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Review Article

Neuropathic pain in cancer: systematic review, performance of screening tools and analysis of symptom profiles

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Abstract

Background: The objectives of this study were to evaluate the methodological quality of rigorous neuropathic pain assessment tools in applicable clinical studies, and determine the performance of screening tools for identifying neuropathic pain in patients with cancer.

Methods: Systematic literature search identified studies reporting use of Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Douleur Neuropathique en 4 (DN4) or painDETECT (PDQ) in cancer patients with a clinical diagnosis of neuropathic or not neuropathic pain. Individual patient data were requested to examine descriptor item profiles.

Results: Six studies recruited a total of 2301 cancer patients of which 1564 (68%) reported pain. Overall accuracy of screening tools ranged from 73 to 94%. There was variation in description and rigour of clinical assessment, particularly related to the rigour of clinical judgement of pain as the reference standard. Individual data from 1351 patients showed large variation in the selection of neuropathic pain descriptor items by cancer patients with neuropathic pain. LANSS and DN4 items characterized a significantly different neuropathic pain symptom profile from non-neuropathic pain in both tumour- and treatment-related cancer pain aetiologies.

Conclusions: We identified concordance between the clinician diagnosis and screening tool outcomes for LANSS, DN4 and PDQ in patients with cancer pain. Shortcomings in relation to standardized clinician assessment are likely to account for variation in screening tool sensitivity, which should include the use of the neuropathic pain grading system. Further research is needed to standardize and improve clinical assessment in patients with cancer pain. Until the standardization

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of clinical diagnosis for neuropathic cancer pain has been validated, screening tools offer a practical approach to identify potential cases of neuropathic cancer pain.

Key words: cancer pain; neuropathic pain; screening tool performance; symptom profile

Editor's key points

- Rigorous pain assessment is needed to identify neuropathic pain in cancer patients for optimal treatment strategies.
- Accuracy of three common screening tools was good; however, there is large variation in sensitivity of these tools and item selection overall is lower compared to non-cancer populations.
- The concordance between clinical diagnosis and screening tool outcomes makes screening tools practical for identifying potential cases of neuropathic cancer pain.

Neuropathic pain affects up to 40% of cancer patients and is associated with increased pain intensity, analgesic consumption and decreased quality of life.[1–4] While the majority of neuropathic pain in cancer patients arises as a direct result of tissue destruction by tumour, a growing proportion is caused by cancer treatments such as surgery or chemotherapy.[1 5]

Rigorous pain assessment is needed to identify the presence of neuropathic pain in order to direct specific treatment strategies.[6 7] In clinical practice inadequate assessment rigour leads to increased heterogeneity of clinical samples with adverse impact on treatment outcomes for patients.[1] In clinical trials, inadequate assessment rigour (and subsequent inclusion of heterogeneous sample populations) has been associated with an increasing number of neuropathic pain studies that fail to meet their primary efficacy end point.[8 9] The recently updated grading system for neuropathic pain[10] offers a standardized set of assessment criteria for identifying possible, probable and definite cases of neuropathic pain in clinical and research settings. The criteria are: (1) history of a relevant neurological lesion or disease of the somatosensory nervous system and pain in a plausible neuroanatomical distribution; (2) pain associated with sensory signs in the same plausible neuroanatomical distribution; and (3) confirmatory diagnostic tests indicate the presence of a lesion or disease of the somatosensory nervous system explaining the pain.[10] Satisfying the three criteria in turn raises the certainty of neuropathic pain from possible, to probable, to definite. However, neither the revised grading system for neuropathic pain[11] nor the original grading system[12] has been widely applied and evaluated in cancer patients. Nevertheless, studies adhering to this grading system were found to have significantly lower estimates of neuropathic pain prevalence than non-rigorous studies.[13] Nevertheless, the neuropathic pain grading system has yet to be widely adopted because the reliability (inter-rater and test-retest) and applicability of the grading system in clinical practice or research remain unclear. In the recent update of the grading system,[10] the authors acknowledged that it cannot yet be used as a 'gold standard.' To date, there is a lack of a gold standard for identifying neuropathic pain, and validated screening tools represent the best alternative.

Although screening tools cannot be used alone to identify neuropathic pain, the discriminatory value of neuropathic pain descriptors and the role of screening tools to identify possible cases of neuropathic pain has been highlighted in the updated grading system for neuropathic pain.[10] The most widely used neuropathic pain screening tools are the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS),[14] the Douleur Neuropathique en 4 (DN4)[15] and painDETECT (PDQ).[16] The LANSS comprises five symptom descriptor items and two sensory examination items; the DN4 comprises seven symptom items and three clinical examination items; and the PDQ comprises nine self-reported symptom items.[17]

These screening tools are recommended by Neuropathic Pain Special Interest Group (NeuPSIG) of the International Association for the Study of Pain (IASP) for screening but not for diagnosis.[7] These tools have been validated in a wide range of pain populations, as well as translated into many languages, to discriminate between pain that is predominantly neuropathic and pain that is predominately nociceptive.[17] However, some reports of their use in cancer populations have suggested that their ability to identify cases of neuropathic pain might be lower than in non-cancer populations in which they were developed.[4 11]

The objectives of our current study were: (1) to evaluate the methodological quality of included studies, and (2) to determine the performance of screening tools for neuropathic pain in cancer patients against clinician assessment of pain type.

Methods

Search methods

We undertook a systematic literature search for all studies that reported use of LANSS, DN4 or PDQ in cancer patients. Electronic database searches were conducted from inception to August 2015 in MEDLINE, EMBASE, CINAHL (searches were updated in March 2017). A search strategy was developed for MEDLINE and altered accordingly for each electronic database (Supplementary Appendix 1). Names and abbreviations of neuropathic pain screening tools were combined with terms for cancer, pain, neuropathic, neuropathy.

Studies were eligible for inclusion if they included:

- Clinical population of patients with pain from cancer or cancer treatment.
- A clinical diagnosis of pain type from a healthcare professional (but not necessarily a pain specialist).
- A classification of pain using one or more of the following screening tools for neuropathic pain: LANSS[14], DN4[15], PDQ.[16]
- Sufficient data for sensitivity and specificity values to be extracted or to be calculated.

All articles were assessed for eligibility by first screening title and abstract and then by full text by two independent assessors. Grey literature search was conducted by reviewing the references lists of included articles and by contacting the authors of the original validation studies for LANSS, DN4 and PDQ to request as yet unpublished reports meeting the eligibility criteria.