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ORIGINAL ARTICLE

Association of Neuropathic Pain with Anxiety Severity in Cancer Patients: A Cross-Sectional Analytic Study

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Abstract

Background: Pain and anxiety are highly prevalent interrelated symptoms in cancer patients; however, the relationship between specific pain mechanisms and anxiety severity remains insufficiently characterized. This study aimed to examine the association between mechanism-based pain classification and anxiety levels in cancer patients.

Methods: A cross-sectional study was conducted among 103 cancer patients attending a tertiary pain clinic. Pain mechanisms were classified using the PainDETECT Questionnaire (PDQ) into nociceptive, unclear/mixed, or neuropathic categories. Anxiety severity was assessed using the Generalized Anxiety Disorder-7 (GAD-7) scale. Associations were analyzed using correlation tests, the Kruskal–Wallis test, and Fisher's exact test, with $p<0.05$ considered statistically significant.

Results: Neuropathic pain was the predominant mechanism (57.3%). Anxiety severity differed significantly across pain types (p=0.004), with patients experiencing neuropathic pain demonstrating higher mean GAD-7 scores (12.98) compared with unclear/mixed (11.82) and nociceptive pain (11.50) (p=0.009). Moderate-to-severe anxiety was present in 98.3% of patients with neuropathic pain. Younger age was weakly but significantly correlated with higher anxiety levels (r=–0.224; p=0.024).

Discussion: The findings suggest that neuropathic pain contributes to a heavier psychological burden than other pain types. Younger age was also identified as a vulnerability factor for anxiety, potentially due to greater psychosocial impact in this age group.

Conclusion: Pain mechanisms are significant predictors of anxiety in cancer patients, with neuropathic pain associated with greater psychological vulnerability. Younger patients also exhibit higher anxiety levels. These findings emphasize the clinical necessity of integrating psychological screening with mechanism-based pain assessment.

Keywords: Anxiety; cancer; neuropathic pain; pain mechanisms; questionnaire

Introduction

Pain is the most common and feared symptom experienced by cancer patients, characterized by complex mechanisms that include inflammatory and neuropathic components.[1–4] The prevalence of pain increases significantly with disease progression, affecting approximately 64% of patients with advanced cancer and reaching up to 70% in those with head and neck malignancies.[5–6] While the administration of analgesics based on the WHO

ladder remains the mainstay of management, basic science research reveals that cancer pain involves a complex system of peripheral and central sensitization that is often not fully understood.[1–4,7]

Routine clinical assessment typically utilizes the Numeric Rating Scale (NRS) to measure pain intensity due to its ease of use and high compliance.[1,8–10] However, intensity scores alone fail to capture the underlying pain mechanisms, which may differentially impact psychological well-being. Anxiety is a substantial and persistent burden in oncology settings, particularly among palliative care patients and women with breast cancer, where it often exceeds rates observed in the general population.[2,11–15] Although the Generalized Anxiety Disorder-7 (GAD-7) scale is validated for identifying psychological distress in cancer patients,[16,17] the specific relationship between distinct pain mechanisms assessed via mechanism-based tools like the PainDETECT Questionnaire (PDQ) and anxiety severity remains an area requiring further elucidation.

In Indonesia, cancer-related pain remains a significant clinical challenge, particularly in tertiary referral centers where patients often present with advanced-stage disease. Sociocultural factors, including strong family involvement in caregiving, varying health literacy levels, and reliance on national health insurance, may influence both pain reporting and psychological responses to illness. The present study was conducted in Medan, North Sumatra, a region characterized by a predominantly Southeast Asian population with diverse ethnic backgrounds. These contextual factors are important, as cultural perceptions of pain expression and emotional distress may affect symptom reporting and coping strategies, thereby influencing measured anxiety levels.

Despite growing international evidence on the coexistence of pain and psychological distress in oncology settings, data from Southeast Asia remain limited, particularly regarding mechanism-based pain classification. Most prior studies have focused on pain intensity rather than differentiating neuropathic and nociceptive phenotypes. Consequently, it remains unclear whether specific pain mechanisms confer differential psychological burden within this regional population.

Based on these considerations, this study aims to analyze the association between pain mechanisms and anxiety levels in cancer patients at the Pain Clinic of Adam Malik Hospital. Specifically, this study defines pain mechanisms using the PDQ to categorize patients into nociceptive, mixed/unclear, or neuropathic pain, and correlates these phenotypes with anxiety severity measured by the GAD-7. This approach seeks to clarify how specific pain phenotypes correlate with the severity of psychological distress, thereby providing novel insights to guide more comprehensive and integrated symptom management strategies.

Subjects and Methods

This study employed an observational analytic cross-sectional design and was conducted at the Pain Clinic of Haji Adam Malik General Hospital, Medan, Indonesia, in June 2025. The study protocol received ethical approval from the Health Research Ethics Committee (No. 264/uns. 2.1.1.29/SPB/2025). Before data collection, written informed consent was obtained from all participants after the study's purpose and procedures were fully explained. The study population comprised patients with a confirmed diagnosis of cancer attending the clinic. A total of 103 subjects were enrolled using a consecutive sampling technique. Of 112 eligible patients approached, 103 consented to participate (response rate 92.0%). Nine patients declined participation, primarily due to fatigue or time constraints. No financial incentives were provided. The inclusion criteria were patients aged 18 years or older who were willing to participate and able to communicate effectively-exclusion Criteria: severe cognitive impairment, history of pre-existing psychiatric disorders, or incomplete medical records.

The research workflow involved collecting

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demographic and clinical data through direct interviews and medical record reviews. The primary research variables included pain mechanisms and anxiety levels. Pain mechanisms were assessed using the PainDETECT Questionnaire (PDQ), a validated instrument that classifies pain based on the total score into nociceptive pain (score ≤12), mixed or unclear pain (score 13–18), and neuropathic pain (score ≥19). Anxiety severity was measured using the Generalized Anxiety Disorder-7 (GAD-7) scale, which consists of seven items with a total score range of 0–21. Anxiety levels were categorized as mild (5–9), moderate (10–14), and severe (15–21). Additional variables collected included age, gender, education level, employment status, health insurance status, chemotherapy history, and primary tumor site.

The PainDETECT Questionnaire (PDQ) and the Generalized Anxiety Disorder-7 (GAD-7) were administered in Indonesian using validated translations. Questionnaires were completed through structured face-to-face interviews conducted by trained research personnel to ensure comprehension, particularly among participants with lower levels of education. Each interview required approximately 15–20 minutes. For participants who were able and preferred to self-complete the questionnaires, clarification was provided when necessary. Data completeness was assessed immediately after questionnaire administration. Cases with incomplete PDQ or GAD-7 responses were excluded from analysis; however, no significant missing data were identified in the final dataset. Although a formal a priori sample size calculation was not performed due to the exploratory nature of the study, the sample size was determined by the total number of eligible patients presenting during the study period.

Statistical analysis was performed using IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY, USA). Patient characteristics were summarized using descriptive statistics, including frequencies and percentages for categorical variables and mean±standard deviation for continuous variables. Bivariate analysis was conducted to examine the associations between patient characteristics, pain mechanisms, and anxiety levels using correlation tests (Pearson or Spearman) and the Kruskal–Wallis test for non-parametric comparisons. A p-value of <0.05 was considered statistically significant.

Results

A total of 103 cancer patients were included in this study. The baseline demographic and clinical characteristics of the study population are summarized in Table 1. The majority of patients were female (63.1%) with a mean age of 53.62±10.87 years. Regarding education, slightly more than half of the participants (52.4%) had completed junior high school or lower. Nearly all patients were covered by the national health insurance (BPJS), and the vast majority (88.3%) had undergone chemotherapy. The most frequently identified primary tumor sites were breast (21.4%), cervix (13.6%), and lung (11.7%).

The study population consisted predominantly of patients of Southeast Asian ethnicity, reflecting the demographic composition of North Sumatra, Indonesia. The majority of participants were of Batak, Malay, and Javanese ethnic backgrounds, consistent with the regional population distribution. All participants were treated within the same tertiary referral center, ensuring relative cultural and healthcare system homogeneity.

The prevalence of specific pain mechanisms and anxiety severity levels is presented in Table 2. Based on the PainDETECT Questionnaire (PDQ), neuropathic pain was the predominant mechanism, identified in more than half of the patients (57.3%), followed by unclear/mixed pain. Only a small proportion of patients presented with purely nociceptive pain. Regarding psychological distress measured by the GAD-7, the majority of the study population experienced moderate anxiety (73.8%), while severe anxiety was reported by 16.5% of patients.

The analysis of the relationship between

Table 1 Patient Characteristics Data

Patient Characteristics	Data
Gender [n (%)]	
Male	38 (36.9)
Female	65 (63.1)
Age (Mean ± SD)	53.62±10.87
Ethnicity [n (%)]	
Batak	45 (43.6)
Malay	26 (25.4)
Javanese	19 (18.4)
Others	13 (12.6)
Education level [n (%)]	
No schooling, elementary, and junior high school	54 (52.4)
Senior high school and university	49 (47.6)
Employment status [n (%)]	
Unemployed	56 (54.4)
Employed	47 (45.6)
Health insurance [n (%)]	
None	0 (0)
BPJS	102 (99)
BPJS and private insurance	1 (1)
Chemotherapy [n (%)]	
Yes	91 (88.3)
No	12 (11.7)
Primary tumor site [n (%)]	
Breast	22 (21.4)
Cervix	14 (13.6)
Lung	12 (11.7)
SCC	6 (5.8)
Prostate	7 (6.8)
Rectum	5 (4.9)
Nasopharynx	6 (5.8)
Bladder	3 (2.9)
Colon	9 (8.7)
Endometrium	5 (4.9)
Larynx	4 (3.9)
Others	10 (9.7)

pain mechanisms and anxiety levels is detailed in Table 3. A statistically significant association was observed between the type of pain mechanism and anxiety severity (p=0.004). Patients classified with neuropathic pain exhibited a distinct distribution of anxiety, with

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Table 2 Distribution of Pain Mechanism (PDQ) and Anxiety Severity (GAD-7)

Variable	Category	n (%)
Pain mechanism (PDQ)	Nociceptive	6 (5.8)
	Unclear/mixed	38 (36.9)
	Neuropathic	59 (57.3)
Anxiety severity (GAD-7)	Mild	10 (9.7)
	Moderate	76 (73.8)
	Severe	17 (16.5)

a high proportion falling into the moderate (76.3%) and severe (22.0%) categories. Conversely, patients with nociceptive pain demonstrated a broader distribution, including a notably higher percentage of mild anxiety (33.3%) compared to the neuropathic group (1.7%).

Regarding the relationship between age and anxiety severity, younger age was significantly associated with higher GAD-7 scores (r=–0.224; p=0.024) (Table 4). When stratified by anxiety category, patients with severe anxiety had a lower mean age compared to those with moderate and mild anxiety. This trend indicates that psychological distress was more pronounced among younger individuals within the cohort. To further illustrate this association, mean age decreased progressively across anxiety categories (mild, moderate, severe), supporting the observed negative correlation. These findings reinforce the vulnerability of younger cancer patients to heightened psychological burden.

Discussion

This study was designed to test the hypothesis that neuropathic pain is associated with greater anxiety severity compared with nociceptive or mixed pain in cancer patients. This study revealed two important findings that support this hypothesis. First, younger patients reported higher levels of anxiety, consistent with the idea that a cancer diagnosis during productive years may disrupt family, career, and social roles, thereby intensifying psychosocial distress. The weak but significant negative correlation between age and GAD-7 scores (r=–0.224, p=0.024) suggests that younger patients are more vulnerable to

Table 3 Association between Pain Mechanism (PDQ) and Anxiety Severity (GAD-7)

Pain Characteristics (PDQ) Nociceptive	Anxiety Levels			p-value
	Mild	Moderate	Severe	
Unclear	2 (33.3)	3 (50)	1 (16.7)	
Neuropathic	1 (1.7)	45 (76.3)	13 (22)	0.004[e]
Pain characteristics (PDQ)	7 (18.4)	28 (73.7)	3 (7.9)	

Note: [e]Fisher Exact Test

Table 4 Correlation Between Age and Anxiety Severity (GAD-7 Score)

Variable 1	Variable 2	Correlation Coefficient (r)	p-value	Interpretation
Age (years)	GAD-7 score	–0.224	0.024	weak negative correlation

anxiety. Increased concerns about financial responsibilities, caregiving roles, and long-term prognosis may explain this vulnerability.

Second, neuropathic pain was strongly associated with higher anxiety scores compared with nociceptive or unclear pain. Neuropathic pain, caused by structural or functional damage to the somatosensory system, produces abnormal sensations such as burning, tingling, or electric shocks, which are inherently threatening to patients. These symptoms, often compounded by central sensitization, may contribute to a greater psychological burden. Beyond the physical component, the unpredictability and uncontrollability of neuropathic pain may erode patients' sense of control, thereby amplifying anxiety.

Our findings align with recent research concerning the impact of age on psychological distress. Haukaas et al. observed that patient characteristics, particularly age, significantly influence distress levels in the diagnostic phase of cancer, supporting the notion that younger individuals often face greater psychological challenges.[18] Other studies likewise suggest that older patients may develop more effective coping mechanisms or possess greater emotional resilience accumulated through life experience, thereby buffering against anxiety.[19] Conversely, younger patients are more prone to existential anxiety and mental health fluctuations when confronted with a cancer diagnosis, as described in longitudinal trajectories of young adult survivors.[20,21]

The link between neuropathic pain and psychological distress is well-supported by current evidence. Neuropathic pain is frequently associated with a higher prevalence of anxiety, sleep disturbance, and impaired well-being compared to nociceptive pain.[22] Recently, Eryiğit and Uzun demonstrated that neuropathic pain severity in cancer patients is strongly correlated with a decline in quality of life. Their study highlighted that higher pain intensity is often more pronounced in women and younger patients and directly contributes to greater functional and psychological impairment.[23] Regional data from the ACoPain SEA study similarly highlighted the high prevalence of neuropathic pain and its contribution to patient suffering in Southeast Asia.[24]

The strengths of this study lie in the use of validated instruments (PDQ and GAD-7) to categorize pain by underlying mechanisms, rather than relying solely on pain intensity scores. This mechanism-based classification allows for a more precise evaluation of the relationship between pain type and anxiety severity, enabling the identification of differences in psychological burden between patients with neuropathic and nociceptive pain. However, several limitations must be acknowledged.

First, the cross-sectional design precludes the determination of causality between pain mechanisms and anxiety; it remains unclear whether neuropathic pain contributes to increased anxiety or whether heightened anxiety amplifies the perception of neuropathic symptoms. Second, the study was conducted at a single tertiary referral center, which may limit the generalizability of the findings to broader cancer populations with different demographic or cultural characteristics. Third, the sample size for the nociceptive pain subgroup was relatively small (n=6), potentially reducing the statistical power for comparisons involving this group. Finally, important potential confounders, including cancer stage, duration of illness, and pre-existing psychiatric history, were not adjusted for in a multivariable analysis.

These results underscore the importance of integrating psychological screening into cancer pain management. Even patients with nociceptive pain reported moderate anxiety levels, suggesting that all cancer pain patients carry a significant psychological burden. A comprehensive assessment should therefore include both physical and psychological dimensions. Routine use of validated instruments such as the PDQ, which has been validated for assessing pain severity and quality and GAD-7 may help clinicians identify high-risk patients, particularly younger individuals and those with neuropathic pain,

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who may benefit from early psychosocial interventions.[25]

Conclusion

This study concludes that pain mechanisms are significant predictors (Fisher's exact test, p=0.004) of anxiety severity in cancer patients. Patients with neuropathic pain exhibited significantly higher anxiety levels compared to those with nociceptive or unclear pain, identifying neuropathic symptoms as a distinct marker of higher psychological vulnerability. Younger age also correlated with increased anxiety. These findings emphasize the clinical necessity of integrating psychological screening with mechanism-based pain assessment to ensure comprehensive symptom management in oncology care. Future longitudinal and multicenter studies are warranted to clarify causal relationships and to evaluate whether targeted interventions for neuropathic pain can reduce anxiety and improve overall patient outcomes.

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