Review Article

# Physical Medicine and Rehabilitation for Complex Regional Pain Syndromes

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## ABSTRACT

Complex Regional Pain Syndrome (CRPS) is a common clinical presentation characterized by a combination of pain, sensory, autonomic, motor, or trophic symptoms that can no longer be attributed to the initial trauma. These signs and symptoms are not localized to the areas of innervation and may include difficulties with mobility, fluctuating skin temperature, sensory loss, and changes in body perception. The diagnosis of CRPS is primarily clinical and in acute phases. Several tests can be useful in determining the diagnosis of CRPS like Thermography, Sweat Testing, Radiographic Testing, Electro-diagnostic Testing and Sympathetic Blocks. Pharmaceutical treatment can be highly beneficial. The most used medicines like Transdermal lidocaine, opioids, antidepressants, anti-inflammatory medications, anticonvulsants, and bisphosphonates. However, physical therapy, rehabilitation therapy, and behavioral therapy are also essential components of the treatment. The purpose of Physical and Occupational Therapy is to help the patient reduce discomfort and enhance mobility while also enhancing the functioning and range of motion of the affected extremity. This article aims to provide a comprehensive summary and critical evaluation to explain the physical therapy and rehabilitation in the treatment of CRPS, as well as a detailed explanation of the importance of these therapeutic approaches in managing and alleviating the symptoms associated with Complex Regional Pain Syndrome.

**Keyword:** Complex regional pain syndrome, Reflex Sympathetic Dystrophy, Rehabilitation.

## Introduction

The term Complex Regional Pain Syndrome (CRPS) describes a collection of clinical manifestations marked by excruciating, continuous pain that is unbearable, independent of any prior injury, and not restricted to the area supplied by a single peripheral nerve [1]. Additionally, it is a condition that progresses and is characterized by excruciating pain, edema, and skin abnormalities. Most frequently, CRPS affects one of the hands, feet, legs, arms, or arms and legs, with pain frequently expanding to the full arm and leg [2]. The wounded limb is usually Where symptoms first appear, although they can also affect other parts of the body and include edema, skin discoloration, aberrant hair or nail development, and dystonia [1]. Although there are little reliable data, it is estimated that there are 5.4 to 26.2 cases of CRPS for every 100,000 person per year [3]. Nearly, 3.8% of the individuals who are harmed, or patients, get it following a fractured wrist [4]. Although the exact origin of CRPS is unknown, the general agreement is that it includes an abnormal inflammatory response together with dysfunction of the autonomic and central

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Nervous systems [5]. The effects on the victims might be quite bad. People with CRPS typically can't use their afflicted limbs, and their capacity to work or engage in communal activities is harshly limited. As a result, their quality of life (QoL) significantly declines, and concomitant depression is quite prevalent [6]. CRPS is composed of two types: Reflex sympathetic dystrophy syndrome, or Type I, develops after a sickness or accident directly damages the nerves in your afflicted limb; causalgia, or Type II, develops after a specific nerve lesion. Type I CRPS sufferers account for around 90% of all cases. After a severe injury to the arm or leg, CRPS patients are common [6]. Since CRPS diagnosis lacked specificity and internal validity, the criterion for diagnosis that the International Association for the Study of Pain (IASP) first established have not been generally adopted [7]. The Budapest criteria have improved diagnostic precision and are currently well-liked. Uncertainties exist about the pathophysiological pathways causing CRPS [6]. According to current research, several processes are involved, including complicated contributions from an unfavorable pro-inflammatory response, a problem with sympathetically mediated vasomotor regulation, unfavorable peripheral and central neural plasticity, and others [7]. The UK Register office statistics indicates that CRPS patients are likely to have uneven care paths, numerous appointments, and frequently subpar results since CRPS is notoriously difficult to manage [8]. In the past five years, the United States of America (USA), the Netherlands, and the United Kingdom (UK) have all produced international clinical recommendations for CRPS [9]. All these recommendations are in favor of using rehabilitation therapy as the primary CRPS treatment, according to published data, expert clinical opinions and interest group perspectives. A wide variety of potential treatment approaches are provided therein, with considerable variations in substance amongst recommendations. Notwithstanding these guidelines, a new Cochrane analysis of CRPS physiotherapy treatments [10] revealed a dearth of multimodal physiotherapy studies, with the majority of the data coming from small trials of single modality interventions. In our research, we explore to provide a general review of CRPS and assess the effectiveness of physical therapy and rehabilitation in the management of CRPS.

## Methods

Study Design: Review article. Study duration Data was collected between 1 June, 2023 and 30 November 2023.

Data collection Medline and PubMed public database searches was carried out for papers written all over the world on complex regional pain syndrome. The keyword search headings included “Complex regional pain syndrome, Reflex Sympathetic Dystrophy, Rehabilitation”, and a combination of these were used. For additional supporting data, the sources list of each research was searched. Criteria of inclusion: the papers were chosen based on the project importance, English language, and 20 years’ time limit. Criteria for exclusion: all other publications that do not have their main purpose in any of these areas or multiple studies and reviews was excluded.

***Statistical Analysis***

No predictive analytics technology was used. To evaluate the initial results and the methods of conducting the surgical procedure, the group members reviewed the data. The validity and minimization of error was double revised for each member's results.

## Results

Epidemiology: In 2016, the USA published the largest population-based study on CRPS to date. An analysis of the Nationwide Inpatient Sample database from 2007 to 2011 in retrospect showed that 22,533 patients, or 0.07%, of the 33,406,123 total study participants, were given a CRPS diagnosis and released. Women's ethnicity, Caucasian ethnicity, greater average family income, and the occurrence of morbid characters including sadness, drug usage, and headaches were all related with CRPS in the population. Lower incidence of CRPS were linked to ailments including anemia, hypothyroidism, diabetes, obesity, and other conditions [11]. In smaller research that analysed 6,575,999 patients in the Truven Market Scan Commercial and Medicare Supplemental database from 2000 to 2012, the overall prevalence of CRPS was found to be somewhat higher, at 1.2%. Positive correlations were found between long-term incapacity, female gender, and several pain diagnoses [12]. Moreover, a different examination of the same database showed that CRPS patients significantly used and spent more money on healthcare 1 year before and during the diagnosis [13]. It's crucial to remember that CRPS is not just an adult diagnosis, but there isn't much information available on how to diagnose and treat the pediatric population [14]. Pediatric patients with CRPS are the topic of a 2021 comprehensive review by Karri et al. [14], which also takes into account neuro-modulation, a well-known adult therapy choice. In order to enhance the patient's QoL, pain alleviation, and functional improvement are the major therapeutic objectives for CRPS in children. Therapy may involve both intense physical therapy and cognitive behavioral therapy [15]. Under the standard of care approach, pediatric patients may be considered for several therapies, including neuro-

modulation techniques like spinal cord stimulation (SCS) or dorsal root ganglion stimulation (DRG) devices. Before installing a device lead.
Developmental and Prognostic Factors: Complex regional pain syndrome often appears following an injury to one or more of the limbs. The "normal" duration for injury recovery determines how long it takes between the injury and the first diagnosis of CRPS. Recovery from a simple radial fracture normally takes 4 to 6 weeks. Complex injuries require more time to heal. The majority of victims appear to be females between the ages of 40 and 60. The fact that women have 3 times as many radial fractures as males does, however, suggest that the female preponderance may potentially be an artifact [16]. Patients with difficult fractures, rheumatologic conditions, or severe pain one week after trauma appeared to be at increased risk of developing CRPS. According to epidemiological statistics, there were between 5.5 and 26.2 new cases of CRPS for every 100,000 persons per year. The variance might be caused by the use of various diagnostic standards. The verified "Budapest Criteria" have only recently gained widespread acceptance [17]. In a longitudinal research about the prognosis, Bean et al.[18] found that 70% of the patients saw improvements within the first year, particularly in the role of the affected extremities and the visual signs (edema, skin tone, and sweating). Of the patients, 25% still satisfied the Budapest Criteria, and just 5% had no complaints. After one year, the long-term results for patients who reported greater levels of anxiety and pain-related concern at the start of therapy were poorer.
Diagnosis: In the past, Reflex Sympathetic Dystrophy (RSD) and Causalgia were the most common labels used to describe Complex Regional Pain Syndrome (CRPS). Both phrases are still occasionally misused, and neither has any established diagnostic standards [19]. The term "CRPS" was coined at an international conference that took place in Orlando, Florida, in 1994 [20] and resulted in the International Association for the Study of Pain (IASP) adopting the first consensus-based diagnostic criteria for CRPS [21]. These 1994 IASP criteria for CRPS were important and necessary, but it became evident that such preliminary consensus-based criteria needed to be modified and validated through systematic validation research, based on knowledge gained from developing and continuously improving diagnostic criteria for psychiatric and headache disorders. To this end, many validation experiments were conducted, culminating in an empirically established set of CRPS criteria (called the Budapest Criteria) that the IASP committee on taxonomy formally recognised as the new IASP criteria in 2012. Building validated and therapeutically relevant criteria became more challenging since the underlying mechanisms and clinical presentation of CRPS might change over time in individuals, even within a single patient [22].
Clinical Symptoms: The most significant symptom of CRPS is pain. It occurs often in the deep tissue and may be constant or cyclical. According to the authors' experience, allodynia is a defining characteristic, particularly in chronic and severe instances, and it worsens with movement and during temperature changes [23]. In addition, sensory abnormalities such as hypoesthesia and impaired heat perception following a glove- or stocking-like design are documented. Some patients claim to feel as though their extremities is no longer a part of their body. All patients have weakened muscles and likely avoid activity out of pain. Contractures progress rapidly. Although the loss of strength and the movement restriction they get better with less discomfort, contractures occasionally get better slowly but don't go away [17]. Inadequately managed acute CRPS, sufferers are more likely to experience tendon and capsule shortening and fibrosis. This could occur in some circumstances, regardless of the course of treatment. Other trophic changes can be seen in the nails, hair, and skin, such as ulcers, increased and reduced hair growth in acute and chronic CRPS, respectively [17]. Edema, which invariably occurs in the acute phase and can expand to spectacular extents, is the primary indication of vascular dysfunction. Patients with persistent CRPS are frequently overestimate the thickness of their own extremities. A hyperhidrosis is the most common sudomotor problem affecting 50% of the patients. The skin color of all patients changes from reddish color (warm CRPS) to blueish livid color (cold CRPS). When contrasting the two sides, the skin temperatures are different. Tremor, myoclonus, and fixed dystonia are more uncommon [18].
Diagnostic Testing: Several tests can be helpful in determining the diagnosis of CRPS even though there is no particular diagnostic test for this disorder. However, the most crucial function of testing is helping rule out other cases [24].
Thermography: Several symmetrical sites on the afflicted and contralateral extremities are measured using an infrared thermometer (accuracy of 0.1°C), allowing comparisons between the 2 extremities. A difference of 0.5°C is often regarded as somewhat asymmetrical in a thermo-neutral environment, whereas a difference of 1.0°C is seen as substantial. If there are several asymmetrical skin temperature sites present, this test's diagnostic value rises. Also, it observed if the injured limb is warmer or cooler than the unaffected limb. Skin temperature is dynamic, therefore the diagnosis of CRPS is not always ruled out by symmetrical thermo-graphic data [25].

Sweat Testing: Several tests that assess sweat output can be used to determine whether a patient has sudomotor dysfunction, which is frequent in CRPS patients. An indicator-starch powder can be used to assess subjective sweat on the limbs. As the limb perspires, the indicator changes color. It has been demonstrated that quantitative sweat testing corresponds with CRPS clinical symptoms [26]. Two useful procedures that assess the sweat productivity of the afflicted and unaffected limbs are the quantitative sudomotor axon reflex test and the resting sweat output test [27]. The test for resting sweat output is used to measure the amount of perspiration produced by the limbs when they are at rest, as its name suggests. A provocative test called the measurements of the quantified sudomotor axon reflex the amount of sweat produced while encountering a cholinergic iontophoresis challenge, such as acetylcholine or methacholine [26].

Radiographic Testing: As early as two weeks following the beginning of CRPS, plain radiographs might reveal patchy osteoporosis [25]. This conclusion might be influenced by the extremity's inactivity and immobilization. Bony formations may seem like diffuse ground glass as CRPS worsens, and cortical erosions may also be seen [24]. Using technetium Labelled Tc 99m bisphosphonates to do a 3-phase bone scan of the afflicted extremity is a highly sensitive (albeit very nonspecific) diagnostic that might identify osseous alterations earlier than plain radiography. The three phases of the blood phase, blood pool, and scan phase all show enhanced periarticular uptake as classic results; however, in certain cases, a reverse or mixed pattern is observed [25]. The patient's symptoms' duration has an impact on this variability. In afflicted limbs, bone densitometry frequently shows decreased bone mineral density and bone content. When a patient is receiving therapy, these indices frequently improve, and they may be used to track treatment effectiveness [24].

Electro-diagnostic Testing: Patients with type II CRPS may benefit from electromyography, which reveals abnormalities associated with nerve damage. The fact that type II CRPS's somatosensory symptoms go beyond the range of the damaged peripheral nerve is a key difference between it and a peripheral mono-neuropathy [24].

Sympathetic Blocks: The analgesic reaction to a block of the sympathetic nerve was regarded as a crucial piece of diagnostic information under the previous naming scheme (RSD rather than CRPS) [25]. In reality, the majority of pain management specialists believed that the most crucial diagnostic tool was a good reply to a block of sympathetic nerves, or the reduction of pain and related symptoms [25]. Sympathetic dysfunction could or might not be a factor depending on the new system (CRPS). As a result, a good reaction to a sympathetic block is not necessary for the diagnosis of CRPS. Due to potential treatment implications, it is crucial to identify patients who do not have sympathetic dysfunction. Patients who have significant pain and clinical signs of vasomotor or sudomotor dysfunction should think about getting a diagnostic sympathetic block. Sympathetic blocks may be necessary for patients who receive symptomatic relief following a sympathetic block in order to manage the sympathetically sustained component of pain [24]. An intravenous phentolamine infusion can be used to achieve a pharmacological sympathetic block, however this method is not very common [25]. A sympathetic trunk block with local anesthetic is the more typical and tried method [24]. For symptoms in the lower extremities, a paravertebral sympathetic block in the lower back is used, and for symptoms in the upper extremities, a cervicothoracic block (also known as a stellate ganglion block) or thoracic sympathetic block in upper limbs is used. Not every diagnostic sympathetic block is made equally, which is significant. The technique must be carried out in a meticulously regulated way to prevent misunderstanding and incorrect diagnosis. The most crucial thing is to establish the lack of a somatic nerve block and gain proof of a sufficient sympathetic block, such as by thermography. The latter is crucial because pain relief brought on by an undiagnosed somatic nerve block that is mistakenly attributed to a sympathetic block may result in a poor diagnosis and course of therapy. The local anaesthetic injection may spread from the sympathetic nerve trunks to the adjacent somatic nerves because the sympathetic nerve trunks that supply the upper and lower extremities are physically close to the somatic nerves. A significant placebo effect might exist [24].

**Treatment**

In conjunction with mental counseling, neuropathic painkillers, physical and occupational therapy, anti-inflammatory drugs, and interventional procedures, CRPS is mostly treated symptomatically [28]. The effectiveness of numerous medications used to treat CRPS are based on how well they work to relieve neuropathic pain [29]. There are few drugs that have assessed in clinical studies for CRPS, and this review discusses the available data. This review also includes information on the neuro-modulation trial data for spinal cord stimulation (SCS) and dorsal root ganglion (DRG) stimulation. Many of the CRPS therapy methods have little supporting data for their efficacy, thus more studies are needed.

Physical and Occupational Therapy: The CRPS treatment recommendations include a multidisciplinary strategy that includes physical

therapy (PT), occupational therapy (OT), and psychological therapy for rehabilitation. Patients with CRPS are frequently steer clear of the afflicted limb because of the extremity discomfort. The purpose of PT and OT is to help the patient reduce discomfort and enhance mobility while also enhancing the functioning and range of motion of the affected extremity [9]. Eighteen RCTs (randomised controlled trials; n = 739) examining interventions based on physiotherapy were examined in a Cochrane review [9]. The majority of the trials under investigation had "low" quality or a "high" risk of bias. Notwithstanding these drawbacks, the Cochrane analysis identified two medications with the most evidence that potentially improve function and discomfort for CRPS I patients. There is a great deal of overlap between graded motor imagery (GMI) and mirror treatment [9].

Three steps are involved in GMI: first, patients begin by using pictures to determine the laterality of their limbs; second, they advance to visualizing moving their limb into a position based on an image; and third, they see the unaffected limb move as it is reflected in a mirror [30]. In two studies using GMI (n=49), individuals with CRPS I experienced less pain and functional impairment after 6 months. Forty-nine mirror treatment has been used for CRPS since it was initially reported for phantom limb pain [31]. In mirror treatment programs, patients first describe the damaged and unaffected limbs. Then they envision moving both extremities [32]. Finally, they gaze at the reflected limb that is immobile. Improvements in pain and functioning were also seen at 6 months in two studies (n=72) using mirror treatment in CRPS Type I patients [10]. Patients with CRPS may experience emotional distress. Patients with CRPS often avoid using the afflicted limb because of the pain it causes and develop a phobia of the limb because of the agony. Patients who have acute pain will experience high levels of emotional stress. In this context, psychological treatment can aid patients with pain management strategies, relaxation training, thermal biofeedback, and graded exposure therapy. Eighteen individuals who underwent either physical therapy (PT) or PT combined with relaxation training participated in a short RCT. Both groups saw equal reductions in pain, range of motion, and edema; however, the PT with relaxation training experienced greater reductions in limb temperature [9]. The goals of physical therapy are to increase functioning, mobility, QoL, and pain management skills. These therapies should be used as soon as possible for CRPS and are regarded as first-line therapy by many pain doctors [9].

Pharmacotherapy: The treatment of CRPS involves the use of several pharmacotherapeutic medications. Transdermal lidocaine, opioids, N-methyl-D-aspartate (NMDA) antagonists, antidepressants, anti-inflammatory medications, anticonvulsants, and bisphosphonates are some of the often-prescribed treatment alternatives in this group. Superior results could be obtained by employing a multimodal pharmacologic regimen that incorporates multiple distinct classes. Anti-inflammatory drugs: Since inflammation is suspected to have a part in the etiology of the condition, oral corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) have been utilized in the treatment of CRPS [33]. A Cochrane review found that oral steroids do not significantly lessen pain in CRPS patients based on three trials that evaluated oral corticosteroids to placebo in that condition. There was pretty shoddy evidence to back this up. Oral corticosteroids appear to lower composite pain levels, according to the review [34]. Another study discovered that oral prednisolone appeared to be more beneficial than piroxicam (NSAID) in reducing composite CRPS scores in post-stroke patients [35]. According to a more recent trial, a 2-month course of low-dose oral prednisolone was both safe and effective for treating post-stroke CRPS [33]. Bisphosphonates: Due to its ability to block osteoclastic activity, this family of drugs is frequently prescribed for bone-related issues. There have been several hypothesised mechanisms of action for bisphosphonates in CRPS. The more widely acknowledged methods include control of inflammation as well as suppression of bone marrow cell migration and proliferation. According to a 2017 meta-analysis, bisphosphonates appear to lessen CRPS Type I patients' discomfort [36]. Low-quality data also tended to imply the similar reaction in CRPS, more so in those with concurrent indications of osteopenia or osteoporosis, according to a Cochrane review [33]. Antiepileptic and antidepressants drugs: The drug in this class with the greatest research on it is gabapentin. Voltage-gated calcium channels' alpha 2-delta subunit is inhibited, which is how it functions. Although gabapentin is frequently used to treat CRPS, there is very little evidence that it works to treat CRPS [33]. Amitriptyline and gabapentin were examined in research for CRPS Type I and pediatric neuropathic pain. Both drugs were shown to greatly lessen pain and impairment. Between the two, no discernible difference in effect was found [37]. Opioids: Since the usefulness of opioids in CRPS has not been investigated, no fact-based judgments can be made [38]. NMDA blockers: It has been proposed that NMDA receptor antagonists, such as ketamine, can reverse central sensitization and unfavorable cortical neuroplastic alterations in CRPS [38]. According to low-quality research, an intravenous ketamine infusion may reduce CRPS patients' discomfort for four to eleven weeks [34]. Ketamine's psychomimetic qualities and adverse effects, however, have limited its

usage [39]. Behavior Modification: By causing central sensitization through adrenergic pathways, elevated catecholamine levels linked to depression might exacerbate CRPS. One of the suggested mechanisms of action of psychotherapy in CRPS is the reversal of this impact [9].

## Conclusion

Complex regional pain syndrome (CRPS) is a condition affecting limbs after physical trauma or nerve damage, leading to chronic pain and mental health issues like depression and anxiety. Despite the unknown cause, research suggests progress is being made. Initial treatment involves neuropathic drugs, physical, occupational, and psychological therapy, as part of a multidisciplinary approach to enhance functioning, mobility, quality of life, and pain management abilities.

## Conflict of Interest

None

## Funding

None

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