Managing Pain From Advanced Cancer in the Palliative Care Setting

Betty Ferrell, PhD, FAAN, Michael H. Levy, MD, PhD, and Judith Paice, RN, PhD, FAAN

Managing complex pain at the end of life is an essential aspect of palliative care. Such care is best guided by a comprehensive evaluation of the physiologic sources of pain to determine appropriate analgesia. Using the case of Mrs. J, a woman with advanced ovarian cancer, key principles of complex pain management at the end of life are reviewed, including optimum use of opioids and co-analgesics. In addition to physical assessment, total care of the patient and family facing imminent death should be based on an assessment of psychological, social, and spiritual factors. The assessment and management of pain and suffering are guided by an interdisciplinary team focused on goals of comfort and facilitating a death that respects the life of the patient who is dying.

At a Glance
- Complex pain management at the end of life includes optimum use of opioids and co-analgesics.
- Assessment of patients and families facing imminent death should be focused on physical, psychological, social, and spiritual well-being.
- An interdisciplinary approach to pain management for patients with advanced cancer should center on the goals of comfort as well as the facilitation of dignity and respect at the end of life.

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across the country. Based on communication with the social worker, the physician’s initial orders and note included a clear directive that the goal of Mrs. J’s care was optimum comfort and peaceful death. Twenty-four hours later, Mrs. J died peacefully with her spouse, daughter, and chaplain at her bedside.

In this article regarding complicated pain in advanced cancer, suggestions for initial assessment of a pain crisis are presented, including the critical step of determining the etiology of pain. The medical evaluation of the pain etiology is combined with comprehensive nursing assessment. Comprehensive care for such patients begins with careful selection of opioid and adjuvant analgesics; guidelines for the selection of those agents are presented. Care also includes psychological, social, and spiritual well-being, and key elements of the assessment are presented with suggestions for intervention (Chochinov, Hack, McClement, Kristjanson, & Harlos, 2002; Covinsky et al., 1994; Daaleman & VandeCreek, 2000; Lo et al., 2002; Rando, 2000). An organized approach involving an interdisciplinary team can attend to a patient in a pain crisis while also caring for other dimensions of patient and family quality of life (American Academy of Hospice and Palliative Medicine, 2004; Berry & Griffie, 2001; Cassidy & Davies, 1998; Doyle, Hanks, & MacDonald, 1998; Ferrell & Coyle, 2006; Furst & Doyle, 1998; Panke & Ferrell, 1998; Taylor, 2003).

## Initial Approach to a Pain Crisis

When a patient is in a pain crisis, the most likely sources of the pain as well as prior responses to pain management interventions must be rapidly and thoroughly assessed (see Figure 1). After the assessment, an interdisciplinary care plan can be initiated to optimize comfort and function. The goal of the care plan is to find the simplest and most effective analgesic and co-analgesic treatment regimen to maximize the patient’s quality of life (see Table 1). Co-analgesic or adjuvant drugs are nonopioid medications that enhance the analgesia provided by opioids through mechanisms aimed at the source or transmission of the pain, resulting in better pain control and/or fewer side effects than treatment with opioids alone (see Figure 2 and Table 2).

In the case of patients such as Mrs. J, for whom death is imminent, priority must be given to controlling the physical pain; however, psychosocial needs cannot be neglected. Optimal comfort and function can be achieved only if psychosocial and spiritual pain are assessed and managed concomitantly with physical pain (Chochinov et al., 2002; Daaleman & VandeCreek, 2000).

## Etiology of Pain in Advanced Cancer

Even in the face of advanced, progressive cancer, multiple sources of pain can be modified by specific local and systemic therapy (Levy & Samuel, 2005; Miaskowski et al., 2005). For example, advanced cancer can invade or compress healthy tissues, causing tissue destruction, reactive inflammation, or distention of an encapsulated organ or hollow viscous. Infection resulting from advanced cancer or local procedures may be another treatable source of pain, as are complications of prior cancer treatment. Clues to somatic (musculoskeletal, soft tissue) and visceral (hollow or encapsulated organs) sources of pain come from the patient’s report of the qualities of the pain, the response of the pain to prior interventions, and the exact location and extent of the patient’s cancer. Tumors also can compress or invade nerves, causing neuropathic pain that typically follows known dermatomes and is described as burning, cold, hot, electric, or numbing. Physical examination can confirm those clues or identify other sources of pain that might be alleviated by source-modifying and/or transmission-modulating co-analgesic therapy (Doyle et al., 1998; Ferrell & Coyle, 2006; Levy & Samuel; Lussier, Huskey, & Portenoy, 2004; Miaskowski et al.) such as anti-inflammatory drugs, antidepressants, and anticonvulsants, or transmission-blocking, invasive procedures, such as a celiac

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**Figure 1. Assessment of Patients With Advanced Cancer**

**Note.** Based on information from Doyle et al., 1998; Ferrell & Coyle, 2006; Levy & Samuel, 2005; Miaskowski et al., 2005.
plexus block, cordotomy, or intrathecal infusions of opioids and local anesthetics (Doyle et al.; Kim, 2005).

Assessment of Physiologic Pain

When assessing cancer pain intensity, a standard measurement tool should be used to determine the severity of the patient’s pain and its response to current therapy, such as a 0–10 numeric or visual analog scale or the Wisconsin Brief Pain Inventory (Levy & Samuel, 2005; Miaskowski et al., 2005). Based on the results of the assessment, opioid analgesic therapy aimed at reducing central perception of the patient’s pain should be provided while searching for and treating the sources of the pain.

Source-modifying therapy may include systemic or local anticancer therapy, anti-inflammatory drugs, antibiotics, and palliative surgery. Analgesic therapy is complicated by side effects such as constipation, nausea, and sedation that may be related to cancer, opioids, or other medications. Assessment of the patient’s concurrent medical conditions and psychosocial status can guide the interdisciplinary treatment plan with specific pharmacologic therapies and psychosocial interventions for these conditions. For example, the anticholinergic effects of tricyclic antidepressants might not be safe for a patient with hypertension or cardiac arrhythmias. Alternatively, psychologic depression reported by the patient as “pain” will not respond to standard analgesic therapy.

Key elements of Mrs. J’s assessment included the multiple small bowel obstructions related to metastatic disease. Her disease had progressed through prior anticancer therapies and the articulated goal was to optimize her quality rather than quantity of life. Physical examination revealed frequent, high-pitched bowel sounds on auscultation, suggesting partial bowel obstruction. In the case of partial small bowel obstruction, the use of nasogastric tubes to decompress the upper bowel obstruction. In bowel obstruction, the use of nasogastric tubes to decompress the upper bowel obstruction.

Table 1. Four Basic Approaches to Pain Relief

<table>
<thead>
<tr>
<th>APPROACH</th>
<th>TARGET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modify the source(s) of pain(s).</td>
<td>Tumor invasion into bone or nerves, tumor distention of hollow or encapsulated organs, fractures, infections, inflammation, noncancer pain (arthritis, degenerative spine disease, etc.)</td>
</tr>
<tr>
<td>Alter the central perception of pain.</td>
<td>Pain center in brain stem, brain cortex involved in pain interpretation, brain cortex involved in psychosocial distress</td>
</tr>
<tr>
<td>Modulate transmission of pain to the central nervous system.</td>
<td>Afferent neurons, spinal synapse, ascending spinothalamic tract, descending pain-modulating tracts</td>
</tr>
<tr>
<td>Block transmission of pain to the central nervous system.</td>
<td>Nerve plexuses, dorsal root ganglion, spinal synapse of afferent neurons, ascending spinothalamic tract, descending pain-modulating tracts</td>
</tr>
</tbody>
</table>

Note. Based on information from Doyle et al., 1998; Ferrell & Coyle, 2006; Levy & Samuel, 2005; Miaskowski et al., 2005.

Figure 2. Pharmacologic Management of Pain in Advanced Cancer

Note. Based on Doyle et al., 1998; Ferrell & Coyle, 2006; Levy & Samuel, 2005; Miaskowski et al., 2005.
gastrointestinal tract can sometimes be avoided, particularly when patients find it offensive. Pharmacologic approaches, including the somatostatin analog octreotide, can reduce gastrointestinal secretions; dexamethasone can reduce inflammation, and antiemetics can afford comfort. When those approaches are applied aggressively, yet vomiting persists, decompression with a nasogastric or venting gastrostomy may be considered.

Management of Physical Pain

Opioid analgesia using single-agent opioids such as morphine, oxycodone, hydromorphone, and fentanyl is the mainstay of relieving a pain crisis in patients with advanced cancer. Optimal opioid analgesia requires that each patient be given the right drug, at the right dose, by the right route, at the right interval on an around-the-clock basis to control persistent pain (Miaskowski et al., 2005). Proportional, supplemental doses of opioids should be available for breakthrough pain (i.e., episodes of pain occurring between doses of analgesics often caused by activity or other stimulus). Immediate-release, supplemental oral opioids are offered every two to four hours at a dose that is equal to one-sixth of the total 24-hour dose of the controlled-release opioid prescribed for control of the patient’s persistent pain. Patients usually experience pain relief if their as-needed IV bolus opioids are available every 15 minutes at a dose that is 50%–100% of their continuous infusion hourly dose (Miaskowski et al.).

Side effects such as constipation, nausea, and sedation should be anticipated, prevented, and managed to optimize comfort and function (Cherny et al., 2001). Side effects often can be relieved by switching to another opioid, for example, from morphine to methadone (Levy & Samuel, 2005; Miaskowski et al., 2005). The addition of co-analgesics directed at the source of the pain or the transmission of pain, or at reducing the side effects of the opioids can improve the patient’s comfort and function (Levy & Samuel; Lussier et al., 2004; Miaskowski et al.). Finally, regional pain can be treated with regional or neuraxial invasive procedures that can sometimes reduce systemic opioid requirements, thereby improving pain control and quality of life (Kim, 2005). In the case study, if Mrs. J’s pain had not been relieved promptly with an IV opioid, the team would have wanted a pain consultation to consider other options. Aggressive consideration of all options is warranted to ensure that patients do not die in pain when first-line approaches fail to provide relief.

Treatment with only one opioid at a time generally is recommended, with a switch to an alternative agent should intractable nausea, sedation, delirium, or myoclonus develop with the initial opioid (Levy & Samuel, 2005; Miaskowski et al., 2005). When rotating opioids, equianalgesic tables should be consulted to adjust for the different potency of each opioid and for the greater bioavailability of the parenteral route of opioid administration compared with the oral route (see Table 3). Switching to methadone should be considered only by experienced clinicians supported by a skilled interdisciplinary team because of its complex equianalgesic dosing and prolonged elimination half-life (Davis & Walsh, 2001; De Conno et al., 1996; Levy & Samuel; Miaskowski et al.).

Table 2. Co-Analgesic Therapy for Common Cancer Pain Syndromes

<table>
<thead>
<tr>
<th>CANCER PAIN SYNDROME</th>
<th>CO-ANALGESIC THERAPY</th>
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</thead>
<tbody>
<tr>
<td>Bone metastases, soft tissue infiltration, arthritis, serositis, and other inflammatory pain</td>
<td>Oral nonsteroidal anti-inflammatory drugs (NSAIDs)</td>
</tr>
<tr>
<td>Postoperative pain (plus arthritis, serositis, and other inflammatory pain syndromes in patients who cannot use oral NSAIDs)</td>
<td>Parenteral or enteral NSAIDs</td>
</tr>
<tr>
<td>Acute nerve compression, visceral distention, increased intracranial pressure, soft tissue infiltration</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Acute spinal cord compression, severe increased intracranial pressure</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Neuropathic pain</td>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td>Bone pain from metastases</td>
<td>Pamidronate 90 mg IV every three to four weeks</td>
</tr>
<tr>
<td>Bowel spasm from obstruction</td>
<td>Scopolamine 0.4 mg IV or SC every four hours</td>
</tr>
</tbody>
</table>

* Starting dose of nortriptyline and desipramine should be 25 mg PO at bedtime (10 mg if frail or older) and increased by one tablet every three to seven days to target dose as tolerated. Serum drug levels should be checked at target dose or at maximum tolerated dose to assess patient adherence and prevent unexpected toxicity. Onset of pain relief should be expected at one to two weeks and mood elevation with four to six weeks of maximum tolerated or target dose.

* Serum drug levels should be followed with carbamazepine to assess compliance and prevent unexpected toxicity. The multiple drug-drug interactions noted require review of all medications before initiation.

* Possible severe bone marrow suppression requires blood counts to be followed closely.

Note. Based on information from Cherny et al., 2001; Doyle et al., 1998; Ferrell & Coyle, 2006; Levy & Samuel, 2005; Lussier et al., 2004; Miaskowski et al., 2005.
Alert and conscious patients experiencing a pain crisis, particularly in the face of nausea and vomiting, are best treated with IV opioids administered through a patient-controlled analgesia pump (Levy & Samuel, 2005; Miaskowski et al., 2005). No preset maximal dose of single-agent opioids has been recommended. The correct dose is the dose that relieves pain without causing intolerable adverse effects. Upward dose titration of opioids should be by 25%–50% for patients with moderate pain and by 50%–100% for patients with severe pain (Levy & Samuel; Miaskowski et al.). During a pain crisis, doses may be titrated upward every hour until the patient’s pain has dropped into the mild or moderate range. Subsequent dose increases can be ordered every four hours for the rest of the first day and then every 24 hours once the crisis has passed. Because of methadone’s long half-life, titration should occur much more gradually, with increases no more frequent than every 24 hours. The risk of the titration guidelines causing respiratory depression in opioid-tolerant patients such as Mrs. J is minimal.

Bone pain can be reduced by non-steroidal anti-inflammatory drugs (NSAIDs) and antosteoclast drugs (bisphosphonates and calcitonin) (Lussier et al., 2004). NSAIDs also can be used to treat acute postoperative pain and pain from other causes of inflammation. Corticosteroids are beneficial when inflammation-associated edema causes pain, such as headache from intracranial tumors; pain from acute compression of spinal cord, nerve roots, or nerve plexuses; and pain from distention of encapsulated viscosa. The latter was the case with Mrs. J and describes why that drug is useful in malignant bowel obstruction. Neuropathic pain can be relieved with tricyclic antidepressants (e.g., nortriptyline, desipramine), anticonvulsants (e.g., gabapentin, carbamazepine), antispasticity drugs (e.g., baclofen), and local anesthetics (e.g., topical lidocaine). Other agents can be important additions to the analgesic regimen. In the case study, octreotide helped reduce gastrointestinal secretions, relieving the pain, nausea, and vomiting associated with partial obstruction.

Upward titration of opioids and adding co-analgesics are sufficient for pain relief in most patients with advanced cancer (Bell, Eccleston, & Kalso, 2003; Hocking & Cousins, 2003; Jatoi, Podratz, Gill, & Hartmann, 2004; Krantz, Kutinsky, Robertson, & Mehler, 2003; Ripamonti & Mercadante, 2004). Patients in their final days and weeks of life typically require a change in drug or route of administration because of difficulties in swallowing, and these are supplemented by intermittent administration of benzodiazepines (e.g., lorazepam, diazepam, clonazepam) and/or neuroleptics (e.g., haloperidol, chlorpromazine) to control their pain, anxiety, restlessness, and delirium. Most patients do not require palliative sedation to die comfortably (Levy & Cohen, 2005; Lo & Rubenfeld, 2005). Palliative sedation via continuous infusion of midazolam, thiopental, or propofol should be viewed as essential, extraordinary care that should be administered only by palliative care experts for the relief of refractory symptoms in the imminently dying patient (Mercadante, 1995, 1998).

### Assessment of Psychosocial Issues Influencing Pain

Successful psychosocial support of the patient and family is contingent on the staff’s clear comprehension of the goals of psychosocial care. Clear communication about the goals of care among the physician, social worker, and other professionals helps create cohesive and consistent care. Involvement of a social worker, psychologist, or chaplain can help to optimize the psychosocial care required by the patient and family and often is valuable support for the nursing staff (Ferrell & Coyle, 2006).

Three essential dimensions of psychosocial assessment and treatment were relevant to Mrs. J as a patient facing imminent death: the psychological, social, and spiritual. Across those dimensions, conducting a psychosocial assessment invites the healthcare professional to closely consider the patient’s experiences using a comprehensive approach (Chochinov et al., 2002; Covinsky et al., 1994).

The psychological evaluation generally includes attention to anxiety, depression, delirium or confusion, and cognitive status. Other important factors to assess include the patient’s psychological response to the current situation. In the case study, an understanding of Mrs. J’s and her family’s coping to date, coupled with their understanding of the current situation, and an initial assessment of their grieving were vital to effective patient management. Although healthcare providers may have seen Mrs. J as a woman who was about to die, her family’s report that she had been close to death on many occasions suggested that they may have believed that she might have survived the last crisis.

Key factors of the social assessment include some knowledge of the family structure and their relationships and patterns of communication, as well as the influence that the family members may have on the patient’s experience (Panke & Ferrell, 1998). Social assessment also includes evaluating the goals of

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**Table 3. Equianalgesic Doses of Opioid Analgesics for Relief of Severe Pain in Advanced Cancer**

<table>
<thead>
<tr>
<th>ANALGESIC</th>
<th>ORAL DOSE (mg)</th>
<th>IV DOSE (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine¹</td>
<td>15</td>
<td>5.00</td>
</tr>
<tr>
<td>Oxycodone²</td>
<td>10</td>
<td>–</td>
</tr>
<tr>
<td>Hydromorphone³</td>
<td>4</td>
<td>1.50</td>
</tr>
<tr>
<td>Fentanyl⁴</td>
<td>–</td>
<td>0.05</td>
</tr>
</tbody>
</table>

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¹ Equianalgesic doses were obtained from a variety of studies and experiences. This table is meant to be a practical guide for initial dosing with the exact dose to be determined in each patient by individual titration.

² Dose interval: every four hours except for methadone (every 6–12 hours), modified-release morphine (every 8, 12, or 24 hours depending on formulation), controlled-release oxycodone (every 12 hours), and transdermal fentanyl (every 48–72 hours)

³ Rectal suppositories are available. Per rectum dose is equal to PO dose.

⁴ Transdermal fentanyl dose should be calculated as follows: mcg/hour of fentanyl every 3 days = mg of morphine PO every 12 hours.

⁵ Oral transmucosal fentanyl citrate dosage must be determined by individual titration. Fentanyl units should be applied to the buccal mucosa over a 15-minute period for breakthrough pain. Dose may be repeated in 15 minutes if needed. Unit dose should be increased if patient needs more than 8 units per day.

Note. Based on information from Doyle et al., 1998; Ferrell & Coyle, 2006; Levy & Samuel, 2005; Miaskowski et al., 2005.
care from the patient’s and family’s viewpoints. In the case study, optimum care was facilitated by understanding that for the patient and family, the goal was pain relief and a comfortable death (Berry & Griffie, 2001).

Consideration of patient and family grieving often has clinical relevance. Patients who have been chronically or seriously ill for months or years face a very different experience than others when confronted with the reality of death. Patients who remain hopeful for a cure, families waiting for a miracle, and those whose faith entails an unwavering hope for cure or long-term survival may begin grieving only when death is imminent.

**Management of Psychosocial Influences on Pain**

Planning care for Mrs. J and her family for the short duration of her stay until her death was undoubtedly a challenge. The team working concertedly to ensure comfort and spiritual care impacted the quality of care and the long-term grieving of the family (Berry & Griffie, 2001).

Given the desire for privacy and intimacy of a family during a patient’s final hours, one psychosocial professional may be designated who can call on other colleagues as needed. The concept of transdisciplinary care can be applied when a single consultant will deliver care relying on colleagues for input and support (Cassidy & Davies, 1998). In the case of Mrs. J, for example, the social worker could consult with chaplaincy and nursing colleagues to address psychosocial needs and call on the chaplain or others as indicated.

In the social dimension, Mrs. J was fortunate to have a supportive family with clear goals of saying good-bye and facilitating a peaceful death. Social support was focused on creating an environment where the family could assist Mrs. J in carrying out those goals. Mrs. J’s prolonged illness, multiple admissions, and final rapid decline may have caused her husband to require increased need for bereavement support. If palliative care is truly to be family centered, failing to direct the family to bereavement services would be a missed opportunity (Rando, 2000).

A patient’s suffering often is not relieved, despite the best physical, psychological, and social support, if spiritual aspects such as beliefs about death, faith in God or a higher power, unrecognized guilt, or unresolved life conflicts are not addressed. The spiritual care for Mrs. J and her family might include the use of a brief spiritual assessment tool (Lo et al., 2002; Taylor, 2003) to assess the importance of a patient’s spirituality (see Figure 3) and referral to the hospital chaplain or outside spiritual counselor, if desired.

Another often-missed opportunity is the use of appropriate ritual. Determining from the family what might be appropriate can create a valued memory for the family in the months and years ahead (Lo et al., 2002). For some families, that ritual may be a prayer or reading of sacred texts. After death, rituals often are important for patients and family members and should be discussed so that appropriate preparations (e.g., having members of the religious community bathe the body, perform special prayers at the bedside) can be made.

Because Mrs. J had been hospitalized on many occasions and cared for repeatedly by the same staff, the staff might be expected to be greatly affected by her death. Support for the nursing staff by the chaplain or social worker undoubtedly will impact their ability to care for future patients with compassion and competence. Psychosocial professionals do a great service in providing follow up for staff who have been most involved in the care of a dying patient.

**Figure 3. The FICA (Faith, Importance, Community, and Action) Tool**

*Note.* Based on information from Puchalski, 2002.

**Figure 4. Resources to Consult When Planning End-of-Life Care**

- American Pain Society Guidelines for Cancer Pain Management (www.ampainsoc.org): principles of pain management with an emphasis on analgesic treatments, revised in 2003
- City of Hope Pain/Palliative Care Resource Center (http://prc.coh.org): offers more than 400 resources and links related to pain and palliative care
- National Comprehensive Cancer Network Guidelines (www.nccn.org): evidence-based guidelines, including areas of pain, palliative care, and other common symptoms in cancer
- National Consensus Project for Quality Palliative Care (www.nationalconsensusproject.org): consensus guidelines published in 2004 to support the development and delivery of palliative care
planning care for patients at the end of life. The case of Mrs. J highlights challenging analgesic needs, but her care represents what is needed for the 570,000 people who die from cancer each year in the United States (Jemal et al., 2008).

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References


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