2 Outcome measures for complex regional pain syndrome type I: an overview in the context of the international classification of impairments disabilities and handicaps

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2.1 Abstract

Purpose: To determine the availability of relevant and objective outcome measures concerning Complex Regional Pain Syndrome Type I (CRPSI) for Rehabilitation Medicine. **Method:** Outcome measures were classified according to the International Classification of Impairments, Disabilities and Handicaps. For each outcome measure a description of concept, operationalisation into variables and instrument was given. We performed a PUBMED MEDLINE search (1980-1998) using the following keywords: complex regional pain syndrome, reflex sympathetic dystrophy, impairment, disability, handicap, (long-term) outcome and effect/efficacy. **Results:** Most outcome measures were concentrated on impairments, whereas measures at the level of disabilities and handicaps, the most relevant levels for rehabilitation medicine, were mentioned in very few studies. Objective outcome measures were merely found at the level of impairment. **Conclusion:** The results indicate a need for the development of relevant outcome measures at the level of disabilities and handicaps that can objectively measure treatment efficacy for CRPSI.

2.2 Introduction

Complex Regional Pain Syndrome Type I (CRPSI; also known as Reflex Sympathetic Dystrophy) is a poorly understood and not well defined symptom complex comprising a combination of sensory, trophic, autonomic and motor impairments [1, 2]. The syndrome usually follows surgery or trauma, and is generally expressed in the extremities. In addition to the impairments, CRPSI can lead to serious disabilities in performing activities of daily life and handicap [3, 4]. In the acute phase of CRPSI, pain in particular may constitute a major cause of disability and/or handicap, whereas during the later stages CRPSI associated motor impairments, together with pain, are thought to bring about disabilities and/or handicaps [1, 5, 6]. The complex entity of CRPSI has often been investigated, leading, however, to confusing and conflicting results and theories about the aetiology and pathophysiology [7]. As the disease is not yet understood, plus the fact that each speciality has its own discipline-specific approach, a wide variety of treatments (more than 50) are found in literature [8]. As a consequence, numerous measures to determine treatment outcome have been described.

In the present paper, the numerous measures that are used to determine treatment outcome in CRPSI research and clinical practice will be classified. So far, one of the difficulties in interpreting reports on treatment efficacy in CRPSI, has been the (objective) quantification of patient findings and the lack of uniform measurement of treatment outcome [9, 10]. Classification of outcome measures may not only be a useful tool to indicate the extent of the (obvious) inconsistency in defining treatment outcome in CRPSI research. The main aim of classifying outcome measures in the present paper is to determine whether relevant and objective outcome measures for rehabilitation medicine are available. It is clear that objective outcome measures are preferable to subjective outcome measures; the latter are more likely to endanger reliability and validity of measurements. As for the relevance of outcome measures: outcome measures are considered most relevant for rehabilitation medicine when they concern the goal of rehabilitation, that is regaining and/or maintaining of functionality by decreasing the consequences of a disease [11, 12]. Outcome measures concerning impairments are considered less relevant for rehabilitation medicine, especially since the relation between the consequences of a disease is often found to be rather ambiguous [13-15].

The international classification of impairments, disabilities and handicaps (ICIDH) [16] is an often-used classification, in which three hierarchical levels of the consequences of a disease on everyday life of patients are distinguished. Outcome measures on the level of impairments, disabilities and handicaps concern the consequences of diseases at the level of the body, the person and the person as a social being, respectively. As for CRPSI, the consequences at the ICIDH level of impairments can be categorised into sensory impairments (e.g. neuropathic pain, allodynia,

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hyperalgesia, hypesthesia, anaesthesia, dysesthesia, hyperpathia), autonomic impairments (e.g. oedema, hyperhydrosis, skin colour change, change of temperature), trophic impairments (e.g. atrophy of skin, nails, muscles and bone), and motor impairments (e.g. dystonia, weakness, spasms, tremor, difficulty initiating movement, increased tone and reflexes, and increase of complaints after exercise) [8]. Disabilities associated with CRPSI are those directly related to the involved extremity (e.g. problems with getting dressed with upper extremity CRPSI or climbing stairs with lower extremity CRPSI) and general disabilities in daily functioning (e.g. slow performance of activities of daily living). Handicaps associated with CRPSI concern limitations in social functioning (e.g. alienation) and problems with role fulfilment (e.g. a grandmother with CRPSI cannot play with her grandchild), as a consequence of pain, other impairments or disabilities [17]. From this list of consequences it becomes clear that CRPSI encompasses all three levels of the consequences of a disease as described in the ICIDH. Although some discussion continues about the sometimes unclear distinction between the theoretical levels of the ICIDH [18, 19], we consider the ICIDH framework useful to classify outcome measures in order to make a statement on availability of relevant and objective outcome measures for rehabilitation medicine.

2.3   Method and data sources

To obtain data, a PUBMED MEDLINE search (1980-1998) was performed using 'complex regional pain syndrome', 'reflex sympathetic dystrophy', 'impairment', 'disability', 'handicap', '(long term) outcome' and 'effect' as keywords. The initial idea of only using randomised clinical trial studies and quasi-experimental studies was not feasible given the relatively small number of studies performed up till now. Therefore, non-experimental and transversal studies with descriptions of one or more outcome measures were also included. Only journal articles in the English or Dutch languages were used. Publications without MEDLINE abstract and studies with less than 8 subjects were excluded. To provide insight in the kind of research that is performed concerning CRPSI, we studied some characteristics of the publications used for classification of outcome measures.

To determine the success of treatment in a reliable and valid manner, well-defined and methodologically sound outcome measures are of major importance [20-22]. In general, an outcome measure can be considered methodologically sound when the theoretical definition of the outcome measure (at the conceptual level) is clearly operationalised into one or more variables [21]. Moreover, an appropriate instrument to assign a value to variables has to be chosen [21]. In this study, we represented each outcome measure in a scheme, in which the concept to be measured, the operationalisation of this concept into variable(s), and the instrument to assign a value to the variables were described. It was not our aim to take reliability and validity of measurements with different instruments into account. Each outcome measure was classified according to the three levels of a consequence of a disease

(impairment, disability and handicap). The earlier described categorisation of impairments [8] was also applied in the tables.

Each publication was analysed to find information about concept, operationalisation of concept into variable(s), instrument and level of the ICIDH classification of the described outcome measures. Almost identical descriptions of concept, operationalisation and/or instrument of two or more outcome measures in different publications were represented as one outcome measure to limit the size of the tables. In case the concepts of outcome measures in different publications were similar, but different operationalisations and/or instruments were described, the outcome measures were shown separately.

2.4   Results

To provide insight in the kind of research that is performed concerning CRPSI, some characteristics of the studies were described (table 2.1). In addition to information about the first author and year of publication, studies were categorized as either transversal or longitudinal depending on the number of measurements. Transversal studies were categorized as either retrospective or prospective depending on whether measurements are done with data that already existed before defining the research questions or yet to be acquired data. Longitudinal studies were categorized as either experimental or non-experimental depending on whether the researcher actively intervenes in the research process or not. Specification of the type of treatment and research field, based on the first author, were presented, as well.

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Table 2.1: Overview of several aspects of the publications studied.

Author(s) (+ref. no.)	Year	Design†	Subjects (n)	Type of treatment	Research field
Atkins et al.[39]	1990	tran., pros.	60	No treatment	Orthopaedic Surgery
Bickerstaff et al.[41]	1991	long., exp.	20 (+20 control)	Nasal calcitonine (Sandoz Basle)	Hum. Metabolism & Clin.Biochemistry
Bickerstaff et al.[42]	1994	long., non-exp.	274	No treatment	Hum. Metabolism & Clin.Biochemistry
Braus et al.[66]	1994	long., exp.	36	Oral corticosteroids (methyl prednisolone) + daily physical therapy	Neuropathology
Cortet et al.[30]	1997	long., exp.	23	Intravenous 2nd generation biphosphonate pamidronate (APD)	Rheumatology
Davidoff et al.[10]	1988	long., exp.	17	Exercise program (8 weeks) + corticosteroids or sympathetic blockade	Rehabilitation Medicine
Field et al.[37]	1992	long., exp.	55	Intravenous regional anaesthesia + cast immobilisation (4 weeks)	Orthopaedics
Field et al.[38]	1993	long., exp.	17	Serial regional intravenous guanethidine blockade	Orthopaedics
Geertzen et al.[40]	1994	long., exp.	26	Regional intravenous ismelin blocks (n = 13) + radical scavenger DMSO (n = 13)	Rehabilitation Medicine
Geertzen et al.[15,45]	1998	tran., retro. + pros.	65	No particular treatment (follow-up after various treatments)	Rehabilitation Medicine
Gobelet et al.[9]	1991	long., exp.	33 (+33 control)	Physical therapy combined with calcitonine	Rehabilitation Medicine
Hamanci et al.[26]	1996	long., exp.	24 (+16 control)	Intramuscular salmon calcitonine treatment	Rehabilitation Medicine
Hassenbusch et al.[32]	1996	long., exp.	30	Peripheral nerve stimulation	Neurosurgery
Hord et al.[34]	1992	long., exp.	12	Intravenous regional bretylium and lidocaine	Anaesthesiology + Orthopaedics
Kaplan et al.[33]	1996	long., exp.	53	Intravenous regional guanethidine Bier block	Anaesthesiology + Pain Management
Kozin et al.[78]	1981	tran., pros.	48 (+16 control)	No particular treatment	Radiology
Langendijk et al.[25]	1993	long., exp.	37	Dimethylsulfoxide DMSO (50%) in a fatty cream	Pharmacy
Mailis et al.[62]	1997	long., exp.	15 (+21 control)	Intravenous administration of sodyum amytal, a medium action barbiturate	Pain Investigation Unit
Muramatsu et al.[29]	1998	long., exp.	17	Movelat cream manipulation (MIRA) therapy and regional anesthesia	Orthopaedic Surgery
*Poplawski et al.[27]	1983	tran., retro. + pros.	62	No particular treatment	Orthopaedics
*Poplawski et al.[27]	1983	long., exp.	27	Regional intravenous block (+corticosteroids) followed by physical therapy	Orthopaedics
Ramamurthy et al.[38]	1995	long., exp.	30 (+30 control)	Intravenous regional block with guanethidine	Anaesthesiology
Rauck et al.[36]	1993	long., exp.	26	Epidural clonidine	Anaesthesiology
Robaina et al.[73]	1989	long., exp.	35	Transcutaneous electrical nerve stimulation + spinal cord stimulation (n = 6 of 35)	Neurosurgery + Anaesthesiology
Schwartzman et al.[34]	1997	tran., retro.	29	Transthoracic or lumbar sympathectomy	Neurology
Subbarao et al.[68]	1981	tran., retro. + pros.	77	No particular treatment (follow-up after various treatments)	Rehabilitation Medicine
Tu et al.[44]	1994	tran., pros.	8	Surgical sympathectomy	Radiology
Vande Streek et al.[63]	1998	tran., pros.	?	No treatment	Nuclear Medicine
Veldman et al.[35]	1995	long., exp.	71	Injection of bupivacaine + methylprednisolone for RSD shoulder complaints	Surgery
Zuurmond et al.[31]	1996	long., exp.	16 (+15 control)	Dimethylsulfoxide in a fatty cream	Anaesthesiology

* The study of Poplawski et al. consists of two parts with distinct designs that are shown separately.
† long. = more than one measurement, tran. = one measurement, retro. = data already available, pros. = data yet to be aquired, exp. = active intervention, non-exp. = no active intervention

2.4.1   Outcome measure at the level of impairment

Sensory impairments

A variety of outcome measures at the ICIDH level of sensory impairments were found (table 2.2). However, only few of the earlier described familiar CRPSI-associated sensory impairments [8, 23] were used as concepts of outcome measures. It is clear that the concept of pain is most frequently used in CRPSI research and practice.

Although there was general acceptance of pain as the main concept, operationalization of this concept differed considerably (table 2.2). In some publications, pain was operationalized by simply describing the type [24] or location [9, 10] of pain. Other operationalizations of the concept of pain were focused on the level of pain, indicated by using the terms degree [25], score [26], intensity [10, 15, 27, 28] or severity [27-29] of pain. Changes in the level of pain were indicated by usage of the terms decrease [30], change [31-33], relief [25, 34, 35] or reduction [32, 36]. These differences in operationalization were not related to the design of the study. From a methodological perspective, it may be expected that pain was operationalized as changes in pain level in longitudinal studies and as pain level in transversal studies, which was, however, not consistently done. In general, operationalizing pain was considered obvious and was not extensively described. In addition to pain, tenderness was the only other sensory impairment that was used as an outcome measure concept in more than one publication. As for the instruments to measure pain, it appeared that pain was mainly measured by scales and questionnaires and virtually no objective instruments were used.

Table 2.2: Outcome measures used in CRPSI research to measure sensory impairments. Insufficient descriptive detail in publications is represented by a question mark.

Concept	Operationalization	Instrument(s)	Reference no.
Pain	Burning pain	Visual analogue scale (VAS)	24
Pain	Change in level of diffuse pain	Visual analogue scale (VAS)	31
Pain	Change in level of diffuse pain	Examination: pressure exerted over tendons	35
Pain	Change in level of mechanical allodynic + spontaneous pain	Verbal digital scale (0–10)	32
Pain	Change in level of pain	Verbal digital scale (0–10)	30
Pain	Change in level of pain	Visual analogue scale (VAS)	25, 30, 34
Pain	Change in level of pain	4-point scale	33
Pain	Change in level of pain	Question(naire) or patient's estimate	32
Pain	Change in level of sensory, affective + miscellaneous pain	McGill pain questionnaire (PRI)	36
Pain	Level of pain	Visual analogue scale (VAS)	10, 26, 36, 40, 47, 73
Pain	Level of pain	McGill pain questionnaire	28, 73
Pain	Level of pain	3, 4 or 6-point scale	27, 29, 66
Pain	Presence or absence of pain	Question(naire) or patient's estimate	39, 41, 42
Pain	Joint pain (at rest or during movement) by palpation	4 or 5-point score	9, 10
Pain	Affective, sensory + evaluative aspects pain	McGill pain questionnaire (PRI + NWC)	10
Pain	Pain as part of general health	RAND-36 questionnaire	79
Hyperalgesia	Intensity of hyperalgesia	6-point scale	66
Tenderness	Tenderness of wrist, MCP, PIP, DIP	Investigation	26
Tenderness	Bony tenderness in response to load compared to other hand	Dolorimeter ratio (kg/m²)	37–39, 41, 42
?	Moving two-point discrimination volar tip thumb + index finger	Disk Discriminator (mm)	79

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Autonomic impairments

Autonomic impairments of CRPSI patients can be categorized as changes in temperature, changes in skin colour, changes in volume and changes in sweat secretion [8]. These four autonomic impairments associated with CRPSI have all been used as outcome measure concepts (table 2.3): a large variety of 'autonomic' outcome measures were found. Some authors consider autonomic impairments as a cluster of signs or symptoms, which was represented by conceptual umbrella terms, such as 'vasomotor instability' [29, 37-39] or 'vasomotor changes' [32]. Most authors, however, did not use such umbrella terms. For clarity, the initial concepts of tumour [31], oedema [9, 15, 26, 40] and swelling [10, 25, 27, 29, 37-39, 41, 42] were grouped as volume. Operationalizations shown in table 2.3 are original operationalizations and were not renamed. Of the autonomic impairments, (changes in) volume was clearly most often used as concept of outcome measures.

Table 2.3: Outcome measures used in CRPSI research to measure autonomic impairments. Insufficient descriptive detail in publications is represented by a question mark. The bottom three rows represent outcome measures that do not fit into the categories of Kurvers (1997).

Concept	Operationalization	Instrument(s)	Reference no.
skin temperature			
calor	elevated skin temperature compared to other side	dorsal side observer's hand + patient's estimate	25, 31
?	bilateral skin temperature	?	28
vasomotor instability	abnormal temperature affected hand	2-point questionnaire	42
calor	2-point temperature profile skin compared to other side	?	10
vasomotor instability	(7-point) temperature profile skin compared to other side	portable thermography	32, 38
?	skin temperature response (to electrical stimulation)	thermometer	34, 62
skin colour			
discoloration	difference in skin colour compared to other side	3-point scale	15, 40
rubor	difference in skin colour compared to other side	observation/examination	25, 31
vasomotor tone changes	change in skin colour compared to other side	examination on 4-point scale	32
vasomotor instability	abnormal skin colour affected hand	2-point questionnaire	42
volume			
volume	diffuse oedema	observation/examination	31
volume	degree of oedema compared to other side	observation	25
vasomotor tone changes	degree of swelling compared to other side	observation	32
volume	degree or severity of oedema dorsal side throughout day	4-point scale	29
autonomic problem	degree or severity of distal oedema	4-point scale	66
volume	degree or severity of oedema	3 or 4 point scale (examination)	9, 15, 26, 40
volume	volume hand compared to other side	ratio water displacement (+ assessment)	10, 37–39, 41, 4
volume	digital circumference compared to other side	arthrocircameter or measuring tape	15, 27, 38, 39
volume	skin thickness compared to other side	skinfold calipers on dorsum hand (mm)	39
perspiration			
vasomotor instability	hyperhidrosis affected hand	2-point questionnaire	42
?	hyperhidrosis affected hand compared to other side	observation	25
?	bilateral electrodermal activity from sweat glands	electrical stimulation and macroelectrode recording	62
vasomotor instability	response to external factors/environmental changes	questionnaire	37–39, 42
?	asymmetrical blood flow in extremities	scintigraphy	43
vasoconctrictor tone	blood flow distal artery muscle affected side	colour duplex Doppler ultrasound	44

Operationalizations of the autonomic impairment concepts, as well as the instruments to measure autonomic impairments were not uniform. Part of the outcome measure operationalizations were expressed as a ratio of affected and unaffected side, whereas the other part only took the affected side into account. The three outcome measures at the bottom of table 2.3 were separated from the other outcome measures. This was done because they could either be considered as an outcome measure with a general operationalization of more than one of the four autonomic impairments [37-39, 42, 43], or because none of the four autonomic symptoms were mentioned specifically in the text [44].

Trophic impairments

Only few outcome measures at the level of trophic impairments were found (table 2.4). Nearly all of these outcome measures were used by highly specialised disciplines, such as Nuclear medicine and Human metabolism & clinical biochemistry.

Table 2.4: Outcome measures used in CRPSI research to measure trophic impairments. Insufficient descriptive detail in publications is represented by a question mark.

Concept	Operationalization	Instrument(s)	Reference no.
trophic changes	degree of trophic changes	examination, 4-point scale	32
?	abnormal hair or nail growth compared to other side	observation	25
skeletal changes	trabecular bone evaluation	radiographic scoring system	41
skeletal changes	cortical bone evaluation of metacarpals	morphometry	41
skeletal changes	bone mineral density compared to other side	Nuclear Data ND 1100 scanner	41
dynamic bone changes	periarticular bone uptake compared to other side	Three-Phase-Bone-Scan (TPBS)	63
osteoporosis	demineralisation	radiography	43
?	increased periarticular activity compared to other side	scintigraphy	43

Motor impairments

A large number of 'motor' outcome measures at the ICIDH level of impairments were found (table 2.5). Lack of unity in defining outcome measures was very obvious with motor impairments: concepts, operationalization as well as instruments differed enormously. Studies mainly focused on operationalization and instruments mentioning the concept to be measured. Information about concepts had to be extracted from all sections of the publications, which made some interpretation unavoidable. In several publications [10, 15, 38, 41, 42] information about concepts could not be found.

Range of Motion (ROM) was the most frequently adopted operationalization of motor impairment outcome measures. Measurement of active or passive ROM was not always specified. Moreover, ROM was not consistently measured in the same joints of upper or lower extremity. In one study [29] the instrument to determine ROM was not specifically mentioned, which forces one to make assumptions when trying to classify the different outcome measures.

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Table 2.5: Outcome measures used in CRPSI research to measure motor impairments. Insufficient descriptive detail about concepts in publications is represented by a question mark.

Concept	Operationalization	Instrument(s)	Reference no.
loss of motor function	pinch grip, elbow flexion and shoulder abduction	Motricity index	26
weakness	grip strength compared to other side	hand held strength gauge	41, 42
joint function	grip strength compared to other side	sphygmomanometer	39
?	grip strength compared to other side	dynamometer	15,38
motor deficits	degree of motor weakness	4 or 6-point scale, examination	32, 66
?	stiffness in fingers	questionnaire	41, 42
loss of motion	stiffness during day	4-point scale on palpation or complaints	27, 29
functio laesa	limited active ROM	observation/examination	31
inflammatory symptom	limited active or passive ROM shoulder	observation/examination	35
motor function	painless passive ROM shoulder	4-point scale with goniometer	66
motor function	passive ROM shoulder, wrist and MCP	goniometer	26
contracture	ROM PIP joint, severity compared to other side	4-point scale	29
joint function	ROM shoulder, elbow and finger	clinical assessment and goniometry	39
joint mobility	ROM fingers	goniometry	37
loss of mobility	ROM compared to other side	4-point mobility scale	9
stiffness	ROM all finger joints compared to other side	goniometer	38
loss of motion	ROM digital joints compared to other side	goniometer	27,28
motor function limitation	ROM fingers when making fist compared to other side	measurement tape	15, 40
motor function limitation	ROM thumb	6-point scale	15,40
motor function limitation	active ROM shoulder+elbow+wrist compared to ROM normal ADL	goniometer	15
?	active ROM compared to other side	measurement tape and goniometer	10

2.4.2   Outcome measures at the level of disability and handicap

Relatively few studies expressed the outcome of a CRPSI treatment in terms of disability and/or handicap (table 2.6). Therefore, we decided to describe the outcome measures of these two levels together. Concepts as well as operationalizations of outcome measures were described in very different ways, although the majority of outcome measure concepts at the level of disabilities were related to occupation. Instruments to assess 'disability' and 'handicap' were scales and questionnaires.

Operationalization into activity level categories in ordinal scales was not always consistent and scales or interviews sometimes contained items with different levels of abstraction [32, 42] including some items at the level of impairments, which made interpretation of treatment outcome difficult. Some instruments (e.g. RAND-36 Questionnaire) contain items at both the level of disabilities and at the level of handicaps [45]. Topics of the structured interview were not always reported [9].

Table 2.6: Outcome measures used in CRPSI research to measure disabilities and handicaps. Insufficient descriptive detail in publications is represented by a question mark.

Concept	Operationalization	Instrument(s)	Reference no.
Disability			
activity level	rating of restriction of activities of daily living related to full-time job (100%)	11-point scale	32
status of daily activities	improvement in certain daily activities	interview 3rd party	32
daily activities	difficulties with using hands last 24 hrs (in upper extremity CRPS)	Visual analog scale (VAS) All Daily Activities	40
hand function	among others: restriction of everyday activities + performing simple tasks	de Bruijn (1987) scoring system	42
vocational or educational status	changes in vocational or educational status compared to premorbid level	questionnaire	68
work status ?	ability to perform occupational activity or ADL after 8 weeks of treatment	analysis/interview	9
employment status	changes in job and/or working time compared to prior CRPS	questionnaire, interview	27
occupational status	long-term changes in occupation	structured interview, 4 categories	45
Handicap			
functional social activity level	subjective grade of ability to return to premorbid levels	questionnaire	68
general health status	9 subscales (e.g. social functioning, role limitation, pain, mental health)	RAND-36 questionnaire	45

2.5 Discussion and conclusion

2.5.1 Level of impairments

Sensory impairments

The almost unanimous choice of pain as the main 'sensory' outcome measure concept may be attributed to the fact that pain is often described as the most unpleasant feature of CRPSI for the majority of patients [1, 5, 8, 46, 47]. The large variability of other sensory impairments between patients and the lack of valid and reliable instruments may also play a role in this choice.

An important aspect in the evaluation of pain that was not taken into account in any of the studies is that, in CRPSI, acute pain in early stages of the disease most likely changes into chronic pain in later stages. Acute and chronic pain can be considered as different clinical entities [48], which may not involve the same dimensions [49, 50]. Therefore, one has to carefully consider the moments of measurement and the choice for a specific instrument to determine long-term pain evaluation in CRPSI; not all instruments are designed to reflect these different dimensions of acute and chronic pain.

To clearly classify the numerous outcome measures, we tried to fit each outcome measure in the scheme of concept, operationalization and instrument. With respect to the operationalization of the outcome measure concept of pain, this gave rise to some difficulties because authors usually failed to present an explicit operationalization. It appeared that the majority of authors consider pain as a clear-

cut concept, thus making some interpretation unavoidable. We realise that one may ask whether 'level of pain' and 'changes in level of pain' are actually operationalizations of pain, but in these cases thorough analysis of the publications failed to provide more detailed information.

Pain clearly is a very complex and diverse concept that can be interpreted or classified in several ways [51]. In one publication, pain was operationalized as mechanical allodynia and spontaneous deep pain [32]. These operationalizations, however, are both discrete sensory impairments in the framework of the ICIDH. In contrast to this framework, in which pain is considered as one of the sensory impairments in CRPSI, pain can also be considered as a separate entity [10, 52], that can be classified into several levels of abstraction: nociception, pain, suffering and pain behaviour [51, 53]. Because pain is often described as the most unpleasant feature of CRPSI and especially since it is the impairment that particularly leads to disability (which can be described in terms of pain behaviour), one may consider this latter classification also applicable to classify the CRPSI outcome measures. Although we acknowledge that the ICIDH is not ideal to classify the concept of pain, there are two reasons why we think the ICIDH is the most suitable framework to classify the numerous outcome measures. First, pain clearly is not the only consequence of CRPSI; using this other classification would not do justice to the other impairments that are found in CRPSI. Second, pain is not present in all CRPSI patients [54, 55]; about ten percent of the patients do not have pain, which makes the alternative classification not applicable to determine outcome for this part of the patient group.

Pain and other sensory impairments were usually measured by scales and questionnaires. A major disadvantage of these instruments is their subjective character [56, 57]. Another problem with measuring pain in CRPSI is that pain of individual patients can change often during the day and the pain level between patients can also vary widely [58]. The instruments to measure pain are not capable of detecting variation in pain level throughout the day. A possibility to overcome these problems is to evaluate 'pain behaviour' in addition to pain as a sensory impairment [51, 53, 59], especially because latest technological developments provide possibilities to objectively measure pain behaviour [60]. For rehabilitation medicine, measuring the concept pain behaviour operationalized as (changes in) the activity pattern is more relevant than measuring pain alone because pain behaviour is an outcome measure at the ICIDH level of disability and not at the level of impairment.

Autonomic impairments
It is clear that the number of 'autonomic' outcome measures by far exceeds the number of other outcome measures at the level of impairments, with the exception of pain. The popularity of 'autonomic' outcome measures together with 'sensory' outcome measures may be related to the current ideas concerning aetiology and pathophysiology of CRPSI. Sensory and autonomic impairments represent the most important features of an inflammatory reaction (dolor, calor, rubor and tumor) which

are thought to play a role in the acute phase of CRPSI [55, 61]. The acute phase is the focus of the majority of CRPSI studies. However, the greater part of CRPSI patients in rehabilitation practice in the Netherlands are already in the later stages of the disease, which makes autonomic outcome measures less relevant for determining treatment efficacy. Autonomic outcome measures are frequently measured by subjective purpose-formulated scales or questionnaires, although objective instruments are available [15, 27, 32, 34, 38, 39, 62].

Trophic impairments

Trophic impairments are not often used as outcome measures. This may be because these impairments are only found in a minority of CRPSI patients [43, 55] which makes 'trophic' outcome measures a less logical choice. Even though objective measurement of trophic impairments is possible, a major disadvantage is that instruments are usually costly and not always available. Moreover, objective measurement requires trained personnel. Trophic impairments are generally measured for diagnosis of CRPSI and not to determine the effect of a treatment, although some authors have investigated the possibilities of using them as outcome measures [63]. It was concluded that the bone scan could be part of an algorithm rather than a discrete outcome measure. Trophic impairments are closely related to autonomic impairment; changes in the nutritional state are one of the consequences of changes in local blood flow, which, for some researchers, may make use of these measures redundant.

Motor impairments

Whether active range of motion (AROM) or passive range of motion (PROM) was measured was not always clear. This is a very important issue, however, because measuring PROM is assumed to be not appropriate for patients with CRPSI since the pain threshold is generally reached quickly [58]. In addition, ROM measurements in CRPSI patients are subject to considerable variation [64], which may have an impact on the objectivity and reliability of measurements. This is also true for grip strength: it was found that for objective medical reports on hand muscle strength, it is recommendable to measure three times in more than one session and, if possible, by more than one person [65]. In the studies that used grip strength as an outcome measure, only few actually used a (potentially) objective method [15, 38, 39, 41, 42]. In only one of these studies [15] was information presented about repeated measurement. Even though motor impairments form a well-known aspect of CRPSI, epidemiological data on this matter are still scarce [6]. Whether this is a matter of lack of interest or lack of objective, reliable and valid instruments is not clear. However, it may be that researchers usually focus on the early stages of CRPSI, whereas motor impairments become more obvious in the later stages.

Sum scores

In order to indicate the 'overall' condition of patients, in several studies, scores were assigned to a number of outcome measures and added to sum scores called reflex

sympathetic dystrophy-score [15, 40], also reflex sympathetic dystrophy-score [25, 31] or shoulder hand syndrome-score [66]. Reflex sympathetic dystrophy (RSD) and shoulder hand syndrome (SHS) are two of the numerous names that are used to describe the disease. In the present study, we decided to use the term CRPSI because this is the term the International Association for the Study of Pain recently agreed upon [67]. Sum scores were made up of a varying numbers of outcome measures that usually had different relative contributions to the total score. This may be related to the discipline involved (e.g. ROM is more important to a rehabilitation specialist or an orthopaedist, whereas changes in temperature may be more relevant for an anaesthesiologist). In these five sum scores, pain was generally considered (one of) the most important concept(s) of outcome measures. In the selection of other outcome measures, however, little consistency in order of importance was found which makes interpretation of treatment outcome and comparison of different studies very complicated. An additional sum score, the impairment level sum score (ISS)[58], was published after the initial MEDLINE-search. In this weighted sum score, pain is also the most important outcome measure concept.

Since the consequences of CRPSI encompass all three levels of the ICIDH, assessing treatment outcome by sum scores of different outcome measures at different ICIDH levels can be considered as a logical strategy. However, with the exception of the variable VAS-ADL in one of the RSD scores [15, 40] and the affective and evaluative variables of the McGill pain questionnaire in the impairment level sum score [58], all of the variables in these scores were exclusively on the level of impairments. Variability among patients regarding the functional impact of various impairments was reported as a reason to solely focus on the level of impairments [58].

2.5.2   Level of Disabilities and Handicaps

The small number of 'disability' and 'handicap' outcome measures that were found, were assessed by means of scales and questionnaires; no objective instruments were used. About half of the outcome measures at the level of disability and/or handicap were employed by researchers in the field of rehabilitation (table 2.1). Apparently, outcome measures at these levels are also considered relevant by researchers in other research fields. With the exception of two studies [27, 68], all studies in which outcome measures at the ICIDH level of disabilities and/or handicaps in CRPSI research were used are written in the last few years. This may also be related to increasing general recognition that the evaluation of treatments should include assessment of a broad set of outcome measures that are important to patients, especially functionality (level of disabilities), role performance (level of handicaps) and quality of life [69-72].

Clearly, assessing treatment outcome at the level of disabilities and/or handicaps is difficult: particularly when it comes to objective outcome measures. In one study [73], it was mentioned that the outcome measures 'increase in hours of sleep' and 'increase

in physical activity' were taken into account. However, the authors failed to report on these outcome measures, which may also indicate that objectively assessing outcome at these two levels is considered relevant but difficult.

2.5.3   General discussion and conclusion

The aim of the present paper was to determine the availability of relevant and objective outcome measures concerning CRPSI for rehabilitation medicine. It appears that there clearly is a gap in the availability of these measures. Gaps in availability of appropriate outcome measures may be the starting point for the development of new instruments that are capable of objective measurement at the higher levels of the ICIDH. This does not implicate that we consider outcome measures at the level of impairment irrelevant for rehabilitation medicine. These outcome measures would be very relevant if there were an unambiguous relationship between impairments and changes in functionality; no clear evidence for such a relation in CRPSI has yet been found. Studies investigating whether patients benefit from treatment in terms of improvement of functional health require disability and/or handicap measures [74]. Insight into a patient's disabilities and handicaps is also important for the choice of treatment.

For this overview of outcome measures used in CRPSI research and clinical practice, 30 publications were analysed. It was not our intention to be fully exhaustive: we omitted studies with small patient numbers because these studies usually report on preliminary results of employment of 'new' outcome measures. Classifying these outcome measures may result in an overview of one-time employed outcome measures, which was not the objective of this study. In the data selection we did not perform cross-referencing because we think that the outcome measures currently classified are representative for the outcome measures applied in CRPSI research in general. In our opinion, cross-referencing would not have added many other outcome measures; it would merely result in a larger number of references in the reference number columns in tables 2.2-2.6. Again, it was not our intention to be fully exhaustive.

The clinical picture of CRPSI has been described by authors from different clinical disciplines, such as anaesthesiologists, hand surgeons, orthopaedists, psychiatrists, and rheumatologists [7]. These different disciplines have not unexpectedly emphasised different signs, symptoms, diagnostic criteria, treatments and outcome measures, which may be a reason for some of the difficulties in reviewing the literature on CRPSI. The fact that little controlled research on CRPSI is done from the perspective of rehabilitation [75] may have contributed to the lack of relevant outcome measures at the level of disabilities and/or handicaps. On the other hand, all disciplines should attempt to determine whether patients benefit from treatment in terms of improvement of functional health.

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Due to the lack of consensus about pathogenesis, current treatments do not always have a rational basis [8]; this may have had an impact on the selection of outcome measures for determining treatment efficacy. Ideally, the selection of certain outcome measures depends on the questions to be answered in different studies [74]; namely, whether the treatment has a biological effect or a clinical effect. Research and treatment of CRPSI may still be in an early experimental phase, despite the amount of research that has already been performed. For studies on pathogenesis, impairment outcome measures probably are the best choice. Clinical decision making can be improved by measuring at the level of disability, however, because these measures provide important and patient relevant information on whether a treatment improves the patient's functional health. Moreover, expressing outcome in terms of disabilities and handicaps, in addition to impairments, facilitates communication between disciplines and between specialists and patients.

In summary, classification of outcome measures in CRPSI research according to the hierarchical levels of the ICIDH shows that the majority of outcome measures describe treatment success at the level of impairment. Little consistency was found in concepts, operationalization of these concepts into variables and the instruments used. Outcome measures at the levels of disability and handicap, the most relevant levels for Rehabilitation Medicine, were mentioned in only very few studies. Objective outcome measures were merely found at the level of impairment. The shortage of relevant and objective outcome measures can not be due to lack of interest in such outcome measures or in CRPSI. This finding calls for development of relevant outcome measures that can objectively measure treatment efficacy at the level of disabilities and handicaps. Recent developments in the field of ambulatory activity monitoring [76, 77] seem to offer good perspectives.

2.6   References

1.   Schwartzman RJ, Kerrigan J. The movement disorder of reflex sympathetic dystrophy. Neurology 1990; 40:57-61.
2.   Atkins RM, Duckworth T, Kanis JA. Algodystrophy following Colles' fracture. J Hand Surg [Br] 1989; 14:161-4.
3.   Borg AA. Reflex sympathetic dystrophy syndrome: diagnosis and treatment. Disabil Rehabil 1996; 18:174-80.
4.   Inhofe PD, Garcia-Moral CA. Reflex sympathetic dystrophy. A review of the literature and a long-term outcome study. Orthop Rev 1994; 23:655-61.
5.   Galer BS, Butler S, Jensen MP. Case reports and hypothesis: a neglect-like syndrome may be responsible for the motor disturbance in reflex sympathetic dystrophy (Complex Regional Pain Syndrome-1). J Pain Symptom Manage 1995; 10:385-91.
6.   Ribbers G, Geurts AC, Mulder T. The reflex sympathetic dystrophy syndrome: a review with special reference to chronic pain and motor impairments. Int J Rehabil Res 1995; 18:277-95.
7.   Fournier RS, Holder LE. Reflex sympathetic dystrophy: diagnostic controversies. Semin Nucl Med 1998; 28:116-23.
8.   Kurvers HA. Reflex Sympathetic Dystrophy : a clinical and experimental study. Department of Neurology. Maastricht: University Hospital Maastricht, The Netherlands, 1997:208.
9.   Gobelet C, Waldburger M, Meier JL. The effect of adding calcitonin to physical treatment on reflex sympathetic dystrophy. Pain 1992; 48:171-5.
10. Davidoff G, Morey K, Amann M, Stamps J. Pain measurement in reflex sympathetic dystrophy syndrome. Pain 1988; 32:27-34.

28

11. Bennekom CAv, Jelles F. Rehabilitation Activities Profile : the ICIDH as a framework for a problem-oriented assessment method in Rehabilitation Medicine. Rehabilitation Medicine. Amsterdam: Free University of Amsterdam, 1995:213.

12. Bangma BD. Revalidatie-geneeskunde, methodologie en praktische uitvoering (in Dutch). Assen/Maastricht: Van Gorcum, 1989.

13. Rondinelli RD, Dunn W, Hassanein KM, et al. A simulation of hand impairments: effects on upper extremity function and implications toward medical impairment rating and disability determination. Arch Phys Med Rehabil 1997; 78:1358-63.

14. Brummel-Smith K. Research in rehabilitation. Clin Geriatr Med 1993; 9:895-904.

15. Geertzen JH, Dijkstra PU, Groothoff JW, ten Duis HJ, Eisma WH. Reflex sympathetic dystrophy of the upper extremity--a 5.5-year follow- up. Part I. Impairments and perceived disability. Acta Orthop Scand Suppl 1998; 279:12-8.

16. WHO. International Classification of Impairments, Disabilities, and Handicaps. Geneva: World Health Organization, 1980.

17. Geertzen JH. Reflex Sympathetic Dystrophy : a study in the perspective of Rehabilitation Medicine. Department of Rehabilitation. Groningen: State University Groningen, 1998:143.

18. Brandsma JW, Lakerveld-Heyl K, Van Ravensberg CD, Heerkens YF. Reflection on the definition of impairment and disability as defined by the World Health Organization. Disabil Rehabil 1995; 17:119-27.

19. Badley EM. An introduction to the concepts and classifications of the international classification of impairments, disabilities, and handicaps. Disabil Rehabil 1993; 15:161-78.

20. Jette AM. Concepts of Health and Methodological Issues in Functional Assessment. In: Granger CV, Gresham GE, eds. Functional Assessment in Rehabilitation Medicine. Baltimore/London: Williams & Wilkins, 1984:46-64.

21. Fuhrer MJ. Overview of Outcome Analysis in Rehabilitation. In: Fuhrer, ed. Rehabilitation Outcomes, Analysis and Measurement. Baltimore/London: Paul H. Brookes Publishing Co, 1987.

22. Zielhuis GA, Heydendael PH, Maltha JC, vanRiel PL. Handleiding medisch-wetenschappelijk onderzoek (in Dutch). Utrecht: Wetenschappelijke Uitgeverij Bunge, 1995.

23. Veldman PH. Clinical aspects of Reflex Sympathetic Dystrophy. Department of Neurosurgery. Nijmegen: Catholic University of Nijmegen, 1995:182.

24. Schwartzman RJ, Liu JE, Smullens SN, Hyslop T, Tahmoush AJ. Long-term outcome following sympathectomy for complex regional pain syndrome type 1 (RSD). J Neurol Sci 1997; 150:149-52.

25. Langendijk PN, Zuurmond WW, van Apeldoorn HA, van Loenen AC, de Lange JJ. [Good results of treatment of reflex sympathetic dystrophy with a 50% dimethylsulfoxide cream] Goede resultaten van behandeling van acute reflectoir-sympathische dystrofie met een 50%-dimethylsulfoxide-creme. Ned Tijdschr Geneeskd 1993; 137:500-3.

26. Hamamci N, Dursun E, Ural C, Cakci A. Calcitonin treatment in reflex sympathetic dystrophy: a preliminary study. Br J Clin Pract 1996; 50:373-5.

27. Poplawski ZJ, Wiley AM, Murray JF. Post-traumatic dystrophy of the extremities. J Bone Joint Surg [Am] 1983; 65:642-55.

28. Ramamurthy S, Hoffman J. Intravenous regional guanethidine in the treatment of reflex sympathetic dystrophy/causalgia: a randomized, double-blind study. Guanethidine Study Group. Anesth Analg 1995; 81:718-23.

29. Muramatsu K, Kawai S, Akino T, Sunago K, Doi K. Treatment of chronic regional pain syndrome using manipulation therapy and regional anesthesia. J Trauma 1998; 44:189-92.

30. Cortet B, Flipo RM, Coquerelle P, Duquesnoy B, Delcambre B. Treatment of severe, recalcitrant reflex sympathetic dystrophy: assessment of efficacy and safety of the second generation bisphosphonate pamidronate. Clin Rheumatol 1997; 16:51-6.

31. Zuurmond WW, Langendijk PN, Bezemer PD, Brink HE, de Lange JJ, van loenen AC. Treatment of acute reflex sympathetic dystrophy with DMSO 50% in a fatty cream. Acta Anaesthesiol Scand 1996; 40:364-7.

32. Hassenbusch SJ, Stanton-Hicks M, Schoppa D, Walsh JG, Covington EC. Long-term results of peripheral nerve stimulation for reflex sympathetic dystrophy. J Neurosurg 1996; 84:415-23.

33. Kaplan R, Claudio M, Kepes E, Gu XF. Intravenous guanethidine in patients with reflex sympathetic dystrophy. Acta Anaesthesiol Scand 1996; 40:1216-22.

34. Hord AH, Rooks MD, Stephens BO, Rogers HG, Fleming LL. Intravenous regional bretylium and lidocaine for treatment of reflex sympathetic dystrophy: a randomized, double-blind study. Anesth Analg 1992; 74:818-21.

35. Veldman PH, Goris RJ. Shoulder complaints in patients with reflex sympathetic dystrophy of the upper extremity. Arch Phys Med Rehabil 1995; 76:239-42.

36. Rauck RL, Eisenach JC, Jackson K, Young LD, Southern J. Epidural clonidine treatment for refractory reflex sympathetic dystrophy. Anesthesiology 1993; 79:1163-9; discussion 27A.

37. Field J, Warwick D, Bannister GC. Features of algodystrophy ten years after Colles' fracture. J Hand Surg [Br] 1992; 17:318-20.

38. Field J, Monk C, Atkins RM. Objective improvements in algodystrophy following regional intravenous guanethidine. J Hand Surg [Br] 1993; 18:339-42.
39. Atkins RM, Duckworth T, Kanis JA. Features of algodystrophy after Colles' fracture. J Bone Joint Surg [Br] 1990; 72:105-10.
40. Geertzen JH, de Bruijn H, de Bruijn-Kofman AT, Arendzen JH. Reflex sympathetic dystrophy: early treatment and psychological aspects. Arch Phys Med Rehabil 1994; 75:442-6.
41. Bickerstaff DR, Kanis JA. The use of nasal calcitonin in the treatment of post-traumatic algodystrophy. Br J Rheumatol 1991; 30:291-4.
42. Bickerstaff DR, Kanis JA. Algodystrophy: an under-recognized complication of minor trauma. Br J Rheumatol 1994; 33:240-8.
43. Kozin F, Soin JS, Ryan LM, Carrera GF, Wortmann RL. Bone scintigraphy in the reflex sympathetic dystrophy syndrome. Radiology 1981; 138:437-43.
44. Tu ES, Mailis A, Simons ME. Effect of surgical sympathectomy on arterial blood flow in reflex sympathetic dystrophy: Doppler US assessment. Radiology 1994; 191:833-4.
45. Geertzen JH, Dijkstra PU, Groothoff JW, ten Duis HJ, Eisma WH. Reflex sympathetic dystrophy of the upper extremity--a 5.5-year follow- up. Part II. Social life events, general health and changes in occupation. Acta Orthop Scand Suppl 1998; 279:19-23.
46. Doury P. Algodystrophy. Reflex sympathetic dystrophy syndrome. Clin Rheumatol 1988; 7:173-80.
47. Geertzen JH. Reflex sympathetic dystrophy. Outcome and measurement studies. Introduction. Acta Orthop Scand Suppl 1998; 279:1-3.
48. Grichnik KP, Ferrante FM. The difference between acute and chronic pain. Mt Sinai J Med 1991; 58:217-20.
49. Reading AE. A comparison of the McGill Pain Questionnaire in chronic and acute pain. Pain 1982; 13:185-92.
50. Choiniere M, Melzack R. Acute and chronic pain in hemophilia. Pain 1987; 31:317-31.
51. Seitz FC. The evaluation and understanding of pain: clinical and legal/forensic perspectives. Psychol Rep 1993; 72:643-57.
52. Butler SH. Reflex Sympathetic Dystrophy : Clinical Features. In: Stanton-Hicks M, Jänig W, Boas RA, eds. Reflex Sympathetic Dystrophy. Boston/Dordrecht/London: Kluwer Academic Publishers, 1990.
53. Loeser JD. What is chronic pain? Theor Med 1991; 12:213-25.
54. Goris RJA, Reynen JAM, Veldman P. De klinische verschijnselen bij posttraumatische dystrofie (In Dutch). Nederlands Tijdschrift voor Geneeskunde 1990; 134:2138-2141.
55. Veldman PH, Reynen HM, Arntz IE, Goris RJ. Signs and symptoms of reflex sympathetic dystrophy: prospective study of 829 patients. Lancet 1993; 342:1012-6.
56. Bouchard TJ. Field Research Methods: Interviewing, Questionnaires, Participant Observation, Systematic Observation, Unobtrusive Measures. In: Dunette MD, ed. Handbook of Industrial and Organizational Psychology. Chicago: Rand McNelly, 1976:364-402.
57. Staples D. Questionnaires. Clin Rehabil 1991; 5:259-64.
58. Oerlemans HM, Goris RJ, Oostendorp RA. Impairment level sumscore in reflex sympathetic dystrophy of one upper extremity. Arch Phys Med Rehabil 1998; 79:979-90.
59. Follick MJ, Ahern DK, Laser-Wolston N. Evaluation of a daily activity diary for chronic pain patients. Pain 1984; 19:373-82.
60. Bussmann JB, van de Laar YM, Neeleman MP, Stam HJ. Ambulatory accelerometry to quantify motor behaviour in patients after failed back surgery: a validation study. Pain 1998; 74:153-61.
61. Daemen MA, Kurvers HA, Kitslaar PJ, Slaaf DW, Bullens PH, Van den Wildenberg FA. Neurogenic inflammation in an animal model of neuropathic pain. Neurol Res 1998; 20:41-5.
62. Mailis A, Plapler P, Ashby P, Shoichet R, Roe S. Effect of intravenous sodium amytal on cutaneous limb temperatures and sympathetic skin responses in normal subjects and pain patients with and without Complex Regional Pain Syndromes (type I and II). I. Pain 1997; 70:59-68.
63. Vande Streek P, Carretta RF, Weiland FL, Shelton DK. Upper extremity radionuclide bone imaging: the wrist and hand. Semin Nucl Med 1998; 28:14-24.
64. Geertzen JH, Dijkstra PU, Stewart RE, Groothoff JW, Ten Duis HJ, Eisma WH. Variation in measurements of range of motion: a study in reflex sympathetic dystrophy patients. Clin Rehabil 1998; 12:254-64.
65. Geertzen JH, Dijkstra PU, Stewart RE, Groothoff JW, ten Duis HJ, Eisma WH. Variation in measurements of grip strength. A study in reflex sympathetic dystrophy patients. Acta Orthop Scand Suppl 1998; 279:4-11.
66. Braus DF, Krauss JK, Strobel J. The shoulder-hand syndrome after stroke: a prospective clinical trial. Ann Neurol 1994; 36:728-33.
67. Colton AM, Fallat LM. Complex regional pain syndrome. J Foot Ankle Surg 1996; 35:284-96.
68. Subbarao J, Stillwell GK. Reflex sympathetic dystrophy syndrome of the upper extremity: analysis of total outcome of management of 125 cases. Arch Phys Med Rehabil 1981; 62:549-54.

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69. Lohr KN, Ware JE. Proceedings of the advances in health assessment conference. J Chron Dis 1987; 40:S1-S211.
70. Lohr KN. Advances in health status assessment. Overview of the conference. Med Care 1989; 27:S1-11.
71. Lohr KN. Applications of health status assessment measures in clinical practice. Overview of the third conference on advances in health status assessment. Med Care 1992; 30:MS1-14.
72. Richards JM, Jr., Hemstreet MP. Measures of life quality, role performance, and functional status in asthma research. Am J Respir Crit Care Med 1994; 149:S31-9; discussion S40-3.
73. Robaina FJ, Rodriguez JL, de Vera JA, Martin MA. Transcutaneous electrical nerve stimulation and spinal cord stimulation for pain relief in reflex sympathetic dystrophy. Stereotact Funct Neurosurg 1989; 52:53-62.
74. Molenaar DS, de Haan R, Vermeulen M. Impairment, disability, or handicap in peripheral neuropathy: analysis of the use of outcome measures in clinical trials in patients with peripheral neuropathies. J Neurol Neurosurg Psychiatry 1995; 59:165-9.
75. Arlet J, Mazieres B. Medical treatment of reflex sympathetic dystrophy. Hand Clin 1997; 13:477-83.
76. Bussmann JB, Tulen JH, van Herel EC, Stam HJ. Quantification of physical activities by means of ambulatory accelerometry: a validation study. Psychophysiology 1998; 35:488-96.
77. Bussmann JBJ. Techniques for measurement and assessment of mobility in rehabilitation medicine: a theoretical approach. Clin Rehabil 1998; 12:513-522.
78. Kozin F, Ryan LM, Carerra GF, Soin JS, Wortmann RL. The reflex sympathetic dystrophy syndrome (RSDS). III. Scintigraphic studies, further evidence for the therapeutic efficacy of systemic corticosteroids, and proposed diagnostic criteria. Am J Med 1981; 70:23-30.
79. Geertzen JH, Dijkstra PU, van Sonderen EL, Groothoff JW, ten Duis HJ, Eisma WH. Relationship between impairments, disability and handicap in reflex sympathetic dystrophy patients: a long-term follow-up study [In Process Citation]. Clin Rehabil 1998; 12:402-12.

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