Original Article

Major Depressive Disorder and Quality of Life in Patients With Coronary Artery Disease Assessed by Myocardial Perfusion Imaging

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Abstract

Background: Major depressive disorder (MDD) may negatively influence cardiovascular prognosis, increasing the morbidity and mortality of patients with coronary artery disease (CAD). Thus, the psychometric assessment of these individuals may contribute to understanding how mental health impacts the pathophysiology of myocardial ischemia.

Objective: To evaluate the prevalence of MDD in patients with CAD undergoing stress and rest myocardial perfusion imaging (MPI) using the psychometric instrument Patient Health Questionnaire-9 (PHQ-9). As secondary objectives, to correlate quality of life (QoL) data obtained using the 12-Item Short Form Survey (SF-12) and Positive and Negative Affect Schedule (PANAS) instruments with the presence or absence of myocardial ischemia detected by MPI.

Methods: The SF-12, PHQ-9, and PANAS questionnaires were administered to 120 consecutive patients referred for MPI for CAD evaluation. The prevalence of MDD was assessed, and the results were correlated with MPI findings and QoL scale scores.

Results: A high prevalence of MDD was identified (58 cases; 48.3%), with no association with risk factors, age, or MPI findings. A significant rate of suicidal ideation was observed among the evaluated patients (15 cases; 12.5%), in addition to reduced QoL in 88.3% of patients (n = 106), with scores below 50 on the physical SF-12, and in 65% (n = 78), with scores below 50 on the mental SF-12, indicating poor perceived mental health.

Conclusion: These findings reinforce the need for a multidisciplinary approach in the management of patients with suspected CAD, including systematic mental health assessment, given the opportunities to improve outcomes during patient interactions with the health care system.

Keywords: Major Depressive Disorder; Quality of Life; Myocardial Ischemia.

Introduction

Coronary artery disease (CAD) is the leading cause of death and disability in the United States and in developed Western countries. Approximately every 40 seconds, an individual experiences an acute myocardial infarction (AMI), with an estimated 720,000 new acute coronary events occurring annually.[1] In 2021, CAD remained the leading cause of death worldwide, accounting for approximately 9.44 million deaths.[2] In Brazil, 2021 data demonstrated an age-standardized CAD mortality rate of 67.1 per 100,000 inhabitants.[3]

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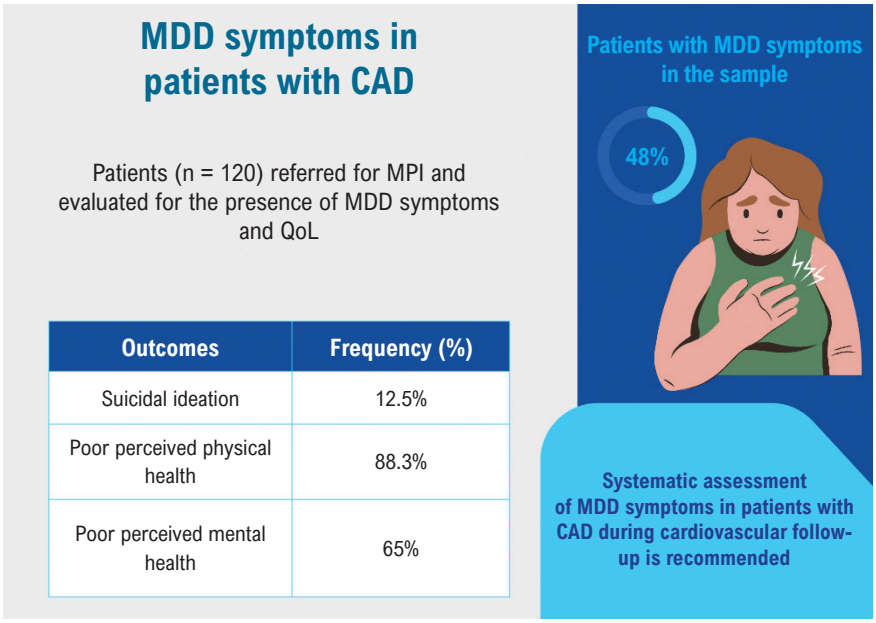
Major depressive disorder (MDD) is associated with significant levels of disability and suffering for both patients and their families,[4] and its appropriate treatment may contribute to restoring quality of life (QoL) and promoting well-being.[5]

Studies conducted in different care settings involving patients with CAD have demonstrated that fewer than half of individuals diagnosed with mental disorders had been previously identified and, among those diagnosed, only a proportion received specialized treatment with a psychiatrist or psychotherapy.[6]

MDD is a multifactorial condition capable of causing relevant physiological alterations. In myocardial perfusion imaging (MPI), some studies suggest the presence of reversible perfusion defects in patients with MDD, which may indicate episodes of transient myocardial ischemia.[7]

This study was based on the hypothesis that correlations exist between MDD symptoms and the main parameters obtained from stress and rest MPI. The primary objective

Central Illustration: Major Depressive Disorder and Quality of Life in Patients With Coronary Artery Disease Assessed by Myocardial Perfusion Imaging



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Major Depressive Disorder and Quality of Life in Patients With Coronary Artery Disease Assessed by Myocardial Perfusion Imaging. CAD: coronary artery disease; MDD: major depressive disorder; MPI: myocardial perfusion imaging; QoL: quality of life.

was to identify the prevalence of MDD in patients referred for cardiovascular evaluation at a federal university hospital through the application of validated psychometric instruments. Additionally, the study aimed to evaluate the prevalence of MDD symptoms using the Patient Health Questionnaire-9 (PHQ-9) in individuals undergoing stress and rest MPI as well as to correlate these symptoms with QoL scores obtained using the 12-Item Short Form Survey (SF-12) and Positive and Negative Affect Schedule (PANAS) instruments, according to the presence or absence of myocardial ischemia.

Associations between MDD symptoms and the main parameters obtained from stress and rest MPI were also investigated to provide an integrated understanding of the interaction between mental health, QoL, and cardiac perfusion abnormalities in this population.

Methods

Study design and population

This was a cross-sectional, observational, prospective analysis based on a primary quantitative database derived from a study conducted at a federal university hospital. Data were collected through structured interviews with closed-ended questions and the application of 3 instruments validated for use nationwide.

The sample was obtained by convenience sampling and included 120 consecutive adult patients undergoing MPI for CAD investigation at the university hospital. Data collection was performed between December 2018 and January 2019.

Information regarding sex, age, and history of systemic arterial hypertension, diabetes mellitus, obesity, dyslipidemia, family history of CAD, menopause, AMI, coronary artery bypass graft surgery, angioplasty with stent implantation, stroke, chronic kidney disease, aortic aneurysm, and vascular disease was collected from medical records.

Data regarding mental health assessment instruments, including SF-12, PHQ-9, and PANAS, as well as parameters obtained from MPI, were also collected. Statistical analysis sought to correlate MPI findings, such as the presence of ischemia, left ventricular ejection fraction (LVEF), and ventricular volumes, with MDD symptoms assessed using psychometric questionnaires.

The study complied with current ethical requirements and was approved by a human research ethics committee under CAAE 89721625.0.0000.5243.

Psychiatric and QoL assessment

The PHQ-9,[8] PANAS,[9] and SF-12[10] scales were used to assess psychiatric symptoms. PHQ-9 was employed to evaluate MDD symptoms, whereas PANAS and SF-12 were used to assess QoL and emotional aspects.

PHQ-9

PHQ-9 is used for MDD diagnosis and symptom severity stratification.[11] The instrument contains nine questions based on the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, fifth edition.

Each item includes the following response options: "not at all," "less than 1 week," "1 week or more," and "nearly every day," corresponding to scores of 0, 1, 2, and 3, respectively. The total score ranges from 0 to 27 points and is classified as follows: i) absence of MDD (0-4 points); ii) mild MDD (5-9 points); iii) moderate MDD (10-14 points); iv) moderately severe MDD (15-19 points); and v) severe MDD (20-27 points).

PANAS

PANAS evaluates two dimensions of individuals' emotional state: positive affect and negative affect.[12] The instrument consists of 20 items distributed across two subscales with 10 questions each, one focused on positive emotions and the other on negative emotions.

Responses range from 1 ("very rarely or never") to 5 ("very frequently or always"). Results were calculated using the application recommended by the investigators responsible for validation of the instrument. Final scores range from 10 to 50 points, with higher values indicating greater intensity of positive or negative emotions.

12-Item Short Form Health Survey

SF-12 is a shortened version translated and validated into Portuguese from the 36-Item Short Form Survey (SF-36).[10] It is a more objective instrument for assessing health-related QoL.

SF-12 consists of 12 items distributed across eight domains grouped into two main components: i) the physical component, which includes functional capacity, physical aspects, pain, and general health status; and ii) the mental component, related to mental health, emotional aspects, social aspects, and vitality.

SF-12 has a final score ranging from 0 to 100, in which 0 represents the worst general health status and 100 the best health status. It demonstrates performance similar to that of SF-36 in the assessment of health-related QoL and is widely documented medical literature, both in its original English version and in versions validated for different languages.

MPI acquisition and analysis

MPI examinations were performed using a single-detector gamma camera (Millenium MPR, GE HealthCare) equipped with a low-energy, high-resolution collimator. Tomographic images were acquired by single-photon emission computed tomography (SPECT), electrocardiogram-gated, using 64 projections and a 64 × 64 matrix.

After acquisition, images were reconstructed by filtered back projection using a Butterworth filter and processed using the e-Soft software, including the Cedars-Sinai and Emory Cardiac Toolbox packages. Global and segmental contractility analysis, as well as LVEF assessment, were performed by gated SPECT. The adopted myocardial segmentation model consisted of 17 segments.

The analyzed MPI variables included the presence of ischemia, defined as an area of radiotracer hypouptake on post-stress images with normalization on rest images, and the presence of fibrosis, defined as an area of persistent hypouptake on both post-stress and rest images. Post-stress and rest LVEF, as well as ventricular volumes under both conditions, were also evaluated.

Statistical analysis

Descriptive analysis was presented in tables, with categorical variables expressed as absolute and relative frequencies (%), and numerical variables presented using appropriate measures of central tendency and dispersion.

Inferential analysis included the following methods: the relationship between numerical MPI parameters and PHQ-9, SF-12, and PANAS scale scores, as well as other numerical variables, was evaluated using Spearman's correlation coefficient. Associations involving categorical variables were analyzed using the Mann-Whitney or Kruskal-Wallis tests. Comparisons between the presence of ischemia on MPI and numerical variables were performed using the Mann-Whitney *U* test, whereas associations with categorical variables were assessed using the chi-square test.

Data distribution normality was verified using the Shapiro-Wilk test and graphical inspection of histograms. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA). Statistical significance was set at 5%.

The analyzed numerical variables did not demonstrate a normal (Gaussian) distribution, as shown by the Shapiro-Wilk test and graphical evaluation of histograms. Therefore, data were summarized using median and interquartile range (Q1-Q3), corresponding to the central 50% of observations between the first and third quartiles. The interquartile range was used as the measure of dispersion associated with the median, analogous to the use of standard deviation in relation to the mean.

Results

The overall profile of the 120 patients included in the study was described using numerical and categorical variables in the total sample. Numerical variables were presented using appropriate measures of central tendency and dispersion, whereas categorical variables were expressed as absolute and relative frequencies (%).

Table 1 presents the characterization of the analyzed demographic and clinical variables, including median, interquartile range (Q1-Q3), and statistical analysis of differences between groups classified according to PHQ-9 results. No statistically significant differences were observed among the analyzed variables when comparing patients with moderate/severe MDD and those with minimal/mild MDD.

Patients had a median age of 62 years and were predominantly female. Arterial hypertension was the most frequent comorbidity, identified in 82% of the sample. Among

Table 1 – Demographic and clinical characteristics of patients according to PHQ-9 results

Variable	Moderately severe/Severe MDD (n and %)	Minimal/Moderate MDD (n and %)	p-value
Age (years) – median (Q1-Q3)	61 (55-66)	63 (58-66)	0.290
Male sex	21 (36.2%)	25 (40.3%)	0.640
Female sex	37 (63.8%)	37 (59.7%)	0.640
Family income (R$) – median (Q1-Q3)	890 (784-1,700)	1,474 (818-2,000)	0.062
Hypertension	38 (80.9%)	44 (83.0%)	0.780
DM	20 (43.5%)	15 (28.3%)	0.120
Smoking	7 (14.9%)	6 (9.6%)	0.420
Obesity	14 (29.8%)	8 (15.1%)	0.070
Dyslipidemia	21 (44.7%)	20 (37.7%)	0.370
FH	23 (48.9%)	18 (39.1%)	0.090
Menopause	25 (53.2%)	23 (43.4%)	0.420
Previous CAD	12 (25.5%)	15 (32.6%)	0.520
AMI	8 (17.0%)	9 (17.0%)	0.960
CABG	4 (8.5%)	5 (9.4%)	0.580
PTCA	6 (12.8%)	10 (21.3%)	0.190
CABG or PTCA	10 (21.3%)	14 (26.4%)	0.550

AMI: acute myocardial infarction; CABG: coronary artery bypass graft surgery; CAD: coronary artery disease; DM: diabetes mellitus; FH: Coronary artery disease family history; MDD: major depressive disorder; PHQ-9: Patient Health Questionnaire-9; PTCA: percutaneous transluminal coronary angioplasty.

women, 48 were postmenopausal, and 44% of participants were smokers or had a history of tobacco use.

MDD was identified in a substantial number of patients: 58 individuals (48%) presented moderately severe/severe MDD. Among these patients, 15 (12.5%) reported suicidal ideation.

Correlation analysis was performed between MPI parameters, age, and scores from the PHQ-9, PANAS, and SF-12 instruments. Table 2 presents Spearman's correlation coefficient (r), the respective p values, and the number of cases included in each analysis involving MPI parameters, age, and psychometric scale scores.

No correlation was observed between post-stress LVEF and PHQ-9, PANAS, and SF-12 scores. Although patients demonstrated poor perceived physical and mental health, there was no direct relationship between these findings and the severity of MPI results.

A significant inverse correlation was observed between resting end-diastolic volume (REDV) and age ($r = -0.225$; $p = 0.013$; $n = 120$), indicating that older age was associated with lower REDV values in the analyzed sample. No statistically significant correlations, at the 5% level, were identified between the remaining MPI parameters and PHQ-9, SF-12, and PANAS scale scores.

Table 3 presents the description of MPI parameters according to score classifications as well as the respective p values obtained from statistical tests. MPI variables were expressed as median and interquartile range (Q1-Q3) and compared using the Mann-Whitney test when two groups were present and the Kruskal-Wallis test when 3 or more groups were analyzed.

When analyzing the relationship between PHQ-9 scores and MPI parameters, no statistically significant correlations were identified.

Table 4 presents the distribution of PHQ-9 and SF-12 score classifications according to the presence or absence of ischemia on MPI as well as the respective p values obtained from statistical tests. Score classifications were expressed as absolute (n) and relative (%) frequencies and compared using the chi-square test.

No statistically significant association at the 5% level was observed between PHQ-9 and SF-12 score classifications and the presence of ischemia on MPI.

Discussion

The present study demonstrated a finding of high clinical relevance: 48% of patients referred for evaluation by MPI presented symptoms compatible with moderate to severe MDD according to the PHQ-9 score. Because of the high prevalence of MDD symptoms observed in the studied population, we believe that systematic assessment of these symptoms in patients referred for CAD investigation is essential, allowing early detection and appropriate management of this condition (Central Illustration).

Table 2 – Correlation between MPI parameters, age, and PHQ-9, SF-12, and PANAS scores

Variable	Parameter	Post-stress LVEF	Rest LVEF	Post-stress EDV	Rest EDV	Post-stress ESV	Rest ESV
Age (years)	r	0.097	0.069	−0.171	−0.225	−0.134	−0.126
	p	0.29	0.46	0.061	0.013	0.14	0.17
	n	120	120	120	120	120	120
PHQ-9 score (depression)	r	0.118	0.109	0.06	0.021	−0.054	−0.048
	p	0.20	0.24	0.51	0.82	0.58	0.60
	n	120	120	120	120	120	120
SF-12 PCS score	r	−0.003	−0.084	−0.039	0.074	0.001	0.075
	p	0.98	0.36	0.67	0.42	0.99	0.42
	n	120	120	120	120	120	120
SF-12 MCS score	r	0.034	0.064	−0.034	−0.020	−0.026	−0.047
	p	0.71	0.49	0.71	0.83	0.78	0.61
	n	120	120	120	120	120	120
Positive PANAS score	r	−0.033	−0.114	0.076	0.041	0.053	0.121
	p	0.72	0.22	0.41	0.65	0.56	0.19
	n	119	119	119	119	119	119
Negative PANAS score	r	−0.093	−0.121	0.160	0.082	0.100	0.090
	p	0.31	0.19	0.08	0.38	0.28	0.33
	n	119	119	119	119	119	119

EDV: end-diastolic volume; ESV: end-systolic volume; LVEF: left ventricular ejection fraction; MCS: Mental Component Summary; MPI: myocardial perfusion imaging; PANAS: Positive and Negative Affect Schedule; PCS: Physical Component Summary; PHQ-9: Patient Health Questionnaire-9; SF-12: 12-Item Short Form Health Survey.

Despite the high prevalence of MDD symptoms, no correlations were identified between MDD scores, QoL indices, and parameters obtained from MPI. No association was observed between MPI abnormalities and greater burden of MDD symptoms. Therefore, MPI did not prove to be an effective marker of cardiovascular severity in patients with MDD symptoms.

When comparing our results with Brazilian population-based data, the prevalence of moderately severe/severe MDD found in our sample (48%) was substantially higher than that reported in large national studies. In an epidemiological survey involving 49,658 Brazilian adults[3] and based on PHQ-9, only 10.5% of individuals presented clinically relevant MDD, defined by a score ≥ 10, a significantly lower value than that identified in our clinical population.

Furthermore, although the population-based study demonstrated an unfavorable impact of MDD on cardiovascular health, reducing by 27% the likelihood of an individual presenting favorable cardiovascular health (odds ratio, 0.73; 95%CI, 0.62-0.86), no prevalence of MDD as high as that observed in our health care setting was identified. These contrasts suggest that patients with suspected or established CAD treated in an outpatient public health care setting present greater emotional and psychological burden, possibly influenced by factors such as recurrent chest pain, fear of future cardiovascular events, functional limitation, and uncertainty regarding prognosis.[13]

In addition, pathophysiological mechanisms related to the interaction between chronic inflammation, oxidative stress, and neuroendocrine activation in ischemic disease may contribute to this scenario.[14] Thus, the nearly 4-fold higher prevalence of moderately severe/severe MDD observed in our cohort reinforces the hypothesis that individuals with CAD constitute a group with high psychosocial vulnerability, requiring systematic screening and integrated cardiometabolic and mental health management strategies.

Several studies have described physiological mechanisms supporting the relationship between MDD and cardiovascular disease. Activation of the hypothalamic-pituitary-adrenal axis in individuals with MDD promotes increased glucocorticoid secretion, associated with peripheral insulin resistance, hyperglycemia, and elevated blood pressure, all recognized cardiovascular risk factors.[15]

Increased glucocorticoid levels are also associated with greater secretion of proinflammatory interleukins, such as interleukin-6 and tumor necrosis factor-alpha. This exacerbated inflammatory response is associated with the risk

Table 3 – Ventricular function variables obtained by MPI and their comparison according to PHQ-9 score classification

Variable	PHQ-9 classification (MDD)	n	Median	IQR	p-value
Post-stress LVEF	Minimal	32	65	52-76	0.47
	Mild/Moderate	53	63	51-73	
	Moderately severe/Severe	35	68	58-75	
Rest LVEF	Minimal	32	61	53-75	0.80
	Mild/Moderate	53	67	55-76	
	Moderately severe/Severe	35	69	60-75	
Post-stress EDV	Minimal	32	55	41-78	0.20
	Mild/Moderate	53	65	52-90	
	Moderately severe/Severe	35	62	51-77	
Rest EDV	Minimal	32	63	46-100	0.86
	Mild/Moderate	53	67	49-85	
	Moderately severe/Severe	35	66	55-85	
Post-stress ESV	Minimal	32	19	10-37	0.52
	Mild/Moderate	53	26	14-38	
	Moderately severe/Severe	35	19	13-30	
Rest ESV	Minimal	32	27	11-48	0.99
	Mild/Moderate	53	23	13-37	
	Moderately severe/Severe	35	19	14-34	

EDV: end-diastolic volume; ESV: end-systolic volume; IQR: interquartile range; LVEF: left ventricular ejection fraction; MDD: major depressive disorder; MPI: myocardial perfusion imaging; PHQ-9: Patient Health Questionnaire-9.

Table 4 – Distribution of PHQ-9 and SF-12 scores according to the presence or absence of ischemia on MPI

Variable	Classification	With ischemia, n (%)	Without ischemia, n (%)	p-value
PHQ-9 Classification (MDD)	Minimal	16 (27.1%)	16 (26.2%)	0.99
	Mild/Moderate	26 (44.1%)	27 (44.3%)	
	Moderately severe/Severe	17 (28.8%)	18 (29.5%)	
Suicidal ideation	Yes	6 (10.2%)	9 (14.8%)	0.44
	No	53 (89.8%)	52 (85.2%)	
SF-12 PCS score > 50 points	Yes	4 (6.8%)	10 (16.4%)	0.10
	No	55 (93.2%)	51 (83.6%)	
SF-12 MCS score > 50 points	Yes	22 (37.3%)	20 (32.8%)	0.60
	No	37 (62.7%)	41 (67.2%)	

MCS: Mental Component Summary; MDD: major depressive disorder; MPI: myocardial perfusion imaging; PCS: Physical Component Summary; PHQ-9: Patient Health Questionnaire-9; SF-12: 12-Item Short Form Health Survey.

of atherosclerosis and alterations in neurotransmitter release, which may contribute to worsening of MDD symptoms.[16] In addition, a possible imbalance of the autonomic nervous system in patients with MDD could favor sympathetic hyperactivity, altering cardiac contractility and increasing susceptibility to arrhythmia development.[16]

Studies using MPI in patients with MDD demonstrated that this population presents greater susceptibility to emotionally induced myocardial ischemia, evidencing myocardial perfusion abnormalities in these individuals.[17]

The analyzed population also demonstrated poor overall perception of physical health. As observed in the physical

component of the SF-12, 106 individuals (88.3%) presented scores below 50. Patients with MDD and CAD may present greater physical limitation, lower functional capacity, and higher prevalence of fatigue and low energy levels.[18]

Furthermore, 78 individuals (65%) presented poor perceived mental health, defined by scores below 50 in the mental component of the SF-12. Patients with this perception tend to present greater emotional and physical impact related to CAD,[19] which may result in greater limitation of daily activities, poorer treatment adherence, and lower engagement in cardiovascular rehabilitation programs.[20]

The 2025 European Society of Cardiology Clinical Consensus Statement on mental health and cardiovascular disease[21] reinforces that systematic assessment of MDD and other mental disorders should be incorporated into the routine care of patients with cardiovascular disease. The document recommends the use of validated tools, such as the Patient Health Questionnaire-2 and PHQ-9, for initial screening after cardiovascular events or in the presence of clinical suspicion, considering the high prevalence of these conditions and their negative prognostic impact.

In our study, a particularly high prevalence of moderately severe/severe MDD was observed among patients referred for MPI (48%), in addition to a substantial rate of suicidal ideation (12.5%), without association with clinical, demographic, or functional variables. In light of the ESC recommendations, our findings reinforce the urgent need to routinely incorporate structured mental health screening into cardiovascular care pathways, considering that psychological distress may be present even in the absence of traditional clinical markers, thereby requiring proactive strategies for identification and intervention aimed at risk reduction, improvement of QoL, and potential modification of clinical outcomes.[21]

Among the limitations of this study, the use of a convenience sample composed of patients referred for evaluation at a university hospital should be highlighted, which may have contributed to a greater burden of comorbidities in the analyzed population. Additionally, patients were evaluated during a period preceding the COVID-19 pandemic, a condition that in several studies was associated with worsening of mental health-related disorders.[22]

Conclusion

This study demonstrated a high prevalence of moderately severe/severe MDD in patients referred for cardiovascular evaluation by MPI. These patients should be identified early and receive follow-up and specific mental health guidance. The implementation of structured protocols for systematic screening of mental disorders in the context of cardiovascular evaluation may represent a relevant strategy for reducing cardiovascular risk, improving QoL, and potentially modifying the clinical outcomes of these individuals.

Author Contributions

Conception and design of the research: Gonçais G, Barbirato GB, Pagnin D, Pagnin VQ, Mesquita CT; acquisition of data: Barbirato GB; analysis and interpretation of the data and writing of the manuscript: Gonçais G, Pagnin VQ, Mesquita CT; statistical analysis: Gonçais G, Pagnin D; critical revision of the manuscript for intellectual content: Pagnin D, Pagnin VQ, Mesquita CT.

Potential Conflict of Interest

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

Sources of Funding

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Study Association

This article is part of the thesis of master submitted by Almeida GG, from Universidade Federal Fluminense.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the CEP-UFF (Universidade Federal Fluminense)

under the protocol number 7.768.804. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013.

Use of Artificial Intelligence

The authors did not use any artificial intelligence tools in the development of this work.

Availability of Research Data

The underlying content of the research text is contained within the manuscript.

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