Original Article

Course of Symptoms and Quality of Life Measurement in Complex Regional Pain Syndrome: A Pilot Survey

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Abstract
Few data have been published regarding the natural history, course of symptoms, and quality of life in Complex Regional Pain Syndrome (CRPS). To obtain preliminary data regarding these important issues in CRPS, a set of patient self-report questionnaires were mailed to patients with the diagnosis of CRPS who had been assessed and/or treated at a tertiary university-based pain center in the United States. Self-reports of demographic information, symptoms, the Neuropathic Pain Scale, and a modified Brief Pain Inventory (mBPI) were received from 31 CRPS patients. Approximately 75% of patients reported initial symptoms of pain, swelling, coldness, and color changes. An additional 71% had weakness and inability to move the extremity as initial symptoms. Weakness at some time during their course of CRPS was described by 97%. A majority reported no overall improvement or worsening of symptoms over time (mean 3.3 years). The pain descriptors with the highest mean values were "deep" (6.4/10), "unpleasant" (6.4), "sensitive" (5.7), "surface" (5.4), and "dull" (5.3) pains. Significant sleep disturbance was reported by 80%. CRPS had a severe impact on quality of life, with substantial interference reported in 9 of 10 mBPI activity items by a majority of these patients. These findings should be viewed with caution and should not be generalized to the entire CRPS population because the cohort was small and select. A large multicenter prospective study needs to be performed to validate these preliminary findings. J Pain Symptom Manage 2000;20:286–292. *© 2000 U.S. Cancer Pain Relief Committee, 2000.*

Key Words
Complex regional pain syndrome, reflex sympathetic dystrophy, pain, quality of life, neuropathic pain

Introduction

Complex regional pain syndrome (CRPS) is a poorly understood clinical syndrome characterized by regional pain and vasomotor disturbances. Little is known of this condition's pathophysiology, natural history, and impact on quality of life. Moreover, although pain and symptom heterogeneity is known to occur among sufferers, there is a scarcity of published reports assessing self-reported symptom progression. Classic teaching is that patients afflicted with this disorder progress through

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three stages,[1] but this teaching is based primarily on clinical experience rather than scientific data.

The aims of this patient survey pilot study were to obtain data regarding the course of symptoms among CRPS patients and how the disorder has affected patient quality of life.

Methods

Subjects

Fifty-five patients who had been evaluated and given the diagnosis of CRPS by a physician at the University of Washington Multidisciplinary Pain Center from 1997 to 1998 were sent a survey with a cover letter. A subsequent telephone call was made by a research coordinator asking for participation in this study. Patient diagnosis of CRPS (or reflex sympathetic dystrophy [RSD]) was made after a history and physical examination by a pain physician on faculty at the pain center; all patients met the current criteria of the International Association for the Study of Pain (IASP) for CRPS.[2]

Measures

Basic demographic data, information about health care utilization, and CRPS history, such as time since onset of pain and other symptoms, were obtained. Respondents were also asked to indicate whether or not they have first- or second-degree relatives with CRPS.

In addition, respondents were asked details concerning the pain and symptoms associated with their CRPS, including their first symptoms, pain location(s), diurnal variation, duration, and the average, worst, and least pain during the past week (on a 0–10 scale, with 0 = "no pain" and 10 = "the worst pain imaginable"). Possible covariates of pain and other CRPS symptoms were also ascertained, including whether or not the pain is worse when the respondent is tired or stressed, history of smoking since diagnosis of CRPS, and impact of distraction on CRPS experience.

The Neuropathic Pain Scale (NPS),[3] a validated 10-item questionnaire used to quantitate the different qualities of neuropathic pain, each on a 0–10 scale, was also included in the survey, as was a modified version of the interference items from the Brief Pain Inventory (mBPI).[4] The mBPI asks respondents to indicate the extent to which pain interferes with daily activities on a 0 ("CRPS/RSD pain has not interfered") to 10 ("CRPS/RSD pain completely interfered") scale. Patients rated the degree pain interfered with general activity, mood, mobility, normal work, relations with others, sleep, enjoyment of life, self-care, recreational activities, and social activities; items concerning the last three activities were added to the measure as they represent additional activities with which pain could potentially interfere.

Results

Demographics

Thirty-one surveys were returned (56% of those sent). The average age of the respondents was 43.8 years (SD = 8.6); 25 (80.6%) were female. Patients first began to notice symptoms of CRPS at the age of 39.2 years (SD = 8.8) and were first diagnosed with CRPS at 40.5 years of age (SD = 8.8). According the patient report, the average mean duration of CRPS of these patients was 3.3 years (SD = 1.8 years, median = 3.1 years, range = 1.1–9.1 years).

Ethnicity was reported as Caucasian by 28 (90.3%) responders, African American by 1 (3.2%), Hispanic by 1 (3.2%), and "other" by 1 (3.2%). Thirty (96.8%) reported an injury as the inciting event that caused the development of CRPS. Four patients (12.9%) claimed to have a relative who also had developed CRPS. Smoking at any time while suffering from CRPS was found in 13 (41.9%) of responders.

First Symptoms Developed

Table 1 shows the "first symptoms of RSD/CRPS" described by patients. Twelve (38.7%) patients reported that the left side was first affected, 38.7% reported the right side, and 9.7% reported that both sides were initially affected. Initial symptoms first developed in the toes and/or feet in 45.2%, fingers and/or hand in 32.3%, the entire leg in 12.9%, and fingers in 6.5%.

Immobilization of Limb

Prior to developing CRPS, 67.7% of patients reported having the affected limb physically immobilized with a cast or sling: 19.4% for less than 1 month, 25.8% for 1–2 months, 6.5% for 3–6 months, and 16.1% for more than 1 year. Additionally, when asked if they had "not moved or slightly moved their CRPS-affected

Table 1
First Symptoms of RSD/CRPS Reported by Patients

Symptom	Responders (%)
Severe pain	100
Abnormal swelling	90.3
Abnormal coldness	74.2
Abnormal color changes	74.2
Weakness	71
Inability to move extremity	71
Muscle spasms	58.1
Feelings as though limb was disconnected	54.8
Abnormal warmth/heat	54.8
Abnormal sweating	48.4
Abnormal movements (tremors)	38.7
Skin dryness	22.6

body part for a period of time," 80.6% of patients agreed: 9.7% for less than 1 month, 12.9% for 1–2 months, 25.8% for 3–6 months, 3.2% for 6 months to 1 year, and 22.6% for more than 1 year.

Course of Symptoms

The majority of patients reported having multiple symptoms during their course of CRPS (Table 2). The most common symptoms in this group were pain (100%), weakness (96.7%), and swelling (96.7%). The only symptoms that were noted to improve by a majority of subjects were skin color (58.1%) and swelling (51.6%). No symptom was reported to have worsened to stayed the same by a majority of patients, although most symptoms were noted by a majority to have either worsened or had no change.

For those patients who noted symptom worsening or symptom improvement, Table 3 shows patient self-reported reasons for symptom severity change. A majority reported that treatment altered the severity of most symptoms, including pain (83.3%), swelling (77.8%), weakness (73.9%), sweating (70.0%), disconnected feeling (64.3%), skin cold (64.3%), skin color (61.9%), and skin warm (53.3%). Time (i.e., the natural history of the condition), was also felt by a majority of patients to be a major reason for symptom severity change, including skin warm (80%), skin cold (71.4%), disconnected feeling (64.3%), skin color (61.9%), weakness (60.9%), and skin dryness (57.1%). No symptom was described as changing in severity by a majority of patients due to another injury or stress.

Current Pain Symptomatology

When asked to rate their pain during the past week on a 0–10 numerical rating scale, patients reported 5.9 (SD = 2.7) "average pain," 3.9 (2.3) "least pain," and 7.3 (2.9) "worst pain." Pain was worse during the day in 32.3% and at night in 19.4%, and almost half (48.4%) stated their pain was at the same level during the day and night.

Current pain location involved the feet in 58.1%, calves in 22.6%, hands in 48.4%, and forearms in 38.7%. Other pain locations were written in by 71% as being affected, including "shoulder" ($n = 5$), "knee" ($n = 5$), "ankle" ($n = 4$), "face" ($n = 1$), "hip" ($n = 1$), "entire left side of body" ($n = 1$), "chest" ($n = 1$), and "neck" ($n = 1$).

Effect of Stress and Distraction on Pain

Approximately three-quarters (77.4%) reported that their CRPS pain was worse under stressful conditions and when tired (80.6%). Only 25.8% claimed that their pain was improved with distraction.

Table 2
Course of Symptoms

Symptom	Never had (%)	Improve (%)	Worsen (%)	No change (%)
Pain	0.0	29.0	29.0	41.9
Weakness	3.2	48.4	25.8	22.6
Swelling	3.2	51.6	6.5	38.7
Skin color	9.7	58.1	9.7	22.6
Skin cold	16.1	32.3	12.9	38.7
Skin warm	25.8	29.0	19.4	25.8
Disconnected feeling	25.8	29.0	16.1	29.0
Sweating	35.5	22.6	9.7	32.3
Tremors	41.9	16.1	19.4	22.6
Dry skin	51.8	9.7	12.9	19.4

Table 3
Patient Explanation for Symptom Improvement or Worsening

Symptom	Treatment (%)	Time (%)	Another injury (%)	Stress (%)
Pain	83.3	55.6	5.6	22.2
Weakness	73.9	60.9	4.3	17.4
Swelling	77.8	50.0	0.0	5.6
Skin cold	64.3	71.4	0.0	14.3
Skin color	61.9	61.9	0.0	4.8
Skin warm	53.3	80.0	13.3	6.7
Disconnected feeling	64.3	64.3	7.1	28.6
Sweating	70.0	50.0	0.0	20.0
Tremors	45.5	45.5	9.1	27.3
Skin dryness	42.9	57.1	0.0	28.6

Results shown are for those patients who reported that their symptoms had changed; patients could check more than one for each symptom.

Neuropathic Pain Scale

The findings on the Neuropathic Pain Scale (NPS) were as follows: intensity of pain 6.3 (SD = 2.9), sharp 5.2 (3.5); hot 5.0 (3.6); dull 5.3 (3.2); cold 4.1 (3.4); sensitive 5.7 (3.5); itchy 2.8 (3.4); unpleasant 6.4 (2.9); deep 6.4 (2.9); and surface pain 5.4 (3.3).

To determine if the quality of pain experienced in this sample of patients differed from those in other patient groups, including another sample of patients with CRPS/RSD,[3,5] a series of ANOVAs was performed using responses to the NPS items as dependent variables, and diagnostic group (postherpetic neuralgia, $n = 128$; previous CRPS/RSD sample, $n = 69$; painful diabetic polyneuropathy, $n = 24$; peripheral nerve injury, $n = 67$; Charcot-Marie-Tooth Neuropathy (CMT), $n = 44$; and current CRPS sample, $n = 31$) as the independent variable. Significant overall differences ($P < 0.05$) emerged for intense, sharp, cold, sensitive, itchy, unpleasant, and surface pain. Pairwise comparisons between the current sample of CRPS patients with the other patient groups on these NPS items indicated that the current sample described their pain as significantly less intense, sharp, sensitive, and unpleasant, but significantly more cold than persons with postherpetic neuralgia. They also described their pain as significantly less unpleasant than those with diabetic neuropathy, peripheral nerve injury, or the previous sample of CRPS patients. However, this sample of CRPS patients described their pain as more itchy than the prior CRPS/RSD sample or the peripheral nerve injury patients. Finally, this sample of CRPS patients described their pain as more cold and sensitive than those with CMT. (See Galer and Jensen[3] and Carter et al.[5] for the means and standard deviations of NPS responses in the other samples.)

Sleep

Only 19.4% of patients reported no sleep interference due to CRPS/RSD, while 19.4% reported one to two nights per week of sleep interference, 22.6% reported three to five nights/week, and 38.7% reported six to seven nights/week.

Quality of Life

In the majority of respondents, CRPS significantly interfered with functional activities, as can be seen in Table 4. In fact, for all items except for "self-care," more than 50% of patients reported substantial interference (score of at least 5/10). Approximately 75% of patients noted substantial interference with general activity, mood, normal work, and recreational activities. Using a device, such as a cane, walker, or wheelchair, to help move was reported by 35%.

Discussion

This pilot study describes the self-reported course of symptoms and quality of life measures among a select group of 31 CRPS patients who had been evaluated at a tertiary university-based pain center in the United States. The "first symptoms" endorsed by at least 75% of these patients encompass the symptoms included in the current diagnostic criteria for CRPS[2]: pain (100%), swelling (90%), coldness (74%), and color changes (74%) (Table 1). Interestingly, the next most common set of initial symptoms was related to motor dysfunction:

Table 4
Patient Mean Scores on the Modified Brief Pain Inventory and the Percentage of Respondents with "Substantial Interference" Defined by a Score of ≥5/10

Activity	Score (SD)	Substantial Interference (%)
General activity	6.81 (3.43)	74.2
Mood	6.35 (3.25)	74.2
Mobility	6.23 (4.03)	67.7
Normal work	6.84 (3.63)	74.2
Relations	5.74 (3.43)	64.5
Sleep	6.10 (3.80)	67.7
Enjoyment	6.94 (3.34)	71.0
Self-care	3.94 (3.56)	45.2
Recreational activities	7.32 (3.31)	77.4
Social activities	6.26 (3.61)	74.2

weakness (71%), inability to move extremity (71%), and muscle spasms (58%). The latter symptoms are not currently included in the IASP diagnostic criteria. Recent studies assessing the validity of the current IASP criteria for diagnosis of CRPS have also reported the importance of motor symptoms and signs in this disorder.[6–8] Additionally, others have also observed that significant motor dysfunction is a common symptom in patients with CRPS and RDS.[9–11] Thus, our data confirm the importance of motor symptomatology in CRPS and provide further evidence for their inclusion in revisions of the CRPS diagnostic criteria.

The initial symptoms of patients with CRPS (or RSD) have not been adequately studied, and much of what has been written in the past is based on personal anecdotal experience. According to Bonica[1] "the first stage of RSD is characterized by constant pain . . . localized edema, muscle spasm . . . limitation of motion . . . skin is usually warm, red, and dry." Thus, the only difference between our patients' reports and Bonica's first stage is that more of our patients described an abnormal coldness as compared to an abnormal warmth. Veldman and colleagues[9] prospectively assessed 829 RSD subjects during their initial evaluation. RSD for less than 2 months was reported by 156 of these patients. Of these 156 "early RSD" patients, 92% reported pain, 97% reported discoloration, 86% reported edema, 98% reported temperature difference, 90% reported limited movement, 98% reported paresis, and 57% reported hyperhidrosis. Regarding the temperature abnormality, this other study did not observe any temporal trend and suggested "a subdivision into primarily warm and cold form."[9] Of note, an equal number of our study patients, approximately 50%, noted the classically described "abnormal warmth or heat" and the more recently described neglect-like symptoms ("feelings as though the limb is disconnected")[11] as part of their initial symptom complex.

The course of symptoms in CRPS (and RSD) has been poorly studied. To our knowledge, our study is the first to ask patients to assess the course of their CRPS symptoms. The majority of our patients reported experiencing the classically described symptoms of CRPS and RSD at some point during the course of their condition, such as pain, swelling, temperature abnormality, and swelling. Additionally, 96.8% reported having associated weakness and 74.2% experienced disconnected feelings in their affected body region—again, suggesting that motor and neglect problems are prevalent in CRPS. The only symptoms that a majority of our patients reported improving since onset were coldness (58.1%) and swelling (51.6%), and approximately one-half (48.4%) reported improved weakness. Interestingly, no symptom was described as worsening by a majority of these patients. Thus, the data from this group of CRPS patients tend to suggest a chronic ongoing condition without any significant changes in symptom severity for a majority of those afflicted.

Several prior studies have provided data on the course of signs, symptoms, or laboratory testing. Veldman et al.[9] compared patients with RSD duration of 0–2 months ("early") versus greater than 12 months ("late") and noted the following: color difference in 97% of "early" vs. 84% of "late" patients, edema in 86% vs. 55%, temperature difference in 98% vs. 91%, limited movement in 90% vs. 83%, tremor in 54% vs. 50%, and hyperhidrosis in 57% vs. 40%, re-

spectively. A prospective study assessing autonomic dysfunction in 21 CRPS patients reported a warmer affected side at the first investigation (median 5 weeks) and a colder limb at follow-up (median 94 weeks).[12] This study did not find any alteration in sudomotor activity with time, noting an increase in sweating at both investigation times.[12] A study using laser Doppler flowmetry reported skin blood flow changes tended to correlate more with skin temperature than with duration of the condition and concluded that large interindividual differences "may reflect dissimilar rates with which pathophysiological processes take place."[13] Clearly, larger prospective studies need to be performed to better define the course of symptoms and signs in CRPS.

When those patients who endorsed a change in symptom severity were asked whether, in their opinion, the improvement or worsening was due to a treatment provided, the natural course of time, another injury, or stress, a majority of patients stated both treatments and time were the sources of symptom change. In most of these patients, treatment was felt to be responsible for a change in the severity of pain, swelling, weakness, sweating, skin coldness, disconnected feeling, skin discoloration, and skin warmth (in order of most to least common). Less than one-half felt that their tremors or skin dryness were altered by treatment. More than 50% also ascribed the following symptoms' change in severity to time alone: skin warmth, skin coldness, disconnected feelings, skin discoloration, weakness, skin dryness, and pain (in order of most to least common). Neither stress nor another injury was felt by a majority of patients to explain any symptom severity change.

The pain intensity, "average" and "worst pain" in the past week, reported by this group of CRPS patients was severe, 5.9/10 and 7.3/10, respectively. This group's "least pain" was in the moderate range, 3.9. The Neuropathic Pain Scale[3] descriptors with the highest mean values were "deep" (6.4), "unpleasant" (6.4), "sensitive" (5.7), "surface" (5.4), "dull" (5.3), and "hot" (5.0). Compared to a prior group of CRPS/RSD patients,[3] both groups of patients did not differ across most descriptors, except the current cohort described their pain as less unpleasant but more itchy. Compared to patients with postherpetic neuralgia and CMT neuropathy,[5] this group of CRPS patients had more cold pain. Interestingly, these CRPS patients described their pain as less unpleasant compared to all other neuropathic pain patients, including those with postherpetic neuralgia, painful diabetic neuropathy, peripheral nerve injury, and CMT neuropathy.

An important finding of this study was that CRPS symptoms significantly interfered with patient quality of life and daily functioning. Approximately 80% noted sleep disturbance due to CRPS, with 62% reporting at least three nights per week with sleep problems. Using a modified Brief Pain Inventory measure (Table 4), an overwhelming majority reported substantial disability due to CRPS. All but one of the 10 activity interference measures had a mean average score of at least 5 (on a 0–10 scale). Moreover, 75% of patients claimed substantial interference ($\geq$5/10 severity ranking) on 4 of the 10 items (general activity, mood, normal work, and recreational activities) and more than 50% endorsed substantial interference with the remaining five of six items (mobility, relations, sleep, enjoyment, and social activities).

The results of this study should be interpreted very cautiously and viewed as preliminary. They cannot be generalized to al CRPS patients. The small number of patients who were included in this study do not represent a cross-section of the overall CRPS population because these patients were referred (or self-referred) to a tertiary university pain center. Furthermore, a selection bias may be present, as the patients that responded to the survey may have been those who were more severely affected by CRPS. Another potential problem with this study is that some of the data collected relied on patient report of prior symptoms. Future studies should be performed in a prospective fashion assessing larger CRPS populations. Additionally, future studies should attempt to better define the correlation between symptom progression or regression due to specific therapies.

In conclusion, this pilot study of a small select cohort of CRPS patients has added further confirmatory data that motor symptoms are often an initial symptom in CRPS and continue to be present in many CRPS patients. In this selected CRPS group, all CRPS symptoms changed little in severity over time. The majority of the patients

in this study reported moderate to severe pain intensity associated with substantial disability. These data should be viewed as preliminary and most likely do not reflect the entire range of symptom course in CRPS. Further studies need to be performed in a prospective manner, using larger and more diverse groups of CRPS patients.

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