

Complex Regional Pain Syndrome (CRPS)

What does the literature report regarding the time interval between the inciting trauma and its subsequent diagnosis?

By

WorkSafeBC Evidence-Based Practice Group

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About this report

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The Evidence-Based Practice Group was established to address the many medical and policy issues that WorkSafeBC officers deal with on a regular basis. Members apply established techniques of critical appraisal and evidence-based review of topics solicited from both WorkSafeBC staff and other interested parties such as surgeons, medical specialists, and rehabilitation providers.

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Question

What evidence is there in the literature on the time interval between trauma and the subsequent diagnosis of Complex Regional Pain Syndrome (CRPS)?

Methods

- A systematic literature search was conducted on April 7, 2010.
- The search was conducted on commercial medical databases, including BIOSIS Previews, EMBASE, Ovid MEDLINE and Ovid MEDLINE Daily Update, which are available through the OvidSP Interface.
- Combination keywords employed in this search included ((complex regional pain syndrome) OR crps OR causalgia OR (reflex sympathetic dystrophy) OR (sudeck atrophy)) AND (onset or (delayed onset)). The search was only limited to studies in humans. One hundred ninety-eight studies⁽¹⁻¹⁹⁸⁾ were identified through this search.
- Upon examination of titles and abstracts of these studies,⁽¹⁻¹⁹⁸⁾ thirteen^(11,13,15,26,28,45,55,70,74,88,126,142,174) articles were retrieved in full for further appraisal.
- Manual searching was also done on the references of the fully retrieved articles.^(11,13,15,26,28,45,55,70,74,88,126,142,174) Fifteen articles^(199-201,203-205,207-215) were retrieved in full as the result of this manual searching.
- A chapter on CRPS⁽²⁰²⁾ written in the textbook “Bonica’s Management of Pain” was also consulted.

Results

- Of the 29 studies/chapters retrieved in full,^(11,13,15,26,28,45,55,70,74,88,126,142,174,199-205, 207-215) sixteen studies^(11,45,55,70,74,126,142,174,204,205,207,209-212,215) provided data relevant to assessing the time interval between injury and the onset of CRPS and are discussed further. Levels of evidence are assigned to these articles as part of our review process.
 1. Arden et al.⁽¹¹⁾ reported two cases (level of evidence 5. Appendix 1) of facial reflex sympathetic dystrophy (CRPS) following vascular surgery of the neck. Two 69-year-old men who underwent transposition of the right external carotid artery developed symptoms that were considered to be CRPS at approximately one month post surgery. The authors also undertook a limited literature search in an effort to find similar cases of facial CRPS. Eight more cases of facial CRPS were found in which the duration between injury/tissue insult and diagnosis ranged from almost immediately to up to 3 months post injury.
 2. Demun et al.⁽⁴⁵⁾ reported a single case of CRPS due to minor electric shock (level of evidence 5. Appendix 1). The progressive onset of paraesthesia and swelling of the hand occurred at five days post injury, at which point a diagnosis of CRPS was made.

3. In his attempt to calculate the incidence of CRPS in the North Manchester district of England, Dunningham⁽⁵⁵⁾ reported on 18 cases of CRPS diagnosed between January 1976 and January 1979. This level 5 evidence paper (Appendix 1) clearly reported the baseline population from which the CRPS patients were diagnosed. The data provided by these 18 cases revealed a mean onset of CRPS of 18 weeks post injury (range: 8 – 52 weeks).
4. Based on a trauma center patient population, Gradl and Schürmann⁽⁷⁰⁾ reported 10 cases of CRPS (level of evidence 5. Appendix 1) following upper limb trauma or surgery. On average, these patients were thought to fulfill the diagnostic criteria of CRPS as proposed by Bruehl et al.⁽²¹⁶⁾ by day 63 post trauma (range: 46-72 days).
5. Okabayashi et al.⁽¹²⁶⁾ reported the onset of symptoms in 36 patients diagnosed with CRPS (type I or II) (level of evidence 5. Appendix 1). They observed that within < 1 month 78% of patients already developed allodynia. Further specific data from this paper is unavailable.
6. In another small case series (n=39 patients) (level of evidence 5. Appendix 1) from a clearly defined population of military personnel with trauma induced peripheral nerve injuries, Roganovic et al.⁽¹⁴²⁾ reported that on average (mean±SD) signs and symptoms of CRPS could be observed as early as 2.6±2.8 days post injury in this population.
7. In a further case series (n=17) (level of evidence 5. Appendix 1) with a clearly defined population, Tountas and Noguchi⁽¹⁷⁴⁾ reported the average delay between injury and the clinical manifestation of CRPS was 2.5 months (range: from 2 days to almost 6 months).
8. Zyluk⁽²⁰⁴⁾ reported on 30 patients diagnosed with CRPS (level of evidence 5. Appendix 1). In this study, the first diagnosis of CRPS was made from 2 to 10 months after the initial injury.
9. In an abstract presentation,⁽²⁰⁵⁾ Zyluk and Puchalski reported on how soon after a traumatic event the diagnosis of CRPS could be made. The authors concluded that, among 64 patients reviewed (level of evidence 5. Appendix 1), the clinical diagnosis of CRPS could be made at 1 week post injury in 34% of patients, at 3 weeks in 72% of patients, and at 4 weeks in 83% of patients. However, 17% of patients first showed clinical features of CRPS later than 1 month post injury (*the abstract did not provide detailed observations and we were not able to translate the full publication of this abstract presentation*).⁽²⁰⁶⁾
10. In their attempt to investigate the incidence of CRPS after distal radial fracture, Dijkstra et al.⁽²⁰⁷⁾ reported on the development of one case of CRPS (level of evidence 5. Appendix 1) seven weeks post fracture.
11. Based on a medical records review, Geertzen et al.⁽²⁰⁹⁾ presented 65 patients (level of evidence 5. Appendix 1) diagnosed with upper extremity CRPS. In this group

- of patients, the mean interval between injury and diagnosis of CRPS was 2.3 months (range: 1-5 months). Seventy-four percent of these patients were diagnosed and treated for CRPS within 2 months post injury while 26% were diagnosed and treated for CRPS between 2-5 months post injury.
12. In their prospective study among patients with Colles' fractures, Atkins et al.⁽²¹⁰⁾ reported the incidence of CRPS post fracture. Among 59 Colles' fracture patients in this series, 23 were thought to be clinically suffering from CRPS (level of evidence 5. Appendix 1). Even though the authors did not explicitly provide data on the duration of CRPS onset in this subset of patients, this data can be inferred from Table 1 in their paper⁽²¹⁰⁾ which shows that, at most, the diagnosis of CRPS was made on average at 8.2 weeks (SD 2.1 weeks) post injury.
 13. In their well defined case series (n=23) (level of evidence 5. Appendix 1) measuring the tightness of plaster casts, Field et al.⁽²¹¹⁾ reported that six of the 23 patients developed CRPS. Clinical features of CRPS were observed by nine weeks post injury. The authors reported no data beyond this time period.
 14. Veldman, one of the experts attempting to standardize the diagnostic criteria of CRPS,⁽²¹⁶⁾ reported the signs and symptoms that were thought to be observed or relevant in the diagnosis of CRPS patients in a large series of patients (n=829) (level of evidence 5. Appendix 1).⁽²¹²⁾ With regard to the time interval between injury and onset of these signs and symptoms, Veldman and Reynen⁽²¹²⁾ reported that signs and symptoms relevant to CRPS were observed within 1 day in 75% of patients. Further, the authors stated that in 7 patients, in whom signs and symptoms were observed greater than one year post injury, the association between injury event and diagnosis of CRPS may well be questionable.
 15. Another large case series (n=506) (level of evidence 5. Appendix 1) of CRPS patients from a well defined population was reported by Kleinert et al.⁽²¹⁵⁾ Kleinert et al.⁽²¹⁵⁾ reported that 57% of cases reported onset of CRPS symptoms in less than 1 month post injury, 23% between 1 to 3 months post injury, 10% between 3 to 6 months post injury and only 10% reported onset of symptoms over 6 months after the inciting trauma.
 16. Hassantash et al.⁽⁷⁴⁾ conducted a meta-analysis of the literature (level of evidence 1. Appendix 1) with the aim of providing a better definition of CRPS type II. In this meta-analysis, the authors assembled data on 1528 patients who were diagnosed with CRPS type II. With regard to the onset of allodynia from the time of injury, the authors found that in 34% of patients it occurred immediately to 1 day post injury, 10% between 1-7 days, 11% from 7 days to 1 month, and only 6% reported it to occur after longer than 1 month post injury. *It should be noted that the primary studies included in this meta-analysis were in the form of case reports or case series* (level of evidence 5. Appendix 1), *further, there was some discrepancy in the reported number of studies selected and included in this meta-*

analysis (110 or 37 primary studies?) Given the fact that it is very likely that the primary studies included in this meta-analysis employed different diagnostic criteria for CRPS type II, it is not clear whether such a meta-analysis was warranted with such a heterogenic study population.

Summary/Conclusion

- Data gathered from primary studies^(11,45,55,70,74,126,142,174,204,205,207,209,211,211,212,215) and one “meta-analysis”⁽⁷⁴⁾ in this systematic review provide us some evidence that signs and symptoms of CRPS may initially develop at up to 6 months post injury. Two studies stated that 10% (52 cases)⁽²¹⁵⁾ and 1% (7 cases)⁽²¹²⁾ of patients experienced the onset of symptoms at over 6 months post injury. Further, it should be noted that Veldman,⁽²¹²⁾ a well known expert in CRPS, discounted any potential causal association between an inciting injury and CRPS when there was a time lag of over one year.

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Appendix 1

WorkSafeBC Evidence-Based Practice Group levels of evidence ^(adapted from 1,2,3,4)

1	Evidence from at least 1 properly randomized controlled trial (RCT) or systematic review of RCTs.
2	Evidence from well-designed controlled trials without randomization or systematic reviews of observational studies.
3	Evidence from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.
4	Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments could also be included here.
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

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Appendix 2

Flow diagram (Study selection)

