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Intense Pain Soon After Wrist Fracture Strongly Predicts Who Will Develop Complex Regional Pain Syndrome: Prospective Cohort Study

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Abstract: Complex regional pain syndrome (CRPS) is a distressing and difficult-to-treat complication of wrist fracture. Estimates of the incidence of CRPS after wrist fracture vary greatly. It is not currently possible to identify who will go on to develop CRPS after wrist fracture. In this prospective cohort study, a nearly consecutive sample of 1,549 patients presenting with wrist fracture to 1 of 3 hospital-based fracture clinics and managed nonsurgically was assessed within 1 week of fracture and followed up 4 months later. Established criteria were used to diagnose CRPS. The incidence of CRPS in the 4 months after wrist fracture was 3.8% (95% confidence interval = 2.9–4.8%). A prediction model based on 4 clinical assessments (pain, reaction time, dysynchiria, and swelling) discriminated well between patients who would and would not subsequently develop CRPS (c index .99). A simple assessment of pain intensity (0–10 numerical rating scale) provided nearly the same level of discrimination (c index .98). One in 26 patients develops CRPS within 4 months of nonsurgically managed wrist fracture. A pain score of ≥5 in the first week after fracture should be considered a "red flag" for CRPS.

Perspective: This study shows that excessive baseline pain in the week after wrist fracture greatly elevates the risk of developing CRPS. Clinicians can consider a rating of greater than 5/10 to the question "What is your average pain over the last 2 days?" to be a "red flag" for CRPS.

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Key words: Complex regional pain syndrome, reflex sympathetic dystrophy, chronic pain, dysynchiria.

Complex regional pain syndrome (CRPS) is a distressing complication of some minor injuries. It is characterized by disproportionate pain and disability, with disturbed autonomic and motor function, usually confined to 1 arm or leg (see[20] for review of clinical features and pathophysiology of CRPS). The incidence of CRPS in Western countries is about 26 per 100,000 person-years (95% confidence interval [CI] = 23–30). That is, about 80,000 Americans are diagnosed with CRPS every year.[8] Total annual lost income due to CRPS exceeds US$1 billion.[18] Despite many treatments for CRPS, including physical and occupational therapy, sympathetic nerve block, spinal cord stimulation, systemic analgesics, and cognitive-behavioral pain management, more than half of all CRPS patients report continuing or worsening symptoms 5 years after diagnosis.[10]

The most common trigger in prevalent cases of CRPS is wrist fracture.[8] The incidence of CRPS after wrist fracture is uncertain because available estimates vary widely (eg,

estimated incidence proportions in the first 3–4 months include <1%,[17] 37%,[2] and 58%[11]). The mechanisms by which wrist fractures trigger CRPS are not known. The best available data, from a large cross-sectional study,[8] exclude cast tightness, preinjury psychological profile or mood, stressful life events, injury severity, location of fracture, mode and biomechanical characteristics of injury, time to surgery and surgical approaches, compensation, and previous illness history.[8] The same study concluded that the presence of several previous or current morbidities, including osteoporosis, migraine, and asthma, and the current use of angiotensin-converting enzyme inhibitors are risk factors for CRPS.

We conducted a multicenter prospective cohort study of patients with wrist fracture. The study was designed to quantify the incidence of CRPS, diagnosed using established criteria, in the 4 months after wrist fracture. A second aim was to develop a prediction rule that uses data from clinical assessments conducted in the first week after wrist fracture to identify people who develop CRPS within 4 months of wrist fracture. We sought to predict who would develop CRPS, not to identify causes of CRPS.[14]

Methods

Study Design and Participants

The cohort was recruited between January 2006 and December 2008. It consisted of a near-consecutive sample of patients who presented with acute wrist fracture to 1 of 3 hospital fracture clinics. Participants were assessed within 1 week of fracture (baseline) and were followed up 4 months later.

Patients were eligible to participate if they had radiologic evidence of fracture to the carpal bones, the distal radius or ulna, or both; were aged between 18 and 75 years; and did not require external fixation other than a cast. Those who presented with additional orthopedic or neurologic injuries or who had an established diagnosis of CRPS were excluded. Written informed consent was obtained from all participants, procedures conformed to the Declaration of Helsinki, and the protocol was approved by the NHS Research Ethics Committee.

Detailed clinical assessment procedures, undertaken in the first week after fracture, are presented in the Appendix and included assessment of the signs and symptoms of CRPS. The following variables were assessed: pain (average pain over the last 2 days and pain on touching together the thumb and index finger, both assessed using a 0–10 numerical rating scale, anchored at left with "no pain at all" and at right with "worst possible pain"); swelling (the circumference of the thumb and the first 3 fingers on the fractured side, expressed as a proportion of that measured on the opposite side); performance on a left/right hand judgment task (response time for correct judgments of images of the affected hand expressed as a proportion of that for correct judgments of images of the unaffected hand[22]); the presence or absence of dysynchiria, a sensory response on the fractured side to stimulation of the opposite side while watching in the mirror the reflected image of the opposite limb being touched[1]; and catastrophizing (using the Pain Catastrophizing Scale[24]).

Outcome Measures

Four months after fracture, participants were telephoned and asked whether they had symptoms of CRPS, as stipulated in the International Association for the Study of Pain (IASP) diagnostic criteria for research that were widely accepted at the time of study design and data collection.[6] Those participants who reported pain, and any other symptoms consistent with CRPS, also underwent a physical examination by a pain specialist to confirm the diagnosis of CRPS using the same criteria. That is, we used the diagnostic criteria for research. The specialist was unaware of the results of the baseline assessments.

Statistical Analysis

The incidence proportion of CRPS 4 months after wrist fracture was estimated in 2 ways. A naïve estimate was obtained by expressing the number of observed cases as a proportion of the number followed up. As it was expected that there would be some loss to follow-up, the primary estimate was obtained by imputing missing CRPS data using a multiple imputation procedure (20 imputations, using the "ice" routine in Stata v10.1 [StataCorp, College Station, TX]) based on age, gender, reaction time, dysynchiria, swelling, pain, and catastrophizing measured at baseline. Where data are missing at random (ie, missing randomly, conditional on covariates), estimates based on multiple imputation are unbiased.[19] The missing-at-random assumption was considered to be plausible.

A predictive model was developed using the following procedures. Before conducting the analysis, we nominated 7 potential predictors based on evidence from cross-sectional studies of an association with CRPS or chronic pain.[1,9,22,25] They were age, gender, response time, dysynchiria, swelling, pain, and catastrophizing. All of the predictors except gender and dysynchiria were treated as continuous variables. Only those variables with significant univariate associations with CRPS (logistic regression, likelihood ratio test, $P < .05$) were considered further. We used the criterion of $P < .05$ (not a higher value, as used by some researchers) because our aim was to develop a clinically useful and therefore parsimonious prediction model. The remaining candidate variables were subject to a bootstrap variable selection procedure.[4] The purpose of this procedure is to generate prediction models that are likely to be applicable to other samples drawn from the same population, rather than just to the sample used in the study. This involved drawing 10,000 bootstrap samples from the original sample and subjecting each bootstrap sample to backwards stepwise regression (P value to remove = .2) in a logistic model. Those variables selected in at least 80% of bootstrap samples were retained in the final model. Regression coefficients were zero-corrected to reduce the bias associated with variable selection procedures.[3] Goodness of fit was evaluated by inspecting calibration

plots[15] and with the Hosmer-Lemeshow test.[16] Discrimination was evaluated by inspecting histograms of prediction scores and was quantified with the *c* index (ie, the area under the receiver operating characteristic curve) and diagnostic (predictive) likelihood ratios. All analyses were conducted using Stata 10.1.

Results

Characteristics of the Participants

A total of 1,661 eligible patients presented to the study clinics during the study period, although because of an administrative error 21 eligible patients were not identified until after the study was completed. Of these, 1,549 (93.3% of eligible patients and 94.5% of identified eligible patients) consented to participate. Baseline data were obtained on average 3.8 days after fracture (SD = 1.9, range = 1–9). Outcome data were obtained from 1,506 participants (90.7% of eligible patients, 91.8% of identified eligible patients, and 97.2% of participants); that is, 97.2% of participants were contacted at follow-up. Missing follow-up cases were due to inability to reach the patient again. The intention was to evaluate the presence of CRPS 4 months (122 days) after fracture. In practice, follow-up occurred a mean of 112 days after fracture (SD = 8, range = 92–131). Characteristics of the participants are given in Table 1.

Incidence of CRPS

Sixty-seven participants satisfied the symptomatic criteria at telephone interview and were asked to attend a physical assessment. All 67 attended and 55 of them were diagnosed as having developed CRPS. The naïve estimate of the risk (incidence proportion) of CRPS 4 months after wrist fracture was 3.7%. Similar estimates were obtained from all 3 centers (3.7%, n = 507; 4·1%, n = 123; and 3.5%, n = 876). The primary estimate, based on multiple imputation, was 3.8% (95% CI = 2.9–4.8%).

Prediction of CRPS

Five of the 7 potential predictor variables (all except age and gender) had statistically significant univariate relationships with risk of CRPS and were subsequently

Table 2. Univariate Relationships Between Putative Predictors and Risk of Developing CRPS

	Odds Ratio*	95% CI	P
Age (years)	1.006	.988–1.024	.528
Gender (0 = female, 1 = male)	.580	.332–1.015	.056
Catastrophizing (0–52 scale)	1.097	1.031–1.167	.003
Pain (0–10 scale)	3.481	2.757–4.395	<.001
Reaction time (affected/unaffected, %)	1.066	1.048–1.084	<.001
Dysynchiria (0 = absent, 1 = present)	35.75	18.07–70.75	<.001
Swelling (affected/unaffected, %)	1.043	1.018–1.068	.001

*All variables except gender and dysynchiria were treated as continuous variables. The odds ratio is the increase in odds per unit increase in the predictor.

considered for inclusion in a logistic model (Table 2). Lowess-smoothed curves relating each predictor to the log odds of developing CRPS (not shown) were near-linear over most of their ranges. The bootstrap variable selection procedure selected 4 variables (pain, reaction time, dysynchiria, and swelling), all in more than 92% of bootstrap samples. The catastrophizing variable was selected in only 40% of bootstrap samples, so it was dropped from the model. The zero-corrected regression coefficients for the 4-variable model are given in Table 3.

The prediction model had excellent discrimination (Fig 1A). The *c* index was .99, indicating that for 99% of randomly chosen pairs of participants in which one participant developed CRPS and the other did not, the participant with the higher risk score was the one who developed CRPS.[15] The Hosmer-Lemeshow test was not statistically significant (*P* = .98), so there was no evidence of a failure of model fit.

Nearly comparable predictive performance was achieved by considering just the pain variable. The pain variable alone had excellent discrimination (*c* index = .98; Fig 2A). No patient with a pain score of 3 or lower went on to develop CRPS, but 46% of the 113 patients with scores of 5 or higher went on to develop CRPS (Fig 2B). To enable risk stratification, pain scores were categorized (arbitrarily) as 0, 1–2, 3–4, 5–6, or 7–8. (No patients reported pain scores of 9 or 10.) The likelihood ratio for patients with pain scores

Table 1. Participant Characteristics at Baseline (N = 1,549)

Age (mean, SD)	43.3 (14.8)
Male gender (n, %)	766 (49.5%)
Right side dominance (n, %)	1,332 (86.0%)
Right sided fracture (n, %)	510 (32.9%)
Left/right judgment performance (mean ratio fractured/unfractured sides, SD)	.97 (.15)
Dysynchiria (n, %)	201 (13.0%)
Swelling ratio (mean ratio fractured/unfractured sides, SD)	1.03 (.08)
Pain on opposition (mean [/10], SD)	1.6 (1.3)
Average pain over previous 2 days (mean [/10], SD)	1.4 (1.1)
Catastrophizing (mean [/52], SD)	7.5 (4.5)

Table 3. Multivariate Logistic Prediction Model of Risk of Developing CRPS

	Coefficient	Odds Ratio*	95% CI
Pain (0–10 scale)	1.194	3.299	2.506–4.342
Reaction time (affected/ unaffected, %)	.038	1.039	1.011–1.068
Dysynchiria (0 = absent, 1 = present)	2.803	16.50	6.12–44.49
Swelling (affected/unaffected, %)	−.078	.925	.883–.969
Constant	−4.621		

*All variables except dysynchiria were treated as continuous variables. The odds ratio is the increase in odds per unit increase in the predictor. Regression coefficients have been zero corrected.
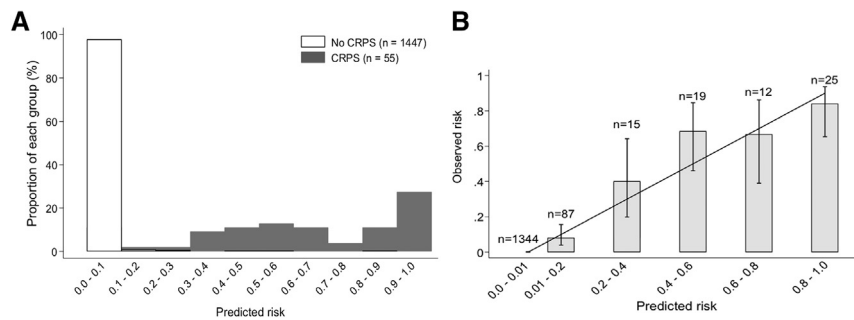
Figure 1. Discrimination and calibration of a multivariate predictive model based on a 4-predictor model incorporating pain, reaction time, dysynchiria, and swelling. **(A)** Histogram showing proportions (%) of each group at each stratum of predicted risk. The small amount of overlap of the 2 groups' distributions is indicative of a high level of discrimination. **(B)** Comparison of observed and predicted risks. Bars are SDs and the line is the line of identity. There is broad agreement between observed and predicted risks.

of 3 to 4 was .89 (95% CI = .29 to 2.72), for those with pain scores of 5 to 6 it was 15.1 (95% CI = 10.6–21.4), and for those with pain scores of 7 to 8 was 78.9 (95% CI = 35–178). These likelihood ratios indicate that patients with pain scores of 5 or higher have greatly elevated odds (risk) of developing CRPS.

Discussion

This study prospectively monitored a cohort of nearly consecutive cases presenting to hospital fracture clinics with nonsurgically managed wrist fracture. There was a high rate of follow-up, and widely accepted diagnostic criteria were used to diagnose CRPS.[6] The data were used to obtain an estimate of the incidence of CRPS after wrist fracture and to develop a clinical prediction rule based on an easy-to-collect self-report measure.

The data show that approximately 4% of people with recent wrist fracture managed nonsurgically develop CRPS within 4 months. This incidence is broadly similar to the incidences estimated in early investigations of algodystrophy after wrist fracture (eg, about 1%,[17] or 3–4%[13]) but much lower than reports from investigations of reflex sympathetic dystrophy (eg, 37%[2]), even though algodystrophy and reflex sympathetic dystrophy are simply different names for the same condition.[29] Estimates of incidence obtained from previous studies may have been biased because some involved retrospective analysis of poorly defined cohorts (eg, [5]) and others

suffered from undefined sampling methods[11] or high rates of loss to follow-up.[12]

Another reason that previous estimates of the incidence of CRPS are difficult to interpret is ambiguity of diagnostic criteria. In early studies, painful disorders that presented with vasomotor or sudomotor changes were assigned various diagnoses using nonstandardized and incompatible diagnostic schemes. This provided the impetus for the IASP to define CRPS as a discrete diagnostic entity,[21] and later to refine those criteria for research applications.[6] Establishment of recognized diagnostic criteria for CRPS has made definitive investigation of CRPS possible. Surprisingly, there have been very few attempts to estimate the incidence of CRPS using these criteria, and those few attempts have yielded very different estimates. Dijkstra and colleagues followed up 72 of 89 consecutive patients (follow-up of 81%) 7 weeks after wrist fracture and reported only 1 case of CRPS (naïve estimate of incidence proportion of 1.4%, 95% CI = .3–7.5%).[12] In contrast, Thomson McBride and colleagues followed up 262 patients about 10 weeks after wrist fracture and reported a 20% incidence,[26] and Demir and colleagues followed up 70 patients about 3 months after a hand or arm fracture and reported 58% incidence.[11] The latter 2 studies did not sample consecutive cases, so it is possible that the very high estimates of incidence obtained in these studies is due to a sampling bias. In the present study, we used the research criteria for diagnosis of CRPS, which is associated with a higher specificity and lower sensitivity
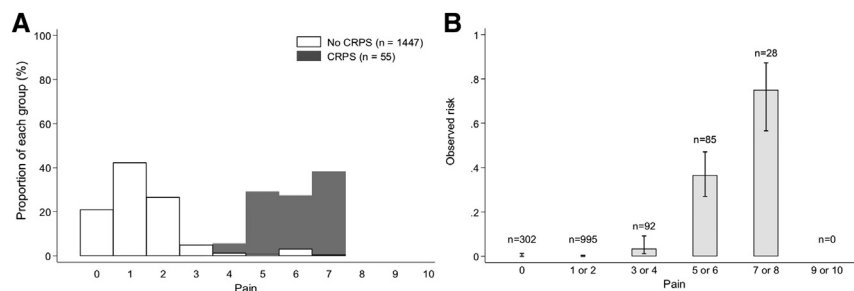

Figure 2. Discrimination and calibration of predictive model based only on pain. **(A)** Histogram showing proportions (%) of each group at each level of pain. The separation of the 2 groups' distributions is indicative of a high level of discrimination. **(B)** Observed risk for different levels of pain intensity. Bars are SDs. The observed risk increased greatly with pain intensity.

than the clinical criteria,[6] so there is a chance that our result slightly underestimates the true incident rate. That we screened for symptoms of CRPS over the telephone may also have resulted in an underestimate—perhaps patients under-report their symptoms on the telephone. However, the opposite is equally possible—perhaps people over-report their symptoms in a face-to-face interview, which would result in false-positive cases. Indeed, an interview by a clinician who is clearly not blinded to signs could introduce significant bias. On these grounds we chose to screen for symptoms over the telephone because of the substantial cost saving of doing so. There are 2 more reasons, based on a prospective investigation of wrist fracture patients that is currently under way (G.L. Moseley et al, unpublished data), that make us confident that our approach did not lead to missed positive cases. First, we replicated the telephone assessment but narrowed our criteria for progressing to physical assessment to answering *yes* to the question of "Do you have ongoing pain?" (G.L. Moseley et al, unpublished data). Our incidence data using this approach are similar to those observed in the present study. Second, we have compared responses to the symptomatic criteria questions between telephone interview and in-person assessment and find very little discrepancy between them. More importantly, there is no systematic effect toward overreporting in one format as compared to the other.

The second aim of the current work was to develop a prediction rule for identifying people who would go on to develop CRPS after wrist fracture. Our goal was to predict CRPS, not to understand causes of CRPS, so we did not attempt to identify or control for confounders. Thus, we caution readers not to infer causal relationships between the 4 predictors (pain, reaction time, dysynchiria, and swelling) and the development of CRPS. The aim was to develop a clinically useful tool, so we sought parsimony. Consequently, we did not attempt to model nonlinear relationships or interactions between predictors.

A simple clinical prediction rule based on 4 clinical findings was able to predict with a high degree of accuracy who would, and who would not, develop CRPS within 4 months of fracture. It is notable that our model did not include age or gender, both of which might be thought to contribute to risk, on the basis of epidemiologic data.[8] However, our model is confined to those who fracture their wrist, not all those who develop CRPS. To our knowledge, this is the first strong evidence that it may be possible to predict accurately which individuals will develop CRPS. The prediction rule was based on measurements, taken in the first week after fracture,

of pain, response time, dysynchiria, and swelling. Assessment of all of these predictors would take about 25 minutes. Therefore, although the prediction rule may be useful for research purposes, it is unlikely to be routinely applied to all patients with wrist fracture in busy fracture clinics.

An important finding was that it was possible to obtain predictions that were nearly as accurate as those obtained using the 4-predictor model using just 1 predictor: average pain severity over the last 2 days, assessed in the first week after wrist fracture. This suggests that it may be possible, in clinical practice, to identify most people who will subsequently develop CRPS simply by asking, in the first week after fracture, about the severity of pain experienced over the preceding 2 days. This simple assessment can be carried out in seconds and can be conducted by telephone if needed. In this population, people with pain intensity ≤4 are unlikely to develop CRPS, but people with pain scores ≥5 are at high risk of developing CRPS. A pain score ≥5 in the first week after fracture should be considered to be a "red flag" for CRPS.

It is generally true that prediction rules do not perform as well when applied to other clinical settings as they did when applied to the sample on which they were developed. This is partly because the process of variable selection can produce poorly calibrated models and can produce bias ("optimism") in measures of model calibration and discrimination.[15] We attempted to calibrate our model appropriately and minimize optimism by using bootstrapping techniques.[15,4] Nonetheless, both prediction rules (ie, the rule based on 4 predictors and the rule based on pain only) should be considered provisional until they are validated in other samples. Given the model's extremely high discrimination (areas under the curve of .99 and .98), we would expect that even if the prediction rules are substantially less discriminative in other samples, they will still have sufficient discrimination to be useful. Potential cultural differences in reporting pain[27] may necessitate recalibration of the model if the model is to be used in other cultural groups.

Currently the best available evidence from high-quality randomized trials and systematic reviews suggests that it may be possible to reduce the incidence of CRPS with high-dose vitamin C[28] and treat CRPS with a range of pharmacologic and physical interventions.[7,23] A simple, accurate prediction tool might enable targeting of preventive strategies or provision of early intervention for high-risk patients. The ability to identify high-risk patients should open up new opportunities to develop and test the effectiveness of interventions designed to prevent and treat CRPS in high-risk patients.

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Appendix: Full clinical assessment protocol (in addition to routine hospital assessment protocol)

Assessment 1 (Within 1 Week of Fracture)

Clinical Assessment

Pain: 1. "On this scale of 0–10, with 0 being no pain at all and 10 being worst possible pain, how much pain are you in right now? Please circle the number that best reflects your response"

0	1	2	3	4	5	6	7	8	9	10
No pain at all									Worst possible pain	

2. "On this scale of 0–10, with 0 being no pain at all and 10 being worst possible pain, how would you rate your average pain over the last two days?"
3. "I will ask you how much it hurts to touch your thumb and first finger together. I will ask you to rate the pain on this scale of 0–10, with 0 being no pain at all and 10 being worst possible pain. Please touch your thumb and first finger together. How would you rate the pain caused by doing that?"

Swelling:

The circumference of the thumb was measured using Jobst finger tape midway between the metacarpophalangeal joint and the interphalangeal joint. The circumference of digits 2 to 4 was measured midway between the metacarpophalangeal joint and the proximal interphalangeal joint. An average of the 4 digits was obtained. Both hands were measured. The order of hands was alternated. The measure from the affected hand was expressed as a proportion of the measure from the unaffected hand.

Complex Regional Pain Syndrome Diagnostic Criteria:

Symptoms: Participants were asked, "In the last three days, have you noticed any of the following symptoms":
A.
   i) The skin of your hand being sensitive or painful to touch?
B.
   ii) One hand feeling warmer or cooler than the other?
   iii) One hand changing color or looking mottled?
C.
   iv) One hand being swollen or feeling swollen?
   v) One hand sweating a lot?
D.
   vi) The fingers of one hand difficult to move, or shaking when you try to move them?

Signs: Clinicians completed the following checklist (note—the arm was often in a plaster cast and therefore only the visible area could be assessed):
Are any of the following signs present:
A.
   i) Hyperalgesia to pinprick (gentle pressure of pin on either hand—patient reports whether the 2 stimuli feel the same or different).
   ii) Allodynia to light touch (paint brush stroking on either hand—patient reports whether the 2 stimuli feel the same or different).
B.
   iii) Changes in skin temperature (infrared tympanic thermometer placed on skin at midpoint of first phalanx of index finger)
   iv) Changes in skin color (observation only)
C.
   v) Edema (see swelling)
   vi) Increased sweating (observation only)
D.
   vii) Tremor or dystonia (observation of thumb to finger opposition)
   viii) Trophic changes—nails, hair skin (observation)
The following conditions constituted minimum criteria for diagnosis of CRPS:
   —At least one symptom from A, B, C, and D.
   —At least one sign in at least 2 of A, B, C, and D.
Catastrophizing: Participants completed the Pain Catastrophizing Scale[3]

Nonclinical Assessment

Dysynchiria:

Dysynchiria was tested in a quiet room. A mirror was placed between the patient's arms, the affected arm hidden from view and the patient watching the reflected image of the opposite limb. Pinprick and allodynia assessments from the diagnostic assessment were repeated, but with patients watching the "virtual limb" and reporting the quality and location of the evoked sensation.[1,2] Dysynchiria was considered positive if the patient reported normal sensation at the stimulated site, but also reported a sensation at the corresponding site on the affected limb.

Left/Right Hand Judgments

A left/right hand judgment task was adapted for use with foot pedals. We used an in-house software program and a 14-inch monitor on a laptop. Fourteen images of 1 hand were copied and flipped to produce 28 images. Each image was presented for 5 seconds or until the participant responded by pressing one of the foot pedals. Images were presented in a random and counterbalanced order so that each image appeared twice per trial. Participants sat comfortably with their hands resting in their lap or on a table in front of them. Left and right responses were indicated by depressing either the top or bottom (alternated between participants) of the foot contralateral to their fractured wrist. Two trials were undertaken. Data

from the second trial were analyzed. Participants were advised to not move during data collection. Accuracy and mean response time (RT) for correct responses were calculated.

Assessment 2 (over phone)

1. "On a scale of 0–10, with 0 being no pain at all and 10 being worst possible pain, how much pain are you in right now?"
2. "On a scale of 0–10, with 0 being no pain at all and 10 being worst possible pain, how would you rate your average pain over the last two days?"
3. "On a scale of 0–10, with 0 being no pain at all and 10 being worst possible pain, how would you rate your worst pain over the last week?"

If participants answered "2" or above for any of those questions, they were asked these questions:

"In the last week, have you noticed any of the following symptoms":

A.
   i) The skin of your hand being sensitive or painful to touch?

B.
   ii) One hand feeling warmer or cooler than the other?
   iii) One hand changing color or looking mottled?

C.
   iv) One hand being swollen or feeling swollen?
   v) One hand sweating a lot?

D.
   vi) The fingers of one hand difficult to move, or shaking when you try to move them?
   vii) Excessive growth of the hair or nails, or dryness of skin, on one hand?

If participants answered in the affirmative for at least 1 symptom from at least 2 of A, B, C, and D, they were called in for assessment from a trained clinician. NOTE: These symptomatic criteria are much less specific and much more sensitive to detect true CRPS cases. This was chosen to minimize the risk of missing true cases because patients underreported symptoms over the phone.

The following signs were assessed:

A.
   i) Hyperalgesia to pinprick (gentle pressure of pin on either hand—patient reports whether the 2 stimuli feel the same or different).
   ii) Allodynia to light touch (paint brush stroking on either hand—patient reports whether the 2 stimuli feel the same or different).

B.
   iii) Changes in skin temperature (infrared tympanic thermometer placed on skin at midpoint of first phalanx of index finger)
   iv) Changes in skin color (observation only)

C.
   v) Edema (see swelling)
   vi) Increased sweating (observation only)

D.
   vii) Tremor or dystonia (observation of thumb to finger opposition)
   viii) Trophic changes—nails, hair, and skin (observation)

The following conditions constituted minimum criteria for diagnosis of CRPS:
   —At least 1 symptom from A, B, C, and D.
   —At least 1 sign in at least 2 of A, B, C, and D.

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