6 Impairments and activity limitations in subjects with chronic upper limb complex regional pain syndrome type I

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Archives of Physical Medicine and Rehabilitation, In press.
6.1 Abstract

Objective: Complex Regional Pain Syndrome type I (CRPSI) is a symptom complex comprised of several impairments, which may lead to activity limitations. Our aim was to determine the degree of impairments and activity limitations and their inter-relationship. Design: Cross-sectional study inter-relating impairments and objectively measured activity limitations. Setting: Ambulatory/home environment. Patients: Thirty non-acute upper limb CRPSI subjects. Main outcome measure(s): Sensory, motor and autonomic impairments, as well as activity limitation outcome measures. The latter were objectively measured with a novel Upper Limb-Activity Monitor (based on ambulatory accelerometry). Results: All subjects were impaired to some degree but with a large variability with respect to magnitude. Regarding activity limitations, the involved upper limb was clearly less active (lower intensity and percentage of activity) than the non-involved side. Impaired active range of motion (adjusted $R^2$ 18-39%) and grip strength (adjusted $R^2$ 12-45%) were the most important factors explaining variance in activity limitations. Conclusions: All subjects were still impaired nearly three years after the causative event. The involved upper limb was also clearly less active than the non-involved side, especially when the subjects were sitting and when the dominant side was involved. The more impairments a subject had, especially motor impairments, the more activity limitations were present.
6.2 Introduction

Complex Regional Pain Syndrome type I (CRPSI; also known as reflex sympathetic dystrophy) remains a poorly understood and variously defined symptom complex. When CRPSI occurs, it usually follows surgery or trauma and it is generally expressed in the extremities. Its course shows large variability, which makes diagnosis and interpretation of clinical findings and research data difficult. Uncertainty surrounding the disorder is also reflected by the wide variety of treatments and, consequently, the numerous measures used to determine treatment outcome. Sensory, autonomic, trophic and motor impairments may be found in CRPSI. Furthermore, activity limitations during normal daily life including occupation and participation problems such as social functioning and role fulfillment have been reported. These studies show that CRPSI encompasses impairments, activity limitations and participation problems as described in the International Classification of Functioning (ICF, ICIDH2). However, most outcome measures used in CRPSI research concentrate on impairments. Up to now, there has been a lack of appropriate instruments to objectively determine activity limitations of subjects with upper limb CRPSI. The small number of instruments used in CRPSI research to determine activity limitations were retrospective scales and questionnaires.

From a rehabilitation viewpoint, it is important to analyse the relationship between impairments and activity limitations in order to address such questions as: ‘does an impairment always lead to activity limitations?’, ‘should treatment or prevention focus on impairment or activity limitations?’ and ‘which impairment mainly affects activities?’. However, only two studies have investigated the relationship between impairment-activity limitations relationship in CRPSI. In both these studies scales and questionnaires were used to determine activity limitations; a Visual Analogue Scale for perceived activity limitations (VAS-ADL) and the Groningen Activity Restrictions Scale for activity limitations (GARS). For this reason, an Upper Limb-Activity Monitor (ULAM) was developed, which allows objective measurement and quantification of upper limb activity while a subject is functioning during normal daily life. The ULAM has proven its ability to noninvasively detect limitations in upper limb activity in chronic upper limb CRPSI subjects. The advantages of the ULAM over scales and questionnaires are, for example, that it is more extensive than a VAS-ADL and, more importantly, it provides objective outcome measures for activity limitations that allows quantification of what subjects actually do in normal daily life and not what they report they are capable of. Our aim was to analyse the relationship between impairments and objectively measured activity limitations in upper limb CRPSI subjects. This will be the first study to determine how impairments and objectively measured activity limitations are interrelated in upper limb CRPSI.
The research questions were:
- What is the degree of impairments and activity limitations?
- What is the relationship between impairments and activity limitations?
- Which impairment(s) mainly explain(s) activity limitations?
- Do other variables influence the relationship between impairment-activity limitations?

6.3 Methods

Design and subjects
Thirty subjects with CRPSI in one upper limb volunteered for this cross-sectional study inter-relating impairments and objectively measured activity limitations. In 15 subjects the dominant side was involved and in the other 15 the non-dominant side. Only 1 subject was male; the average age was 55.1 (sd ± 14.9, range 20-81) years. Mean duration of CRPSI was 33 months (table 6.1). Inclusion criteria were: 1) presence of Veldman’s criteria 13 at diagnosis and 2) ongoing CRPSI-related complaints at enrollment into the study. The criteria of Veldman were a) four or five of the following: unexplained diffuse pain, different skin color relative to other side, diffuse edema, different skin temperature relative to other side, limited active range of motion, b) occurrence or increase of signs and symptoms after use, and c) presence of signs and symptoms in an area larger than was initially involved, including the area distal to primary injury. These criteria do not substantially differ from the IASP criteria 3, 34. Subjects were excluded if co-morbidities affecting upper limb usage or general mobility were present. Informed consent was obtained from all subjects and the study was approved by the Medical Ethics Committee of Erasmus MC.

Impairment outcome measures
The ‘Impairment level Sum Score’ (ISS) 11, a validated set of five items (temperature, VAS-pain, McGill-pain, AROM, volume) especially developed for upper limb CRPSI, was used to determine the degree of impairment. However, because the ISS, as most other sum scores 4, 11, 16, 35-37, is based on diagnostic criteria, it was considered incomplete to study the present population. Since it has recently been recognised that motor impairments are not only prominent in chronic CRPSI 8, 13, 18, 19, 38-42 but are also a distinct component to be incorporated in the IASP criteria for CRPSI 4, loss of grip strength was chosen as an additional item:
- **ISS-Temperature**
  An infrared thermometer a was used (measurement range 0–42.2°C, accuracy ± 0.2 °C). Temperature can be reliably measured dorsally perpendicular to the middle of the hand after 10-15 minutes acclimatisation 43. Normal temperature difference between both hands was set at ≤ 0.3 °C 11.
- **ISS-VAS**
  Pain resulting from effort was measured with a Visual Analogue Scale (VAS)
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• **ISS-McGill**
The McGill Pain Questionnaire (MPQ) is often used in CRPSI research\(^{45-47}\). The total number of words chosen from the list of sensory, affective and evaluative pain words from the reliable\(^{48}\) Dutch language version (MPQ-DLV) was used to assess pain during the previous week.

• **ISS-AROM**
Maximum active range of motion (AROM) within pain threshold was measured. Percentages of normal AROM (involved versus non-involved side) were determined for the wrist (dorsal/palmar flexion) and MCP and PIP (flexion/extension) of the two most impaired digits. Each joint movement was measured three times and averaged\(^{11,49,50}\).

• **ISS-Volume**
Volumetric measurements of the hands were taken with a volumeter\(^{b}\) which determines fluid overflow. The difference in volume between both hands was considered in relation to the volume of the unimpaired hand. A difference in volume up to 3.5% was considered normal\(^{11}\).

• **Strength**
A portable hand-held dynamometer\(^{c}\) was used, which allows quantification and, if performed in a standardized manner, reproducible and reliable\(^{51}\) determination of grip strength. Only four-point grip strength was measured because several forms of grip strength were well correlated in CRPSI subjects\(^{25}\). Subjects were instructed to squeeze as hard as possible with hands in the ‘lumbrical’ grip (thumb at bottom and digits II-IV on top of the device). Strength was measured three times after one practice and the average was calculated for both the involved and non-involved side.

Oerlemans et al. converted the ISS impairment items to a range of 1-10 (based on intra-individual comparisons for AROM, volume and temperature of both hands)\(^{11}\). A score of 1 was interpreted as absence of that impairment. In the present study, to make grip strength comparable with ISS scores, intra-individual comparisons for grip strength were also ascribed scores of 1 to 10 (if strength of the involved side was >90% of the non-involved side then the score was 1, if strength of the involved side is 0-10% then 10 was scored, the intermediate strength differences were ascribed scores 2-9). This score was added to the five ISS scores to create the Total Impairment Score ranging from 6-60, with a higher score indicating more severe impairment.

**Activity Limitations outcome measures**
The Upper Limb-Activity Monitor (ULAM) is an extended version of the ‘classic’ Activity Monitor (AM) which has been developed and validated in our department\(^{52-57}\). The AM allows objective measurement of mobility-related activities such as lying, sitting, standing, walking, cycling and general movement. This portable device enables detailed long-term ambulatory measurement of what subjects actually do.
during normal daily life and can therefore be used to determine activity level and, if present, activity limitations. The ULAM was developed to determine activity limitations of subjects with disorders related to the upper limbs. It enables one to determine whether or not the upper limbs are active when a subject is performing one of the mobility-related activities. The combination of mobility-related activities and upper limb activity allows one to obtain more specific information than with less advanced techniques, such as a wrist actigraph or actometer.

Uni-axial piezoresistive acceleration sensors attached to thighs (sensitive direction in sagittal plane), trunk (sensitive direction in sagittal and longitudinal plane) and forearms (sensitive direction in sagittal plane being in the anatomical position) are connected to a small recorder that is worn around the waist (figure 6.1). The raw acceleration signals are expressed in g (9.81 ms$^{-2}$) and are a combination of two components: gravitational acceleration and accelerations due to activity. The raw data was stored digitally on a PCMCIA flash card with a sample frequency of 32 Hertz downloaded onto a PC for subsequent analysis.

Automatic detection of mobility-related activities and upper limb activity was done by kinematic analysis based on Signal Processing and Inferencing Language (SPIL) routines, yielding ‘C’-code. For detection, three feature signals are derived from each raw acceleration signal: the angular, motility and frequency feature (time resolution 1 second). The subsequent steps of analysis have been described previously. To detect upper limb activity, the motility feature (Finite Impulse Response filter 0.3-16 Hz, envelope of the AC component of the acceleration signal), which is the variability around the mean in the raw acceleration signal expressed in g (9.81 ms$^{-1}$), is used. This variability can be considered as a measure for the intensity of upper limb activity: the more intensely active, the higher the motility value. For a more technical description of the detection method we refer to other studies.

Based on previous research, the following outcome measures were used:

- **Mean intensity of upper limb activity of the involved side during sitting and standing**
  The mean intensity of upper limb activity of the involved side was expressed in mean (scaled) motility values during the time the involved upper limb was active while the subjects were sitting and standing. The lower the mean intensity of upper limb activity the more limited the activity.

- **Percentage of upper limb activity of the involved side during sitting and standing**
  The percentage of upper limb activity of the involved side was expressed as the percentage of the time that the involved upper limb was active (i.e. exceeding a threshold in the motility value) while the subjects were sitting and standing. The lower the percentage of upper limb activity the more limited the activity.
• **Proportion of activity between both upper limbs during sitting and standing**
  The proportion of activity of one upper limb relative to the other upper limb was expressed as a ratio: the percentage of activity of the non-dominant side relative to the percentage of activity of the dominant side. These ratios were normalised based on a reference value derived from ten healthy subjects in an earlier study. For subjects with dominant side involvement, a ratio higher than 1 was associated with activity limitations. For subjects with non-dominant side involvement, a ratio lower than 1 was associated with activity limitations. The higher/lower these respective ratios, the more limited the activity.

• **Percentage of dynamic mobility-related activities**
  In addition to outcome measures related to the upper limbs, the percentage of the measurement period during which dynamic mobility-related activities (i.e. walking, cycling and general non-cyclic activity) were performed was also used as activity limitation outcome measure. The lower the percentage of dynamic mobility-related activities, the more limited the activity.

*Figure 6.1: A subject wearing the Upper Limb-Activity Monitor*

*Other variables*
Some demographic variables, such as age, gender, marital status and employment status, may influence the relationship between impairments and activity (limitations). Duration of CRPSI, time between onset and diagnosis and whether or not receiving therapy/medication may also influence this relationship. Involvement of dominant or non-dominant side should also be taken into account, because the inter-relation between impairment and activity may differ depending on whether or not the dominant side is involved.
Protocol
To reduce interference with normal daily life, the ULAM was fitted at home and worn for 24 hours. Subjects were instructed to continue their ordinary activities, except for swimming, bathing or showering. To avoid bias, initially, the exact technique and output parameters were not explained: the subjects were just told that the sensors detect movement of body parts to which they were attached. After 24 hours, the device was removed, subject characteristics and activities performed were noted and the six impairments were measured. At this stage, complete information was given about what the ULAM actually measures: a 24-hour activity pattern of whether the upper limbs are active or not plus which mobility-related activity was performed. All subjects agreed with this protocol. Measurements on the second day took approximately 1.5 hours; the order of measurement was the same for each subject with grip strength being measured last to avoid provoking physical complaints (e.g. pain) or increasing temperature.

Statistics
Non-parametric statistical methods were used: Spearman rank coefficients were used to describe correlations between outcome measures and other variables, the Wilcoxon signed rank test was used to determine whether outcome measures differed between involved and non-involved sides, and the Mann-Whitney test was used to determine whether activity limitation outcome measures differed between subjects with dominant and non-dominant side involvement. After confirmation that linear regression was allowed to analyse the relationship between impairment-activity limitations, simple linear regression was carried out for each dependent variable with impairment outcome measures as independent variables. Statistically significant (p ≤ 0.05) impairments that explained 10% or more of the variance in the simple models were included in the multiple models. Separate regression models were made for the two subgroups for the proportion of activity between both upper limbs during sitting and standing. SPSS for Windows (version 10.0) statistical package was used for data analysis.

6.4 Results

Subject characteristics
Most subjects were aged 40-70 years (table 6.1). Only one man participated, and overall the main precipitating event was one or more fracture(s). Most subjects had CRPSI for more than 1 year, with a mean duration of 32.8 months (sd 31.3 months, range 4-143 months). In about one third, the time between onset and diagnosis was more than 2 months (range 3-33 months).
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Table 6.1: Several characteristics of the thirty subjects with upper limb CRPSI. 

\( n = \text{number of subjects}, \% = \text{percentage of subjects} \)

<table>
<thead>
<tr>
<th>Subject characteristics</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-30</td>
<td>2</td>
<td>6.7</td>
</tr>
<tr>
<td>31-40</td>
<td>3</td>
<td>10.0</td>
</tr>
<tr>
<td>41-50</td>
<td>5</td>
<td>16.7</td>
</tr>
<tr>
<td>51-60</td>
<td>10</td>
<td>33.3</td>
</tr>
<tr>
<td>61-70</td>
<td>5</td>
<td>16.7</td>
</tr>
<tr>
<td>71-80</td>
<td>3</td>
<td>10.0</td>
</tr>
<tr>
<td>80+</td>
<td>2</td>
<td>6.7</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>Female</td>
<td>29</td>
<td>96.7</td>
</tr>
<tr>
<td>Causative event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fracture</td>
<td>15</td>
<td>50.0</td>
</tr>
<tr>
<td>Other</td>
<td>11</td>
<td>36.7</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>4</td>
<td>13.3</td>
</tr>
<tr>
<td>Time since onset (months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3-12</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>12+</td>
<td>21</td>
<td>70</td>
</tr>
<tr>
<td>Duration between onset &amp; diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \leq 2 \text{ months} )</td>
<td>19</td>
<td>63.3</td>
</tr>
<tr>
<td>&gt; 2 months</td>
<td>11</td>
<td>36.7</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, part time</td>
<td>7</td>
<td>23.3</td>
</tr>
<tr>
<td>No, retired</td>
<td>4</td>
<td>13.3</td>
</tr>
<tr>
<td>No, work compensation</td>
<td>10</td>
<td>33.3</td>
</tr>
<tr>
<td>No, housewife</td>
<td>9</td>
<td>30.0</td>
</tr>
</tbody>
</table>

**Impairments**

Impairment scores ranged considerably (table 6.2): nearly all possible values were present for each outcome measure. Median scores for ISS-AROM, Strength, ISS-McGill and ISS-VAS were higher than for ISS-Volume and ISS-Temperature. The only impairment that was present to a some degree in all subjects was impaired AROM. None of the subjects was completely unimpaired as indicated by the minimum Total Impairment Score of 13. Total Impairment Scores were not related to any of the other variables such as age or other demographic variables, duration of CRPSI, time between onset and diagnosis and having therapy or not. No significant differences were found between those with dominant side and those with non-
dominant side involvement with respect to impairment outcome measures or any other variables. ISS-VAS did not correlate well with ISS-McGill ($r_s=0.21$). Momentary pain (additionally measured with a VAS) ranged from 0-70 mm (median 13 mm) and was significantly correlated with ISS-VAS pain resulting from effort ($r_s=0.71$, $p=0.000$). Momentary pain was significantly less than pain resulting from effort ($p=0.000$).

**Table 6.2: Descriptive statistics (median scores and range) for the impairment outcome measures.**

<table>
<thead>
<tr>
<th>Impairment (possible range)</th>
<th>Median [range]</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISS-VAS (1-10)</td>
<td>5 [1-10]</td>
</tr>
<tr>
<td>ISS-McGill (1-10)</td>
<td>6 [1-10]</td>
</tr>
<tr>
<td>ISS-AROM (1-10)</td>
<td>7 [3-10]</td>
</tr>
<tr>
<td>ISS-Volume (1-10)</td>
<td>2 [1-10]</td>
</tr>
<tr>
<td>ISS-Temperature (1-10)</td>
<td>3 [1-10]</td>
</tr>
<tr>
<td>Strength (1-10)</td>
<td>6 [1-10]</td>
</tr>
<tr>
<td>Total Impairment Score (6-60)</td>
<td>31.5 [13-52]</td>
</tr>
</tbody>
</table>

**Activity limitations**

The mean intensity and percentage of upper limb activity of the involved side were significantly less than the non-involved side, during both sitting and standing (upper part table 6.3). The percentage of dynamic mobility-related activities did not differ significantly between subjects with dominant side involvement and those with non-dominant side involvement (lower part table 6.3); also, between these two subgroups there were no significant differences for the mean intensity and percentage of upper limb activity of the involved sides. Compared to the mean activity intensity of the dominant (4.04 g) and non-dominant (3.66 g) side of 10 healthy subjects during sitting $^{33}$, in these CRPSI subjects the activity of the involved side was low (3.10 g). This is also true for the percentage of upper limb activity during sitting (healthy subjects: dominant side 37.5%, non-dominant side 35.6%).

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Table 6.3: Activity Limitation outcome measures (I)
Descriptive statistics (mean and standard deviation; SD) for the mean intensity of upper limb activity (expressed as scaled (*100) motility values) and the percentage of upper limb activity (expressed as % of the time the limb was active during a specific mobility-related activity). The upper part presents within subject comparisons between involved and non-involved side (Wilcoxon signed rank). The lower part presents between subject comparisons between subjects with dominant and non-dominant side involvement (Mann-Whitney). n = number of subjects.

<table>
<thead>
<tr>
<th>Activity limitations</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Within subject comparison:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensity sitting (g *100)</td>
<td>3.10</td>
<td>± 0.99</td>
<td>4.17</td>
<td>± 1.66</td>
<td>0.001</td>
</tr>
<tr>
<td>Intensity standing (g *100)</td>
<td>9.96</td>
<td>± 3.16</td>
<td>12.88</td>
<td>± 3.38</td>
<td>0.001</td>
</tr>
<tr>
<td>Percentage sitting (%)</td>
<td>29.20</td>
<td>± 8.54</td>
<td>34.94</td>
<td>± 9.96</td>
<td>0.008</td>
</tr>
<tr>
<td>Percentage standing (%)</td>
<td>72.86</td>
<td>± 10.96</td>
<td>78.06</td>
<td>± 10.06</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Between group comparison:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of dynamic mobility-related activities (%)</td>
<td>10.32</td>
<td>± 4.04</td>
<td>12.22</td>
<td>± 5.68</td>
<td>0.604</td>
</tr>
<tr>
<td>Involved side: Intensity sitting (g *100)</td>
<td>2.98</td>
<td>± 1.08</td>
<td>3.21</td>
<td>± 0.91</td>
<td>0.455</td>
</tr>
<tr>
<td>Involved side: Intensity standing (g *100)</td>
<td>10.82</td>
<td>± 3.72</td>
<td>9.11</td>
<td>± 2.30</td>
<td>0.254</td>
</tr>
<tr>
<td>Involved side: Percentage sitting (%)</td>
<td>27.76</td>
<td>± 9.56</td>
<td>30.63</td>
<td>± 7.42</td>
<td>0.237</td>
</tr>
<tr>
<td>Involved side: Percentage standing (%)</td>
<td>72.69</td>
<td>± 10.66</td>
<td>73.23</td>
<td>± 11.4</td>
<td>0.820</td>
</tr>
</tbody>
</table>

Table 6.4 gives data on the proportion of activity between both upper limbs during sitting and standing separately for both subgroups. Not all subjects were limited with respect to these outcome measures, as indicated by the fact that most interquartile ranges included the reference value: seven subjects (23%) were classified as limited. After subsequent analysis of the percentages of activity of both upper limbs of the individual subjects, it appeared that for the subjects with dominant side involvement, limitations in the proportion of upper limb activity during sitting were due to a decreased percentage of upper limb activity of the involved dominant side; during standing, the activity of the non-involved (non-dominant) upper limb was increased. Unlike the subjects with dominant side involvement, there were no such patterns with respect to increase and/or decrease of percentage of upper limb activity in those with non-dominant side involvement.
Table 6.4: Activity Limitation outcome measures (II)
Median scores [and interquartile range] for the proportion of activity between both upper limbs during sitting and standing for both subgroups. For dominant side involvement, a ratio higher than 1 was associated with activity limitations. For non-dominant side involvement, a ratio lower than 1 was associated with activity limitations. The higher/lower these respective ratios, the more limited a subject was.

<table>
<thead>
<tr>
<th>Proportion of upper limb activity</th>
<th>During sitting</th>
<th>During standing</th>
</tr>
</thead>
<tbody>
<tr>
<td>non-dominant : dominant side</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominant involvement (n=15)</td>
<td>1.20 [0.85 – 1.61]</td>
<td>1.13 [1.05 – 1.19]</td>
</tr>
<tr>
<td>Non-dominant involvement (n=15)</td>
<td>0.88 [0.74 – 0.98]</td>
<td>0.98 [0.96 – 1.01]</td>
</tr>
</tbody>
</table>

Impairment-activity limitations relationship
The Total Impairment Score, ISS-AROM and Strength were significant in each simple model for the mean intensity and percentage of activity of the involved upper limb during sitting and standing (table 6.5). In addition, ISS-VAS and ISS-Temperature were significant in both the simple models during sitting. Since age was considered as a potential confounder for activity (i.e. the older, the less active), it was always included in the multiple models. In the multiple models AROM (p=0.009) and age (p=0.001) were significant contributors to the percentage of upper limb activity during standing. The variability in upper limb outcome measures explained by impairments and age ranged from 24% to 52%. Because the percentage of dynamic mobility-related activities (average 11.3%) performed by CRPSI subjects did not differ from earlier findings in healthy subjects 65, 66, indicating that the CRPSI subjects were not limited with respect to mobility, it was decided not to make regression models for this ULAM outcome measure.

Regarding the proportion of activity between both upper limbs during sitting and standing, ISS-AROM and the Total Impairment Score were significant in three of the four simple regression models made for both subgroups (table 6.6). Strength was significant in each simple model. The multiple regression models for the two subgroups explained variances ranging from 34-57%.
Table 6.5: Impairment-activity limitation relationship (I)
Simple and multiple regression models with activity limitation outcome measures (mean intensity and percentage of upper limb activity during sitting and standing) as dependent variables and impairment outcome measures as independent variables. For the simple models, the adjusted R squares are shown. For the multiple models, the standardized beta regression coefficients and the total adjusted R square are shown for impairments that were significant in the simple regression models (and age). Intensity sitting and standing = Mean intensity of upper limb activity of the involved upper limb during sitting and standing separately, Percentage sitting and standing = Percentage of upper limb activity of the involved upper limb during sitting and standing respectively, - not significant in the simple model and therefore not included in the multiple model, *** p ≤ 0.001, ** p ≤ 0.001, *p ≤ 0.05.

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Intensity sitting β</th>
<th>Adj R sq</th>
<th>Intensity standing β</th>
<th>Adj R sq</th>
<th>Percentage sitting β</th>
<th>Adj R sq</th>
<th>Percentage standing β</th>
<th>Adj R sq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple models:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISS-VAS</td>
<td>0.12</td>
<td>0.00</td>
<td>0.12</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISS-McGill</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISS-AROM</td>
<td>0.34**</td>
<td>0.23**</td>
<td>0.18**</td>
<td>0.07</td>
<td>0.00</td>
<td></td>
<td></td>
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Other variables
The relative temperature score (the degree to which the involved side is colder or warmer than the non-involved side) was significantly correlated with the percentage of upper limb activity ($r_s = 0.38$, $p=0.037$): the colder the hand, the less the percentage of activity. Also, the involved side of subjects having CRPSI for longer than 12 months was significantly colder compared to those with CRPSI of shorter duration ($p=0.02$). Duration of CRPSI, time between onset and diagnosis, employment status, marital status and level of education were not related to the upper limb activity outcome measures.
Table 6.6: Impairment-activity limitation relationship (II)
Simple and multiple regression models with activity limitation outcome measures (proportion of upper limb activity during sitting and standing) as dependent variables and impairment outcome measures as independent variables, for both subgroups separately. For the simple models, the adjusted R squares are shown. For the multiple models, the standardized beta regression coefficients and the total adjusted R square are shown for impairments that were significant in the simple regression models (and age). Proportion sitting = Proportion of upper limb activity of the non-dominant side relative to dominant side during sitting, Proportion standing = Proportion of upper limb activity of the non-dominant side relative to dominant side during standing, - not significant in the simple model and therefore not included in the multiple model, *** p \leq 0.001, ** p \leq 0.001, *p \leq 0.05.

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</table>

Multiple models:

| Age                | 0.41                            | 0.36                            | 0.28                            | 0.14 |
| ISS-AROM           | -0.31                           | -0.57                           | -0.28                           | 0.37 |
| Strength           | -0.30                           | -0.01                           | -0.56                           | -0.42 |
| Total Adjusted R sq. | 0.57 **                      | 0.43 *                          | 0.34 *                          | 0.37 * |

6.5 Discussion

Impairments
There was large intersubject variability in magnitude of impairments, which is in accordance with other studies 11, 12. The mutual impairment correlations did not differ from the findings of Oerlemans et al. 11 in more acute CRPSI, with the exception of the present significant correlations between VAS-AROM (r=0.50) and VAS-Volume (r=0.37). None of the impairments was related to duration of CRPSI. In our chronic population, impaired strength, AROM and pain were most prominent, which supports earlier findings that motor impairments become more important as the complicated syndrome becomes chronic 8, 13, 18, 19, 36-42.
AROM was most impaired in our group of subjects, but did not differ between subjects with multiple fractures or another causative event. In contrast to other motor impairments, because AROM and strength are relatively constant throughout the day, they were considered more suitable as outcome measures. The problem remains, however, that although rigidly standardized in every aspect, AROM and grip strength measurements may be subject to considerable systematic and random variation, which was anticipated by determining average scores of three movements per joint. Geertzen et al. also reported AROM differences between involved and non-involved side in shoulder, elbow and wrist, but considered these differences not clinically relevant because AROM was within the range needed for normal daily life. Since small reductions in mobility of especially the hand are thought to predominantly affect fine motor skills, we considered AROM of wrist and fingers more important outcome measures than AROM of shoulder and elbow. We did not notice other motor impairments such as tremors, spasms or dystonia during the measurements on the second day. These latter impairments have been reported in small patient groups with more generalized and severe CRPSI, but are not common. Also, their underlying mechanism is unclear.

Temperature and volume appeared least impaired. Regarding skin temperature, Oerlemans et al. pointed out that unequivocal measurement is difficult, because temperature may change with time in CRPSI and may be higher or lower than on the contralateral side. Moreover, objective and subjective temperature measurements do not always correspond in CRPSI. To partly overcome such validity problems, we differentiated between a warmer or colder involved side compared to the non-involved side. The finding that the involved sides were significantly colder in CRPSI of longer duration was in accordance with findings from advanced techniques measuring the vascular reflex response during a complete thermoregulatory cycle. No subjects was in the ‘acute phase’ (< 3 months), so we could not contribute to the discussion about subsequent stages in CRPSI.

ISS-McGill was poorly correlated with other impairments both in our study and in that of Oerlemans et al. The McGill Pain Questionnaire (MPQ) assesses sensory, affective and evaluative aspects of pain and, for this reason, measures beyond impairment level. Our data were in accordance with the finding that chronic pain patients such as in CRPSI choose affective and especially evaluative aspects with greater frequency than acute patients. Sensory indicators tingling, stiff and nagging, affective indicator tiring and evaluative indicators tolerable/bearable and annoying (Dutch Language Version) were indicated most often. ISS-VAS was more strongly correlated with ISS-McGill’s affective and evaluative aspects than with its sensory aspects; although a VAS is intended to measure pain intensity, chronic CRPSI subjects may indeed use it to reflect affective and evaluative aspects of pain. Because acute pain becomes chronic pain as the CRPSI syndrome continues, the MPQ is important to monitor changes over time. Although not all CRPSI patients have pain, it is too important an aspect to quantify using only a simple VAS.
Activity limitations

Although our subjects with dominant side involvement were somewhat less active, in general, CRPSI in one upper limb does not appear to limit general mobility. The involved side was on average significantly ‘disused’ or ‘spared/protected’, both during sitting and standing. Unfortunately, it was not possible to detect to what degree disuse and/or sparing/protecting were responsible for this inactivity. Moreover, because upper limb activity during standing in our CRPSI group did not differ from healthy subjects, upper limb activity during sitting seems to be the most important aspect when determining activity limitations resulting from an upper limb disorder.

In our study, the lack of significant differences for mean intensity and percentage of activity of the involved upper limb between both subgroups (table 6.4) seems to indicate that both subgroups were equally limited; however, dominant side involved subjects were more limited. With respect to intensity and percentage of upper limb activity, equal absolute values of the dominant and non-dominant involved sides are due to a relatively larger decrease in activity of the dominant involved side than of the non-dominant involved side; in ‘healthy’ upper limb activity the dominant side is more active than the non-dominant side. Since our two subgroups were similar with respect to duration of CRPSI, impairment outcome measure scores and a number of other relevant variables, it can be concluded that the impact on normal daily life of CRPSI in the dominant side is larger than when the non-dominant side is involved. This is in accordance with earlier findings and supports the intuitive idea that a dominant upper limb involvement generally has greater impact than non-dominant involvement.

Subjects with dominant side involvement who were classified as limited showed a clearly decreased percentage of activity of the involved dominant side during sitting and a clearly increased percentage of activity of the non-involved (non-dominant) side during standing. It may be relatively easier to activate the non-involved (non-dominant) upper limb to compensate for decreased activity of the involved limb during standing in order to do what one wants to do. However, since upper limb activity during sitting requires more precision skills (fine motor skills, manipulative upper limb usage), compensating decreased activity of the involved limb with the non-involved (non-dominant) limb may be more difficult during sitting. It was difficult to compare our findings with other studies reporting 77% 24, 62% 16 and 78% 20 of the subjects with chronic CRPSI being limited because the ULAM measurement technique we used was not used in these other studies.
Impairments and activity limitations in chronic CRPSI

Relationship between impairments and activity limitations
Impaired AROM and grip strength and to a lesser extent pain resulting from effort were the most important factors explaining variance in activity limitations in normal daily life in chronic upper limb CRPSI. The fact that the Total Impairment Score was significant in each simple regression model underlines the fact that heterogeneous presence of impairments is a complicating factor when studying the ‘impairment-activity limitation’-relationship in CRPSI. In our opinion, however, it would have been inadequate to take only one or a few impairments into account.

In the studies by Geertzen et al., a VAS for perceived activity limitations (VAS-ADL) and two subscores of the Groningen Activity Restrictions Scale (GARS), performance of activities of daily life (ADL) and instrumental activities of daily life (IADL), were used as outcome measures for activity limitations. Pain appeared to be the most important impairment limiting activity, which is in contrast to the present findings and may have been due to different operationalisation of pain degree.

One may hypothesize that the ULAM is inherently more related to motor impairments since it measures only activity limitations and not other limitations (e.g. situational or communicational limitations), thereby being more associated with pain resulting from effort (‘activity’) than with momentary pain. However, the items assessed with the GARS and VAS-ADL were also solely activity limitations. Therefore, it was considered unlikely that different operationalisations explain why pain was less important than motor impairments. Moreover, since our data on momentary pain did not differ from Geertzen et al. (range 0-80 mm, mean 12 mm) we think this excludes volunteer/selection bias with respect to pain. The different results with respect to pain may have been due to different characteristics of the instruments used to determine activity limitations: the ULAM is a non-retrospective, objective outcome measure to quantify what subjects actually do and did not quantify perceived or self-reported limitations as did the VAS-ADL and GARS.

The importance of motor impairments in chronic CRPSI was stressed by Geertzen et al. and others. Clinically, this may indicate that increasing AROM and grip strength as early as possible is as (or even more) important than pain management when treating CRPSI in order to prevent or reduce CRPSI-related complaints. Our aim was to find out which impairment(s) were most prominent and least variable among 30 subjects with chronic upper limb CRPSI as well as which impairment(s) explained most of the variability at the ICF activity level. It appeared that motor and sensory impairments were most prominent and equally variable. However, impaired AROM and grip strength clearly explained a higher percentage of the variability in activity limitations.

Therefore we conclude that the more impaired a subject was, the more activity limitations were present. It should be noted, however, that caution is needed when
relating quantified impairment to quantified activity limitations. This cross-sectional study does not allow us to conclude that an impairment always leads to activity limitations; linear regression analysis does not say anything about causality between variables. For example, it cannot be said that the percentage of activity was less because a hand was colder, or the other way around (i.e. because of a lower activity percentage, a hand becomes colder). This may also partly explain why the relationship between the ICF consequences of a disease is often found to be ambiguous. It was our intention to determine which impairment(s) explained most of the variability in activity limitations.

Other variables
There was no relationship between the duration of CRPSI and either of the outcome measures, which was probably due to large intersubject variability in the presence and severeness of impairments and activity limitations. Age was always included in the regression models, although it was not always significantly related to the activity limitation outcome measures. The present subjects were representative of the CRPSI population with respect to age. Although CRPSI affects predominantly women, men were clearly underrepresented in this study. This homogeneity with respect to gender should be taken into account when findings are extrapolated to the male CRPSI population. This study clearly demonstrates the important influence of the involved side (dominant or non-dominant) on the degree of activity limitations.

Similar to Geertzen et al., we found no evidence that early diagnosis and subsequently early initiation of therapy might give better long-term outcome. As stated, causative event, employment status, marital status and level of education were not related to any of the upper limb activity outcome measures; this might be due to the relatively small number of subjects or possible selection bias. Finally, it can not be excluded that factors other than those examined in the present study need consideration. Other impairments such as hyperhydrosis, discoloration, dystonia, tremor or psychosocial factors such as motivation, kinesiophobia, presence of social life events may also explain some of the variance in the activity limitation outcome measures, but were not assessed in this study.

Practical and methodological issues
Our aim was to use outcome measures that were workable and allowed quantification. In addition, the outcome measures had to be as far as possible objective, reliable and valid to factually describe the ‘impairment-activity limitation’ relationship in subjects with chronic upper limb CRPSI. A potential limitation of this study, however, was its cross-sectional nature. Since CRPSI is a chronic disease with exacerbations and remissions even throughout the same day, this may hamper reliable measurement of some of the outcome measures. Despite this, the fact that the ULAM outcome measures were relatively comprehensive, plus the small group of subjects and resulting potential lack of explanatory power and biological variance in daily activity, the explained variances in the multiple models were not low.
Linear regression was used because there was no co-linearity between impairment variables. Because of the subject-to-variable ratio, no independent variables other than impairment and age were included in the multiple models.

With a novel device like the ULAM, activity limitations of subjects with an upper limb disorder can be viewed from a perspective other than the usual one. The additional value of the ULAM is that it allows objective and ambulatory determination of (in-)activity of both upper limbs while a subject is performing specific mobility-related activities. This technique also enables differentiation between the impact of dominant side or non-dominant side involvement on activity during normal daily life, a topic that has not yet been investigated. Of course, a new technique also has some disadvantages. The recorder and sensor could be smaller and lighter, little is known about between-day variability in activity patterns of subjects, and fitting the ULAM at home to reduce interference with normal life is time-consuming. In addition, manipulative/fine upper limb activity, holding of objects and leaning are currently not 100% well detected with the ULAM. Since a large number of upper limb CRPSI subjects also experience problems with these forms of upper limb usage in addition to decreased gross motor activity, the explained variances from the regression models probably would have been higher had we been able to detect all forms of upper limb usage 100% correctly. Fortunately, development of instruments, such as the ULAM, is an ongoing process of extending possibilities and optimizing current properties.

6.6 Conclusion

These thirty subjects with chronic upper limb CRPSI showed large variability with respect to magnitude of impairments. All subjects were impaired to some degree, but AROM, strength and pain were far more severe than impaired volume or temperature. Subjects with dominant and non-dominant side involvement were equally impaired and both subgroups were also comparable with respect to other relevant variables. With respect to activity limitations, the involved upper limbs were all less active for the mean intensity and percentage of upper limb activity; the subjects clearly spared or protected their involved side during normal daily life. This impact of upper limb CRPSI was more obvious during sitting than during standing. As measured with the ULAM, subjects with dominant side involvement had more activity limitations than subjects with non-dominant side involvement. Analysis of the relationship between impairment-activity limitation showed that impairments associated with upper limb CRPSI are not related to the percentage of dynamic mobility-related activities performed. However, impaired AROM and grip strength, and to a lesser extent pain resulting from effort, were the most important factors explaining variance in activity limitations in normal daily life in these 30 subjects with chronic CRPSI of one upper limb. Thus the more impaired a subject was, the more activity limitations were present.
Acknowledgments
The authors would like to thank J.J. van Hilten (Department of Neurology, LUMC, Leiden, the Netherlands) and H.J. Krijnen (Pain Clinic / Department of Anesthesiology, Ikazia Hospital, Rotterdam, the Netherlands) for their help in recruiting the subjects, H.M. Oerlemans (Department of Allied Health Services, University Hospital Nijmegen, the Netherlands) for information related to the Impairment Sum Score.

Suppliers
a. Braun Pro 3000 Type 6014, Kronberg, Germany
b. Volumeters Unlimited, Idywild, USA
c. Microfet, Force Evaluating and Testing System, Hoggan Health Industries Inc., Draper, USA
d. Analog Devices, ADXL201 (size 1x1x0.5 cm)
e. TEMEC Instruments BV, Kerkrade, the Netherlands

6.7 References
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