Original Scientific Paper

CHARACTERISTICS OF CANCER PAIN AND CAUSES OF INADEQUATE ANALGESIA IN PATIENTS RECEIVING PALLIATIVE CARE

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ABSTRACT

Background: Cancer pain is a frequent and complex symptom that often remains inadequately treated. This study aimed to determine the prevalence of different types of cancer pain and to identify factors contributing to insufficient analgesic management.

Methods: A retrospective analysis was conducted on 394 patients evaluated at the Pain Therapy Outpatient Clinic of the Center for Palliative Care and Pain Therapy, University Clinical Center Tuzla, Bosnia and Herzegovina. Pain intensity was assessed using the Numeric Rating Scale, while pain type was determined using the LANSS scale. Statistical analysis was performed using MedCalc (version 9.4.2.0), with significance set at $\alpha = 0.05$.

Results: Nociceptive pain was predominant (298 patients), followed by mixed neuropathic–nociceptive pain (64 patients). 16 patients had combined nociceptive–bone pain, 14 had pure neuropathic pain, and 2 had neuropathic–bone pain. Moderate pain was reported by 192 patients, severe pain by 148 patients, and mild pain by 54 patients. cancer pain was most common among women with gynecological cancers, followed by breast, liver, and pancreatic cancers. Before referral, the most frequently used analgesics were weak opioids (260 cases), non-opioids (108), and NSAIDs (21), while strong opioids were used in only four cases.

Conclusion: The findings indicate a high prevalence of moderate to severe cancer-related pain and substantial underuse of strong opioids, suggesting the need for improved pain assessment and optimized analgesic strategies.

Keywords: *Palliative care, cancer, pain, opioids, insufficient management.*

INTRODUCTION

Cancer-related pain is one of the most prevalent and burdensome symptoms in advanced malignancy, affecting 75–90% of patients (1). Despite evidence that up to 95% of cancer pain can be effectively controlled, 40–50% of patients continue to experience moderate to severe pain, and 25–30% report very severe or unbearable pain (2). More than half of patients entering inpatient palliative care present with moderate to severe pain, and although 71% achieve pain relief by discharge, those with bone and cartilage cancers experience the least improvement (3). Data from the Swedish Palliative Care Register, covering 315,000 patients from 2011 to 2022, show that pain during the last week of life occurs in 81% of cancer patients, with severe pain documented in 35% (4).

Cancer pain is multifactorial and may be categorized by pathophysiological mechanisms into nociceptive and neuropathic pain, which differ in both clinical presentation and underlying biology (5,6). Approximately 70% of cases are tumor-related nociceptive pain, arising from visceral or somatic structures (7). Visceral pain commonly results from tumor invasion of hollow organs, ischemia, or adverse effects of cancer therapy (8). Neuropathic pain originates from structural damage to the somatosensory pathways caused either by tumor infiltration or by oncologic treatments such as surgery, chemotherapy, or radiotherapy (9,10). Clinically, it manifests as burning sensations, electric-shock-like pain, stabbing, or numbness (11).

The prevalence of cancer pain is approximately 33% overall but significantly higher in specific cancer types, including head and

neck (67–91%), prostate (56–94%), uterus (30–90%), urogenital tract (58–90%), breast (40–89%), and pancreas (72–85%) (12). Bone metastases occur in 60–84% of patients with advanced cancer and are associated with severe, difficult-to-control pain, contributing to poor quality of life and inadequate pain relief in nearly half of affected individuals (13,14).

Optimal pain management requires timely integration of palliative care into treatment (15). Accurate assessment of the type and intensity of pain is essential, using appropriate scales, which directly influences the choice of analgesic therapy. Inadequacy of these procedures could be a crucial factor in poor treatment with a decrease in the patient's functional capacity and an increase in anxiety and depression. Underdosing of analgesics and poor assessment of pain intensity as a result of a lack of education on the part of the physician, combined with irregular intake of recommended doses by the patient, increase the patient's suffering caused by pain. (16). Continuous evaluation of pain and individualized analgesic therapy are necessary for adequate therapy, which can be achieved in more than 75% of patients with rational use of analgesics and adjuvant drugs (17). Approximately 10% require interventional pain-management techniques (18). Opioid rotation is often necessary to improve analgesic effect due to individual variability in opioid response (19), influenced partly by demographic factors and largely by genetic polymorphisms of μ-opioid receptors (20).

METHODS

This retrospective study included patients with confirmed malignant disease who were evaluated for cancer-related pain at the Pain Therapy Outpatient Clinic of the Center for Palliative Care and Pain Therapy (CPNJiTB), University Clinical Center Tuzla, Bosnia and Herzegovina. Over a one-year period, 448 patients were screened. Exclusion criteria were: (1) age under 18 years, (2) uncontrolled vomiting preventing the intake of oral analgesics, and (3) non-cancer-related pain. After excluding 54 patients, a total of 394 patients were included in the final sample.

Pain intensity was assessed using the Numeric Rating Scale (NRS, 0–10). Scores of 1–3 were categorized as mild pain, 4–6 as moderate pain, and 7–10 as severe or unbearable pain. The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and signs (LANSS) was used to classify pain mechanisms (21). Data were collected on sex, primary tumor site, presence of metastases, and analgesic therapy prescribed prior to the first specialist assessment, typically initiated within primary care. The intensity of pain is assessed using the NRS (Numeric Rating Scale), at the first examination of the patient, when the previous pain therapy was evaluated, and if necessary, the dose or type of analgesic was corrected. In the following days, the pain was re-evaluated daily (by phone contact with the patient or caregiver) and the adequacy of analgesia was assessed, using the NRS scale. This resulted in the causes of inadequate analgesia listed in Table 3.

Statistical data processing was performed using the biomedical application software MedCalc for Windows version 14.8.1. The numerical data were presented using measures of central tendency and dispersion. Statistical analysis was performed using descriptive methods, calculating the mean and standard deviation, and using the t-test and chi-square (χ^2) test. Statistical analysis was performed with a confidence interval of 95%, and a p-value of < 0.05 was considered significant.

ETHICAL CONSIDERATIONS

The study was conducted anonymously and in accordance with international ethical standards and the principles of the Declaration of Helsinki. No personally identifiable information was collected. Ethical approval was granted by the Ethics Committee of the University Clinical Center Tuzla (Decision No. 02-09/2-23/20).

RESULTS

A total of 394 patients completed the study, of whom 204 (51.78%) were male and 190 (48.22%) female. The largest proportion of participants suffered from primary lung tumors (n = 110; 27.9%), followed by tumors of the liver and pancreas (n = 66; 16.7%) and esophagus, stomach, and intestines (n = 46; 11.7%). Additional tumor localizations included breast tumors (n = 39; 9.9%), urological tumors (n = 38; 9.6%), gynecological tumors (n = 36; 9.1%), ENT tumors (n = 19; 4.8%), and a category classified as other tumors (n = 40; 10.2%), which included hematologic malignancies, brain tumors, bone/cartilage tumors, and tumors of unknown primary origin.

To illustrate the distribution of tumor types among all participants, a bar chart was generated (Figure 1).

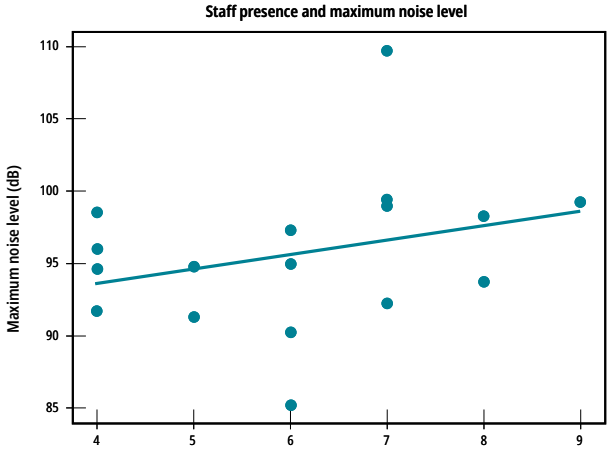

Figure 1. Distribution of tumor types

PAIN FREQUENCY AND CHARACTERISTICS IN RELATION TO SEX

Among 190 female participants, nociceptive pain was recorded in 136 patients (71.58%), which was statistically significantly higher ($p < 0.0001$; Chi-square = 117.93) compared to 30 patients (15.79%) who experienced mixed neuropathic–nociceptive pain, 14 (7.37%) with combined nociceptive–bone pain, 8 (4.21%) with pure neuropathic pain, and 2 patients (1.05%) with combined neuropathic–bone pain.

Combined nociceptive–bone pain was most frequently observed in female patients with lung tumors (n = 6) and breast tumors (n = 4). Mixed nociceptive–neuropathic pain occurred in 14 patients with breast cancer, 6 patients in the "other tumors" category, and in 4 patients each with ENT tumors and gynecological tumors.

Table 1. Pain Intensity by Gender.

Pain intensity (NRS)	Men n (%)	Women n (%)	p value	Total n (%)
Mild (1–3)	28 (13.73%)	26 (13.68%)	0.847	54 (13.70%)
Moderate (4–6)	101 (49.51%)	91 (47.89%)	0.359	192 (48.73%)
Severe (7–10)	75 (36.76%)	73 (38.42%)	0.909	148 (37.56%)
Total	**204**	**190**	—	

Table 2 summarizes the distribution of analgesic use prior to the first pain-clinic assessment, stratified by sex. In both men and women, weak opioids were the most commonly prescribed analgesics, while non-opioid medications were used less frequently. Strong opioids were prescribed only in a very small proportion of cases and exclusively among male patients. No statistically significant sex differences were observed in the overall pattern of analgesic use.

Table 2. Analgesics Used Prior to Pain Clinic Assessment by Gender.

Analgesic Class	Men n (%)	Women n (%)	p value	Total n (%)
Non opioids (Metamizole / NSAIDs)	68 (33.33%)	61 (32.11%)	0.92	129 (32.74%)
Weak opioids	132 (64.22%)	129 (67.89%)	0.43	261 (65.99%)
Strong opioids	4 (1.96%)	0 (0%)	—	4 (1.02%)
Total	**204 (51.78%)**	**190 (48.22%)**	—	

Among female patients, the most common cause of inadequate analgesia was under-dosing of the prescribed analgesic, recorded in 33.68% of cases. Irregular intake of the recommended dose accounted for 21.58%, while a combination of under-dosing and irregular use was identified in 19.47% of cases. Inaccurate assessment of pain intensity—where the actual pain experienced was stronger than the evaluated level—was responsible for inadequate analgesia in 25.26% of women.

Among male patients, under-dosing was also the leading cause of inadequate analgesia (34.80%). This was significantly more frequent than irregular intake (23.04%) ($p = 0.01$; $\chi^2 = 6.3$). A combined pattern of under-dosing and irregular use occurred in 25.98% of men, while inadequate assessment of pain intensity accounted for 16.18% of cases.

Together, these findings indicate that insufficient dosing of prescribed analgesics—most often initiated in primary care—is the predominant factor contributing to inadequate pain control in both sexes (Table 3).

Table 3. Causes of Inadequate Analgesia.

Cause of Inadequate Analgesia	Men n (%)	Women n (%)	p value	Total n (%)
Under dosing of analgesics	71 (34.80%)	64 (33.68%)	0.89 (χ^2 = 0.016)	135 (34.26%)
Irregular medication intake	47 (23.04%)	41 (21.58%)	0.82 (χ^2 = 0.051)	89 (22.59%)
Under dosing + irregular intake	53 (25.98%)	37 (19.47%)	0.15 (χ^2 = 2.01)	90 (22.84%)
Incorrect pain assessment	33 (16.18%)	48 (25.26%)	0.035 (χ^2 = 4.42)	81 (20.56%)
Total	**204 (51.78%)**	**190 (48.22%)**	—	

Under-dosing of prescribed analgesics was the most frequent cause of inadequate analgesia (34.26% overall), significantly more common than irregular intake or inaccurate pain assessment ($p = 0.0004$; $\chi^2 = 12.62$). Although slightly more prevalent in men, no statistically significant sex differences were observed. Incorrect assessment of pain intensity was the only category showing a significant difference between sexes ($p = 0.035$).

DISCUSSION

The findings of this study confirm that cancer-related pain remains a highly prevalent and clinically significant problem among patients with advanced malignancies. When compared with international data, the prevalence, type, and intensity of pain in our cohort largely align with previously published

literature, although notable differences were observed in opioid prescribing patterns and the causes of inadequate analgesia.

A study conducted in Spain (22) on 860 patients reported that 306 patients reported some type of pain, implying a prevalence of 35.6%. 50.1% were men. The most commonly treated tumor types were breast cancer (33%), followed by urogynecological tumors (24.6%), lung cancer (16.1%), head and neck cancer (9.3%), digestive system cancer (8.5%). The proportion of pain was similar between genders, but the proportion of non-cancer-related pain was higher among women ($p < 0.05$). Regarding analgesic treatment, only 60/306 patients (19.6%) received strong opioids. The study by Karri et al. states that pain can also occur as a side effect of oncological treatment (eg radiation) suggesting that the actual prevalence of pain may be slightly higher due to radiation-related pain, but could be balanced by patients who feel relief, especially those with bone metastases with radiotherapy (23).

In our study, moderate pain was registered in a total of 192 patients, statistically significantly more ($p = 0.002$) than patients with severe pain or patients with mild pain ($p < 0.0001$). There is no statistically significant difference in pain intensity depending on gender. Most cases (35 or 17.16%) with pain intensity from 7 to 10 were registered in patients with lung cancer, followed by patients with liver/pancreas cancer (18 or 8.82%), and 10 patients (4.9%) with tumors of the urogenital tract. In a study in India (Gupta et al.), moderate to severe pain was registered in 62.7% of patients, chronic pain in 26.98% and neuropathic pain in 13.49%. Pain intensity is highest in hematological tumors (77.78%), ENT tumors (64.29%) and genitourinary tract (60%). Neuropathic pain is most common in patients with breast tumors (41.67%), and (20%) in patients with genitourinary tumors (24).

In the study conducted by Jamora et al. observed a high prevalence (62.8%) of pain in 94 oncology patients, with the majority of patients experiencing mild pain (67.8%) with a low impact of pain (67.8%) on daily personal life, while the study by Mañas et al. conducted more than fifteen years ago, reveals a high prevalence (31%) of neuropathic pain among cancer pain patients visiting oncology units (25, 26). In a study by Niv et al., the prevalence of nocioceptive pain was the highest in patients with breast cancer (41.67%), which is often complicated by metastatic invasion of bone or nerve structures and can be very painful, because an activated osteoclast causes bone lysis, damaging peripheral nerves, which leads to neuropathic pain (27).

In our study, weak opioids were the most commonly prescribed analgesics before the first visit to our pain clinic (in 260 patients or 65.99%), which is significantly higher ($p < 0.0001$) statistically than the use of non-opioid drugs (129 patients or 32.74%). Strong opioids were prescribed only in 4 male patients (1.02%). There is no statistically significant difference in the use of analgesic types depending on gender.

Gomez et al., following WHO recommendations on pain intensity in oncology patients reported a mean pain score of 5.6, suggesting that patients had moderate pain intensity, while those with breakthrough pain, with a mean score of 7.3, had severe pain, which seems to be in agreement with other patient cohorts (28). Some authors have argued that the correlation between pain prevalence and primary tumor location is at best inconclusive, while others have reported that the highest frequency of pain occurs in patients with lung, head and neck, hematological, and gastrointestinal tumors (29,30). In the study by Vadalouka et al., neuropathic pain is often multifactorial in etiology with direct tumor infiltration, nerve/plexus compression; chemotherapy/radiotherapy-induced neuropathic pain, surgically induced scars or nerve damage as some of the most common causes (31).

In our study, underdosing of analgesics, prescribed by family medicine doctor, is the most common cause of inadequate analgesia, which is significantly higher ($p = 0.0004$) statistically than irregular use of analgesics or poor assessment of pain intensity ($p < 0.0001$). Observed by gender, there is no statistically significant difference in the causes of inadequate analgesia.

Despite numerous guidelines and protocols, only about 20% of patients with any type of pain received the third step of analgesic treatment, significantly lower than recommended (32,33). This could be due to a certain reluctance of Spanish doctors to prescribe these drugs, which are considered the first choice for intense pain, especially of oncological origin. In this sense, it might be interesting to know if the patients with the most pain are those who receive higher doses of opioids, but this information is beyond the scope of this study (21).

CONCLUSIONS

The complexity of cancer pain treatment is caused by multifactorial causes, and a combination of nociceptive, neuropathic and mixed pain. Bone metastases further complicate the adequacy of analgesic therapy. Combining analgesics, re-evaluation of pain and effectiveness of therapy are essential for better analgesia.

Given that moderate pain, intensity 4-6 according to NRS, was the most common, analgesics from the group of weak opiates were dominantly used, while strong opiates are used much less often, which is certainly one of the reasons for inadequate analgesia in a large number of patients. This is related to the need for additional education of doctors for better assessment of the intensity and type of pain and more frequent evaluation and correction of analgesic therapy. At the same time, the patient and caregivers, in the interest of better pain coverage, should regularly take the recommended therapy and communicate more often with health professionals.

ETHICS STATEMENT

The study was conducted anonymously and following international ethical standards. In addition, the study strictly adhered to the principles of the Declaration of Helsinki. Participants were fully informed about the purpose, procedures, potential risks, and benefits of the study before agreeing to participate. The anonymity of the participants was maintained by not collecting any personally identifiable information. Decision of the Ethics Committee of the Public Health Institution University Clinical Center Tuzla, number 02-09/2-23/20, dated 21.05.2020.

AUTHORS CONTRIBUTION

Authors declared that all contributed equally. All authors approved the submitted version.

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CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

GENERATIVE AI STATEMENT

The authors used a generative AI tool to assist with language editing, formatting, and journal-specific manuscript preparation. All AI-assisted output was critically reviewed, revised, and verified by the authors, who take full responsibility for the final content. No AI tools were used for data collection, analysis, or interpretation.

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