menopause women, postmenopausal women have reduced cardiac function due to aging and hormone levels[1-3].

Regarding the diagnostic accuracy tests, the geometric index RRtri presented the potential to predict the last postmenopausal time. Besides, in our results, the greatest sensitivity values have been observed in the geometric indices, and this could be related to their ability to discriminate changes in autonomic modulation. Studies[6-9] showed that some linear and nonlinear HRV indices have good diagnostic accuracy in certain populations.

Table 3. Sensitivity, specificity, ROC curve, and positive and negative predictive values of heart rate variability indices to predict late postmenopausal.

Variables	ROC (95%CI)	p	Sensitivity	Specificity	PPV	NPV	Cutoff
MEANRR	0.57 (0.48–0.66)	0.157	48.53 (36.2–61.0)	70.91 (57.1–82.4)	1.67	0.73	>936.599975586
SDNN	0.59 (0.50–0.68)	0.0658	80.88 (69.5–89.4)	43.64 (30.3–57.7)	1.44	0.44	≤31.299999237
RMSSD	0.545 (0.453–0.635)	0.4008	60.29 (47.7–72.0)	56.36 (42.3–69.7)	1.38	0.70	≤21.200000763
RRtri	0.608 (0.516–0.695)	0.040[a]	88.24 (78.1–94.8)	32.73 (20.7–46.7)	1.31	0.36	≤9.666999817
TINN	0.583 (0.490–0.671)	0.1319	76.47 (64.6–85.9)	50.91 (37.1–64.6)	1.56	0.46	≤150
LF, ms²	0.563 (0.471–0.652)	0.2544	69.12 (56.7–79.8)	54.55 (40.6–68.0)	1.52	0.57	≤240
LF, nu	0.522 (0.430–0.613)	0.6817	52.94 (40.4–65.2)	63.64 (49.6–76.2)	1.46	0.74	≤58.299999237
HF, ms²	0.581 (0.489–0.669)	0.1319	75.00 (63.0–84.7)	47.27 (33.7–61.2)	1.42	0.53	≤233
HF, nu	0.520 (0.428–0.611)	0.7115	52.94 (40.4–65.2)	63.64 (49.6–76.2)	1.46	0.74	>41.099998474
LF/HF	0.521 (0.429–0.611)	0.6984	52.94 (40.4–65.2)	63.64 (49.6–76.2)	1.46	0.74	≤1.404000044
SD1	0.559 (0.467–0.649)	0.2718	58.82 (46.2–70.6)	58.18 (44.1–71.3)	1.41	0.71	≤14.800000191
SD2	0.600 (0.508–0.688)	0.0604	70.59 (58.3–81.0)	52.73 (38.8–66.3)	1.49	0.56	≤36.299999237
SD1/SD2	0.505 (0.413–0.596)	0.9310	17.65 (9.5–28.8)	67.27 (53.3–79.3)	0.54	1.22	>1.893000007
SAMPEN	0.544 (0.451–0.634)	0.4052	38.24 (26.7–50.8)	74.55 (61.0–85.3)	1.50	0.83	>1.827000022
ALFA1	0.545 (0.453–0.635)	0.3951	66.18 (53.7–77.2)	47.27 (33.7–61.2)	1.26	0.72	≤1.129999995
ALFA2	0.502 (0.411–0.594)	0.9645	67.65 (55.2–78.5)	45.45 (32.0–59.4)	1.24	0.71	≤0.587000012
ALFA1/ALFA2	0.508 (0.416–0.599)	0.8787	80.88 (69.5–89.4)	30.91 (19.1–44.8)	1.17	0.62	≤2.587248325

[a]p<0.05. 95%CI: 95% confidence interval; PPV: positive predictive value; NPV: negative predictive value; MEANRR: median of RR intervals/ms; SDNN: mean standard deviation of all normal RRis/ms; RMSSD: square root of the mean of squared differences between successive beat intervals/ms; HF: high frequency; LF: low frequency; LF/HF: low-frequency/high-frequency ratio; SD1: standard deviation of the RRis; SD2: standard deviation of long-term continuous RRis; SD1/SD2: ratio between short and long variations of the intervals; RRtri: triangular index; TINN: RRi triangular interpolation; SAMPEN: sample entropy; ALPHA1: short-term fractal scaling exponent; ALPHA2: long-term fractal scaling exponent; ALPHA1/ALPHA2: short-term fractal scaling exponent/long-term fractal scaling exponent ratio.

Out of various conventional HRV parameters, Hämmerle et al.[6] indicated the geometric index RRtri as an independent predictor of cardiovascular and all-cause mortality in a cohort of patients with atrial fibrillation. Silva et al.[7] observed that some geometrics indices showed better sensitivity and specificity for discriminating autonomic dysfunction in individuals with type 1 diabetes mellitus compared to individuals without the disease. Pivatelli et al.[8] reported that the parasympathetic indices presented the highest discriminatory power of coronary arterial disease, and among the nonlinear indices, only approximated entropy presented the highest discriminatory power. Using nonlinear dynamics methods, Corrêa et al.[9] found a significant difference between groups with and without pulmonary infections in the postoperative period of myocardial revascularization, through the cutoff levels set by the ROC curve for total DFA, entropy, and Lyapunov exponent, suggesting that these methods may have a prognostic value for these patients.

This study presents some limitations: (1) we only use HRV evaluation and did not perform other types of cardiovascular risk factors assessment, but this was the proposal to evaluate the predicted power of the HRV indices alone; (2) there was a difference in the age of the groups; however, due to the clinical characteristics of postmenopausal women, this was expected and had already been described in previous studies. Therefore, we do not believe that they could influence our findings; and (3) finally, there are limitations inherent to the study design, which does not allow establishing a cause-effect relationship of the outcomes.

Further studies are needed to monitor these postmenopausal phases for longer. The study of HRV, by being a noninvasive, low-cost, and risk-free method, can be clinically relevant in their diagnostic evaluation. The cutoff points in the HRV indices could be related to other physiologic parameters, such as quality of life and vasomotor symptoms, as well as being used as measures for interventions in this population, such as exercises and hormone therapy.

CONCLUSION

The geometric index RRtri was significantly lower in late postmenopausal women and presented the potential to predict late postmenopausal. The increase in postmenopausal time decreases global HRV indices.

AUTHORS' CONTRIBUTIONS

TDC: Data curation, Supervision, Writing – original draft. **ARN:** Data curation. **LSP:** Formal Analysis. **FRO:** Formal Analysis. **ECB:** Supervision. **JMSJ:** Conceptualization. **LCMV:** Conceptualization. **ICES:** Conceptualization, Supervision, Writing – review & editing.

REFERENCES

1. Almeida Júnior ÁD, Carvalho TD, Norberto AR, Figueiredo FWDS, Martinelli PM, de Abreu LC, et al. Autonomic cardiac modulation in postmenopausal women with dry eye syndrome: a cross-sectional analytical study. Rev Assoc Med Bras. 2021;67(8):1143-49. https://doi.org/10.1590/1806-9282.20210529
2. Martinelli PM, Sorpreso ICE, Raimundo RD, Leal Junior OS, Zangirolami-Raimundo J, Lima MVM, et al. Heart rate variability helps to distinguish the intensity of menopausal symptoms: a prospective, observational, and transversal study. PLoS One. 2020;15(1):e0225866. https://doi.org/10.1371/journal.pone.0225866
3. de Rezende Barbosa MPDC, Vanderlei LCM, Neves LM, Takahashi C, Torquato PRDS, Fortaleza ACS, et al. Impact of functional training on geometric indices and fractal correlation property of heart rate variability in postmenopausal women. Ann Noninvasive Electrocardiol. 2018;23(1):e12469. https://doi.org/10.1111/anec.12469
4. Rezende Barbosa MP, Netto Júnior J, Cassemiro BM, de Souza NM, Bernardo AF, da Silva AK, et al. Impact of functional training on cardiac autonomic modulation, cardiopulmonary parameters and quality of life in healthy women. Clin Physiol Funct Imaging. 2016;36(4):318-25. https://doi.org/10.1111/cpf.12235
5. Rezende Barbosa MP, Vanderlei LC, Neves LM, Takahashi C, Torquato PR, Silva AK, et al. Functional training in postmenopause: cardiac autonomic modulation and cardiorespiratory parameters, a randomized trial. Geriatr Gerontol Int. 2019;19(8):823-8. https://doi.org/10.1111/ggi.13690
6. Hämmerle P, Eick C, Blum S, Schlageter V, Bauer A, Rizas KD, et al. Heart rate variability triangular index as a predictor of cardiovascular mortality in patients with atrial fibrillation. J Am Heart Assoc. 2020;9(15):e016075. https://doi.org/10.1161/JAHA.120.016075
7. Silva AKF, Christofaro DGD, Bernardo AFB, Vanderlei FM, Vanderlei LCM. Sensitivity, specificity and predictive value of heart rate variability indices in type 1 diabetes mellitus. Arq Bras Cardiol. 2017;108(3):255-62. https://doi.org/10.5935/abc.20170024
8. Pivatelli FC, Santos MA, Fernandes GB, Gatti M, Abreu LC, Valenti VE, et al. Sensitivity, specificity, and predictive values of linear and nonlinear indices of heart rate variability instable angina patients. Int Arch Med. 2012;5(1):31. https://doi.org/10.1186/1755-7682-5-31
9. Corrêa PR, Catai AM, Takakura IT, Machado MN, Godoy MF. Heart rate variability and pulmonary infections after myocardial revascularization. Arq Bras Cardiol. 2010;95(4):448-56. https://doi.org/10.1590/s0066-782x2010005000123

10. Catai AM, Pastre CM, Godoy MF, Silva E, Takahashi ACM, Vanderlei LCM. Heart rate variability: are you using it properly? Standardisation checklist of procedures. Braz J Phys Ther. 2020;24(2):91-102. https://doi.org/10.1016/j.bjpt.2019.02.006

11. Vanderlei LCM, Pastre CM, Hoshi RA, Carvalho TD, Godoy MF. Noções básicas de variabilidade da frequência cardíaca e sua aplicabilidade clínica. Rev Bras Cir Cardiovasc. 2009;24(2):205-17. https://doi.org/10.1590/S0102-76382009000200018

12. Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its associated cutoff point. Biom J. 2005;47(4):458-72. https://doi.org/10.1002/bimj.200410135

13. Bagnoli VR, Fonseca AM, Arie WMY, Neves EM, Azevedo RS, Sorpreso IC, et al. Metabolic disorder and obesity in 5027 Brazilian postmenopausal women. Gynecol Endocrinol. 2014;30(10):717-20. https://doi.org/10.3109/09513590.2014.925869

14. Sanchez-Barajas M, Ibarra-Reynoso LDR, Ayala-Garcia MA, Malacara JM. Flow mediated vasodilation compared with carotid intima media thickness in the evaluation of early cardiovascular damage in menopausal women and the influence of biological and psychosocial factors. BMC Womens Health. 2018;18(1):153. https://doi.org/10.1186/s12905-018-0648-3