Does the Aging Process Significantly Modify the Mean Heart Rate?

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Abstract

Background: The Mean Heart Rate (MHR) tends to decrease with age. When adjusted for gender and diseases, the magnitude of this effect is unclear.

Objective: To analyze the MHR in a stratified sample of active and functionally independent individuals.

Methods: A total of 1,172 patients aged ≥ 40 years underwent Holter monitoring and were stratified by age group: 1 = 40-49, 2 = 50-59, 3 = 60-69, 4 = 70-79, 5 = ≥ 80 years. The MHR was evaluated according to age and gender, adjusted for Hypertension (SAH), dyslipidemia and non-insulin dependent diabetes mellitus (NIDDM). Several models of ANOVA, correlation and linear regression were employed. A two-tailed p value <0.05 was considered significant (95% CI).

Results: The MHR tended to decrease with the age range: 1 = 77.20 ± 7.10; 2 = 76.66 ± 7.07; 3 = 74.02 ± 7.46; 4 = 72.93 ± 7.35; 5 = 73.41 ± 7.98 (p < 0.001). Women showed a correlation with higher MHR (p <0.001). In the ANOVA and regression models, age and gender were predictors (p < 0.001). However, R² and ETA² < 0.10, as well as discrete standardized beta coefficients indicated reduced effect. Dyslipidemia, hypertension and DM did not influence the findings.

Conclusion: The MHR decreased with age. Women had higher values of MHR, regardless of the age group. Correlations between MHR and age or gender, albeit significant, showed the effect magnitude had little statistical relevance. The prevalence of SAH, dyslipidemia and diabetes mellitus did not influence the results. (Arq Bras Cardiol. 2013;101(5):388-398)

Keywords: Aging; Heart Rate; Electrocardiography, Ambulatory.

Introduction

The aging process, in spite of recent medical advances, still constitutes an inexorable phenomenon. The number of elderly individuals has grown in almost all regions of the world, particularly where strategies to improve living conditions have been implemented1.

In recent decades, there has been a change in the age profile of Brazil. Considered for a long time as a young population, the number of elderly individuals is progressively increasing2,3.

On account of that, large-scale studies have been performed on the different aspects of the aging issue4-6, understood as a complex and multifactorial process, comprising biological changes with consequences on quality of life and general health status7.

There are several features related to cardiovascular senescence, ranging from decreased left ventricular compliance due to collagen accumulation and fibrosis to alterations in the conduction system, with reduction in pacemaker cells and fatty infiltration, leading to loss of specialized fibers and intrinsic decrease in sinus automatism8,9. Moreover, dynamic histochemical and immunohistochemical alterations during the aging process are associated with autonomic reactions involved in the reduction of heart rate in the elderly10, resulting in diagnostic and therapeutic implications11.

There is little scientific literature that aims to measure the effect size and relevance of MHR at Holter with advancing age. Searching the Medline and Embase databases for publications from 2005 on, using the keywords 'mean heart rate' and "aging" or "elderly", only one article addressed the issue, albeit indirectly due to its design, as well as its small sample size and specific population12.

The present study aims to investigate the values of MHR in functionally and mentally active adults and elderly individuals, submitted to physical examination with 24-hour Holter monitoring. Several and exhaustive statistical analysis models will be used in order to identify, quantify and assess the relevance of MHR trends associated with age,
dependent or not on other factors, including gender and presence of three high prevalence comorbidities among the elderly: systemic arterial hypertension (SAH), dyslipidemia and non-insulin dependent diabetes mellitus (NIDDM).

Methods

A cross-sectional, descriptive and analytical study was carried out. The study complied with the ethical principles in the Declaration of Helsinki and the requirements of the 196/96 National Health Council Resolution, including complementary requirements and was approved by the institutional Research Ethics Committee #100710, on July 19, 2010. All individuals enrolled in the study consented to participate and signed the free and informed consent form.

The sample size, of around a thousand individuals, was previously calculated using the GPower software, based on the following parameters: alpha = 0.05, 1-β = 0.80, effect = 0.10. Data collection was performed consecutively and prospectively and the sample consisted of adult and elderly individuals of both genders, aged ≥ 40 years, submitted to Holter monitoring for 24 hours in a cardiology reference private practice from July 2010 to December 2012. The main reason for the examination was routine cardiological assessment in asymptomatic individuals or investigation of nonspecific symptoms, such as palpitations, dizziness or atypical chest pain.

The recording of the electrocardiographic tracing was performed during spontaneous situations occurring outside the hospital and medical environment. Every beat that generated electrical activity at any time of the recording was counted. The method has been validated by several researchers national and international cardiology associations.

The Holter recorder used in the study was a Cardiolight Cardsios digital model with Memory Card, which performed 3-channel continuous recording, subsequently analyzed by the CardioSmart Professional CS 540 program. All recording devices were installed in the same location by the same professional and the tests were processed in a single computer. Moreover, the analysis of the examination and the production of the final report were made by the same cardiologist, experienced in Holter System.

Before the enrollment, individuals initially selected by the age criterion (≥ 40 years) and under outpatient care, were invited for an interview, where cognitive capacity was evaluated, albeit subjectively (understand without difficulty the content of direct questions related to anamnesis) and functional independence (walking without external aid, pain or difficulty in walking).

We selected only those individuals that met both criteria and agreed to take part in the research. Complaints indicating major diseases (history of myocardial infarction, angina pectoris, invasive hemodynamic procedure, cardiac surgery and permanent pacing) represented additional exclusion criteria.

We also excluded those who reported using insulin, digitals, antiarrhythmics, beta-blockers or drugs that had a direct action on heart rate (such as the nebivolol), and the pharmacological survey was carried out in two stages (on the day of installation and removal of the recording device) and by evaluating the compatibility between the anamnesis, the reported diseases and prescribed medications.

We also subsequently excluded those whose tests had a recording duration < 22 hours, those with more than 5% of artifacts, atrial fibrillation or dynamic alterations in the ST segment and T wave, high rate of supraventricular or ventricular ectopy (> 10,000/24h), or those who had evidence of abnormal sinus activity, be it of functional or organic etiology, manifested by atypical MHR values (< 60 or > 90 bpm). After echocardiography, we selected subjects with ejection fraction (EF) > 50%. The sample selection flowchart is shown in figure 1.

The resulting sample consisted of 1,172 individuals and was separated by gender and grouped into five strata according to the age (in years): 1 = 40-49; 2 = 50-59; 3 = 60-69; 4 = 70-79; 5 ≥ 80. There were no missing data. Anthropometric data were obtained (weight and height) using an electronic calibrated scale with a maximum capacity of 200 kg and a ruler for measuring height ranging between 1.30 and 2 meters. The Body Mass Index (BMI) was calculated using the formula: weight (kg) / height (m)².

Sample characterization data were obtained through a sociodemographic questionnaire, as well as reference to three chronic diseases: systemic arterial hypertension, diabetes mellitus and dyslipidemia.

The calculations were performed using SPSS platform 20, with the exception of the homoscedasticity test, and MHR jacknife estimates were performed in Stata 12. The 95% Confidence Interval (95%CI) was used and a significance value of p < 0.05 (two-tailed). Nonparametric data were represented by the total number and percentage. The chi-square test or Fisher’s test were employed when appropriate for comparisons between groups.

Parametric variables were described as mean, standard deviation, standard error and interquartile range. Several bootstraps were employed to corroborate the sample values of MHR, with 1,000 samples and random counts of the 95%CIs for each situation: MHR for the entire sample; MHR for gender differences; MHR in five age groups.

The Kolmogorov-Smirnov test was used for exploration of the normality pattern and Levene’s test for equality of variance. This was carried out both in the whole sample and in subgroups divided according to gender or age. In comparisons between two independent samples, the mean difference was calculated by Student’s t test. Even though the distribution was normal, the same thing was done with the Mann-Whitney test, due to its more conservative characteristic and lower probability of Type I error.

Subsequently, the analysis of MHR between age groups was performed by Kruskal-Wallis (also due to its more conservative characteristic and lower probability of type I error) and three ANOVA models: One-way (age groups), 5x2 (age groups and gender) and 5x2x2x2 (age groups, gender, SAH, dyslipidemia and diabetes mellitus). In the third ANOVA model, the difference between subgroups was calculated using Tukey’s post hoc test.
Figure 1 – Sample selection flow chart. CHD: coronary heart disease; AMI: acute myocardial infarction; PCI: percutaneous coronary intervention; APCs: atrial premature complexes; VPCs: ventricular premature complexes; MHR: mean heart rate; EF: ejection fraction

Results

The general characteristics of the sample distribution according to age groups and gender are shown in table 1. The age of the sample ranged between 40 and 100 years, with a mean of 65.69 ± 11.65 years.

It can be observed that females predominated in the five age groups, but this pattern was not significantly different between the age groups of the sample population. With advancing age, there was an increased prevalence of SAH, diabetes mellitus, dyslipidemia, and number of medications (p < 0.001) and decreased BMI, ejection fraction and percentage of non-sedentary individuals.

The mean MHR in the sample population was 74.45 ± 7.55 bpm (95% CI = 74.02 to 74.88). In addition to the narrow confidence interval, the internal validity of
Table 1 – Clinical characterization of the sample according to the age groups

| AGE RANGE (years) | 40-49 | 50-59 | 60-69 | 70-79 | ≥ 80 | p |
|------------------|-------|-------|-------|-------|------|---|
| N = 1172         | n(%)  | n(%)  | n(%)  | n(%)  | n(%) |   |
| GENDER           | 0.511            |
| Female           | 92(7.8)          | 118(10.1) | 255(21.8) | 195(16.6) | 105(9.0) |   |
| Male             | 46(3.9)          | 63(5.4)  | 154(13.1) | 99(8.4)   | 45(3.8) |   |
| COMORBIDITY      |                  |
| SAH              | 33(2.8)          | 78(6.7)  | 218(18.6) | 175(14.9) | 103(8.8) | < 0.001 |
| Dyslipidemia     | 18(1.5)          | 69(5.1)  | 164(14)   | 123(10.5) | 59 (5.0) | < 0.001 |
| Diabetes         | 6(0.5)           | 19(1.6)  | 52(4.4)   | 51(4.4)   | 26(2.2)  | 0.002  |
| PHYSICAL ACTIVITY| < 0.001          |
| Sedentary        | 89(7.6)          | 92(7.8)  | 164(14.0) | 167(14.2) | 107(9.1) |   |
| Walking          | 20(1.7)          | 41(3.5)  | 204(17.8) | 116(9.9)  | 32(2.7)  |   |
| Physical exercises| 29(2.5)        | 48(4.1)  | 41(3.5)   | 11(0.9)   | 11(0.9)  |   |
| BMI              | 27.5 ± 5.2       | 27.6 ± 3.6 | 27.2 ± 4.3 | 26.6 ± 4.4 | 26.1 ± 4.9 | 0.003 |
| N. of MEDICATIONS| 1.1 ± 1.1        | 1.1 ± 0.9 | 1.9 ± 1.8 | 2.1 ± 1.8 | 2.7 ± 2.1 | 0.001 |
| EJECTION FRACTION| 71.5 ± 7.6    | 68.1 ± 5.9 | 68.7 ± 6.8 | 67.2 ± 6.7 | 65.9 ± 7.1 | 0.003 |

SAH: systemic arterial hypertension; BMI: body mass index.

these values was corroborated by successive spontaneous bootstrap estimates (95% CI = 74.00 to 74.90) and the use of jackknife estimates (95% CI = 74.01 to 74.89). The analysis was also performed in subgroups according to gender, age range and the association between them. In all cases, the values obtained directly resembled those found by the jackknife and the bootstrap estimates (Table 2).

The median and interquartile ranges of MHR were analyzed for the whole sample according to gender and stratified according to gender and age. The distributions showed typical pattern of normality without outliers or atypical values. MHR was higher among women and this pattern persisted in all age groups; we also identified a trend decline in MHR with age, regardless of gender (Figure 2A, B, C, D).

The mean MHR was significantly higher in females, both at Student’s t test and at the Mann-Whitney test (p < 0.001). However, the magnitude of this difference was considerably small (d = 0.281). Both tests for comparisons of MHR means in two independent samples were reapplied regarding the presence of DM, dyslipidemia and diabetes, with nonsignificant results. Levene test for homogeneity of variance was satisfactory in all these analyses (Table 3).

In analyses involving the five age groups, different ANOVA models were employed, as well as the Kruskal-Wallis test (Table 5). With regard to the association between higher MHR and female gender, all tests resulted in significant differences. As for the association between MHR and age group, the One Way ANOVA and 5x2 (factors = age group and gender) were significant. This was not observed with the 5x2x2x2x2x2 ANOVA (previous factors + SAH + dyslipidemia + DM), probably due to the reduction in power caused by the magnification of factors.

However, in post hoc analysis of the subgroup, Tukey’s test showed differences in MHR, reaching levels of significance when the comparison was made between non-contiguous age groups. SAH, dyslipidemia and diabetes mellitus had no predictive influence, either separately or in interaction. Due to the multiple comparisons, when Bonferroni correction was applied, the threshold values for the interaction between age group and SAH (p = 0.046) were not considered significant. In situations where there was actually a significant difference, the values of R² and ETA² found in the several models indicated a diminished contribution of the involved variable. Similar phenomenon occurred with the five linear regression models.

In the first two models, a simple regression was applied, for the age group and for age as discrete variable. In the third, the three comorbidities were added and inserted simultaneously. Hierarchical regression was applied to the fourth and fifth models, the first in two stages and containing only age and gender, and the second in three stages, once again including the comorbidities (Table 6). Again, in all regression models significance was found for age range and gender. Nevertheless, the participation of these two variables was limited, given the reduced values of
Table 2 – Mean Heart Rate (MHR) values and confidence intervals (CI) according to gender, age and association between gender and age range

| Age range          | MHR (bpm) | SD  | SE  | 95%CI          | BOOTSTRAP 95%CI |
|--------------------|-----------|-----|-----|----------------|-----------------|
| TOTAL              | 74.45     | 7.55| 0.22| 74.02-74.88    | 74.00-74.90     |
| GENDER             |           |     |     |                |                 |
| Female             | 75.18     | 7.49| 0.27| 74.65-75.72    | 74.61-75.72     |
| Male               | 73.07     | 7.48| 0.37| 72.34-73.80    | 72.36-73.81     |
| AGE RANGE          |           |     |     |                |                 |
| 40-49 years        | 77.20     | 7.10| 0.60| 76.00-78.39    | 75.91-78.42     |
| 50-59 years        | 76.66     | 7.07| 0.52| 75.83-77.70    | 75.55-77.76     |
| 60-69 years        | 74.02     | 7.46| 0.36| 73.29-74.74    | 73.30-74.78     |
| 70-79 years        | 72.93     | 7.35| 0.42| 72.09-73.78    | 72.07-73.80     |
| ≥ 80 years         | 73.41     | 7.98| 0.65| 72.12-74.69    | 72.21-74.56     |
| GENDER X AGE RANGE |           |     |     |                |                 |
| 40-49 years        |           |     |     |                |                 |
| Female             | 78.25     | 6.83| 0.76| 76.74-79.75    | 76.8-79.58      |
| Male               | 75.08     | 7.25| 1.08| 72.96-77.21    | 73.04-77.04     |
| 50-59 years        |           |     |     |                |                 |
| Female             | 77.63     | 7.22| 0.67| 76.31-78.96    | 76.36-78.25     |
| Male               | 74.84     | 6.45| 0.92| 73.02-76.65    | 73.27-76.45     |
| 60-69 years        |           |     |     |                |                 |
| Female             | 74.83     | 7.43| 0.46| 73.93-75.74    | 73.94-75.75     |
| Male               | 72.65     | 7.34| 0.59| 71.49-73.81    | 71.52-73.82     |
| 70-79 years        |           |     |     |                |                 |
| Female             | 73.23     | 6.99| 0.52| 72.20-74.26    | 72.24-74.22     |
| Male               | 72.33     | 8.02| 0.73| 70.88-73.78    | 70.71-73.95     |
| ≥ 80 years         |           |     |     |                |                 |
| Female             | 74.19     | 7.96| 0.71| 72.78-75.59    | 72.62-75.72     |
| Male               | 71.57     | 7.97| 1.09| 69.43-73.72    | 69.24-73.70     |

Table 3 – Parametric and nonparametric tests for comparisons between the means of MHR in two independent samples, according to gender and comorbidities

| GROUPS:            | Student’s r | Levene | p       | Cohen’s d | Mann-Whitney | p       |
|--------------------|-------------|--------|---------|-----------|--------------|---------|
| Gender             | 4.594       | 0.738  | < 0.001 | 0.281     | 129.992      | < 0.001 |
| SAH                | 1.726       | 0.693  | 0.085   | -         | 160.944      | 0.069   |
| Dyslipidemia       | -0.614      | 0.425  | 0.539   | -         | 161.495      | 0.600   |
| Diabetes           | 0.437       | 0.243  | 0.662   | -         | 77.153       | 0.753   |

SAH: systemic arterial hypertension; MHR: mean heart rate.

standardized beta coefficients. In the hierarchical models, when analyzing the individual role of comorbidities, it was not significant from a statistical point of view.

The VIF values around 1 and the computation of the Durbin-Watson equation close to 2, added to the successful result of the Cook-Weisberg homoscedasticity test (p = 0.892) indicated excellent sample suitability to the models chosen for regression testing. This was also corroborated by analyzing the standardized regression residuals involving frequencies of distribution, cumulative probability and critical values of Z-distribution in scatter plots.
Discussion

The predominance of women as the age progresses has been probably due to a longer life expectancy in females, when compared with male elderly individuals\(^{19}\).

The three comorbidities assessed in the study (SAH, diabetes and dyslipidemia) showed homogenous distribution and had no influence on MHR behavior. In terms of prevalence, they showed a similar pattern customarily described in epidemiological studies carried out in other locations in Brazil\(^{20,21}\).

In the CARLA (Cardiovascular Disease, Living and Ageing) study, which had a sample of 1,779 individuals, age ranged between 45 and 83 years and no consistent association was observed between parameters of heart rate variability and major cardiovascular risk factors\(^{22}\).

Although it is generally considered that sinus automatism decreases with the aging process\(^{12-15}\), the prognostic value, therapeutic potential and clinical significance have been questioned in view of varying results and interpretation\(^{23,24}\).

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**Figure 2** – Distribution of Mean Heart Rate (MHR) values. A - Sample population. B - Stratification according to gender. C - Stratification according to age range and gender. D - Chart showing MHR decrease with increasing age, with comparative curve for both genders.
Table 4 – Bivariate, point biserial and partial correlation for mean heart rate (MHR) versus age, gender, disease, ejection fraction (EF) and Body Mass Index (BMI)

| VARIABLE                      | R       | R²      | p      |
|-------------------------------|---------|---------|--------|
| AGE                           | -0.198  | 0.039   | < 0.001|
| GENDER                        | -0.133  | 0.017   | < 0.001|
| Gender adjusted for Age       | -0.141  | 0.019   | < 0.001|
| SAH                           | -0.050  | 0.0025  | 0.085  |
| SAH adjusted for Age          | -0.002  | < 0.0001| 0.941  |
| DYSLIPIDEMIA                  | 0.018   | 0.0003  | 0.539  |
| Dyslipidemia adjusted for Age | 0.048   | 0.0003  | 0.100  |
| DIABETES                      | 0.013   | 0.0001  | 0.662  |
| Diabetes adjusted for Age     | 0.048   | 0.0001  | 0.695  |
| EJECTION FRACTION (EF)        | -0.009  | < 0.0001| 0.834  |
| EF adjusted for Age           | -0.019  | 0.0003  | 0.669  |
| BMI                           | 0.002   | < 0.0001| 0.952  |
| BMI adjusted for Age          | -0.011  | 0.0001  | 0.700  |

SAH: systemic arterial hypertension.

In Japan\textsuperscript{14}, the mean values of NN intervals at 24-hour Holter in 15 individuals aged > 65 years were analyzed in two stages, with a 15-year interval, showing slight shortening of sinus cycle, although reaching statistical significance ($0.976 \pm 0.115 \times 0.903 \pm 0.117, p = 0.0019$). Nevertheless, the authors of this article calculated the difference according to Cohen’s formula and corrected for each year of life, with negligible results ($d = 0.0413$).

In Denmark, a study of which sample consisted of 260 healthy subjects aged between 40 and 79 years, a MHR of 74 ± 18 bpm was obtained\textsuperscript{25}. The lower standard deviation value in this study suggests greater sample homogeneity, in addition to greater precision due to the use of long-term tracings.

In a case-control study performed in the state of Rio Grande do Sul, Brazil\textsuperscript{26}, the recording of HR at rest in the control group of 5,410 patients with a mean age of 55.4 ± 10.4 years showed a mean value of 72.1 ± 12.6 bpm. This value was also close to the current findings described in Holter monitoring. However, dissimilar from the 24-hour ambulatory ECG, routine and direct HR measurements are subject to variations caused by several types of interference, such as ambient temperature, presence of the examiner and the individual’s emotional status\textsuperscript{27}. Again, the standard deviation obtained from the resting HR was quite higher than that resulting from the measurement of MHR by 24-hour monitoring.

This aspect of the matter can be illustrated by the analysis of another study\textsuperscript{28}, which used both measurements (resting HR and MHR). First, the resting HR of 32 patients aged 100 to 106 years was compared to that of 89 healthy individuals (aged 63 to 95 years). There was a difference between the first (76.8 ± 12.7) and the latter (74.9 ± 5.9), with statistical significance ($p < 0.005$). But when the MHR was measured by 24-hour Holter, it was around 72 bpm and there was no significant difference between the groups.

These findings are similar to those found in the present study. The authors attributed the increase in resting HR in centenarians to the previous effort made when lying on the stretcher, or some emotional expectation before the examination.

The Baltimore Longitudinal Study on Ageing (BLSA)\textsuperscript{29} evaluated 69 men and 29 women aged 60 to 85 years. Patients were divided into three groups: 59 subjects aged between 60 and 69 years, 32 aged between 70 and 79 years, and only 7 members aged ≥ 80 years. All were considered “healthy” according to the following criteria: absence of systemic disease or overt heart disease, no heart abnormalities at physical examination, blood pressure of 160/95 mmHg; ECG with no significant morphological alterations; satisfactory lung function, exercise testing within normal limits, no antiarrhythmic and beta-blocker drug use. The dynamic electrocardiography recordings lasted between 17 and 26 hours.

There was no significant variation in MHR with age. However, MHR in women (76.9 ± 8.0) was significantly higher than that of men (69.8 ± 8.8), with $p < 0.001$.

When compared to the present study, and although it corroborates our findings, the BLSA showed greater differences regarding gender, which may be due to the smaller sample size and greater variability during the electrocardiographic recording. Another important aspect of the BLSA study is the excessive proportion of men (70%). This fact was due to the enrollment procedure, which was voluntary and active on the part of the patients. Additionally, the measurements obtained in inpatients may result in bias, as they may not reflect the natural environment\textsuperscript{30}.

The physiopathology of the chronotropic response is considered to be complex, multifactorial and not completely understood. The slight increase in heart rate may be attributed to transient alterations in blood flow on
Table 5 – Parametric and nonparametric tests for comparisons between the means of MHR in five age groups, followed by post hoc evaluation for subgroups

| Degrees of freedom | Test | R² | Eta² | p     |
|--------------------|------|----|------|-------|
| ANOVA ONE WAY      | 4    | F = 12.962 | 0.034 | 0.043 | < 0.001 |
| KRUSKAL-WALLIS     | 4    | H = 48.739 | 0.007 | -     | < 0.001 |
| ANOVA 5x2           |       | 0.630 |      |       |         |
| Age group          | 4    | F = 10.421 | -    | 0.035 | < 0.001 |
| Gender             | 1    | F = 20.033 | -    | 0.019 | < 0.001 |
| Group*Gender       | 4    | F = 39.347 | -    | 0.003 | 0.572   |
| ANOVA 5x2x2x2x2    |       | 0.129 |      |       |         |
| Age group          | 4    | F = 1.899  | -    | 0.007 | 0.108   |
| Gender             | 1    | F = 4.250  | -    | 0.004 | 0.039   |
| SAH                | 1    | F = 2.278  | -    | 0.002 | 0.131   |
| Dyslipidemia       | 1    | F = 1.840  | -    | 0.002 | 0.175   |
| Diabetes           | 1    | F = 0.935  | -    | 0.001 | 0.334   |
| Group*Gender       | 4    | F = 0.541  | -    | 0.002 | 0.706   |
| Group*SAH          | 4    | F = 2.425  | -    | 0.009 | 0.046   |
| Group*Dyslipidemia | 4    | F = 1.528  | -    | 0.006 | 0.192   |
| Group*Diabetes     | 4    | F = 1.674  | -    | 0.006 | 0.154   |
| POST HOC (Tukey)   |      |       |      |       |         |
| 40-49 x 50-59 years| -    | -     | -    | 0.967 |         |
| 40-49 x 60-69 years| -    | -     | -    | 0.001 |         |
| 40-49 x 70-79 years| -    | -     | -    | < 0.001 |      |
| 40-49 x ≥ 80 years | -    | -     | -    | < 0.001 |      |
| 50-59 x 60-69 years| -    | -     | -    | < 0.001 |      |
| 50-59 x 70-79 years| -    | -     | -    | < 0.001 |      |
| 50-59 x ≥ 80 years | -    | -     | -    | < 0.001 |      |
| 60-69 x 70-79 years| -    | -     | -    | 0.001  |         |
| 60-69 x ≥ 80 years | -    | -     | -    | 0.291  |         |
| 70-79 x ≥ 80 years | -    | -     | -    | 0.905  |         |

SAH: systemic arterial hypertension; MHR: mean heart rate.

the atrial wall\(^{31}\), progressive reductions in systolic volume or ventricular compliance alterations produced by diastolic dysfunction\(^{32}\).

Several factors related to the autonomic modulation during the aging process, agonist and antagonist ones, may be related to the maintenance of the MHR equilibrium status. The reduced decrease in MHR, substantially lower than the intrinsic sinus rate decrease\(^{14}\), would eventually result from the action of other adaptation mechanisms of the cardiovascular system in the elderly, such as increase in sympathetic tone after a lower myocardial performance during daily activities, including varying degrees of physical exertion. Several studies have identified a trend of predominant sympathetic modulation over the parasympathetic one with advancing age\(^{23,33}\).

Although the mechanisms responsible for it are not completely understood, the small decrease in MHR with age, regardless of gender and ethnicity, has been demonstrated in other studies with elderly individuals submitted to 24-hour Holter monitoring\(^{27,34,35}\).

Further investigations, involving echocardiographic measurements and heart rate variability, may explain the phenomenon and confirm some of the hypotheses. Among the limitations of this study, one might question the representativeness of the sample, as there was no randomization during the process of participant inclusion and the source population consists of patients from a single cardiology referral center. In fact, considering the institutional-based sampling, there is potentially a trend of predominance of individuals with higher prevalence of diseases\(^{36}\). Another factor to be considered is the lack of direct measurement of blood pressure levels and clinical parameters, but the echocardiographic evaluation sought to avoid the inclusion of individuals with evident heart disease.
Data related to thyroid function were not available in approximately 25% of the sample. Although an eventual thyroid dysfunction may interfere with MHR values, we believe this factor did not have any significant influence on the present study, as the remaining 75% showed normal hormone levels and no subjects enrolled in the study reported the use of thyroid-dysfunction medication. Additionally, the prospective and sequential data collection, the complete filling out of data, the participants’ selection and exclusion criteria and the stringent statistical calculations were relevant measures in minimizing biases. The distribution of individuals across the age groups and the expected ratio between men and women in terms of “real life” also suggest that the research sample is inserted within the expected population standard.

Conclusions

MHR decreased with increasing age in both genders. For similar age groups, females had significantly higher MHR values than their male counterparts and this phenomenon was reproduced in both the total sample and when stratified by age. The prevalence of comorbidities such as hypertension, non-insulin dependent diabetes mellitus and dyslipidemia had no detectable influence on MHR patterns. Both the association between MHR and age range as the association between MHR and gender were significant in several models of statistical analysis. However, the magnitude of this association in both situations is considerably small. The findings were consistent, reproducible and corroborated in several statistical models.

Author contributions

Conception and design of the research e Writing of the manuscript: Santos MAA, Sousa ACS, Reis FP, Santos TR, Lima SO, Barreto-Filho JA; Acquisition of data: Santos MAA, Santos TR; Analysis and interpretation of the data: Santos MAA, Sousa ACS, Reis FP, Barreto-Filho JA; Statistical analysis: Santos MAA; Critical revision of the manuscript for intellectual content: Santos MAA, Sousa ACS, Reis FP, Lima SO, Barreto-Filho JA.

Potential Conflict of Interest

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

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of master and doctoral submitted by Marcos Antonio Almeida Santos from Universidade Tiradentes and Universidade Federal de Sergipe.
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