Complex Regional Pain Syndrome following Spine Surgery: Clinical and Prognostic Implications

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Introduction

CRPS is an orthopedic, neurological, and traumatological disease [1–3] which occurs following extraneous trauma, such as surgery, fractures (1–2%), peripheral nerve damage (2–5%), and infections. In the long run, CRPS can lead to dystrophy and atrophy of parts of the extremities. Typical symptoms include circulatory disorders, edema, skin changes, pain, and loss of function [4].

To date, the etiology of CRPS remains unclear. It is believed to involve a neuronal inflammation reaction in combination with cortical reorganization. The etiology has been reported to be an abnormal healing process [5]. Therefore, symptoms include a circulus vitiosus of pain and a consecutive sympathetic reaction [6]. The neuronal changes convert the somatosensory impulse leading to the extension of pain beyond the defined neuronal supply area. Hemisensory symptoms [7, 8] and vascular changes [9] have been described in patients with CRPS.

In 1995, the International Association for the Study of Pain (IASP) defined the term 'complex regional pain syndrome' (CRPS) [10]. According to the IASP definition, CRPS should be diagnosed if the following criteria are observed:

- Pain syndrome following a initiating pain occurrence.
- Spontaneous pain or allodynia/hyperalgesia, where the spread of pain is not limited to the area of the af-
CRPS following Spine Surgery

Eur Neurol 2012;68:52–58 53

affected nerve, and the pain strength is not limited to the
initiating event.

Studies have found that the IASP criteria for CRPS suf-
f er from a lack of specificity [11, 12] due to the fact that
the IASP CRPS criteria can be met solely based on self-
reported symptoms (which can be historical). Therefore,
modified diagnostic criteria (‘Budapest criteria’) were
proposed [13, 14] and validated recently [15].

There are two main types of CRPS:
• CRPS type I (classic M. Sudeck): lack of specific nerve
damage.
• CRPS type II (causalgia): following specific nerve
damage, not essentially limited to the location of in-
jury.

CRPS is predominantly a clinical diagnosis, but labo-
 ratory tests like thermography, MRI, three-phase bone
scan, and conventional X-ray of the affected extremity
can confirm the diagnosis or exclude other diseases [16].
It is unknown how frequently CRPS occurs after spinal
operations, and whether the course and severity of the
disease differs from CRPS of different origins.

In this study, we retrospectively analyzed the data of
CRPS patients treated in our pain department over 6
years. The aim of the study was to (1) determine the fre-
cquency of spinal surgery preceding CRPS (CRPS-SS) in
these patients, (2) examine if the course of the disease dif-
ers from that in patients with CRPS of other origins
(CRPS-OO), and (3) identify if there are prognostic fac-
tors indicating an unfavorable outcome.

Methods

We reviewed the medical charts of all CRPS patients treated at
our institution, an interdisciplinary academic pain center, be-
tween January 1, 2003 and December 31, 2008. Diagnostic criteria
were applied according to the IASP criteria [17]. Age, sex, CRPS
type, CRPS etiology, and the patients’ clinical symptoms and
signs were recorded. The length of follow-up and outcome in
terms of resolution of autonomic sequelae and pain were not-
ed. In cases that underwent spinal surgery previous to onset of
the disorder, the surgical reports and radiologic exams were re-
corded.

Descriptive statistics were applied to the age and length of fol-
low-up data. Differences between the normal age distributions of
two groups of patients (patients with CRPS-SS vs. patients with
CRPS-OO) were analyzed using an unpaired t test. Differences in
the length of follow-up, which lacked a normal distribution, were
analyzed using a Mann-Whitney test. The correlation of prior
spine surgery with CRPS II was assessed using Fisher’s exact test.
Data are presented as means ± SD.

Results

A total of 35 patients (18 women and 17 men) were in-
cluded in the study. All of the patients were treated under
the diagnosis of CRPS (I or II). The mean age at the time of
diagnosis was 47.7 ± 18.1 years (range: 6–77). In 18
patients, the upper extremities were affected, while in 17
patients the lower extremities were affected. Twenty-sev-
en patients had CRPS I, and 8 patients had CRPS II (table 1).

Six of the patients had undergone spinal operations
shortly before the onset of symptoms of CRPS (median:
5 days, range: 1–14) and had no other trauma preceding the
development of the CRPS symptoms. The mean age of these patients (49.17 ± 12.6 years, range: 32–69) did
not differ significantly (p = 0.79) from that of the patients
with CRPS-OO (47.03 ± 19.2 years, range: 6–77). Five of
these patients underwent prior lumbar spine surgery. These
patients had CRPS of the lower extremity. One pa-
tient, who had undergone cervical multisegmental dorsal
decompression for cervical myelopathy, suffered from
CRPS of the upper extremity. Prior spinal surgery was
closely associated with CRPS II (p = 0.0161, Fisher’s exact
test). The clinical features of these patients are given in
table 2.

The mean length of follow-up (length of treatment at
our institution) was 12.69 ± 17.20 months (range: 1–96).
The mean follow-up was 26.17 ± 35.82 months (range:
1–96) in patients with prior spine surgery compared to
9.89 ± 9.10 months (range: 1–36) in patients with CRPS
of different origins. This difference in the mean follow-up
was not statistically significant (Mann-Whitney test, p =
0.3566). In patients with CRPS I, the mean follow-up was
10.15 ± 9.30 months (range: 1–36), whereas it was 21.25
± 31.72 months (range: 3–96) in patients with CRPS II.
This difference was not statistically significant (Mann-
Whitney test, p = 0.7673).

A complete remission of CRPS symptoms was ob-
served in 18 patients. Eleven patients experienced partial
remission. No remission was seen in 6 patients.

Three of the 6 patients with prior spine surgery had a
complete remission, 2 had a partial remission, and 1 had
no remission. Fifteen of the patients without prior spine
surgery had a complete remission, 9 had a partial remis-
sion, and 5 had no remission. Outcomes according to pri-
or spine surgery/no prior spine surgery and type of CRPS
are given in table 3.

Sympathetic blocks were performed in 18 patients (8
patients with CRPS of the upper extremity and 10 pa-
tients with CRPS of the lower extremity). We observed a
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age</th>
<th>Sex</th>
<th>Type of CRPS</th>
<th>Therapy</th>
<th>Follow-up months</th>
<th>Outcome</th>
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<tr>
<td><strong>Prior spine surgery</strong></td>
<td></td>
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<tr>
<td>Cervical spine surgery</td>
<td>57</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>4</td>
<td>CR</td>
</tr>
<tr>
<td><strong>Lower extremity</strong></td>
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<tr>
<td>Lumbar disc operation L4/5</td>
<td>45</td>
<td>f</td>
<td>II</td>
<td>MT, PT, LD, SB</td>
<td>96</td>
<td>NR</td>
</tr>
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<td>Dorsoventral spondylodesis L5/S1</td>
<td>48</td>
<td>m</td>
<td>II</td>
<td>MT, PT, LD, SB</td>
<td>32</td>
<td>CR</td>
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<tr>
<td>Lumbar disc operation L5/S1</td>
<td>44</td>
<td>f</td>
<td>II</td>
<td>MT, PT, LD, SB</td>
<td>14</td>
<td>PR</td>
</tr>
<tr>
<td>Lumbar disc prosthesis L4/5</td>
<td>32</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>8</td>
<td>CR</td>
</tr>
<tr>
<td>Hemilaminectomy L5 and nucleotomy L4/5 and L5/S1</td>
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<td>m</td>
<td>II</td>
<td>MT, PT, LD</td>
<td>3</td>
<td>PR</td>
</tr>
<tr>
<td><strong>No prior spine surgery</strong></td>
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<tr>
<td><strong>Upper extremity</strong></td>
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<td>Laceration injury left hand</td>
<td>40</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>12</td>
<td>CR</td>
</tr>
<tr>
<td>Tendon rupture right middle finger</td>
<td>51</td>
<td>f</td>
<td>II</td>
<td>MT, PT, LD, SB</td>
<td>12</td>
<td>NR</td>
</tr>
<tr>
<td>Radius fracture</td>
<td>65</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>36</td>
<td>PR</td>
</tr>
<tr>
<td>Contusion right hand</td>
<td>29</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>8</td>
<td>NR</td>
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<td>Shoulder luxation</td>
<td>71</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>7</td>
<td>CR</td>
</tr>
<tr>
<td>Laceration injury left hand</td>
<td>53</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>8</td>
<td>PR</td>
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<td>Median and ulnar entrapment</td>
<td>62</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
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<td>CR</td>
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<tr>
<td>Herpes zoster</td>
<td>74</td>
<td>f</td>
<td>II</td>
<td>MT, PT, LD</td>
<td>3</td>
<td>CR</td>
</tr>
<tr>
<td>Carpus and middle hand fracture</td>
<td>57</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>4</td>
<td>CR</td>
</tr>
<tr>
<td>Contusion right hand</td>
<td>35</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>9</td>
<td>PR</td>
</tr>
<tr>
<td>Radius fracture</td>
<td>47</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>4</td>
<td>CR</td>
</tr>
<tr>
<td>Minor trauma</td>
<td>36</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>1</td>
<td>CR</td>
</tr>
<tr>
<td>Tendon operation hand</td>
<td>77</td>
<td>m</td>
<td>II</td>
<td>MT, PT, LD</td>
<td>7</td>
<td>CR</td>
</tr>
<tr>
<td>Radius fracture</td>
<td>66</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>7</td>
<td>PR</td>
</tr>
<tr>
<td>Minor trauma</td>
<td>14</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>4</td>
<td>CR</td>
</tr>
<tr>
<td>Tendovaginitis</td>
<td>65</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>7</td>
<td>CR</td>
</tr>
<tr>
<td>Radius fracture</td>
<td>71</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>14</td>
<td>CR</td>
</tr>
<tr>
<td><strong>Lower extremity</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Minor trauma</td>
<td>22</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>6</td>
<td>CR</td>
</tr>
<tr>
<td>Fracture of malleolus lateralis</td>
<td>39</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>22</td>
<td>PR</td>
</tr>
<tr>
<td>Metatarsal fracture</td>
<td>39</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>8</td>
<td>PR</td>
</tr>
<tr>
<td>Hip prosthesis</td>
<td>63</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>26</td>
<td>PR</td>
</tr>
<tr>
<td>Minor trauma</td>
<td>14</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>2</td>
<td>PR</td>
</tr>
<tr>
<td>Tibia fracture</td>
<td>6</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>3</td>
<td>CR</td>
</tr>
<tr>
<td>Minor trauma</td>
<td>50</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>3</td>
<td>CR</td>
</tr>
<tr>
<td>Metatarsal fracture</td>
<td>38</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD, SB</td>
<td>5</td>
<td>CR</td>
</tr>
<tr>
<td>Peroneal paresis</td>
<td>49</td>
<td>m</td>
<td>I</td>
<td>MT, PT, LD</td>
<td>9</td>
<td>NR</td>
</tr>
<tr>
<td>Operation of Baker’s cyst</td>
<td>28</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD, SB, SCS</td>
<td>12</td>
<td>NR</td>
</tr>
<tr>
<td>Core decompression right foot</td>
<td>43</td>
<td>f</td>
<td>I</td>
<td>MT, PT, LD, SB, SCS</td>
<td>36</td>
<td>NR</td>
</tr>
<tr>
<td>Vertebral fracture with nerve root lesion</td>
<td>60</td>
<td>m</td>
<td>II</td>
<td>MT, PT, LD</td>
<td>3</td>
<td>PR</td>
</tr>
</tbody>
</table>

MT = Medical therapy; PT = physiotherapy; LD = lymphatic drainage; SB = sympathetic block; SCS = spinal cord stimulation; CR = complete remission (complete absence of symptoms, restitution ad integrum); PR = partial remission (amelioration but persistence of pain; neurological deficits, and/or trophic changes); NR = no remission (neurologic deficits and/or trophic changes not altered).
complete remission in 8 of these patients (44%). In the patients with CRPS that resulted after lumbar spine surgery, 4 of 5 patients had sympathetic blocks. Two of these patients had a complete remission (50%), 1 had a partial remission, and 1 experienced no remission. In 14 patients with CRPS-OO, 6 (42%) had a complete remission after sympathetic blocks. Thus, sympathetic blocks were equally successful in patients with CRPS-SS and in patients with CRPS-OO.

**Discussion**

In this study, we identified a relatively high proportion of CRPS patients treated in our department who previously underwent spinal surgery. The clinical findings indicated typical CRPS symptoms, including autonomic, motor, and sensory abnormalities. In some patients, besides typical CRPS symptoms of distal generalization, distinct symptoms of a radicular lesion were obvious. In these patients (4/6), CRPS II was diagnosed. Thus, the frequency of CRPS II was significantly higher in patients with CRPS following CRPS-SS than in patients with CRPS-OO. Diagnostic methods like three-phase bone scintigraphy were equally helpful for diagnosing CRPS-SS and CRPS-OO, and sympathetic blockades were equally helpful in both groups.

In general, it can be assumed that the frequency of CRPS-SS is low. Given that during the 6 years, approximately 12,000–15,000 spine operations were performed in the service area of our institution, we can roughly estimate that CRPS occurs at a frequency of less than 1 in 2,000 patients following spinal surgery. On the other hand, the question of how often patients with CRPS underwent spinal surgery prior to the onset of CRPS symptoms can be addressed with more certainty using the data obtained in our study. We found that nearly one third of the patients experiencing CRPS of the lower extremities had spinal surgery prior to the onset of their symptoms. Prior spinal surgery was associated with CRPS II in our study. These patients had a tendency towards a longer and more severe disease course than patients with CRPS I. However, due to the low number of patients, this tendency was not statistically significant. Anyhow, CRPS I can

**Table 2. Diagnoses and clinical features of CRPS patients after spine surgery**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age</th>
<th>Sex</th>
<th>Type of CRPS</th>
<th>Time between operation and onset of CRPS</th>
<th>Symptoms</th>
<th>Diagnoses and clinical features of CRPS patients after spine surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper extremity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical spine surgery</td>
<td>57</td>
<td>m</td>
<td>I</td>
<td>1 day</td>
<td>no radicular motoric deficit, slight diffuse weakness of the arm</td>
<td>diffuse hypesthesia, no radicular pattern, hyperthermia, edema, later complete resolution of autonomic symptoms</td>
</tr>
<tr>
<td>Lower extremity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumbar disc operation L4/5</td>
<td>45</td>
<td>f</td>
<td>II</td>
<td>7 days</td>
<td>pronounced L5 paresis</td>
<td>diffuse hypesthesia after onset of CRPS (radicular before onset of CRPS)</td>
</tr>
<tr>
<td>Dorsoventral spondylodesis L5/S1</td>
<td>48</td>
<td>m</td>
<td>II</td>
<td>14 days</td>
<td>L5 paresis in acute phase</td>
<td>diffuse hypesthesia after onset of CRPS (radicular before onset of CRPS)</td>
</tr>
<tr>
<td>Lumbar disc operation L5/S1</td>
<td>44</td>
<td>f</td>
<td>II</td>
<td>14 days</td>
<td>S1 paresis</td>
<td>alldynia, burning and tingling pain, hypesthesia beyond radicular limits</td>
</tr>
<tr>
<td>Lumbar disc prosthesis L4/5</td>
<td>32</td>
<td>f</td>
<td>I</td>
<td>2 days</td>
<td>weakness of the foot without clear radicular attribution</td>
<td>no radicular sensory deficit</td>
</tr>
<tr>
<td>Hemilaminectomy L5 and nucleotomy L4/5 and L5/S1</td>
<td>69</td>
<td>m</td>
<td>II</td>
<td>3 days</td>
<td>discrete L5 and S1 paresis</td>
<td>burning dysesthesia, alldynia in the distal L5 and S1 dermatome, proximal S1 hypesthesia</td>
</tr>
</tbody>
</table>

CRPS following Spine Surgery

Eur Neurol 2012;68:52–58

55
also occur following spine surgery. One of the possible mechanisms might be a sympathetic reaction following the mobilization of the sympathetic trunk during ventral access to the spine, as the case of CRPS following lumbar disc prosthesis shows (tables 1, 2) [18].

Causalgia (now defined as CRPS II) is a well-known complication of spine surgery. A number of studies have reported the development of CRPS symptoms after spinal surgery.

Sachs et al. [19] reported 11 patients with CRPS after spinal surgery; however, CRPS occurred mainly after stabilization. Similar to our results, the CRPS symptoms could be relieved by sympathetic blocks in half of the patients. de Weerdt et al. [20] performed thermographic measurements on 48 patients who had undergone surgery for lumbar disc herniation. Twenty-six of these patients had mild residual pain and 12 patients experienced more severe residual pain. Two of the patients with mild pain and 4 of the patients with severe residual pain showed hyperthermia of the affected limb with a greater than 1.25°C temperature difference. The authors concluded that ‘patients with lasting pain can be considered to be suffering from a sympathetic reflex dystrophy, i.e. a disturbance of vasomotor control’. Likewise, Bernini and Simeone [21] reported that three-phase bone scintigraphy may be useful for the diagnosis of CRPS-SS and sympathetic blocks can relieve CRPS symptoms. It is important to note that the IASP defined the criteria for CRPS in 1993. Since most of the case reports were published before 1994, these studies adhered to the former nomenclature.

In most of the published cases, reflex sympathetic dystrophy (which is now defined as CRPS) or causalgia was diagnosed after lumbar spine operations. There are only five case reports of causalgia/CRPS II secondary to lumbar disc prolapse that were diagnosed prior to spinal operations [21–25].

Thus, CRPS following spine surgery has been described much more frequently than CRPS following (conservatively treated) nerve root compression. One could conclude that the emergence of CRPS II requires an additional impact on the nerve rather than mere nerve root compression. This impact might occur during intraoperative manipulation, but in some cases it can also be due to a nerve injury. This assumption might be enforced by the finding that in our CRPS-SS patients CRPS II was more common (4/6) than in the CRPS-OO patients (4/29).

In 2 of the 6 cases, the probable pathomechanism was not nerve root affection. These 2 cases were diagnosed with CRPS I. The first (cervical) case was diagnosed with CRPS I, not CRPS II, because the patient’s symptoms did not correspond to any of the nerve roots in question and intraoperative nerve root damage during dorsal decompression was unlikely. To our knowledge, this is the second reported case of CRPS occurring secondary to cervical spinal surgery [26].

In 1998, Condon et al. [22] reported a case of CRPS secondary to an L5 nerve root compression due to an extraforaminal disc prolapse at the L5/S1 level. Symptoms in this case immediately resolved after a combined sympathectomy and discectomy that were carried out using a retroperitoneal approach. In 1994, Adachi et al. [23] described a somewhat similar case of CRPS secondary to nerve root compression by extraforaminal disc prolapse. In this case, however, the symptoms resolved after one sympathetic block. In a recent study, 15 cases of causalgia (CRPS II) secondary to lumbar disc prolapse subjected to lumbar discectomy were reported; however, the authors did not state the incidence of the condition in their patients [27]. In all of these studies, CRPS following lumbar disc prolapse or lumbar operation was not compared to CRPS following other injuries. In our present study, patients with CRPS-SS were compared to CRPS-OO for the first time, and revealed a similar remission rate, success rate of sympathetic blockades, etc.

Treatment in all patients consisted of medical therapy, physiotherapy, and lymph drainage. In approximately half of our patients, additional sympathetic blocks were necessary. We did not perform neurolytic blocks, but we

<table>
<thead>
<tr>
<th>CRPS I CR</th>
<th>CRPS I PR</th>
<th>CRPS I NR</th>
<th>CRPS II CR</th>
<th>CRPS II PR</th>
<th>CRPS II NR</th>
<th>Σ CRPS I</th>
<th>Σ CRPS II</th>
<th>Σ CRPS I+II</th>
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<tbody>
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<td>3</td>
<td>2</td>
<td>27</td>
<td>8</td>
<td>35</td>
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</tbody>
</table>

SS = Prior spine surgery; OO = no prior spine surgery; CR = complete remission (complete absence of symptoms, restitution ad integrum); PR = partial remission (amelioration but persistence of pain, neurological deficits, and/or trophic changes); NR = no remission (neurologic deficits and/or trophic changes not altered).
used local anesthetics for diagnostic purposes and local anesthetics combined with steroids for therapeutic purposes. By repeating this therapeutic procedure up to three times during an interval of weeks, we observed complete remission in 8 of 18 patients.

Three of our patients received spinal cord stimulation (SCS) therapy, and among these was 1 patient with CRPS II that developed after a lumbar disc operation. In cases with radiculopathy after lumbar disc operations, SCS appears to be an effective treatment option in carefully selected patients [28, 29]. There is only one randomized controlled trial for SCS in CRPS I [30] and only case reports and single observations for the use of SCS in CRPS II patients. In a meta-analysis, SCS treatment was supported in cases with CRPS I (grade A evidence) and CRPS II (grade D evidence) [31]. In contrast with these conclusions, the 2 patients in our study treated with SCS for CRPS I showed modest success. Meanwhile, the patient with CRPS II following a lumbar disc operation experienced reliable pain relief through SCS during 8 years of SCS treatment.

The importance of initiating CRPS therapy early has been pointed out frequently [1, 3]. Early therapy, however, requires early diagnosis of the disorder. In our opinion, since CRPS occurs relatively rarely following spinal surgery, it should not have a substantial impact on the indications for and timing of these operations. However, it is critical to be aware of the possibility that CRPS may occur, to promote early diagnosis and more successful therapies [24, 32–36].

References


