



Physiology in Aging

How do I best treat pain in my older patient with cancer?

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1. Introduction

Despite decades of attention, pain in patients with cancer is too often inadequately treated, especially in older adults [1,2]. Multiple evidence-based guidelines are available to assist providers in the assessment and management of cancer related pain [3,4]. For older adults, there are additional challenges to address. There are well-documented patient and provider-related barriers in the literature that contribute to under treatment of pain in this population [5]. Because older adults are heterogeneous, with changes in cognition, function and various comorbidities, the evaluation of pain can be complex, requiring additional elements of assessment. As pain severity increases so does functional impairment [6]. This becomes increasingly relevant in patients with cancer as performance status dictates treatment and outcomes. The difference between managed and unmanaged pain can then impact not only quality of life but whether a patient is a candidate for cancer-directed therapies. Additionally, the fear that analgesics will cause more harm than benefit needs to be overcome in order to optimize pain treatment in older adults.

2. Pain Assessment

The foundation of successful pain management in patients with cancer starts with screening for the presence and severity of pain. For maximum effectiveness, this must be incorporated as a routine practice [7]. Understanding the patient's pain experience and preferred language used to describe their pain can alleviate barriers and misunderstandings in assessment [8]. A validated tool such as the Brief Pain Inventory is helpful to systematically measure both the intensity of pain using a numeric rating scale (NRS) and the level of pain interference with

important life activities [9]. Self-report is preferred whenever possible and patients with mild to moderate dementia can reliably answer simple questions about the presence or absence of pain. For patients with severe dementia unable to self-report, many behavioral assessment tools are available, such as the Pain Assessment in Advanced Dementia Scale (PAINAD) and the Checklist of Nonverbal Pain Indicators (CNPI) [10]. These tools have been extensively reviewed elsewhere with no one tool emerging as superior [11]. Once screening reveals the presence of pain greater than 2 on NRS, a new location of pain or change in an existing pain, a thorough assessment must follow. Uncontrolled pain may be due to the cancer, treatments related to the cancer, or due to non-cancer related comorbidities. One study of patients presenting to an oncology clinic found that 27% had pain unrelated to cancer [12]. In older adults, chronic nonmalignant pain occurs frequently and may already be contributing to suffering and disability [13]. Adding to the complexity, patients with cancer frequently have more than one pain related to cancer or cancer treatment, with varied underlying physiologies [14].

Because cancer patients have multiple sources and types of pain and older adults have more chronic painful conditions, a thorough history, physical examination and review of imaging is essential. Each area of pain must be assessed separately to guide the appropriate management. In addition, assessment of pain in an older adult requires additional important elements of geriatric assessment. Table 1 shows the components of a comprehensive cancer pain assessment in an older adult with elements in common which a comprehensive geriatric assessment highlighted [15]. Impairments in these areas should prompt consideration for referral to a geriatric oncology specialist [16]. Several essential areas to specifically note, including sensory, cognitive, mood, and functional status evaluation can significantly impact pain experience and management. Deficits in sensory and cognitive function influence patient self-report of pain and treatment history as well as the ability to follow pain management plans. For patients who have memory deficits,

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Table 1
Overview of cancer pain assessment in an older adult.*

Domain	Assessment features
Pain Characteristics	Location, frequency, character, aggravating and alleviating factors, natural history
Pain Intensity	Now, average, worst, lowest
Pain Presence	At rest, with activity
Functional Status	Self-reported ADLs [42], IADLs [43]
Pain Interference	Physical, Psychological, Spiritual, Social, Falls , Sleep, Appetite
Pain-related Behavior Changes	Facial expressions, Vocalizations, Body movements, Changes in interpersonal interactions and routines, Social withdrawal, Mental status changes
Pain treatment history	Prior pharmacologic and non-pharmacologic treatments
Cancer History	Stage, Sites of metastasis, treatment history
Painful Comorbid Conditions	Osteoarthritis, Osteoporosis, Prior fractures, Diabetic neuropathy, Post-herpetic neuralgia, Myofascial pain syndromes
Psychological Screening	Geriatric Depression Scale [44] PHQ-2 [45], PHQ-4 [46]
Coping Style	Adaptive (i.e., distraction) vs. Maladaptive (i.e., catastrophizing)
Sensory deficits	Hearing, Vision screening
Cognitive Assessment	MMSE [47], MoCA [48], Mini-Cog [49]
Proxy Report	Family or professional caregiver, Primary nurse in a facility

ADL = Activities of Daily Living, IADL = Instrumental Activities of Daily Living, PHQ = Patient health questionnaire, MMSE = Mini Mental State Exam, MoCA = Montreal Cognitive Assessment.

* Elements unique to older adult assessment are bolded.

corroboration from a caregiver yields important information about pain history, impact on activity and mood, and effectiveness of interventions. Anxiety and depression are common in both older adults with cancer and those with chronic pain, and both conditions negatively affect both pain outcomes and quality of life [17,18].

3. Management

One of the first steps in pain management is developing an understanding of the patient's goals and making sure that these goals are realistic and attainable. Providers must understand the patient's priorities regarding pain management with measurable functional goals [19]. While minimizing pain is one goal that becomes increasingly important as patients approach the end of life, even late in the course of an illness, maintaining function is frequently a higher priority [20]. Determining these goals is important to establish a process of shared decision making and overcome common barriers to successful pain management.

Cancer directed treatment is often the most effective means of pain relief; however, pain management should not be withheld while waiting for this result. Instead, once controlled, pain levels should be monitored for improvement in the underlying cause of the pain. This is typically evidenced by decreased episodes of breakthrough pain or complete absence of pain on current medications. In this case, careful, monitored dose reduction is appropriate.

The World Health Organization (WHO) 3-step pain ladder is a well-established guide for analgesic selection based on levels of pain intensity in managing cancer pain. While the pain ladder is in some cases considered outdated, the concept of starting an opioid for moderate to severe pain and escalating potency of medication in the face of uncontrolled pain is validated in multiple studies conducted since its inception in the mid-1980s [21].

Opioid medications are recommended for the management of moderate to severe cancer-related pain and are safe for use in older adults when used with appropriate caution and monitoring [22,23]. Initial choice of opioid should be guided by the patient's previous experience of tolerability and effectiveness of specific opioid medications. Older

adults will often have had exposure to an opioid medication during a dental or surgical procedure in the past and therefore have some knowledge of their response to the medication.

The "start low and go slow" philosophy is recommended for starting opioid analgesics in older adults. This means lower doses are started to assure tolerability with frequent reassessment and adjustment to achieve adequate relief. Educating the patient about the plan is essential so that they understand that the initial dose will likely not be the final dose, and that the goal is to attain adequate control and minimize side effects of medications as much as possible. Immediate release or short acting agents are initiated first. Extended release medications should not be used for initial dose titration. The choice of starting dose of medication should be 25–50% of the usual starting dose in younger patients due to age-related changes in renal function and drug metabolism. Follow up should be timely to assess effectiveness and potential side effects [24]. For example, starting a low dose of morphine scheduled every 6 h should be followed up no later than 48 h after initiation and the dose adjusted if needed. Follow up may include phone calls, more frequent office visits, or visiting nurse services.

Older adults are at increased risk of experiencing side effects from opioids and should be carefully re-evaluated when initiating and titrating medications. Patients do not become tolerant to opioid-induced constipation, and therefore it should be emphasized that a bowel regimen should be started immediately to prevent constipation. A prophylactic bowel regimen that includes both a softener and stimulant should be prescribed to prevent constipation. Delirium can be precipitated by both opioid medications and uncontrolled pain, and requires close monitoring [25,26]. Even though a recent meta-analysis did not show an increased fall risk for older adults taking opioids, caution is still advised when initiating and escalating doses of opioids, particularly in someone with a history of falls [27].

Some cancer related pain, especially metastatic bone pain and neuropathic pain, is incompletely responsive to opioid medications. Localized pain is often best managed with a non-pharmacologic approach such as radiation or nerve block. Single fraction radiation has been proven as effective as multiple fraction regimens for palliation of painful bone metastases [28]. For multifocal pain not amenable to this approach, or in the event of contraindications to a nerve block such as coagulopathy, additional adjuvant analgesics are necessary. Among these are acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentinoids and serotonergic norepinephrine reuptake inhibitors such as duloxetine. Recent Cochrane reviews on the use of acetaminophen and NSAIDs for cancer related pain concluded that there is no high-quality evidence to recommend for or against use [29,30]. The risks associated with acetaminophen are associated with the use of excessive doses, which often occur inadvertently. Daily doses in older adults should be limited to 3 g for most patients and 2 g for those with liver disease or daily intake of more than three alcoholic drinks. NSAIDs should be used cautiously in selected patients and only short term due to the high risk of adverse events in older adults. The risk of gastrointestinal bleeding increases with age, dose and length of therapy, and often times symptoms may not precede bleeding events. NSAIDs also pose significant cardiovascular and renal risks in older adults. Clinical experience suggests use on a case by case basis. For example, the addition of short course NSAIDs to opioids for uncontrolled metastatic bone pain in a patient undergoing radiation therapy could be considered.

Corticosteroids are often added to a pain regimen as an alternative anti-inflammatory agent. While this approach may have short term benefit, evidence of benefit is weak and the optimal drug, dose and duration are not adequately defined for specific recommendations [31]. The adverse effects of steroids increase with dose and duration of use so if used the lowest effective dose and shortest course are recommended. Delirium can occur at any time during treatment but typically occurs early in the course.

Evidence for the management of cancer related neuropathic pain is limited and typically the evidence-based guidelines for management of all cause neuropathic pain are followed. Although limited, the available evidence supports benefit from gabapentin and pregabalin in combination with opioids in the treatment of cancer related neuropathic pain [32,33]. Gabapentinoids exhibit few drug interactions. They are excreted renally and dose reduction is necessary in renal insufficiency. As with other analgesics, both gabapentin and pregabalin dosing should start low and the dose increased every few days until adequate analgesia is achieved, dose limiting side effects occur, or the maximum recommended dose is achieved. The most common side effects are sedation, dizziness, and peripheral edema, which are more common in older adults.

Duloxetine may be effective for chemotherapy induced peripheral neuropathy [34]. Duloxetine is typically started at a dose of 30 mg and increased to 60 mg at 2 weeks. Improvements in painful neuropathy are noted at the 60 mg and 120 mg doses but not at lower doses. The most common side effects are dry mouth, nausea, constipation, diarrhea, fatigue, somnolence and insomnia. Risks of clinically significant hyponatremia and falls are increased in older adults. Duloxetine should be avoided in patients with liver function abnormalities and those with heavy alcohol consumption due to reports of elevated liver enzymes, hepatitis, and liver failure.

As noted above, the risks of sedation, confusion, and delirium are frequent side effects of medications in older adults and the risk increases as medications are added. While medications must be included in a differential diagnosis when these symptoms arise, a complete evaluation for underlying causes should be considered [8], including electrolyte abnormalities, infections, exacerbation of medical comorbidities, fecal impaction, urinary retention, brain metastasis, and even medication withdrawal [35].

Patients and family members often inquire about medical cannabis use for many symptoms including pain, and cannabis use is increasing in older adults [36]. One recent study specifically demonstrated safety and efficacy in older adult patients with side effects of dizziness and dry mouth [37], however concern for adverse cardiovascular effects is warranted and increasing reports of serious events even in patients with low cardiac risk should be noted [38,39]. Furthermore, evidence of benefit in cancer pain management is lacking. Randomized controlled trials of a cannabis-derived fixed ratio tetrahydrocannabinol (THC), cannabidiol (CBD) oromucosal spray failed to show benefit over placebo [40] and a recent Cochrane database review concluded that cannabinoids have not been shown effective for neuropathic pain of any cause [41]. Providers should be prepared to discuss the potential risks associated with cannabis use as they would with any other medication being recommended.

When patients have multiple different sources of pain, the approach to treatment may necessarily vary based on which type of pain is exacerbated. Pain from nonmalignant causes may be exacerbated by inactivity or cancer treatment. It is important to consider that not all pain in a patient with cancer is cancer related and not all pain in a patient with cancer should be treated with escalating opioids. Pain that would not typically be treated with an opioid should not be treated with escalating opioids just because a patient has cancer. Guidelines for the management of the individual pain syndrome should be followed. For example, a patient with acute post thoracotomy pain that is well-controlled with gabapentin and a low dose opioid who develops an exacerbation of myofascial neck pain can be effectively treated with local measures and physical therapy rather than escalation of the existing medication regimen.

Risk assessment for abuse and diversion should be performed in all patients starting opioid therapy with appropriate ongoing monitoring. While older adults treated for cancer related pain are generally low risk, patients with a personal history of drug or alcohol abuse or addiction or serious psychiatric illness may be high risk. In these cases, referral to a pain specialist should be considered. Additionally, risk of

diversion or accidental ingestion by a third party, such as a grandchild, should be evaluated and safe medication storage should be reviewed.

4. Conclusion

Cancer related pain is common but can be safely and effectively managed in older adults. Thorough assessment is paramount, with attention to presence of comorbid conditions including sensory and cognitive impairment. Non-pharmacologic approaches should be considered whenever possible and pharmacologic management should be closely monitored with use of the minimum amount of medications necessary to achieve pain control. Given the many complicating factors in this population, a low threshold should be used for consultation for both comprehensive geriatric assessment and pain management.

Author Contribution

Dr. Malec and Dr. Levine participated in the conception and design, data collection, analysis and interpretation of data, manuscript writing, and approval of final article.

Conflicts of Interest

Dr. Malec and Dr. Levine have nothing to disclose.

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