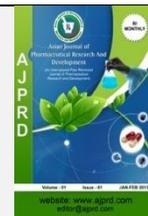


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Review Article

## Recommendations for Pain Management in Cancer Patients

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### ABSTRACT

Pain is a symptom that is reported in cancer patients with the prevalence varying from 33% to 64%. Addressing pain remains a critical aspect of cancer treatment with research showing that pain management in this population remains inadequate. Addressing pain is instrumental because of the impact it has on a patient's life. It affects clinical outcomes, contributes to poor quality of life, and leads to psychological distress. Barriers remain the key challenge that contributes to inadequate management. Addressing these barriers can lead to better outcomes. Carrying out a comprehensive patient assessment and screening is recommended before beginning pain management. Pain is multidimensional in nature and for many patients, different factors may be contributing to pain. Conducting a comprehensive assessment helps to identify these factors. Comprehensive assessment also helps to capture important information that can contribute to better pain management. After conducting an assessment, pain management should begin. Cancer pain can be managed using pharmacological and non-pharmacological interventions. The interventions should aim to improve patient comfort and function. The interventions should also provide more benefits than adverse effects. One of the mainstay interventions in managing cancer pain is opioids. Opioids should be given in accordance with recommendations from different guidelines to ensure they are effective.

**Keywords:** pain, cancer pain, assessment, pain management, barriers, opioids

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### INTRODUCTION

Pain is commonly reported in cancer patients. Pain can vary from 33% in patients on curative treatment to 59% in patients who are on anticancer treatment.<sup>1</sup> For patients in metastasis or terminal stage, the pain can be as high as 64%.<sup>1</sup> A follow-up review also showed the rates of pain to vary from 39.3% to 66.4%.<sup>2</sup> For patients receiving anti-cancer treatment and those who were at an advanced level of the disease, the pain rates were 55% and 66.4% respectively.<sup>2</sup> Different factors contribute to pain reported by cancer patients. In some patients, factors such as fear, anxiety, and depression are significant contributing factors to pain.<sup>3</sup> In other patients, increased survival accompanied by curative treatment and life-prolonging treatment contributes to persistent pain.<sup>4</sup> Among cancer survivors, factors such as peripheral neuropathy because of chemotherapy, brachial plexopathy attributed to radiation, postsurgical pain, and chronic pelvic following radiation contribute to pain.<sup>5,6</sup>

Addressing pain is vital for cancer patients. The presence of severe pain affects a patient's clinical outcome.<sup>2</sup> It also contributes to poor quality of life and psychological distress.<sup>7</sup> For most cancer patients, pain is not adequately addressed because of a number of factors. Other than poor pain control, poor communication makes it difficult to adequately address pain.<sup>7</sup> Other factors that contribute to poor pain management are poor pain monitoring, poor self-reporting of pain, and poor utilization of healthcare. Pain in cancer patients can also occur because of limited clinical advancement and research.<sup>6</sup> Addressing the barriers can significantly improve patient outcomes. The aim of this review is to identify recommendations for effective pain management in cancer patients. The review begins by identifying barriers that make it difficult to manage pain before discussing recommendations that can ensure effective pain management that leads to positive outcomes.

## Barriers that Affect Pain Management

Although pain medications and treatment have improved over the years, effective pain management is a challenge for cancer patients. The high prevalence of pain is an indicator of the challenge that effective pain management is in this group.<sup>2</sup>In most instances, cancer patients end up in emergency rooms and primary care settings because of pain.<sup>3</sup> One of the reasons why effective pain management remains a predominant challenge among cancer patients is because of the existing barriers. Several categories of barriers exist that make effective pain management a challenge. They include patient-related barriers, system-related barriers, and clinician/professional barriers.<sup>7,8,9</sup> Barriers related to racial and socioeconomic disparities can also affect pain management. Addressing these barriers remains a significant challenge despite years of advanced research and treatment.

### Patient-Related Barriers

Patient-related barriers emanate from several factors. One of these is patient beliefs.<sup>10</sup> Some of the common pain beliefs are fear of addiction, fear of tolerance, concerns over side effects, fear of injections, fear that pain is an indication of disease progression, belief that cancer pain is hard to manage, and belief that good patients do not complain about pain.<sup>8,9</sup> Fear or the belief that pain medication results in addiction are commonly reported among cancer patients.<sup>8,10</sup> Fear that pain analgesics may result in physical dependence, psychological addiction, and tolerance.<sup>9</sup> Patients who have a concern about side effects are also likely to avoid reporting pain.<sup>8</sup> Side effects such as nausea, drowsiness, constipation, and mental confusion have been reported among patients using analgesics.<sup>8</sup> For some patients, these symptoms can be intolerable and inform their decision not to seek treatment for pain management. Patient beliefs can have both direct and indirect effects on pain intensity.<sup>9</sup> Directly, negative beliefs about analgesics lead to high pain intensity even with great compliance with the medication. Indirectly, these beliefs affect pain communication and medication adherence. Patients are less likely to report or communicate pain if they believe that pain medications are likely to have negative effects. They are also less likely to adhere to medication regimens.

Pain-related barriers may also result from poor communication between the patient and the physician. Inadequate pain communication can affect pain management including medication prescription and the regimen.<sup>9</sup> Poor communication may result from the patient's hesitation and unwillingness to report pain to the physician which can result in a prescription that is not adequate to address the pain. Several patient beliefs hinder communication in cancer patients experiencing pain. They are the belief that communicating about pain may distract the doctor from treating the disease, the belief that good patients do not complain about pain, the belief that pain may be a sign of disease progression, and the belief that pain is an unavoidable consequence of cancer.<sup>11</sup> Quality of communication also matters. In some instances, patients reported that they wanted to be more active in information exchange.<sup>9</sup> The need to be open and honest was also reported

as a key factors that informed the quality of the communication.

Another patient-related barrier that can hinder effective pain management is inadequate medication adherence. Patients are likely to report poor pain control if they do not adhere to medication adherence.<sup>9</sup> Considering the fact that medication adherence is dependent on self-administration, failure to administer medication as prescribed can affect adherence and hence poor pain management. Factors such as hesitation to use medication, partial use, or non-use are reported especially in patients who hold beliefs that analgesics have negative side effects or potential to result in addiction. Poor communication has also been shown to affect medication adherence.<sup>9</sup>

Other patient-related barriers that affect pain management are financial barriers that make it difficult for patients to afford medication, cultural barriers and religious beliefs, reluctance to use pain medications or report pain, and limited self-knowledge on pharmacological and non-pharmacological pain interventions.<sup>7,8,12,13</sup> Cultural and religious beliefs may influence one's perceptions of pain and whether or not they receive medication to manage it.<sup>14</sup> Beliefs that pain is a test of faith or part of God's plan, a sign of progress towards recovery, and the belief that pain should be endured bravely are some of the existing cultural and religious barriers that impede effective pain management.<sup>15</sup> Limited self-knowledge about the available pain interventions can also impede the ability of patients to get adequate pain management. Addressing these barriers is vital to ensure optimal patient outcomes.

### System-Related Barriers

System-related and regulatory barriers are an additional set of challenges that make effective cancer pain management difficult. These barriers affect the provision of optimal care and make it difficult to access the medication needed for pain. System-related barriers may result from a number of factors. Inadequate reimbursement for pain services due to ineffective reimbursement policies for example can affect the ability of patients to manage cancer pain effectively.<sup>16,6</sup> Such barriers make it difficult for patients to get their prescriptions because they cannot afford medications. System-related barriers may also result from lack of access to pain medications, disparities in pain management, inadequate support services, and financial barriers that affect the ability of patients to access pain management resources.<sup>16</sup> Regulatory barriers such as fear and concerns of being investigated by state and federal authorities also affect the ability of patients to manage pain effectively.<sup>6</sup> In the US, requirements to promote transparency over the prescription of controlled services through the use of prescription drug monitoring programs (PDMPs) is another system barrier that can affect pain management.<sup>7</sup> The introduction of PDMPs has led to more prior authorization requirements for opioid prescription which may act as a barrier. Although some states are exempting cancer patients from such reviews and checks, others are using PDMPs which can act as a barrier to opioid prescription and pain management.<sup>17</sup> Addressing the legal and administrative constraints that hinder effective pain

management among cancer patients can lead to positive outcomes.

### *Clinician/Professional Barriers*

Clinician barriers can also affect pain management. Several clinician-related barriers that impede pain management in cancer patients have been identified in research.<sup>7,18</sup> Inadequate pain assessment and management is a commonly reported clinician-related barrier to pain management.<sup>18,19,20</sup> Inadequate pain assessment can be attributed to a number of factors. Failing to use standardized pain assessment tools, failing to take patient history, and failing to carry out a psychosocial evaluation are some of the factors that can lead to inadequate pain assessment.<sup>19,21</sup> Inadequate pain assessment can also be a result of limited clinician knowledge of the proper way to carry out pain assessment.

Clinician barriers can also result from reluctance to report pain or give a pain score.<sup>18</sup> Reluctance to report pain or give a pain score can affect the ability of clinicians to manage pain. The belief that reporting pain may interfere with treatment or that failing to report pain is being a good patient contributes greatly to this barrier.

Inadequate knowledge among clinicians is a common clinician-related barrier that affects pain management. Knowledge deficits are a common barrier reported among clinicians.<sup>20</sup> Several areas of knowledge deficits such as the pathophysiology of cancer pain, regular medication for cancer pain, adjuvant medications, addiction, and failure to understand equianalgesic dose titration of opioids have been reported among clinicians.<sup>7,21</sup> Another study by Silvonemi et al. showed that oncologists had a greater basic knowledge of cancer pain management compared to other specialists such as general practitioners, internal medicine specialists, and geriatric specialists.<sup>22</sup> However, the study generally reported low knowledge of pain management and recommended training on effective pain management. Training on pain management is one area that is lacking in medical school and residence. A survey reported that the quality of pain management training provided in residency and medical school was 3 and 5 respectively.<sup>23</sup> This explains why residents report a lack of confidence in their ability to manage pain effectively.<sup>7</sup> Addressing knowledge deficits reported by clinicians can improve pain management among cancer patients.

### *Racial/Ethnic Disparities*

Racial and ethnic disparities are also contributing barriers to effective pain management among cancer patients. Research has established that minority patients who are receiving cancer treatment are at a higher risk of being undertreated for pain because of racial and ethnic disparities.<sup>24,25,26</sup> Significant variation in access to opioids is commonly reported in this group.<sup>7</sup> Patients may also not receive appropriate pain assessment and management which can impede proper pain management. System-related barriers such as inadequate access, patient-related barriers such as patient beliefs, and clinician barriers such as poor communication can also affect access. Underestimation of pain is also commonly reported among minority patients.<sup>7</sup>

Underestimation of pain leads to negative effects such as less prescription of opioids. According to Dickason et al. African American patients are less likely to be given opioids than whites. Addressing these disparities is vital to improve outcomes for cancer patients.<sup>27</sup> The reported disparities make it difficult for cancer patients to receive the right treatment for pain which negatively affects their quality of life.

### *Assessing Pain in Cancer Patients*

Screening and carrying out a comprehensive assessment are vital in managing cancer pain. Research has shown that failure to carry out a comprehensive assessment of pain can lead to undertreatment.<sup>28</sup> Initial assessment is done to determine the intensity of pain, the pathophysiology, and the impact of pain on the ability of the patient to function.<sup>29</sup> Comprehensive assessment is also done to determine if a patient is going through any psychosocial issues because they can increase the intensity of pain.<sup>30</sup> Various guidelines recommend the need for comprehensive pain assessment before commencing pain management therapy.<sup>31,32,33</sup> The aim of carrying out an initial comprehensive pain assessment is to determine the multidimensional nature of patient pain and capture critical information pain the patient's treatment history, whether or not there are presence of comorbid conditions, and the psychosocial history including history of substance use disorder (SUD).<sup>4,31</sup>

Screening should be performed at every encounter with the patient meaning it should be ongoing and should be documented using a quantitative or semiquantitative tool.<sup>31</sup> Some of the standardized scales that are used in documenting pain are the visual analog scale (VAS), the verbal rating scale (VRS) and the numerical rating scale (NRS).<sup>34</sup> The NRS has a score of 0 to 10 with 0 representing no pain and 10 representing worse pain. The VRS has a score of 1 to 6.1 represents no pain and 6 represents severe pain.<sup>34</sup> The aim of comprehensive pain assessment is to evaluate the intensity, etiology, and pathophysiology of pain.<sup>7,28</sup> Noting down the patient's goal pain score is important in designing a development plan. It also helps in the effective and individualized management of pain.<sup>4</sup> Asking key screening questions is vital when carrying out an initial assessment. One of the key screening questions that is asked to patients is "What has been your worst pain in the last 24 hours on a scale of 0–10?"<sup>4,35</sup> 0 represents no pain and 10 represents severe pain. Paice et al. recommend using something as simple as a two-question verbal screen to screen for pain.<sup>31</sup> The two questions can be ("Have you had frequent or persistent pain since the last time you were seen?" and if the answer is yes, "How severe has this pain been, on average, during the past week?")<sup>31</sup> Such simple screening can help to identify patients that should undergo initial comprehensive pain assessment that can identify the cause of the pain and lead to development of a treatment plan.<sup>31</sup>

Assessment and reassessment of pain should also aim to identify the pain characteristics including causes, onset, type, site, duration, intensity, and quality of pain.<sup>4,36</sup> The quality of pain can be described as throbbing, aching, gnawing, sharp, cramping, stabbing, tingling, ringing, shooting, or pain felt as pressure.<sup>5</sup> Assessment should also

seek to identify whether the patient is experiencing or not experiencing radiating pain, whether the patient is experiencing relief or temporal patterns of the pain, and whether the patient is experiencing pain at rest or when moving.<sup>4</sup> Other factors that the clinician should aim to identify when assessing or reassessing pain are trigger factors of the pain, the signs and symptoms, whether the patient is using any analgesics, and whether they are effective or not. Asking questions such as when the pain started, how long it has lasted, where the pain is, and how strong is the pain can help to identify the patient's pain score and lead to the development of a pain plan.<sup>37</sup>

### Recommendations for Pain Management

After conducting a comprehensive assessment for pain, the next step is pain management. Optimal management of pain is vital to ensure the patient leads a quality life and has good outcomes. Pain management can be done using both pharmacological and non-pharmacological interventions. Whether using pharmacological or non-pharmacological interventions, pain management should be done with the aim of enhancing patient comfort and improving function.<sup>31</sup> A clinician should also ensure patient safety and limit adverse events when managing pain.<sup>31</sup> Engaging the patient and their family or caregivers is also vital throughout the process of pain assessment and management.<sup>38</sup> Fallon et al. recommend the need to inform the patient about pain and pain management and to encourage them to take an active role in pain management to improve outcomes.<sup>4</sup> Patient involvement improves pain management outcomes because it improves communication, understanding, and prescribing. Besides, involving patients and their families or caregivers is important because they are likely to be involved in pain management.

Pain intensity is a key factor when it comes to the type and dose of analgesic drugs used in managing pain.<sup>7</sup> Using the right analgesic and in the right amount is vital in ensuring the patient gets optimal pain relief and does not get adverse effects. The World Health Organization proposes using an Analgesic Ladder that comprises a stepwise approach to manage pain.<sup>39</sup> In step 1, the ladder recommends using over-the-counter analgesics such as paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) to manage pain.<sup>4,7</sup> In step 2, the ladder recommends using opioid analgesics such as codeine and tramadol to manage pain.<sup>4,7</sup> In the third step, the ladder recommends using stronger opioids such as morphine to manage pain.<sup>7</sup> These are used to manage pain that is classified as severe. Administering the right analgesics depending on the classification of pain is vital in ensuring effective pain management.

### Pharmacological Interventions

Over-the-counter analgesics such as paracetamol and NSAIDs can be used to manage mild pain.<sup>38</sup> An example of paracetamol that is recommended for managing mild cancer pain is acetaminophen.<sup>31</sup> NSAIDs can also help in managing mild pain because of their analgesic, anti-inflammatory, and antipyretic properties.<sup>7</sup> NSAIDs can be used alone or in combination with an opioid although there is no evidence to support or refute its effectiveness when used together.<sup>40</sup> The use of NSAIDs together with opioids improved analgesia

and reduced opioid consumption in patients experiencing cancer pain.<sup>41</sup>

In addition to paracetamol and NSAIDs, adjuvant analgesics can also be used in managing mild pain.<sup>31</sup> Adjuvant analgesics are medications that help to manage nociceptive pain.<sup>7</sup> Adjuvants alone or in combination with opioids can also be used to manage neuropathic pain. Examples of adjuvants are selected antidepressants such as duloxetine, venlafaxine, and amitriptyline, and anticonvulsants such as gabapentin and pregabalin.<sup>7</sup> Research has established that antidepressants are effective in managing moderate pain, more so neuropathic pain in cancer patients.<sup>42,43</sup> Anticonvulsants were also found to have similar effects on neuropathic pain.<sup>42</sup>

In managing moderate pain, "weak opioids" such as tramadol, codeine, and hydrocodone are recommended particularly for patients who have not been on opioids.<sup>38</sup> Tramadol is widely used in palliative care.<sup>4</sup> Despite its widespread use, research has shown it can have adverse effects on patients including nausea, vomiting, dizziness, and constipation.<sup>44,45</sup> Tramadol has also been shown to lead to serotonin toxicity because of the effect it has on serotonin metabolism. Although the WHO Ladder recommends the use of weak opioids in managing moderate pain, there is no sufficient data to prove its efficacy.<sup>4</sup> To increase the efficacy of weak opioids, they can be combined with non-opioid analgesics.

Strong opioids are the analgesic of choice when it comes to managing moderate to severe cancer pain.<sup>31</sup> Before initiating opioids, clinicians need to consider the patient's initial exposure to opioids.<sup>7</sup> Current medications and the patient's end-organ function can also be considered.<sup>7</sup> For instance, in opioid-naïve patients, a clinician can consider using weak opioids first before proceeding to strong opioids. However, if weak opioids are not effective, strong opioids such as oral immediate-release morphine can be initiated.<sup>7</sup> Morphine is often used as the firstline of opioids because of affordability and ease of administration. For an opioid-naïve patient, the initial dose of morphine for immediate release should comprise 5mg every 4 hours as needed.<sup>46</sup> For oxycodone, the dose should be 2.5mg to 5 mg every four hours as needed.<sup>7</sup> Prescribing the right amount of opioids for opioid-naïve patients is very important. The CDC recommends the need for clinicians to prescribe the initial dose of opioids in the right quantity and as needed for the expected duration of pain.<sup>47</sup> Scarborough et al. even note that the clinician can choose to errors based on the patient or clinical picture.<sup>7</sup> For instance, if there are concerns for potential side effects, a clinician can choose to give 2.5 mg instead of 5 mg of oral oxycodone.<sup>7</sup> What is important is to reassess the patient 24 hours after administering the initial dose to ensure it is adequate in managing pain and whether the benefits outweigh the risks.<sup>47</sup> Opioid titration is done to ensure the drugs take effect as soon as possible. Titration refers to the process where the dose of opioids is modified to increase the speed with which pain relief is achieved without adverse side effects.<sup>4</sup> Titration should begin at the minimum recommended dose before being increased to achieve desired pain relief with little to no side effects.

Paice et al. recommend the need for clinicians to assess for side effects of opioids to ensure effective pain management. Side effects can be normal and expected or adverse effects that are not expected.<sup>31</sup> Adverse effects may necessitate a change of opioid regimen. Some of the common side effects that are reported with opioid use are constipation, mild nausea, and sleepiness.<sup>7</sup> Adverse side effects that are reported from using opioids are constipation, nausea, bloating, mental clouding, respiratory depression, central nervous system, and opioid-induced hyperalgesia.<sup>4,31</sup> Assessing for SUD is also important.<sup>7</sup> SUD can affect and complicate pain management. If an assessment determines that a patient is likely to develop adverse side effects, opioid reduction should be done to reduce the adversity.

### Non-Pharmacological Interventions

Non-pharmacological interventions such as integrative therapies, psychological approaches, physical rehabilitation, and neurostimulatory therapies can also help.<sup>31</sup> Examples of integrative therapies are acupuncture, massage, mindfulness, and music. Evidence on the effectiveness of integrative therapies has been mixed with some studies showing it is effective in managing pain and others showing no significant statistical differences.<sup>48,49,50</sup> The results of mindfulness in managing pain have also been mixed.<sup>51</sup> Some studies have shown its effectiveness in managing pain while other studies have shown that it has no significant statistical significance.<sup>52</sup> Other types of integrative therapies such as music and massage have also been shown to provide relief for patients experiencing pain. Physical medicine and rehabilitation include physical therapies, occupational therapies, recreational therapies, and exercise programs.<sup>31</sup> Research showed that physical therapy was effective in improving the quality of life and physical function.<sup>53</sup> Interventional therapies include the use of nerve blocks and neuraxial infusion to manage pain.<sup>31</sup> Medical marijuana is another non-pharmacological intervention that has drawn significant attention when it comes to the management of cancer pain.<sup>7</sup> The impact of medical marijuana in managing cancer pain cannot be ascertained though because of a lack of studies to show effectiveness.

### CONCLUSION

Inadequate pain management remains a significant problem among cancer patients despite the availability of effective options to manage pain. Different factors contribute to poor pain management among cancer patients. Barriers for example are a key factor when it comes to poor pain management in cancer patients. Addressing these barriers can lead to positive outcomes when it comes to managing pain. Carrying out a comprehensive pain assessment is the first step towards effective pain management. The assessment should be ongoing to ensure patients receive adequate measures to help manage pain. Optimal pain management is vital to ensure that patients lead a quality pain-free life, have comfort, and improved function. Using pharmacological and non-pharmacological interventions in managing pain has a greater likelihood of leading to better outcomes. Whichever intervention is chosen, patient safety is relevant. The intervention chosen should provide greater benefits in terms of relieving pain and fewer adverse effects.

To increase effectiveness, it is important to involve the patient and their families or caregivers in pain management. Clinicians can use the WHO ladder to guide the pain management process with different pain medications being used depending on the intensity of pain. When it comes to using strong opioids for pain management, the physician should assess the patient for adverse side effects and SUD to ensure the patient gains benefits from the medications.

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