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Complex regional pain syndrome type I of the knee: A systematic literature review

Bussel, CM van
Stronks DL,
Huygen FJPM

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ABSTRACT

Background and Objective: In our Center for Pain Medicine, a group of patients reported to have symptoms possibly attributable to complex regional pain syndrome (CRPS) of only the knee(s). Therefore, this study aimed to investigate whether the literature reports on patients with CRPS type I in the knee(s) alone and, if so, to summarize the reported diagnostics, aetiology and treatment strategies of CRPS of the knee(s).

Databases and Data treatment: Medline, Embase, Cochrane Library, PubMed and Web of Science were searched for articles focusing on a painful disorder of the knee, most likely CRPS type I. Screening on title and abstract was followed by full-text reading and searching of reference lists to determine the final set of relevant articles.

Results: Of the 513 articles identified, 31 met the inclusion criteria. These articles reported on a total of 368 patients diagnosed with CRPS of the knee(s) based on the diagnostic criteria used at the time of publication. Knee surgery, especially arthroscopic surgery, was the most common inciting event in developing CRPS of the knee(s). Various treatment strategies were applied with variable outcomes.

Conclusions: The scientific literature does report cases of CRPS type I of only the knee(s). This applies when using the diagnostic criteria prevailing at the time of publication and, obviously for a smaller number of cases, also when using the current Budapest criteria set. Arthroscopic knee surgery is described multiple times as the inciting event. We recommend to include CRPS of the knee in future research on the aetiological mechanisms of and optimal treatment for CRPS.

1. INTRODUCTION

Complex regional pain syndrome (CRPS) type I, formerly known as reflex sympathetic dystrophy (RSD) or algodystrophy, is a collection of locally appearing painful conditions following a trauma, which mainly occur distally in the affected limb and exceed in both intensity and duration the expected clinical course of the original trauma. The symptoms are not confined to the innervation zone of an individual nerve (1). Involvement of the whole extremity can occur. The main clinical features of CRPS are continuing pain, and sensory, vasomotor, sudomotor and motor trophic disturbances (2). CRPS is a clinical diagnosis based on signs and symptoms described in criteria sets and, over the years, different diagnostic criteria sets have been developed. Currently, the use of the Budapest criteria set is recommended (3). Laboratory tests and radiology have only limited additional value in the diagnostic process and are mainly used to exclude another diagnosis. The natural history of CRPS is not always positive and can result in permanent disability. Treatment remains a challenge because the underlying pathophysiologic mechanisms are only partly understood (4).

In our expert center for CRPS, we receive referrals from throughout the Netherlands and see many patients for a second opinion. Our interest was drawn by a group of patients with CRPS-like symptoms confined only to the knee(s); this was the rationale to perform this systematic review.

The following research questions were addressed: 'Are there any descriptions in the medical literature of complex regional pain syndrome type I only affecting the knee(s), and diagnosed with the criteria used at the moment of publication?' and 'If so, what does the literature report on diagnostics, etiology and treatment of complex regional pain syndrome type I affecting only the knee(s)?'

2. LITERATURE SEARCH METHODS

2.1 Search strategy

To find relevant articles, searches were made in Embase, OVID-SP, Cochrane Central, PubMed and Web of Science covering the period 21 December 2012 to 4 January 2013.

The search strategy was divided into elements for CRPS and those for the knee. For optimal results from all five databases, elements from both groups were applied in the correct format for the search in each database. Details on the strategies and results are given in Appendix 1.

2.2 Inclusion/exclusion criteria

Articles were not excluded on the basis of study design. After the search, the title and abstract of each article were checked for relevance. Because the search was made in different databases, Endnote X5 for Windows (Thomson Reuters, New York, NY, USA) was used to ensure that no article was included more than once. The main topic of the article had to be a painful disorder of the knee, most likely diagnosed as CRPS type I. The reference lists of the identified articles were checked for additional studies possibly missed by the search strategies.

Excluded articles had either the wrong main topic, e.g., patients suffered from CRPS type I in a location other than the knee, or patients were suffering from a partial CRPS type I. Partial CRPS type I was considered by authors of some articles as being a CRPS-like syndrome, not completely matching the criteria used at the time of publication. Other excluded articles described patients with CRPS of the knee attributable to verifiable nerve damage (this disorder was most likely CRPS type II). Also excluded were articles written in languages other than Dutch, English or German, because none of the authors mastered these languages, as well as studies involving children with CRPS aged ≤ 18 years.

3. RESULTS

After filtering with EndNote, the search resulted in 513 articles. After screening the titles and abstracts, 436 articles were excluded either because the main topic was incorrect, or children aged ≤ 18 years were involved, or the articles described CRPS as a result of nerve damage. This left 77 articles of which 26 were written in French, Italian, Spanish or Portuguese and were therefore excluded. This left 51 articles. After full-text reading of these papers, another 20 were excluded because CRPS was only considered as a differential diagnosis. This left 31 relevant articles to present in this review: 10 case reports, 10 case series, five retrospective studies, five prospective studies and one case-controlled study. Checking the reference lists of these articles yielded no additional relevant publications. A flow chart showing the in- and exclusion of the articles is presented in Appendix 2.

3.1 Diagnostics

3.1.1 Criteria sets

The 31 included articles comprised a total of 368 patients diagnosed with RSD, algodystrophy or CRPS based on criteria sets used at the time of publication. Table 1 shows how many patients (based on the symptoms mentioned in the articles) met the various criteria sets used over time in diagnosing CRPS, i.e., the criteria of Veldman, the International Association for the Study of Pain (IASP) criteria, the Bruehl and Harden criteria, and the Budapest criteria. In 187 patients, based on the symptoms mentioned in the articles, it

was not possible to confirm whether the patients met one or more of the criteria sets. Nevertheless, these patients were diagnosed by the authors as having RSD, algodystrophy or CRPS of the knee(s) (5-17).

Table 1. Multiple-response frequency table of the included patients meeting the criteria sets

Criteria set used:	Meeting the criteria set		Percentage of cases
	n	%	
Veldman	4	0.85	1.09
Bruehl and Harden	56	11.87	15.22
Budapest	79	16.67	21.47
IASP	148	31.52	40.22
Not possible to confirm	187	39.09	50.81
Total	474	100.00	128.81

Note: Because some patients met more than one criteria set, the percentage of cases does not sum to 100

3.1.2 Lumbar sympathetic blockade

Six articles were found in which the authors described using the relief of symptoms after a lumbar sympathetic blockade as a confirmation, or as an (additional) criterion, for diagnosing RSD or CRPS in patients with extensive knee pain.

The authors of five publications stated that CRPS can be confirmed by at least partial relief of the symptoms after receiving a lumbar sympathetic blockade, besides clinical appearance suggestive for RSD or CRPS. Of these, Cooper *et al.* and Braverman *et al.* reported on patients who matched the Bruehl and Harden, IASP, and the Budapest criteria set (4, 18). Because the authors of the other three publications did not describe (all) the symptoms patients were suffering from, we were unable to confirm their diagnosis of CRPS or RSD based on the criteria sets (8, 15, 16).

In contrast, Neuschwander *et al.* used (partial) relief of symptoms after a lumbar sympathetic blockade only as confirmation of the diagnosis CRPS or RSD (17).

3.1.3 Radiographs/Bone scans

In 13 articles, the authors used a form of radiology as a diagnostic tool or as a confirmation of the diagnosis of RSD, algodystrophy or CRPS of the knee.

Finsterbush *et al.* used abnormalities on a skyline view of the patellofemoral joint or a bone scan as an additional criterion (besides the clinical appearance of the patients) in diagnosing RSD of the knee (19). Malhotra *et al.* used a three-phase bone scan to substantiate the diagnosis of RSD, when RSD was suspected on the basis of clinical appearance (15).

Radiographic investigation of the knee showed patchy bone atrophy in five studies involving patients already diagnosed with RSD of the knee (5, 7, 9-11).

O'Brien *et al.* reported that 19 of the 60 patients diagnosed with RSD had positive findings on pre-treatment bone scans; they stated that if a patient had asymmetry of uptake in the knee(s) on the bone scan this is a supportive but not necessary finding in diagnosing RSD (16). Loew and Isakov *et al.* stated that pathological findings on a three-phase bone scan can be supportive in the clinical diagnosis of RSD of the knees. The scans revealed increased bone uptake in the patellae, femoral condyles or upper part of the tibia (2, 20).

In all patients who developed RSD or CRPS after renal transplantation, radiographs showed patchy osteopenia and bone scintigraphy showed increased uptake in the affected areas; the authors considered these findings as supportive in diagnosing RSD or CRPS (21-23).

3.2 Aetiology

3.2.1 CRPS after (arthroscopic) knee surgery

The authors of ten articles reported on patients with RSD or CRPS of the knee after undergoing (arthroscopic) surgery of the knee (6, 11-14, 16, 20, 24-26).

Cooper *et al.* reported on a group of 14 patients of whom 11 underwent a patellar operation before the onset of RSD symptoms (18). The authors of three articles reported on 32 patients who developed RSD of the knee after undergoing a total knee replacement (4, 13, 19).

Burns *et al.* compared eight patients with CRPS of the knee after total knee arthroplasty with patients who had no complaints after total knee arthroplasty and with patients with preoperative osteoarthritic knees; they stated that prompt diagnosis and early treatment is most important in treating CRPS of the knee (27). Others stated that CRPS should also be considered when a knee does not recover after knee surgery (8).

3.2.2 CRPS after trauma or injury

In 1954 three cases of RSD of the knee after a distortion or contusion were described by Baur (5). In 1995, Isakov *et al.* presented a case of RSD of the knees that developed after burning both knees (2). Miller reported a case of RSD after injuring the left knee; the patient felt a "twinge" and within two weeks developed intense pain and other symptoms (28). In another case, a left patella fracture and emergency surgery was complicated by developing CRPS (29).

A study of 67 patients with unexplained knee pain revealed (in retrospect) that 14 patients were suffering from RSD; all of these patients had injured one knee and had persistent complaints (9).

Ten studies described patients with RSD or CRPS of the knee after a minor twist, injury or trauma (10-12, 15-19, 26, 30, 31).

3.2.3 Non-traumatic CRPS

Two patients were described as being diagnosed with RSD or algodystrophy of the knee without a known trauma or injury before the symptoms occurred (7, 16).

The authors of three articles reported the occurrence of RSD in the lower extremities in patients after renal transplantation. A total of seven patients had severe pain in one or both of the knees and ankles; clinical examination revealed increased local temperature, trophic changes and periarticular soft tissue swelling (21-23).

Table 2. Number and percentage of reported eliciting factors

Aetiology	Number of cases (n)	Percentage (%)
Trauma or injury	197	53.53
(Arthroscopic) knee surgery	162	44.02
Non traumatic	9	2.45
Total	368	100

3.3 Treatment

In the included articles many different strategies are described in the treatment of CRPS of the knee, with variable results.

In 11 articles, the authors mentioned the use of physiotherapy (besides other therapy) in patients with CRPS or RSD of the knee (2, 4, 7, 12, 14, 15, 19, 20, 24, 27, 29).

A lumbar sympathetic blockade was performed in 12 studies; this blockade was sometimes used as a single therapy and sometimes combined with another therapy, e.g., physiotherapy (4, 8, 11-14, 16-20, 25). Seven patients with the diagnosis CRPS of the knee were treated with intravenous regional anaesthesia with clonidine and the authors reported this to be a useful treatment in the management of CRPS of the knee, without significant side-effects (26). A study of 30 patients, all diagnosed with CRPS according to the IASP criteria, examined the efficacy of shockwave therapy in the management of CRPS of the medial femoral condyle; only one patient had persisting pathology signs on MRI at six months follow-up (32).

Ching *et al.* reported on a patient with Behçet's disease and CRPS of her left knee (diagnosed according to the Budapest criteria set). The patient was given thalidomide for the Behçet's disease, which resulted in an unexpected gradual improvement of the pain in her knee (30). Ogilvie-Harris and Roscoe described 19 patients suffering from extensive knee pain and (retrospectively) 11 of these patients met the IASP criteria in diagnosing CRPS; the remaining eight patients did not meet any of the criteria sets. All patients received non-steroidal anti-inflammatory drugs (NSAIDs) and intensive physiotherapy and, if a patient did not respond, he/she received a sympathetic blockade (12).

Burns *et al.* compared eight patients with CRPS of the knee (according to the Bruehl and Harden, IASP and Budapest criteria), which developed after a total knee arthroplasty,

with eight patients with uncomplicated total knee arthroplasty. All patients received NSAIDs and physiotherapy and, if needed, manipulation under anaesthesia. The authors concluded that, when managed early, patients complicated with CRPS after total knee arthroplasty have a similar prognosis to patients with uncomplicated total knee arthroplasty (27).

Mak *et al.* reported on a man with CRPS of the knee (diagnosed according to the Bruehl and Harden criteria set) that developed after a patella fracture; the patient received an infusion of bupivacaine with fentanyl for five days, continuous passive stretching at night-time and daily physiotherapy, resulting in a pain score of zero and sustained improvement in mobilization and function (29). Another patient with the diagnosis algodystrophy of the knee received NSAIDs, prednisone and physiotherapy, and was considered to be cured after two years of therapy (7). Furthermore, the patient described by Malhotra *et al.* with RSD of the knee had almost complete relief of the symptoms after physiotherapy, microwave diathermy and NSAIDs (15).

Two case reports reported on patients with CRPS or RSD of the knee who, despite various pain medication, physiotherapy, transcutaneous electrical nerve stimulation (TENS) and passive motion, never became symptom-free of CRPS of the knee (24, 28).

The authors of seven studies state that therapy should be started as soon as possible to ensure the best outcome for patients (4, 11, 12, 14, 18, 19, 27). This is in contrast to a study performed by O'Brien *et al.* These authors included 60 patients diagnosed with RSD of the knee who were divided into three groups; early (< 6 months), medium (6-12 months) and late (>12 months) diagnosis. The study showed no difference between the three groups of RSD patients in outcome (knee pain, other knee symptoms and range of motion) after treatment (16).

4. DISCUSSION AND CONCLUSIONS

This review investigated whether the literature describes patients suffering from CRPS type I of only the knee(s) and, if so, what the aetiology, diagnostics and treatment were in those patients.

4.1 Limitations in the inclusion of articles

Our search included descriptions of CRPS, RSD, algodystrophy, and derivatives of these terms and descriptions of the knee. CRPS, RSD and algodystrophy are only three of the many descriptions used over the course of time for (or related to) CRPS. Therefore, we may have missed some publications if the authors used yet another description for the same disorder. In addition, we were unable to examine the studies published in the French,

Italian, Spanish or Portuguese language. Of these 26, only nine studies were potentially valuable. We consider this as a possible shortcoming of this review.

4.2 Diagnosis

All the articles included in this review were studies in which patients are described as having RSD, algodystrophy or CRPS of the knee(s). For the diagnosis of these disorders, some authors used only the clinical appearance, others claimed that abnormalities on radiological investigations are needed (beside clinical appearance), and yet others state that at least partial relief of the symptoms after a lumbar sympathetic blockade is needed to make a diagnosis of CRPS. In addition, some authors did not describe all the symptoms (besides extensive knee pain) a patient was suffering from after minor trauma or surgery; in these cases, we were unable to confirm their diagnosis.

Radiographs and bone scans were used in almost every study included in this review. In seven studies, abnormalities found on radiographs (besides the clinical features) were considered supportive in diagnosing RSD or CRPS. The authors of one article stated that the use of a skyline view of the patella would be helpful because, so they say, in RSD of the knee the patella is always involved (19). Currently, however, the diagnosis of CRPS is clinically based and no further tests are acquired.

Some authors stated that RSD is a condition 'better overtreated than underdiagnosed' (14). Tietjen concluded that if the existence of CRPS of the knee was more widely known in the medical world, this would help in diagnosing patients with extensive knee pain after a trauma, injury or surgery as patients with CRPS. For knee pain, he advises the use of arthroscopic techniques to rule out causes other than RSD, thereby reducing the amount of unnecessary surgery on knees with RSD (9). His study was published in 1986, and after that date several cases of RSD or CRPS have been described (as shown in this review) after arthroscopic knee surgery. Therefore, the question arises whether we should consider arthroscopic knee surgery to be a risk factor for developing CRPS of the knee.

4.3 Treatment

The literature is inconsistent and/or unclear about the best time to start therapy and which therapy should be applied to treat CRPS. Comparison of the studies in this review was difficult because of the differences in study design, and the variable time after diagnosis and start of treatment. Moreover, the authors used different treatment strategies and primary outcome measures. Uncertainty about the best treatment for CRPS of the knee seems to be no different than uncertainty for CRPS on other (more distal) locations.

4.4 Budapest criteria set

The Budapest criteria set is currently recommended for the diagnosis of CRPS. One of the requirements in diagnosing CRPS according to this set is continuing pain, which is dispro-

portionate to the inciting event. The criteria set does not include that the patient must have at least partial relief of the symptoms after a lumbar sympathetic blockade, or that radiographs or bone scans must show abnormalities in the affected area when compared with the unaffected area. This could imply that patients with a diagnosis of RSD/CRPS without any inciting event, or based on their clinical appearance and at least partial relief of the symptoms after a blockade, or based on their clinical appearance and radiographic evidence of abnormalities, would nowadays probably not receive the diagnosis of CRPS.

In conclusion, our review of the literature reporting on CRPS affecting only the knee(s) reveals that at least 79 patients (more than 20% of the reported cases) are described who met the current Budapest diagnostic criteria set. Therefore, we conclude that patients suffering from CRPS of only the knee(s), have been described in the medical literature.

In addition, we summarized the authors' description of the diagnostics, aetiology and treatment of CRPS affecting only the knee(s). On this basis, we recommend to consider CRPS of only the knee(s) as a medical entity, similar to the more frequently described CRPS of the hand or foot. Because CRPS as a medical condition is only partially understood, we recommend that future research on the aetiological mechanisms and optimal treatment of CRPS should also include CRPS of only the knee. That CRPS of the knee often appeared after arthroscopic knee surgery is an important finding; this implies that this procedure is a possible inciting factor for the development of CRPS; the same applies when a knee does not recover adequately after an arthroscopic knee surgery.

APPENDIX 1

Search strategies in detail

Embase: 441 hits

('complex regional pain syndrome'/exp OR (CRPS OR 'complex regional pain' OR Sudeck* OR Sudek* OR Suedeck* OR (RSD* AND (reflex* OR sympathet* OR dystroph*)) OR algodystroph* OR algesidystroph* OR algoneurodystroph* OR ((posttraumatic OR 'post traumatic' OR sympathet* OR reflex*) NEAR/3 (osteoporos* OR dystroph*)):ab,ti) AND (Knee/de OR 'knee meniscus'/de OR 'patellofemoral joint'/de OR 'knee ligament'/exp OR 'knee injury'/exp OR 'knee disease'/exp OR 'knee surgery'/exp OR 'knee arthroscopy'/de OR 'below knee amputation'/de OR (knee* OR menisc* OR genu* OR genopath* OR patell* OR femoropatellar* OR (semilun* NEAR/3 (bone* OR cartilage*)):ab,ti)

OVID-SP: 252 hits

(exp "complex regional pain syndromes"/ OR (CRPS OR "complex regional pain" OR Sudeck* OR Sudek* OR Suedeck* OR (RSD* AND (reflex* OR sympathet* OR dystroph*)) OR algodystroph* OR algesidystroph* OR algoneurodystroph* OR ((posttraumatic OR "post traumatic" OR sympathet* OR reflex*) ADJ3 (osteoporos* OR dystroph*)):ab,ti.) AND (Knee/ OR exp "knee joint"/ OR "knee meniscus"/ OR exp "Medial Collateral Ligament, Knee"/ OR "Genu Valgum"/ OR exp "Knee Injuries"/ OR "Osteoarthritis, Knee"/ OR "Patellofemoral Pain Syndrome"/ OR (knee* OR menisc* OR genu* OR genopath* OR patell* OR femoropatellar* OR (semilun* ADJ3 (bone* OR cartilage*)):ab,ti.)

Cochrane Central: 4 hits

((CRPS OR "complex regional pain" OR Sudeck* OR Sudek* OR Suedeck* OR (RSD* AND (reflex* OR sympathet* OR dystroph*)) OR algodystroph* OR algesidystroph* OR algoneurodystroph* OR ((posttraumatic OR "post traumatic" OR sympathet* OR reflex*) NEAR/3 (osteoporos* OR dystroph*)) AND (knee* OR menisc* OR genu* OR genopath* OR patell* OR femoropatellar* OR (semilun* NEAR/3 (bone* OR cartilage*)):ab,ti)

PubMed as supplied by publisher: 3 hits

(CRPS[tiab] OR complex regional pain*[tiab] OR Sudeck*[tiab] OR Sudek*[tiab] OR Suedeck*[tiab] OR (RSD*[tiab] AND (reflex*[tiab] OR sympathet*[tiab] OR dystroph*[tiab])) OR algodystroph*[tiab] OR algesidystroph*[tiab] OR algoneurodystroph*[tiab] OR ((posttraumatic[tiab] OR post traumatic*[tiab] OR sympathet*[tiab] OR reflex*[tiab]) AND (osteoporos*[tiab] OR dystroph*[tiab]))) AND (knee*[tiab] OR menisc*[tiab] OR genu*[tiab] OR genopath*[tiab] OR patell*[tiab] OR femoropatellar*[tiab] OR (semilun*[tiab] AND (bone*[tiab] OR cartilage*[tiab]))) AND publisher[sb])

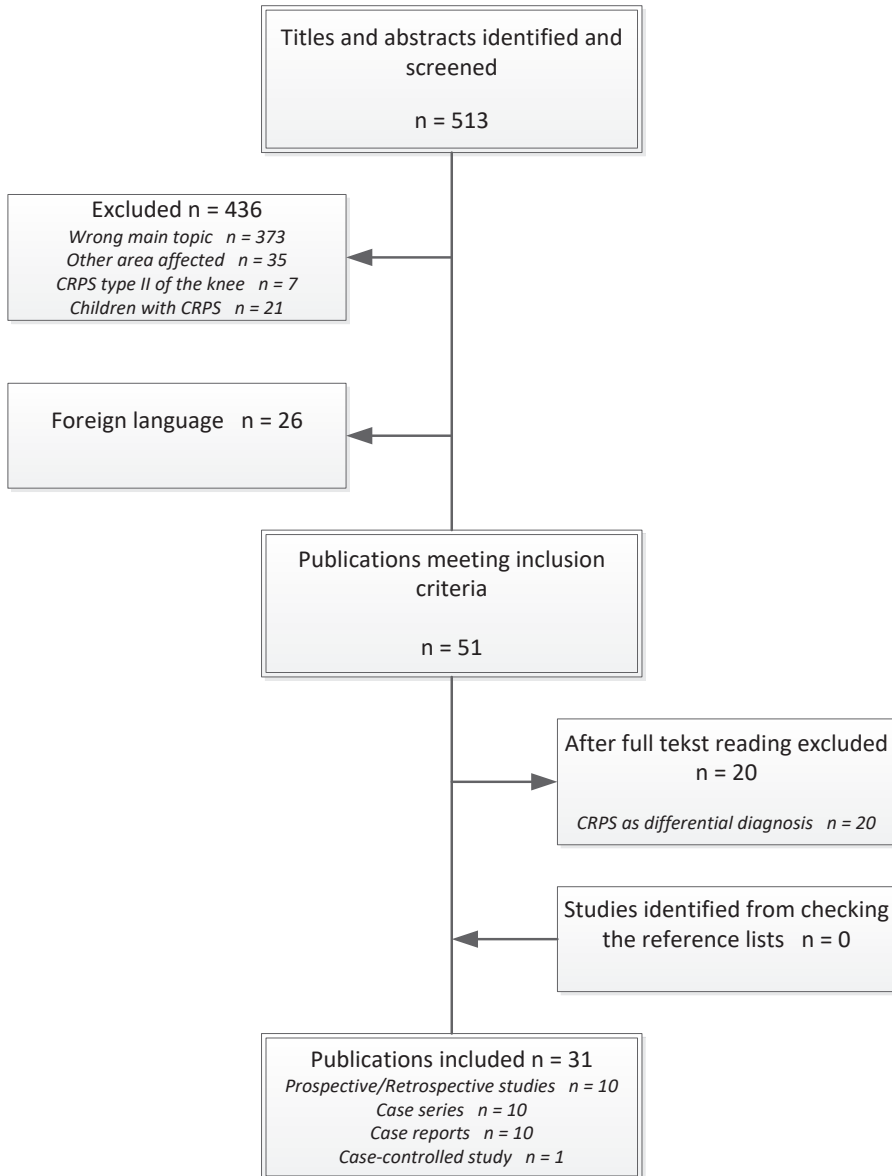
Web of Science: 158 hits

TS=((CRPS OR "complex regional pain" OR Sudeck* OR Sudek* OR Suedeck* OR (RSD* AND (reflex* OR sympathet* OR dystroph*)) OR algodystroph* OR algesidystroph* OR algoneurodystroph* OR ((posttraumatic OR "post traumatic" OR sympathet* OR reflex*) NEAR/3 (osteoporos* OR dystroph*)) AND (knee* OR menisc* OR genu* OR genopath* OR patell* OR femoropatellar* OR (semilun* NEAR/3 (bone* OR cartilage*)))

Total amount of articles: 858. After removing duplicates: 513

APPENDIX 2

Flow Chart



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