Differences in Linear and Nonlinear Heart Rate Variability Based on Pain Intensity in Non-Specific Chronic Low Back Pain: a Cross-Sectional Study

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Abstract

This study investigated the association between linear (spectral analysis) and nonlinear [Shannon entropy (SE), conditional entropy (CE), and symbolic analysis (SA)] heart rate variability (HRV) parameters and pain intensity in individuals with non-specific chronic low back pain. Fifty-two participants were stratified into 2 groups, mild-to-moderate pain and severe pain, based on the Visual Analog Scale (VAS). The RR intervals were recorded at rest in the supine position for10 min with an HR monitor. A series of 250 beats was selected to analyse variance, spectral analysis, SE, CE [complexity index (CI), normalized CI (NCI)] and SA (0V and 2ULV patterns), as well as 0V (no significant variation) and 2ULV (two significant unlike variations), which reflect sympathetic and vagal modulation, respectively. Independent t-tests and Pearson's correlation assessed group differences and the VAS-HRV relationship ($p<0.05$). The severe pain group showed higher LF and 0V% values and lower HF, 2UV%, SE, CI, and NCI values ($p < 0.05$). While linear HRV parameters did not show a significant correlation with pain intensity, nonlinear measures, particularly NCI, demonstrated a statistically significant moderate negative correlation. In conclusion, this study showed that higher pain intensity is associated with decrease in HRV.

1. Introduction

Chronic pain is one of the leading causes of disability worldwide, with high morbidity and a significant impact on patients' quality of life [1]. Assessing its intensity remains a challenge due to its subjective nature (Nesse & Schulkin, 2019). However, physiological features of pain may correlate with its intensity. For instance, chronic pain has been shown to induce dysfunction of the autonomic nervous system (ANS), characterized by sympathetic hyperactivity and reduced parasympathetic modulation [2]. This dysregulation not only perpetuates the pain experience but also increases the risk of comorbidities such as cardiovascular diseases [3].

In this context, heart rate variability (HRV) has emerged as a promising objective tool to assess autonomic balance and determine its relationship with pain intensity [3]. In patients with low back pain (LBP), a predominance of sympathetic activity and a reduction in parasympathetic function have been observed [4]. However, linear HRV parameters have not demonstrated a significant correlation with pain intensity in this condition [5]. As an alternative, nonlinear HRV analyses offer a more comprehensive perspective on autonomic dynamics and may show a stronger correlation with pain intensity. Therefore, this study aims to assess differences in both linear and nonlinear HRV variables based on pain intensity (moderate vs. severe) in patients with NSCLBP, considering their potential utility as objective biomarkers of chronic pain intensity.

2. Methods

2.1. Study design

This is a cross-sectional study conducted at the University of Pernambuco, Petrolina campus, to assess the differences in HRV based on pain intensity levels in participants with non-specific chronic low back pain. Participants were stratified into two groups according to visual analogue scale (VAS): mild to moderate pain (VAS ≤7) and severe pain (VAS >7).

2.2. Participants, eligibility criteria, and recruitment

Participants were individuals aged 18-59 with localized pain in the lumbosacral area for at least 3 months, with no associated pathologies. Exclusion criteria included conditions such as disc herniation, fractures, rheumatic diseases, and pregnancy.

2.3. General characteristics

General characteristics were assessed through interviews, including demographic information and medical history. Anthropometric data (body mass, height, and BMI) were measured.

2.4. Measurements

2.5. Pain intensity

Pain intensity was assessed using the Visual Analog Scale (VAS), a widely validated tool for the subjective measurement of pain. This scale consists of a 10 cm horizontal line, with endpoints representing the extremes of the symptom: “no pain” on the left end (0 cm) and “worst imaginable pain” on the right end (10 cm). Participants indicated their pain level by placing a mark along this line, with the distance from the left end to the mark serving as the quantitative measure of perceived pain, expressed in centimetres (0–10) (Delgado et al., 2018).

2.6. Heart rate variability (HRV)

The RRi sequence length (n = 256 beats) with the greatest stability was selected for each group of patients. The same sequence was used for both analyses (linear and nonlinear). The mean and standard deviation of the RRi were calculated.

2.6.1. HRV spectral analysis

Frequency domain analysis was performed using an autoregressive model of Malliani et al. [6] on previously selected RRi sequences. Two main spectral components were considered: LF, from 0.04 to 0.15 Hz and HF, from 0.15 to 0.50 Hz, which represent sympathetic and vagal modulations in normalized units, respectively. The spectral components were expressed as normalized units (LFnu and HFnu) and ratio (LF/HF). Normalization consisted of dividing the power of a given spectral component (HF or LF) by the total power minus the power below 0.04 Hz and multiplying this ratio by 100. All the volunteers presented a respiratory rate in the HF range.

2.6.2. Shannon entropy

The RRi series were transformed into a sequence of numbers (symbols) ranging from 0 to 5 and organized into three beat sequences from which patterns were observed. The shape and distribution of these patterns were calculated with SE. The SE is large if the distribution is flat (all patterns are identically distributed, and the series carries the maximum amount of information). However, if there is a subset of more probable patterns, while others are missing or infrequent (e.g., in a Gaussian distribution), the SE is small [7].

2.6.3. Symbolic analysis

Symbolic analysis was carried out by grouping the patterns into four families as follows: 0V: all the symbols are equal, i.e., 2, 2, 2 or 4, 4, 4; 2LV: the three symbols form an ascending or descending ramp, i.e., 5, 4, 2 or 1, 3, 4; The rate of occurrence for each pattern is defined as 0V% or 2LV%. It has been observed that 0V% and 2LV% can function as markers of sympathetic and vagal modulation, respectively [8].

2.6.4. Conditional entropy

According to Porta et al [8], CE measures the amount of information carried by the most recent sample of patterns that cannot be derived from a sequence of L past values. Conditional entropy is assessed with the CI. We normalized this index with the SE of the RRi to obtain a NCE that expresses complexity in terms of dimensionless units. This index ranges from 0 (null information) to 1 (maximum information). The larger both indexes are, the greater the complexity and the lower the regularity.

2.7. Statistical analysis

Statistical analysis was performed using SPSS. Normality was checked with the Shapiro-Wilk test. Differences between groups were assessed using an independent t-test for HRV variables, and Pearson’s correlation coefficient was used to assess correlations between VAS and linear and nonlinear HRV measures. Significance was set at 5%, and data are presented as mean ± standard deviation.

3. Methods

The study population consisted of 81 patients evaluated for eligibility, of whom 52 met the inclusion criteria. These participants were subsequently stratified into two groups: mild to moderate pain (n = 30) and severe pain (n = 14). No differences were observed in baseline characteristics.

In the frequency domain analysis of HRV, the severe group exhibited a LFnu (52.56 [42.62 - 60.31]) higher than the mild-Moderate group (37.38 [20.62 - 46.09]). Following this trend, the mild-Moderate group showed a significantly higher HFnu (62.61 [53.91 - 79.38]) than the severe group (47.44 [39.69 - 57.32]). Both findings demonstrated statistically significant differences between the groups ($p < 0.05$, 95% CI).

In the symbolic analysis of HRV, the severe group exhibited a percentage of no-variation patterns (0V%) of 17,06 [15.39 - 25.55], higher than the 10.21 [4.71 - 16.88] recorded in the mild-Moderate group. Similarly, the mild-Moderate group showed a higher percentage of patterns with two non-similar variations (2UV%), with 27.06 [17.25 - 33.73] compared to 16.92 [10.98 - 23.53] in the severe group. Both findings demonstrated statistically significant differences between the groups ($p < 0.05$, 95% CI).

Statistically significant differences were found between the groups ($p<0.05$). Compared to the mild-moderate group, the severe group exhibited significantly lower values for Shannon Entropy (SE: 3.35 [95% CI, 3.18–3.45] vs. 3.63 [95% CI, 3.37–3.92]), Conditional Entropy (CE: 0.99 [95%

CI, 0.93–1.09] vs. 1.15 [95% CI, 0.96–1.27]), and Normalized Conditional Entropy (NCE: 0.73 [95% CI, 0.69–0.79] vs. 0.78 [95% CI, 0.75–0.85]).

Correlations between linear frequency domain indices and VAS were weak (r = ± 0.24) and did not reach statistical significance (p = 0.12; 95% CI). In contrast, moderate and statistically significant correlations (r = - 0.43 to + 0.41) were found between symbolic analysis variables and VAS scores (p < 0.05; 95% CI), with a positive association observed for 0V% and a negative association for 2V%. Regarding geometric analysis, moderate inverse correlations were identified between SE and CI with VAS, while NCI exhibited moderate-to-strong inverse correlations (r = -0.38 to -0.53) with VAS (p < 0.05; 95% CI). (Table 1)

Table 1. Sociodemographic characteristics of the sample, stratified by pain intensity (VAS).

Characteristic	Mild-Moderate Pain (n=36)	Severe Pain (n=16)	p-value
Sex, n (%)			0.999
Men	29 (80.6)	13 (81.3)	
Women	7(19.4)	3 (18.8)	
Age (years)	37.47 (12.66)	37.81 (10.23)	0.919
Weight (kg)	68.47 (11.75)	72.53 (10.17)	0.214
Height (m)	1.63 (0.09)	1.63 (0.07)	0.951
BMI (kg/m²)	25.63 (3.37)	27.24 (3.74)	0.152

Values are presented as Mean (Standard Deviation) for continuous variables or as n (%) for categorical variables. P-values were calculated using an independent samples t-test, except for the 'Sex' variable, for which the Chi-squared test was used.. Abbreviations: BMI, Body Mass Index; VAS, Visual Analog Scale.

Table 2. Spearman correlations (r^2) and p-values between VAS and HRV variables

Variable	r^2	p-value
LF	0.24	0.122
HF	-0.24	0.122
0V%	0.41	0.006*
2UV%	-0.43	0.004*
SE	-0.46	0.002*
CI	-0.38	0.011*
NCI	-0.53	<0.001*

Significant correlations (p < 0.05) marked with an asterisk (*) Abbreviations: LF, Low Frequency; HF, High Frequency; 0V%, zero variations (%); 2UV%, two unlike variations (%); SE, Shannon Entropy; CI, Conditional Index; NCI, Normalized Conditional Index

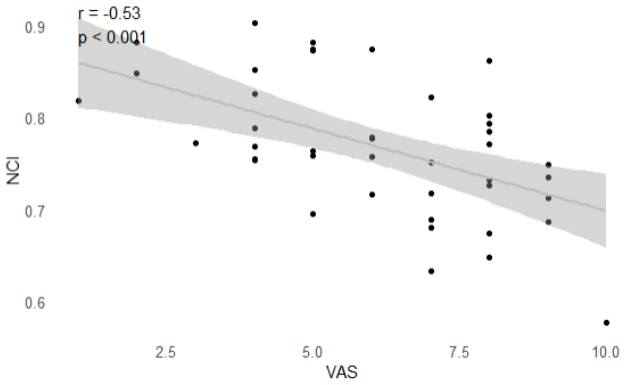


Figure 1. Spearman correlation coefficient (r) and p-value are shown. The solid red line represents the linear regression fit. Significant correlations are indicated by p < 0.05. Abbreviation: NCI, Normalized Complexity Index; VAS, Visual Analogic Scale.

4. Discussion

Our findings demonstrate that individuals with severe non-specific chronic low back pain (NSCLBP) exhibit significant autonomic nervous system (ANS) dysfunction, specifically characterized by sympathetic hyperactivity and impaired vagal modulation. These alterations were further evidenced by a demonstrable reduction in complexity and higher regularity in the severe NSCLBP group when compared to the mild-to-moderate NSCLBP group.

These relationships between alterations in the autonomic nervous system and chronic pain can be explained through HRV indices, which have shown increased sympathetic activity along with a deficit in vagal activity [9]. This combination may reduce the effectiveness of descending inhibitory pain pathways, facilitating central sensitization and contributing to the development of chronic pain.

Regarding pain intensity, it is still not entirely clear how HRV varies according to its level [3]. Some studies on chronic cervical pain have reported weak correlations between linear HRV indices and pain intensity [12]. In contrast, our study identified significantly stronger correlations using nonlinear metrics.

These results support the idea that nonlinear heart rate variability may serve as an additional tool to assess the impact of chronic pain on the autonomic nervous system, as it captures the chaotic dynamics of heart rate and provides a deeper understanding of the system's complexity and adaptability in response to persistent pain [10]. This type of analysis allows for the identification of dynamic and unpredictable behaviours in heart rate variability that may go unnoticed with spectral analysis, and is, furthermore, more robust and sensitive in detecting subtle autonomic dysfunctions [13]. In this regard, nonlinear analysis could be particularly useful for identifying autonomic alterations associated with chronic pain, as the regulatory mechanisms

of the autonomic nervous system are often disrupted in a complex and nonlinear manner.

While the findings of this study are revealing, it is important to acknowledge its main limitations for a correct interpretation. The study has three principal constraints: its cross-sectional design, which precludes the establishment of causality; the absence of a pain-free control group; and the unequal sample sizes between groups, which may reduce statistical power. Future research employing longitudinal designs, control groups, and more balanced samples is essential to validate and expand upon these findings.

5. Conclusion

In conclusion, our study reveals a significant relationship between pain intensity and alterations in heart rate variability (HRV), especially using nonlinear analysis. Chronic pain patients showed sympathetic dominance and reduced parasympathetic activity, as well as more rigid and less adaptable autonomic function. These changes could affect pain modulation and the body's ability to handle the associated physiological stress.

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