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# Complex Regional Pain Syndrome I (CRPS I): Prospective Study and Laboratory Evaluation

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**Abstract:**

**Objective:** To relate clinical features to autonomic laboratory indices used in the diagnosis of Complex Regional Pain Syndrome type I (CRPS I) (reflex sympathetic dystrophy) to generate improved diagnostic criteria.

**Description:** CRPS I is a chronic pain syndrome, characterized by diffuse limb pain with allodynia and prominent vasomotor and sudomotor dysfunction.

**Methods:** We conducted a prospective study on 102 patients referred for possible CRPS I. These patients completed a structured questionnaire and underwent neurologic examination, with special attention to the evaluation of clinical features of vasomotor, sudomotor, motor, and sensory, including pain, dysfunction. All patients were tested using a standard autonomic protocol that compared side-to-side skin temperature, resting sweat output, and quantitative sudomotor axon reflex test (QSART) measurements. Composite autonomic clinical (CRPS-Sx) and laboratory (CRPS-LAB) scores were defined. The clinical (subjective and objective) and the laboratory data were analyzed using Pearson's correlation analysis and Bonferroni's probability value to assess concordance and their value in correctly diagnosing CRPS I.

**Results:** All cases occurred after limb injury. One-third of cases did not fulfill our criteria of CRPS I. Highly significant correlations ($p < .001$) were found among certain clusters of symptoms and signs that shared unifying pathophysiologies. CRPS-Sx correlated with CRPS-LAB ($p = .035$). The indices that correlated most reliably with clinical data and with each other were RSO, QSART, and skin temperature reductions.

**Conclusion:** Clinical and autonomic laboratory probability scores correlate in an internally consistent manner. Both CRPS-Sx and CRPS-LAB are sensitive and reliable tools to formulate a correct diagnosis of CRPS I and can be combined to provide an improved set of diagnostic criteria for CRPS I.

**Key Words:** RSD—QSART—Vasomotor—Sympathetic—Autonomic.

Posttraumatic chronic limb pain is a major health problem, with disruption to the individual's domestic, occupational, and social activities of daily living and has an enormous economic impact on society.[1] The pathogenesis of the disorder is still controversial. Of particular interest is the potential pathophysiologic role of the sympathetic nervous system. The prominence of vasomotor and sudomotor symptoms and signs and the relief obtained after sympathetic block suggest a potential pathophysiologic role of sympathetic dysfunction.

There are numerous terms used to describe this condition, including reflex sympathetic dystrophy (RSD), minor causalgia, posttraumatic pain syndrome, sympathetically mediated pain, shoulder-hand syndrome, and Sudeck's atrophy. Recently, the term "Complex Regional Pain Syndrome type I" (CRPS I) has been recommended when no major nerve trunk injury is involved and CRPS II when nerve trunk injury is involved.[2] We use the term CRPS I in this article. Most clinical descriptions on CRPS I have been anecdotal or based on reviews. The lack of clearly defined

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diagnostic criteria makes such literature difficult to interpret. We therefore undertook a prospective evaluation of 102 consecutive patients referred to the Mayo Autonomic Reflex Laboratory with a suspected diagnosis of CRPS I, posing two questions. First, what are the demographic and clinical features of the condition? Second, how do the clinical features relate to laboratory indices? Clinical features are focused on the pain characteristics and the recognition of dysfunction and asymmetry of vasomotor and sudomotor effector function; laboratory indices are based on a quantitative analysis of the latter (autonomic dysfunction) alone.

The recognition of florid CRPS I is not problematic. The recognition of milder cases is considerably more difficult because of the changing clinical features of this syndrome as it evolves over time (vasodilatation at first, then vasoconstriction, and finally dystrophic changes), the dynamic alterations including diurnal fluctuations, and the subjectivity of some complaints, resulting in significant interobserver variability and observer bias. Laboratory indices may help in several ways. These can measure changes in autonomic function with greater sensitivity, specificity, and objectivity. If good correlation is found with the clinical score, a set of diagnostic criteria can be generated that would reduce observer bias and enhance diagnostic sensitivity and specificity. We had undertaken a large retrospective study (407 patients). The diagnosis of CRPS I was defined using a clinical probability scale. We identified the clinical and laboratory indices that were most important from the diagnostic and predictive (of response to sympathetic block) standpoint. Clusters of clinical tests are able to generate sensitivity and specificity of 90%. The best predictors of a response to sympathetic block were QSART response, allodynia, a unilateral warmer extremity, and to a lesser extent, absence of psychiatric factors. That retrospective study provides the hypothesis that drives the present prospective study. In this study, we evaluate prospectively if certain clinical characteristics and laboratory indices correlated well with the diagnosis of CRPS I. By combining the statistically most robust indices, we wished to generate new diagnostic criteria that would enhance our ability to diagnose CRPS I.

For the purposes of this study, we used a set of criteria for CRPS I that incorporates the IASP definition,[3] then builds upon it, by incorporating symptoms and signs that were found to best predict the diagnosis of CRPS I.[4] We end up with a clinical probability diagnostic scale, similar to what we had proposed earlier.[4] A summary of the data has appeared elsewhere.[5]

## METHODS

### Patient selection

Detailed description of the laboratory evaluation of CRPS I has been described elsewhere.[6] We studied 102 consecutive patients who presented with a posttraumatic chronic limb pain syndrome in which the diagnosis of CRPS I was entertained, and they were referred to us to for evaluation to either confirm or rule out this diagnosis. Exclusionary criteria were the presence of another obvious cause for the pain (e.g., documented nerve lesion, therefore fulfilling criteria for CRPS II, mechanical/structural factors, central lesions) previous sympathectomy or the presence of medications or other factors known to interfere with autonomic laboratory tests or their interpretation.

### Patient preparation

Patients were required to have been indoors for at least 30 minutes, after which they underwent 20 minutes of additional equilibration within the Autonomic Reflex Laboratory before the recordings. The laboratory was maintained at a temperature of 22°C. For upper extremity studies, men were asked to undress to the waist. Women were asked to undress to the waist, including removal of brassiere, and were provided with a sleeveless gown. For lower extremity studies, subjects were asked to undress to their underwear. Stockings were removed prior to testing.

*Structured questionnaire*

Each patient was asked to complete a questionnaire consisting of two parts: the first, filled out by the patient, contained questions on symptoms; the second, designed in a similar way, contained questions on signs and was completed by one of the examiners.

Part I consisted of 25 questions and focused on the initial offending event, time of symptoms onset and duration, the quality of the most bothersome pain (burning, shooting/stabbing, dull/aching/tearing), and the presence of abnormal perception of pain to usually nonpainful mechanical (both static and dynamic) and thermal stimuli (allodynia). Pain severity was analyzed using a verbal scale (absent, mild, moderate, severe) and a visual analog scale (VAS). Autonomic symptoms (vasomotor, sudomotor symptoms and trophic changes) were graded in a similar fashion. A set of questions was devoted to investigate the degree of impact of the pain syndrome on patients' quality of life. The questionnaire was formulated in a redundant fashion in an attempt to improve accuracy by internal consistency.

The second portion consisted of a set of questions, organized in clusters, in a parallel fashion to Part I: presence of allodynia to passive movement, pressure, light touch and cold, vasomotor, sudomotor, trophic status, motor testing, and assessment of movement disorders (alterations in tone, posture, or the presence of involuntary movements). The examiner graded each component at the time of the neurologic examination.

### Sudomotor recordings

*Measurement of resting sweat output (RSO)*

Large capsules (5.31 $cm^2$) were strapped on identical sites, and resting sweat activity was measured over the unstimulated limb. Recordings were done bilaterally and simultaneously at identical sites. For both the upper and lower extremities, four sites were studied. The hypothenar eminence and the medial forearm were used for study of the upper extremity, and recordings were made over the extensor digitorum brevis muscle and medial leg bilaterally for study of the lower extremity. RSO is recorded over 5 minutes in the four sites simultaneously. The RSO over the last of the 5 minutes was read by the computer. The choice of 5 minutes is a compromise between the attainment of steady state and practicality. By 3–4 minutes, near steady state conditions are achieved.[6]

*Quantitative sudomotor axon reflex test (QSART) recordings*

QSART recordings were done over the medial forearm for upper extremity studies. For lower extremity studies, recordings are made over the extensor digitorum brevis muscle and the medial distal leg. All recordings were bilateral and simultaneous. The stimulus used was iontophoresis of 10% acetylcholine applied through one compartment, and its response was recorded by a sudorometer connected to a different compartment, where sweat output is mediated by the axon reflex of postganglionic sympathetic fibers.[6,7]

### Measurement of skin vasomotor function

Skin temperature is an accurate surrogate index of skin blood flow. Side-to-side comparisons of the skin temperature were made for evidence of vasomotor asymmetry. Skin temperature over the digital pads was determined using infra-red thermometry (more accurate than telethermography for small areas) and other sites using telethermography. To avoid spurious differences due to inhomogeneity of skin temperatures, skin temperature was averaged over defined areas and compared for homologous sites. For the upper extremity, the ventral aspect of the forearm was divided horizontally into medial and lateral halves and vertically into upper, middle, and lower thirds resulting in six areas. The thenar, mid-palm, and hypothenar areas of the palm were also studied as were the pads of each of fingers.

For the lower extremity, the thigh and anterior leg were each divided into six areas, using the same approach we used for the forearm. The skin over the extensor digitorum brevis was studied as were the pads of each toe. The mean skin temperature of each area was compared with the homologous contralateral areas, and the values were entered into a chart of these areas.

### Controls and criteria for abnormality

RSO was recorded from the hypothenar eminence, distal forearm, distal leg, and foot in 24 normal subjects. There were no significant sex or age differences, and the data were therefore pooled. Median values with 5th to 95th in brackets were 0.54 (0.20–1.02), 0.09 (0.04–0.15), 0.11 (0.06–0.56), and 0.14 (0.03–0.56) for hypothenar, forearm, distal leg, and foot, respectively. Responses were considered asymmetric when a difference of 40% occurred.

Control values for QSART were derived from studies on 223 normal subjects aged 10 to 83 years.[6,8] Latency, volume, and morphologic differences of QSART responses were compared between sides. The presence of an ultrashort latency (<0.2 minute) was considered abnormal and likely comprises an augmented somatosympathetic response.[6] The stimulus (electric current) is slightly painful. It generates a somatic afferent volley followed by a sympathetic efferent response that is recordable as a skin potential but is not discernable as an increase in sweat volume. In some patients with CRPS I, there is a discernable sweat response, presumably from an augmented somatosympathetic response. A difference in sweat volume of $\geq$50% or a response showing persistent sweat activity were also considered abnormal, as was a value that fell outside of the control range, appropriate for age and gender. Control data for skin temperature were based on age- and sex-matched controls ($n$ = 25). In controls differences between sides did not exceed 0.8°C. A difference $\geq$1°C between homologous sites was considered abnormal if it occurred at several different sites, indicating a diffuse distribution of vasomotor changes. The changes seen were usually distal, but if asymmetry was seen only in the pads, a difference of 2° was required.

### Definition of CRPS I

We generated a clinical CRPS I probability scale and a laboratory CRPS I probability scale. The clinical scale incorporates the criteria of CRPS I recommended by IASP, but contains additional criteria based on our retrospective study.[4] The clinical scoring of CRPS I is shown in Table 1. This clinical CRPS I probability scoring scale (CRPS-Sx) was determined by a combination of symptoms and signs of allodynia (defined as pain perception to a normally nonpainful stimulus), vasomotor changes, and swelling. It can be subdivided into two major subdivisions: the allodynia (CRPS-Sx-allo) and vasomotor (CRPS-Sx-VM) subscales. CRPS-Sx has a maximal score was 7 (definite CRPS I). Levels of probability are:

| Score | Diagnosis |
|---|---|
| 7 | Definite CRPS I |
| 4–6 | Probable CRPS I |
| 2–3 | Possible CRPS I |
| 0–1 | Not CRPS I |

**TABLE 1.** *Clinically based CRPS I probability scoring system (CRPS-Sx)*

| Parameter CRPS I | Definite | Probable | Possible | No |
|---|---|---|---|---|
| CRPS-Sx-allo | | | | |
| 1a. Allodynia (touch) | | | | |
| 1b. Allodynia (pressure) | 3/3 | 2/3 | 1/3 | 0/3 |
| 1c. Allodynia (movement) | | | | |
| CRPS-Sx-VM | | | | |
| 2a. Vasomotor (history) | | | | |
| 2b. Vasomotor (exam) | 4/4 | ≥2/4 | ≥1/4 | 0–1/4 |
| 2c. Swelling (history) | | | | |
| 2d. Swelling (exam) | | | | |

| Score | Diagnosis |
|---|---|
| >6 | Definite CRPS I |
| 4–6 | Probable CRPS I |
| 2–3 | Possible CRPS I |
| 0–1 | Doubtful |

The laboratory scoring scale for CRPS I (CRPS-LAB) corrects for the effects of age and gender on the sudomotor responses and allows therefore to pool the data (Table 2). CRPS-LAB incorporates a composite score of QSART, RSO, and telethermography (vasomotor). The subsets can be separately evaluated. The higher the score, the greater the probability of CRPS I. CRPS-LAB has a maximal score of 9, and levels of probability are:

| Score | Diagnosis |
|---|---|
| >6 | Definite CRPS I |
| 4–6 | Probable CRPS I |
| 2–3 | Possible CRPS I |
| 0–1 | Doubtful |

### Statistics

Patients were analyzed using Systat for Windows (Systat Intelligence Software, Evanston, IL, U.S.A.). The clinical profile of these patients was obtained using descriptive statistics. To relate CRPS-Sx to CRPS-LAB, Pearson's correlation analysis, which computes the Pearson product-moment correlation coefficients were used. Systat computes the Bartlett chi-square test for significance of correlations. For individual correlations, we used the Bonferroni-adjusted probabilities, which generates a matrix of Bonferroni probabilities describing the significance of correlations among categories of symptoms and signs. The same method was used to evaluate the concordance of clinical with laboratory scores. Statistical significance was accepted at the $p < .05$ level.

## RESULTS

### Demography, type of injury, and effect of chronic pain

A total of 102 patients referred to the Autonomic Reflex Laboratory with limb pain, where CRPS I was considered, were prospectively evaluated. Each patient completed a structured questionnaire and was examined by one of three examiners, who had earlier been validated for interexaminer agreement in pain and neurologic evaluation. Demographic features are shown in Table 3. There was an over-representation of women, who comprised approximately three-fourths of the patients seen. All patients had had an antecedent injury. The most common specific injury was a sprain or strain type injury. The causes listed under "other injuries" were numerous, including soft-tissue injury, joint trauma, surgical operation, and repetitive trauma.

**TABLE 2.** *Laboratory-based CRPS I grading scale (CRPS-LAB)*

| Score | Description |
|---|---|
| Sudomotor Index | |
| 1 | Any of the following changes:<br>Unilateral reduction or increase in sweat volume by 25–50% on the affected side<br>Ultrashort latency, ipsilateral, contralateral or both<br>Persistent sweat activity, ipsilateral, contralateral, or both |
| 2 | Single QSART site with an increase or decrement by ≥50% on the affected side |
| 3 | Two or more QSART sites with an increase or decrement by ≥50% on the affected side or bilateral increase or reduction by ≥50% |
| Vasomotor Index | |
| 1 | Skin temperature asymmetry (increase or reduction) on affected side by ≥0.5°C diffusely or by 1° over pads |
| 2 | Skin temperature asymmetry (increase or reduction) on affected side by<br>a 1.0°C in a limited distribution (<3 sites)<br>b Skin temperature asymmetry ≥1.0°C, diffuse but atypical distribution |
| 3 | Skin temperature asymmetry (increase or reduction), ≥1.0°C diffuse, maximal distally |
| Resting Sweat Index | |
| 1 | Unilateral reduction or increase, 25–50% |
| 2 | Unilateral reduction or increase, ?50% involving a single site |
| 3 | Two sites with an increase or reduction of ?50% |

**TABLE 3.** *Demography, injury type, and effect of chronic pain*

| | |
|---|---|
| *N* | 102 |
| Age | 45 ± 16 |
| Sex distribution | 76 F, 26 M |
| Distribution of pain | |
| Upper extremity | 41 |
| Lower extremity | 61 |
| Type of antecedent injury (%) | |
| Sprain-strain | 35 |
| Fracture | 8 |
| Immobilization | 1 |
| Other injuries | 56 |
| Activities of daily living (%) | |
| No interference | 2 |
| Mild interference | 8 |
| Moderate interference | 35 |
| Severe interference | 55 |

**TABLE 4.** *Characteristics of pain*

| | Severity of pain | | | | |
|---|---|---|---|---|---|
| Type of pain | Total (%) | Severe (%) | Moderate(%) | Mild (%) | Absent (%) |
| Dull | 53 | 17 | 23 | 5 | 7 |
| Burning | 25 | 5 | 6 | 4 | 10 |
| Shooting/stabbing | 22 | 9 | 7 | 2 | 4 |
| Duration of pain (months) | | Severity of pain (VAS) | | | |
| <6 | 26 | <4 | 9 | | |
| 6-12 | 19 | 4—7 | 27 | | |
| >12 | 55 | >7 | 64 | | |

## Pain

Characteristics of pain are shown in Table 4. The number of patients who had had the condition for less than 1 year (45%) was slightly less than those who had had the condition for more than 1 year (55%), and most of these latter patients (45% of total) had had the pain for 1–5 years. These patients were either severely impaired (55%) or were at least moderately impaired (35%) in their ability to perform activities of daily living such as work in their occupations or at home. Patients typically had several types of pain, but when asked for the most dominant or common pain, about one-half (53%) reported a dull pain, one-fourth had burning, and 22% had sharp pain as the predominant pain (see Table 4). The severity of the pain (verbal) was either moderate or severe in the majority of patients. By visual analog scale of pain severity, the majority had severe (64%) pain, defined as a score >7 on a 10-point scale (see Table 4).

## Clinical autonomic changes

By history, swelling was noted in 75% of patients (Table 5), although this was found at the time of evaluation in slightly less than half of the patients (44%), and was most commonly mild objectively.

**TABLE 5.** *Comparison of clinical autonomic indices by history and by examination*

| History | %Abnormal | Examination | %Abnormal |
|---|---|---|---|
| Swelling | | | |
| Absent | 25 | Absent | 56 |
| Mild | 25 | Mild | 32 |
| Moderate | 32 | Moderate | 10 |
| Severe | 17 | Severe | 2 |
| Color changes | | | |
| Absent | 30 | Absent | 69 |
| Present | 70 | Present | 31 |
| Sweating | | | |
| Normal | 67 | Normal | 84 |
| Decreased | 13 | Decreased | 10 |
| Increased | 20 | Increased | 6 |

An alteration in sweating was less common; 67% reported no change, and 84% were considered normal on clinical examination. Vasomotor alterations, most commonly described as a red or bluish discoloration, either at rest or more commonly, with the limb dependent, were reported in approximately one-half (49%) of patients. Unilateral coldness was reported in 21% of patients. On examination, these alterations were seen in only 31% of patients. Trophic changes were present in 20% and consisted of thinning of hair and either increase or reduction of skin and nail thickness. Contractures were seen in 13% of patients.

## Neurologic function

Strength was intact in 60% of patients and reduced to varying degrees in the remainder, typically related to the pain or allodynia (Table 6). Tremor and dystonia were uncommon, seen in only 4% of patients.

## Autonomic function tests

QSART was normal in 38% of patients and abnormal in 62%, 38% showing a reduction and 24% an increase. RSO was abnormal in 29% of subjects and normal in 71%, most of the abnormalities being a reduction (Table 7). Skin temperature distribution was abnormal in 58%, a reduction being twice as common as an increase on the affected side.

## Correlation of clinical with laboratory indices

To evaluate the reliability of the questionnaire, we undertook correlation analysis of symptoms with the relevant neurologic examinations, using Pearson's correlation analysis with Bonferroni-adjusted probabilities. We undertook analysis of clusters of symptoms and signs. Reliability should result in internal consistency, with significant correlations within clusters of autonomic symptoms sharing the same underlying autonomic mechanism:

1. Vasomotor cluster: skin color; skin temperature; swelling by history; swelling by examination; sweating by history ; sweating by examination.

**TABLE 6.** *Clinical autonomic findings on examination*

| Allodynia to | Touch (%) | Cold (%) | Pressure (%) | Movement (%) |
|---|---|---|---|---|
| Absent | 64 | 70 | 34 | 46 |
| Mild | 16 | 15 | 26 | 33 |
| Moderate | 15 | 8 | 33 | 12 |
| Severe | 5 | 7 | 8 | 9 |
| Strength | | | | |
| Normal | 60 | | | |
| Mild reduction | 13 | | | |
| Moderate reduction | 16 | | | |
| Severe reduction | 10 | | | |
| Tremor | | | | |
| Absent | 96 | | | |
| Mild | 1 | | | |
| Moderate | 3 | | | |
| Contractures | | | | |
| Absent | 80 | | | |
| Present | 20 | | | |
| Impaired joint movements | | | | |
| Absent | 77 | | | |
| Present | 23 | | | |
| Dystonia | | | | |
| Absent | 96 | | | |
| Present | 4 | | | |
| Trophic changes | | | | |
| Absent | 87 | | | |
| Present | 13 | | | |

2. Pain cluster: Shooting pain; dull pain; burning pain; type of injury.
3. Motor function: motor strength; joint movement; contractures; activities of daily living.
4. Allodynia to: light touch; pressure; movement; cold.

For each category (1–4), correlation was excellent with $p < .001$.

Within CRPS-LAB scores, good concordance was also generally found. RSO reduction correlated significantly with QSART reduction ($p < .001$), and significantly but somewhat less with temperature reduction ($p = .032$). Similarly QSART reduction correlated significantly with temperature reduction ($p = .02$).

We next correlated clinical (CRPS-Sx) with laboratory scores (CRPS-LAB). In a subanalysis using Bonferroni-adjusted probabilities, certain correlations were found. CRPS-Sx correlated significantly with CRPS-LAB ($p = .035$). It correlated even better with the combination of RSO + QSART ($p = .009$). It also correlated with QSART reduction ($p = .025$) and RSO ($p = .049$).

**TABLE 7.** *Summary of autonomic function tests*

| Test | QSART | RSO | Vasomotor |
|---|---|---|---|
| % Normal | 38 | 71 | 42 |
| % Abnormal | 62 | 29 | 58 |
| % Reduced | 38 | 22 | 39 |
| % Increased | 24 | 7 | 19 |

**TABLE 8.** *Comparison of CRPS I probability scoring scales using clinical (CRPS IPSS) and laboratory (CRPS-LAB) indices*

| CRPS-Sx | % | CRPS-LAB | % |
|---|---|---|---|
| <2 | 31 | <2 | 29 |
| 2–3 | 45 | 2–3 | 29 |
| 4 | 8 | 4 | 20 |
| >4 | 15 | >4 | 22 |

Within the CRPS-Sx category, the allodynia component (CRPS-Sx-allo; see Table 1) correlated with the vasomotor component (CRPS-Sx-VM; $p < .001$). The best correlation was with the triad of reductions in QSART, RSO, and temperature ($p < .001$). There was no significant correlation with increments of these indices. CRPS-Sx-allo also correlated with QSART reduction ($p = .04$), RSO reduction ($p = .01$), and temperature reduction ($p = .007$).

CRPS-Sx-VM also correlated significantly ($p < .001$) with the triad of reductions in QSART, RSO, and temperature, but not with their increments. A comparison of probability scores for the two scales are shown in Table 8.

## DISCUSSION

To achieve our specific aim of generating a CRPS I probability scale and to evaluate its reliability, it was necessary to study the broad spectrum of post-traumatic chronic limb pain syndromes, ranging from patients with clinically definite CRPS I to patients who obviously did not have it. This entry criterion (of including all patients referred with post-traumatic limb pain with the referring diagnosis of suspected CRPS I) should not be confused with the diagnostic criteria for CRPS I. We selected the entry criterion that was representative of a large population of patients seen in pain practice.

In this prospective study of post-traumatic limb pain, two of three patients referred with chronic limb pain fulfilled clinical and laboratory criteria for possible CRPS I, and 44% fulfilled the stricter criteria for probable CRPS I. The pain had significant impact on the patients; the severity of chronic limb pain was perceived to be at least moderately severe in more than 50% of patients, and 90% of patients had at least moderate interference with their activities of daily living.

In spite of extensive publications on CRPS I, the clinical descriptions have been largely derived from retrospective reviews. This prospective study confirms the key conclusions of our large retrospective study of 407 patients referred for possible CRPS I,[4] and a characteristic clinical pattern emerges, based on the clinical probability scoring

scale for CRPS I. These patients have chronic limb pain that is of at least moderate severity, with allodynia to pressure, movement, touch, or cold. The main pain is most commonly dull and deep, occurring in about half the patients, whereas the other half has a pain that is evenly distributed between a superficial burning pain or sharp stabbing pain. A history of vasomotor changes and swelling is common, occurring in at least two-thirds of patients, whereas sudomotor symptoms are relatively uncommon. The changes are usually absent in the majority at the time of the examination (but can still be found on autonomic function tests).

Our findings lend support to the criteria suggested by other workers. Several attempts have been made to define the criteria for the clinical diagnosis of CRPS I. There is good general agreement that CRPS I is characterized by diffuse pain, typically distal, developing following injury, with superficial and deep allodynia, and commonly associated with vasomotor, sudomotor, swelling, and trophic changes.[9–11] There is good agreement that chronic diffuse limb pain is mandatory, associated with allodynia and autonomic dysfunction. The latter is manifested as unilateral vasomotor, sudomotor alterations and the related manifestation of swelling.

Controversy exists on the prevalence of motor deficits, tremor, and dystonia. In this prospective study, the frequency of motor involvement is common, with an impairment of strength seen in 40% of patients, but the frequency of dystonia is lower than recently reported.[12] The differences likely relate in part to diagnostic criteria (what might be diagnosed as dystonia by some investigators might be recognized as bracing of muscles by others) and referral bias.

There are several findings that suggest sympathetic involvement in CRPS I pain. First, allodynia, a key criterion of CRPS I and predictor of response to sympathetic block,[4] is significantly correlated with the CRPS-Sx cluster, with vasoconstriction (lower skin temperature), and with indices of sudomotor dysfunction (RSO and QSART). The two limbs of the clinical scale (CRPS-Sx-allo and CRPS-Sx-VM) are highly correlated. The severity of pain is also significantly correlated with indices of sympathetic dysfunction. Our earlier retrospective study demonstrated that bilaterally absent QSART (presumably indicating denervation) is highly predictive of a poor response to sympathetic block. Of interest is the apparent paradox of the correlation of CRPS-Sx with a reduction in RSO and QSART but not with an increment. Indeed the best correlation of both CRPS-Sx-allo and CRPS-Sx-VM was with the gestalt of reductions in RSO, QSART, and skin temperature. This finding is identical to an earlier retrospective study in which the gestalt of: (a) Swelling on examination, (b) The clinical diagnosis CRPS I, (c) Severe pain, and (d) Vasomotor alterations on examination, correlated best with a reduction in QSART.[4] A similar dissociation between sudomotor and vasomotor regulation has recently been reported.[13] The mechanism of these changes is uncertain. Possibly, it relates to the dynamic nature of the alterations and different stages in the evolution of the syndrome (i.e., increments in RSO-QSART occur early in acute-subacute phase). Sudomotor activity is dependent on skin temperature,[14] and these reductions may be due in part to the lower temperature. The reduction in temperature is however relatively small; a more likely possibility is that both the changes in temperature (and blood flow) and in the QSART reflect some common microenvironmental changes as part of the disease process.

There are several features in the present study that lend support to the use of clinical and laboratory CRPS I probability scoring systems. First, there is the close correlation of indices within clusters assumed to have the same underlying pathophysiologic mechanisms. These include the pain, vasomotor, and allodynia clusters. Second, there is good correlation among clinical symptoms, signs, and laboratory measurements that are manifestations of the same autonomic physiologic perturbation, such as sympathetic vasomotor or sudomotor overactivity. Third, there is good correlation among the two major limbs of the CRPS-Sx scoring scale (the allodynia and vasomotor components). Finally, there is good correlation between the clinical (CRPS-Sx) and laboratory (CRPS-LAB) scales. Considering these findings, we propose a modified scoring system, which combines CRPS-Sx and CRPS-LAB. The following recommendations are suggested.

**Recommendations**

Regardless of etiopathogenetic considerations, the best current clinical approach to the diagnosis of CRPS I is to use a combined clinical and laboratory approach, with particular emphasis on:

1. Severity of pain (at least moderate severity and out of proportion with the presenting clinical signs)
2. Distribution of pain (diffuse and maximal distally)
3. Allodynia.

These components of the CRPS-Sx should be combined with CRPS-LAB, which focuses on QSART asymmetry, RSO, and possibly skin vasomotor alterations. This approach results in the following modification of our current scale:

I Definite CRPS I = allodynia to touch, pressure and movement + asymmetry of QSART (grade 3) or RSO (grade 3 asymmetry)

II Probable CRPS I = CRPS-Sx (probable) + any of the following on CRPS-LAB: (a) QSART3 or RSO3 and (b) QSART2 + RSO2 or VM2

III Possible CRPS I: Chronic limb pain + QSART1 or RSO1 or VM1

This combined scale combines the strengths of the clinician and the laboratory. CRPS-LAB is more accurate, sensitive, and specific in detecting side-to-side and absolute changes in autonomic indices, thereby enhancing the clinical evaluation of vasomotor and sudomotor alterations. CRPS-Sx, on the other hand, provides the unique historical aspects of the patient's symptoms and provides essential information on allodynia. The two approaches should not be viewed as competitive but complementary. Finally, regardless of whether sympathetic dysfunction is etiologically related[15] to CRPS I or not,[16,17] sympathetic dysfunction is an integral component in making the clinical diagnosis, and the combined approach sharpens the clinical diagnosis of CRPS I.

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