Archives of Psychiatry and Psychotherapy, 2023; 1: 79–93

10.12740/APP/155142

Quality of life and functionality in patients suffering from chronic pain, anxiety and depression

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Abstract

Mental illnesses are common in patients with chronic pain, and this association may result in changes in functional status. This study assessed the functionality and quality of life of patients with chronic pain, anxiety, and depression.

Methodology: A total of 103 patients were interviewed at Federal University of Minas Gerais' (UFMG) *Hospital das Clínicas* Pain Center, in 2020 and 2021. The presence of depression and anxiety symptoms, pain intensity, quality of life, and functionality was assessed. The cohort studied was stratified into groups suffering from mild, moderate, and intense pain in accordance with the visual numeric scale, and these patients then underwent descriptive and comparative analyses. Subsequently, a multivariate analysis was performed, followed by linear regression analysis to identify risk factors and variables that contributed to the pain being felt.

Results: In total, 16.5% of the patients were diagnosed with symptoms of anxiety, 13.59% with depression, and 34.95% presented symptoms of both anxiety and depression. The functionality assessment revealed severe incapacity, with the highest levels of incapacity present in those suffering from the most intense pain. Patients with symptoms of anxiety and depression presented a worse quality of life than those without these symptoms, with some aspects directly related to pain intensity.

Conclusion: Chronic pain, in the presence of symptoms of anxiety and depression, produces severe functional psychosocial incapacity and a low quality of life, which are directly related to pain intensity. Skin color, suicidal ideation, and psychosocial issues are associated with depression, anxiety, and chronic pain.

INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience, that serves as a biological warning for real or potential tissue damage. It is a multidimensional phenomenon that involves physical, psychological, and sociocultural aspects that impact health and well-being. It may be classified based on the etiology, anatomical location, or duration. Chronic pain is continuous or intermittent for more than three months [1]. Chronic pain is considered a public health problem that affects 20–35% of the global population, varying from 19% in Europe [2], to between 14.6 and 64% in the USA [3]. In South America, the cities of Rio de Janeiro and Santiago have a high prevalence of chronic pain at 31% and 33%, respectively [4]. Pain has multiple serious consequences, including mental disorders, inability to work, social isolation, and suicidal thoughts [5]. Evidence suggests that moderate-to-severe pain, accompanied by psychological disorders, results in a decline in functionality, including changes in routine day-to-day activities [6].

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Chronic pain is associated with various alterations in psychological function. A single experience with chronic pain can lead to alterations in mood (depression, anxiety, and stress), a desire to feel more in control (self-efficacy and self-esteem), responsibility issues (guilt and shame), and feelings of mourning/loss. Although patients suffering from chronic pain experience substantial alterations in all aspects of their psychology, the most commonly examined areas are depression and anxiety and, to a lesser degree, somatization, anger/hostility, and self-efficacy issues [7]. Mental illnesses may be present in up to 75.3% of patients suffering from chronic pain, with anxiety and depression in 30–40% of these patients occurring in a more pronounced manner in women [8]. In 2020, within the context of COVID-19, there was a parallel outbreak of fear and concern associated with the high rates of coronavirus infection, overloaded healthcare systems, and extreme social distancing measures. Uncertainty regarding disease and death was added to confinement, loss of income, restrictions on activity and boredom [9].

The objective of this study was to assess the presence of symptoms of anxiety and depression in patients suffering from chronic pain and their influence on functionality and quality of life, in terms of the complex biopsychosocial interactions involved.

METHODOLOGY:

This study was conducted in an observational, transversal, individual, uncontrolled, and descriptive manner at the Multidisciplinary Pain Center of UFMG's *Hospital das Clínicas* (HC-UFMG). To participate in this study, patients signed a free and informed consent form. The study followed the ethical standards of Resolution No. 196/96 of the National Health Council and was approved by UFMG's Ethics in Research Committee.

The data were collected using semi-structured, standardized questionnaires and mobile devices during individual, in-person interviews. Socioeconomic data were collected, and instruments were used to assess pain intensity (Visual Numeric Scale – VNS), quality of life (Medical Outcomes Study 36 – Short Form Health Survey – SF-36), functionality (the Pain Disability Questionnaire – PDQ), and depression and anxiety (Hospital Anxiety and Depression Scale – HAD, and Depression tracking, in two questions), respectively.

The VNS is a valid and reliable scale for measuring pain intensity. It allows for comparison among patients and is more sensitive to clinical changes in pain intensity. It is the most widely recommended scale for patients suffering from chronic pain and the most widely accepted scale in studies [10-12]. The VNS consists of an 11-point ruler numbered from 0 to ten, which is shown to patients. The following instruction should be given: *"zero means no pain and ten means the worst pain that you can imagine. Choose the number that best describes your pain over the last 24 hours* [13].

The SF-36 subjectively measures individuals' well-being. It is widely used in the literature and has excellent and well-known psychometric properties of reproducibility and validity [14]. It is a multidimensional questionnaire composed of thirty-six items grouped into eight domains: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health. It is scored from 0 to 100, with zero representing the worst state of health and 100 representing the best state of health [13-15].

The PDQ was developed to demonstrate the interaction of biopsychosocial factors in the development of pain and disability [16-18]. It is a concise survey that can be completed quickly and features reliable psychometric measurements It is composed of two domains: the functional condition, comprised of nine items, and the psychosocial component, comprised of six items. It is scored from 0 to 150 and classifies patients as having zero, moderate, or severe or extreme disability [17]. The HAD has frequently been used in population studies and its psychometric properties have been studied in many populations [19]. The HAD was developed to identify symptoms of anxiety and depression in non-psychiatric patients and, to prevent criterion contamination, all somatic indicators were excluded [21], with the depression symptoms focused on anhedonia and a lack of positive affectivity [22]. It is divided into two sub-

scales to assess anxiety and depression separately, each consisting of seven questions. A result of less than eight is considered negative and has a specific sensitivity of 80% for both subscales [22,23]. Although this instrument does not replace a clinical diagnosis, which must be performed by a licensed psychiatric specialist, the terms anxiety and depression were used to identify patients that present a symptomology compatible with the diagnosis based on the HAD, with the patients being considered anxious or depressed when they present a score equal to or greater than eight.

Depression tracking on a two-question scale, was developed to facilitate the identification of depression in clinical medicine. It is based on two questions posed during the assessment of mental disorders during primary care (PRIME-MD) and consists of a 27-item questionnaire [24]. Tracking in the two-question questionnaire had a sensibility of 96% and negative predictive value of 98%, while its specificity was 57% and the positive predictive value was 33% [25]. A total of 103 patients were interviewed between January 2020 and June 2021. The sample was defined based on a conveniently available pool of subjects; therefore, a sample size calculation was not performed. Previously published studies used sample sizes similar to those used in this study [19,26-29]. This served as a benchmark for the utilization of this number of patients. The patients included were of both sexes, over the age of eighteen years, and were regularly monitored at the Multidisciplinary Pain Center. Patients with cognitive deficits or dementia were excluded from this study.

Considering the non-parametric nature of the data median, minimum, and maximum values were obtained along with the interquartile range (P25 and P75). Absolute frequency (n) and percentage (%) figures are presented for the descriptive characterization analysis for both the general population and the three pain groups: mild, moderate, and intense. Comparative analyses of groups were performed utilizing the *Kruskal-Wallis Test*, followed by Dunn's post-hoc test for multiple two-by-two comparisons. The *Chi-Squared Test* was used to compare the frequencies obtained among the groups. The *Kappa Coefficient* was utilized to assess the level of agreement between the results obtained from the Depression Tracking Scale and the HAD. The Mann-Whitney Test was utilized for two-by-two comparisons. This test is recommended for non-parametric data. The epsilon^2 ordinal methodology was utilized to define the size of the effect, as proposed by Cohen and Mangiafico [30,31]. Variables with a *p*-value less than or equal to 0.30 were included in the final multivariate regression model. Owing to the characteristics of each response variable, logistic regression and multivariate regression were utilized, with the strength of the association determined using the odds ratio (OR) with a 95% confidence interval (CI). Adjustments to the model were performed based on the Log likelihood (Logistic Regression) and Root MSE (Linear Regression) values. In all analyses performed, the differences obtained were considered statistically significant when the *p*-value was less than 0.05 ($p<0.05$). Statistical analyses were performed using the GraphPad Prism® program (GraphPad Software, version 8.0, La Jolla California USA, www.graphpad.com) for Windows and the Stata® program (version 14.0; Stata Corporation, College Station, TX, USA).

RESULTS

The study population and its sociodemographic characteristics are described in Table 1.

Table 1. Sociodemographiccharacteristics of the study population, considering the general sample.

Variable	Overall (n=103)	
	n	%
Age(years)		
Median (P25-P75)	55 (48 – 63)	
Min – Max	22 – 79	

	18 – 30	4	3.88
	31 – 40	5	4.85
	41 – 50	24	23.30
	51 – 60	35	33.98
	61 – 70	25	24.27
	71 – 80	10	9.71
Sex (n=103)			
	Female	75	72.82
	Male	28	27.18
Marital Status (n=103)			
	Married or stable relationship	59	57.28
	Single	24	23.30
	Separated or divorced	13	12.62
	Widowed	7	6.80
Race/Color (n=103)			
	White	41	39.81
	Brown	38	36.89
	Black	23	22.33
	Yellow	1	0.97
Education (n=103)			
	Illiterate	3	2.91
	Complete Elementary School	21	20.39
	Incomplete Elementary School	29	28.16
	Complete High School	35	33.98
	Incomplete High School	5	4.85
	Technical Degree	3	2.91
	Complete Higher Education	6	5.83
Work Situation (n=103)			
	Retirement by disability	36	34.95
	Disability related to pain	23	63.89
	Disability not related to pain	13	36.11
	Sick leave	23	22.33
	Unemployed or inactive	14	13.59
	Retirement by age/time of contribution	9	8.74
	Employed or active	9	8.74
	Others: houseworker, does not work and does not look for a job	9	8.74
	Other social benefits	2	1.94
	Student	1	0.97

% Percentage

According to the HAD scale data, 16.5% (17/103) of the patients were diagnosed with symptoms of anxiety, 13.59% (14/103) with symptoms of depression, and 34.95% (36/103) with symptoms

of both. In patients suffering from anxiety, the median score obtained for the HAD was nine, with the group suffering from intense pain registering a median score of eleven, followed by nine for the group suffering from moderate pain, and six for the group suffering from mild pain. The median depression scores were eight. In the group suffering from intense pain, the median score was nine, followed by eight in the population suffering from moderate pain, and 4.5 in the group suffering from mild pain. There were no significant differences in the median scores and frequencies of anxiety and depression in each group (p>0.05). Regarding the total indices obtained from the HAD (the sum of the anxiety and depression scores), the general median score was nineteen. Patients in the intense and moderate pain groups also presented a median score of nineteen, while for the mild pain group, the score was 12.5. The difference between the groups was not significant (p = 0.058), and the size of the effect was considered small (epsilon^2 ordinal 0.05 to 0.06) (Table 2).

Table 2. Comparative analysis of anxiety and depression, according to the Hospital Anxiety and Depression Scale (HAD)

ANXIETY*	Overall (n=103)		Mild pain (n=12)		Moderate pain (n=45)		Severe pain (n=46)		p value	H test	epsilon^2 ordinal	Effect size
Total (%)	53 (51.46%)		5 (41.67%)		23 (51.11%)		25 (54.35%)		0.095 KW	4.705	0.05	Small
median	9		6		9		11					
DEPRESSION*	Overall (n=103)		Mild pain (n=12)		Moderate pain (n=45)		Severe pain (n=46)		p value	H test	epsilon^2 ordinal	Effect size
Total (%)	50 (48.54%)		3 (25.00%)		22 (48,89%)		25 (54,35%)		0.060 KW	5.625	0.06	Small
mediana	8		4.5		8		9					
ANXIETY AND DEPRESSION	n	%	n	%	n	%	n	%	p value	H test	epsilon^2 ordinal	Effect size
Anxiety (n=53)	17	32.08	3	5.66	7	13.21	7	13.21	0.702 Q	---	---	---
Depression (n=50)	14	28.00	1	2.00	6	12.00	7	14.00				
Anxiety and depression	36	34.95	2	1.94	16	15.53	18	17.48				
TOTAL INDEX	Overall (n=103)		Mild pain (n=12)		Moderate pain (n=45)		Severe pain (n=46)		p value	H test	epsilon^2 ordinal	Effect size
mediana	19		12,5		19		19		0.058 KW	5.686	0.06	Small

Frequência absoluta; % Porcentagem; KW Teste de Kruskal Wallis; Q Teste de Qui-Quadrado.
Ponto de corte utilizado para o diagnóstico de ansiedade e depressão, segundo Zigmond e Snaith (1983)[1]: ≥ 9

According to the Depression Tracking Scale, a large proportion of the patients were assessed in the study (47.57%). The degree of agreement between the two instruments was assessed using the Kappa agreement coefficient. According to the data obtained, the expected agreement between depression diagnosis scales was 50.07%. However, the level of agreement obtained was 87.38%, with a Kappa index of 0.75 (p<0.001).

A total of twenty-seven patients (26.21%) presented with suicidal ideation during this study. Regarding pain intensity, according to the VNS instrument, no significant difference was observed among the frequencies of individuals identified as having suicidal ideation in the groups suffering from mild, moderate, and intense pain (p = 0.913). Regarding the HAD-A instrument, the patients identified in the study as suffering from anxiety, presented a median score

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of five in the VNS, while those not suffering from anxiety presented a median score of seven. Regarding the HAD-D instrument, the median VNS score was seven among patients with depression, and six among those without depression. The same result was observed when the Depression Tracking Scale was used. There was no significant difference between the patients suffering from anxiety and those who were not, or between those suffering from depression and those who were not (>0.05), and the size of the effect was considered small across the variables of pain intensity, and the presence of anxiety or depression registered by both the assessment instruments utilized (epsilon^2 ordinal 0.02).

The general data from the SF-36 in patients with anxiety indicate a low quality of life. The components with the worst results, in descending order, were limitations owing to emotional and physical aspects, followed by pain, functional capacity, general state of health, vitality, mental health, and social aspects. Categorization among the groups suffering from mild, moderate, and intense pain demonstrated that, regarding "functional capacity" and "limitation owing to emotional aspects," the patients presented significant differences. Patients suffering from intense pain presented a significantly lower score for the "functional capacity" aspect compared to the groups suffering from mild and moderate pain (p = 0.031). Regarding the "limitation owing to functional aspects, the group with intense pain presented a significantly lower score than the patients with mild pain (p=0.046). For the "pain" component, as expected, the score among the groups suffering from mild pain was higher than that for the group suffering from severe pain (p<0.0001). The total PDQ score indicates severe disability in the general population examined in this study (total score = 94). When stratifying the patients based on pain intensity, it was noted that the group of patients suffering from mild pain presented a better result than that of the patients suffering from intense pain in terms of the psychosocial component (p=0.003), and a better result than that of patients suffering from moderate or intense pain for the functional condition component and in the total for the indices (p≤0.001). When analyzing the size of the effect, minimal to large effects were observed among the variables of anxiety, functionality, and quality of life (epsilon^2 ordinal value of 0.01 to 0.30), with a medium or large effect observed for the variables with a significant p-value (Table 3).

Table 3. Characterization of quality of life and level of disability of anxious patients, according to the SF-36 and PQD instruments

Instrument	Overall (n=53)	Mild pain (n=5)	Moderate pain (n=23)	Severe pain (n=25)	p value ^{KW} H test		epsilon^2 ordinal	Effect size
	Median	Median	Median	Median				
SF-36 Social Aspects	37.5	62.5	37.5	25	0.161	3.655	0.07	Small
SF-36Functional Condition	25	45	40	15	0.031 $^{a.b}$	6.975	0.13	Medium
SF-36Pain	12	42	12	0	<0.001 ^{a}	14.730	0.28	Large
SF-36 General Health Status	30	50	30	30	0.822	0.392	0.01	Minimun
SF-36 Emotional Aspects	0	33.33	0	0	0.046 ^{a}	6.151	0.12	Medium
SF-36 Physical Aspects	0	0	0	0	0.360	2.044	0.04	Small
SF-36 Mental Health	36	44	36	32	0.391	1.876	0.04	Small
SF-36Vitality	35	40	35	25	0.448	1.605	0.03	Small
Psychosocial PDQ	42	26	42	46	0.003 ^{a}	11.670	0.22	Medium
Functional PDQ	54	32	48	60	0.001 $^{a.b}$	13.660	0.26	Large
Total Index PDQ	94	58	86	106	<0.001 $^{a.b}$	15.850	0.30	Large

KW Kruskal Wallis Test. a Significant differences were observed between the Mild Pain and Severe Pain groups (p<0.05).

^{b} Significant differences were observed between the Moderate Pain and Severe Pain groups (p<0.05

The general SF-36 data for patients with depression also indicate a low quality of life. The components with the worst results, in descending order, were limitation owing to emotional and physical aspects, followed by pain, functional capacity, social aspects, vitality, general state of health, and mental health. Categorization among the groups suffering from mild, moderate, and intense pain demonstrated that, in relation to the "social aspects," the patients presented significant differences: patients suffering from mild pain presented a significantly higher score than those suffering from intense pain (p=0.037). For the "pain" component among the group suffering from mild pain, the score registered was significantly higher than that for the group suffering from moderate or intense pain (p=0.008), indicating a better quality of life for these patients in terms of these two parameters. The total PDQ score indicates a disability in the population in this study (total score = 99). When stratifying the patients based on pain intensity, the group of patients with mild pain was observed to have better results than those with intense pain in the psychosocial component, and in the total for the indices (p=0.008 and p=0.013, respectively). When analyzing the size of the effect, minimal to medium effects were observed among the variables of depression, functionality, and quality of life (epsilon^2 ordinal value of 0.01 to 0.30), with a medium effect observed for the variables with a significant p-value (Table 4).

Table 4. Characterization of quality of life and level of disability of depressed patients, according to the SF-36 and PQD instruments.

Instrument	Overall (n=50)	Mild pain (n=3)	Moderate pain (n=22)	Severe pain (n=25)	p value [KW]	H test	epsilon^2 ordinal	Effect size
	Median	Median	Median	Median				
SF-36 Social Aspects	25	75	25	25	0.037 [a]	6.603	0.135	Medium
SF-36 Functional capacity	17.5	25	25	15	0.355	2.072	0.042	Small
SF-36 Pain	5	62	5	0	0.008 [b]	9.622	0.196	Medium
SF-36 General Health Status	31	50	33.5	30	0.529	1.273	0.026	Small
SF-36 Emotional Aspects	0	0	0	0	0.579	1.094	0.022	Small
SF-36 Physical Aspects	0	0	0	0	0.820	0.396	0.008	Minimun
SF-36 Mental Health	34	48	32	36	0.465	1.530	0.031	Small
SF-36 Vitality	27.5	35	27.5	25	0.888	0.238	0.005	Minimun
Psychosocial PDQ	56	26	44	48	0.008 [c]	9.781	0.200	Medium
Functional PDQ	57	46	55	58	0.214	3.083	0.063	Small
Total Index PDQ	99	74	96	106	0.013 [c]	8.717	0.178	Medium

KW Kruskal Wallis Test.

[a] Significant differences were observed between the Mild Pain and Moderate Pain groups (p<0.05).

[b] Significant differences were observed between the Mild Pain and Severe Pain and Severe Pain groups (p<0.05)

[c] Significant differences were observed between the Mild Pain and Severe Pain groups (p<0.05

According to the results, the majority of patients presented with some type of comorbidity (74.76%). The most frequently identified comorbidity was systemic arterial hypertension (29.14%), followed by *diabetes mellitus* (11.43%), dyslipidemia (9.71%), and thyroid disease (7.43%), with 25.24% of patients not presenting any comorbidity. In terms of pain intensity, according to the VNS instrument, no significant difference was observed in the frequency of co-

morbidities among the groups with mild, moderate, or intense pain ($p = 0.812$).

An analysis of the correlation between anxiety and pain intensity, comorbidity, quality of life, and functionality revealed that anxiety was negatively correlated with various aspects of the SF-36 instrument: social aspects (-0.389), general state of health (-0.388), limitations owing to emotional aspects (-0.395), vitality (-0.398), and mental health (-.606). Even though the coefficient indicated a weak correlation, with the exception of mental health, for which the correlation was moderate, anxiety was the highest in patients with the lowest values in the indices indicated in the SF-36 ($p<0.05$). Conversely anxiety presented a weak positive correlation with the psychosocial component (0.426), and the total for the PQD indices (0.282). The "SF-36 General state of health," "SF-36 Mental health," "SF-36 Vitality," and "PDQ Psychosocial component" variables presented a significant correlation with the three groups of patients, after taking pain intensity into consideration. For the group suffering from intense pain, in addition to the abovementioned parameters, the presence of comorbidities, social aspects (SF-36), and the total for the indices (PQD) also presented a positive correlation between anxiety and pain intensity ($p<0.05$). Patients with depression had a negative correlation with the following aspects of the SF-36: social aspects (-0.490), functional capacity (-0.296), pain (-.315), general state of health (-0.331), limitations owing to emotional aspects (-.0347), mental health (-.0636), and vitality (-0.551). In the PDQ, a positive correlation was observed for all items in this instrument: the psychosocial component (0.588), functional condition (0.337), and the total for the indices (0.493).

When analyzing the groups, patients suffering from depression and moderate or intense pain presented a significant correlation with the social aspects (SF-36), limitations owing to emotional aspects (SF-36), mental health (SF-36), vitality (SF-36), the psychosocial component, and the total for the indices (PQD).

Regarding the three pain intensity categories, based on the VNS, the variables of age, sex, race/skin color, family income, financial alterations, pain duration and intensity, pain frequency and causes, SF-36, PQD, and suicide ideation presented a significant p-value (≤0.30) in the bivariate analysis and were selected for the final multivariate logistic regression model. The following variables were selected to comprise the final multivariate anxiety and depression model: age (years); sex; marital status; race/skin color; education level; family income; financial impacts; employment status; pain duration (in categories); pain intensity, frequency, location, and cause thereof; SF-36; PDQ; suicide ideation; and the practice of physical exercise ($p\leq0.30$). Table 5 shows the results of the final multivariate regression model. The race/skin color variable was associated with a 7.32-fold higher risk of anxiety and depression. Suicidal ideation presents a 16.07-fold higher risk of association with anxiety and depression. The psychosocial components of the PDQ present a 1.19-fold higher risk of anxiety and depression. The mental health item had an OR value of 0.82, suggesting a negligible risk of association with anxiety (protection factor). The limitations owing to the emotional aspect variable did not present an association with anxiety (OR near 1), although this is considered important in explaining the final model

Table 5. Logistic Regression (factors associated with Anxiety and Depression – HAD) – FINAL MODEL

LINEAR REGRESSION (HAD – TOTAL INDEXES)				
Explanatory variables	Final Model **			
	Odds Ratio	CI (95%)		p value
RACE/COLOR	7.32	2.00	26.72	0.003*
SF36_ LIMITATION BY EMOTIONAL ASPECTS	0.97	0.95	0.99	0.017*
SF36_MENTAL HEALTH	0.82	0.77	0.86	0.000*
PQD_ PSYCHOSOCIAL COMPONENT	1.19	1.06	1.32	0.002*
SUICIDAL IDEATION	16.07	1.30	199.08	0.031*

* significant p values ($p<0.05$)

** Root MSE = 5,047 / Nr. Of observations = 102 / R2 = 0.74

DISCUSSION

A high frequency of psychiatric disturbances in patients suffering from chronic pain is recognized, and it is possible that there is a subjacent pathophysiological process. The temporal relationship between mental health and chronic pain is not clear, although it appears bidirectional. The factors that determine pain reporting, intensity, and feelings of disability are not yet fully understood. The biopsychosocial model is described by an integrated mixture of biological, physical, and social dimensions [32]. Pain carries the personal meaning of self-dissatisfaction, physical and mental disability, and social dysfunction. Personality traits may also be implicated in the development and adjustment of chronic pain. Although older studies do not confirm a typical pain personality, new evidence suggests that different types of chronic pain share a profile of greater damage avoidance (HA) and less self-control (SD) [33].

Anxiety and depression, among other psychological functioning issues associated with chronic pain, are part of a general condition that by itself only increases the experience of pain [34]. Suffering amplifies pain through poor adaptive responses that lead to the creation or exacerbation of physical and mental suffering [35]. In general, there seems to be a notable overlap between the cerebral structures that confer vulnerability or are affected by the chronification of pain and pathologically negative mood. However, it is not surprising that these conditions are frequently associated [36].

It is important to consider the fact that many studies utilize self-reporting of depression and anxiety as a diagnostic tool; in this study, two instruments with good psychometric properties have been utilized in two questions: the HAD and the Depression Tracking Scale. Other relevant data is the type of instrument utilized, as the assessment of mood, within the context of pain, may produce biased estimates as a result of including items related to the pain pattern, such as: a reduced interest in activities, insomnia, psychomotor agitation or retardation, fatigue, or a reduced ability to concentrate or items related to appetite and a loss of energy that may be influenced by medications, such as analgesics [37]. This was one of the reasons for the selection of the HAD instrument, which excluded somatic symptoms from its items. We noted a high prevalence of anxiety and depression symptoms in the presence of persistent pain, which was more common in the presence of both. However, when a single disorder was present, anxiety demonstrated a higher prevalence. As observed by McWilliams, Goodwin, and Cox [38], anxiety was more strongly associated with chronic pain than with depression in our sample. Most previous studies have shown greater associations with depression, and these relationships have been practically uncontested over the past decade [7]. Anxiety and depression were clearly distinct from each other. Anxiety is centered on the emotion of fear and involves feelings of concern, apprehension, and dread; in contrast, depression is dominated by feelings of sadness, hopelessness, and melancholy [39-41]. Pain may have a greater impact on the domains that are directly linked to the physical experience of pain, especially anxiety, possibly owing to an increase in the tendency to note and respond to physical sensations [7], along with an interpretation of them as threatening, thus increasing feelings of anguish and discomfort, and perpetuating the cycle [42,43].

When we compared the results of the HAD-D with depression tracking in the two-question instrument, we see remarkably similar values. The level of agreement was found to be significant. This is important, as it demonstrates the ability to track patients suffering from depression and chronic pain using an instrument composed of only two questions, which may be performed quickly and simply in day-to-day life. Additionally, we may consider that the assessment of symptoms of depression, using more than one tool, allows for the development of a clearer picture of the symptomology of patients, examining the coherence of their responses and the complementary nature of the items in the questionnaires, and identifying those that require complementary monitoring by a specialist with greater precision.

When stratifying patients with anxiety and depression in relation to pain intensity assessed using the VNS, we did not observe statistically significant differences among the groups. The literature on the influence of depression and anxiety on the perception of pain intensity is unclear.

Studies indicate an altered perception of pain in patients suffering from depression, who seem to perceive stimuli as less painful [44], while others maintain that anxiety may lead to heightened reactiveness to pain [45]. These results led us to question whether intensity is a relevant parameter for the assessment of pain in the presence of symptoms of depression and anxiety.

When patients were categorized based on pain intensity using the VNS, the number of patients in the group suffering from mild pain was considered low, although this was explained by the fact that the samples were obtained from a multidisciplinary pain center, which is a benchmark in the state of Minas Gerais, Brazil. Consequently, the majority of patients treated at this center presented with moderate or severe pain. The categories used in this study (mild, moderate, and intense pain) were chosen with the goal of identifying significant differences among the populations studied, using declarations made by the patients themselves, as indicated by the VNS instrument.

The data for this study were collected in 2020 during the COVID-19 pandemic, which overloaded healthcare systems and led to prolonged and repeated social isolation measures. Studies indicate that social distancing and quarantine have an effect on people's mental health [9,46-48]. Additionally, the majority of patients had their treatments postponed, cancelled, or otherwise made unavailable owing to the pandemic. This serious interruption of treatment may have a negative impact on the health and well-being of people suffering from chronic pain [49). Therefore, it should be remembered that, in this study, conducted within the scope of the pandemic, the results may have been influenced by the presence of mental alterations resulting from the conditions of the pandemic [50,51].

Mental alterations are associated with disability [52]. Cognitive and emotional triggers and behavioral responses may exacerbate pain and disability. In this study, we observed that both anxiety and depression were correlated with the worst functionality results, as measured using the PDQ. The findings indicate that, in clinical terms, exaggerated and dysfunctional pain is associated with fear and avoidance behaviors. Patients begin to abandon their daily activities and become physically inactive. Consequently, an increased risk of mental deterioration arises, leaving these patients more vulnerable to pain and suffering, which leads to more symptoms of anxiety and depression [53], completing a vicious cycle.

Chronic pain has been associated with grave consequences in terms of well-being and is a medical condition that results in the worst quality of life, comparable to that of patients receiving palliative care [54,55]. In the presence of anxiety, the domains most affected were "limitation owing to emotional and physical aspects," "pain, and "functional capacity." The categorization of pain intensity leads to the conclusion that more intense pain has the greatest effect on "functional capacity" in relation to the groups suffering from mild and moderate pain. Therefore, it can be inferred that pain intensity in patients with anxiety, is directly related to their quality of life, especially in terms of functional aspects. This was also observed in the functionality data assessed using PDQ. These data are compatible with evidence that anxiety is related to a improve ability to note the physical domains of painful experiences [7]. These data demonstrate the clinical need to recognize anxiety to implement measures that favor improvements in functionality and quality of life in patients with chronic pain.

Patients suffering from depression present with a low quality of life, similar to patients suffering from anxiety. The worst results are related to "limitations owing to emotional aspects," demonstrating that depression affects emotional issues, especially those that involve feelings of sadness. We observed that, for patients suffering from depression, the presence of pain resulted in improved scores in the "social aspects" when compared to patients suffering from mild pain, suggesting that the latter interferes less with patients' social lives and isolation than severe pain does. The "pain" component in the group suffering from mild pain, as was expected, resulted in a significantly higher score than the group suffering from moderate and intense pain, indicating a better quality of life for these patients in terms of this parameter. These data do not allow for the observation of an agreement between the pain intensity in the VNS instrument, and the pain domain of the SF-36. The data obtained from the SF36 and PDQ in this study, al-

low for the demonstration of the biopsychosocial model, insofar as patients suffering from chronic pain and symptoms of anxiety and depression present alterations in quality of life and physical, mental, and social functionality.

In this study, most patients presented with some type of comorbidity. Patients with chronic pain and other chronic diseases present with higher levels of mortality, dependence on medication, more frequent usage of healthcare services, and greater expenses [2,56]. We observed that patients with anxiety and comorbidities, who belong to the group suffering from intense pain, present with a higher level of disability and a lower quality of life. These results corroborate the literature, showing that the presence of more than one chronic disease increases the level of disability [57].

In the multivariate analyses performed using linear regression, the factors associated with symptoms of anxiety and depression were race/skin color, with a 7.32-fold increase in the risk of association with anxiety and depression. Our data contrasts with that of the "black-white depression paradox" theory, which proposes that black populations, despite being exposed to greater suffering, social inequality, discrimination and "health problems," present lower rates of mental illness, such as depression [58], owing to their greater resilience. It is important to mention that past research highlights a disparity in the diagnosis of depression in the Afro-American population, which may represent a bias in the theory of the paradox. Additionally, these patients have less access to physical and mental healthcare resources and are thus less often diagnosed with and treated for mental conditions. Conversely, prior research demonstrates, as does this study, that Black patients present a higher frequency and intensity of depression in the presence of chronic pain [57]. Suicidal ideation presented a 16.07-fold higher risk of anxiety and depression. Suicidal ideation is estimated to occur in approximately 5-50% of patients suffering from chronic pain [59]. The nature of the relationship between chronic pain and suicide is unclear and rarely studied. People suffering from chronic pain express the desire to die more frequently. The presence of severe, long-lasting pain associated with sleep disorders, catastrophizing, and impaired mental health associated with unfavorable socioeconomic conditions and disability, are recognized factors. Depression is a risk factor independent of suicidal ideation and is well established in the literature [60,61]. Therefore, the degree of mental disability is directly related to the mental health of patients with chronic pain. The psychosocial component of the PDQ presents a risk 1.19 times higher association for anxiety and depression.

This study should be assessed through the lens of the multidimensional biopsychosocial pain model, which has replaced restrictive unidimensional and biomedical theories. The biopsychosocial model is described by an integrated mixture of biological, physical, mental, and social dimensions, suggesting that the body and mind are connected, and that patients and diseases may only be completely understood holistically [8]. It is based on Melzack and Wall [62], and on the "Gate Control Theory of Pain," which describes pain as a system in which the peripheral sensory inputs rise to higher centers, to be modulated down following motivational-affective and cognitive-evaluative influence. More recently, this theory has been associated with the "neuromatrix theory of pain," which is a broader and more complex neural signature characteristic of the brain [63,64]. Past experiences related to motivation and learned memory traits, influence the experience of pain, with such influences being a dominant factor in many, if not the majority, of chronic pain conditions. The strong clinical implication of this perspective is that chronic pain requires manipulation of the emotional circuitry of the central nervous system, along with the nociceptive circuitry [65]. Therefore, pain may be easily modulated by mood, attention, rewards, and expectations [66]. Hence, pain specialists recognize the importance of a broader, multidimensional, multimodal, and interdisciplinary approach to chronic pain management. Within this context, psychological and behavioral interventions are widely accepted as important, if not critical components of effective pain treatment. The results of this study demonstrate the emotional and physical behavioral levels of patients with chronic pain and symptoms of anxiety and depression. Considering that depression and anxiety are associated with multiple negative results [60], subdiagnosis is especially problemat-

ic. The clinical significance of these results is the need to track mental disorders in patients with chronic pain, such as stress, self-esteem, self-efficacy, anger, hostility, guilt, and grief or loss. New studies are necessary to assess other issues beyond mood. Research suggests that, to help individuals interrupt the pain cycle, we should prioritize aspects of psychological function [7], especially the use of interventions, such as acceptance and commitment therapy for people suffering from chronic pain [48].

LIMITATIONS

Transversal studies cannot define causality, which is a characteristic of this study's design. Additionally, the data were collected at a single location, and there was no control group of healthy patients; thus, it was not possible to generalize the results for the entire population. The sample was selected from a conveniently available pool of subjects; therefore, this study was not population based. Future studies using longitudinal and experimental designs are necessary to better understand these relationships. Other psychological functioning processes should also be investigated to fully understand the implications of chronic pain on health and well-being.

CONCLUSION

In this study, we observed a high prevalence of anxiety and depression among patients with chronic pain. These patients presented with severe physical and mental disabilities and low quality of life. In particular, the presence of disability appears to have a strong influence, contributing to the worsening of quality of life. The treatment of psychiatric disorders may be a critical component of the treatment of pain, and failure to recognize or treat mental illnesses in patients.

Disclosures
Michelle dos Santos Severino Costa: conception, planning, analysis, interpretation and writing of the work.
Renato Gomez Santiago: coordination, planning, analysis, interpretation and critical review of the work's writing.
The authors approved the final version submitted. The research complied with the ethical norms of Resolution 196/96 of the National Health Council and was approved by the Research Ethics Committee of Universidade Federal de Minas Gerais.
I certify that this manuscript represents an original work and that it, or part of it, or any other work with substantially similar content of my own, has been published or is being considered for publication in another journal, whether in print or electronic format.
The authors have no conflicts of interest to this work.

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