

## PAIN MANAGEMENT IN HOSPITALIZED CANCER PATIENTS: SYSTEMATIC REVIEW

<sup>1</sup>\*Calista Giovani, <sup>2</sup>Theodora Monica Carissa, <sup>3</sup>Claudia Priska Adelin

<sup>1</sup>\*General Practitioner, Samarinda Medika Citra General Hospital, Samarinda, Indonesia

<sup>2</sup>General Practitioner, Wava Husada General Hospital, Kepanjen, Malang Regency, Indonesia

<sup>3</sup>General Practitioner, Rumah Sehat UGM Primary Clinic, Special Region of Yogyakarta, Indonesia

### Correspondence Author:

[calista.giovani110@gmail.com](mailto:calista.giovani110@gmail.com)

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### ABSTRACT

**Introduction:** Cancer pain affects a significant percentage of patients globally, impacting their quality of life. Despite available guidelines, undertreatment remains a concern, with barriers to effective pain management, highlighting the need for a systematic review. This review aims to assess current practices, identify barriers, evaluate intervention effectiveness, explore patient experiences, and investigate adherence to guidelines, providing comprehensive insights for optimizing pain management in hospitalized cancer patients.

**Methods:** The researchers in this study followed the 2020 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines to ensure that their work met the required standards. This was done to ensure the precision and reliability of the conclusions derived from the research.

**Result** Our search produced 16 results. After looking at the titles and summaries, we found several papers that fit our criteria. At first, we excluded few articles because they were written in review and case report style. But after reading the full papers carefully, we included five papers in our final analysis. These papers included cross-sectional, retrospective chart review study, retrospective analysis of pancreatic cancer patients receiving CPN for pain, a multicenter, prospective, longitudinal study of inpatients with cancer pain who received SPC, and blinded, randomized, sham-controlled pilot cross-over trial.

**Conclusion:** Our systematic review on pain management in hospitalized cancer patients highlights the correlation between pain documentation adequacy, opioid prescriptions, and the need for targeted palliative care education. Additionally, insights from interventions such as CT-guided CPN, SPC, and TENS underscore their potential benefits, calling for further exploration within the systematic review's overarching aim of understanding effective pain management strategies for hospitalized cancer patients.

## INTRODUCTION

Pain is a widespread and devastating symptom that impacts millions of cancer patients globally. On average, 30-50% of patients undergoing active cancer therapy and 75-90% with advanced disease experience chronic pain, requiring pain management. Pain, with its sensory and emotional aspects, significantly affects the quality of life for cancer patients in terms of physical, behavioral, and social well-being. However, among cancer patients displaying pain symptoms, almost 30-50% endure moderate-to-severe pain. While manageable, this pain can negatively impact the patients' quality of life.<sup>1,2</sup>

Inefficient treatment of cancer pain is a frequently reported issue, despite the availability of effective therapies and pain management guidelines. The application of pain management guidelines in clinical practice remains problematic. A review assessing compliance with the Joint Commission standards for pain management in cancer patients revealed that pain intensity and reassessment were documented in 53% and 44% of cases, respectively. Additionally, inappropriate pain assessment delays pain relief. According to the World Health Organization (WHO), the objective of cancer pain management is to alleviate pain to a level that enables an acceptable quality of life. Inadequate pain relief may result from barriers such as improper identification, assessment, or documentation of the pain intensity. The WHO recommends initiating treatment with a combination of mild analgesics (paracetamol and/or non-steroidal anti-inflammatory drugs [NSAIDs]) and opioids for the initial management of moderate-to-severe pain. Patients should not rely solely on mild analgesics if experiencing this level of pain.<sup>3</sup>

The Brief Pain Inventory (BPI) is a commonly used tool for pain assessment, considering factors such as pain location, intensity, treatment, and its impact on daily activities. The scale ranges from 0 to 10, where 0 indicates no pain and 10 signifies the worst imaginable pain. Despite available guidelines and education on the assessment and management of cancer-related pain, underestimated or undertreated pain remains a significant global public health concern for patients with solid and hematological malignancies. Furthermore, effective and personalized treatment begins with the accurate self-reporting assessment of pain. Inadequate pain assessment hinders optimal treatment for cancer patients.<sup>4,3</sup>

Conducting a systematic review on pain management in hospitalized cancer patients serves multiple purposes. First and foremost, it aims to assess the current practices employed in the management of pain among this specific patient population. By systematically evaluating various approaches and interventions, the review seeks to provide a comprehensive understanding of the existing landscape, encompassing both pharmacological and non-pharmacological methods, as well as the incorporation of guidelines and protocols within hospital settings.

One crucial aspect of the systematic review is the identification and analysis of barriers hindering the effective implementation of pain management strategies. This involves exploring challenges related to healthcare policies, healthcare provider practices, patient-related factors, and systemic issues within hospitals. Understanding these barriers is essential for developing targeted interventions that address specific challenges and improve overall pain management outcomes for cancer patients during hospitalization.

Another key objective of the systematic review is to evaluate the effectiveness of different pain management interventions. This involves assessing outcomes associated with various treatments and identifying any gaps or inconsistencies in the existing evidence. By synthesizing this information, the review aims to provide insights into which interventions are most successful in achieving optimal pain relief and enhancing the overall quality of life for hospitalized cancer patients. Patient experience is also a focal point of the review, as it seeks to understand the perspectives and preferences of cancer patients regarding pain management during hospitalization. This includes exploring patient satisfaction levels and identifying areas for improvement in the delivery of care. Acknowledging the subjective experiences of patients is crucial for tailoring interventions to meet individual needs and preferences.

Furthermore, the systematic review aims to investigate the adherence of hospitals and healthcare professionals to established pain management guidelines and protocols. By assessing the extent of compliance, the review can identify factors influencing adherence and suggest areas where modifications or improvements may be necessary to enhance the overall quality of care.

## METHODS

### Protocol

The researchers in this study followed the 2020 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines to ensure that their work met the required standards. This was done to ensure the precision and reliability of the conclusions derived from the research.

### Criteria for Eligibility

This study considered articles that met specific criteria. Eligible articles were required to be English-language research papers focusing on pain management in hospitalized cancer patients and published after 2019 within the designated timeframe for this systematic review. Excluded from the evaluation process were articles falling under categories such as editorials, lacking a DOI, previously published review articles, or duplicating content from prior journal publications.

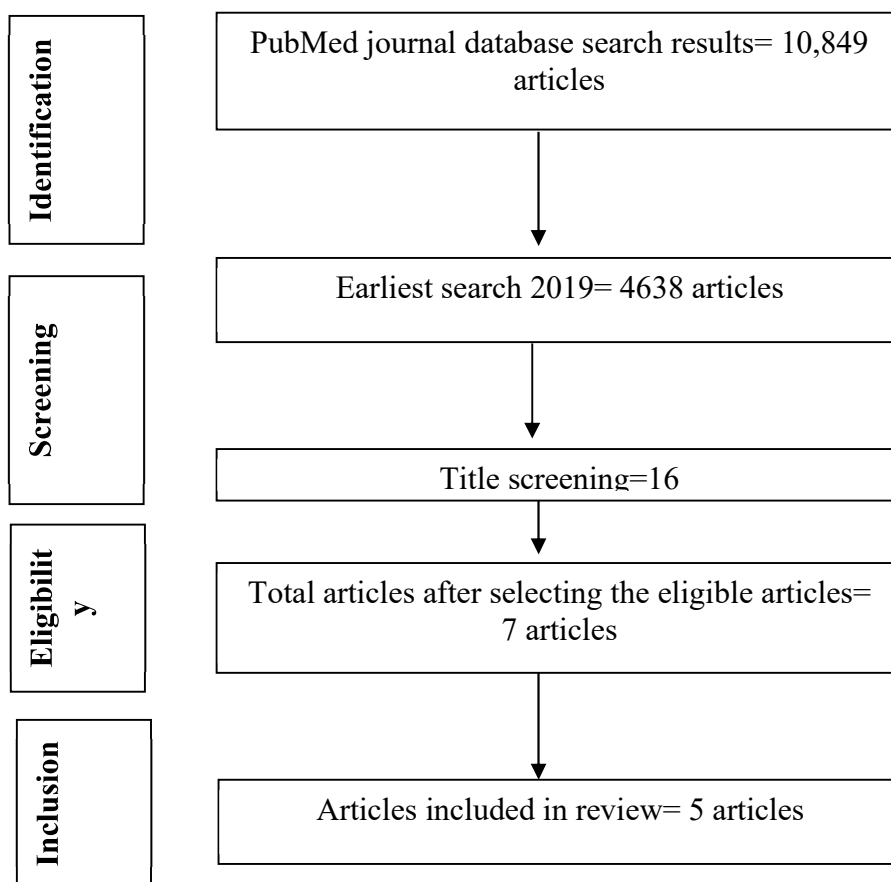
**Search Strategy**

We conducted a comprehensive literature search using PubMed journal database, focusing on studies published from 2019 to 2024. The search terms employed were as follows ("cancer pain"[MeSH Terms] OR ("cancer"[All Fields] AND "pain"[All Fields]) OR "cancer pain"[All Fields]) AND ("manage"[All Fields] OR "managed"[All Fields] OR "managements"[All Fields] OR "managements"[All Fields] OR "manager"[All Fields] OR "manager s"[All Fields] OR "managers"[All Fields] OR "manages"[All Fields] OR "managing"[All Fields] OR "managment"[All Fields] OR "organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "management"[All Fields] OR "disease management"[MeSH Terms] OR ("disease"[All Fields] AND "management"[All Fields]) OR "disease management"[All Fields]) AND ("inpatient s"[All Fields] OR "inpatients"[MeSH Terms] OR "inpatients"[All Fields] OR "inpatient"[All Fields]).

**Inclusion and exclusion criteria**

The studies included had specific criteria: (1) they needed to be original research related to pain management in hospitalized cancer patient; (2) they could be Randomized Controlled Trials (RCTs) or observational studies (cohort or case-control studies); (3) relevant data had to be accessible. On the other hand, certain studies were excluded if they: (1) were ongoing or lacked available data; (2) were duplicates, in which case the most recent article was selected; (3) were not in English.

**Figure 1. Article search flowchart**



**Data Retrieval**

The authors conducted a thorough examination of relevant studies, specifically selecting those that met precise inclusion criteria. They focused on original, unpublished papers in English to ensure a refined and high-quality selection. The analysis covered essential information, such as study particulars, authors, publication dates, locations, and research methodologies, aligning with the study's objectives.

Author	Origin	Method	Sample Size	Result
ALMouaa lamy et al., 2021. <sup>6</sup>	SAU	Cross-sectional, retrospective chart review study.	451 patients (selected through computerized random sampling).	The pain was assessed using the Brief Pain Inventory in almost all patients (n = 450, 99.8%). The pain was categorized as mild in 386 (85.6%) patients, moderate in 46 (10.2%) patients, and severe in 19 (4.2%) patients. Opioid prescriptions were significantly higher among patients with moderate (76.1%) and severe pain (89.5%) compared to those with mild pain (39.1%; p < 0.0001).
Lu et al., 2023. <sup>7</sup>	China	Retrospective analysis of pancreatic cancer patients receiving CPN for pain.	63 patients with pancreatic cancer underwent CPN between June 2018 and June 2021	Both groups were comparable in demographic characteristics and baseline pain conditions measured using the numeric rating scale (5.77 ± 1.23 vs. 6.27 ± 1.21; p = 0.141). The pain scores were significantly reduced in both groups; early CPN resulted in significantly lower scores from 3 to 5 months. The opioid consumption gradually decreased to a minimum at 2 weeks but increased at 1 month (35.56 ± 30.14 mg and 50.48 ± 47.90 mg, respectively); significantly larger consumption from 2 to 4 months was seen in the delayed group. The total pain interference was lower than baseline in all patients, with significant improvement after early CPN in sleep, appetite, enjoyment of life, and mood. The average survival time of the two groups was comparable.
Tagami et al., 2024. <sup>8</sup>	Japan	Multicenter, prospective, longitudinal study of inpatients with cancer pain who received SPC.	Of 396 screened cancer patients, 67 were enrolled at least twice during the study period.	Cancer pain management based on the PROs was achieved in 87.9% (385/438) of all cases. In 94.5% (364/385) of these cases, cancer pain management was achieved within 1 week, and the median time to pain management was 3 days (95% confidence interval [CI], 2-3). The mean worst pain intensity in the last 24 h at the start and end of observation were 6.9 ± 2.2 and 4.0 ± 2.3, respectively, with a difference of -2.9 (95% CI, -3.2 to -2.6; p < 0.01). Overall, 81.6% of the patients reported satisfaction with cancer pain management, and 62 adverse events occurred.
Siemens et al., 2020. <sup>9</sup>	USA	A blinded, randomized, sham-controlled pilot cross-over trial.	201 patients were admitted, 124 were excluded and 77 charts were abstracted.	Of 632 patients screened, 25 were randomized (sequence IMT-PBT = 13 and PBT-IMT = 12). Finally, 11 patients in IMT-PBT and 9 in PBT-IMT completed the study (N = 20). The primary outcome did not differ between groups (IMT minus PBT: -0.2, 95% confidence interval -0.9 to 0.6). However, responder rates were higher in IMT (17/20 [85%] vs. 10/20 [50%], p = 0.0428). Two patients experienced an uncomfortable feeling caused by the current, one after IMT and one after PBT. Seven patients (35%) desired a TENS prescription. Women and patients with incident pain were most likely to benefit from TENS.
Tonev et al., 2022. <sup>10</sup>	Bulgaria.	Retrospective study.	total of 70 patients were admitted, 41 were excluded, and 29 charts were abstracted	A higher ASA score is the only determinant positively influencing opioid consumption (= 0.018) and pain flare as well (OR = 15.00; 95% CI: 2, 24-100, 48; = 0.005). Lower dose 4 mg dexamethasone was revealed as a moderate analgesic agent in steroid naïve patients with no side effects, whereas in steroid non-naïve patients the predominantly higher dose 8 mg dexamethasone had minimal impact on pain flares prevention at the expense of more pronounced immunosuppression (= 0.039).

**RESULT**

Our search produced 16 results. After looking at the titles and summaries, we found several papers that fit our criteria. At first, we excluded few articles because they were written in review and case report style. But after reading the full

papers carefully, we included five papers in our final analysis. These papers included cross-sectional, retrospective chart review study, retrospective analysis of pancreatic cancer patients receiving CPN for pain, a multicenter, prospective, longitudinal study of inpatients with cancer pain who received SPC, and blinded, randomized, sham-controlled pilot cross-over trial.

A cross-sectional, retrospective study conducted by Al-Mouaalamy et al. was aimed to investigate physicians' adherence to WHO guidelines in the assessment and management of pain among oncology patients based on available pain scores in the Pain and Palliative Care Nursing Order Set (PNOC) at the King Abdulaziz Medical City in Jeddah (KAMC-JD). KAMC-JD is a tertiary hospital located in the Makkah region of the Kingdom of Saudi Arabia, featuring 558 functional beds. The PNOC within KAMC-JD serves as a tertiary cancer center, comprising an 88-bed adult general oncology inpatient unit, a 22-bed bone marrow transplant unit, and a 32-bed pediatric hematology and oncology unit.<sup>6</sup>

The study, approved by the King Abdullah International Medical Research Center ethics review board (SP21J/216/05), was conducted from January 1, 2020, to December 31, 2020. Informed consent was waived due to the study design. The inclusion criteria covered all adult cancer patients admitted to the PNOC during the study period, excluding those not meeting the criteria or requesting privacy. Out of 2,133 eligible patients, a sample size of 451 was determined through computer-generated random sampling, utilizing Raosoft software with a confidence level of 95% and an error margin of 5%.<sup>6</sup>

Data were extracted from the BESTCare Health Information System (HIS), focusing on variables such as pain assessment scoring, opioids prescribed (including drug name and dosage per day), and demographic details (age, gender, area of residence, code status, co-morbidities, admitting diagnosis, admitting specialty, admission date and time, length of stay, and previous opioid usage with drug name and dosage per day). The study design and methodology were aligned with ethical considerations, ensuring a comprehensive evaluation of pain management practices among the included cancer patients at KAMC-JD.<sup>6</sup>

In a retrospective cohort analysis, Lu et al examined the medical records of patients with advanced pancreatic cancer who underwent celiac plexus neurolysis (CPN) for moderate to severe pain at a specialized oncology hospital from June 2018 to June 2021. The study, regulated by the Institutional Review Board, included 56 patients (39 males, 17 females) after excluding those with specific pain control solutions. Patient demographics revealed a majority with pancreatic body and tail cancer, stage IV conditions, and malnutrition. All patients received prior oncology treatment, with varying time gaps between the first visit and CPN.<sup>7</sup>

Both groups reported moderate to severe baseline pain (NRS  $5.77 \pm 1.23$  and  $6.27 \pm 1.21$ ), showing a significant reduction post-CPN. Early CPN demonstrated consistently lower pain scores, with significant differences from 3 to 5 months. Breakthrough pain decreased significantly after CPN, with no notable between-group differences in frequency. Analgesic consumption, initially comparable, saw a minimum at 2 weeks post-CPN followed by an increase at 1 month. Delayed CPN group exhibited greater opioid consumption from 2 to 4 months, starting earlier than the early CPN group. Adverse reactions were similar between groups, with dizziness, hypotension, and diarrhea being the most frequent. One patient in the delayed group experienced transient hemochezia.<sup>7</sup>

Post-CPN, overall pain interference significantly decreased, especially in the early group. Mood-related interference, sleep, and appetite improvement were notably better in the early group. However, no significant differences were observed in activity-related interference. Survival rates showed an average time of 11.18 months for the early CPN group and 8.75 months for the delayed group, with no significant difference. The study provides insights into CPN outcomes, suggesting potential benefits in pain management, mood improvement, and interference reduction in daily activities for patients with advanced pancreatic cancer.<sup>7</sup>

A prospective multicenter observational study in Japan spanned from November 1, 2020, to June 30, 2021, involving five inpatient specialized palliative care (SPC) consultation teams and four palliative care units in tertiary care hospitals. The study focused on cancer patients expressing a need for comprehensive pain management (CPM) and admitted to oncology or palliative care units. Of the initially screened 396 patients, 355 were included in the analysis, with a median age of 62.9 years. The most common primary cancer site was the lung (22.3%), and 20.7% had comorbidities, including 38 with diabetes mellitus.<sup>8</sup>

The study evaluated 438 cases of cancer pain, revealing mixed pain as the most common type (33.8%) and bone tumor or metastasis as the predominant pathophysiological mechanism (83 cases). Regular opioids were used in 77.9% of cases, with oxycodone being the most frequently used. CPM was achieved in 87.9% of cases, with a median duration of 3 days. The worst and average pain intensity significantly improved, as did pain interference with general activities and sleep. Opioid usage increased between the beginning and end of observation, while the number of daily rescue medications decreased. Patient Global Impression of Change (PGIC) indicated improvement in 84.5% of cases.<sup>8</sup>

Regular opioids, NSAIDs, acetaminophen, and analgesic adjuvants were used in 93.6%, 48.4%, 44.1%, and 34.7% of cases, respectively, with a significant increase in the median morphine equivalent daily dose (MEDD). Adverse events,



primarily caused by opioids, occurred in 62 cases, with somnolence and delirium being the most common. In subgroup analysis, achievement rates for 33%, 50%, and 100% pain reduction and Patient Perception of Goal Achievement (PPG) scores were assessed. Predictive factors for CPM achievement within 3 days included higher daily dose of regular opioids and average pain intensity within the last 24 hours.<sup>8</sup>

This was a blinded, randomized, sham-controlled pilot crossover trial (DRKS00007990; ClinicalTrials.gov Identifier NCT02655289) conducted at the University Medical Center Freiburg, Germany, involving patients from the inpatient specialist palliative care ward and acute pain service. The primary objective was to assess the efficacy and safety of Transcutaneous Electrical Nerve Stimulation (TENS) in addition to standard care for advanced cancer pain patients. A secondary goal was the exploratory identification of subgroups benefiting from TENS.<sup>9</sup>

Recruitment occurred between February 2016 and February 2018, with 632 patients screened, and 25 eligible patients randomized. The study completion rate was 20 out of 26 recruited patients. The dropout analysis revealed that 23.1% of dropouts tended to have a higher Eastern Cooperative Oncology Group (ECOG) level and higher average pain levels before receiving Perceptual-Decision Training (PBT). Baseline characteristics were well-balanced, with slight differences between sequences in cancer entity, ECOG, and DN4. Duration of TENS use and TENS-related adverse events were recorded. The results showed no statistically significant differences in change scores between the two sequences, and the sensitivity analysis of post-treatment scores was consistent.<sup>9</sup>

Exploratory subgroup analysis indicated that 85% of patients experienced at least a "slight improvement" during the TENS application in the IMT phase compared to 50% in the PBT phase. Changes within groups showed a decrease in average pain, worst pain, least pain, mood, walking ability, and relations during IMT. Safety analysis revealed minimal TENS-related adverse events, and 35% of patients requested a prescription for the TENS device after testing both modes.<sup>9</sup>

This retrospective examination included 29 American Society of Anesthesiologists (ASA) III-IV patients aged 18 or older, treated with single-fraction 8 Gy/1 or multi-fraction 20 Gy/5 radiotherapy for painful uncomplicated or complicated bone metastases. Inclusion criteria involved patients with pathologically proven primary solid malignancy, indications for radiotherapy, corticosteroid coanalgesic administration, pain intensity  $\geq 2$  on a numeric rating scale (NRS), and complete medical records. Exclusion criteria included incomplete radiotherapy, contraindications to steroids, painless bone metastases, and inadequate medical records.<sup>10</sup>

All patients received parenteral dexamethasone, along with background and breakthrough pain medication. Data on demographics, Eastern Cooperative Oncology Group (ECOG) and ASA scores, comorbidities, primary cancer site, radiated bone lesions, complete blood count (CBC), and side effects were collected. Pain severity (NRS) and analgesic consumption data were recorded at admission, daily during hospital stay, and for 10 days post-radiotherapy.<sup>10</sup>

Within a year, 70 patients were admitted, 41 were excluded, and 29 charts were analyzed. No significant between-group differences were observed in demographics, ECOG, ASA, comorbidities, malignancy, radiotherapy, or analgesic consumption. A tendency for more primary breast cancer in the corticosteroid-naïve group and more primary cancers from other sites in the corticosteroid non-naïve group was noted. No significant differences were found between groups in preventing radiation-induced pain flare and nausea/vomiting, despite higher dexamethasone doses in the corticosteroid non-naïve group. Pain flares occurred in 34% of patients, with 28% in the steroid-naïve group and 40% in the steroid non-naïve group. Dexamethasone side effects, particularly associated with hyperglycemia and immunosuppression, were observed only in the steroid non-naïve group. Immunosuppression, measured by WBC elevation, was more pronounced with 8 mg dexamethasone compared to 4 mg. A higher ASA score positively influenced opioid consumption and pain flares.<sup>10</sup>

## DISCUSSION

The discussion presents an insightful analysis of cancer pain management, focusing on pain assessment, analgesic prescriptions, and adherence to guidelines. Clinician-related barriers, including inadequate knowledge and malpractice, underscore the importance of evaluating current practices. The study reveals pain intensity as a significant predictor of opioid prescription, aligning with the three-step ladder of cancer pain management advocated by the WHO. Non-opioid analgesics, such as acetaminophen and NSAIDs, are more likely to be prescribed for patients with moderate to severe pain, in accordance with guidelines.<sup>6</sup>

High rates of pain assessment compliance (99.8%) demonstrate adherence to cancer pain management guidelines. While reassessment after opioid administration data was unavailable, the study suggests effective pain reassessment practices. Physicians appear to adhere to WHO guidelines in prescribing opioids, but the study identifies potential gaps in optimal opioid selection and dosages. Further investigation and tailored palliative care educational programs may be warranted.<sup>6</sup>

The use of acetaminophen as the most common non-opioid analgesic aligns with guidelines, but the study questions its efficacy in patients already on potent opioids. The choice of analgesics is recommended to be individualized, considering pain assessment, type, and site of pain. The study employed the Brief Pain Inventory (BPI) for pain assessment, a widely-

used tool with validated reliability. However, the retrospective nature of data collection, limitations in assessing drug patterns by cancer grade, and the absence of opioid use patterns by patients are acknowledged.<sup>6</sup>

This study highlights the benefits of early celiac plexus neurolysis (CPN) in preventing pain progression, reducing opioid consumption, and enhancing overall quality of life (QoL) for patients with pancreatic cancer, a malignancy known for its significant pain burden and challenging palliative care. Chemical neurolysis, often utilizing alcohol or phenol under imaging guidance, offers substantial pain relief, especially for patients with limited life expectancy, with evidence suggesting superior outcomes compared to general analgesia.<sup>7</sup>

The study underscores the significance of early CPN decision-making, with retroperitoneal tumor invasion emerging as a crucial factor influencing pain relief effectiveness. Despite the potential benefits, our findings reveal a considerable time gap between the initial visit and CPN implementation, emphasizing the need for timely interventions to optimize outcomes. While both early and delayed CPN groups demonstrated decreased opioid consumption compared to baseline, the early group exhibited significantly reduced numeric rating scale (NRS) scores and fewer breakthrough pain incidents from 3 to 5 months postoperatively. This suggests a more favorable prognosis with early CPN, emphasizing the importance of optimal timing for administering neurolytic solutions into the preaortic space.<sup>7</sup>

Opioids remain a mainstay in cancer pain control, and our study aligns with the broader analgesic strategy, demonstrating ongoing adjustments post-CPN. The delayed group required earlier and higher opioid dose adjustments, consistent with pain progression. Timely neurolysis has been shown to reduce the need for opioids until the end of life, aligning with our results that suggest a potential break in the opioid consumption spiral when CPN is administered early. The study's QoL analysis indicates a greater improvement in overall pain interference for patients receiving early CPN, particularly in sleep, appetite, and mood-related aspects. However, early CPN did not show a significant improvement in work and walking. Integrating early supportive care in advanced cancer patients is associated with improved mood, QoL, and longer survival, supported by our findings.<sup>7</sup>

In the novel multicenter study, Tagami et al investigated the time required to achieve Comprehensive Pain Management (CPM) goals through Supportive and Palliative Care (SPC) in an inpatient setting, utilizing Patient-Reported Outcomes (PROs) and quantitative measures. Our study is the first to systematically explore the clinicodemographic predictors of refractory cancer pain and associated treatment durations by inpatient SPC consultation teams and palliative care units.<sup>8</sup>

Results demonstrated that daily SPC support significantly improved cancer pain within a short timeframe, with the median time to achieve CPM equal to or exceeding that reported in previous studies. The study considered patients with or without adequate standard CPM, revealing that opioid-naïve users and those with lower initial Morphine Equivalent Daily Dose (MEDD) often required a longer duration to achieve CPM. Despite a relatively low median MEDD, our comprehensive approach aimed to address various medication levels in managing cancer pain. Patients with factors such as neuropathic pain, incident pain, higher initial pain intensity, a history of addictive behavior, psychological distress, and younger age required a longer time to achieve stable pain control. Notably, higher regular opioid doses and background pain intensity contributed to CPM failure. Daily inpatient SPC support was associated with higher CPM achievement rates based on PROs, indicating potential benefits in both satisfaction and quantitative measurements.<sup>8</sup>

In comparing the effects of Interferential Therapy (IMT) and Placebo TENS (PBT) on average pain intensity, no significant differences were observed, but IMT showed higher responder rates based on a 7-point Verbal Rating Scale (VRS). While both interventions were safe, the study did not detect statistically significant group differences, aligning with previous randomized controlled trials (RCTs) on TENS in cancer patients. Notably, IMT had more responders than PBT on the VRS, suggesting the potential responsiveness of a 7-point VRS for pain relief over an 11-point Numeric Rating Scale (NRS) in assessing short-term TENS interventions.<sup>9</sup>

Within the IMT group, notable changes were observed in worst pain, mood, walking ability, and relations, suggesting potential clinical relevance. PBT demonstrated changes only in average pain and worst pain, with a clinically relevant decrease in worst pain. Comparable changes within groups were reported in other RCTs, emphasizing the importance of assessing diverse outcome measures to capture the impact on physical function and psycho-social outcomes. Concerning safety, IMT was well accepted, and its safety profile was comparable to another RCT. Dropouts in the study were associated with higher Eastern Cooperative Oncology Group (ECOG) levels and pain levels before PBT. The burden of using TENS, particularly the disturbance caused by device cables, was a usability problem leading to study discontinuation after the second period.<sup>9</sup>

Subgroup Analyses:

1. Gender: Women were more likely to report improvement from TENS, highlighting potential gender differences in treatment response. This finding aligns with emerging discussions on sex differences in pain perception, although primarily based on animal models.
2. Incident Pain: Patients with incident cancer pain were more likely to benefit from TENS, addressing a condition identified for improvement in cancer pain management. The study provides novel insights into the effectiveness of TENS in addressing incident pain, an aspect not extensively explored in previous TENS trials in palliative care.

The study design and washout phase were deemed appropriate, following methodological recommendations and considering potential biases. This RCT contributes valuable data on the feasibility, efficacy, and safety of TENS in advanced cancer patients in a palliative care setting, addressing a significant gap in the existing evidence base.<sup>9</sup>

Managing painful bone cancer metastatic lesions poses significant challenges due to the complex nature of pain generation involving inflammation and constant remodeling activities at the bony site. The tumor's growth may lead to additional pain sources, such as neuropathic pain due to spinal cord or nerve root compression. Opioids are the primary treatment, complemented by bisphosphonates, radiation therapy (RT), and monoclonal antibodies to alleviate pain. While bisphosphonates may cause hypocalcemia, requiring supplementation, RT effectively reduces local inflammation and shrinks tumors.<sup>19</sup>

In the study by Dimitar et al, bisphosphonate use and patients' baseline calcium levels did not differ between groups, minimizing interference with pain assessment. RT, particularly a single 8 Gy fraction, was employed, demonstrating efficacy comparable to multiple-fraction courses. Corticosteroids like dexamethasone, administered prophylactically, controlled pain by reducing peritumoral inflammation and edema. However, this study's corticosteroid usage did not show a significant impact on pain between groups. Notably, corticosteroid-naïve patients had a pain flare rate of 28%, aligning with previous findings for uncomplicated bone metastases. Higher-dose prophylactic dexamethasone (8 mg) showed more pronounced immunosuppression, potentially reflecting a heightened inflammatory response in complicated bone metastases. The study suggests that 4 mg dexamethasone prophylaxis could be a relevant alternative in immunotherapy patients.<sup>19</sup>

Non-opioid analgesics like NSAIDs and paracetamol were used consistently but did not reveal an opioid-sparing effect due to even distribution between groups. However, in all-patient comparison, these analgesics showed an opioid-sparing effect in ASA III patients compared to ASA IV patients, emphasizing the importance of ASA classification in predicting survival and treatment outcomes. Opioid use was associated with increased hazards of death, reinforcing the need for an individualized approach considering symptom burden, comorbidities, performance status, and quality of life. The study introduces the ASA classification as a valuable prognostic factor, aiding in decision-making for the management of painful bone metastases within a multidisciplinary framework.<sup>19</sup>

## CONCLUSION

In the context of our systematic review on pain management in hospitalized cancer patients, our findings highlight the adequacy of pain documentation practices at KAMC-JD, emphasizing the correlation between moderate to severe pain and increased opioid prescriptions. These results underscore the importance of targeted educational programs in palliative care to guide prescribing practices. Future prospective studies within the scope of our review should delve into analgesic prescription patterns based on cancer type, economic factors, and temporal changes in dosing. Regarding the application of CT-guided CPN for advanced pancreatic cancer, our study contributes valuable insights to the systematic review. The early implementation of CT-guided CPN demonstrated benefits in pain management, reduced opioid consumption, and improved quality of life. However, these advantages were not associated with enhanced survival. To provide comprehensive evidence on the optimal procedural timing, larger randomized-controlled trials should be considered in the systematic review.

The findings related to SPC and TENS underscore the potential of these interventions in achieving favorable outcomes in cancer pain management. SPC demonstrated positive results in achieving CPM with fewer adverse events, emphasizing its comprehensive approach. TENS, while safe, showed no significant difference between IMT and PBT in analgesic effects, calling for further exploration in the systematic review, especially in terms of gender and incident pain aspects. Our real-world data on dexamethasone's efficacy in preventing RT-induced pain flares in a diverse case mix of bone metastases adds a critical perspective. The findings highlight the need for larger studies to determine optimal doses, particularly in high-risk patients, providing valuable insights for the systematic review's overarching aim in understanding pain management strategies for hospitalized cancer patients.

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