Biopsychosocial complexity is correlated with psychiatric comorbidity but not with perceived pain in complex regional pain syndrome type 1 (algodystrophy) of the knee

Aurélie Vouilloz*, Olivier Deriaz, Gilles Rivier, Charles Gobelet, François Luthi

Clinique Romande de réadaptation SuvaCare, avenue Grand-Champsec 90, 1951 Sion, Switzerland

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A B S T R A C T

Aim: The aim of this study was to compare the characteristics of patients suffering from complex regional pain syndrome type 1 (CRPS), also known as reflex sympathetic dystrophy or algodystrophy, of the knee with those of a matched group of patients experiencing post-traumatic knee pain. The comparisons looked at biopsychosocial complexity (simple versus complex), psychiatric comorbidity and pain intensity.

Methods: Cross-sectional, single-centre, case-control study using the INTERMED scale, psychiatric diagnostic tools (ICD-10) and visual analogue pain scale. Contingency table and Chi² tests. One-way analysis of variance for continuous dependent variables. Difference between groups: Tukey's variance test, after the event. For nominal dependent variables, multivariate logistic analysis.

Results: Biopsychosocial complexity did not differ between the two groups (p = 0.7). The “complex” patients displayed significantly more psychiatric comorbidity (odds ratio 2.94, 95% confidence interval 1.1–7.8, p < 0.01), independently of whether or not CRPS was present. The pain perceived varied with biopsychosocial complexity only in the control group. The “complex” control patients reported more pain than the “simple” control patients (p < 0.05). The perceived intensity of pain was not different between the “simple” and “complex” patients with CRPS.

Conclusions: Biopsychosocial complexity was comparable between the two groups, and was strongly associated with the presence of psychiatric comorbidity. However, unlike with other pain syndromes, with CRPS the intensity of the perceived pain did not vary with biopsychosocial complexity. Early identification of “complex” patients could make it possible to quickly institute targeted management for both groups of patients.

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1. Introduction

Complex regional pain syndrome type 1 (CRPS type 1) – i.e. algodystrophy – specifically affecting the knee was first described in 1939, by René Leriche [1]. Its medical aspects have been studied extensively since the 1960s [2–4], particularly by the French school of rheumatology [5,6]. In terms of prevalence, the knee is the third most common site for the syndrome [6], as confirmed by accident-insurance sources (www.unfallstatistik.ch) [7].

In recent years, it has been generally accepted that CRPS, like all other chronic pain syndromes, should be seen in biopsychosocial (BPS) terms. Its management should therefore focus on the syndrome's medical, psychological and social components [8,9]. As far as we know, however, no research has used validated methods to study patients with CRPS in terms of BPS complexity.

The INTERMED method was developed and validated about 10 years ago, and has become an appropriate tool for this task [10,11]. Its predictive validity has been studied in various populations, particularly patients suffering from chronic low back pain [12,13], rheumatoid arthritis [14] or neurological disorders [15]. This tool has been recognized as identifying “complex” patients at risk of showing a reduced response to treatment and increased use of the health care system. The knee was chosen as a useful model with which to assess CRPS from the perspective of BPS complexity [16], since the prevalence of post-traumatic knee pain makes it easy to obtain matched groups not suffering from CRPS. This obviates the need to resort to comparisons with patients suffering from different medical problems, such as low back pain, neuropathy or chronic headaches [17–19].

The influence of psychological disturbances in cases of CRPS nevertheless remains controversial, and the current state of knowledge does not enable any conclusions to be drawn [20]. Some writers have found a higher prevalence of neuroticism [21], but that is not confirmed by others [18,22]. Also, some authors suggest that anx-
The aim of this study was to describe the characteristics of a group of patients suffering from post-traumatic CRPS of the knee, and to compare them with those of a group of matched patients suffering from post-traumatic knee pain without CRPS. The data compared in greatest detail relate to BPS complexity (measured by INTERMED in both groups), psychiatric comorbidity as diagnosed by a psychiatrist and pain intensity.

2. Methods

2.1. Population study

This was a single-centre cross-sectional study. From 2002 to 2005, 514 patients with post-traumatic knee pain were admitted to a rehabilitation hospital. The reasons for admission to hospital were persistent pain, functional limitations or persistent inability to work. The patients were receiving interdisciplinary treatment, including physiotherapy and occupational therapy.

The inclusion criteria for this study were as follows: patient with CRPS confirmed by a senior physician specializing in physical medicine and rehabilitation or in rheumatology, aged between 18 and 65, no financial compensation (disability benefit) being received, and no central-nervous-system lesions. The diagnosis of CRPS was made based on Doury’s criteria [27]. The diagnosis of CRPS also met the “International Association for the Study of Pain” (IASP) criteria at the time of the study [28]. In case of conflict between the criteria, those of Doury took precedence over the IASP’s, as the former also take into account X-ray and laboratory findings. Combined use of the two methods was chosen to facilitate comparisons with international literature. Sixty-one patients with CRPS of the knee were included during the course of the study: 51 men (84%) and 10 women (16%), aged 42 ± 12 (mean ± SD).

The control group also comprised 61 patients: 51 men and 10 women, aged 41 ± 10. The same inclusion criteria were applied, with the exception that CRPS was ruled out by a senior physician. Inclusion was also carried out consecutively, based on the hospital’s database. The control group was matched for age, sex, type of initial injury, and the presence of degenerative disorders [29] (Table 1).

2.2. Methods and measurements

The initial social and medical data – known at the time of the patient’s accident – were collected from participants’ medical and accident-insurance files. These included: marital status, level of occupational training, native language, type of occupation and employment before the accident, disability benefit by a family member, legal proceedings in progress, circumstances of the accident and type of surgery undertaken. Also quantified was the period during which the symptoms developed before admission to rehabilitation.

For all the patients, BPS complexity was measured using the INTERMED scale. This is a validated tool, which had already been compared against other instruments, such as SF-36, HADS, VAS, and other relevant scales [10,11]. The INTERMED is an observer-rated instrument used to assess biopsychosocial and health care-related aspects of disease. It synthesizes information from four domains: biologic, psychological, social and health care. The interview is conducted by specially trained nurses, during the three days following admission. Each of the four areas (Table 2) contains variables known to influence the degree of clinical complexity. The scale is subdivided into three sections reflecting developments over time: the patient’s medical history, current condition, and prognosis. Each variable can be given a score of 0 to 3. The score in each of the four areas can thus go from 0 to 15, and the total INTERMED score can range from 0 to 60. A high score indicates high BPS complexity. Conforming to the practice with data in the literature [30], patients with a greater or equal to 21 points score were considered “complex” cases, while those with a less than 21 points score were considered “simple” cases. The INTERMED score was calculated after the interview. Detailed information about the semi-structured questionnaire can be found at: http://www.intermedfoundation.org/.

The psychiatric diagnoses were made by senior psychiatrists, using the diagnostic criteria in ICD-10 [31], following an initial assessment carried out by the rehabilitation physician responsible for the patient. The INTERMED score, used for research purposes,

### Table 1
Characteristics of the patients. Matched criteria.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>CRPS N=61 (%)</th>
<th>Controls N=61 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td>42 ± 12</td>
<td>41 ± 10</td>
</tr>
<tr>
<td>Initial lesion (non-exclusive)</td>
<td>Meniscal lesion</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Fracture, temur, tibia, patella</td>
<td>21</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Anterior cruciate ligament lesion</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Posterior cruciate ligament lesion</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Radiologic degenerative disorders</td>
<td>Absent</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>16</td>
<td>14</td>
</tr>
</tbody>
</table>

Mean ± SD. CRPS: Complex regional pain syndrome.
was not known to either the rehabilitation physician or the psychiatrist.

The intensity of pain at rest was measured in the same way in both groups, using a visual analogue scale (VAS), a simple method validated in patients displaying a lesion to the musculoskeletal system, and in patients with CRPS [32].

### 2.3. Statistics

The differences between the groups (CRPS and control) were calculated using contingency tables and chi squared ($\chi^2$) tests for the nominal dependent variables, and by one-way analysis of variance for the continuous dependent variables. For pain, two-way analysis of variance was used (for BPS complexity and CRPS diagnosis or control). The mean values are shown, together with the corresponding standard deviations (SDs). The differences between the groups were determined after the event using Tukey’s test. A multivariate logistic analysis was used for the nominal dependent variables with a number of independent variables (Jump software, version 4.0, from SAS Institute, Cary NC 27513, USA).

### 2.4. Ethics

This study was approved by the regional medical ethics committee, and the data were processed in accordance with Switzerland’s federal law on data protection.

### 3. Results

#### 3.1. Comparisons between patients with complex regional pain syndrome and controls

The two groups were comparable in terms of their social and medical characteristics. In particular, occupation before the accident, whether or not there were legal proceedings in progress and whether or not a disability benefit was received by the household were distributed similarly (see Table 3). Furthermore, there was no difference in relation to the circumstances of the accident or to the type of surgery. The duration of symptoms before admission to hospital (246 days for the CRPS patients and 296 days for the controls) ($p = 0.21$) was similar.

The mean scores for BPS complexity as measured by the INTERMED scale were also comparable (Table 3): 19 ± 6 points and 20 ± 6 points for the CRPS group and the controls respectively ($p = 0.4$).

Twenty percent of the patients (12 cases) with CRPS showed current psychiatric comorbidity on admission, against 23% of the controls (14 cases) ($p = 0.7$). The conditions diagnosed among the CRPS patients were all mood disorders (nine cases of adjustment disorders and three of depressive states). Among the controls, 10 cases of mood disorders, one of bipolar disorder, one of social phobia and two of post-traumatic stress disorder were recorded. In neither group did the psychiatrists diagnose any somatoform disorder or personality disorder. The existence of psychiatric comorbidity was strongly correlated with BPS complexity (odds ratio 2.94, 95% confidence interval 1.1-7.8, $p<0.01$) and was independent of whether or not the patients had CRPS ($p = 0.66$) (Fig. 1).

Pain intensity was known in 110 of the patients (92%). The VAS scores were 56/100 ± 3.5 mm and 53.5/100 ± 3.1 mm ($p = 0.6$) for the CRPS patients and the controls respectively. The perceived intensity of pain varied according to the degree of BPS complexity only in the control group (Fig. 2). In other words, the “complex” controls reported feeling significantly worse than the “simple” controls ($p < 0.05$). The “complex” controls also tended to feel more pain than the CRPS patients, though without reaching the significance level ($p = 0.07$). On the other hand, the pain did not appear to be influenced by BPS complexity in cases of CRPS. Indeed, the pain score did not differ between the patient groups considered “complex” or “simple” (Fig. 2). In both groups (CRPS and controls) patients with psychiatric comorbidity stated that they had more pain ($p = 0.03$). The VAS scores were 65/100 ± 20 mm and 63/100 ± 27 mm for the CRPS patients and the controls respectively, as against 53/100 ± 19 mm and 51/100 ± 27 mm in the absence of a psychiatric diagnosis.

#### Fig. 1. Psychiatric comorbidity in relation to the INTERMED score in post-traumatic knee pain with or without CRPS type 1. Percentage of psychiatric comorbidity in relation to the degree of biopsychosocial complexity, as measured by the INTERMED score (score ≥ 21 points is considered as “complex”, score < 21 points is considered as “simple”) in the two groups. In cases of post-traumatic knee pain, the existence of psychiatric comorbidity was 40% (10 cases) and 6% (two cases) in the “complex” and “simple” CRPS patients respectively ($p = 0.0001$). The extent of psychiatric comorbidity was 42% (13 cases) and 3% (one case) in the “complex” and “simple” controls respectively ($p = 0.0001$).

NS = difference not significant. CRPS = complex regional pain syndrome.
3.2. Clinical and radiological characteristics of complex regional pain syndrome patients (n = 61)

All the patients displayed unlocalized and ill-defined knee pain. Eight of them (7%) were given a neurological examination to screen for a peripheral neurological lesion, and a diagnosis was arrived at for four of them. The neurologists nevertheless felt that these cases of neuropathy (mostly involving the saphenous nerve and its branches) played only a minor role in producing the pain. All the patients complained of symptoms that were compatible with CRPS in 14 patients (21%) was particularly useful, given that obvious vasomotor or “trophic” signs were absent.

4. Discussion

The two groups showed similar BPS complexity, as measured using the INTERMED scale. The mean scores (19 ± 6 points and 20 ± 6 points for the CRPS patients and controls respectively) were slightly higher than those obtained with patients who had rheumatoid arthritis (17 points) [14], but comparable to those of patients with multiple sclerosis (19 points) [15] and patients admitted to the hospital’s medical department (21 points) [30]. In contrast, they were lower than those of a group of chronic back-pain patients who were assessed during an expert assessment exercise (30 points) [12]. However, the duration of symptoms in the last group was particularly long (several years) and probably reflects an especially complex BPS situation (patients undergoing medical expert assessment).

The prevalence of psychiatric comorbidity did not differ between the two groups studied, at 20% for the CRPS patients and 23% for the controls. The study by Monti et al., which was also based on a psychiatric assessment, reported comparable figures (24%) [19]. A prevalence of 20–30% for diagnoses made in other patients admitted to hospital, particularly in the medical departments, is also documented [30,33,34]. Our results showed that in cases of post-traumatic knee pain, the degree of BPS complexity
as measured by INTERMED was associated with the presence of psychiatric disorders, independently of whether or not there was CRPS. The assessment of BPS complexity was therefore an important aspect in both groups of patients studied, as has already been emphasized with other pain patients, particularly those with low back pain [12].

Mood disorders (adjustment and depressive disorders) accounted for most of the diagnoses made in the two groups. This is consistent with the conclusions of other authors [18,19,22,24]. No personality disorders were diagnosed, a finding that contrasts with other studies [19]. The epidemiological data on personality disorders as cases of comorbidity with chronic pain are, however, far from uniform [24]. The assessment criteria vary between studies, making comparisons difficult. The use of questionnaires is common, although they are only screening tools when not confirmed by a psychiatrist, and it is recommended that such diagnoses should be made only after lengthy observation (ICD-10) [31], to avoid overestimating the disorders.

The intensity of pain perceived did not differ between the CRPS patient group and the controls. However, if the pain is seen in perspective against the degree of BPS complexity as measured by INTERMED, significant differences can be seen between the two groups studied. In the controls, the pain was correlated with the degree of BPS complexity, whereas that was not the case in the CRPS patients. This observation, which as far as we know is being reported for the first time, is interesting. Indeed, it is generally accepted that BPS complexity plays a part in how pain is experienced, independently of the diagnosis made and the seriousness of the lesions [14] or the specific features of the lesion, such as in chronic low back pain patients [12]. The results from the control group therefore agree with the literature. In contrast, the interactions seem to be more complex in the CRPS patients. Taken in isolation as one of the components of BPS complexity, however, the presence of a psychiatric comorbidity predicts that the perception of pain would be comparable in the CRPS patients and the controls. In other words, in both groups, the patients with a psychiatric condition stated that they experienced more pain. With patients suffering from CRPS, however, it is probable that other factors, correlated with INTERMED, influenced the perception of pain differently. The somatic and social aspects were carefully controlled, so they are probably not relevant to explaining this observation. It is, however, possible that psychological factors linked to how each patient related to the health care system are involved. As an example, a diagnosis of CRPS, as opposed to a condition considered less specifically painful, could play an important part in patients’ communications with those around them. It would, in a sense, legitimate the pain expressed by patients, particularly when communicating with health and insurance professionals [18]. It would reassure patients, who could finally use a term to describe the variety and unpredictability of the symptoms they were experiencing, and be better equipped to deal with them. Other studies will be needed to confirm this suggestion. In particular, psychological and contextual factors that are correlated with INTERMED and that could modify CRPS patients’ perception of pain should be studied.

Disproportionate pain is one of the main criteria universally quoted in CRPS classifications [27,32,35]. This diagnostic criterion was chosen because of the observed lowering of the pain threshold secondary to both local and central lesions, in cases of CRPS [36]. But our results show that disproportionate pain is also found in “complex” control patients. The concomitant measurement of BPS complexity could thus balance this diagnostic criterion. Where the influence of BPS complexity has not been considered, a diagnosis of CRPS could be made through excessive development (in the sense that it is medically difficult to explain) of the condition over time. The risk seems to be all the greater in cases of CRPS in a lower limb, particularly at the knee, where vasomotor or “trophic” disorders are often less obvious [27].

The descriptions provided by our group of CRPS patients confirm that symptoms and vasomotor or “trophic” signs are less obvious in cases affecting the knee, which corresponds with the literature [24,27]. Such signs and symptoms were not found in 21% of patients. If this study had been based only on the IASP 1994 criteria, it would have been difficult to classify these patients reliably into a specific group. The IASP 1994 criteria were already considered rather unspecific [37], and it now appears that in cases of CRPS of the knee they also lack sensitivity when compared with a radiographic and clinical classification, such as Douuy’s [27]. Although much more specific, the most recent diagnostic criteria proposed by the IASP [35] do not seem to provide a definite advantage in cases of CRPS of the knee. Indeed, by following the current proposals, the 14 patients affected (21%) would have been classified as “CRPS, not otherwise specified”. The clinical picture most suggestive of CRPS of the knee accordingly remains the simultaneous existence of joint stiffness and diffuse pain [4,6,38]. In this situation, however, we consider that it is also useful to have a radiological assessment in order to differentiate CRPS from other situations that give rise to stiffness, such as arthrofibrosis of the knee, which should be dealt with differently [38]. Without being specific, imaging techniques therefore seem to be useful in two ways: both to confirm the diagnosis of CRPS in any situation where it is difficult for clinical assessment to decide definitely and to be specific in relation to a differential diagnosis and a treatment plan.

Naturally, this study has its limitations: it was a cross-sectional study, and as such cannot deliver information about, for instance, the influence of BPS complexity on the prognosis. The INTERMED scale was administered only at the time of admission to hospital, and it is therefore impossible to know the proportion of patients whose situation was already “complex” before their accident. However, considerable care was given to collecting the basic social and medical variables – i.e. those that existed before the accident and could have introduced distortions into the interpretation – and no difference was found between the groups. Finally, men were more numerous than women, despite the fact that a number of studies indicates that CRPS affects women more than men [3]. This can definitely be explained by the way the patients were selected, our hospital being associated with a Swiss accident insurance scheme whose subscribers are mainly men working in the secondary sector. In our opinion, despite this bias in selection, our results are potentially useful, as the aim of the investigation was not to study the prevalence of CRPS but to understand better how it relates to the BPS situation. At all events, the syndrome’s prevalence remains little known [8].

To conclude, this study has shown that patients suffering from CRPS of the knee exhibit a degree of BPS complexity which, when measured by INTERMED, is comparable to that of control patients suffering from post-traumatic knee pain. The prevalence of psychiatric comorbidity varies with the degree of BPS complexity, but seems to be independent of a CRPS diagnosis. These results are compatible with the working hypothesis, which postulated that BPS complexity would have a similar effect in both the groups studied. In contrast, the intensity of perceived pain does not seem to be similarly influenced by BPS complexity in the CRPS patients and the controls. Only in the latter group was BPS complexity found to adversely affect the perceived pain, as has been reported in other patient populations suffering from non-specific chronic pain [12]. It is possible that unidentified factors that are correlated with INTERMED played a part in producing this novel observation. Early identification of “complex” patients could encourage interdisciplinary care, particularly in pain treatment and in the psychological and social domains, in both groups of patients. This would allow better allocation of the available treatment resources.
and the establishment of treatment programmes that better meet patients’ needs.

Conflict of interest

None of the authors has any conflicts of interest to declare.

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