Classification of Cancer Pain Syndromes

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Cancer patients experience pain in multiple sites and from several pathophysiologies of the symptom complex. The fluctuating nature of cancer pain intensity is a relevant clinical feature and depends on disease patterns and pain mechanisms. Breakthrough pain is defined as episodes of pain that "break through" the control of an otherwise effective analgesic therapy.

The terms "cancer pain" and "cancer-related pain" distinguish pain in cancer patients from pain in patients without malignancies, but they do not convey details of the characteristics, etiology, and pathophysiology of pain. Cancer patients may experience many different types of pain. This fact was recognized decades ago, and systematic assessment of cancer pain syndromes has evolved since the pioneering work of Kathleen Foley, who first described the complex phenomenology of cancer pain in the 1970s.[1,2] Another important early description of cancer pain came from the hospice experience in the United Kingdom.[3] After these initial empiric efforts, the definition of pain associated with cancer was refined as schemes by Foley and Twycross were perfected with more detailed lists of significant clinico-anatomic entities. These updated lists were derived from the experience of different authors from several centers.[4-7]

It was already evident from the earliest reports that the prevalence of pain among cancer patients was high, and that cancer pain may result from antineoplastic treatments or the tumor itself. It is now recognized that cancer patients experience pain in multiple sites and from several pathophysiologies of the symptom complex. The importance of classifying cancer pain syndromes depends on the goal of the clinical or research task for which the classification is to be used. Cancer pain classification schemes may be temporal, etiologic, anatomic, pathophysiologic, or syndromic.

Pain Assessment and Clinical Presentations

Pain History
A pain history must be comprehensive and elicited directly from the patient, whenever possible. In particular, questions about pain location, radiation, referral, quality, intensity, duration, and temporal variation, as well as provocative and palliative factors, must be noted. The PQRST mnemonic is quite useful in the clinical setting: P = provocative/palliative factors; Q = quality; R = region, radiation, referral; S = severity, using intensity rating scales; T = temporal features.[8]

Number of Pain Sites
The location and number of pain sites are often formally recorded by the patient or clinician on body charts. This information is also included in many pain assessment tools.[9,10] Multiple sites of pain are common, especially when pain is related to metastatic disease. The number of different pains reported varies considerably, but most authors agree that between 70% and 80% of cancer patients have pain from two anatomically distinct sites.[3,11] One report recognized more specifically the presence of two or more distinct pain syndromes in 70% of cases.[11] Differences in assessment methods can be a source of significant variability in the descriptions of pain syndromes.

Temporal Variation
After a pain history is taken and the location of the pain described, the next fundamental clinical characteristic to be assessed is pain intensity.[12] Pain intensity is assessed by validated subjective ratings using visual analog scales, numeric or verbal rating scales, or pain questionnaires.[10,13,14] Intensity is often the main feature of pain guiding therapeutic interventions. The fluctuating nature of cancer pain intensity is a relevant clinical feature and depends on disease patterns and pain mechanisms. The occurrence of significant episodes of pain that "break through" the control of an otherwise effective analgesic therapy led to the definition of breakthrough pain. This term is used primarily by North American cancer pain specialists.[15-17]
Portenoy and colleagues have defined breakthrough pain as "a transitory exacerbation of pain that occurs on a background of otherwise stable pain in a patient receiving chronic opioid therapy." There are three important aspects of this phenomenon:

1. **Intensity**: Breakthrough pain manifests as an increase in pain intensity. To be clinically meaningful, a certain intensity level has to be set as a threshold, ie, a level that would prompt changes in therapy. This severity threshold can change. Pain described as greater than moderate-to-severe or excruciating was the level used in the original definition.[15] On a numeric (0 to 10) rating scale, most breakthrough pain requiring treatment was rated of 5 or more.[18] In accordance with these definitions, treatment strategies for breakthrough pain have been investigated.[19,20]

2. **Temporal Factors**: Breakthrough pain is by definition transitory, to be distinguished from an increase in the intensity of background pain. To be considered transitory, the pain episode has to be linked to a reversible provocative factor (eg, movement) or be terminated by analgesic measures.

3. **Therapy**: The third concept links breakthrough pain with an established ongoing analgesic regimen usually based on opioid administration. Pain, therefore, breaks through the analgesia provided by regularly administered medications. This characteristic limits the concept and, in subsequent definitions, has been eliminated to give a more general meaning to breakthrough pain.[21]

**Epidemiology and Clinical Implications**

Between 40% and 80% of cancer pain patients experience breakthrough pain.[15,18,22-24] We can conservatively estimate a prevalence of 65%.[22,24] In one survey, breakthrough pain was independently associated with more severe pain intensity on multivariate analyses.[24] Another study confirmed that breakthrough pain has a negative effect on quality of life, function, and mood.[22]

One important aspect of the management of breakthrough pain is the identification of precipitating factors. Some breakthrough pains are precipitated by volitional actions (movement, posture, and touch), and in such cases, breakthrough pain is synonymous with incident pain.[15,18,22] Breakthrough pain may also occur spontaneously as a result of some automatic, involuntary action (visceral reflexes such as bowel spasm, ureteral distension, or swallowing). Breakthrough pain can otherwise be spontaneous or the result of therapeutic failure, such as pain worsening at the end of analgesic efficacy. In the clinical setting, the causes of some breakthrough pain are difficult to identify.

The pathophysiology of breakthrough pain has been poorly studied. In one International Association for the Study of Pain (IASP) Task Force study, the presence of breakthrough pain was strongly associated with bone pain syndromes, especially vertebral bone pain (87%), and with pain due to plexopathies (78%) suggesting the existence of breakthrough pain with different mechanisms and pathophysiologies (personal communication, Caraceni and Portenoy, 2001).

**Controversies**

Although breakthrough pain is considered an important aspect of cancer pain, its diagnosis and definition is controversial. Different definitions are possible, ranging from general to specific (as discussed above), depending on intensity, duration, relationship to the therapeutic regimen, precipitating factors, and so on. When the concept has been used in other than an Anglo-Saxon cultural setting, the wide variation in interpretation suggests cultural differences will have to be better appreciated before the concept can be universally applied.[24]

**Classification Schema**

**Temporal Classification**

Traditional ways of classifying pain in the cancer population include distinguishing between pain associated with therapy, the tumor, or unrelated to both,[2] and between chronic and acute pains associated with therapies or due to untreatable cancer. The latter concept has been described by some as "untreatable cancer pain." Although many cancers are incurable, progress in antineoplastic therapy has allowed patients to live with cancer as a chronic disease.

We contend that the distinction between acute and chronic pain is not as applicable when considering pain in relation to progressive cancer. Pain is considered chronic when it persists for at least 6 months. Chronic pain may be due to secondary central nervous system processes (spinal and
supraspinal) initiated by tissue injuries that evolve and are maintained beyond healing of the initial lesion.

When cancer progresses, tissue changes are dynamic, develop spontaneously, and respond to environmental or therapeutic changes. Acute and chronic processes are, therefore, intermingled in such a way as to be practically impossible to untangle. In the case of treatment-related pains, a distinction has been made between acute and subacute procedural pain associated with different therapeutic techniques (Table 1) and chronic painful sequelae of therapies that last for years, if not indefinitely (Table 2).

The following discussion will focus on pain syndromes related directly to cancer progression or invasion. Therapy-related pains will be considered in this review only for their interference and overlap with the diagnosis of disease-related syndromes.

**Etiologic Classification**

Early reports, confirmed by more recent surveys, showed that in cancer centers, 70% of patients with pain have a pain syndrome directly related to the cancer, 20% have treatment-related pain (excluding immediate postoperative pain), and 10% have some unrelated chronic pain syndrome.[1,2] Subsequently, a substantial overlap of pain syndromes due to cancer and its treatment has been observed.[25] Some authors have suggested a fourth category called "pain associated with chronic disease or debility" that would include myogenic pain.[3,25,26] These percentages can change depending on the center’s experience and on the assessment method. For instance, if emphasis is placed on assessing every pain vs the most significant pains or those requiring specific medical attention, the resulting numbers will change.

In a recent study, pain specialists were asked to evaluate only the pain that they were actively treating in patients with pain due only to cancer progression. With this very conservative definition, treatment-associated pain was nonetheless reported to overlap in 20% of patients with cancer-induced pain, a figure higher than the 12% rate reported by Twycross and Fairfield in 1982.[3]

**Anatomic Classification**

Cancer may affect any body tissue, and pain may be classified according to anatomic location, ie, structure(s) or tissue(s) involved by disease. Table 3 summarizes how various researchers have distinguished pain syndromes due to neoplastic lesions of bone, viscera, neural, or soft tissue.[1,3,11,24-26] Each study may have a different selection bias, reporting respectively on inpatients admitted to a specialized cancer center,[2] hospice inpatients,[3,26] or patients who are referred to a pain specialist.[11,24,25]

**Syndromic Classification**

The diagnosis of a pain syndrome in a cancer patient is based on repeated recognition of a cluster of symptoms and signs, including pain, which, combined with other relevant information from the history and examination, identify a clinical entity that can be used to define that specific situation (eg, brachial plexopathy, bone pain due to vertebral metastases). Although different lists have been published indicating the numerous pain syndromes associated with cancer, an established classification system has never been validated, and each clinician will offer a different level of detail to the description of cases based on experience, available imaging studies, and clinical needs. For example, a painful lesion of one vertebra can be described from an anatomic point of view as osteolytic or osteoblastic; involving the body, articular processes, pedicles, and/or spinous process; with or without compression fracture, spine instability, epidural extension, or foraminal encroachment; and may include histologic information.

The most recent attempt to provide a comprehensive description of the syndromic classification of cancer pain with some anatomic detail is reported in Table 4.[24] This scheme is a modified version of previous lists.[2,4,27-29] By using this list in an international survey, it was possible to show that some tumors are more often associated with some syndromes than others (Table 5) and that some characteristics of pain considered important in planning a treatment strategy, such as pain intensity, presence of breakthrough pain, and neuropathic pain, are more typical of some syndromes.[24]

All the listed entities have clinical characteristics that can vary according to the stage of disease and will usually evolve. Therefore, cancer pain management requires frequent reevaluation of the patient and refinement of the pain "diagnosis" repeatedly over time. A good clinical description of these syndromes can be found in comprehensive reviews and specific articles dedicated to single syndromes or tumors.[4,6,7,12,28-63]

The pain syndromes associated with hematologic malignancies are the least studied. Only a few were seen in the above-mentioned study. In a survey of 469 patients with advanced hematologic malignancies followed by a palliative home-care service, 244 (52%) had pain, and 284 pain
syndromes were identified and described (see Table 6).[64] These syndromes were classified as due to bone marrow expansion in 33% of cases, lymphadenopathy and visceral involvement in 18%, osteolysis in 16%, oral mucositis in 11%, herpetic neuralgia in 6%, meningeal disease in 5%, and other causes in 11%. Generalized bone pain was noted in 51% of patients.[64]

To highlight the importance of diagnosing cancer pain syndromes, Figures 1 through 7 illustrate the differential diagnosis of back pain due to cancer. Pain in the back, one of the most common pain sites in advanced cancer (see below) can be the result of bone lesions (Figure 1, Figure 2, and Figure 3), retroperitoneal or paraspinous lesions (Figure 4 and Figure 5), or root (Figure 2 and Figure 3), spinal cord, or meningeal lesions (Figure 6 and Figure 7).[65]

**Pathophysiologic Classification**

Determining the pathophysiologic mechanisms of pain is essential to selecting the appropriate therapeutic strategies.[66,67]

The classic distinction between nociceptive and neuropathic pain has been applied to cancer pain usually with further separation between nociceptive somatic and nociceptive visceral pain. The distinction between somatic and visceral nociceptive pain follows traditional semielogic teachings (see below for a more detailed discussion under staging systems).[68]

**Neuropathic Pain**

Nociceptive pain is caused by the direct activation of nociceptors that are located in the somatic and visceral structures sensitive to pain. Neuropathic pain is due to pathologic functioning of the nervous system and can be "generated" by peripheral and central nervous system processes. Several different changes occur in the central nervous system after the pain-generating stimulus is initiated. Damage to peripheral and central nervous system structures can result in other neuropathic pain syndromes, eg, phantom pain or postherpetic neuralgia. Identifying the mechanisms of neuropathic pain is again important in selecting therapeutic strategies.

The debate in cancer pain relating to confirmation of neuropathic pain mechanisms has important implications for other pain conditions, such as low back pain. A complete discussion of these issues is beyond the scope of this review, but we contend that neuropathic mechanisms are operating in most painful conditions of intermediate-to-long duration (those not due to acute activation of nociceptors).[69] It has been noted that pain caused by trauma or surgical incision of the skin is likely to be sustained by neurogenic mechanisms of peripheral inflammation and central sensitization, even in the first postoperative days.[70]

The most common use of the term neuropathic pain in cancer is restricted to pain with particular clinical characteristics or to pain caused by lesions of the peripheral or central nervous system. A distinction should be made between the site(s) of nervous system injury and the neuropathic mechanisms underlying pain. The clinical characteristics of neuropathic pain are variably described. Some authors have suggested that negative and positive neurologic symptoms and signs are necessary to make a diagnosis of neuropathic pain (Table 7).[67,71-73]

Neuropathic pain in cancer patients has been variously defined. Vainio and Kalso describe their patient population as affected by brachial or lumbosacral plexopathy with radiating pain.[74] Arner and Arner reported the finding of continuous vs intermittent neurogenic pain.[75] Cherny and colleagues,[76] and Grond and colleagues identify any pain due to a neurologic lesion as neuropathic.[11] Caraceni and colleagues included patients in a study of neuropathic cancer pain only if a neurologic lesion was the cause of the pain and if the patients complained of lancinating or burning pain, or allodynia.[77] Other authors have discussed the need to distinguish between nociceptive nerve pain (for example, inflammatory nerve trunk pain) and neuropathic pain (pain perpetuated by neurologic dysfunction).[78-80] Neuropathic pain in cancer is used as a general term, lacking a universally accepted and homogeneously applied definition.[81]

With these and other limitations noted,[82,83] the IASP Task Force on Cancer Pain attempted a pathophysiologic classification by conducting a survey of cancer pain syndromes (see Table 8).[24] The pain classifications were provided by pain specialists, who received a well-known textbook chapter to use as a general guide.[4]

**Psychogenic Pain**

The category of psychogenic pain is always theoretically considered in pain assessment,[84] but its practical application in cancer patients with pain remains, at best, unclear. It will be considered again in the staging system section.

Some authors refer to pain that has no evident organic explanation in patients with active cancer as idiopathic.[4] It is likely that psychological status has a role in modulating the perception of pain in cancer, although we lack good evidence on how this mechanism is clinically relevant. One observation suggested that pain was rated as more intense when the patient thought it was due to cancer progression.[85] This correlates with the observation that concurrent anxiety increases the perceived intensity of the pain. Other authors favor the theory that depression is a relevant factor in
modulating the perception and expression of pain in patients with metastatic cancer,[86] but recent evidence in the post-bone-marrow transplant mucositis model suggests that psychological factors and coping styles are modest predictors of pain intensity compared with biomedical factors (ie, mucositis severity).[87] Psychogenic mechanism has been considered relevant in only 1.8% of patients in another survey.[24] In conclusion, it is important to test and validate an operational classification system of cancer pain that is grounded in pathophysiologic mechanisms, including more refined definitions of neuropathic pain and psychological characteristics that may be relevant to patients with cancer pain.

Cancer Pain Staging Systems

A number of attempts to classify cancer pain according to different criteria have been made. At present, none seem to completely meet the needs of both clinicians and researchers working in this field.

International Association for the Study of Pain Taxonomy

The use of the IASP Taxonomy[84] in this field has been criticized because it is not aimed at establishing a prognosis and lacks some factors considered important in cancer pain prognosis.[11,81] The only study that implemented this classification system in patients with cancer integrated its use with the traditional concepts listed above (see also Table 1). The authors identified 4,542 pain syndromes in 2,266 patients.

The IASP Taxonomy is based on five axes. Axis I (regions) describes pain location; axis II (systems), the body system of pain origin; axis III, temporal characteristics of pain, pattern of occurrence; axis IV, patient’s statement of intensity, time since onset; and axis V, etiology. If we follow the taxonomy by axis, the following are relevant observations:

- **Axis I, Region** It could be shown that the location of the pain was related anatomically to the type of primary tumor in cancer of the head and neck, respiratory system, and gastrointestinal system, whereas for all other cancers, the most prevalent pain region was the lower back, lumbar spine, sacrum, and coccyx (36% of all patients).
- **Axis II, System** The musculoskeletal system or connective tissue was responsible for pain in most patients except in those affected by gastrointestinal tumors (60% of these patients had pain related to gastrointestinal system involvement).
- **Axis III, Temporal characteristics pattern of occurrence** Continuous nonfluctuating pain was reported in 34%, and 36% had fluctuating pain superimposed on continuous pain. Paroxysmal pains were recorded in 12% of patients.
- **Axis IV, Intensity and time since onset** In 42% of cases, patients had severe pain of more than 1-month duration.
- **Axis V, Etiology** Neoplasm was the etiology of pain in 81% of cases (see also Table 1). Interestingly, psychogenic pain was diagnosed in only one patient who had head and neck cancer.

The IASP Taxonomy is a broad classification system with the scope to give a code number to every clinical pain syndrome. It, therefore, may lack some of the details that can be important in classifying cancer patients. Axis V is probably not very helpful in assessing pain in patients with a known active cancer. Axis I and III provide interesting information, but it would be useful to assess the prognostic relevance of different axis III descriptions compared with other clinical characteristics that have temporal implications and are not included in this classification (such as breakthrough pain and incidental pain).[15,88] Unfortunately, the IASP Taxonomy does not coincide with coding systems used for financial reimbursement in some countries.

The Edmonton Staging System

This classification system includes most factors that, according to clinical experience, might predict response to analgesic treatment.[88,89] The most recent version of the staging system is reported in Table 9. The factors currently included are those that were demonstrated to be correlated with pain control after logistic regression analyses.[89] The presence of any of the factors listed under stage II classify the patient as a potentially poor responder. The operational definitions adopted for pain mechanisms reflect classic clinical physiologic knowledge.[68] Visceral pain is pain due to a visceral lesion; the pain is not well localized, "aching," "dull," and occasionally like a "cramp." Bone and soft-tissue lesions cause pain described as an "ache" in the affected area that is well localized and aggravated by pressure or movement. Radicular
neuropathic pain is located in the region of distribution of the affected nerve root "associated or not with motor or sensory deficit, autonomic changes, paresthesias or paroxysmal episodes of pain." It is usually described as "burning" or "electric." Among other pain characteristics, incident pain was chosen as a negative prognostic factor. Incident pain is pain aggravated by body movement, swallowing, defecation, or urination that occurs on a baseline level of well-controlled or slight pain at rest. This definition partially overlaps the definition of breakthrough pain (see above discussion). Therefore, incident pain is a type of breakthrough pain related to movement in many descriptions. The Edmonton Staging System defines incident pain as all forms of pain precipitated by voluntary or involuntary stimulation of the painful area. An addictive personality may worsen prognosis as well as the presence of psychological distress. Drug or alcohol abuse can be assessed by history or by specific instruments such as the CAGE (Cut down, Annoyed, Guilty, Eye opener).[90] The construct of psychological distress is more difficult to define. The authors state that "patients with somatization accompanied by symptoms such as depression, anxiety, hostility, or neuroticism severe enough to jeopardize the success of the analgesic treatment" are psychologically distressed. In the setting of terminal illness, anxiety, depression, adjustment disorders, and cognitive deficits are common and when properly treated may not confer a worse prognosis for analgesic response. An evaluation of this system in 276 patients led to a high rate of good responses in the favorable prognostic group (93%), but also in the poor prognostic group (55%). Among patients classified as stage I, 93% achieved good pain control, and among patients classified as stage II, only 44% had poor pain control. The staging is, therefore, interesting but requires more study. Each factor should be defined more precisely, especially neuropathic pain and psychological distress. Also the concept of tolerance needs further elaboration, because, in this setting, an increased need for opioids may more likely reflect pain escalation due to disease progression than pure pharmacologic tolerance. (Opioid tolerance is defined as a 5% or more increase per day in the initial opioid dose. Lower increases in dose confer better prognosis.) The two possibilities have very different implications. A validation process would require replication of the staging results with the same or modified characteristics in a training population, aiming at better predictive values, and confirmation of such in an independent testing population.

**Clinical Implications**

In focusing on the care of the individual patient, it is useful to be familiar with the characteristics of the typical syndromes found in association with different tumor types and anatomic locations. An understanding of the etiology of pain in relation to the cancer is useful in recognizing these complications and in treating them. Pain in cancer is often a presenting symptom, and may herald severe complications that can be prevented by an accurate diagnosis of the pain syndrome. In the experience of one pain consultation service at a tertiary cancer center, the assessment of pain led to a diagnosis of new neoplastic lesions in 64% of cases and to the initiation of new specific oncologic therapy in 20% of cases.[91] Pain is often a sign of disease progression in cancer patients and can precede radiologic evidence of new metastases by weeks or months.[36] In the case of bone pain, the intertrabecular dissemination of cancer cells can cause pain although diagnostic studies (radiographs and bone scintigraphs) remain negative. In some cases, magnetic resonance imaging (MRI) of bone metastases may be positive while other tests are negative.[92] Bone pain intensity, location, quality, and temporal characteristics can be helpful in predicting an impending fracture,[35] or can raise the index of suspicion for neurologic complications such as radiculopathy and epidural spinal cord compression. In spite of a large clinical experience with these types of bone pain,[36,37,93] few empiric studies are available to guide the clinician in using these observations.[94]

**Cancer Staging**

Certain painful disease complications are important for staging and prognosis. It has already been shown that if pain is considered among the oncologic response variables, it can be a substitute or an adjunct to other oncologic parameters, such as tumor response or performance status. Pain intensity is also associated with objective measure of tumor activity.[95] Consideration of the pain history and pathophysiology along with disease information is important but not often fully appreciated.[24] As complex as it could be, it is likely that staging and prognostic variables can be influenced by the type of tumor and the availability and use of specific antineoplastic therapies. Therefore, a classification system has to be validated in different
neoplasms with different biological behaviors. A good example is provided by the observation that about 50% of bone metastases are asymptomatic; when and how they become painful is unknown.\[96\]

Some of these issues could be clarified by animal models that link the biological factors of a tumor with the pathophysiology of pain. These studies may throw light on the clinical aspects of cancer pain syndromes that may make the present traditional syndromic or mechanistic classifications obsolete.\[97\]

**Cancer Prognosis**

Predicting the results of therapies, whether analgesic or tumor-directed, would probably be the most relevant aim of a classification system that includes the cancer pain syndrome. This aim is the most difficult and demanding in terms of research effort, considering that many variables are likely to be involved. However, only after identifying patients with similar painful lesions and pathophysiology will it be possible to assess the relevance of prognostic factors and to define a staging system that will determine prognosis as precisely as does using performance status of patients with the same stage of a given cancer.

Homogeneity of the patient population is a typical requirement in oncology research. It is possible that different staging concepts will apply to advanced cancer patients approaching end of life. In one series on the prognosis of advanced cancer patients, tumor histology was unrelated to life expectancy.\[98-100\] Similar differences may apply to the study of cancer pain syndromes, but we lack studies that specifically address these issues.\[101\]

**Opioid Responsiveness**

Some of the clinical characteristics reviewed above are associated with pain intensity, as already mentioned, and also with pain response to treatment, or more specifically, opioid responsiveness. In one study, more severe pain was associated with somatic pathophysiology and presence of breakthrough pain according to multivariate analyses.\[24\] Another report found that bone pain exacerbated by motion was the most important predictor of unsuccessful management of pain at a multidisciplinary pain clinic.\[102\] Visceral pain was associated with better outcome, in terms of severity, than other syndromes.\[24,102\]

Control of neuropathic pain is more difficult, according to clinical observations.\[75\] Due to its relatively reduced responsiveness\[103\] to opioid analgesics, higher doses may be needed,\[76,104\] and wider use of adjuvant drugs is necessary to improve analgesia.\[77,105\] Mercadante developed a systematic assessment of opioid responsiveness using a score that, after slight changes, has been defined as the combination of (1) the Opioid Escalation Index (OEI), reflecting opioid requirement, and (2) pain intensity (visual analog scale) at a given OEI level (Table 10).\[106\] By using this method, several observations by the same authors suggest that opioid responsiveness, and therefore, pain management outcomes are negatively influenced by incidental pain,\[107\] bone pain with an incidental component,\[44\] perhaps neuropathic pain,\[106,108\] and diagnosis of mesothelioma.\[109\]

These observations partially recall the previous discussion of the need for refinement of the definition of neuropathic pain and of the multiple factors, including primary disease, that may influence outcome. Multivariate analysis techniques have yet to be applied to the concept of opioid responsiveness, as defined by Mercadante, to select relevant clinical aspects to be tested in prospective trials.

**Conclusions**

We have reviewed the many different constructs produced by the accurate evaluation and continuous clinical observation of cancer pain syndromes, and the attempts to develop criteria to classify cancer pain patients according to clinically relevant characteristics. The importance of making the "pain diagnosis" in clinical practice cannot be overemphasized. Fully delineating the pathophysiology of the pain leads to the selection of appropriate therapeutics. In the clinical research setting, we must also describe completely the syndromes being treated if we are to make real progress in therapeutic investigation.

Although the rich phenomenology of cancer pain is not depicted in full detail here, it is the hope of the authors that it is reflected by the philosophy of the review. We hope to engender further discussion to promote multidisciplinary interest. We believe this subject deserves more attention from oncologists and that the resulting increase in clinical knowledge will lead to improved pain management and better clinical oncologic investigation.
References:


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