

# CORRELATION BETWEEN DEGREE OF AUTONOMIC NERVOUS SYSTEM IMPAIRMENT AND QUALITY OF LIFE INDICES IN OLDER ADULTS

## Correlação entre grau de comprometimento do sistema nervoso autônomo e índices de qualidade de vida em idosos

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### ABSTRACT

**INTRODUCTION:** The increase in the world's elderly population in recent decades calls for research on quality of life during the aging process. Heart rate variability (HRV) evaluates the modulation of the autonomic nervous system (ANS) and indicates the heart's ability to respond to multiple physiological and environmental stimuli, as well as to disease. **OBJECTIVE:** To investigate the perceived quality of life of older people and its association with HRV. **METHOD:** Twenty-nine subjects (69 ± 7.76 years) were selected at a preventive medicine center and completed a questionnaire (World Health Organization quality of life assessment — old module: WHOQOL-OLD). The HRV data were collected for 20 minutes in the supine position using a Polar RS800CX frequency meter. **RESULTS:** Using the median value as a cut-off point, the sample was divided into two groups: WHOQOL-OLD ≥ 92 (n = 15: better quality of life) and WHOQOL-OLD ≤ 91 (n = 13; lower quality of life). For the HRV time-domain variables RMSSD and pNN50, there were higher values in the WHOQOL-OLD ≥ 92 group (p = 0.0413 and p = 0.0222, respectively). For the frequency-domain variables, low-frequency (LF), high-frequency (HF) and Total Power, there were also higher values in the WHOQOL-OLD group ≥ 92 (p = 0.0195, p = 0.0170 and p = 0.0287, respectively). The non-linear variable SD1 was significantly higher in the WHOQOL-OLD ≥ 92 group (p = 0.0413), while DET% was significantly higher in the WHOQOL-OLD ≤ 91 group (p = 0.0253). **CONCLUSIONS:** Better quality of life in older adults is associated with normal ANS function, represented by higher values found through three HRV analysis methods. This indicates the importance of a healthy lifestyle for healthy aging, which includes improvement in autonomic function and, consequently, quality of life.

**KEYWORDS:** aging; quality of life; autonomic nervous system.

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**INTRODUÇÃO:** O aumento do tamanho da população idosa mundial nas últimas décadas tem demandado investigações sobre a qualidade de vida durante o processo de envelhecimento. A Variabilidade da Frequência Cardíaca (HRV) avalia a modulação do Sistema Nervoso Autônomo (SNA) e indica a capacidade do coração em responder a múltiplos estímulos fisiológicos e ambientais, bem como em doenças. **OBJETIVOS:** Investigar a percepção da qualidade de vida de idosos e sua associação com a VFC. **MÉTODOS:** Vinte e nove indivíduos ( $69 \pm 7,76$  anos) foram selecionados em um Centro de Medicina Preventiva, e preencheram um questionário (World Health Organization quality of life assessment – old module: WHOQOL-OLD). Os dados da VFC foram coletados durante 20 minutos, com indivíduos em posição supina, com uso do frequencímetro Polar RS800CX. **RESULTADOS:** Utilizando o valor de mediana como ponto de corte, a amostra foi dividida em dois grupos: WHOQOL-OLD  $\geq 92$  (N = 15: idosos com melhor qualidade de vida) e WHOQOL-OLD  $\leq 91$  (N = 13: idosos com menor qualidade de vida). Considerando a VFC, no domínio do tempo, as variáveis RMSSD e pNN50 apresentaram maiores valores no grupo WHOQOL-OLD  $\geq 92$  ( $p = 0,0413$  e  $p = 0,0222$ , respectivamente). No domínio da frequência, as variáveis LF, HF e Total Power apresentaram maiores valores no grupo WHOQOL-OLD  $\geq 92$  ( $p = 0,0195$ ,  $p = 0,0170$  e  $p = 0,0287$ , respectivamente). No domínio não linear da VFC, a variável SD1 foi significativamente maior em WHOQOL-OLD  $\geq 92$  ( $p = 0,0413$ ), enquanto o DET% apresentou-se significativamente maior em WHOQOL-OLD  $\leq 91$  ( $p = 0,0253$ ). **CONCLUSÕES:** Melhor qualidade de vida está associada ao bom funcionamento do SNA, representado pela maiores valores nos três domínios da VFC em idosos, enfatizando a importância de estilo de vida saudável no envelhecimento saudável, com melhora da função autonômica e, conseqüentemente, da qualidade de vida. **PALAVRAS-CHAVE:** envelhecimento; qualidade de vida; sistema nervoso autônomo.

## INTRODUCTION

The aging of the population is a worldwide concern, especially the increasing number of individuals over 80 years of age, which involves epidemiological changes. This age group is today's fastest growing population segment and includes more than 14.2% of the elderly population.<sup>1</sup>

According to Minayo et al.,<sup>2</sup> quality of life is a human perception associated with the degree of satisfaction in aspects of life such as family, love, the social environment and spirituality. It presupposes a combination of all the elements that society considers standard for comfort and well-being.

The international scientific literature shows an inverse correlation between quality of life and frailty, depression, and institutionalization; these vulnerability factors are associated with lower quality of life scores for older adults.<sup>3</sup> Other studies maintain that physical activity and social support directly contribute to multiple quality of life domains. Brazilian studies on quality of life assessment in long-lived people are incipient and involve different instruments, making it difficult to compare the data.<sup>4</sup>

The World Health Organization Quality of Life Assessment (WHOQOL), defines quality of life as “an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”.<sup>5</sup>

Several versions of this instrument have been developed, such as the WHOQOL-100 and the WHOQOL-BREF.<sup>6</sup> Although these instruments have been extensively tested in a number of countries and the results reflect different cultures

and populations, such as youngsters, adults and older adults, there has been an increasing interest in specific instruments for assessing the quality of life of older adults.<sup>7</sup>

The WHOQOL-OLD<sup>6</sup> focuses on the specific characteristics of this population group, who are in a stage of life where the major organ systems no longer work together seamlessly. This instrument considers cross-cultural factors and how different age groups create specific situations that may have a direct or indirect impact on the daily life of this population. The original project was carried out at 22 centers in 21 countries, and its final version contains four items, each involving 6 facets. Module scoring may consist of a single six-facet set or a total score based on the sum of all 24 items.

The WHOQOL-OLD module can be used in a variety of studies where quality of life issues are crucial, since it allows possible consequences of quality-of-life policies for older adults to be identified and provides a clearer understanding of areas of investment for improving their quality of life.<sup>8</sup>

The autonomic nervous system (ANS) is responsible for regulating the cardiovascular system, supplying afferent and efferent nerve fibers to the heart.<sup>9</sup> Changes in heart rate, called heart rate variability (HRV), are normal and expected, indicating the heart's ability to respond to multiple physiological and environmental stimuli as well as to compensate for disease-induced disorders.<sup>9</sup>

HRV analysis using time- and frequency-domain methods (linear measures) and nonlinear methods (chaos/complexity) is considered an important means of assessing a patient's health status, allowing actions that may eventually reverse health impairment.<sup>9</sup>

High HRV values are a sign of good adaptation, characterizing an individual as healthy due to efficient autonomic mechanisms. Low HRV values, however, are often indicative of ANS insufficiency and could represent a physiological malfunction.<sup>9</sup>

Thus, detecting altered autonomic activity is crucial in clinical practice for a number of conditions, including anxiety, depression and chronic fatigue.<sup>10-13</sup> High HRV values indicate adequate cardiac activity as well as lower risk of acute myocardial infarction and heart failure,<sup>14</sup> whereas lower HRV values are related to a higher risk of cardiovascular disease and mortality.<sup>15,16</sup>

The present study correlated WHOQOL-OLD global scores (i.e., the sum of all 24 items) with HRV data in an attempt to determine whether individuals with better quality of life are likely to have better ANS function.

Thus, this study aimed to investigate perceived quality of life and its association with HRV to assess autonomic modulation in older adults.

## MATERIALS AND METHODS

This study was conducted at a preventive medicine center in São José do Rio Preto that is linked with the largest hospital in the northwestern region of the state of São Paulo, Brazil.

Inclusion criteria were: physically active elderly individuals, regardless of sex, who were enrolled in a preventive medicine program designed to improve quality of life through physical activity. Exclusion criteria were: sequelae of neurological diseases or significant cognitive deficit.

This study was approved by the Research Ethics Committee of the School of Medicine of São José do Rio Preto (FAMERP) and the director of the institution (Protocol No. 371232/2013) and was accredited by the Comissão Nacional de Ética em Pesquisa do Ministério da Saúde (Health Ministry National Research Ethics Committee — CAAE: 12698813.7.0000.5415). The study was explained in detail to all prospective participants, and they confirmed their willingness to participate by providing written informed consent. The participants were informed that there were no risks involved in heart rate measurement or administration of the questionnaire. This study adhered to the ethical principles outlined in the Helsinki Declaration (2000).

The WHOQOL-OLD,<sup>6</sup> a quality of life assessment scale developed by the World Health Organization Quality of Life Group, was used in this study. Cross-cultural aspects were also considered, so that cultural differences among populations would not interfere with the results.

The questionnaire consisted of Likert-scale question modules (preference scale) covering the following facets: Sensory Abilities, Autonomy, Past, Present and Future Activities, Social Participation, and Death and Dying.

The median WHOQOL-OLD score was considered the cut-off point for dividing the participants into groups. Thus, Group 1 consisted of those with WHOQOL-OLD scores  $\geq 92$  ( $N = 15$  patients), indicating higher levels of quality of life, while Group 2 consisted of those with WHOQOL-OLD scores  $\leq 91$  ( $N = 13$  patients) indicating lower levels of quality of life.

Heart Rate Variability data were recorded in the morning with a Polar RS 800CX monitor for 20 minutes, with the patients resting in the supine position. Kubios HRV software was used for HRV analysis (Biosignal Analysis and Medical Image Group, University of Eastern Finland, Kuopio, Finland).<sup>17</sup>

The following HRV variables were used in this study:

- time-domain methods: mean of all normal RR intervals (mean RR), mean heart rate (mean HR), standard deviation of all normal RR intervals (SDNN), root-mean square of differences between adjacent normal RR intervals (RMSSD), and percentage of adjacent RR intervals with a difference of duration greater than 50 milliseconds (pNN50);
- frequency-domain methods: high-frequency (HF  $\text{ms}^2$ ) band (i.e., > 0.15 to 0.4 Hz), low-frequency (LF  $\text{ms}^2$ ) band (i.e., 0.04 to 0.15 Hz), absolute and relative changes between the components of the ANS (LF/HF) and total power;
- nonlinear methods: Poincaré standard deviation (SD1, SD2 and SD1/SD2), approximate entropy (ApEn), sample entropy (SampEn), detrended fluctuation analysis (DFA) alpha1, mean diagonal length (Lmean), maximal diagonal length (Lmax), recurrence rate (REC%), determinism (DET%), Shannon entropy (ShanEn), multiscale entropy (MSE-1, MSE-5, MSE-10, MSE-20).

No other interventions were performed apart from assessing heart rate variability and administering the WHOQOL-OLD questionnaire.

Normally-distributed variables were assessed with an unpaired Student's *t*-test, while non-normally distributed variables and discrete variables were analyzed with the Mann-Whitney test. The Kolmogorov-Smirnov test was used to test normality. Statistical analysis was performed in StatsDirect version 1.9.15, assuming  $p < 0.05$  as a significant value.

## RESULTS

According to Table 1, Group 1 (WHOQOL  $\geq 92$ ) and Group 2 (WHOQOL  $\leq 91$ ) were similar regarding the following variables: age ( $p = 0.2381$ ), gender ( $p = 0.9511$ ), weight ( $p = 0.5627$ ), waist circumference ( $p = 0.4873$ ), hypertension ( $p = 0.5568$ ) and diabetes mellitus ( $p = 0.8556$ ).

Table 2 shows the results of the three HRV methods. In the time domain, Group 1 had higher RMSSD and pNN50 values ( $p = 0.0413$  and  $p = 0.0222$ , respectively). In the frequency domain, Group 1 had LF, HF and total power values ( $p = 0.0195$ ,  $p = 0.0170$  and  $p = 0.0287$ , respectively).

**Table 1** Demographic and clinical data of the sample of older adults.

	WHOQOL-OLD $\geq 92$	WHOQOL-OLD $\leq 91$	p-value
Age (years)	67.5 $\pm$ 7.5	70.7 $\pm$ 7.9	0.2381 <sup>#</sup>
Sex (M/F)	4 / 11	5 / 8	0.9511 <sup>*</sup>
Weight (kg)	65.6 $\pm$ 13.3	68.9 $\pm$ 10.8	0.5627 <sup>#</sup>
BMI (kg/m <sup>2</sup> )	26.1 $\pm$ 4.16	26.9 $\pm$ 4.23	0.5728 <sup>*</sup>
Hypertension %	60	46	0.5568 <sup>*</sup>
Diabetes Mellitus %	20	23	0.8556 <sup>*</sup>

WHOQOL-OLD: World Health Organization quality of life assessment — old module; M: male; F: female; BMI: body mass index; <sup>#</sup>unpaired *t*-test; <sup>\*</sup>Fisher's exact test; p-value significance <0.05. Results are expressed as Mean  $\pm$  Standard Deviation (SD).

**Table 2** Heart rate variability measurement associated with WHOQOL-OLD instrument in older adults.

HRV	WHOQOL-OLD $\geq 92$	WHOQOL-OLD $\leq 91$	p-value
Time Domain			
Mean HR	66.9 $\pm$ 7.8	71.1 $\pm$ 14.2	0.5250
Mean RR	909.2 $\pm$ 104.1	878.6 $\pm$ 182.5	0.5551
SDNN	33.8 $\pm$ 12.1	28.5 $\pm$ 13.1	0.1077
RMSSD	19.8 $\pm$ 11.1	13.2 $\pm$ 7.7	0.0413
pNN50	3.4 $\pm$ 7.6	1.2 $\pm$ 2.9	0.0222
Frequency Domain			
LF ms <sup>2</sup>	266.2 $\pm$ 316	132.9 $\pm$ 176.2	0.0195
HF ms <sup>2</sup>	145.2 $\pm$ 184.2	69.8 $\pm$ 117.2	0.0170
LF/HF ms <sup>2</sup>	2.2 $\pm$ 1.4	2.4 $\pm$ 1.8	0.9990
Total Power ms <sup>2</sup>	999.4 $\pm$ 896	673.1 $\pm$ 867.1	0.0287
Non-linear Methods			
SD1	14 $\pm$ 7.8	9.3 $\pm$ 5.4	0.0413
SD2	45.5 $\pm$ 15.7	38.8 $\pm$ 18.2	0.0977
ApEn	1.2 $\pm$ 0.1	1.1 $\pm$ 0.3	0.4956
DFA1	1.1 $\pm$ 0.2	1.2 $\pm$ 0.2	0.7168
Lmean	19.1 $\pm$ 7.4	28.7 $\pm$ 20.1	0.1555
Lmax	661.2 $\pm$ 294.1	790.2 $\pm$ 328.7	0.0626
REC%	45.4 $\pm$ 8.9	51.2 $\pm$ 12.1	0.0626
DET%	99.1 $\pm$ 0.6	99.3 $\pm$ 1.0	0.0253
ShanEn	3.7 $\pm$ 0.3	3.9 $\pm$ 0.5	0.1300
MSE-1	1.2 $\pm$ 0.2	1.1 $\pm$ 0.3	0.4956
MSE-5	1.3 $\pm$ 0.2	1.2 $\pm$ 0.3	0.4130
MSE-10	1.5 $\pm$ 0.3	1.3 $\pm$ 0.3	0.3389
MSE-15	1.6 $\pm$ 0.3	1.3 $\pm$ 0.3	0.1521
MSE-20	1.5 $\pm$ 0.4	1.6 $\pm$ 0.7	0.7856

WHOQOL-OLD: World Health Organization quality of life assessment — old module; HRV: heart rate variability; HR: heart rate; RR: mean of RR Intervals; SDNN: standard deviation of all normal RR intervals; RMSSD: root-mean square of the differences between adjacent normal RR intervals; pNN50: percentage of adjacent RR intervals with a difference of duration greater than 50 milliseconds; LF: low-frequency; HF: high-frequency; SD: Poincaré standard deviation; ApEn: approximate entropy; DFA1: detrended fluctuation analysis (DFA) alpha 1; Lmean: mean diagonal length; Lmax: maximal diagonal length; REC%: recurrence rate; DET%: determinism percentage; ShanEn: shannon entropy; MSE: Multiscale Entropy; results are expressed as Mean  $\pm$  SD; unpaired *t*-test for all variables; p-value significance <0.05.

For non-linear methods, Group 1 had higher SD1 values ( $p = 0.0413$ ), while determinism (DET%) was higher in Group 2 ( $p = 0.0253$ ).

## DISCUSSION

In the present study, significantly higher values for the time-domain variables RMSSD and pNN50 were observed in Group 1 (WHOQOL-OLD  $\geq 92$ ). These variables represent parasympathetic function and their high values indicate good functioning of the parasympathetic nervous system and good general health.<sup>17</sup>

High HRV values were also found for the frequency domain variables LF, HF and total power in Group 1 (WHOQOL-OLD  $\geq 92$ ). According to Billman,<sup>18</sup> LF corresponds to the combined activity of the vagal and sympathetic components of the heart (50 and 25%, respectively), and HF indicates the action of the vagus nerve on the heart. Therefore, we observed a predominance of parasympathetic modulation in older adults with WHOQOL-OLD scores  $\geq 92$ , indicating that this system may contribute to a better quality of life and emotional state in this sample of individuals.

Since the human body is a dynamic, complex system involving nonlinear behavior, interpreting its biological behaviors requires nonlinear methods. According to chaos theory, elements that are highly sensitive to initial conditions, although seemingly random, are deterministic.

The Poincaré plot is a nonlinear method of HRV analysis that shows the degree of complexity of RR<sup>17</sup> intervals. Three indices are obtained from this method: SD1, SD2 and the SD1/SD2 ratio. SD1 represents the dispersion of points perpendicular to the line of identity and seems to be an instantaneous index of the beat-to-beat variability, corresponding to parasympathetic modulation. In this study, high SD1 values were observed in older adults with WHOQOL-OLD scores  $\geq 92$ , again indicating optimal vagal activity. Moreover, a low rate of determinism (DET%) was also observed in this group, indicating more dynamic biological system behavior and, therefore, normal ANS function.

Although the patients were similar in demographic characteristics and comorbidities, they were divided (based on the median value) into high or low levels of quality of life (WHOQOL-OLD  $\geq 92$  and WHOQOL-OLD  $\leq 91$ , respectively), which facilitated the observation of differences in three methods of HRV assessment.

The aging of the population is one of today's most challenging public policy issues in both industrialized and less industrialized countries.<sup>19,20</sup> According to a national survey published by the Brazilian Institute of Geography and Statistics,<sup>21</sup> the number of people in Brazil aged 60 years or over has increased from 9.7% in 2004 to 14.3% in 2015.

This increasing number of older adults is accompanied by an increase in diseases that affect this age group, resulting in decreased quality of life.<sup>19</sup> Since aging can result in multiple functional impairments and the need for intensive care, the importance of healthy aging should be emphasized. Quality of life is defined as an individual's perception of their position with respect to their social and cultural context, goals and expectations.<sup>22</sup> Although disease, disability, low socioeconomic conditions and poor social integration may reduce an individual's quality of life, currently available instruments provide a better understanding of this variable among the aging population.<sup>23,24</sup>

Improving quality of life has become a critical and important measure in recent years, especially in public health campaigns focused on healthy aging for those who are not in the hospital and do not have disabling morbidities.

Several currently available instruments for measuring quality of life are based on the WHOQOL,<sup>19</sup> including the WHOQOL<sup>19</sup> and the WHOQOL-BREF,<sup>5</sup> which have been internationally validated.<sup>25</sup> They consist of eight questions pertaining to four domains: Physical Health, Psychological Health, Social Relationships and Environment.<sup>6,26</sup> These tools reflect social status and the quality of the individual's environment, which influence physical and psychological health and determine individual well-being.<sup>16</sup>

Since the WHOQOL-OLD<sup>6</sup> was developed for cross-cultural investigations about the quality of life of older adults, it prioritizes factors related to old age.<sup>19,26,27</sup> The validation of this instrument in Brazil was reported by Guillemin.<sup>28</sup>

In humans, ANS is of vital importance in adjusting the body's response to internal and environmental stimuli.<sup>10,11,29,30</sup> Alterations in this system have been observed in a number of diseases.<sup>25-27</sup> Given that change in ANS activity is related to the onset of disease, it plays an important role in determining quality of life.<sup>16</sup> HRV is related to ANS function and can contribute to quality of life analysis.<sup>16</sup> Lu et al.<sup>16</sup> suggest that the better quality of life of healthy individuals reflects adequate autonomic balance and that this could help diagnose diseases before they manifest clinically.

HRV analysis is a noninvasive method of assessing ANS activity<sup>31</sup> and is related to variations between heartbeats due to sympathetic innervation (acceleration) and parasympathetic innervation (vagus nerve — deceleration). Thus, higher HRV values indicate better ANS function<sup>27</sup> and optimal regulatory capacity.<sup>32</sup> On the other hand, low HRV values indicate ANS deficiency<sup>33</sup> and disease status.<sup>34</sup>

Interventions in particular aspects of quality of life could lead to important health benefits, as well as to the rehabilitation and recovery of older adults. Thus, factors that may affect the quality of life of older adults must be examined,

especially their social environment, while they pursue a predominantly active lifestyle. Such efforts will certainly improve their health and enhance their quality of life.

This study has certain limitations, including: being conducted at a single prevention center, a relatively small sample size, and lack of association with variables such as smoking, alcohol consumption and medications.

## CONCLUSION

Our results strongly suggest that better quality of life in older adults is associated with good functioning of the

autonomic nervous system, represented by greater HRV values according to three assessment methods. Long-term prospective studies will confirm these results.

## CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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