

## Effects of Age and Aerobic Fitness on Heart Rate Recovery in Adult Men

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### Abstract

**Background:** Physiological aging leads to cardiac autonomic dysfunction, which is associated with the onset and worsening of cardiovascular disease and an increased risk of death. Currently, physical exercise is considered a cardioprotective strategy and more research is needed on its benefit on cardiac autonomic function.

**Objective:** To evaluate the autonomic control of heart rate in healthy young and middle-aged volunteers with different levels of aerobic fitness.

**Methods:** The study included 68 volunteers, stratified for age and level of aerobic fitness. Based on aerobic fitness assessed by the submaximal exercise test, subjects were separated into two groups, good fitness and poor fitness. Assessment of cardiac autonomic control was performed based on measurements of heart rate variability at rest and heart rate recovery post-exercise. Analysis of variance with two factors was used to compare the variables investigated.

**Results:** The heart rate variability is significantly lower in middle-aged volunteers than in young individuals, regardless of the aerobic fitness level ( $p < 0.01$ ). Higher levels of aerobic fitness in middle-aged volunteers are associated with earlier post-effort vagal reentry - rate of HR decline after 1min30s: 39.6% good aerobic fitness vs. poor 28.4% ( $p < 0.01$ ).

**Conclusion:** Better levels of aerobic fitness act beneficially on the autonomic control of post-exercise heart rate, preserving the vagal reentry velocity in healthy middle-aged volunteers. However, it does not attenuate the decrease in heart rate variability due to the natural aging process. (Arq Bras Cardiol 2012;99(3):802-810)

**Keywords:** Autonomic nervous system; heart rate; physical fitness; exercise; middle aged; young adult.

### Introduction

The heart rate variability (HRV) is a non-invasive tool used for the analysis of cardiac autonomic modulation, being a functional indicator of the autonomic nervous system<sup>1</sup>. Studies have shown that there is a decrease in HRV with advancing age<sup>2-6</sup> and that this reduction is associated with the emergence or worsening of cardiovascular disease, increasing the risk of death from all causes<sup>7-11</sup>.

However, the cardioprotective role of physical exercise is a consensus in the literature and is considered important in maintaining health in all age groups. However, its effect on HRV after aerobic training programs and the expected positive correlation between higher levels of aerobic fitness and HRV remains controversial. Studies have shown that older adults engaged in physical activity for several years have higher levels of HRV than sedentary ones<sup>12-14</sup>. On the other hand, there is evidence that aerobic training programs do not exert significant influence on HRV indices in middle-aged individuals<sup>5,15-17</sup>.

Another evaluation measure of cardiac autonomic function is heart rate recovery (HRR) post-exercise, defined as the rate of decline in HR after cessation of the effort<sup>18</sup>. There are reports

in the literature that middle-aged and elderly individuals have delayed HR recovery after exercise test, when compared to young individuals<sup>19,20</sup> and that HRR measures are directly related to the level of aerobic fitness<sup>21,22</sup>. Furthermore, healthy trained individuals have a faster post-exercise HRR than sedentary controls<sup>20,23,24</sup>.

In this context, the objective of this study was to evaluate the cardiac autonomic function, using the analysis of HRV at rest and HRR after submaximal exercise test in healthy young and middle-aged individuals.

### Methods

#### Study population

A total of 68 volunteers were recruited, aged 20-60 years, male, healthy and nonsmokers. Due to the sample age distribution, we chose to study primarily 50 of these volunteers, divided into two groups: young (20-30 years) and middle-aged (40-60 years). Thus, we investigated four experimental groups: young individuals with good aerobic fitness (YGF,  $n = 11$ , age =  $24.7 \pm 2.8$ ), young individuals with poor aerobic fitness (YPF,  $n = 12$ , age =  $24.9 \pm 2.3$ ), middle-aged individuals with good aerobic fitness (MAGF,  $n = 13$ , age =  $47.3 \pm 6.6$ ) and middle-aged individuals with poor aerobic fitness (MAPF,  $n = 14$ , age =  $48.0 \pm 5.4$ ). The remaining 18 volunteers, aged 31 to 39 years were considered only for the multiple regression analysis, described in the statistical

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analysis subsection. All volunteers were recruited considering the following exclusion criteria: i) use of medication and ii) having signs or symptoms of cardiovascular diseases detected by clinical evaluation.

### Ethical aspects

The experimental protocol was approved by the Ethics Committee in Research of Instituto Nacional de Cardiologia. All volunteers were informed and instructed about the study participation and signed the free and informed consent form.

### Volunteer assessment

All volunteers underwent evaluation, consisting of: i) history (personal data, investigation of lifestyle and physical activity, history of previous diseases and risk factors for cardiovascular system diseases) and ii) physical examination (general assessment, height and total body mass measurement, overall osteoarticular assessment, heart and respiratory rate measurement and systolic and diastolic blood pressure measurement at rest).

## Experimental protocol

### Electrocardiographic signal acquisition and processing (ECG)

ECG signals were acquired in an adequate environment, with controlled temperature and low noise, always in the afternoon, between 2 pm and 5 pm. To undergo the experimental protocol, the subjects were previously instructed to follow the following procedures: i) do not drink alcohol or caffeinated beverages for 24 hours prior to the examination, ii) have a good night's sleep, iii) not to exercise for 24 hours prior to the examination iv) avoid food intake of at least two hours before the test.

For the acquisition of the ECG signal three pairs of skin electrodes were placed to obtain the modified Frank's derivations X, Y and Z<sup>8</sup>. After electrode placement, the volunteers remained at rest in the supine position for a minimum period of 10 minutes for HR stabilization before the acquisition of the ECG signal for HRV analysis. Signal acquisition was performed with spontaneous breathing during the first 15 minutes. Then the volunteers were instructed to breathe in accordance with the rhythm determined by the examiner for five minutes, with the inspiration lasting 2 seconds and expiration lasting 3 seconds. Thus, the respiratory rate was controlled (CR) at a frequency of 12 respirations per minute (rpm), corresponding to 0.2 Hz to attain a 2:3 ratio between inspiration and expiration.

The electrocardiographic signal processing for the analysis of the autonomic modulation of heart rate was performed as follows: from the digitized ECG signal, we performed the automatic detection of R waves. Then the values of intervals between the R waves at the ECG (RRI) were calculated to establish the tachogram. The signal was processed to exclude artifacts and premature beats and immediately before and after beats, and to obtain the normal values of RRI (NNI) that were used to construct the tachogram considered for analysis. Following the recommendations of the American and

European Societies of Cardiology<sup>1</sup>, regarding the duration of the electrocardiographic signs of short duration, we used the first five minutes of uninterrupted signal without the presence of artifacts and extrasystoles.

For the study of HRV in the time domain we calculated variables from the INN tachogram and based on statistical relationships, given by (TASK FORCE, 1996):

- SDNN – standard-deviation INN intervals;
- RMSSD – root mean square of the differences of successive beats, given by:

$$RMSSD = \sqrt{\frac{\sum_{i=1}^{n-1} (N_i - N_{i+1})^2}{n-1}} \quad (1)$$

in which, n is the total number of INN intervals in the evaluated signal and the duration of the i-esimo interval is INN;

The variable SDNN reflects the participation of all rhythmic components responsible for variability, being related to the contributions of both branches of the autonomic nervous system, while the variable RMSSD reflects the contributions of variations at high frequencies, which are related to vagal action<sup>1</sup>.

To investigate the HRV in the frequency domain, each tachogram of NNI was interpolated using a linear spline to obtain equally spaced samples, and resampled at a rate of 2 Hz to be used in the calculation of the estimated power spectral density (PSD) function through fast Fourier transform (FFT).

Based on the PSD, two frequency bands were considered: low frequency (LF, 0.04-0.15 Hz), related to the baroreflex mechanism, and high frequency (HF, 0.15-0.4 Hz), related to respiration and vagal activity<sup>25,26</sup>. The LF/HF ratio was then estimated, which characterizes the sympathovagal balance<sup>25</sup>.

## Submaximal exercise test

### Aerobic fitness classification

The classification of volunteers in relation to the level of submaximal aerobic fitness was carried out through a submaximal exercise test (test withdrawal criteria: reaching 85% of maximal predicted heart rate for age (220 minus age), using Bruce protocol<sup>27</sup>. From the total time spent performing the submaximal exercise test (ET), a descriptive analysis of this variable was performed. The median of the ET time between all tests performed for each age group was used to classify the population in relation to the level of submaximal aerobic fitness as described below. The Borg scale of subjective perception of effort was used to monitor effort at every step of the exercise test.

Moreover, at the beginning and end of each stage of that test, heart rate (HR) was measured, as well as systolic (SBP) and diastolic (DBP) blood pressure. Regarding the level of submaximal aerobic fitness, the sample was qualitatively classified as: (a) good aerobic fitness (GF): individuals who had an ET greater than the median, stratified by age, or (b) poor aerobic fitness (PF): individuals who had ET less than the median, stratified by age.

### Recovery protocol after submaximal exercise test

It was carried out so that post-exercise recovery was performed in a slow, gradual manner, minimizing adverse effects, such as fainting, and other abnormal pressure decreases. With this purpose, it was divided into three sequential steps:

Step 1 - during the gradual withdrawal of the treadmill inclination, during 1 min and 30 s, the speed was gradually reduced until it reached 1.6 Km / h;

Step 2 – the volunteer walked at a speed of 1.6 km / h for 1 min and additional 30 s;

Step 3 - the volunteer remained standing on the treadmill for 2 min, ending the recovery protocol post-exercise.

The HRR was defined as the difference between the peak HR and the HR achieved at each stage of recovery defined above normalized by peak HR and studied in each of the following phases:

$$(1) \text{ Deceleration 1 (D1): } \frac{HR_{peak} - HR_{phase 1}}{HR_{peak}} \cdot 100;$$

$$(2) \text{ Deceleration 2 (D2): } \frac{HR_{peak} - HR_{phase 2}}{HR_{peak}} \cdot 100;$$

$$(3) \text{ Recovery (R): } \frac{HR_{peak} - HR_{phase 3}}{HR_{peak}} \cdot 100;$$

### Statistical analysis

In all statistical tests, the level of significance was set at  $\alpha = 0.05$ . Numerical data are presented as mean  $\pm$  standard deviation (SD). The visual presentation of the results is shown in the boxplot chart format.

The sample analysis was performed on the variable RMSSD based on the work of Marocolo et al.<sup>28</sup>, considering a difference between the means of sedentary and physically active groups of 34.4 ms, standard deviation of 28.8 ms in both groups and distribution of individuals between groups with a ratio of 1:1, whereas error values  $\alpha = 0.05$  and  $\beta = 0.1$ . The sample size was calculated using the software Statgraphics 5.1, resulting in 10 subjects for each age group.

The variables analyzed were: resting HR, resting RR, SBP, DBP, body mass index (BMI), perceived exertion at the last stage of the submaximal ET (PSE), ET time, HRR at stages D1,

D2 and R and HRV indices (SDNN, RMSSD, HF, LF, LF/HF) during spontaneous breathing and CR. For such variables, we used the bi-factorial analysis of variance (two-way ANOVA) with the factors age and aerobic fitness, followed by Bonferroni post-test. The HRV variables were transformed into their natural logarithms (LnT), in order to normalize the probability distribution functions<sup>8</sup>.

In order to verify the correlation between HRV parameters and the age variable, an analysis was performed using Pearson's linear correlation.

The stepwise multiple linear regression analysis was performed to obtain which physiological variables (age, HR, RR, SBP, DBP, HRR - D1, D2 and R, BMI, ET time) were responsible for possible alterations in parameters of HRV analysis in healthy men aged 20 to 60 years. In this particular case, we considered data from 68 subjects, with added data from 18 volunteers aged 31 to 39 years.

## Results

### Sample characteristics

The physiological variables, BMI, SBP, DBP, resting HR, resting RR and PSE were not significantly different between groups (Table 1).

Regarding the total duration of the exercise test (ET time), the analysis of variance indicated significant differences ( $p < 0.0001$ ) as a function of age range and physical fitness (Table 1). It was observed that the ET time was significantly lower ( $p < 0.0001$ ) in groups with PF compared to individuals with GF, both in young and middle-aged volunteers. Additionally, the ET time was significantly lower ( $p < 0.001$ ) in middle-aged subjects compared to young individuals for both levels of aerobic fitness (Table 1).

### Effect of age ranges and aerobic fitness on HRV

The HRV parameters both in spontaneous breathing and in controlled breathing were significantly lower in middle-aged subjects compared to young volunteers, except for the variable Ln (LF/HF) reflecting the sympathovagal balance (Table 2). There were no significant differences between groups when aerobic fitness was analyzed (Table 2).

**Table 1 - Characterization of experimental groups**

Experimental Group		N	Age	BMI (Kg/m <sup>2</sup> )	RPE	HR (irpm)	SBP (mmHg)	DBP (mmHg)	ET Time (min)
Age	Fitness								
20-30	GF	11	24.7 $\pm$ 2.8	25.3 $\pm$ 0.03	15.5 $\pm$ 1.9	17.4 $\pm$ 3.8	122.9 $\pm$ 9	79.7 $\pm$ 11.1	10.5 $\pm$ 0.7 <sup>§</sup>
	PF	12	24.9 $\pm$ 2.3	27.0 $\pm$ 0.08	14.5 $\pm$ 3.5	16.6 $\pm$ 3.8	121.8 $\pm$ 13.1	77.08 $\pm$ 8.7	8.1 $\pm$ 1.1
40-60	GF	13	47.3 $\pm$ 6.6	26.3 $\pm$ 3	14.9 $\pm$ 1.3	15.5 $\pm$ 4.2	124.7 $\pm$ 16.2	81.7 $\pm$ 9.8	8.5 $\pm$ 0.9 <sup>§#</sup>
	PF	14	48.0 $\pm$ 5.4	27.0 $\pm$ 3.7	13.3 $\pm$ 2.7	15.0 $\pm$ 3.8	127.4 $\pm$ 9.7	82.0 $\pm$ 9.1	6.1 $\pm$ 1 <sup>#</sup>

BMI: body mass index; <sup>#</sup>  $p < 0.001$  in relation to 20-30 between group with the same physical fitness, but different age ranges; <sup>§</sup>  $p < 0.0001$  between groups of the same age range, but with different physical fitness; GF: good physical fitness; PF: poor physical fitness; N: sample size; HR: heart rate at rest; RPE: ratings of perceived exertion (Borg Scale); SBP: systolic blood pressure; DBP: diastolic blood pressure; ET time: total time spent at the submaximal exercise test. Values described as mean  $\pm$  standard-deviation.

**Table 2 - Analysis of HRV parameters. Values described as mean  $\pm$  SD**

Experimental group	N	Ln (SDNN) (ms)	Ln (RMSSD) (ms)	Ln (LF) (ms <sup>2</sup> )	Ln (HF) (ms <sup>2</sup> )	Ln (LF/HF)	
<b>Spontaneous breathing</b>							
20-30	GF	11	4.2 $\pm$ 0.4	4 $\pm$ 0.6	7 $\pm$ 0.7	6.6 $\pm$ 0.8	0.4 $\pm$ 0.7
	PF	12	4.1 $\pm$ 0.3	3.9 $\pm$ 0.4	6.7 $\pm$ 0.7	6.7 $\pm$ 0.8	-0.01 $\pm$ 0.5
40-60	GF	13	3.6 $\pm$ 0.6 <sup>*</sup>	3.2 $\pm$ 0.7 <sup>**</sup>	6.2 $\pm$ 1.1	5.2 $\pm$ 1.4 <sup>**</sup>	1.1 $\pm$ 0.8 <sup>*</sup>
	PF	14	3.6 $\pm$ 0.4 <sup>**</sup>	3.1 $\pm$ 0.7 <sup>**</sup>	6 $\pm$ 1	4.6 $\pm$ 1.2 <sup>***</sup>	1.2 $\pm$ 0.7 <sup>***</sup>
<b>Controlled breathing</b>							
20-30	GF	11	4.0 $\pm$ 0.4	4 $\pm$ 0.6	6.2 $\pm$ 0.7	7.4 $\pm$ 1.2	-1.2 $\pm$ 1
	PF	12	4.2 $\pm$ 0.3	4.2 $\pm$ 0.4	6.4 $\pm$ 0.8	7.8 $\pm$ 0.7	-1.3 $\pm$ 0.7
40-60	GF	13	3.6 $\pm$ 0.4 <sup>*</sup>	3.3 $\pm$ 0.7 <sup>*</sup>	5.5 $\pm$ 1.1	5.5 $\pm$ 1.1 <sup>**</sup>	-0.3 $\pm$ 0.9 <sup>*</sup>
	PF	14	3.7 $\pm$ 0.5 <sup>**</sup>	3.5 $\pm$ 0.7 <sup>**</sup>	5.4 $\pm$ 1.2 <sup>*</sup>	6.2 $\pm$ 1.3 <sup>**</sup>	-0.8 $\pm$ 0.7

N: sample size; <sup>\*</sup>  $p < 0.05$ ; <sup>\*\*</sup>  $p < 0.01$ ; <sup>\*\*\*</sup>  $p < 0.001$  between groups with the same physical fitness - good fitness (GF) or poor fitness (PF) – however, at different age ranges.

### Analysis of the correlation between HRV parameters and the age variable

The analysis of Pearson's linear correlation between the HRV parameters in spontaneous breathing and in controlled breathing and the variable age of volunteers was significant for all studied parameters. There was a negative correlation between the age variable and Ln (SDNN), Ln (RMSSD), Ln (LF), Ln (HF) and a positive correlation with Ln (LF/HF). Of these parameters, the one that showed the highest correlation with age in both spontaneous breathing and in controlled breathing was Ln (HF) in the frequency domain and Ln (RMSSD) in the time domain; these parameters represent cardiac vagal modulation (Table 3).

### Analysis of multiple linear regression

For the multiple regression analysis, Ln (RMSSD\_S) was tested as the dependent variable, as it represented the variable in the time domain with the highest correlation with age and greater simplicity in the calculation. Initially, the following independent variables were entered in the multiple regression model: ET time, SBP, BMI, RR, HRR (D1, D2 and R), resting HR and age (20-60 years).

After analysis of collinearity and adjustment of the stepwise multiple regression model, the following independent variables remained in the final model: age and resting HR (Table 4). The coefficient of determination was  $R^2 = 64.9\%$  ( $p < 0.001$ ).

The equation of the final model was adjusted as follows:

$$\text{Ln (RMSSD_S)} = 8.52 - (0.06 \times \text{resting HR}) - (0.03 \times \text{age})$$

The multiple regression analysis shows that the variable cardiac vagal modulation represented by the variable Ln (RMSSD) in spontaneous breathing (Ln (RMSSD\_S)) was explained (approximately 65%) by resting HR and age (Table 4).

The independent variables in the final multiple regression model, resting HR and age were inversely associated with the dependent variable Ln (RMSSD\_S) (Graphs 2 and 3).

### Post-hoc analysis of statistical power

The post hoc evaluation of the power of statistical test (1- $\beta$ ) was performed using as basis of comparison the means of the HRR variables in phases D1 and D2 between the groups of middle-aged volunteers with good aerobic fitness versus those with poor aerobic fitness, considering a one-tailed approach. The analysis showed that, with the sample size used in this study for the analysis of the variable D1, the statistical test showed a 95% power to the variable D2, 90%.

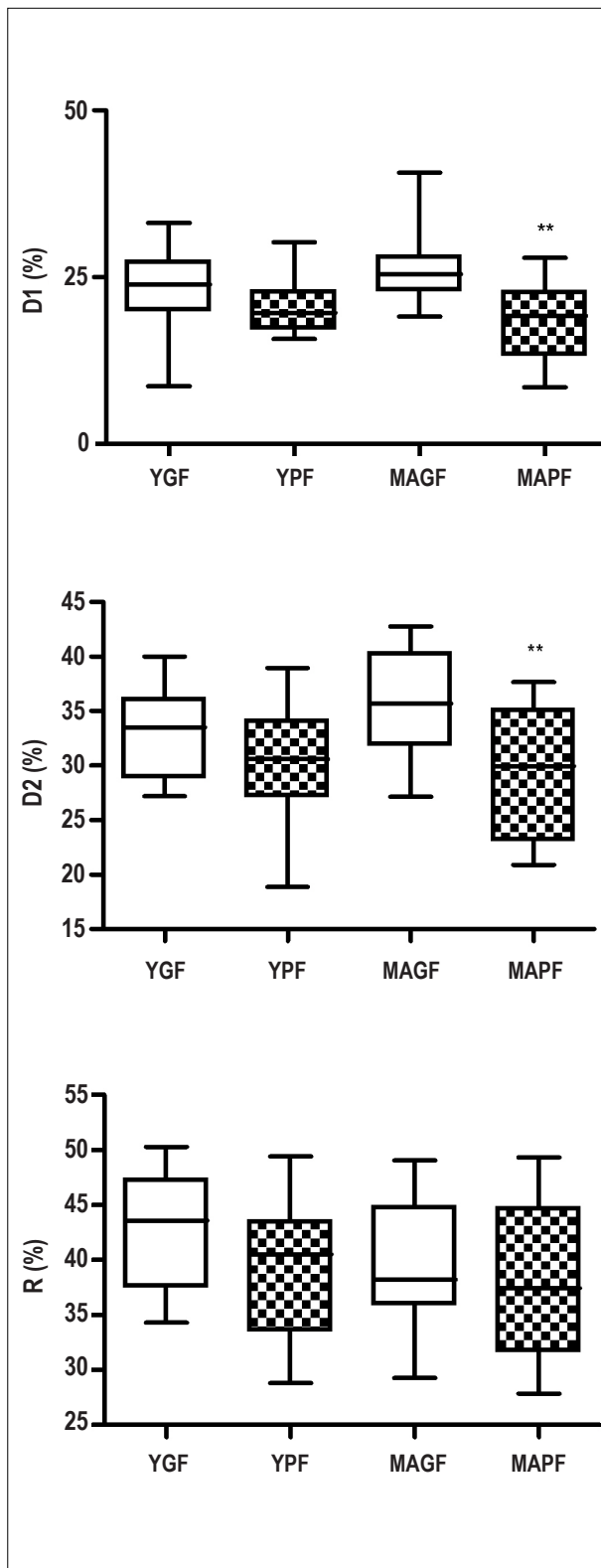
The variable LnRMSSD bin spontaneous breathing showed a 95% power in the recruited sample when comparing young subjects with middle-aged ones with good aerobic fitness, as well as young individuals versus middle aged ones with poor aerobic fitness.

### Discussion

The autonomic modulation of HR, as measured by HRV at rest was significantly lower in middle-aged volunteers compared with young individuals, characterizing the deleterious effect of aging on cardiac autonomic function. This finding was similar to several published studies that evaluated healthy subjects at similar age ranges to the ones in the present work<sup>2,4,6,15,29</sup>. However, better aerobic fitness values were not effective in attenuating the reduction in HRV with age.

Migliaro et al.<sup>29</sup> found similar results to those of the present study, as they did not find significant differences in resting HRV between young sedentary and non-sedentary individuals. Evaluating the effect of a short-duration aerobic training program of mild to moderate intensity on heart rate variability in middle-aged individuals (40-60 years), Smith<sup>15</sup> found no alteration in HRV indices, although he showed improvement in aerobic fitness. On the other hand, De Meersman<sup>30</sup> showed that physically active individuals have a higher cardiac vagal modulation than sedentary individuals, in both young volunteers and middle-aged individuals.

The HRR, in the present study was lower in middle-aged volunteers with poor aerobic fitness, when compared to



**Graph 1** – Boxplots of HRR after submaximal exercise test at the phases: (a) D1; (b) D2 and (c) R in the studied groups. YGF: young individuals with good physical fitness; YPF: young individuals with poor physical fitness; MAGF: middle-aged individuals with good physical fitness; MAPF: middle-aged individuals with deficient physical fitness.

volunteers with good aerobic fitness. These results corroborate the findings of Cole et al.<sup>19</sup> and Du et al.<sup>23</sup>, as in the first study, the authors found an association between low HRR values in subjects with poor aerobic fitness and, in the second, when studying women marathon runners (32-42 years), the authors showed that the HRR was faster in the marathon runners than in the sedentary control group.

Several authors have demonstrated the prognostic and predictive role of HR response after exercise testing<sup>18,19,31,32</sup>. Still, few studies were carried out in order to understand the interaction between HRR measures, aerobic fitness and mortality. In a pioneering study, Kokkinos et al.<sup>33</sup>, evaluating the association between HRR (1<sup>st</sup> and 2<sup>nd</sup> min of recovery), aerobic fitness and risk of mortality from all causes in a cohort of 5,974 men with a follow-up period of 6.2 years, showed that in individuals with low aerobic fitness and low HRR, the mortality risk was approximately seven times higher when compared to subjects with good aerobic fitness and high HRR. The authors emphasize that the aerobic fitness associated with HRR substantially affects mortality. This study demonstrates the impact of aerobic fitness on the HRR.

The results regarding the cardiac autonomic function found in our study (HRV at rest and HRR after exertion) were discrepant by showing that HRV decreases with aging, but there is no effect of aerobic fitness on its values. Moreover, the HRR was not different among age groups, even though there were significant differences as a function of aerobic fitness.

The current literature has shown the lack of correlation between measures of HRV at rest and HRR<sup>34-36</sup>. The role of these measures in the autonomic nervous system remains to be elucidated. It is believed that the HRV indices related to vagal activity reflect the magnitude of the vagal autonomic modulation, whereas those related to HRR reflect the autonomic tone itself<sup>37</sup>. More studies are needed to clarify this issue.

The analysis of stepwise multiple linear regression adopted in this study showed that, in the sample studied, alterations in cardiac vagal tone measured by Ln (RMSSD) index is significantly explained by alterations in resting HR and age, with little or no participation of the HRR and indistinct at the level of aerobic fitness.

The information described in the literature indicates that normal aging leads to reduced HRV. However, the role of exercise training and improved levels of aerobic fitness in this process remain unclear. This study, based on an adjusted protocol of post-submaximal exercise recovery, showed that middle-aged individuals with good aerobic fitness have a faster HR recovery after exercise than middle-aged individuals with poor aerobic fitness.

## Conclusion

Better levels of aerobic fitness are beneficial to the autonomic control of heart rate after exertion, preserving the velocity of vagal reentry in middle-aged volunteers. However, such fitness levels do not seem to attenuate the reduction in heart rate variability at rest due to the natural aging process in the analyzed age group.

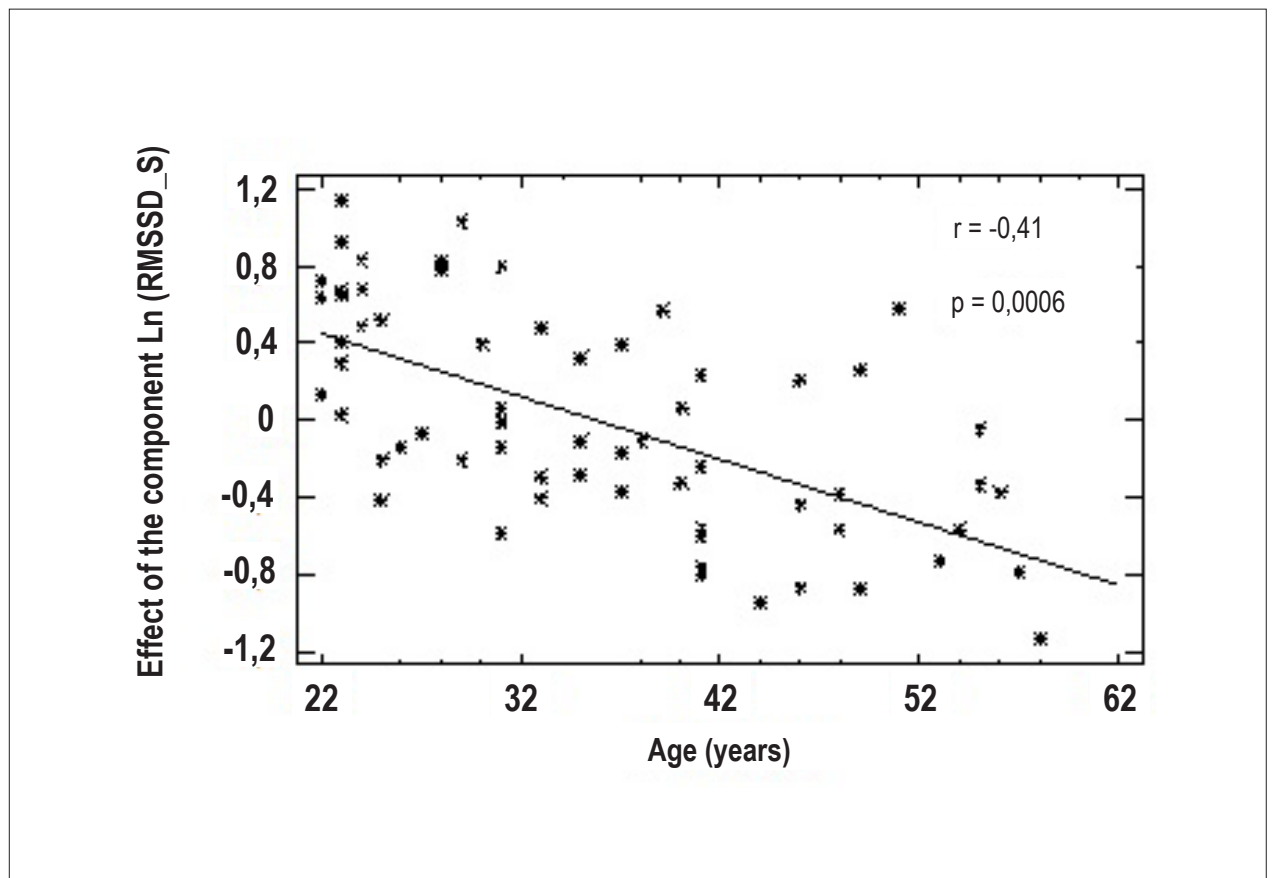
**Table 3 - Pearson's linear correlation between parameters of HRV, in spontaneous and controlled breathing and the variable age**

Ln(SDNN) x Age	Ln(RMSSD) x Age	Ln(LF) x Age	Ln(HF) x Age	Ln(LF/HF) x Age
<b>Spontaneous Breathing</b>				
r = - 0,5 p = 0,0002	r = - 0,5 p = 0,0001	r = - 0,4 p = 0,0059	r = - 0,6 p < 0,0001	r = 0,5 p < 0,0003
<b>Controlled Breathing</b>				
r = - 0,4 p = 0,001	r = - 0,4 p = 0,0008	r = - 0,4 p = 0,007	r = - 0,5 p < 0,0001	r = 0,4 p < 0,005

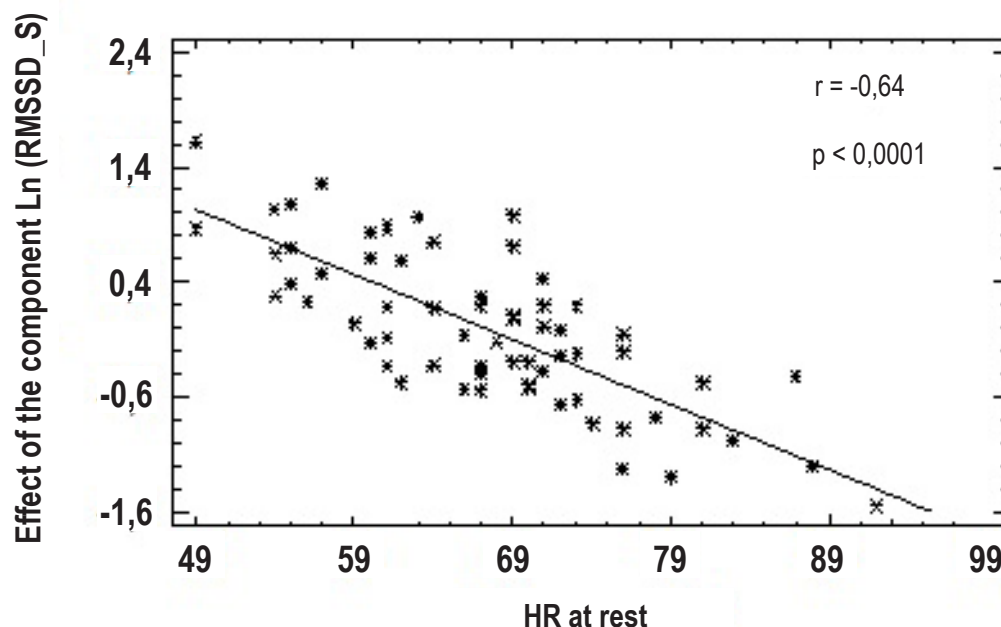
*In bold the VFC variables that show a higher correlation with the variable age.*

**Table 4 - Multiple regression analysis for the dependent variable Ln (RMSSD) in spontaneous breathing**

Dependent variable Ln (RMSSD) in spontaneous breathing				
Parameter	Estimate	Standard-deviation	T Statistics	P value
Constant	8.5	0.4	18	< 10 <sup>-4</sup>
Age	- 0.03	0.01	- 6.3	< 10 <sup>-4</sup>
HR at rest	- 0.06	0.01	- 9.4	< 10 <sup>-4</sup>



**Graph 2 – Regression chart between the independent variable age and the dependent variable Ln (RMSSD\_E) in multiple regression. Note the significant value of the partial regression coefficient (p < 0.001). S - spontaneous breathing.**



**Graph 3** – Regression chart between the independent variable HR at rest and the dependent variable Ln (RMSSD\_S) in multiple regression. Note the significant value of the partial regression coefficient ( $p < 0.001$ ). S - spontaneous breathing.

#### Potential Conflict of Interest

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

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#### Study Association

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