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REVIEW ARTICLE

What Is the Evidence that Neuropathic Pain Is Present in Chronic Low Back Pain and Soft Tissue Syndromes? An Evidence-Based Structured Review

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Abstract

Objectives. The objectives of this evidence-based review were to review the evidence for whether neuropathic pain (NP) is associated with chronic low back pain (CLBP) and soft tissue syndromes (STS), and review the reported prevalence percentages for NP within these syndromes.

Methods. Of 816 reports, 11 addressed the diagnosis of NP in CLBP and five of NP in STS. Studies were grouped by the method of arrival at an NP diagnosis, e.g., physical examination, type of NP inventory utilized, etc. The reported prevalence of NP was determined by aggregating all the patients in all the studies in each grouping. Similarly, the reported prevalence of NP within CLBP and STS was determined by aggregating all the patients with NP from all the studies in those groups. Each study was independently rated by two raters according to 11 quality criteria generating a quality score. The strength and consistency (SAC) of the evidence represented by each grouping was rated according to Agency for Health Care Policy and Research guidelines.

Results. In each grouping, 100% of the studies reported some prevalence of NP (none reported zero prevalence). Aggregated NP prevalence for CLBP was 36.6% (SAC level A [consistent multiple studies]) and for STS 41.1% (SAC level A). There was significant variation in prevalence according to the method utilized to diagnose NP.

Conclusion. There is consistent evidence by all methods that NP is present in CLBP and STS. Reported prevalence percentages by all methods are substantial. This has significant implications for the treatment of CLBP and STS.

Key Words. Prevalence Neuropathic Pain; Chronic Low Back Pain; Soft tissue Syndromes; Evidence-Based Structured Review; Leeds Assessment of Neuropathic Symptoms and Signs (LANSS); Neuropathic Pain Diagnostic Questionnaire (DN4); Pain Detect Questionnaire

Introduction

Neuropathic pain (NP) is defined as pain initiated or caused by a primary lesion or dysfunction of the nervous system and historically has been classified according to etiology

(e.g., painful diabetic neuropathy, trigeminal neuralgia, spinal cord injury, etc.) [1]. In the last 15 years, the number of measures/scales have been developed to identify and/or to measure NP. These are the following: NP Scale (NPS), Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), the Self-Report LANSS (S-LANSS), the NP Questionnaire (NPQ), the NP Symptom Inventory (NPSI), the NP Diagnostic Questionnaire (DN4); the Pain Quality Assessment Scale (PQAS), the NPQ Short-Form (NPQ-SF), Pain Detect, and the identification (ID) scale (neuropathic pain screening questionnaire) [2–6]. Of these, a number were designed to differentiate patients with NP from patients without NP: LANSS, NPQ, DN4, Pain Detect, and ID scale [3,7–9]. These scales have been shown to be reliable and valid [3,4,8,10,11].

The arrival of these scales has fueled a debate in the literature relating to whether NP should be an all or none diagnosis based on classification according to etiology or whether there may be various degrees of "neuropathic" components in some chronic pain conditions [10,12–15]. Two of these are chronic low back pain (CLBP) and soft tissue syndromes (STS) (STS as defined here are generally divided into two subcategories: disorders of muscles [musculoskeletal conditions] and disorders of the synovial and tendons. As such, STS have been thought by some authors to encompass musculoskeletal pain, myofascial syndromes, fibromyalgia, fasciitis, tendinitis, bursitis, etc.).

Back pain is the most frequently reported chronic pain condition and may present with nociceptive,neuropathic, or both pain components, and it is claimed that about 4% of adult population experiences CLBP with a neuropathic component [11]. The question of whether NP is a component in conditions such as CLBP and STS where according to the etiological classification, it should not be present except where there is nerve root compression has recently been addressed in a number of studies. These studies have utilized physical examination findings, pharmacological diagnostic approaches, and NPSs to determine which patients have NP.

The objectives of this evidence-based structured review was to review CLBP and STS studies where an attempt had been made to determine if there is an NP component present and determine the quality of each study. A second objective was to arrive at an evidence consistency rating for whether NP is present in CLBP and STS from all the studies combined for these groups (CLBP and STS) as per the Agency for Health Care Policy and Research (AHCPR) Guidelines (Table 1, Section 2) [16]. A third objective was to determine a combined aggregate prevalence percentage for NP in CLBP and STS from all the available studies combined in these groups and also for the subgroups (per method of arrival at a NP diagnosis). The hypotheses of this evidence-based structured review were the following: 1) a significant percentage of patients in each grouping should be reported to have an NP component; and 2) there should be significant variations in the percentages of the patients identified as having an NP component for the different methods utilized to arrive at this diagnosis.

Table 1 Levels of evidence as developed by the Agency for Health Care Policy and Research for guideline development [16]

Type of Evidence and Strength/Consistency of the Evidence Guidelines According to the AHCPR
Type of Evidence Guidelines (section one):
i. Meta-analysis of multiple well-designed controlled studies.
ii. At least one well-designed experimental study.
iii. Well-designed, quasi-experimental studies such as nonrandomized controlled, single group pre-post, cohorts, time series, or matched case-controlled studies.
iv. Well-designed non-experimental studies, e.g., comparative, correlational, descriptive, case control.
v. Case reports and clinical examples.
Strength and Consistency of Evidence Guidelines (section two):
A. There is evidence of type I or consistent findings from multiple studies of type II, III, or IV.
B. There is evidence of type II, III, or IV, and findings are generally consistent.
C. There is evidence of type II, III, or IV, but findings are inconsistent.
D. There is little or no evidence, or there is type V evidence only.
E. Panel consensus: Practice recommended on the basis of opinion of experts.

AHCPR = Agency for Health Care Policy and Research.

Methods

Relevant references were located by the following procedure. MEDLINE, Embase, AMED, Psychological Abstracts, Science Citation Index, and the National Library of Medicine Physician Data Query databases were reviewed utilizing the following subject headings: pain, chronic pain, chronic pain patients, low back pain (LBP), CLBP, failed back surgery syndrome, STS, fibromyalgia, fibromyalgia syndrome, STS tendinopathy, tendinitis, musculoskeletal pain, chronic widespread pain, myofascial pain, myofascial pain syndrome, tender point, and trigger points. Each of these was exploded with NP, LANSS, S-LANSS, NPQ, Pain Detect (DN4), ID scale, the NP Inventory, the NPSI, PQAS, NPQ-SF, and all retrieved references reviewed.

The searches were not restricted to the English language and conducted back to 1966, except for Science Citation index, which was conducted back to 1974. The upper limit of each search was 2011.

A manual search was also performed using key pain journals, pain meeting abstracts, and textbooks. For the following journals, the following years were reviewed: *Pain*, 1975–2011; *Spine*, 1986–2011; *The Pain Clinic*,

1986–2011; *Clinical Journal of Pain*, 1985–2011; *Pain Medicine*, 2000–2011. Abstracts of the following meetings were reviewed for the following years: International Association for the Study of Pain 1981, 1984, 1987, 1990, 1993, 1996, 1999, 2002, 2005, 2008, and 2011, and the American Pain Society Meetings, 1982–2011.

Three pain textbooks were reviewed for possible references. These were *Evaluation and Treatment of Chronic Pain*, Third Edition, G. Aronoff (ed.), 1999; *Handbook of Pain Management*, Second Edition, C.D. Tollison, Jr., J.R. Satterthwaite, J.W. Tollison (eds.), 1994; and *Textbook of Pain*, Third Edition, P. Wall, R. Melzak (eds.), 1993.

Eight hundred and sixteen references were found and subjected to a cursory review. Studies were excluded from detailed review if they did not contain the following elements: 1) addressed chronic LBP or STS; and 2) dealt with NP, and contained a procedure by which a determination was made as to whether the population under study had/did not have a NP component. Additionally, studies were excluded from detailed review if they had the following, making them ineligible for this review: isolated a population with suspected NP on which tests were done [17]; NPQ validation studies [18,19]; dealt with other populations besides chronic LBP and STS [20–25]; did not arrive at a NP component population percentage [26,27]; NPQ development studies [28–30]; and did not clarify how an NP component diagnosis was reached [31]. Studies were included for detailed review if they were not excluded by the previous exclusion criteria. Of the original 816 references, 800 were excluded by this process leaving 16 studies that fulfilled these exclusion/inclusion criteria.

These 16 studies [4,5,32–45] were reviewed in detail and sorted into two lines of evidence: CLBP and STS. Research information from these studies was then abstracted into tabular form and is presented according to these lines of evidence (Appendix Tables A1 and A2). Appendix Tables A1 and A2 were arranged to present the author, year publication, study question, design, sample size, how NP diagnosed, type statistical analysis, findings of the study, type of evidence the study represents according to Table 1 subsection 1, and quality score (assigned according to procedure later). The quality of studies was determined according the systems developed by Hoogendoorn et al. [46] and De Vet et al. [47] These researchers developed and tested a list of 23 criteria to be used to assess methodological quality of prospective, historical cohort, and case control studies. For details of how these criteria were developed, the reader is referred to the original studies [46,47]. Ten criteria were selected from their list that were appropriate to the studies analyzed (Appendix Table A3). In addition to the selected criteria, one criterion was added (positive if the data were collected by means of a standardized method of acceptable quality to measure NP). This resulted in a total of 11 criteria. For each analyzed study, each criterion was rated either present/fulfilled (+), not present/unfulfilled (–), or not applicable (NA).

NA was used as follows. There were three types of studies analyzed for quality: case control, cohort, and correlational. Some criteria in Appendix Table A3 pertained only to case control studies, while others applied only to cohort studies, etc. As such, NA was used if the criterion in question pertained to another type of study other than the one being reviewed. In addition, NA was used when that criterion did not pertain to the study in question. NA was not used when information was not available or not described [48]. Under those circumstances, a negative was assigned [48]. A negative was also assigned if the item did not meet the preselected criteria [48]. Each study was rated independently for each criterion by the senior author and another author. Both raters chose either a positive, negative, or NA for each criterion for each analyzed.The value assigned by each author for each criterion was then compared in a meeting. Any differences in the assigned values were resolved by mutual agreement. This resulted in a final decision as to whether each criterion received a negative, positive, or NA categorization. Values were then summarized and placed into tabular format (Appendix Table A3). A quality score was obtained by counting the number of positives obtained. This score was divided by 11 (the total number of criteria) minus the number of NAs and multiplied by 100, which gave the percentage quality score.

Studies scoring less than 50% historically have been rated as “low quality” [48]. These studies are usually not utilized to arrive at conclusions about a reviewed topic. For the purposes of this review, we arbitrarily set the acceptable quality score at 60% in order to avoid marginal studies. Studies scoring less than 60% were then not to be utilized in arriving at a conclusion about this topic.

The senior author independently abstracted the data into Appendix Tables A1 and A2. However, data abstraction was checked independently by the other author. Any discrepancies in this classification were also resolved by mutual agreement. In addition, the other author checked the classifications of the reviewed studies, that is, whether the reviewed study was a cohort, case control, etc. Any discrepancies in this classification were also resolved by mutual agreement.

The categorization of the type of evidence the studies represented (Appendix Tables A1 and A2) was based on the guidelines developed by the AHCPR for categorizing the levels of evidence represented by reviewed studies (Table 1) evidence guidelines [16]. Studies were categorized I through V according to this scheme. This categorization was also independently arrived at by the senior author and the other author. Any discrepancies were again resolved by mutual agreement in a meeting format.

The strength and consistency of the research evidence in each study grouping: Appendix Tables A1 and A2 were then rated according to the AHCPR consistency of evidence guidelines developed for this purpose (Table 1, subsection II) [16]. These guidelines allow the researcher to categorize the reviewed evidence as being consistent,

generally consistent, inconsistent, or demonstrating little or no evidence for supporting the hypothesis under study. Ratings according to these guidelines (Table 1) were performed independently by the senior author and the other author. Any discrepancies were later resolved by mutual agreement.

Finally, data from Appendix Tables A1–A3 were formatted into summary Tables 2 and 3. These tables were designed to summarize the overall findings of this structured review for CLBP and STS. The heading for these two tables are the various methods by which the presence of NP was determined, e.g., by the LANSS questionnaire. The subheadings for these two tables were the following: number of studies in group; % of studies in group with each type of evidence category; % average quality score of the studies in the group; total number of CLBP patients in the group of studies; % of CLBP patients in this group of studies with NP; and strength and consistency of the evidence (by AHCPR) for the question of whether CLBP patients and STS patients have an NP component to their pain.

Results

The results of this evidence-based review are summarized in Tables 2–3. Relevant findings were the following:

There were 11 studies which utilized various methods to determine the presence/absence of NP in CLBP. Of these 72.7% were type 3, and 27.3% were type 4 (Table 1). The % average quality score of the 11 studies was 97.7%. The total number of patients with CLBP in these 11 studies was 13,518. Of these 36.6% had NP according to the various methods utilized. According to the AHCPR guidelines the strength and consistency of this evidence was A (consistent finding from multiple studies of type 2, 3, or 4) (Table 1).

There were five studies that utilized various methods to determine the presence/absence of NP in STS. Of these 80% were type 3 and 20% type 4 (Table 1). The % average quality score of the five studies was 97.5%. The total number of patients with STS in these studies was 1619. Of these, 41.1% had NP according to the various methods utilized. According to the AHCPR guidelines, the strength and consistency of this evidence was A (consistent findings from multiple studies of type 2, 3, or 4) (Table 1).

Discussion

A number of observations can be derived from the results of Tables 2 and 3. First, none of the studies for CLBP or STS reported the frequency of NP to be zero. Thus, according to this evidence, both CLBP and STS populations contain some patients with NP. This supports the first hypothesis of this evidence-based structured review. Second, the overall combined frequency of NP is substantial: 36.6% for CLBP and 41.1% for STS. Surprisingly, the aggregated frequency of NP in STS is greater than in CLBP. Third, the prevalence range in CLBP for NP by different methods ranges from 16.7% to 54.4% and in STS from 13.0% to 43.3%. Fourth, the prevalence of NP in CLBP and STS differs significantly according to the method utilized to generate this diagnosis. Fifth, the different NPQs/inventories appear to generate significantly different NP prevalence rates in both CLBP and STS. Potential reasons for some of these observations will be discussed later.

If the significant aggregated prevalence of NP in CLBP reported here is correct, what are the potential explanations for this finding? Attal et al. [35] has postulated that CLBP is not restricted to typical radiculopathy. He has demonstrated [35] that in CLBP the proportion of patients with NP is highest in those who have typical radicular pain and have undergone surgery. This is typically the failed back surgery patient. Attal and others have postulated that NP here would be the result of lesions of nociceptive sprouts within the degenerative discs, post-surgical scars, and local nerve lesions [35]. Another issue here is whether sciatica, whether it is operated on or not, persists. Here, there is evidence from one epidemiological study [49] of 622 patients. Of these, 53% had sciatic symptoms after 4 years. Of those who had recovered from sciatica, 61% still had LBP. There is then some evidence that sciatica can persist, and these patients could be a large group within CLBP patients generating some of the data within the studies reviewed here. Typically, radicular pain is considered to radiate below the knee, while pain radiating to the knee only has been called pseudoradicular [50]. However, quantitative sensory testing has demonstrated that CLBP patients with pseudoradicular pain have similar sensory profiles to radicular patients but with less sensory loss. From this study, it has been postulated that the symptoms and signs of either pseudoradiculopathy or radiculopathy reflect a disease continuum rather than different disease entities. Thus, the hypotheses from these studies could also be an explanation for the presence of significant numbers of patients with NP in CLBP.

The aggregated prevalence of NP by all methods combined was greater for STS than for CLBP. Why should STS patients have NP if by diagnosis they do not have a nerve injury? Recent evidence in reference to fibromyalgia that has historically been considered an STS provides some clues. It appears that fibromyalgia patients may have central pain processing abnormalities and some characteristics of NP such as hyperalgesia [51]. Patients with chronic widespread pain who do not appear to fulfill diagnostic criteria for fibromyalgia have similar NP symptoms as in fibromyalgia [27]. In addition, the best predictor of whether a chronic widespread pain patient fulfills the diagnostic criteria of 11 trigger points for a diagnosis of fibromyalgia is the LANSS score [27]. The LANSS score also differs significantly between fibromyalgia patients (greater score) vs rheumatoid arthritis patients [26]. There has also been one study [52] that has been able to separate symptoms of musculoskeletal pain patients into clusters of symptoms representative of a mechanism-based classification of nociceptive, peripheral neuropathic or

Table 2 Summary of studies addressing the prevalence of neuropathic pain in chronic low back pain determined by various methods

Characteristics of the Studies	By Physical Examination	By Pharmacological Diagnostics Approach	By DN4 Questionnaire	By LANSS Questionnaire	By Pain Detect Questionnaire	By All Methods Combined
Number of studies in this group	1 (32)	2 (34, 33)	1 (35)	3 (36, 37, 38)	4 (39, 40, 4, 5)	11 (32, 34, 33, 35, 36, 37, 38, 39, 40, 4, 5)
% of studies in group with each type of evidence category						
Type 2	0	0	0	0	0	0
Type 3	100	0	100	100	100	72.7
Type 4	0	100	0	0	0	27.3
% Average quality score of the studies in the group	100	87.5	100	100	100	97.7
Total number of chronic LBP patients in this group of studies	717	60	132	2,403	10,206	13,518
% of chronic LBP patients in this group of studies with neuropathic pain	N = 240 33.4 (3 or more characteristics of neuropathic pain radiating beyond the knee, positive Lasègue, absent patellar reflex.	N = 10 16.7	N = 24 18.2	N = 1,308 54.4	N = 3,375 33.1%	N = 4,951 36.6
Strength and consistency of the evidence for the question of whether chronic LBP patients have a neuropathic pain component	? (not enough studies)	B	? (not enough studies)	B	A	A

DN4 = Neuropathic Pain Diagnostic Questionnaire; LANSS = Leeds Assessment of Neuropathic Symptoms and Signs; LBP = low back pain.

Table 3 Summary of studies addressing the prevalence of neuropathic pain in soft tissue syndromes determined by questionnaire

Characteristics of the Studies	By DN4 Questionnaire	By LANSS Questionnaire	By Pain Detect Questionnaire	By All Methods Combined
Number of Studies in Group	2 (41, 42)	1 (43)	2 (44, 45)	5 (41, 42, 43, 44, 45)
% of studies in group with each type of evidence category				
Type 2	0	0	0	0
Type 3	50	100	100	80
Type 4	50	0	0	20
% Average quality score of the studies in this group	93.7	100	100	97.5
Total number of patients with soft tissue syndrome in this group of studies.	148	86	1,385	1,619
% of patients with soft tissue syndrome in this group of studies with neuropathic pain.	N = 253 35.8	N = 11 13.0	N = 601 43.3	N = 665 41.1
Strength and consistency of the evidence for the question of whether patients with soft tissue syndromes have neuropathic pain	B	? (not enough studies)	B	A

DN4 = Neuropathic Pain Diagnostic Questionnaire; LANSS = Leeds Assessment of Neuropathic Symptoms and Signs.

central sensitization pain. These reports then support the concept that STS could have an NP component.

Why should different NPQs/inventories generate widely different NP prevalence estimates? One reason could be that CLBP and STS groups do not represent uniform diagnostic groups. For example, failed back surgery CLBP patients may be more likely to have NP vs other CLBP diagnostic groups, such as spinal stenosis [53]. As an example therefore, the CLBP studies reviewed here could have varied by the percentages of patients with failed back surgery syndrome. This then could lead to different prevalence estimates of NP between the questionnaires/inventories for allegedly the same population of CLBP. Second, the NPQs/inventories differ in their sensitivities and specificities for the diagnosis of NP. The LANSS has a sensitivity ranging from 82% to 91% and a specificity of 80–90% compared with clinical diagnosis. The DN4 has a sensitivity of 83% and a specificity of 90% compared with clinical diagnosis. The pain detect is entirely a self-report tool of nine items that do not require a clinical examination. This tool has a sensitivity of 85% and specificity of 80% [8]. Overall, all these sensitivities and specificities are in the high range, but nevertheless, minor differences could have led to different NP prevalence estimates for the different NPQs/inventories (Tables 2 and 3). Third, the NPQs/inventories generally utilize similar language to discriminate patients with/without NP. Researchers have claimed that this is a powerful evidence for reliability-validity of this type of approach [8]. However, a closer examination of these tools indicates that they do differ on some items/questions within the tool. For example, a question about numbness is absent in the LANSS but present in the DN4 and pain detect. Pain evoked by light touch question is present in the LANSS and pain detect but absent in the DN4. There are also other differences in items [8]. The subtle differences in these questionnaires/inventories could then also have contributed to the differences in the generated prevalence rates for NP in the studies compiled for Tables 2 and 3. Finally, a major issue is that the whole concept of NP is somewhat amorphous. The questionnaires utilized in the reviewed studies use signs and symptoms that we believe indicate a NP component, but current research has not clarified that signs and symptoms reliably do so.

How does the prevalence of NP in CLBP and STS reported here compare with the prevalence of NP in the general population? In one general population telephone survey of 1207 subjects using the DN4 questionnaire, 35% had chronic pain. Of these, 17.9% had NP symptoms [54]. In another general population study where telephone interviews and clinical examinations were utilized, 9.8% of 3,575 community respondents had NP by clinical examination. Utilizing the LANSS, an 8.8% prevalence was found [55]. In another study utilizing the DN4 questionnaire of 23,712 subjects who responded to a postal survey, 31.7% reported chronic pain. Of these, 6.9% had pain with NP characteristics [56]. Another study utilized patients from six family practices in the United Kingdom generating a sample of 6,000 adults who were administered in the LANSS in a postal survey. Here, 2,957 patients responded of whom 48% had chronic pain, and of these, 16.9% had a positive LANSS [57,58]. Overall, these studies generate a range for NP in the general population of 6.9–17.9%. In addition, it appears that when utilizing the clinical examination as the gold standard, NP prevalence was actually lower for the LANSS (8.8% vs the

clinical examination of 9.8%) [55]. The gold standard was utilized by only one study in CLBP patients [32]. Here, there were 717 patients examined (Table 2). The prevalence of NP was much greater than in the general population [55] (33.4% vs 9.8%). This is to be expected as CLBP is a highly selected population. Comparing this gold standard to our findings with the LANSS, the LANSS found a greater prevalence of NP (54. 4%) than the gold standard (33.4%) (Table 2). However, utilizing all methods combined (Table 2), the prevalence of NP in CLBP (36.6%) was very close to that of the gold standard. Finally, the fact that a number of studies (presented earlier) have found a significant percentage of subject participants with NP indirectly supports the findings of this review.

Most of the information summarized in this review was generated through the use of NPQs/inventories. The question then is what are the advantages of utilizing such questionnaires/inventories to diagnose NP? First, these tools can serve as a screening function that would then lead to a closer physical examination by a clinician. Second, the use of these tools could lead to a better understanding by clinicians of the difference between nociceptive and NP [59]. Third, it is agreed that NP is often more severe and more difficult to treat and is generally undertreated. Currently, there are pharmacological agents available to treat NP, although it is not clear if these agents are NP-specific or treat pain in general. Improving clinician's understanding of NP through the use of these tools could then lead to a more successful multimechanistic treatment approach by clinicians of NP [59]. Fourth, these inventories could serve as screening tools for nonspecialists to improve the index of suspicion for the diagnosis of NP [8]. Finally, NP inventories can be used as standardized case identification tools in epidemiological studies [37,55,56,58], thus advancing NP research.

Some researchers have claimed that the LANSS does not compare well with the gold standard [55]. As such, what should be the next step in the development of this area of research? First, experts in this area should formally agree as to what clinical examination criteria should be included for a clinical diagnosis of NP, i.e., a generally accepted gold standard. Second, once the gold standard is developed/accepted, a large study should be done within CLBP patients. Within this group, actual diagnoses such a failed back surgery syndrome, radiculopathy, fibromyalgia, etc. should be carefully recorded. Each of these groups should be administered all the available NPQs/inventories. Sensitivities/specificities for each of the questionnaires/inventories could then be developed against the gold standard for each of the CLBP diagnostic groups. Such a design would solve the problem of which is the tool with the best sensitivity/specificity and perhaps which tool should be utilized for diagnostic purposes.

What are the clinical implications for the pain clinician from the results of this evidence-based structured review? It is the opinion of this research group that pain clinicians could consider including a NPQ/inventory into the routine examination of patients with CLBP and STS. A positive result on the questionnaire/inventory could then lead to a more detailed physical examination for the presence of NP or to consideration for treatment/nontreatment of NP with appropriate pharmacological agents. This recommendation is being made with the understanding that this may be unrealistic for many busy pain practices where multiple questionnaires are already being utilized.

Conclusions

According to the reviewed studies, there are significant percentages of patients with CLBP and STS who have a NP component to their pain.There is, however, significant variation in the prevalence of NP within these syndromes depending on the method utilized to diagnose NP.

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Appendix

Table A1 Studies addressing the prevalence of neuropathic pain (NP) in chronic low back pain (CLBP) determined by various methods

Authors (Year)	Study Question	Design	How NP Diagnosed	Statistical Analysis	Findings	Type of Evidence	Quality Score
Freynhagen et al. (2006) [32]	What % of CLBP pts. have NP?	717 CLBP pts. examined by physician and patient completed questionnaires.	Physician completed questionnaires	%	33% had three or more characteristics of NP.	3	100.0%
Sorensen et al. (1996) [34]	What % of CLBP pts. have NP?	40 CLBP pts. were subjected to a pharmacological diagnostic approach to diagnose NP.	Pain considered NP if 50% or greater response to both IV lidocaine and epidural local anesthetic	%	20% had NP.	4	87.5%
Sorensen et al. (1996) [33]	What % of CLBP pts. have NP?	20 CLBP pts. were subjected to a pharmacological diagnostic approach to diagnose NP.	Pain considered NP if it decreased 50% or greater to both IV lidocaine and epidural local anesthetic	%	10% had NP.	4	87.5%
Attal et al. (2011) [35]	What % of CLBP pts. groups designated by the Quebec Task Force classification have NP?	132 CLBP pts. divided into four groups based on physical examined history and task force criteria administered DN4.	DN4 (Douleur Neuropathique en 4 questions) score equal to or greater than 4/10	%	Overall, 37.1% of CLBP pts. had NP, but prevalence differed between groups.	4	100.0%
Hassan et al. (2004) [36]	What % of CLBP pts. have NP?	100 CLBP pts. administered LANSS.	LANSS	%	41% had NP.	3	100.0%
El Siss et al. (2010) [37]	Of pts. with CLBP, what % have NP?	1,134 CLBP administered LANSS.	LANSS score greater than 12	%	628 (55%) had >12 NP scores.	3	100.0%
Kaki et al. (2005) [38]	What % of CLBP pts. have NP?	11,698 CLBP pts. administered LANSS.	LANSS	%	639 (54.7%) had scores >12 indicative NP.	3	100.0%
Beith et al. (2011) [39]	What is the % of pts. with NP referred for physical therapy for CLBP?	Pain detect administered to 343 pts. with CLBP referred for physical therapy.	Pain detect	%	16% (N = 54) had NP.	3	100.0%
Morso et al. (2011) [40]	What % of CLBP pts. (3–12 months) have NP?	145 CLBP pts. administered pain detect.	Pain detect (PDQ)	%	19.3% had NP, 26.2% uncertain, 53.1% non-neuropathic.	3	100.0%
Freynhagen et al. (2006) [4]	Of pts. with CLBP, what % have NP?	8,000 CLBP administered pain detect.	Pain detect	%	Of 8,000 pts., 37.0% had NP (>>19)	3	100.0%
Schmidt et al. (2009) [5]	What is the estimate of NP within CLBP within general population?	11,092 subjects from study of the general population had been administered pain detect.	Pain detect (PDQ)	Probabilistic imputation approach modeling	19.4% of 1,718 pts. with CLBP had NP but NP finding more likely in pts. with significant pain.	3	100.0%

LANSS = Leeds Assessment of Neuropathic Symptoms and Signs; PDQ = Pain Detect Questionnaire.

Table A2 Studies addressing the prevalence of neuropathic pain (NP) in soft tissue syndromes determined by questionnaire

Author (Year)	Study Question	Design, Type Study	How NP Diagnosed	Statistical Analysis	Findings	Type of Evidence	Quality Score
Masters and Lind (2010) [41]	What % of musculoskeletal pts. have NP?	133 musculoskeletal pts. classified as either somatic, somatic referred, neuropathic, or combination of these	DN4 score 4/10 or greater	%	8% NP 29 mixed Total: 37%	4	100.0%
Van Wilgen and Keizer (2011) [42]	Do some pts. with tendinopathy have NP?	15 pts. with tendinopathy given DN4 interview	DN4	%	27% had desensitization.	3	87.5%
Gisk et al. (2000) [43]	Of pts. with musculoskeletal pain, what % have NP symptoms?	86 pts. with musculoskeletal pain given LANNS	LANNS	%	13% had a score of 12 or more indicative NP.	3	100.0%
Jespersen et al. (2010) [44]	What % of CPPs with musculoskeletal pain have NP?	1,322 CPPs completed pain detect of which 1,304 have musculoskeletal pain	Pain detect ≥>18	%	540 or 41.4% had NP.	3	100.0%
Amris et al. (2011) [45]	What % of musculoskeletal pts. with CWP have NP?	81 pts. with CWP administered PDQ	PDQ	%	61 or 75.3% had NP.	3	100.0%

CPP = chronic pain patient; CWP = chronic widespread pain; DN4 = Douleur Neuropathique en 4 questions; LANSS = Leeds Assessment of Neuropathic Symptoms and Signs; PDQ = Pain Detect Questionnaire.

Table A3 Quality ratings for studies in Appendix Tables A1 and A2

Criterion	32	34	33	35	36	37	38	39	40	4	5	41	42	43	44	45
1. Positive if the study had a clearly defined objective	+	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	+	+	+	+
2. Positive if the main features (description of the sampling frame, distribution of the population according to age and sex) of the study population were described	+	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	+	+	+	+
3. Positive if the participation rate at baseline was at least 80%	+	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	+	+	+	+
4. Positive if cases and controls were drawn from the same population and clear definitions of cases and controls were given	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
5. Positive if the participation rates of cases and controls selected and invited to participate at baseline were at least 80%	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	(NA)	NA	NA	NA	NA	NA
6. Positive if data were collected by means of standardized methods of acceptable quality for neuropathic pain	+	(+)	+	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	+
7. Positive if the exposure was measured in an identical manner among cases and controls	NA	NA	NA	NA	NA	NA	NA	(+)	NA	NA	(NA)	NA	NA	NA	NA	NA
8. Positive if the method used for the statistical analysis was appropriate for the study	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	+	+	+	+
9. Restriction to a homogenous study population	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	+	+	+	+
10. Allocation procedure not leading to bias	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	+	+	+	+
11. Smallest group bigger than 50 participants	(+)	(-)	(-)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	–	+	+	+
Overall quality score	100.0%	87.5%	87.5%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	87.5%	100.0%	100.0%	100.0%

NA = not applicable.