Journal of Family Medicine

Open Access

Austin Publishing Group

Research Article

Exploring the Relationship between Pain, Psychiatric Factors, and Quality of Life in Patients with Complex Regional Pain Syndrome Type 1 after Distal Radius Fracture: An Observational, Descriptive, Cross-Sectional Study

Sebastián Eustaquio Martín Pérez[1,3*]; Jorge Hernández Marichal[1]; Sergio Martínez Puente; Ignacio Suárez Solo de Zaldívar[1]; Isidro Miguel Martín Pérez[2,3]

[1]Musculoskeletal Pain and Motor Control Research Group, Faculty of Health Sciences, Universidad Europea de Canarias, 38300 Santa Cruz de Tenerife, Spain

[2]Departamento de Medicina Física y Farmacología, Área de Radiología y Medicina Física, Facultad de Ciencias de la Salud, Universidad de la Laguna, 38200, Santa Cruz de Tenerife, España

[3]Escuela de Doctorado y Estudios de Posgrado, Universidad de La Laguna, 38200 Santa Cruz de Tenerife, Espana

***Corresponding author: Sebastián Eustaquio Martín Pérez**

Musculoskeletal Pain and Motor Control Research Group, Faculty of Health Sciences, Universidad Europea de Canarias, 38300 Santa Cruz de Tenerife, Spain

Email: sebastian.martin@universidadeuropea.es

Isidro Miguel Martin Perez (IMP)

Departamento de Medicina Fisica y Farmacologia, Area de Radiologia y Medicina Fisica, Facultad de Ciencias de la Salud, Universidad de la Laguna, & Escuela de Doctorado y Estudios de Postgrado, Universidad de La Laguna

Email: isidromartinperez@gmail.com

Received: December 20, 2023
Accepted: January 12, 2024
Published: January 20, 2024

Abstract

Introduction: Complex Regional Pain Syndrome type 1 (CRPS-1) is defined as a group of sensory and motor disorders that occur as a result of traumatic tissue damage, such as fractures of the distal radius. Pain persistence induces supramedullary neuroplastic changes, resulting in a central sensitization syndrome, in which psychological, affective, and behavioral dimensions interact to amplify the experience of pain. The primary objective of this study was to quantify the relationship between the intensity and duration of perceived pain and psychological factors and quality of life in CS patients diagnosed with CRPS-1 after distal radius fracture.

Materials and Methods: An observational descriptive, cross-sectional study using non-probability convenience sampling was conducted from January 27, 2023 to June 11, 2023. Pain intensity, kinesiophobia, anxiety, depression, hypervigilance, catastrophizing, perceived stress, and quality of life were measured. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Co.), which included descriptive and normality analyses and multiple correlational regression strength calculation.

Results: A total of 26 participants were selected: n=17 women (65.4%) and n=9 men (n=34.6%) with central sensitization diagnosed with CRPS-1 after distal radius fracture. Pain intensity correlated positively and strongly with kinesiophobia (TSK-11*) (β=0.3697, t=2.760, p=0.014)* and negatively with performance-related quality of life *(β=-0.4778, t=-3.301, p=0.005).* The correlation between pain duration correlated with depression was positive and very strong (β=0.7576, t=4.474, p<0.001).

Conclusion: In patients with CRPS after a distal radius fracture who have been diagnosed with CS, pain intensity has been shown to have a positive association with levels of kinesiophobia, while pain duration is significantly related to elevated levels of depression.

Keywords: Complex regional pain syndrome; Central sensitization; Fracture; Kinesiophobia; Stress; hypervigilance; Anxiety; Catastrophizing

Citation: Martín Pérez SE, Hernandez Marichal J, Martinez Puente S, Suarez Solo de Zaldívar I, Martín Pérez IM. Exploring the Relationship between Pain, Psychiatric Factors, And Quality of Life in Patients with Complex Regional Pain Syndrome Type 1 after Distal Radius Fracture: An Observational, Descriptive, Cross-Sectional Study. J Fam Med. 2024; 11(1): 1346.

Introduction

Complex Regional Pain Syndrome type 1 (CRPS-1) is a group of sensory and motor disorders that occur as a result of a traumatic tissue injury such as fractures or dislocations [1-3]. Its annual incidence stands at 13.63 cases per 100,000 inhabitants, being more frequent in a ratio of 1.20 to 1 in women compared to men [4]. Although its etiology is multifactorial, it is produced by the massive release of neurotransmitters and pro-inflammatory substances from the dorsal root ganglia to the fracture region as a consequence of a dysfunction of the sympathetic Autonomic Nervous System (ANS) [5]. This excess of nociceptive information induces peripheral sensitization that leads to hyperalgesia, allodynia, impaired sweating and atrophy of the skin or joints, stiffness, *etc.* [6-8].

The persistence of these mechanisms triggers neuronal hyperactivity in ascending nociceptive transmission that causes not only the activation of the central Nervous System (CNS), but also of the supramedullary structures related to the ANS, causing a phenomenon called secondary or Central Sensitization (CS) [9-11] resulting in an increase in perceived pain intensity, hypersensitivity, skin redness, sweating, and a moderate loss of mobility in the affected limb.

The loss of quality of life of most of these patients is mediated, in turn, by the psychological reactions that emerge during the course of the disease, among which kinesiophobia and hypervigilance stand out [12,13], as well as the emergence of negative thoughts such as catastrophizing that feed back into aversive behavior towards pain [14-16]. In addition, in conjunction with affective disorders (e.g., *depression, anxiety,* etc.) [17] may act by aggravating the perception of their illness and act as predictors of poorer recovery and failure to respond to conventional treatments [18]. Recently, some imaging studies have identified the existence of alterations in neurocognitive domains in patients affected by CRPS that alter cortical areas related to learning and memory, which could explain a decrease in the coping capacity of this syndrome [19,20].

As noted above, the identification and monitoring of psychological factors, which may act as drivers of the long-term subjective pain experience, are especially important in those patients diagnosed with CRPS type 1 after a distal radius fracture since symptoms and signs compatible with CS phenomenon begin to appear in these patients. However, despite the available knowledge on how these psychological responses influence the experience and duration of CRPS, no previous descriptive study has investigated the magnitude and direction of these relationships through multiple linear regression analysis models whose analysis would allow us to understand how these psychological and quality perception factors linked to the centralized pain experienced by the patient diagnosed with CRPS interact with each other. For this reason, the main objective of this study was to quantify the relationship between the intensity and duration of perceived pain and psychological factors and quality of life in CS patients diagnosed with CRPS-1 after distal radius fracture.

Materials and Method

Study Design

An observational, descriptive, cross-sectional study was conducted according to the Statement for Reporting Observational Studies (STROBE) reporting standard [21] using non-probabilistic convenience sampling to quantify the association between pain intensity and psychological factors in a sample of CRPS-1 subjects with CS after radial fracture. The study was conducted from January 27 to June 11, 2023 at the European University of the Canary Islands (Campus Casa Salazar, Tenerife, Spain). Prior to inclusion in the study, each participant was required to sign written informed consent to participate and be registered in an anonymous database.

Participants

After signing the informed consent form, the JHM investigator conducted a clinical interview to assess whether the candidates met the previously established inclusion criteria: (1) men and/or women over 18 years of age, (2) diagnosed with CRPS-1 after a radius fracture, (3) medically validated for the presence of CS-related pain using the Spanish version of the Central Sensitization Inventory (CSI) (>40) and (4) expressed their Willingness to participate by signing an informed consent form. On the other hand, the exclusion criteria were: (1) adults who suffered from cognitive impairment or psychiatric disorder and (2) who had hearing limitations or problems understanding the Spanish language.

Collection of Information and Measuring Instruments

After evaluating the eligibility criteria and signing the informed consent to participate in the study, the ISSZ investigator collected data from March 2, 2023 to April 23, 2023 in a hospital clinic of the European University of the Canary Islands (Campus Casa Salazar, Tenerife, Spain). Information was obtained from interviews that were conducted with the aim of identifying and collecting affiliation data (e.g., *sex, age, employment status, marital status, type of fracture*) and anthropometric data (e.g., *weight, height, BMI).*

CS was then assessed using the Spanish version of the CSI, a two-part scale that assesses a total of 25 common health-related symptoms and their relationship to CS, with scores ranging from 0 (*no*) to 4 (*always*), with a maximum of 100. The instrument is reliable and valid for populations vulnerable to pain, showing high internal consistency (α=0.872) and test-retest reliability (r=0.91) [22]. Subjects who met the inclusion criteria were then administered questionnaires, scales, and assessment instruments that measured the primary variables (pain intensity and duration) and secondary variables related to psychological function (kinesiophobia, catastrophizing, anxiety, stress, depression, hypervigilance) and quality of life.

Study Variables

Primary

Pain intensity was assessed using the *Numeric Pain Rating Scale* (NPRS) [23], a validated subjective measurement instrument for acute and chronic pain that is simple to apply and frequently used to assess changes in pain intensity. It consists of a numbered line of 10 cm in which the patient indicates the level of pain, ranging from 0 (*no pain*) to 10 (*worst pain ever perceived*). On the other hand, the duration of pain was obtained by estimating the time (in *months)* from the medical diagnosis to the time of measurement.

Secondary

Kinesiophobia: Kinesiophobia is the fear of movement or the fear of re-injuring oneself during movement and is considered one of the most important predictors of persistent pain. This variable was measured using the *Tampa Scale for Kinesiophobia* (TSK-11-SV) [24], a reliable and validated instrument con-

sisting of 11 items that must be answered using a Likert-type scale, with the assigned range being from 1 (*strongly disagree*) *to 4* (*strongly disagree*). The results of the scale are interpreted based on the final values obtained, with a higher score indicating a higher degree of kinesiophobia.

Anxiety: Anxiety is the tendency to see or react to different situations as more threatening (anxiety *trait*) or as a temporary period of duration and intensity characterized by tension, worry, and increased activity of the autonomic nervous system (*anxiety state*). In this study, anxiety was assessed with the Spanish version of the *State-Trait Anxiety Inventory* (STAI) [25], which measures anxiety status across 20 items with four options using a Likert-type response scale, which scores from 0 (*not always*) to 3 (*a lot*).

Perceived stress: Perceived stress is a set of psychological changes that cause various ailments in the stomach, respiratory system, skin, nervous system and/or musculoskeletal system. To evaluate this variable, the *Perceived Stress Scale* (PSS) [26] was used, which contains a total of 14 items with a score ranging from 0 (*never*) to 5 (*very frequent*) and which allows us to establish that the higher the score, the higher the level of perceived stress.

Depression: Depression is an affective disorder characterized by emotional irritability or loss of interest or pleasure in daily activities. This dimension was measured with the *Beck Depression Inventory (BDI)* [27] composed of 21 items that assess attitudes and symptoms characteristic of depression and in which participants must choose which statements best describe how they feel during the previous week, including the day the test was administered. At the end, each score must be added up, taking as a reference the score of 63 as the maximum value and 0 as the lowest.

Hypervigilance: Hypervigilance is defined as a state of alertness and signs of impending pain that occurs when threat values are high and causes the individual to engage in aversive behavior toward pain. To analyze this variable, the *Pain Vigilance and Awareness Questionnaire* (PVAQ) [28] was used, which assesses pain awareness, vigilance, and observation. The questionnaire consists of 9 statements, and patients must indicate their value on a scale from 0 (*never*) to 5 (*always*).

Catastrophizing: Catastrophizing measures excessively negative orientation to harmful stimuli in a painful situation. This study used the Spanish version of the *Pain Catastrophizing Scale (*PCS) [29] which consists of 13 statements describing pain-related emotions and thoughts, in which subjects must indicate their level of agreement with these statements on a scale of 0 (*not at all*) to 4 (*always*). Their interpretation implies that the higher the score obtained, the greater the presence of catastrophic behavior in the individual.

Quality of life: Health-related quality of life is the importance people place on their lives in the physical, mental, and social aspects that make up their health and are influenced by personal experiences, beliefs, expectations, and perceptions. To measure this variable, the Spanish version of the SF-36 Health Questionnaire was used [30]. In this tool, composed of 36 items, it evaluates different response options through a Likert-type scale, ranging from 3 to 6, so higher scores reflect a higher quality of life.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics software for Windows, version 20.0 (IBM Co.), for data analysis and representation. First, the ISSZ researcher made a record in an electronic database of the results of the assessment instruments. JHM verified the accuracy of the data by completing the double data entry. Second, the SEMP researcher performed descriptive calculations to characterize the sample based on the parameters of centralization (*mean and median*), dispersion (*standard deviation and variance*) and position (*first quartile and third quartile*). Thirdly, the assumption of normality of each of the variables was tested using the *Shapiro-Wilk* test, establishing the level of statistical significance at $p<0.05$. If these criteria for bivariate correlations were met, Pearson's correlation coefficient was used to determine the relationship between the primary and secondary variables, as well as the coefficient of determination and alignment of each association. In the event that any of them were not met, it was decided to resort to Spearman's correlation coefficient rho to calculate the strength of association between them. The significantly associated variables were entered into independent multiple linear regression models whose result was expressed through the correlation coefficient (R), the adjusted coefficient of determination (R2-Adjust) and the mean square error (RMSE) with their corresponding result of the Snedecor F contrast test (F-value). The correlation strength of each independent variable within the regression model was described from the standardized beta coefficients (β) with its corresponding result of the T-student significance test. For its interpretation, 0.26 to 0.49 (*weak) was considered*; 0.50 to 0.69 (*moderate*); 0.70 to 0.89 (*strong*); and 0.90 to 1.00 (*very strong*). No other selection criteria were applied to include independent variables in the multiple regression model. Statistical significance was established at $p<0.05$.

Ethical Considerations

All patients and controls approved in writing by assent or informed consent according to whether they were minors or adults in their voluntary participation in the study. This study was approved by the institutional ethics committee CEIm 23/171-OS_X_TFM.

Results

Sample Description

A total sample of 26 subjects with CRPS after a distal radius fracture who suffered from CS pain was included. A total of n=17 women (65.4%) and n=9 men (n=34.6%) aged between 47 and 79 years (mean=63.35 years, SD=8.75) were selected (Figure 1). The weight of our population ranged from 45.60 kg to 98.20 kg in the highest case (mean=78.14 kg, SD=12.65). Regarding their height, the subjects in the sample had a height that ranged from 1.64 m to 1.88 m (mean=1.74 m, SD=0.0586) obtaining a variation in Body Mass Index (BMI) from 14.39 to 30.99 kg/m2 (mean=25.92 kg / m^2, SD=4.24). Regarding the type of distal radius fracture, more than half of the sample had Colles's fracture (n=18, 69.2%), followed by Smith fracture (n=4, 15.4%) and Galeazzi and Monteggia fracture (n=4, 15.4%) (Table 1 & Figure 1).

Description of the Study Variables

Pain intensity was moderate (mean NPRS=7.50, SD=1.42) while pain duration was 12.96 months (SD=4.14) The CS of the sample measured with the CSI was mean=44.9 (SD=3.08). Regarding the psychological variables related to pain, Kinesiophobia (TSK-11-SV) reached a mean=25.65 (SD=7.27), State-Trait Anxiety (STAI) mean=53.27 (SD=11.54), Perceived Stress (PSS) mean=33.77 (SD=6.40), depression (BDI) mean=24.96

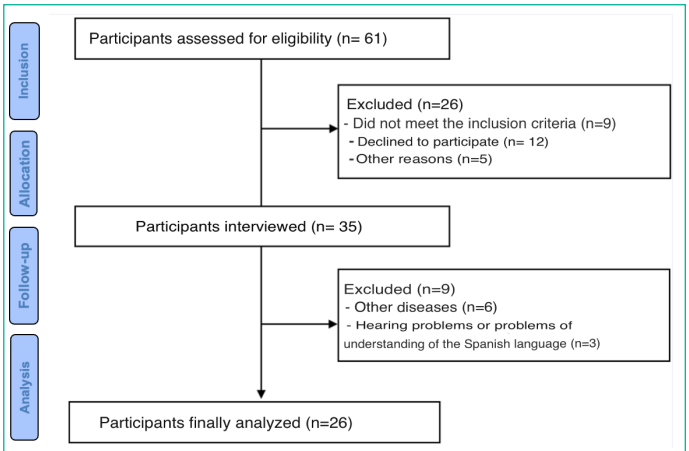

Figure 1: Flowchart for Participant Selection.

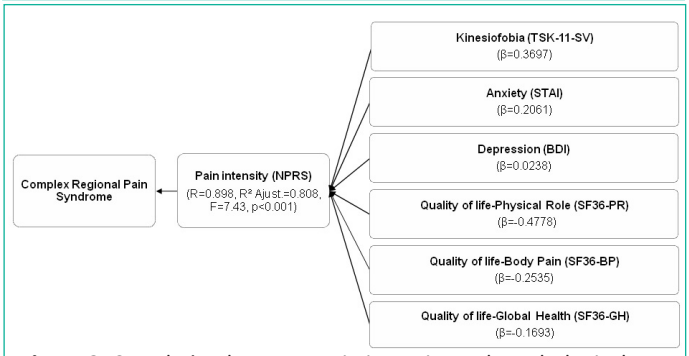

Figure 2: Correlation between pain intensity and psychological factors in patients diagnosed with CRPS after distal radius fracture with CS.

(SD=14.76), hypervigilance (PAVQ) obtained a mean=23.8 (SD=11.0) and catastrophizing (PCS) mean=39.7 (SD=13.6). In relation to the variable of quality of life (SF-36), quality of life related to physical function (mean=67.5, SD=11.5), physical role (mean=55.2, SD=26.3), body pain (mean=73.6, SD=13.4), general health (mean=50.8, SD=20.6), vitality (mean=65.0, SD=6.37), social functioning (mean 54.6, SD=31.8), emotional functioning (mean=81.3, SD=8.67) and mental health (mean 73.1, SD=13.3) (Table 2).

Multiple Correlation Analysis

Regarding the multiple regression model for the association between pain intensity (NPRS) and psychological and quality of life dimensions, a strong predictive value was found (R=0.898, R2-adjusted = 0.612, F=7.43, p<0.001) with an acceptable adjustment (VIF<1.0) and a tolerance greater than 0.620. Statistical power was good (Power (1-β) = 0.99). In this model, only the standardized regression coefficients of kinesiophobia (TSK-11*) (β=0.3697, t=2.760, p=0.014)* and quality of life related to physical performance *(β=-0.4778, t=-3.301, p=0.005)* were statistically significant (Figure 2 & Table 3). Correlation between pain intensity and psychological factors in patients diagnosed with CRPS after distal radius fracture with CS.

In the multiple regression model for the association between pain duration (*months*) and psychological reactions to pain and quality of life, it was observed that the predictive value was very strong (R=0.962, R2-adjusted=1.11, F=9.65, p<0.001) with a good fit (VIF<1.3) and a tolerance greater than 0.421. Statistical power was good (Power (1-β)=0.99). In this model, only the standardized regression coefficient of depression (BDI) (β=0.7576, t=4.474, p<0.001) was statistically significant (Figure 3 & Table 4). Correlation between pain duration and psychological factors in patients diagnosed with CRPS after distal radius fracture with CS.

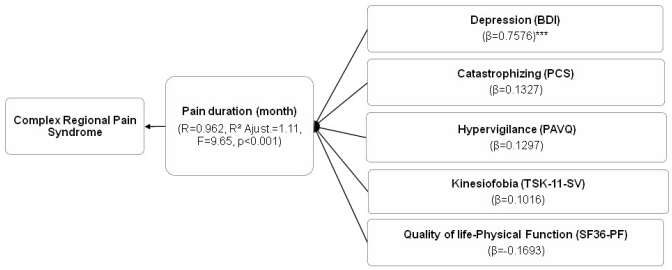

Figure 3: Correlation between pain duration and psychological factors in patients diagnosed with CRPS after distal radius fracture with CS.

Table 1: Demographic description of the sample.

Variable	N	Mean	Median	SD	Var.	W	p	25th	75th
Age (years)	26	63.35	65.50	8.75	76.55	0.967	0.548	57.25	68.75
Weight (kg)	26	78.14	79.05	12.65	160.00	0.941	0.139	72.70	86.5
Stature (m)	26	1.74	1.73	0.058	0.003	0.973	0.693	1.69	1.78
BMI (Kg/m2)	26	25.92	27.29	4.238	17.96	0.910	0.026*	24.10	28.93

Note: N: Sample Size; SD: Standard Deviation; W: Statistical of the Shapiro-Wilk goodness-of-fit test; 25th, 25th percentile; 75th, 75th percentile. Shapiro-Wilk goodness-of-fit test *p≤0.05.

Table 2: Description of the study variables.

Variable	Mean	Median	SD	Var.	W	p	25th	75th
Pain intensity (NPRS)	7.50	7.00	1.42	2.02	0.911	0.028**	7.00	8.75
Duration of symptoms (months)	12.96	12.00	4.14	17.16	0.882	0.006**	10.00	14.00
Central Awareness (CSI)	44.92	45.00	3.08	9.51	0.943	0.161	42.00	46.75
Kinesiophobia (TSK-11-SV)	25.65	26.50	7.27	52.88	0.934	0.098*	22.00	30.75
Anxiety (STAI)	53.27	52.50	11.54	133.16	0.954	0.290	44.25	60.00
Perceived stress (PSS)	23.77	33.00	6.40	40.90	0.944	0.171	30.00	36.75
Depression (BDI)	39.73	22.50	14.76	217.80	0.857	0.002**	12.75	27.75
Hypervigilance (PAVQ)	67.46	21.00	11.04	121.78	0.789	<.001***	18.00	27.00
Catastrophizing (PCS)	55.19	40.00	13.59	184.68	0.972	0.680	30.75	50.75
Quality of Life-Physical Function (SF36-PF)	73.58	68.00	11.48	131.70	0.915	0.035*	58.00	72.00
Quality of Life-Physical Role (SF36-PR)	50.77	55.00	26.32	692.96	0.887	0.008**	45.00	63.75
Quality of Life-Body Pain (SF36-BP)	65.04	71.00	13.40	179.69	0.938	0.120	65.00	80.00
Quality of Life-Global Health (SF36-GH)	54.62	40.00	20.58	423.38	0.813	<.001***	40.00	75.00
Quality of Life-Vitality (SF36-V)	81.35	64.00	6.37	40.52	0.904	0.019**	62.00	68.00
Quality of Life - Social Function (SF36-SF)	73.08	60.00	31.78	1009.85	0.886	0.008**	20.00	80.00
Quality of Life - Emotional Role (SF36-ER)	23.77	80.00	8.67	75.12	0.832	<.001***	75.00	80.00
Quality of Life-Mental Health (SF36-MH)	39.73	80.00	13.35	178.15	0.838	<.001***	70.00	80.00

Note: N: Sample Size; SD: Standard Seviation; W: Statistical of the Shapiro-Wilk goodness-of-fit test; 25th, 25th percentile; 75th, 75th percentile; Shapiro-Wilk goodness-of-fit test. *p≤0.05, **p≤0.001. p≤0.001.

Table 3: Correlation between pain intensity and psychological factors in patients diagnosed with CRPS after distal radius fracture with CS.

Var. depend.	Var. independent.	R	R^2 Adjust.	RMSE	F-value	p-value	β	t	p
Pain intensity		0.898	0.807	0.612	7.43	<,001			
	Kinesiophobia						0.3697	2.670	0.014*
	Anxiety						0.2061	1.630	0.123
	Perceived stress						-0.0711	-0.474	0.642
	Depression						0.0239	0.137	0.893
	Hypervigilance						0.2791	1.433	0.171
	Catastrophizing						0.076	0.656	0.521
	Quality of Life-Physical Function						-0.1383	-1.009	0.328
	Quality of Life-Physical Role						-0.4778	-3.301	0.005**
	Quality of Life - Body Pain						-0.2535	-1.875	0.079
	Quality of Life-Global Health						-0.1693	-0.581	0.573
	Quality of Life-Vitality						-0.1413	-0.470	0.647
	Quality of Life - Social Function						-0.1232	-0.915	0.38
	Quality of Life - Emotional Role						-0.0573	-0.499	0.627

Abbreviation: R^2 Adjust, R squared adjusted; RMSE, root mean square error; β, standardized beta coefficient. *p≤0.05, **p≤0.001. ***p≤0.001.

Table 4: Correlation between pain duration and psychological factors in patients diagnosed with CRPS after distal radius fracture with CS.

Var. depend.	Var. independent.	R	R^2 Adjust.	RMSE	F-value	p-value	β	t	p
Pain duration		0.962	0.829	1.11	9.65	<.001			
	Kinesiophobia						0.1016	0.956	0.360
	Anxiety						-0.1081	-0.961	0.357
	Perceived stress						-0.0216	-0.183	0.858
	Depression						0.7576	4.474	<0.001***
	Hypervigilance						0.1297	0.718	0.488
	Catastrophizing						0.1327	1.307	0.218
	Quality of Life-Physical Function						-0.1693	-0.581	0.573
	Quality of Life-Physical Role						-0.1413	-0.470	0.647
	Quality of Life - Body Pain						-0.1232	-0.915	0.380
	Quality of Life-Global Health						-0.0573	-0.499	0.627
	Quality of Life-Vitality						-0.0775	-0.298	0.771
	Quality of Life - Social Function						-0.0325	-0.173	0.865
	Quality of Life - Emotional Role						-0.0576	-0.302	0.768

Abbreviation: R^2 Adjust, R squared adjusted; RMSE, root mean square error; β, standardized beta coefficient. *p≤0.05, **p≤0.001. ***p≤0.001.

Discussion

The aim of this study was to describe and quantify the association between psychological and quality of life variables with the intensity and duration of centralized pain experienced by people with CRPS after a distal radius fracture.

The first multiple regression model showed that the increase in pain intensity observed in this patient profile is significantly associated, on the one hand, with high kinesophobia scores, and, on the other hand, with low quality of life scores related to the ability to perform physical tasks. These findings suggest that perceived pain intensity in patients with CRPS is associated with altered pain coping behaviors, such as kinesiophobia, which is the independent variable that best predicts the perception of pain intensity suffered by these people. Our results also show that the presence of kinesiophobia in patients with CS affected by CRPS seems to act by promoting anticipatory overprotective responses that strengthen the fear-avoidance cycle by positive feedback and lead the patient to a decrease in physical activity and an alteration in quality of life [31]. In relation to this idea, Gheldof *et al.* (2006) [32] found, in a cross-sectional study conducted in a work setting, that fear of re-injury partially mediated the relationship between pain intensity and disability. Our findings are consistent with those obtained by this group, as we have similarly observed a correlation between the severity of a patient's symptoms and their ability to perform physical tasks associated with daily living. Therefore, the degree to which the patient experiences their symptoms is closely related to a decrease in their overall quality of life. Also, Swinkels-Meewisse (2006) [33] expands the concept that the severity of persistent pain is closely related to the patient's perceived functional status and disability. A cross-sectional study of CRPS patients conducted by Marinus *et al.* (2013) [34] revealed that pain intensity contributed significantly to limitations in physical activity and participation in patients with CRPS in the lower extremities. Recently, in a correlational study of patients with CRPS due to radial fractures, Martín-Pérez et *al.* (2023) [35], reported a moderate degree of correlation between pain intensity and kinesiophobia, hypothesizing that this aversive behavior may contribute to the patient's perception of physical disability.

The results of the second multiple regression model reveal a very strong and significant association (R=0.962, R^2 Adjust. R^2=1.11, F=9.65, p<0.001) between the duration of pain and depression (β=0.7576, t=4.474, p<0.001). This finding is consistent with previous observational studies that identify depression as the most common psychological factor in patients with CRPS type I [36,37]. According to Park *et al.* (2020) [38] chronic pain and depression may share mechanisms that result in bidirectional effects, which would indicate a feedback loop that contributes to their persistence over time. Similarly, Kroenke *et al.* (2011) [39] showed that pain and depression are mutually reinforcing in symptoms lasting at least 12 months, suggesting a possible causal relationship between them. This influence can be attributed to the patient's personality, as other studies have pointed out that patients with pain and neurotic personality experience higher levels of depression due to an alteration in their ability to cope. The importance of personality differences is an

important aspect to consider when interpreting these results, as we believe that it could help to distinguish more accurately between a major depressive disorder and a transient depressive reaction due to persistent pain.

Limitations

Throughout this research, a number of limitations have been identified that may affect the external validity of the results. The sample was recruited using non-probabilistic techniques, which may have resulted in a biased sample. In addition, the use of a single reference centre for participant selection may have introduced biases into the results. However, we believe that this recruitment system is the easiest to implement from an organizational point of view and allows us to achieve a representative sample size.

On the other hand, when considering the conduct of a cross-sectional descriptive observational study to answer the study question, the results presented cannot provide information on the fluctuation of psychological factors over time or how the relationships between variables may change over an extended study period over time. Therefore, it is evident that there is a need to promote prospective observational cohort studies, as they would allow the interactions of outcome variables to be evaluated over time, providing valuable information for the description of the study phenomenon.

Our work corroborates the lack of high-quality methodological research that exists on the relationship between psychological variables and the development of CRPS. Regarding the limitations, it is worth highlighting the lack of participants in the study whose origin of CRPS was different from a radius fracture, nor did it consider the presence of individual non-modifiable cofactors such as personality or the presence of chronic diseases (e.g., diabetes, hypertension, hypercholesterolemia, etc.) or modifiable cofactors such as the consumption of drugs for pain control (e.g., selective serotonin reuptake inhibitors (SSRIs). opiates, *etc*.) In addition, the absence of stratification of the analysis according to the time elapsed since the onset of symptoms could also potentially affect the results of the different psychometric tests that evaluate psychological factors.

These aspects require the construction of observational studies that analyze the results according to subgroups of clinical interest, since it would allow a more precise evaluation of the magnitude to which the characteristics of clinical presentation of pain are related to the rest of the variables.

Conclusion

In patients with CRPS after a distal radius fracture who have been diagnosed with CS, pain intensity has been shown to have a positive association with levels of kinesiophobia, while pain duration is significantly associated with elevated levels of depression.

Author Statements

Financing

Authors certify that they have no affiliations or financial involvement in any organization or entity with a direct financial interest in the topic or materials discussed in the article.

Conflict of Interest

The authors declare no conflict of interest.

Ethical Considerations

- That the work is original and is not in the process of being evaluated by any other scientific journal.

- That the procedures followed in the research have been carried out in accordance with the ethical standards of the human experimentation committee and in accordance with the Council for International Organizations of Medical Sciences (CIOMS) and the Declaration of Helsinki.

- That we guarantee the right of its patients to privacy and confidentiality as described in the corresponding section of these rules.

- That we are in possession of the informed consent of the patients for participation in the study and the publication of the results.

- That we comply with the authorship requirements as set out in its Publication Guidelines. In addition, we declare that we are in possession of the necessary publication permissions from the authors and the publisher of this publication.

That none of the authors has a conflict of interest.

References

1. Miller C, Williams M, Heine P, Williamson E, O'Connell N. Current practice in the rehabilitation of complex regional pain syndrome: a survey of practitioners. Disabil Rehabil. 2019; 41: 847-53.

2. Harden NR, Bruehl S, Perez RSGM, Birklein F, Marinus J, Maihofner C, et al. Validation of proposed diagnostic criteria (the 'Budapest Criteria') for Complex Regional Pain Syndrome. Pain. 2010; 150: 268-74.

3. Misidou C, Papagoras C. Complex Regional Pain Syndrome: an update. Mediterr J Rheumatol. 2019; 30: 16-25.

4. Lorente A, Mariscal G, Lorente R. Incidence and risk factors for complex regional pain syndrome in radius fractures: meta-analysis. Arch Orthop Trauma Surg. 2023; 143: 5687-99.

5. Birklein F, Ajit SK, Goebel A, Perez RSGM, Sommer C. Complex regional pain syndrome - phenotypic characteristics and potential biomarkers. Nat Rev Neurol. 2018; 14: 272-84.

6. Maihöfner C, Seifert F, Markovic K. Complex regional pain syndromes: new pathophysiological concepts and therapies. Eur J Neurol. 2010; 17: 649-60.

7. Popkirov S, Hoeritzauer I, Colvin L, Carson AJ, Stone J. Complex regional pain syndrome and functional neurological disorders - time for reconciliation. J Neurol Neurosurg Psychiatry. 2019; 90: 608-14.

8. Chang C, McDonnell P, Gershwin ME. Complex regional pain syndrome - Autoimmune or functional neurologic syndrome. J Transl Autoimmun. 2021; 4: 100080.

9. Arslan D, Ünal Çevik I. Interactions between the painful disorders and the autonomic nervous system. [Otonom sinir sistemi ve ağrılı bozukluklar arasındaki etkileşimler]. Agri. 2022; 34: 155-65.

10. Wen B, Pan Y, Cheng J, Xu L, Xu J. The role of neuroinflammation in complex regional pain syndrome: A comprehensive review. J Pain Res. 2023; 16: 3061-73.

11. Karpin H, Vatine JJ, Bachar Kirshenboim Y, Markezana A, Weissman-Fogel I. Central sensitization and psychological state distinguishing complex regional pain syndrome from other chronic limb pain conditions: A cluster analysis model. Biomedicines. 2022; 11: 89.

12. Barnhoorn KJ, Staal JB, van Dongen RT, Frölke JP, Klomp FP, van de Meent H, et al. Are pain-related fears mediators for reducing disability and pain in patients with complex regional pain syndrome type 1? An explorative analysis on pain exposure physical therapy. PLOS ONE. 2014; 10: e0123008.

13. de Jong JR, Vlaeyen JW, de Gelder JM, Patijn J. Pain-related fear, perceived harmfulness of activities, and functional limitations in complex regional pain syndrome type I. J Pain. 2011; 12: 1209-18.

14. Margalit D, Ben Har L, Brill S, Vatine JJ. Complex regional pain syndrome, alexithymia, and psychological distress. J Psychosom Res. 2014; 77: 273-7.

15. Jeong S, An J, Cho S. Role of affective instability on suicidal risk in complex regional pain syndrome: a diary approach (preliminary report) [preliminary report]. Korean J Pain. 2021; 34: 94-105.

16. Lee DH, Noh EC, Kim YC, Hwang JY, Kim SN, Jang JH, et al. Risk factors for suicidal ideation among patients with complex regional pain syndrome. Psychiatry Investig. 2014; 11: 32-8.

17. Scarff JR. Managing psychiatric symptoms in patients with complex regional pain syndrome. Innov Clin Neurosci. 2022; 19: 56-9.

18. Cave SA, Reynolds LM, Tuck NL, Aamir T, Lee AC, Bean DJ. Anxiety, Disability, and Pain Predict Outcomes of Complex Regional Pain Syndrome: an 8-year Follow-up of a Prospective Cohort. J Pain. 2023; 24: 1957-67.

19. Halicka M, Vittersø AD, Proulx MJ, Bultitude JH. Neuropsychological changes in complex regional pain syndrome (CRPS). Behav Neurol. 2020; 2020: 4561831.

20. Nimbley E, Caes L, Noel M, Jordan A. Distress and resilience narratives within pain memories of adolescents and young adults with complex regional pain syndrome: A multi-method study. J Pain. 2023; 24: 1275-87.

21. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008; 61: 344-9.

22. Cuesta-Vargas AI, Roldán-Jiménez C, Neblett R, Gatchel RJ. Cross-cultural adaptation and validity of the Spanish central sensitization inventory. SpringerPlus. 2016; 5: 1837.

23. McCormack HM, Horne DJ, Sheather S. Clinical applications of visual analogue scales: a critical review. Psychol Med. 1988; 18: 1007-19.

24. Gómez-Pérez L, López-Martínez AE, Ruiz-Párraga GT. Psychometric properties of the Spanish version of the Tampa Scale for kinesiophobia (TSK). J Pain. 2011; 12: 425-35.

25. Guillén-Riquelmen A, Buela-Casal G. Factorial structure of the State-Risk Anxiety Questionnaire (STAI) for patients diagnosed with depression. Ment Health. 2015; 38: 293-8.

26. Remor E. Psychometric properties of a European Spanish version of the Perceived Stress Scale (PSS). Span J Psychol. Spanish version. 2006; 9: 86-93.

27. Bonicatto S, Dew AM, Soria JJ. Analysis of the psychometric properties of the Spanish version of the Beck Depression Inventory in Argentina. Psychiatry Res. 1998; 79: 277-85.

28. Esteve R, Ramírez-Maestre C, López-Martínez AE. Empirical evidence of the validity of the Spanish version of the pain vigilance awareness questionnaire. Int J Behav Med. 2013; 20: 59-68.

29. Olmedilla Zafra A, Ortega Toro E, Abenza Cano L. Validation of the Pain Catastrophizing Scale in Spanish athletes. Cuad Psicol Deporte. 2013; 13: 83-94.

30. Vilagut G, Ferrer M, Rajmil L, Rebollo P, Permanyer-Miralda G, Quintana José M et al. The Spanish SF-36 health questionnaire: A decade of experience and new developments. Health Gazette. 2005; 19: 135-50.

31. Roh YH, Gong HS, Baek GH. Prognostic value of pain sensitization during early recovery after distal radius fracture in complex regional pain syndrome. Pain Med. 2019; 20: 1066-71.

32. Gheldof EL, Vinck J, Van den Bussche E, Vlaeyen JW, Hidding A, Crombez G. Pain and pain-related fear are associated with functional and social disability in an occupational setting: evidence of mediation by pain-related fear. Eur J Pain. 2006; 10: 513-25.

33. Swinkels-Meewisse IEJ, Roelofs J, Oostendorp RAB, Verbeek ALM, Vlaeyen JWS. Acute low back pain: pain-related fear and pain catastrophizing influence physical performance and perceived disability. Pain. 2006; 120: 36-43.

34. Marinus J, Moseley GL, Birklein F, Baron R, Maihöfner C, Kingery WS, et al. Clinical features and pathophysiology of complex regional pain syndrome. Lancet Neurol. 2011; 10: 637-48.

35. Martín Pérez SE, Losada Delgado P, Pérez Acosta PRKC, Alonso Pérez JL, Sosa Reina MD, et al. Association between pain intensity and psychological variables in patients with complex regional pain syndrome. A correlational cross-sectional study. 2023; 52: 23-6.

36. Pendón G, Salas A, García M, Pereira D. Complex regional pain syndrome type 1. Complex Reg Pain Syndr Type 1: Analysis of 108 patients Revista Sociedad Española Dolor. 2019; 26: 6-13.

37. Taylor SS, Noor N, Urits I, Paladini A, Sadhu MS, Gibb C, et al. Complex regional pain syndrome: A comprehensive review. Pain Ther. 2021; 10: 875-92.

38. Park HY, Jang YE, Oh S, Lee PB. Psychological characteristics in patients with chronic complex regional pain syndrome: comparisons with patients with major depressive disorder and other types of chronic pain. J Pain Res. 2020; 13: 389-98.

39. Kroenke K, Wu J, Bair MJ, Krebs EE, Damush TM, Tu W. Reciprocal relationship between pain and depression: a 12-month longitudinal analysis in primary care. J Pain. 2011; 12: 964-73.