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Relationship between the number of comorbidities, quality of life, and cardiac autonomic modulation in patients with coronary disease: a cross-sectional study

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SUMMARY

OBJECTIVE: The aim of this study was to evaluate if there is a relationship between the number of comorbidities, autonomic modulation, and quality of life in patients diagnosed with coronary artery disease.

METHODS: A cross-sectional study was conducted at an outpatient rehabilitation center in Presidente Prudente-SP, Brazil. A total of 27 participants (65.33±9.23 years) diagnosed with coronary artery disease were assessed, from a cardiac rehabilitation program, independent of sex or age. The number of comorbidities was evaluated using the Self-Administered Comorbidity Questionnaire, and quality of life was evaluated using the Medical Outcome Study 36-Item Short Form Health Survey (SF-36) (eight domains: functional capacity, physical aspects, pain, general health status, vitality, social aspects, emotional aspects, and mental health). To evaluate the cardiac autonomic modulation, the heart rate was registered beat to beat using an heart rate monitor in the supine position during rest for 30 min. A total of 1000 RR intervals were considered to calculate linear (time domain: RMSSD, SDNN; frequency domain: LF, HF, LF/HF) and nonlinear indices (SD1, SD2, SD1/SD2) of heart rate variability.

RESULTS: A negative correlation was observed between the aggregation of comorbidities and the pain domain of the SF-36 (r=-0.427; p=0.03). No significant correlations were observed between other variables (p>0.05).

CONCLUSION: The number of comorbidities is inversely related to the pain domain of the SF-36, suggesting that a higher pain level is related to a higher number of comorbidities in coronary artery disease patients.

KEYWORDS: Comorbidity. Chronic disease. Coronary artery disease. Heart rate. Quality of life.

INTRODUCTION

Chronic disease aggregation, defined as comorbidity[1], promotes impaired functional capacity, reduced quality of life (QoL), and increased mortality[2], and it represents a challenge to health systems, due to the increase in costs and utilization of services[3].

Among chronic diseases, coronary artery disease (CAD) is the main cause of mortality and morbidity in the world[4]. CAD is associated with various chronic diseases, such as osteoarthritis, peripheral arterial disease, chronic obstructive pulmonary disease, diabetes mellitus, asthma, and depression[2].

Reduced QoL[5] and impaired autonomic modulation[6] in CAD patients have been reported in the literature. Previous studies found that reduced QoL could be related to the presence of comorbidities in CAD patients[7-9]. However, although the literature has suggested that a greater number of comorbidities causes longer hospital stays and mortality[10], only one study[8] considered the number of comorbidities to evaluate the relationship between QoL and comorbidities. Likewise, CAD patients with comorbidities are more likely to present reduced heart rate variability (HRV)[11], which indicates autonomic modulation impairment. However, to date, knowledge about the relationship between the presence of comorbidities and autonomic modulation in CAD patients is limited to specific chronic conditions, such as depression[11].

Therefore, it is relevant to investigate if the number of comorbidities associated with CAD is also related to the impairment of cardiac autonomic modulation and QoL. Understanding these aspects may help in the development of public policies for health prevention and promotion and in the identification of patients with worse prognoses, who need greater support during treatment.

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This study aimed to evaluate if there is a relationship between the number of comorbidities, autonomic modulation, and QoL in CAD patients. We hypothesized that a higher number of comorbidities in CAD patients is related to a greater autonomic and QoL impairment.

METHODS

Study design and setting

This was a cross-sectional study, conducted from 2018 to 2019, at the Center for Physical Therapy and Rehabilitation Studies and Treatment of São Paulo State University (UNESP), Faculty of Sciences and Technology, Presidente Prudente (SP), Brazil.

The experimental procedure was divided into two steps. In the first step, an initial assessment was performed, composed of personal data collection, anthropometric evaluation, and application of the Self-Administered Comorbidity Questionnaire[12], to assess the number of comorbidities, and the Medical Outcome Study 36-Item Short Form Health Survey (SF-36)[13] was performed to assess QoL. In the second step, a cardiac autonomic modulation assessment was performed at rest, by recording the heart rate (HR) beat to beat using an HR monitor.

All procedures were approved by the research ethics committee of the institution (CAAE: 79213417.0.0000.5402). Participants were previously informed about the aims and procedures of this study and provided a written informed consent.

This cross-sectional study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations[14].

Participants

A total of 27 patients from a cardiac rehabilitation program (CRP) performed at the Center for Physical Therapy and Rehabilitation Studies and Treatment of São Paulo State University (UNESP), Faculty of Sciences and Technology, Presidente Prudente (SP), Brazil, were invited to participate in the study regardless of sex and age.

The participants met the following eligibility criteria: (1) a medical diagnosis of CAD, regardless of sex and age, and (2) agreed to participate in the study. Exclusion criteria were as follows: participants with atrial fibrillation, who had a pacemaker or cardiac transplant, did not understand the questionnaires or refused to participate in the study, or participants who presented errors >5% on the HRV record.

Sample characterization

For sample characterization, the personal data of the participants (e.g., sex, age, and medications) were collected, and the body weight; height; and waist, abdominal, and hip circumferences were measured.

Exposure variable

Comorbidities evaluation

The "Self-Administered Comorbidity Questionnaire"[12] was used to verify the number of comorbidities. This questionnaire presents 13 previously selected medical conditions (i.e., heart disease, high blood pressure, lung disease, diabetes, stomach disease, kidney disease, liver disease, anemia or another blood disease, cancer, depression, osteoarthritis, back pain, and rheumatoid arthritis) as well as the option to add up to three additional conditions in an open-ended manner. For each condition, the participants were instructed to answer the following questions: "Do you have any of the following problems?" "Do you receive treatment for it?" and "Does it limit your activities?" For each affirmative answer, the participant received 1 point. Considering the 13 defined medical problems and 3 optional conditions, the maximum score is 48 points.

Outcomes

Quality of life evaluation

QoL was assessed using the "Medical Outcome Study 36-Item Short Form Health Survey (SF-36)"[13]. The questionnaire consists of eight multi-item dimensions, namely, functional capacity, physical aspects, pain, general health status, vitality, social aspects, emotional aspects, and mental health. For each dimension, item scores are coded, summed, and transformed on a scale ranging from 0 (worst health) to 100 (best health).

Cardiac autonomic modulation

The analysis of cardiac autonomic modulation was performed using HRV indices. A capture strap was placed on the participants' chest in the region of the distal third of the sternum, and the HR monitor Polar RS800CX (Polar Electro OY, Finland) was placed on the wrist to record HR beat to beat. The participants were instructed to remain awake, without speaking, spontaneously breathing, at rest, in the supine position for 30 min.

All the procedures were performed in a room with a temperature between 21 and 23°C and humidity between 40 and 60%, between 2:00 and 6:00 p.m., to avoid variations in the circadian cycle. Participants were instructed not to consume substances that stimulate the autonomic nervous system for at least 12 h before the evaluation.

For the HRV analysis, the RR interval series was transferred to Polar Precision Performance software (Kempele, Finland)[15].

After digital and manual filtering of the data to eliminate premature ectopic beats and artifacts, 1000 consecutive RR intervals from the period of greatest signal stability were selected. Only series with more than 95% sinus beats were used in the analyses[16]. HRV was analyzed by linear, in the time and frequency domains, and nonlinear methods, calculated using the software Kubios HRV version 2.0 (Kubios, Biosignal Analysis, and Medical Image Group, Department of Physics, University of Kuopio, Finland)[16].

In the time domain, the RMSSD (root mean square of the differences between adjacent normal RR intervals, in a time interval, expressed in milliseconds) and SDNN indices (standard deviation of all normal RR intervals recorded in a time interval, expressed in milliseconds)[15] were calculated.

In the frequency domain, the spectral components of low frequency (LF: 0.04–0.15 Hz) and high frequency (HF: 0.15–0.40 Hz) were used, expressed in milliseconds squared (ms^2) and normalized units (nu). Fourier Fast Transform (FFT) was used as an algorithm for the spectral analysis[15].

For nonlinear HRV analysis, the indices were calculated using quantitative analysis of the Poincaré plot: SD1 (dispersion of the points perpendicular to the line of identity and representing the instantaneous record of the beat-to-beat variability), SD2 (dispersion of points along the identity line and representing HRV in the long-term records), and the SD1/SD2 ratio (the ratio between the short and long duration variations in RR intervals)[15].

Data analyses

For the sample characterization, the descriptive statistical method was used and the results are presented as mean and standard deviation (parametric data) or median and interquartile interval (non-parametric data), minimum and maximum (continuous data), and absolute numbers and frequencies (categorical data).

The normality of the data was assessed by the Shapiro-Wilk test. The relationship between the number of comorbidities and HRV indices and the scores of the SF-36 components was evaluated by the Pearson or Spearman correlation, according to the normality of the data.

The level of significance was set at <5%, and the SPSS statistical package was used (version 22.0) (SPSS Inc., Chicago, IL, United States).

RESULTS

Table 1 presents the characterization of the participants. The sample was composed predominantly of older males (masculine sex: 66.67%, n=18; older people: 74.07%, n=20).

Table 2 shows the results of the Self-Administered Comorbidity Questionnaire. Hypertension (66.7%, n=18), back pain (37%, n=10), and diabetes mellitus (33.3%, n=9) were the main comorbidities reported by the participants.

Table 3 shows the correlation between the number of comorbidities, HRV indices, and QoL components evaluated by the SF-36. A significant negative correlation was found between the number of comorbidities and the pain domain (r=-0.427; p=0.03). No significant correlation was observed between the other SF-36 domains or HRV indices and the number of comorbidities.

DISCUSSION

The present study investigated the relationship between the number of comorbidities, autonomic modulation, and QoL in patients diagnosed with CAD. The main findings suggest that a higher number of comorbidities is related to a higher pain level. Furthermore, the number of comorbidities is not related to cardiac autonomic modulation in CAD patients.

Table 1. Sample characterization.

Variables		
Age (years)	65.33±9.23	44.00–83.00
BMI (kg/m2)	27.12±3.67	19.90–37.83
AC (cm)	96.91±10.13	79.00–120.00
WHR	0.94 [1.12]	0.53–1.72
Medications in use		
Anxiolytic	3 (11.1)	
Platelet antiaggregant	25 (92.6)	
Antiarrhythmic	1 (3.7)	
Anticonvulsants	2 (7.4)	
Antidepressant	4 (14.8)	
Anti-ischemic	3 (11.1)	
Beta-blockers	22 (81.5)	
Diuretic	4 (14.8)	
Hypoglycemic	7 (25.9)	
Hypolipidemic	25 (92.6)	
Proton-pump inhibitors	9 (33.3)	
Levothyroxine	1 (3.7)	
Others	8 (29.6)	
Vasodilator	21 (77.8)	

Data represented as mean±standard deviation; minimum – maximum, median [interquartile range], and number (percentage). BMI: body mass index; AC: abdominal circumference; WHR: waist-to-hip ratio.

The main comorbidities reported were hypertension, back pain, and diabetes mellitus. Hypertension and diabetes mellitus are risk factors for CAD[17,18]. The interaction between a variety of pathophysiological, genetic, and environmental mechanisms is responsible for the genesis of hypertension and the development of related target-organ damage, including CAD[17]. Furthermore, prolonged exposure to the elevated blood glucose levels, associated with other risk factors such as hypertension and dyslipidemia, is responsible for microvascular and macrovascular diabetic complications, such as CAD[18].

Previous studies have also found a strong association between the presence of back pain and the occurrence of CAD[19]. The adoption of a sedentary lifestyle as a result of pain makes the individual more susceptible to the occurrence of cardiovascular diseases such as CAD[19]. Furthermore, data in the literature show that the presence of inflammation, elevated cortisol levels, and sympathetic – parasympathetic imbalances may be common factors between heart disease and back pain[19].

Our results showed a negative correlation between the number of comorbidities and the pain domain of the SF-36, which suggests that a higher number of comorbidities associated with CAD is related to a higher pain level, since a lower score in the SF-36 amounts to a worse condition. This result corroborates with the findings of Assari et al.[8], who also found a negative correlation between the total comorbidity score and the pain domain of the SF-36 in individuals with CAD.

The high prevalence of back pain may justify, at least in part, the correlation observed between the number of comorbidities and the pain domain of the SF-36. According to

Table 3. Correlation between the number of comorbidities, the HRV indexes, and SF-36 domains.

Variables	r	p	
Functional capacity	-0.355	0.07	–
Physical aspects	-0.319	0.11	–
Pain	-0.427	0.03	Moderate
General health status	-0.180	0.37	–
Vitality	-0.185	0.36	–
Social aspects	-0.132	0.51	–
Emotional aspects	-0.140	0.49	–
Mental health	-0.250	0.21	–
Mean RR	0.340	0.08	–
RMSSD	0.211	0.30	–
SDNN	0.015	0.94	–
HF (ms2)	0.246	0.22	–
HF (un)	0.236	0.24	–
LF (ms2)	0.073	0.72	–
LF (un)	-0.230	0.25	–
LF/HF	-0.226	0.26	–
SD1	0.211	0.29	–
SD2	-0.001	1.00	–
SD1/SD2	0.281	0.16	–

Bold indicates statistically significant value. rMSSD: square root of the mean of the square of the differences between adjacent normal RR intervals, expressed in ms2; SDNN: standard deviation of all normal RR intervals recorded in a time interval, expressed in milliseconds; LF: low frequency component; nu: normalized units; HF: high frequency component; LF/HF: LF/HF ratio; SD1: standard deviation of the variability of RR intervals in short term; SD2: standard deviation of RR intervals in long term.

Table 2. Self-Administered Comorbidity Questionnaire results.

Comorbidities	Patients who received treatment				Limitation	
	n	%	n	%	N	%
Heart disease	27	100	26	96.3	10	37
Hipertension	18	66.7	18	100	6	33.3
Lung disease	0	0	0	0	0	0
Diabetes	9	33.3	9	100	2	22.2
Stomach disease	2	7.4	2	100	0	0
Kidney disease	1	3.7	0	0	0	0
Liver disease	0	0	0	0	0	0
Blood disease	0	0	0	0	0	0
Cancer	1	3.7	1	100	0	0
Depression	3	11.1	3	100	0	0
Osteoarthritis	3	11.1	3	100	2	66.7
Back pain	10	37	4	40	6	60
Rheumatoid arthritis	1	3.7	0	0	1	100
Other	5	18.5	2	40	2	40

Vlaeyen et al.[20], the presence of back pain generates negative repercussions on QoL. In addition, other comorbidities that also promote chronic pain, such as osteoarthritis and rheumatoid arthritis[21], were also reported by the study participants.

The presence of pain represents a limiting factor to perform daily life tasks, which contributes to a negative perception of QoL, especially in older people[22]. More than half of all participants were diagnosed with back pain or osteoarthritis, and 100% of participants with rheumatoid arthritis reported having an activity limitation, which corroborates with the literature[20,21]. For this reason, the number of comorbidities should be considered at the time of decision-making regarding the treatment of CAD patients.

No significant correlations were found for the other SF-36 domains. In general, individuals diagnosed with CAD present reduced QoL when compared to individuals without the disease[23]. However, it is important to highlight that exercise-based CRP improves the QoL of CAD patients[24]. Therefore, it is possible to suggest that the participation of study participants in a CRP motivated an improvement in their perception of QoL, despite the number of associated comorbidities.

Regarding cardiac autonomic modulation, no correlation was observed between the number of comorbidities and HRV indices. It has already been well established in the literature that CAD patients present reduced cardiac autonomic modulation compared to the general population[6]. This may have influenced our results, confounding the changes promoted by chronic diseases associated with CAD. Furthermore, data from previous studies suggest that physical exercise programs, such as CRP, can modulate cardiac autonomic control, through the promotion of reduced sympathetic influence and increased parasympathetic tone and, consequently, HRV improvement[25].

Cardiovascular dynamics present a complex structure defined by non-stationary, intermittent, scale-invariant, and nonlinear behaviors[26]. In this context, previous studies have suggested that traditional linear HRV indices are not able to characterize the complex dynamics of heartbeats generation[27]. Also, it has been shown that nonlinear HRV indices can discover new information not obtained by linear HRV indices[28]. Thus, it is possible to suggest that the nonsignificant results that have been found in this study may be due to effect of the limitations of the methods used. Therefore, future studies to determine if the number of comorbidities is related to cardiac autonomic modulation assessed through nonlinear HRV indices in CAD patients may be interesting.

Another point to be discussed is that the HRV analysis may be influenced by different factors, such as age, gender, and body composition[29], and has some limitations for assessing cardiac autonomic dysfunction[30]. However, it is important to highlight that HRV is a validated and widely used method for ANS assessment, and the necessary procedures[29] for an appropriate assessment of autonomic modulation by means of HRV were followed in this study. Future research using other methods, such as the study of the interaction between the regulation of the heart and peripheral blood flow[31], to evaluate the relationship between the number of comorbidities and cardiac autonomic modulation in CAD patients may proportionate relevant information about this topic.

There are some limitations in our study that should be considered. It is important to point out that more than 80% of the participants used beta-blockers, which may alter cardiac autonomic modulation. Niemelä et al.[32] studied the influence of beta-blocker therapy on HRV in individuals with stable CAD and observed improvement in linear indices in the experimental group compared to placebo. Furthermore, the information about comorbidities in this study was self-reported, which could represent a source of error. Finally, the small sample size may also be reported as a limitation. Despite these limitations, to the best of our knowledge, this is the first study to evaluate the correlation between the number of comorbidities and impaired cardiac autonomic modulation in CAD patients.

CONCLUSION

The results suggest that the number of comorbidities is inversely related to the pain domain of the SF-36, which suggests that a higher pain level is related to a higher number of comorbidities in CAD patients. Furthermore, the number of comorbidities is not related to cardiac autonomic modulation or the other SF-36 domains.

AUTHORS' CONTRIBUTIONS

HBV: Conceptualization, Methodology, Investigation, Supervision, Formal Analysis, and Writing – original draft. **VESS:** Conceptualization, Methodology, Investigation, Supervision, and Writing – original draft. **TRMB:** Conceptualization, Methodology, Investigation, and Writing – original draft. **FMV:** Data curation, Formal Analysis, and Writing – review & editing. **MJLL:** Investigation, Data curation, and Writing – review & editing. **AFBB:** Conceptualization, Methodology, and Writing – review & editing. **LMV:** Conceptualization, Methodology, and Writing – review & editing. **ACB:** Investigation and Writing – review & editing. **LCMV:** Conceptualization, Methodology, Project administration, Supervision, and Writing – review & editing.

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