

When Management of Cancer-Related Pain Is Complicated by Coexisting Opioid Use Disorder

A Case Review

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Patients with cancer are living longer, and many experience pain secondary to tumor invasion or as a consequence of cancer-directed therapies. Opioid use disorders and associated morbidity and mortality have increased with dramatic rise during the SARS-CoV-2 pandemic. National and international stakeholders have developed clinical practice guidelines in an effort to curb opioid misuse and overdose-related death. However, to ensure that patients with cancer do not experience barriers to adequate pain management, most of these guidelines are not intended for patients with cancerrelated pain or for those receiving palliative or hospice care. Oncology, palliative, and hospice care providers are increasingly tasked with the management of severe disease-related pain in the setting of coexisting opioid use disorder without research on the most effective risk and harm reduction strategies to guide care. Clinicians should be familiar with addiction medicine and chronic pain literature and be able to incorporate some of these best practices. This case study reviews the management of severe cancer-related pain in a patient with co-occurring opioid use disorder, utilizing many of the best practices in available clinical practice guidelines for the management of chronic non-cancer-related pain.

KEY WORDS

cancer, opioid use disorder, pain, palliative, substance use disorder

ore than half of patients with cancer will experience pain during anticancer treatment, and nearly 40% continue to experience pain in survivorship.¹ Chronic pain experienced by long-term cancer survivors may be related to tumor infiltration or by disease-modifying

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therapies (eg, chemotherapy-induced peripheral neuropathy, postthoracotomy syndrome, complications of chemoradiation for head and neck malignancies). Opioid medications are some of the most important and commonly used tools that clinicians have in managing moderate to severe cancer-related pain. However, the use of opioid medications is not without risk. Emergency department visits for opioid-related events in persons with cancer have increased 2-fold since 2006, most significantly for those with substance use disorders (SUDs).²

Recent education, legislation, and prescribing guidelines have aimed to improve safe practice in the management of chronic pain.^{3,4} Pain management guidelines include recommendations for the use of opioid risk assessment tools and monitoring practices and include risk reduction strategies for patients diagnosed with, or at risk of developing, a use disorder. However, most guideline development and professional organization recommendations for best practice specifically carve out exceptions for the management of cancer-related pain and management of patients receiving palliative or hospice care.³ This leaves providers caring for patients with cancer and SUD without effective evidence-based interventions.

Social isolation, loss of work and housing, and increased rates of anxiety and depression are some of the negative consequences of the SARS-CoV-2 pandemic. These are also known risk factors for relapse of SUDs. Support systems like Alcoholics and Narcotics Anonymous were less accessible early in the pandemic. At the same time, alcohol sales increased by a quarter and an analysis of urine drug screens showed a 10% to 32% increase in positivity rates for heroin, methamphetamine, cocaine, and nonprescribed fentanyl.⁵ Not surprisingly, overdose-related deaths during the SARS-CoV-2 pandemic have reached an all-time high, with increases as high as 98% in several western states.⁶

CASE STUDY

J.W. is a 68-year-old African American woman who started experiencing right upper extremity pain in February 2020. Over the course of several months, she received fragmented medical care, presenting to multiple emergency departments

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within different medical systems with increasing pain and edema and decreased function in the right arm. She was eventually found to have a large solitary chest wall/axillary lesion, measuring 10 cm in diameter at time of diagnosis. The tumor was completely encasing her brachial plexus. After biopsy and positron emission tomography/computed tomography, she was diagnosed with a stage II diffuse large B-cell lymphoma, and she received an early referral to palliative care for complex pain management needs. At the time of referral, she exhibited intractable pain, severe lymphedema, and flaccid paralysis of her right upper extremity.

J.W.'s history was notable for a recent move into transitional housing after experiencing homelessness. She had a remote history of heroin use, treated with medication for opioid use disorder (OUD) for several years, but was off treatment at the time of consult. She did not have reliable transportation, and because of facility restrictions in place, limiting in-person medical visits during the beginning of the SARS-CoV-2 pandemic, her first several palliative care visits were completed via telemedicine. J.W. denied heroin use since establishing with the oncology clinic and receiving prescription opioids for her cancer-related pain.

Early in the treatment of her cancer, she underwent a brachial plexus neurolysis, which was unsuccessful in managing her pain. In addition, J.W.'s pain was treated with systemic nonsteroidal anti-inflammatory medications, duloxetine, gabapentin, and pregabalin. She was prescribed short- and long-acting opioids. Noting the above described risk factors, opioids were prescribed in 7-day quantities and were dispensed from a pharmacy that could supply unit dosing. Despite drastic improvement in lymphedema and moderate improvement in paralysis with initiation of chemotherapy, her pain remained poorly controlled. Her short-acting opioid use never decreased with steady escalations of her long-acting oral opioids, and she was eventually transitioned to monotherapy transdermal fentanyl. With this, she reported mild improvement in her pain. Shortly after this transition, she presented to a local emergency department with hypoxia and altered level of consciousness. She disclosed heroin use to the emergency medical providers. Her post hospital palliative care follow-up appointment was conducted in person, and she was accompanied by her community health social worker. At that visit, she disclosed daily heroin use over the preceding several weeks. She also continued to report severe, debilitating pain in the right upper extremity that made several activities of daily living tasks such as bathing, dressing, and cooking for herself difficult.

CLINICAL PRACTICE GUIDELINE DEVELOPMENT

Clinical practice guidelines developed for the treatment of chronic noncancer pain speak to the importance of opioid risk reduction but carve out exceptions for those with cancer undergoing active treatment.³ The Centers for Disease Control and Prevention (CDC) developed clinical practice guidelines for the management of chronic noncancer pain in 2016. The guidelines include recommendations on screening for risk of OUDs and risk mitigation strategies to employ. These recommendations include limits on daily dosing, the use of signed agreements, urine drug screening, medication-assisted therapy (MAT), prescription drug monitoring programs (PDMPs) monitoring, and prescribing rescue doses of naloxone.³ The CDC guidelines specifically state that they are "not intended for patients undergoing active cancer treatment, palliative care, or end-of-life care." This was reiterated in an additional statement published in 2019 after case reports of patients receiving cancer treatment being denied opioid prescriptions because of insurance company and pharmacy chain policies and restrictions based on the CDC guidelines.7-10

Cancer pain guidelines often fail to fully address how to approach care for patients who are deemed high risk for development of or have already been diagnosed with SUDs.^{4,11} Many national and international organizations, including the American Society of Clinical Oncology, World Health Organization, The European Society for Medical Oncology, and the National Comprehensive Cancer Network (NCCN), have developed clinical practice guidelines specifically addressing the treatment of cancer- and treatmentrelated pain.^{4,11-13} Most guidelines recommend starting with nonopioid therapies for mild cancer pain. However, a Cochrane review in 2017 concluded that there was not enough high-quality evidence to either confirm or deny the effectiveness of acetaminophen in managing cancer pain.¹⁴ These guidelines also recognize that although potentially beneficial, nonsteroidal anti-inflammatory drugs are frequently contraindicated owing to preexisting renal or cardiac disease, risk of gastrointestinal bleeding, anticoagulation use, and disease- or treatment-related thrombocytopenia. The European Society for Medical Oncology and World Health Organization guidelines either fail to address concerns related to use disorders, misuse, or addiction or only discuss it when considering opioid weaning, at which point the recommendation is made to consult an addiction specialist. The NCCN guidelines recognize that a history of SUD is a risk factor for undertreatment of cancer pain and provides recommendations for screening and the management of patients at risk for or with a history of use disorders.⁴ Recommendations include utilizing risk screening tools, such as the Screener for Opioid Assessment for Patients with Pain-Revised or the Opioid Risk Tool, monitoring PDMPs, maximizing nonopioid therapies, considering a written agreement, and giving referral to an interdisciplinary team including addiction medicine.⁴ The NCCN guidelines were further updated in 2021 with extensive revisions in the area of risk mitigation for patients considered



high risk for opioid therapy.⁴ There is a universal call from guideline developers for health care providers to increase their own education around assessment and risk for opioid-related complications and increased understanding of common opioid-related concerns (tolerance, dependence, addiction, etc). Unfortunately, at this time, recommendations for the use of universal precautions and risk mitigation are based on insufficient evidence and expert panel opinion only. There are currently no studies showing improved outcomes, and these guidelines may not be routinely put into practice.

OPIOID USE AND RISK IN PATIENTS WITH CANCER

Persons with a history of cancer, including those in active treatment, in remission, and those who have been cured, have higher rates of opioid use than their peers.¹⁵⁻¹⁸ Rates of opioid prescribing in this population have been reported to be as much as 1.22 times higher than that in age- and sex-matched controls.¹⁷ This higher use persists, even a decade or more after completion of cancer therapy.¹⁷ Risk factors for chronic opioid therapy include younger age, rural populations, lower socioeconomic status, mood disorders, tobacco or alcohol abuse, and chronic daily opioid use before or during cancer treatment.¹⁷⁻¹⁹ Malignancies most commonly associated with long-term opioid use include lung, head and neck, cervical, gastrointestinal, and genitourinary cancers.¹⁶

At least 1 recent study has shown that this higher use of opioids is not necessarily associated with an increase in opioid misuse and may be better explained by the higher incidence of chronic pain in this population and can be as high as 35%.²⁰ Other studies have shown that the risk of OUDs or nonmedical use of opioids (NMUO) for persons with a cancer diagnosis is as high as 20%.^{16-18,20} It is likely that there is some overlap between chronic cancerrelated pain and NMUO. In this setting, it is reasonable to consider a trial of opioid medications despite risk of abuse if the pain is severe, there are no reasonable alternatives, and risk mitigation strategies can be deployed.¹⁹ However, active OUD is associated with increased symptom burden and can lead to decreased quality of life, higher mortality rates, and increased health system utilization, including emergency department visits.²¹ Opioid overdose emergency department visits in patients with cancer have more than doubled since 2006, with most of these overdoses being with prescription opioids.² Patients with coexisting SUD, mood disorders, and chronic pain had the highest rates of increase.

MEDICAL LEGAL IMPLICATIONS

There are potential medical/legal liabilities associated with opioid prescribing. Medical providers have faced state board sanctions and loss of license. Some have been fined millions of dollars, and others are facing life sentences for inappropriate opioid prescribing.²¹ Clinical practice guidelines developed for the management of chronic pain recommend the use of screening tools and formal agreements for responsible prescribing and to mitigate risks associated with OUDs. But these guidelines specifically exclude guidance on the management of cancer-related pain. As such, completion of an opioid risk screening tool, the use of random urine drug screening, and/or written treatment agreements are not consistently used in the practice where this patient received her care. However, an opioid risk screening was informally completed during this initial palliative consultation, and the information obtained during the initial visit guided the decision to more aggressively pursue nonopioid and interventional pain management modalities. When it was determined that opioids remained an important part of the treatment regimen, a prescription for naloxone was given, there were limits placed on quantities of opioids prescribed at 1 time, and the PDMP was monitored with every prescription written. In addition, the prescriber worked collaboratively with a pharmacy that could provide medications in unit dosing as well as J.W.'s community health social worker.

Much of this patient's care was provided via telemedicine owing to restrictions in place early in the pandemic that significantly limited accessibility of in-office medical visits. At telemedicine follow-up visits on multiple occasions, the patient denied heroin use and the prescribing provider was dependent on this self-reporting. The patient eventually disclosed use to an outside provider during an emergency department visit and was open to discussing their daily use with the prescribing provider at follow-up visits. The lack of institutional policy mandating baseline urine drug screen for new opioid prescriptions and the lack of UDS accessibility during telemedicine visits led to an unfortunate situation in which the pain management resources available to the patient became more restricted with the eventual self-disclosure of use, theoretically discouraging the patient from future disclosure for fear of stigma and decreased options for pain management.

DISCUSSION OF ETHICAL DILEMMAS

Justice

All patients have the right to safe, unbiased, respectful, and individualized pain management. In 2017, Paice and Coyne⁸ presented a case study exploring the barriers that patients with cancer-related pain face in accessing appropriate opioid therapy as a consequence of limitations put in place in response to the ongoing opioid epidemic. Since the publication of this case study, the rate of opioid-related overdose deaths has almost doubled, with over 93 000 reported opioid-related deaths in 2020.⁶ Efforts to curb the opioid epidemic continue to create significant barriers in



timely access to medications and public health campaigns have been found to negatively impact patients with cancer receiving opioid therapy owing to fear of stigma associated with use.^{22,23} And pain control for patients facing advanced cancer may actually be worsening. A recent study found a significant increase in emergency department visits for uncontrolled pain over the same timeframe that opioid prescriptions for patients with advanced cancer substantially decreased.²⁴

Before the diagnosis of cancer as the etiology of J.W.'s severe pain, she received fragmented care and small quantity opioid prescriptions from multiple emergency departments. She was navigating the health care environment with nearly every risk factor identified for disparities in access to adequate pain management (elderly, racial minority, poverty and history of OUD).

Nonmaleficence

The principle of nonmaleficence directs health care providers to avoid needless injury or harm to the patient. Care of the cancer patient with coexisting malignant pain and use disorders is incredibly challenging. Providing treatment directed toward pain relief using opioid therapy can increase the risk of harm by exacerbating the disease of use disorder and associated complications. Alternatively, avoiding or severely limiting opioids when managing cancer pain in patients with use disorders when pain is not adequately controlled by nonopioid therapies is likely to have a significant negative impact on quality of life and well-being and could lead to use of opioids being obtained and used illegally. In addition, poorly controlled cancer pain correlates with decreased survival.^{25,26} There are times when OUD is so severe that even with multiple safeguards in place, it is deemed too dangerous to treat cancer pain with opioid medications.²⁷ Ideally, oncologists and their patients would have access to experts such as addiction medicine, pain and palliative care specialists, as well as mental health providers with additional training in the complexities of addiction to safely navigate this tight rope. However, access to addiction medicine specialist is poor nationwide, significantly more so in rural communities.²⁸ Hospice and palliative nurses involved in the care of these complex cases should advocate for pain management modalities that do not come with an unacceptable risk of contributing to patient harm.

DISCUSSION

Although transdermal fentanyl seemed to have some activity in effectively reducing the pain experience for this patient, referencing the ethical principal of nonmaleficence, the risk of continued prescribing with active heroin use was too great. Not only was there a significant risk of self-harm in terms of unintentional overdose, but there is

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also a risk of community harm if the patient was diverting prescribed medications to obtain heroin for injection. This patient welcomed the engagement of her community health social worker, who, while opioids were being prescribed, took responsibility for picking up her prescriptions and assisted with monitoring between office visits. In addition, the palliative oncology social worker was closely involved and attended many of the office visits in conjunction with the palliative advanced practice registered nurse (APRN). The patient verbalized a desire to stop using heroin and welcomed a referral to a pain psychologist who had experience working with patients who had comorbid OUDs. She was also referred to a buprenorphine harm reduction clinic that worked collaboratively with the palliative APRN; providing a microinduction approach as the transdermal fentanyl dose was gradually reduced. This approach reduced the risk of increase in pain or withdrawal symptoms with a transition to buprenorphine.

SPECIAL CONSIDERATIONS IN THE SETTING OF TERMINAL ILLNESS

J.W. was receiving curative intent treatment for a good prognosis, stage II, diffuse large B-cell lymphoma, which requires a different approach from that which could be considered for a patient with terminal cancer. The number of opioid prescriptions written to persons with advanced cancer has decreased in recent years. At the same time, there has been an increase in advanced cancer-related pain visits to the emergency department, suggesting that efforts to address the opioid epidemic are having a significant negative impact on pain management at the end of life.²⁶ The American Society for Pain Management Nursing and the Hospice and Palliative Nurses Association published a position statement in 2018 focused on the management of pain at the end of life.²⁹ Most people identify a pain-free status as an important factor in what is considered a "good death." Unrelieved pain in the last days to months of life is both physically and psychologically harmful and it is recommend that hospice and palliative providers work closely with addiction medicine specialists to provide safe and appropriate pain management at the end of life when there is a risk of substance misuse. In this setting, a goal of avoiding opioids is not always practical or feasible. A harm reduction approach to the care of persons with SUDs includes a focus on reducing the negative impacts of the harmful behavior without a focus on abstinence.³⁰ Using a harm reduction approach in the setting of a terminal illness, health care clinicians provide ongoing medical care and counseling on how to reduce negative outcomes of the illness or SUD.^{31,32} Han³³ recently proposed a model of using a geriatric medicine approach in combination with harm reduction to better care for aging patients with complex comorbid medical conditions occurring simultaneously



with SUDs. Oncology and palliative care clinicians may choose to pursue a harm reduction approach when caring for patients with painful terminal illness and active SUDs using a similar approach of focusing on individual counseling, supporting patient-specific goals, and risk reduction without a primary focus on fixing or curing the underlying problem, to help a person feel as well as they can for as long as they are alive, within the context of their illness.

NURSING IMPLICATIONS

Management of cancer pain while trying to avoid relapse of OUD is complex and requires a thoughtful multidisciplinary approach. Guidelines and interventions intended to reduce misuse, abuse, and aberrant behavior with chronic opioid dosing continue to carve out exceptions for oncology, despite NMUO medications being more prevalent in persons with cancer than previously understood.^{18,34,35} There remains a dearth of literature on how best to support these patients, but this is slowly changing. Arthur and colleagues³⁶ recently published on a multidisciplinary intervention targeting advanced cancer patients exhibiting aberrant behavior and showed that their multidisciplinary "chat" with the patient, combined with shortening intervals between refills, reducing quantity per prescription, and utilizing more nonopioid therapies, led to a significant decrease in aberrant behaviors.

Close collaboration between the oncology and palliative care teams, mental health providers, and addiction medicine can help provide an umbrella of support for patients, leading to a more holistic approach to the management of a psychologically and physically complex illness with the ultimate goal of providing effective pain management while reducing opioid-related morbidity and mortality. It is important that oncology and palliative nurses approach patients with SUDs in an open, accepting, and nonjudgmental fashion. Nurses, regardless of setting, can advocate for institutional policy changes that focus on assessing and identifying risk and active SUDs. Nurses can advocate for creating destigmatized health care settings for this vulnerable patient population.

Pain management guidelines recommend engaging with addiction medicine specialists and considering MAT when appropriate, but this care is inaccessible to many owing to a lack of available prescribers or insurance coverage. The passage of the 2016 Comprehensive Addiction and Recovery Act and the 2018 Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment act giving advance practice providers the opportunity to prescribe buprenorphine for SUDs has significantly increased access to this resource. In June 2016, nurse practitioners, physician assistants, clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwifes became eligible to obtain X-waivers. By May 2019, there were more than

11 000 advanced practice providers with waivers.37 Recently, additional work has been done to continue to increase access to MAT therapy. Advanced practice registered nurses and physician assistants can now obtain an X-waiver to treat up to 30 patients at a time without needing to complete the previously required 24 hours of continuing education.³⁸ Palliative care APRNs are ideal providers to seek X-waivers to further increase accessibility for buprenorphine MAT therapy. In addition, palliative nurses should encourage counseling support and frequently reassess openness for treatment of SUDs. Prescribers can shorten interval time between follow-ups and referring for evidencebased nonpharmacologic pain treatment when appropriate and available while also maximizing nonopioid therapies. When an opioid is prescribed, it should always come with a coprescription for naloxone, and only after review of the PDMP.

CONCLUSION

Patients with a history of SUDs and those who are dealing with active or relapsed OUDs experience a multitude of barriers to equitable access to cancer care and associated supportive care. Caring for a patient at risk of or experiencing relapsed OUDs while also dealing with pain related to an early cancer diagnosis is complex and fraught with ethical dilemmas and should be provided in a multidisciplinary fashion whenever feasible. The incidence and risk of OUD in patients with cancer are higher than previously understood, but pain management guidelines and recommendations continue to carve out exceptions for patients with a cancer diagnosis and those receiving palliative or hospice care. Failing to address or reduce the risk of OUDs increases the risk of an accidental overdose, which is antithetical to life-prolonging and curative anticancer therapies. Treating patients with active OUD, utilizing many of the tools provided in the management of chronic noncancer pain, providing MAT, or working collaboratively with addiction medicine and psychosocial support services as appropriate could reduce the incidence of opioid-related morbidity and mortality while still safely managing cancer and cancer-related pain. More research is needed to determine which of these interventions are the most successful in improving outcomes in this vulnerable patient population.

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Pament: The registration fee for this test is \$21.95. DISCLOSURE STATEMENT

The authors and planners have disclosed that they have no financial relationships related to this article.