

A "TNM" SYSTEM FOR EVALUATING AND TREATING CANCER PAIN

The Edmonton classification system

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Top-line summary

Cancer pain syndromes affect many or most people with cancer. At present no well-defined, internationally accepted assessment instrument exists to help determine which cancer pain syndromes are more difficult or time-consuming to control. A standardized, comprehensive and simple classification of cancer pain would enable clinicians to better manage patients and allocate resources, and researchers to compare results of outcome surveys and clinical trials — promoting the incorporation of good-quality evidence into patient care. Here, *Oncology Exchange* presents the Edmonton Classification System for Cancer Pain (ECS-CP). The authors describe its evolution from the Edmonton Staging System, recent research to validate the tool and standardize its use, and expectations for future development.

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The majority of people with advanced cancer are expected to develop pain syndromes, and these vary in complexity.¹ While we anticipate achieving good pain management for the majority of cases,^{2,3} some of those with complex pain syndromes are more difficult to treat. Clinicians may need to introduce multiple interventions and more time may be required to achieve stable pain control.

NEED FOR STANDARDIZED PAIN ASSESSMENT

Patients with the same age, gender and diagnosis may present with very different factors that have important implications for pain management (see box, opposite). Oncologists would certainly not discuss the outcome of treating lung cancer patients (i.e. with surgery, radiation, chemotherapy or targeted agents) without some differentiation. A brief review of the cancer pain abstracts presented at the 2002 International Association for the Study of Pain Conference in San Diego, however, illustrates that standard practice is to merely state the number of cancer patients with pain included in the study population. The tumour-node-metastasis (TNM) classification system used by oncologists to describe cancer populations provides a common language for clinicians and researchers. The lack of a comparable standardized approach in the cancer pain literature makes it difficult to compare research results of analgesic management for cancer pain.⁴

A variety of characteristics contribute to the complexity of cancer pain management, including neuropathic pain⁵⁻⁹

breakthrough pain^{5,7,10,11} psychological distress,¹²⁻¹⁶ idiopathic pain,^{8,9,17} history of addiction,¹⁸⁻²¹ tolerance,^{4,22} predisposition to side effects,^{5,23} genetic factors^{5-11,13-21,23,24} and presence of delirium.⁹ Diverse interpretations of the pain experience and of the many factors that may contribute to it complicate the development of a standardized pain classification system.

EXISTING SYSTEMS

Some classification systems focus on specific aspects of pain syndromes. The International Association for the Study of Pain has developed a classification of cancer pain consisting of a catalogue of lesions and diseases that can cause pain.^{25,26} This provides important information but is not linked to predicted complexity of pain management. Other systems have focused on pain pathophysiology, using mechanisms of cancer pain syndromes.²⁷ The pharmacologic approach uses different drugs for a short time to determine cancer pain pathophysiology, and subsequently the effectiveness of drug treatment regimens.²⁸ Review articles on the management of cancer pain emphasize the pharmacologic approach, however they





seldom mention the many characteristics that can influence the outcome or success of pain management.^{29,30} Hwang et al developed a Cancer Pain Prognostic Scale which requires multiple assessments to predict the likelihood of pain relief within 2 weeks for cancer patients with moderate to severe pain.¹² While this scale provided comprehensive cancer pain assessment that moves beyond the basic underlying pathophysiology, its complexity limited everyday clinical acceptance.

The recognized value of the TNM system used by oncologists³¹ prompted development of a more comprehensive system for cancer pain classification.^{32,33} The Edmonton Staging System (ESS) attempted to classify cancer pain on the basis of 7 characteristics thought to have clinical prognostic value. Depending on the combination of these features, patients were defined as having good or poor prognosis for pain control.³² The characteristics were mechanism of pain (visceral, bone or soft tissue, neuropathic, mixed, unknown), incidental pain (presence or absence), daily opioid usage, cognitive function (impaired or normal), psychological distress (present or absent) tolerance (present or absent according to an average daily increase in opioid consumption of more than 5% over the first three weeks of followup) and past history of alcoholism or drug addiction (positive or negative).

A number of studies have used the ESS and found it useful for providing more information about the cancer pain syndromes of the research populations.³⁴⁻³⁹ Difficulty with interpretation

and definitions, however, has likely limited its general use and acceptance. Since the original ESS validation studies, our clinical experience has confirmed difficulties with the definitions and use of this system. In particular, incidental pain, psychological distress and history of addiction are controversial and hard to interpret. The tolerance calculation is difficult to implement and impractical in some clinical settings. The terminology of good or poor prognosis may have little value when many of the poor-prognosis patients will, in fact, achieve stable pain control. This problem was confirmed by the recent study comparing the Cancer Pain Prognostic Scale with the ESS.¹² At 3 weeks, both predictive systems were reported to have performed poorly. Collectively, these findings attest to the need for a more valid, widely accepted and user-friendly assessment tool in classifying cancer pain.

EDMONTON SYSTEM REVISION

Having noted the limitations of the ESS, an expert panel consisting of physicians and researchers in our program began work on developing a revised Edmonton Staging System (rESS). The initial version of the rESS was based on a literature review and extensive clinical experience with the use of the ESS. The major change from the ESS was a reduction in the number of features from 7 to 5:

- mechanism of pain
- incidental pain
- psychological distress
- addictive behaviour
- cognitive function

Opioid dose was not included as it was felt to be more useful as an outcome measure. Tolerance was excluded due to the difficulty in incorporating this variable into the initial assessment. Subsequent validation studies have included tolerance as an outcome measure using an opioid escalation dose (OED) calculation, as modified by Mercadante et al.⁴⁰ Other changes were made to the number of options with regard to each feature and in the definitions of terms. The number of pain mechanism options was reduced from 5 to 4, reflecting the complexity

Two cases

1 Consider a 65 year-old man with lung cancer and bone metastases complaining of pain localized to the right arm and leg. You note that he moves comfortably and independently, is alert and oriented, and presents his history in a very coherent manner. He has a stable marriage and home life, no psychiatric history, and no history of substance abuse. His pain management consists of codeine 30 mg orally as required and he states that with this regime he has very little pain most of the time.

2 Another 65 year-old man with lung cancer and bone metastases is complaining of a burning, stabbing pain down his right leg at presentation. He appears reasonably comfortable at rest but cannot move without evidence of severe discomfort, and he has difficulty recounting his history coherently. This man has been divorced 3 times, lives alone, has a history of depression and suicide attempts, and a long history of alcohol and benzodiazepine abuse. His analgesic requirements have increased from morphine 5 mg every 4 hours to 100 mg every 4 hours over the last 7 days.

These two examples illustrate that cancer pain syndromes and the anticipated complexity and difficulty of achieving stable pain control vary enormously.

of treating neuropathic pain over other pain mechanisms. The expert panel introduced new definitions for incidental pain, psychological distress, addictive behaviour and cognitive

PROTOCOLS & PRACTICES

function — with the explicit appreciation that this would be an ongoing evolution.

RESEARCH AGENDA

Since initial development, we have conducted 3 validation studies of

the rESS: a Pilot Study (Study 1), a Regional Multicentre Study (Study 2), and a Construct Validation Study using Content Experts (Study 3). Study 1, involving 82 advanced cancer patients, was designed to determine patient accrual patterns, conduct

power analysis calculations and refine daily collection methods for further validation studies. Based on its findings, definitions of 4 of the 5 features and the design of the subsequent regional multicentre study were refined. An additional category for “no pain syndrome” was added to the mechanism of pain feature, to exclude the possibility that an absent descriptor might be interpreted as failure to complete the assessment.

Study 2 was a multicentre validation study involving advanced cancer patients in 3 Alberta settings: a tertiary palliative care unit, an acute hospital and a hospice palliative care unit.⁴¹ It focused on gathering inter-rater reliability estimates and predictive validity evidence. Of 746 patients included, 619 (83%) had a pain syndrome. Inter-rater reliability estimates ranged from 0.67 (pain mechanism) to 0.95 (presence of addiction). Univariate analysis demonstrated that younger patients (< 60 years), those with neuropathic pain, incidental pain, psychological distress, or comorbid psychological distress and addiction required a significantly longer time to achieve stable pain control ($p < 0.05$). In multivariate analysis, only age, neuropathic pain and incidental pain were significantly associated with time to reach stable pain control. Further, patients with neuropathic or incidental pain used significantly more modalities — both pharmacologic and nonpharmacologic — to achieve stable pain control ($p < 0.01$). Patients with neuropathic pain, incidental pain and presence of psychological distress or addiction required a higher final mean morphine equivalent daily dose ($p < 0.01$).

Construct validation to develop consensus definitions in the ongoing development of the rESS was recognized as central to work in this area. Study 3's purpose was to gather further construct validity evidence and develop and evaluate an administration manual to ensure standardized use.⁴² Two content expert panels, representing regional (Panel A, $n = 18$) and national and international (Panel B, $n = 52$) palliative medicine and pain specialists, were selected to participate in a modified Delphi survey. Most

FIGURE 1. Edmonton Classification System for Cancer Pain

Please consult www.palliative.org (> Clinical Information > Assessment Tools) for definition of terms and guidelines for use.

Patient Name: _____ Patient ID No: _____

For each of the following features, circle the response that is most appropriate, based on your clinical assessment of the patient.

1. Mechanism of Pain

- No** — No pain syndrome
- Nc** — Any nociceptive combination of visceral and/or bone or soft tissue pain
- Ne** — Neuropathic pain syndrome with or without any combination of nociceptive pain
- Nx** — Insufficient information to classify

2. Incident Pain

- Io** — No incident pain
- Ii** — Incident pain present
- Ix** — Insufficient information to classify

3. Psychological Distress

- Po** — No psychological distress
- Pp** — Psychological distress present
- Px** — Insufficient information to classify

4. Addictive Behavior

- Ao** — No addictive behavior
- Aa** — Addictive behavior present
- Ax** — Insufficient information to classify

5. Cognitive Function

- Co** — No impairment. Patient able to provide accurate present and past pain history unimpaired
- Ci** — Partial impairment. Sufficient impairment to affect patient's ability to provide accurate present and/or past pain history
- Cu** — Total impairment. Patient unresponsive, delirious or demented to the stage of being unable to provide any present and past pain history
- Cx** — Insufficient information to classify.

ECS-CP profile: _____

(COMBINATION OF THE FIVE CIRCLED RESPONSES, ONE FOR EACH CATEGORY)


Assessed by: _____ Date: _____

participants either agreed or strongly agreed with including the 5 existing features in the pain classification system, ranging from 67% (Panel A, cognitive function) to 100% (Panel B, mechanism of pain). Based on participant feedback, definitions for incidental pain, psychological distress, addictive behaviour and cognitive function were revised, and the guidelines for use were also revised. The name of the feature incidental pain was changed to incident pain. Participant feedback led to inclusion of an “unable to classify” option for each of the features. The psychological distress and addictive pain features were separated to improve clinical and analysis utility.⁴³ To reflect its intended use as a classification system, the name of the instrument was changed to the Edmonton Classification System for Cancer Pain (ECS-CP). **Figure 1** shows the ECS-CP.

NEXT STEPS FOR THE ECS-CP

Many factors have been proposed as prognostic for pain control; the ECS-CP attempts to simultaneously integrate these within a cohesive framework. Initial reliability and validity evidence provides a solid foundation for further validation studies. The items included represent a first attempt to define a standard core of variables — additional items such as tolerance and age are worthy of further research. The clinical practice setting, social and cultural circumstances of the environment of origin — Edmonton — have influenced the creation of the ECS-CP and currently limit generalizability of findings; further validation studies are planned using the revised definitions in a diverse international sample of palliative cancer pain patients.

It took approximately 50 years to develop international acceptance for the TNM classification system⁴⁴ and TNM continues to evolve. Our past and present research agenda to develop a classification system for cancer pain is the beginning of a journey with great potential that will inevitably involve much complexity and many tangential issues. By definition it will be an ongoing evolution — well worth it to achieve the goal of enabling

clinicians to manage patients' cancer pain more efficiently. 

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