American Pain Society
RESEARCH
EDUCATION
TREATMENT
ADVOCACY
PUBLISHED BY ELSEVIER

The Journal of Pain, Vol ■, No ■ (■), 2014: pp 1-14
Available online at www.jpain.org and www.sciencedirect.com

Critical Review

The Outcome of Complex Regional Pain Syndrome Type 1: A Systematic Review

Debbie J. Bean,*,† Malcolm H. Johnson,*,† and Robert R. Kydd*

*Department of Psychological Medicine, University of Auckland, Auckland, New Zealand.
†The Auckland Regional Pain Service, Auckland District Health Board, Auckland, New Zealand.

Abstract: **The purpose of this systematic review was to examine the outcome of complex regional pain syndrome (CRPS) type 1. We searched MEDLINE, Embase, and PsycINFO for relevant studies, and included 18 studies, with 3,991 participants, in this review. The following data were extracted: study details, measurement tools used, and rates or severity scores for the symptoms/signs of CRPS at baseline and follow-up, or in groups of patients with different disease durations. A quality assessment revealed significant limitations in the literature, with many studies using different diagnostic criteria. The 3 prospective studies demonstrated that for many patients, symptoms improve markedly within 6 to 13 months of onset. The 12 retrospective studies had highly heterogeneous findings, documenting lasting impairments in many patients. The 3 cross-sectional studies showed that rates of pain and sensory symptoms were highest among those with the longest duration of CRPS. Additionally, most studies showed that motor symptoms (stiffness and weakness) were the most likely to persist whereas sudomotor and vasomotor symptoms were the most likely to improve. Overall, this suggests that some CRPS patients make a good early recovery whereas others develop lasting pain and disability. As yet little is known about the prognostic factors that might differentiate between these groups.**

Perspective: ***We found evidence that many CRPS patients recover within 6 to 13 months, but a significant number experience some lasting symptoms, and some experience chronic pain and disability. The quality of the evidence was poor. Future research should examine the factors associated with recovery and identify those at risk of poor outcomes.***

Key words: *Complex regional pain syndrome, outcome, prognosis, recovery, systematic review.*

Complex regional pain syndrome (CRPS) is a painful condition that can occur after fracture, stroke, surgery or trauma, and most commonly affects a hand, wrist, foot, or ankle. In CRPS, pain is accompanied by a range of symptoms, including allodynia, hyperalgesia, swelling, and abnormalities in color, temperature, sweating, nail and hair growth, and movement.

No funding was received for this systematic review but we wish to thank the Oakley Mental Health Research Foundation for support with our CRPS research in general.
All authors wish to declare that they have no conflict of interest.
Supplementary data accompanying this article are available online at www.jpain.org and www.sciencedirect.com.
Address reprint requests to Debbie J. Bean, MSc, Department of Psychological Medicine, Faculty of Medical and Health Sciences, University of Auckland, Private Bag 92019, Auckland, New Zealand. E-mail: d.bean@auckland.ac.nz
1526-5900/$36.00

http://dx.doi.org/10.1016/j.jpain.2014.01.500

Traditionally, CRPS was considered a progressive condition with distinct "stages." For example, Bonica[10] described 3 stages. Stage 1, the "acute stage," was characterized by a painful, swollen, warm, red limb. In stage 2, the "dystrophic stage," the limb was said to cool and appear cyanotic, with changes to hair and nail growth, osteoporosis, stiffness, and muscle wasting. In stage 3, the "atrophic stage," irreversible atrophy of bones, muscles, and nails was described. However, relatively little research data have been offered to support the 3 specific stages, and at least 1 study has refuted the idea that 3 stages exist.[11] Long-term follow-ups of CRPS patients report contradictory findings regarding the outcome of the condition. A number of studies have found that although the nature of symptoms might fluctuate over time, CRPS tends to persist, and only a minority of patients recover from the condition.[14,15,21,41,44,47] For example, a prospective study of 42 patients with CRPS

after fracture found that no patient was symptom-free 12 months later.[6] A follow-up of 134 CRPS patients at a mean of 5.8 years after diagnosis found that 64% still met the International Association for the Study of Pain (IASP) diagnostic criteria for CRPS,[15] and 1 study of more than 600 CRPS patients showed that symptoms tended to be worse in those with a longer duration of CRPS compared to those with a shorter duration.[41] In addition, research has suggested that over time, CRPS patients can develop more widespread pain, and some researchers have described symptoms of CRPS "spreading" to affect multiple limbs.[41,46]

In contrast, there are also studies that present more optimistic data and suggest that the majority of patients will recover from the condition within 12 months.[8,17,24,38,49] A population-based study of medical records found that 74% of CRPS cases resolved, usually spontaneously, at a mean of 11.6 months post onset.[38] A prospective study requiring patients to have no treatment found that of the 30 participants, only 3 had severe symptoms and had to withdraw from the study for treatment, and of the 27 remaining participants, only 1 continued to have CRPS at the 1-year follow-up.[49] Several studies have also shown that the majority of CRPS patients will return to employment following the condition.[17,18]

This review aims to examine these discrepancies in the literature, to synthesize the published data concerning the course of CRPS symptoms over time, and to answer the following questions: In what proportion of CRPS patients do symptoms persist? To what extent do CRPS symptoms persist? We chose to limit the review to CRPS type 1 (CRPS-1, without a major nerve injury) because CRPS type 2 (CRPS-2) is associated with a specific nerve injury that likely affects outcome. We hypothesized that the majority of patients would show improvements in CRPS symptoms with time, but some would display chronic severe symptoms.

Methods

Selection of Studies

We systematically reviewed prospective, retrospective, and cross-sectional studies that provided data on the outcome of CRPS type 1. A literature search was conducted using the databases MEDLINE, Embase, and PsycINFO, from inception until April 4, 2012 (search date). We used the search terms recommended for systematic reviews on prognosis[2]: "exp epidemiologic studies," "incidence.sh," "follow-up studies.sh," "prognos:.sh," "predict:.tw," OR "course:.tw" AND "complex regional pain syndrome.mp," "Reflex sympathetic dystrophy.mp," OR "algodystrophy.mp." The search was limited to peer-reviewed journals and to studies including human subjects. The personal electronic libraries of the researchers were also searched for possible references. The reference lists of all relevant papers were searched by hand and an electronic search for citing articles of each paper was also conducted to ensure that all possible references were obtained.

Studies were considered for inclusion in the systematic review if they

1. Reported on "complex regional pain syndrome type 1," "reflex sympathetic dystrophy" (RSD), "algodystrophy," or "sudeck's dystrophy." Studies with patients combined from several diagnostic groups (eg, CRPS-1 and CRPS-2) were included if >80% of the sample had CRPS-1;
2. Had the stated aim of investigating the course, natural history, or outcomes of CRPS; or
3. Had one of the following characteristics:
   a. Reported on rates or severity of CRPS symptoms/signs or presence of CRPS diagnosis at more than 1 time point, where the time points are at least 6 months apart, or
   b. Provided cross-sectional or correlational data comparing the symptoms/signs of CRPS between patients with differing CRPS duration or correlating symptom severity with duration, or
   c. Were retrospective studies documenting self-report of how symptoms changed over time, or
   d. Were retrospective studies or audits documenting residual symptoms/signs in a follow-up of a cohort more than 6 months after the CRPS patients were identified. Cohorts had to have been previously assembled or patients previously identified, so that the review only included retrospective studies that had a chance of capturing CRPS cases that had resolved.

Studies were excluded if they 1) had a sample size of less than 10; 2) were not published in full article format or data could not be extracted from the article; 3) conducted in pediatric samples or in adult samples where the CRPS onset was during childhood (as there is suggestion that CRPS can manifest differently in children and adolescents); 4) published in languages other than English, French, or German; or 5) had follow-up or response rates <50%.

Quality and Relevance Assessment and Data Extraction

To assess study quality and relevance of studies for this review, we used a modified version of the quality evaluation method recommended for systematic reviews of prognostic variables.[12,28] Few studies assessed prognostic variables. Therefore, our review focused on clarifying the course of CRPS, so we excluded quality items on prognostic factor measurement and confounder measurement.

We assessed quality and relevance on the following 4 sources of bias: study participation (sampling method described, sample described, inclusion/exclusion criteria described, diagnostic criteria described, response rate, representative sample, assembled at common time point >3 months, follow-up >6 months), study attrition (attrition described, attrition adequate, information on drop-outs), outcome measurement (outcomes defined, objective, measured appropriately), and analysis (relevant statistical analysis conducted, and statistical analysis appropriate). For each question, each study was scored

positive (Y), negative (N), or unclear (?). For retrospective and cross-sectional studies, attrition items were scored not applicable (N/A). A detailed description of the quality assessment criteria is available in Supplementary Table 1 in the supplementary information online.

We extracted data on the study population, diagnostic criteria, symptom duration at baseline and follow-ups (where applicable), the measurement tools used to assess each of the symptoms/signs of CRPS, and the mean and standard deviation scores on those measures at each time point. The symptoms/signs investigated were pain, sensory symptoms, function (range of motion/stiffness and limb strength), temperature asymmetry, color asymmetry, swelling, abnormal sweating, and hair and nail growth abnormalities. We also extracted data on scores or measures of general recovery from CRPS. As a number of studies did not report mean scores, but rather the proportion of the sample with each symptom/sign either present or absent, for these studies, the percentage of the sample with the symptom/sign at each time point was recorded.

Data Synthesis

As there was significant heterogeneity in research methods, it was not possible to pool data quantitatively in any meaningful way. Instead, a qualitative analysis and synthesis of the data is presented here. We present the results of the prospective, retrospective, and cross-sectional studies separately.

Results

Studies Selected

The literature search yielded 1,741 papers. The titles, abstracts, and, where necessary, full text of these were screened by the primary author (D.J.B.). Ninety of these were selected for a closer review and were examined in detail. Of these, 18 studies (with 19 publications) met the inclusion and exclusion criteria and were selected for this review (Table 1). The second author screened any of the studies where it was unclear whether they met the inclusion/exclusion criteria, and a decision was made by consensus.

Of the 18 studies included in the review, there were 3 prospective studies, 12 retrospective studies, and 3 cross-sectional or correlational studies. The median sample size of the studies was 71, but samples ranged from 17 to 888. The total number of participants included in this review is 3,991. The study characteristics are described in Table 1. Few studies used the same diagnostic criteria. Three used the 1994 IASP criteria,[33] 2 used the "Budapest" criteria (now also known as the new IASP criteria),[26] 3 used the criteria described by Zyluk,[49] and the rest used their own criteria or did not describe the criteria used. This reflects the changing taxonomy of CRPS over the years. Earlier studies used criteria for algodystrophy or RSD, whereas later studies tended to use the newer criteria for CRPS. There are large variations between the criteria, so, for example, studies that used the 1994 IASP criteria would have captured many more patients than studies that used the new IASP (Budapest) criteria.[14]

Quality Assessment

The results from the quality and relevance assessment are presented in Table 2. In keeping with guidelines on quality assessment for systematic reviews of this nature, we chose not to create a "quality score" for each study, but instead discuss the quality of the studies qualitatively.[12,28] We note 4 major sources of bias in the included studies:

1. Unrepresentative Samples: As shown in Tables 1 and 2, most studies used samples that are unlikely to represent the CRPS population as a whole: some recruited only patients with a particular "trigger" for their CRPS, such as a fracture, which has been suggested to influence outcome.[38] Some recruited from specialist centers where patients with more severe cases of CRPS are likely to be referred, others included only patients with a previous "good outcome," which is also likely to influence later prognosis, and 1 study only included those with CRPS for more than 1 year. We determined that only 6 out of the 18 included samples met our criteria for using a "representative sample." In addition, only 3 studies met our criteria for being considered an "inception" cohort (ie, samples selected at a common time point less than 3 months after developing their CRPS). Thus, most of the studies likely failed to include any CRPS patients who could have recovered in the first few months of their condition.
2. Attrition: Loss to follow-up is major source of bias for the studies included in this review, particularly if those lost to follow-up are those with a likely better or poorer outcome. Only 6 of our 18 included studies could be scored for attrition, and of these, only 2 met our minimum criteria (<20% attrition). Three of the studies were cross-sectional (which meant that any patients who had recovered were not included), and 9 were retrospective follow-ups of a previously identified cohort. For these retrospective studies, we did not score them for "attrition" but rather for "response rate" (ie, the percentage of the previously identified cohort that was included in the study). Of these 9 studies, 4 had response rates below our required cut-off of 75%, and the other 5 did not report response rate clearly in the published article. Thus, attrition is a major and obvious source of bias in the included studies.
3. Measurement: Inadequate measurement of outcomes is a source of bias for this review. We assessed whether outcome measures were defined, whether any measures were objective, and whether they were measured appropriately. We found that 15 of the 18 papers defined their outcomes, 11 studies included at least 1 objective measure (ie, not self- or physician report), and 9 studies used some kind of standardized measure or scale. Overall, the studies performed better for this source of bias than for other major sources of bias, but the huge variation

Table 1. Characteristics of the Included Studies

Reference	Setting, Location, and Publication Year	Sample and Method	Diagnostic Criteria Used	Mean CRPS Duration at Baseline/ Cohort Assembly	Mean CRPS Duration at Follow-Up/ Time of Survey
Prospective studies					
Atkins et al[3]	Hospital Casualty Department, Sheffield, United Kingdom, 1989	Assessed 109 unselected Colles fracture patients at 9 wk and 6 mo. Reports on persisting symptoms in 19 of the 27 patients with features of algodystrophy at baseline.	Own	9 wk	6 mo
Bickerstaff and Kanis[8]	Hospital Casualty Department, Sheffield, United Kingdom, 1994	Assessed 274 Colles fracture patients at 7 wk, then monthly until symptoms abated (6 mo for asymptomatic patients). Included 77 who developed algodystrophy. No mention of response/ dropout rates. Reports the percentage of algodystrophy patients with persisting symptoms at 6 and 12 mo.	From Atkins et al[4]	7 wk	6 and 12 mo
Zyluk[49]	Surgical Department, Pomeranian Medical University, Poland, 1998	Assessed 30 RSD patients at 1, 2, 6, and approx. 13 mo. Patients were required to receive no treatment. Three patients with severe symptoms withdrew for treatment, so the study reports on the rates of symptoms in the remaining 27.	From Zyluk[49]	At time of diagnosis: mean of 12 wk	6 and 13 mo postdiagnosis
Retrospective studies					
Subbarao and Stillwell[45]	Clinic/setting not described, United States, 1981	Chart review of 125 upper limb RSD patients who had been discharged a mean of 14 mo earlier. Follow-up questionnaires sent to 123. Of those, 77 (63%) responded. Paper reports on rates of symptoms noted in this questionnaire.	From Pak et al[35]	22 wk	22 mo
Gougeon et al[25]	French Society of Rheumatology, France, 1982	File review of 573 RSD cases from a survey of society members, 370 files selected for review. Of these, 227 files mentioned the duration of disease until resolution. Reports on percentage whose symptoms had resolved by 6, 12, and 36 mo.	Not described	n/a	Followed up until cured or 3 y max
Fialka et al[20]	Physical Medicine & Rehabilitation Department, Vienna, Austria, 1991	Followed 17 patients with lower limb RSD post-fracture, for a mean of 39 mo. Performed physical assessment at follow-up. Reports on remaining symptoms, as well as scintigraphy.	Own	14 wk	3.5 y

Table 1. Continued

Reference	Setting, Location, and Publication Year	Sample and Method	Diagnostic Criteria Used	Mean CRPS Duration at Baseline/ Cohort Assembly	Mean CRPS Duration at Follow-Up/ Time of Survey
Ehrler et al[19]	Functional Rehabilitation Centre, Strasbourg, France, 1995	Follow-up questionnaire sent to 47 algodystrophy patients who had taken part in a study 9 y earlier. 25 (53%) responded. Reports on percentage that continue to experience pain, stiffness, and reduced strength.	Not described	2 groups: 1 = 1 wk, 2 = 28 wk	Both groups 9 y later
Laulan et al[32]	Orthopedic Services, University Hospital Trousseau, Tours, France, 1997	Recruited all 125 distal radius fracture patients seen over a 7-mo period for surgical treatment and followed-up at 12 mo. Of the 26 who had "definite algodystrophy" at 12 wk, all were followed-up. Reports on those with stiffness and pain at 12 mo.	Own	n/a	12 mo postfracture
Geertzen et al[22,23]	Department of Rehab., University Hospital Groningen, The Netherlands, 1998	Invited all 93 patients treated for RSD from 1988–1994 for follow-up. 65 (70%) responded. Reports on measures of pain, quality of life and physical function.	Own	n/a	5.5 y
Galer et al[21]	University of Washington Multidisciplinary Pain Center, USA, 2000	Questionnaire sent to 55 CRPS patients treated from 1997 to 1998. 31 (56%) responded. Asked patients to describe which symptoms had improved, worsened or remained unchanged.	1994 IASP[33]	n/a	3.3 y
Zyluk[50]	Surgical Dept, Pomeranian Medical University, Poland, 2001	Chart review of all 146 patients treated for RSD from 1986 to 1997. Assessed the 94 (64%) with a previous good response to treatment, at mean 11 mo post-treatment. Paper describes remaining symptoms.	From Zyluk[50]	Not stated, majority duration <4 mo (17 wk)	11 mo posttreatment completed
Bejia et al[7]	Rheumatology Department, University Hospital Monastir, Tunisia, 2005	Reviewed 60 algodystrophy cases seen from 1989 - 2003. Classified the outcome for each patient (poor/ moderate/good/very good), and reports the percentage left with atrophy and pain.	Not described	13 wk	15 mo
de Mos et al[15]	Integrated Primary Care Info. Project (GP Database), Erasmus Medical Centre, Rotterdam, The Netherlands, 2009	Identified all 259 patients diagnosed with CRPS a minimum of 2 y earlier, from 48 clinics in GP database. Visited and assessed 62% of these patients. 40 later	1994 IASP[33]	1st mention in GP database; confirmed by patients	5.8 y

Table 1. Continued

Reference	Setting, Location, and Publication Year	Sample and Method	Diagnostic Criteria Used	Mean CRPS Duration at Baseline/ Cohort Assembly	Mean CRPS Duration at Follow-Up/ Time of Survey
		identified as not appropriate (never had CRPS/developed CRPS before the study period). Final sample: 102 CRPS patients (100 CRPS-1, 2 CRPS-2). Reports on percentage with symptoms/signs of CRPS at assessment.			
Savas et al[39]	Department Physical Medicine & Rehab, Suleyman Demireal University Medical School, Turkey, 2009	Physical examination of all 30 CRPS-1 patients previously discharged with a good outcome 18 mo later. Reports on remaining symptoms at this assessment.	From Zyluk[50]	Unclear	18 mo posttreatment
Sharma et al[44]	RSD Association of America Website, United States, 2009	Asked RSD website users to complete online survey. Received 1359 responses. 35% excluded (likely never met diagnostic criteria). 888 responses included. Reports percentage describing remission at some point, percentage pain-free, and symptom change over time.	Modified Budapest[26] (used symptom report only as no physical examination)	n/a	5.5 y
Cross-sectional or correlational studies					
Veldman et al[47]	Department of Surgery, Nijmegen University Hospital, The Netherlands, 1993	Recorded symptoms reported by 829 consecutive RSD patients. Assessed symptom prevalence in groups according to CRPS duration.	From Veldman et al[47]	Group 1: 0–2 mo (n = 156) Group 2: 2–6 mo (n = 242) Group 3: 6–12 mo (n = 200) Group 4: >12 mo (n = 231)	
Schwartzman et al[41]	Pain Clinic, Drexel University College of Medicine, United States, 2009	Retrospectively analyzed questionnaires completed by 656 CRPS-1 & 2 patients seen over a 10.5-y period. Correlated symptom severity scores with CRPS duration, reported on percentage with particular symptoms at different stages of CRPS duration.	Budapest[26]	1–46-y range. No mean duration reported.	
De Boer et al[14]	Outpatient clinics of 5 hospitals participating in the TREND knowledge consortium (Trauma Related Neuronal Dysfunction), The Netherlands, 2011	Replicated the Veldman et al[47] study with a group of 692 ambulatory CRPS-1 patients.	1994 IASP[33]	Group 1: 0–2 mo (n = 48) Group 2: 2–6 mo (n = 211) Group 3: 6–12 mo (n = 70) Group 4: >12 mo (n = 352)	

in measurement practices and lack of objective measures still likely affected results.

4. Statistics: Only 7 of the 18 studies performed relevant statistical testing, for example, looking for statistically significant reductions in symptom severity over time or comparing differences in measures of the affected and unaffected limbs at a follow-up. All 7 studies that performed statistical testing were deemed to use statistics appropriately. However, a possible source of bias is the lack of statistical testing in the 11 other studies. This means that we did not know if differences between groups in the cross-sectional studies, or changes in symptom severity over time in prospective studies, could be chance findings, and had to take the raw data on its merit.

Results From Prospective Studies

The 3 prospective studies presented the most optimistic outcome data and demonstrated consistent symptom improvements over time.[3,8,49] Two of these studies systematically measured the symptoms/signs of CRPS early after diagnosis and then again at a 12- to 13-month follow-up,[8,49] whereas the other study briefly noted data from a 6-month follow-up.[3] The 2 prospective studies that measured pain or tenderness found that the proportion of CRPS patients with pain reduced from 100% at first assessment to 18% and 7% respectively at the 12- to 13-month follow-up.[8,49] The 2 studies that assessed the presence of swelling reported rates of 87 to 100% at first assessment, which reduced to 12 to 15% at the final follow-up.[8,49] Only 1 of the prospective studies measured changes in temperature disturbance, limb discoloration, sweating abnormalities, trophic changes to hair and nails, and sensory disturbances, and this study noted significant reductions in rates of signs over the course of 13 months.[49] One study found significant reductions in rates of "vasomotor instability" (a combination of abnormalities in limb color, temperature, and sweating) over the course of 12 months, from 91% at baseline to 29% at follow-up.[8] Another study grouped symptoms into a category labeled "vasomotor instability or swelling" and found that 42% of patients experienced these symptoms at the 6-month follow-up.[3]

The symptoms/signs that were least likely to resolve in the prospective studies were stiffness and limb strength. Bickerstaff and Kanis[8] found that 65% of patients continued to have stiffness at 12 months, and the grip strength of the affected limb was equivalent to 45% of the strength of the unaffected limb. This contrasted with a grip strength ratio of 80% in Colles' fracture patients who did not develop algodystrophy. Zyluk[49] reported that 89% of RSD patients had reduced grip strength at the 13-month follow-up and reported that grip strength was 45% that of the unaffected limb. Zyluk[49] also found that stiffness was highly prevalent, with 78% of RSD patients experiencing "stiffness in the morning" at the 13-month follow-up. Atkins et al[3] reported lower rates of joint stiffness at the 6-month follow-up (21%), but it is unclear from the results they present whether joint stiffness may also have affected the 42% of patients noted to have "vasomotor instability or swelling."

Only 1 of the prospective studies had an overall measure of CRPS severity, the "Zyluk assessment of result." This study reported that 73% of patients had a good result (no pain and full finger flexion), 13% had a moderate outcome (pain after load and loss of flexion of less than 3 cm), whereas 13% had a poor result (persistent severe pain and loss of flexion greater than 3 cm).[49]

Of note, 2 of the prospective studies used the same criteria for "algodystrophy" and the other used criteria for "reflex sympathetic dystrophy." All 3 prospective studies required 4 different symptoms/signs of CRPS to be present in order to meet diagnostic criteria, although the algodystrophy criteria were broader as a wider range of symptoms were accepted.

Results From Retrospective Studies

Measures of Overall Rates of CRPS Symptoms or Severity

There were 12 retrospective studies included in the review. Seven reported on results of an overall measure of CRPS presence or severity, with the majority of these studies quantifying the percentage of an original cohort who continued to have symptoms/signs of CRPS at a long-term follow-up assessment. The results are presented in Table 3. This shows that the outcomes were highly variable and are presented here in order from the most to the least positive. Gougeon et al[25] found that all but 22% of algodystrophy patients were "cured" at the 3-year follow-up according to a chart review. A 9-year follow-up questionnaire sent to algodystrophy patients reported that 40% of patients had not "normalized."[19] Another study of algodystrophy patients indicated that 58% had "sequelae" with an elevated algodystrophy score calculated from a clinical and radiologic examination at 12 months postfracture.[32] A study of CRPS patients reported that 64% continued to meet the 1994 IASP criteria for CRPS at an examination at a mean of 5.8 years postdiagnosis.[15] Finally, a physical examination of CRPS patients who had previously had a good outcome found that 90% continued to experience symptoms 18 months after treatment.[39] Overall, these findings are highly heterogeneous, with ratings as low as 22% and as high as 90% for those who continue to have symptoms at long-term follow-up.

One study rated patients' outcome according to a clinical grading system and found that 63% of algodystrophy patients had a very good or good outcome, 29% had a moderate outcome, and 9% had a poor outcome according to a chart review.[7] Another interviewed patients about their clinical course and found that 30% considered themselves recovered, 54% rated their symptoms as stable, and 16% stated that their symptoms were progressive at a mean of 5.8 years after diagnosis.[15]

One retrospective study reported on a measure of overall symptom severity in a cohort of patients examined at a mean of 5.5 years.[22,23] They used the "RSD score"—a 60-point rating scale—and reported that although the score for RSD patients' unaffected hands was 0.7/60 (on a scale of 0–60 where 0 = no RSD and 60 = worst RSD), on the affected side it was a mean of 6/60. They also reported that quality of life scores among patients were similar to population norms.

Measures of Pain

Ten retrospective papers reported on measures of pain among cohorts of patients followed up at least 1 year after diagnosis, and these are presented in Table 4. Five of these studies reported on the percentage of patients who continued to experience pain, and these results were highly variable. The most positive results showed that only 19% of algodystrophy patients continued to experience pain at 1 year; however, 27% of the "algodystrophy" sample in this study had never experienced pain at any time, which questions the

Table 2. Results of the Quality and Relevance Assessment for the Included Studies

	Sampling Method Described?	Sample Described?	Inclusion/ Exclusion Criteria Described?	Diagnostic Criteria Described?	Response Rate >75%?	Representative Sample?	Assembled at Common Time Point <3 Mo?	Follow-Up at Least 6 Mo?	Attrition Described?	Attrition Adequate (<20%)?	Information About Completers vs Dropouts?	Outcomes Defined?	Outcomes Objective?	Outcomes Measured Appropriately?	Relevant Statistical Analysis Conducted?	Analysis Appropriate?
Prospective studies																
Atkins et al[3]	Y	Y	Y	Y	?	N, fracture	Y	N	Y	N	N	N	N	?	N	n/a
Bickerstaff and Kanis[8]	Y	N	N	Y	?	N, fracture	Y	Y	Y	Y	n/a	Y	Y	Y	Y	Y
Zyluk[49]	Y	Y	N	Y	?	Y	N	Y	Y	N	Y	Y	Y	Y	N	n/a
Retrospective studies																
Subbarao and Stillwell[45]	Y	Y	Y	Y	N	Y	N	Y	Y	N	N	Y	N	N	N	n/a
Gougeon et al[25]	Y	N	N	N	?	?	N	Y	n/a	n/a	n/a	N	?	?	N	n/a
Fialka et al[20]	N	Y	Y	Y	?	?	N	Y	n/a	n/a	n/a	Y	Y	Y	Y	Y
Ehrler et al[19]	N	N	N	N	?	?	N	Y	Y	N	N	N	Y	?	N	n/a
Laulan et al[32]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N	N	n/a
Geertzen et al[22,23]	Y	Y	Y	Y	N	Y	N	Y	n/a	n/a	n/a	Y	Y	Y	Y	Y
Galer et al[21]	Y	Y	Y	Y	N	N, pain center	N	n/a	n/a	n/a	n/a	Y	N	Y	N	n/a
Zyluk[50]	Y	Y	Y	Y	N	N, good outcome	N	Y	n/a	n/a	N	Y	Y	Y	N	n/a
Bejia et al[7]	Y	Y	N	N	?	?	N	n/a	n/a	n/a	n/a	Y	N	?	N	n/a
de Mos et al[15]	Y	Y	Y	Y	N	Y	n/a	Y	n/a	n/a	n/a	Y	Y	?	Y	Y
Savas et al[39]	Y	Y	Y	Y	?	N, good outcome	N	Y	n/a	n/a	n/a	Y	Y	Y	Y	Y
Sharma et al[44]	Y	Y	Y	Y	?	N, online support group	N	N	n/a	n/a	n/a	Y	N	N	N	n/a
Cross-sectional studies																
Veldman et al[47]	Y	Y	Y	Y	Y	Y	N	n/a	n/a	n/a	n/a	Y	Y	?	N	n/a
Schwartzman et al[41]	Y	Y	Y	Y	Y	N, chronic	N	N	n/a	n/a	n/a	Y	N	Y	Y	Y
de Boer et al[14]	Y	Y	Y	Y	?	N, regional referral center	N	N	n/a	n/a	n/a	Y	Y	Y	Y	Y

Abbreviations: Y, positive; N, negative; ?, unclear.

similarity of this sample to others diagnosed with RSD or CRPS.[32] An assessment of CRPS patients at a mean of 5.8 years after diagnosis found that 32% still reported experiencing pain.[15] Two postal questionnaire studies found that 36% of algodystrophy patients still reported pain at a 9-year follow-up,[19] and 47% of RSD patients had hand pain at 22 months.[45] Studies that examined patients at follow-up found that 71% of RSD patients with a previously good outcome still had pain 11 months posttreatment,[50] and of CRPS patients, 86% had pain on movement and 76% had pain at rest 18 months post-treatment.[39]

Three retrospective studies reported results of measures of pain intensity. Savas et al[39] found that on a visual analog scale (0–10 cm), the mean pain score of CRPS patients was 2.8 ± 2.0 cm at a follow-up of 18 months post-treatment. Geertzen et al[22,23] reported even lower pain severity ratings at 5.5-year follow-up of RSD patients, with a mean visual analog score of 1.2 ± 1.8 cm. Fialka et al[20] reported low-moderate pain intensity among a group of RSD patients at a 42 month follow-up: on a scale of 0 (no pain) to 5 (intolerable pain), the mean score was 2.1 ± 1.1 cm.

Two retrospective self-report studies asked groups of CRPS patients to recall how pain had changed over time. Galer et al[21] found that 29% of CRPS patients believed their pain had improved over time, 42% described no change, and 29% indicated that their pain had worsened. A survey of RSD patients found that, on average, patients believed their pain had improved slightly since first developing their symptoms, but 79% stated that their symptoms had never gone into remission.[44] This last study was limited as it surveyed patients who were current users of an RSD website, so any who had recovered were unlikely to be included. The results of the retrospective studies that measured the prevalence or intensity of pain are presented in Table 4.

Measures of Function

Eight retrospective studies reported on follow-up measures of limb function among cohorts of CRPS patients. All of these studies showed that limb strength and/or stiffness continue to be affected in the long term. For example, Geertzen et al[22,23] found that there were small but statistically significant differences in the range of motion between the affected and unaffected limbs of RSD patients at a mean follow-up time of 5.5 years. They also reported that the grip strength of the RSD affected hand was 73% that of the unaffected hand, and that 62% of patients were limited in the activities of daily living. Similar significant range of motion and strength differences between the affected and unaffected limbs of CRPS patients were reported by Savas et al[39] at a mean of 18 months posttreatment. Fialka et al[20] found that 58.8% of patients had a slightly reduced range of motion, but none exhibited a markedly reduced range of motion at the 39-month follow-up. Zyluk[50] found that 28% of RSD patients had "morning stiffness" and 78% described decreased function of the hand 11 months after treatment. Grip strength of the affected hand was 37% of the strength of the unaffected side. Ehrler et al[19] reported that 36% of algodystrophy patients indicated that they had reduced

Table 3. Results of Retrospective Studies Measuring General Outcomes of CRPS

Reference	Sample	Mean Follow-Up Time Point	Measure	Result
Bejia et al[7]	60 algodystrophy patients	15 mo	Criteria of French Society for Rheumatologists	Very good result: 16%; good result: 46.5%; moderate result: 28.7%; poor result: 8.8%
Gougeon et al[25]	227 algodystrophy patients	Until cured, max 3 y	Chart review to determine % "cured"	21.6% not "cured" after 3 y
Ehrler et al[19]	25 algodystrophy patients	9 y	Questionnaire to determine % "normalized"	60% "normalized"; 40% symptomatic
Laulan et al[32]	26 algodystrophy patients post–distal radius fracture	12 mo	% with "sequelae" on physical examination	57.7% had "sequelae"
De Mos et al[15]	102 CRPS patients	5.8 y	% who still meet 1994 IASP Criteria for CRPS	64% meet 1994 IASP criteria
Savas et al[39]	30 CRPS patients with previous good outcome	18 mo after treatment	% who met own criteria for CRPS % who were symptom-free	0 met criteria for CRPS; 10% were symptom-free, 90% symptomatic
Geertzen et al[22,23]	65 RSD patients	5.5 y	RSD Score (min = 0, max = 64, worse scores indicate more severe RSD); Short-form 36 (quality of life)	Unaffected side = 0.7 ± 1.5; affected side = 5.6 ± 8.6; SF-36 scores similar to population norms

strength in the limb, and 28% described stiffness 9 years after diagnosis. Subbarao and Stillwell[45] found that 51% of their sample experienced stiffness in the hand at the 22-month follow-up. Of the 102 patients visited by de Mos et al,[15] at a mean of 5.8 years since CRPS onset, 59 to 60% described a reduced range of motion or weakness of the limb, and these were observed by the researchers in 41 to 44%. Galer et al[21] surveyed CRPS patients and asked them to recall the course of symptoms over time. They reported that weakness was noted to have improved by 48% of patients, but 25% noted that weakness tended to worsen and 23% noted no change. Overall, the retrospective studies that report on functional outcomes concur with the findings of the prospective studies, indicating that functional limitations such as weakness, stiffness, and reduced range of motion may be quite prevalent in the long term for CRPS patients.

Diagnostic Criteria Used in the Retrospective Studies

The diagnostic criteria used by the studies once again differed greatly. Three of the retrospective studies did not describe their criteria. Four required 4 symptoms/signs from a list of varying possible clinical features.[22,23,39,44,50] Two studies required 3 symptoms/signs from a list of possible clinical features along with particular radiologic findings.[20,32] Two studies used the broad 1994 IASP criteria.[15,21] One study described a range of symptoms/signs but did not state which were required for diagnosis.[45] It appears that studies that used criteria for "algodystrophy" tended to produce more optimistic results than studies that examined "RSD" or "CRPS." Also, studies that conducted a chart review produced more optimistic results than studies that examined patients at follow-up.

Results From Cross-Sectional Studies

Three cross-sectional studies were included in the review. Two of the studies took samples of patients with diagnoses of RSD or CRPS and divided them into 4 groups on the basis of their duration (less than 2 months, 2–6 months, 6–12 months, and more than 12 months).[14,47] They measured the percentage of each group with each of the symptoms of CRPS and reported these rates. One of the studies compared these 4 groups for statistically significant differences in the rates of symptoms.[14] The other study measured symptoms as well as CRPS duration and performed correlations to see whether symptom prevalence or severity significantly correlated with CRPS duration.[41] These 3 studies had large sample sizes in comparison with the majority of the other papers (656–829 subjects).

The cross-sectional studies generally reported poorer outcomes than the prospective studies and the retrospective studies. For example, for pain, the 2 comparative studies reported that 85 to 92% of RSD/CRPS patients had pain during the first 2 months, and this increased steadily so that among those with CRPS for more than 1 year the rates were 95 to 97%.[14,47] The correlational study reported a significant correlation of r = 0.6 for the numerical pain rating scale scores and CRPS duration, indicating that pain intensity increases with CRPS duration.[41] The cross-sectional studies reported similar patterns of increasing rates for sensory symptoms such as allodynia and hyperesthesia, although the actual rates of symptoms were lower than those for pain.[14,47] The comparative studies

Table 4. Results of Retrospective Studies Measuring Pain Outcomes in CRPS

Reference	Sample	Mean Follow-Up Time Point	Measure	Result
Laulan et al[32]	26 algodystrophy patients post–distal radius fracture	12 mo	% with pain	19%
De Mos et al[15]	102 CRPS patients	5.8 y postdiagnosis	% reporting spontaneous pain	32%
Ehrler et al[19]	25 algodystrophy patients	9 y	% with pain	36%
Subbarao and Stillwell[45]	77 RSD patients	22 mo	% with pain in hand	41%
Zyluk[50]	94 RSD patients with previous "good" outcome	11 mo posttreatment	% not completely pain-free	71%
Savas et al[39]	30 CRPS-1 patients with previous "good" outcome	18 mo posttreatment	% with hand pain after use; % with hand pain at rest; Mean VAS pain intensity	86%, 76%; 2.8 ± 2.0 cm
Geertzen et al[22,23]	65 RSD patients	5.5 y	Mean VAS pain intensity last 24 hours	1.2 ± 1.8 cm
Fialka et al[20]	17 lower limb RSD patients	42 mo	Mean 0–5 pain-rating (0 = no pain, 5 = intolerable pain)	2.1 ± 1.1
Galer et al[21]	31 CRPS patients	3.3 y	Self-report—has pain changed over time?	Improved: 29%; No change: 42%; Worse: 29%
Sharma et al[44]	888 CRPS patients using RSD Association America Website	5.5 y	Self-report (retrospective): pain NRS at onset of symptoms and now	Onset estimate: 8.2/10; current intensity: 6.9/10

Abbreviations: VAS, visual analog scale; NRS, numerical rating scale.

showed that the proportion of patients experiencing temperature disturbance, limb discoloration, and swelling tended to decrease with increasing CRPS duration,[14,47] but this contrasted with the results of the correlational study, which reported significant positive correlations between rates of these symptoms and CRPS duration.[41] The results of the cross-sectional studies are presented in Table 5.

Each of the 3 cross-sectional studies used different diagnostic criteria for CRPS. One of the studies used Veldman's criteria, which required the presence of at least 4 symptoms/signs of CRPS from a list of 5 possible clinical features, and also required that symptoms/signs worsened with use of the limb and that pain was present in a larger and more distal area of the limb than the original injury or surgery.[47] Schwartzman reported using the Budapest criteria, which are much stricter.[41] The third study used the 1994 IASP criteria for CRPS and also reported on the relatively low number of patients in their cohort who would have met Veldman's criteria (42%) and the Budapest criteria (38%), and that the proportion of patients meeting these different criteria differed depending on the CRPS duration.[14] Thus, it is likely that the patient group captured differs greatly among the 3 cross-sectional studies.

Discussion

The 18 studies reviewed here document highly variable outcomes of CRPS. The quality assessment revealed a number of significant limitations in the literature, which are discussed below. Bearing this in mind, we first comment on the general findings. The best rates of recovery were shown by the prospective studies, which found that the proportion of patients with pain, swelling, limb discoloration, and temperature disturbance reduced dramatically within 6 to 13 months. However, functional outcomes such as weakness, stiffness, and limited range of motion persisted in a majority of patients for more than 1 year. In contrast, the cross-sectional studies found that rates of pain, sensory symptoms, and motor dysfunction were highest among those with the longest duration of CRPS, which could be interpreted to mean that these symptoms progress and worsen over time. However, because cross-sectional studies cannot capture cases that have resolved, this interpretation would be inappropriate. Instead, these results can only indicate that there is a cohort of CRPS patients with long-term symptoms including pain, sensory disturbance, and impaired limb function.

The retrospective studies also showed that it is not uncommon for patients to have sequelae including pain and limb dysfunction many years after a diagnosis of CRPS. However, the studies' findings were highly disparate, and there were several possible reasons for this. Studies that conducted careful interviews and examinations tended to identify more symptoms than those that conducted chart reviews or posted questionnaires. Studies that measured symptom severity showed that some persisting symptoms are fairly mild. For example, Geertzen et al[22,23] found at follow-up that average pain scores were 1.2/10, and range of motion was 84 to 99% of the unaffected limb. It is unclear whether such mild symptoms would have been categorized as "present" or "absent" in studies that dichotomized patients, and this likely contributed to the variability in results.

There were some common findings across all 3 types of studies included in the review. First, the vasomotor and sudomotor symptoms of CRPS (discoloration, temperature disturbance, altered sweating, and edema) tend to be most common in the early stages of the condition and had the greatest likelihood of resolving. Second, pain and sensory symptoms persisted in some patients but not all, and long-term follow-ups show fairly low rates of mean pain intensity. Third, we found that motor symptoms such as weakness, stiffness, and limited range of motion are the symptoms most likely to persist in the long term.

Overall, this review shows that CRPS has a highly variable course, with some patients experiencing a relatively

Table 5. Results of Cross-Sectional and Correlational Studies on the Course of CRPS

Reference	Group	Pain	Allodynia	Hyperesthesia	Temperature Disturbance	Discoloration	Edema	Altered Sweating	Reduced Strength
De Boer et al[14]	<2 mo	85%	31%	21%	68%	62%	60%	31%	33%
	2–6 mo	87%	28%	28%	58%	65%	45%	18%	43%
	6–12 mo	93%	41%	39%	57%	62%	49%	20%	52%
	≥12 mo	95%	45%	41%	51%	48%	38%	20%	67%
	Between-group differences	*	*	*	ns	*	*	ns	*
Veldman et al[47]	<2 mo	92%		69%	98%	97%	86%	57%	
	2–6 mo	88%		75%	91%	96%	80%	56%	
	6–12 mo	97%		72%	89%	90%	61%	42%	
	≥12 mo	97%		85%	91%	84%	55%	40%	
Schwartzman et al[41]		NRS correlated with duration (r = 0.6*), SF-McGill did not correlate with duration (ns).	Intensity of touch allodynia correlated with duration (r = 0.5*)	n/a	% with temperature disturbance in each category correlated with duration (r = 0.4*)	% with color disturbance in each category correlated with duration (r = 0.5*)	% with edema in each category correlated with duration (r = 0.5*)	No correlation between % with altered sweating in each category and duration (r = 0.2, ns)	No correlation between % with loss of strength in each category and duration (r = 0.2, ns)

Abbreviations: ns, not significant; NRS, numerical rating scale; SF-McGill, Short-Form McGill Pain Questionnaire.
*$P < .01$ (statistically significant difference).

brief syndrome (with some sequelae such as weakness and stiffness) whereas others experience lasting pain and symptoms. Interestingly, studies have documented high prevalence rates for CRPS after events such as fracture or surgery (up to 36%),[4,27,37,43] and it might be that having features of CRPS briefly after such events is quite common; nevertheless, many symptoms resolve spontaneously, as was found by Zyluk.[49] However, in severe cases of CRPS, disability may last years,[41] and invasive treatments such as spinal cord stimulation[42] or amputation[9] are performed. This suggests that there is huge variability in the course of CRPS and lends support to the idea the subtypes of CRPS patients might exist. Two studies[11,15] performed cluster analyses and showed that there were 3 subtypes of CRPS patients, including a group with florid symptoms across all categories. De Mos et al[15] showed that this group experienced the poorest outcomes. Clinically, it would be useful to be able to identify those at risk of poor outcomes early in the trajectory of their CRPS, so that treatments can be targeted for these individuals.

Relatively few studies have assessed prognostic factors in CRPS, and a recent systematic review concluded that there were few quality studies and most of the evidence on prognostic factors is contradictory, although they did identify that sensory disturbance and cold skin temperature are associated with poor outcomes.[48] The studies included in this review listed the following prognostic factors associated with poor outcome: longer pain duration,[31,34] more intense pain,[20] delay to receive treatment,[7,19] male sex,[7] female sex,[25] younger age,[7] a more severe fracture, poorer grip strength, and low mobility.[32] The following have been reported to predict good outcome: having a fracture as the initiating event, the absence of sensory symptoms, the presence of swelling,[38] having a warm limb in the early stages, no delay between the injury and CRPS onset,[7] and having a single joint involved.[25] Research in other pain conditions has identified the importance of psychosocial factors for predicting the transition from acute to chronic pain. For example, factors such as depression, expectations, pain-related fear, and avoidance of movement predict poor outcome in low back pain.[13,30] As yet, it appears that little research has assessed whether psychological factors predict the transition from the acute to the chronic stages in CRPS. Although studies that have assessed whether psychosocial factors predict the onset of CRPS after fracture or surgery have produced mixed results,[5,16,27,29,36] future researchers may wish to assess the role of such factors in CRPS recovery. Another factor that has been shown to predict CRPS following fracture and CRPS recurrence following surgery is activity of the sympathetic nervous system.[1,40] It may also be valuable to assess whether sympathetic nervous system activity predicts the course or outcome of the condition.

Limitations

This review highlighted several limitations in the literature. At the most, 3 studies agreed on a diagnostic criteria,[14,15,21] and many studies either followed their own criteria or did not describe them. Although considerable efforts have been made by researchers to develop a common name (ie, "complex regional pain syndrome") and diagnostic criteria (eg, the 1994 IASP criteria and the "new IASP" or "Budapest criteria"), even some studies published since this time have not used these terms or criteria. The differences in the criteria used, not to mention the way such criteria are interpreted, likely contributed to the variation in study results. For example, many studies assessing "algodystrophy" reported more favorable outcomes than those assessing RSD or CRPS. As the diagnostic criteria for algodystrophy often required fewer signs and symptoms or did not require the presence of pain,[3,32] this suggests that those with a more limited set of symptoms at the outset might make a fuller recovery. A recently published study that used the stricter Budapest diagnostic criteria found that of those with CRPS-1 after fracture, none were symptom-free at 12 months.[6] This study did not meet the inclusion criteria for this systematic review and only briefly mentions its 12-month outcome data, but it does contrast strongly with the positive data reported by the 3 prospective studies included in this review, which all used "looser" diagnostic criteria. It is important that future research use a common diagnostic criteria for CRPS, and that researchers adopt a consistent set of measurement tools for assessing the signs and symptoms of CRPS.

Another major finding of this review was that the literature as a whole suffers from several sources of bias, and higher-quality studies are needed to understand the outcomes of CRPS. First, few studies included samples that could be considered "representative" of the CRPS population as a whole, and many did not adequately describe their recruitment processes. Future studies should seek to recruit from a wide variety of settings to include a broad range of CRPS patients and should state whether samples are consecutive patients or selected in another manner. Even when such processes were described, the samples recruited were often unrepresentative. For example, 2 studies recruited only patients who had previously responded well to treatment,[39,50] which would be expected to bias results, and another study excluded severe cases who had to withdraw for treatment.[49] Second, several studies suffered from high attrition or low response rates. This is particularly problematic where there is a difference between those who do and those who do not participate. It is possible that those who have recovered would be less inclined to complete a follow-up than those who are still symptomatic and therefore motivated to support research into their condition. Future studies should try to reduce barriers to participation to ensure adequate participant recruitment and retention. The other limitations of the literature included differences in measurement tools used and lack of relevant statistical testing. Also, the review process was limited in that we used just 1 reviewer to search the literature, with a second reviewer assessing suitability for inclusion when there was any doubt.

In conclusion, we found evidence from prospective studies that the rates of symptoms of CRPS reduce significantly over the first 6 to 13 months, but the results from retrospective studies indicate that the outcomes of CRPS are highly variable, and the cross-sectional studies demonstrate that there are a group of patients for whom pain and sensory symptoms persist in the long term. Overall, the quality of the evidence was poor, and the data should be interpreted with caution. At present, there are few studies that have assessed prognostic factors in CRPS, and such studies could help to identify those at risk of poor outcomes as well as help researchers identify possible target variables for treatment.

Supplementary Data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jpain.2014.01.500.

References

1. Ackerman WE 3rd, Ahmad M: Recurrent postoperative CRPS I in patients with abnormal preoperative sympathetic function. J Hand Surg Am 33:217-222, 2008

2. Altman DG: Systematic reviews of evaluations of prognostic variables. BMJ 323:224-228, 2001

3. Atkins RM, Duckworth T, Kanis JA: Algodystrophy following Colles' fracture. J Hand Surg 14:161-164, 1989

4. Atkins RM, Duckworth T, Kanis JA: Features of algodystrophy after Colles' fracture. J Bone Joint Surg Br 72:105-110, 1990

5. Beerthuizen A, Stronks DL, Huygen FJPM, Passchier J, Klein J, Spijker AV: The association between psychological factors and the development of complex regional pain syndrome type 1 (CRPS1)—A prospective multicenter study. Eur J Pain 15:971-975, 2011

6. Beerthuizen A, Stronks DL, Van't Spijker A, Yaksh A, Hanraets BM, Klein J, Huygen FJPM: Demographic and medical parameters in the development of complex regional pain syndrome type 1 (CRPS1): Prospective study on 596 patients with a fracture. Pain 153:1187-1192, 2012

7. Bejia I, Khalifa AB, Salah ZB, Bejaoui S, Touzi M, Bergaoui N: Predictifs factors of the algodystrophy evolution in a rheumatology department among 60 cases [in French]. Tunis Med 83:163-167, 2005

8. Bickerstaff DR, Kanis JA: Algodystrophy: An underrecognized complication of minor trauma. Br J Rheumatol 33:240-248, 1994

9. Bodde MI, Dijkstra PU, den Dunnen WFA, Geertzen JHB: Therapy-resistant complex regional pain syndrome type I: To amputate or not? J Bone Joint Surg Am 93:1799-1805, 2011

10. Bonica JJ: Causalgia and other reflex sympathetic dystrophies, in Bonica JJ (ed): Management of Pain. Philadelphia, Lea & Feibiger, 1990, pp 220-243

11. Bruehl S, Harden RN, Galer BS, Saltz S, Backonja M, Stanton-Hicks M: Complex regional pain syndrome: Are there distinct subtypes and sequential stages of the syndrome? Pain 95:119-124, 2002

12. Centre for Reviews and Dissemination: Systematic Reviews: CRD's Guidance for Undertaking Reviews in Health Care. York, CRD, University of York, 2009

13. Chou R, Shekelle P: Will this patient develop persistent disabling low back pain? JAMA 303:1295-1302, 2010

14. De Boer RDH, Marinus J, Van Hilten JJ, Huygen FJ, Van Eijs F, Van Kleef M, Bauer MCR, Van Gestel M, Zuurmond WWA, Perez RSGM: Distribution of signs and symptoms of complex regional pain syndrome type I in patients meeting the diagnostic criteria of the International Association for the Study of Pain. Eur J Pain 15: 830.e1-830.e8, 2011

15. de Mos M, Huygen FJPM, van der Hoeven-Borgman M, Dieleman JP, Ch Stricker BH, Sturkenboom MCJM: Outcome of the complex regional pain syndrome. Clin J Pain 25: 590-597, 2009

16. Dilek B, Yemez B, Kizil R, Kartal E, Gulbahar S, Sari O, Akalin E: Anxious personality is a risk factor for developing complex regional pain syndrome type I. Rheumatol Int 32: 915-920, 2012

17. Duman I, Dincer U, Taskaynatan MA, Cakar E, Tugcu I, Dincer K: Reflex sympathetic dystrophy: A retrospective epidemiological study of 168 patients. Clin Rheumatol 26: 1433-1437, 2007

18. Dumas S, Pichon B, Dapolito AC, Bensefa-Colas L, Andujar P, Villa A, Descatha A: Work prognosis of complex regional pain syndrome type I: Multicenter retrospective study on the determinants and time to return to work. J Occup Environ Med 53:1354-1356, 2011

19. Ehrler S, Didierjean A, Foucher DG: The prognosis of algodystrophic syndrome of the hand. Late results in 47 patients [in French]. Ann Chur Main Memb Super 14:109-110, 1995

20. Fialka V, Zifko I, Bochdansky T, Schneider B, Schimmerl S: Late sequelae of reflex sympathetic dystrophy: Results of clinical, scintigraphic and dynamometric investigations. Eur J Phys Rehabil Med 3:59-64, 1991

21. Galer BS, Henderson J, Perander J, Jensen MP: Course of symptoms and quality of life measurement in complex regional pain syndrome: A pilot survey. J Pain Symptom Manage 20:286-292, 2000

22. Geertzen JH, Dijkstra PU, Groothoff JW, ten Duis HJ, Eisma WH: Reflex sympathetic dystrophy of the upper extremity—A 5.5-year follow-up. Part I. Impairments and perceived disability. Acta Orthop Scand Suppl 279:12-18, 1998

23. Geertzen JH, Dijkstra PU, van Sonderen EL, Groothoff JW, ten Duis HJ, Eisma WH: Relationship between impairments, disability and handicap in reflex sympathetic dystrophy patients: A long-term follow-up study. Clin Rehabil 12:402-412, 1998

24. Goris RJA, Leixnering M, Huber W, Figl M, Jaindl M, Redl H: Delayed recovery and late development of complex regional pain syndrome in patients with an isolated fracture of the distal radius: Prediction of a regional inflammatory response by early signs. J Bone Joint Surg Br 89:1069-1076, 2007

25. Gougeon J, Eschard JP, Moreau Hottin J: Reflex dystrophies: Course, polyarticular forms and recurrent forms [in French]. Rev Rhum Mal Osteoartic 49:809-814, 1982

26. Harden RN, Bruehl S, Perez RSGM, Birklein F, Marinus J, Maihofner C, Lubenow T, Buvanendran A, Mackey S, Graciosa J, Mogilevski M, Ramsden C, Chont M, Vatine J-J: Validation of proposed diagnostic criteria (the "Budapest criteria") for complex regional pain syndrome. Pain 150: 268-274, 2010

27. Harden RN, Bruehl S, Stanos S, Brander V, Chung OY, Saltz S, Adams A, Stulberg SD: Prospective examination of pain-related and psychological predictors of CRPS-like phenomena following total knee arthroplasty: A preliminary study. Pain 106:393-400, 2003

28. Hayden JA, Cote P, Bombardier C: Evaluation of the quality of prognosis studies in systematic reviews. Ann Intern Med 144:427-437, 2006

29. Hootkani AR, Fayyazi MRF, Hasankhani EG: Relationship between anxiety, depression, and personality type and the incidence of reflex sympathetic dystrophy in patients with distal radius fracture. Iran J Med Sci 33:74-78, 2008

30. Iles RA, Davidson M, Taylor NF, O'Halloran P: Systematic review of the ability of recovery expectations to predict outcomes in non-chronic non-specific low back pain. J Occup Rehabil 19:25-40, 2009

31. Katz MM, Hungerford DS: Reflex sympathetic dystrophy affecting the knee. J Bone Joint Surg Br 69:797-803, 1987

32. Laulan J, Bismuth JP, Sicre G, Garaud P: The different types of algodystrophy after fracture of the distal radius. Predictive criteria of outcome after 1 year. J Hand Surg 22: 441-447, 1997

33. Merskey H, Bogduk N: Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms, 2nd ed. Seattle, IASP Press, 1994

34. Ogilvie-Harris DJ, Roscoe M: Reflex sympathetic dystrophy of the knee. J Bone Joint Surg Br 69:804-806, 1987

35. Pak TJ, Martin GM, Magness JL, Kavanaugh GJ: Reflex sympathetic dystrophy. Review of 140 cases. Minn Med 53: 507-512, 1970

36. Puchalski P, Zyluk A: Complex regional pain syndrome type 1 after fractures of the distal radius: A prospective study of the role of psychological factors. J Hand Surg 30:574-580, 2005

37. Roumen RM, Hesp WL, Bruggink ED: Unstable Colles' fractures in elderly patients. A randomised trial of external fixation for redisplacement. J Bone Joint Surg Br 73: 307-311, 1991

38. Sandroni P, Benrud-Larson LM, McClelland RL, Low PA: Complex regional pain syndrome type I: Incidence and prevalence in Olmsted county, a population-based study. Pain 103:199-207, 2003

39. Savas S, Baloglu HH, Ay G, Cerci SS: The effect of sequel symptoms and signs of complex regional pain syndrome type 1 on upper extremity disability and quality of life. Rheumatol Int 29:545-550, 2009

40. Schurmann M, Gradl G, Zaspel J, Kayser M, Lohr P, Andress HJ: Peripheral sympathetic function as a predictor of complex regional pain syndrome type I (CRPS I) in patients with radial fracture. Auton Neurosci 86:127-134, 2000

41. Schwartzman RJ, Erwin KL, Alexander GM: The natural history of complex regional pain syndrome. Clin J Pain 25: 273-280, 2009

42. Sears NC, Machado AG, Nagel SJ, Deogaonkar M, Stanton-Hicks M, Rezai AR, Henderson JM: Long-term outcomes of spinal cord stimulation with paddle leads in the treatment of complex regional pain syndrome and failed back surgery syndrome. Neuromodulation 14:312-318, 2011 [discussion 318]

43. Sennwald GR: Fasciectomy for treatment of Dupuytren's disease and early complications. J Hand Surg Am 15:755-761, 1990

44. Sharma A, Agarwal S, Broatch J, Raja SN: A web-based cross-sectional epidemiological survey of complex regional pain syndrome. Reg Anesth Pain Med 34:110-115, 2009

45. Subbarao J, Stillwell GK: Reflex sympathetic dystrophy syndrome of the upper extremity: Analysis of total outcome of management of 125 cases. Arch Phys Med Rehabil 62: 549-554, 1981

46. van Rijn M, Marinus J, Putter H, Bosselaar S, Moseley G, van Hilten J: Spreading of complex regional pain syndrome: Not a random process. J Neural Transm 118:1301-1309, 2011

47. Veldman PH, Reynen HM, Arntz IE, Goris RJ: Signs and symptoms of reflex sympathetic dystrophy: Prospective study of 829 patients. Lancet 342:1012-1016, 1993

48. Wertli M, Bachmann LM, Weiner SS, Brunner F: Prognostic factors in complex regional pain syndrome 1: A systematic review. J Rehabil Med 45:225-231, 2013

49. Zyluk A: The natural history of post-traumatic reflex sympathetic dystrophy. J Hand Surg 23:20-23, 1998

50. Zyluk A: The sequelae of reflex sympathetic dystrophy. J Hand Surg 26:151-154, 2001