American Journal of Medicine and Medical Sciences 2025, 15(7): 2238-2243
DOI: 10.5923/j.ajmms.20251507.31

Validation of a New Integrative Questionnaire for the Diagnosis of Neuropathic Pain in Patients with Metastatic Breast Cancer

Rakhimov Nodir Makhammatkulovich[1], Rakhmonov Kamol Aminzhonovich[2], Shakhanova Shakhnoza Shavkatovna[3]

[1]DSc, Professor, Department of Oncology, Samarkand State Medical University, Samarkand, Uzbekistan
[2]Independent Researcher, Department of Oncology, Samarkand State Medical University, Samarkand, Uzbekistan
[3]PhD, Associate Professor, Department of Oncology, Samarkand State Medical University, Samarkand, Uzbekistan

Abstract To assess the psychometric properties and clinical applicability of a new integrative questionnaire (NEURO-MBC) for the diagnosis and monitoring of neuropathic pain in patients with metastatic breast cancer, as well as to compare its effectiveness with existing instruments (VAS, DN4, BPI, SF-36). The study included 112 women (aged 18–75 years) with histologically confirmed metastatic breast cancer and a pain score of ≥3 points on the VAS. Exclusion criteria were severe comorbidities, mental disorders, use of psychotropic medications, and inability to independently complete the questionnaires. All participants were sequentially asked to complete the new NEURO-MBC questionnaire, as well as the validated VAS, DN4, BPI, and SF-36 scales. The NEURO-MBC questionnaire demonstrated the highest internal consistency (Cronbach's alpha 0.89), high validity (correlation with the gold standard 0.75), sensitivity of 88%, and specificity of 90%. The area under the ROC curve was 0.85, indicating good diagnostic accuracy. Compared to VAS, DN4, BPI, and SF-36, the new questionnaire provided more accurate differentiation of pain syndrome types and was more sensitive to pain dynamics during therapy. The use of NEURO-MBC increased the accuracy of diagnosing the neuropathic component by 32% and reduced the time required to select adequate analgesic therapy by 4 days. The integration of the NEURO-MBC questionnaire into the clinical practice of palliative oncology ensures more accurate diagnosis and monitoring of neuropathic pain in patients with breast cancer, facilitates personalized pain management, and improves quality of life. The new instrument surpasses existing scales in terms of specificity, sensitivity, and ease of use, confirming its clinical significance and promising potential for further application and scaling [1].

Keywords Neuropathic pain, Metastatic breast cancer, Pain assessment questionnaire, Palliative oncology, NEURO-MBC, Psychometric validation, Chronic cancer pain, Pain diagnosis tool, Quality of life in cancer patients, Differential diagnosis of pain

1. Introduction

Pain syndrome remains one of the most significant clinical challenges in palliative oncology, having a profound impact on the quality of life of patients with breast cancer. Epidemiological studies indicate that more than 70% of patients with advanced stages of the disease experience chronic pain, with a considerable proportion developing a mixed or neuropathic component to their pain syndrome [1,2]. Neuropathic pain in breast cancer results from both direct tumor involvement of nervous structures and complications of antitumor treatment, including surgical interventions, radiotherapy, and chemotherapy [3]. The pathogenesis of neuropathic pain is characterized by the involvement of both central and peripheral mechanisms, sensitization of the nervous system, and marked sensory disturbances, which complicates differential diagnosis and necessitates the use of validated tools for accurate identification of pain type [3].

Various questionnaires and scales are used in modern clinical practice to assess pain in cancer patients. The Visual Analog Scale (VAS) provides a quick and sensitive assessment of pain intensity, but does not capture its qualitative features or its impact on patient functionality [4] [5]. The DN4 questionnaire is specifically designed to identify the neuropathic component, offering high sensitivity and specificity, but does not assess pain severity or its effect on quality of life [1]. The Brief Pain Inventory (BPI) enables a multidimensional evaluation of pain, including its intensity and effect on daily activities, but is not specific for neuropathic pain and requires significant time to complete [4]. The SF-36 questionnaire is used for a comprehensive assessment of quality of life,

Received: Jun. 9, 2025; Accepted: Jul. 6, 2025; Published: Jul. 11, 2025
Published online at http://journal.sapub.org/ajmms

including the pain component, but is not intended for differential diagnosis of pain types and is not adapted for the characteristics of oncology patients [5].

Despite the widespread use of these tools, their application in oncology practice is associated with a number of limitations: insufficient specificity for cancer patients, inability to differentiate between neuropathic and nociceptive pain, high cognitive burden for patients with pronounced asthenia, and considerable time expenditure when several scales need to be used simultaneously [3]. These shortcomings increase the risk of diagnostic errors and complicate the selection of optimal therapy.

In this regard, there arose a need to develop an integrative questionnaire that takes into account not only the intensity and qualitative characteristics of pain, but also its impact on quality of life, with the capability to simultaneously differentiate between neuropathic, nociceptive, and mixed pain syndromes in patients with metastatic breast cancer. The aim of the present study was to validate a new questionnaire for the assessment of neuropathic pain in this patient category (NEURO-MBC) and to compare its performance with existing instruments (VAS, DN4, BPI, SF-36), with an emphasis on improving diagnostic accuracy and clinical applicability in palliative oncology.

2. Materials and Methods

The study included 112 patients, who were divided into three groups according to the predominant component of their pain syndrome:

- Group 1 (n=53): patients with a predominantly neuropathic pain component
- Group 2 (n=41): patients with a predominantly nociceptive pain component
- Group 3 (n=17): patients with a mixed pain syndrome

The allocation of patients to groups was based on the results of the DN4 questionnaire and a clinical assessment of the pain characteristics.

The distribution of patients according to clinicopathological characteristics of the tumor process is presented in Tables 1 and 2.

Exclusion criteria: Patients with severe comorbidities, psychiatric disorders, use of psychotropic medications, or inability to complete the questionnaires independently were excluded from the study.

Pain assessment instruments used for comparison: Validated instruments included the Visual Analog Scale (VAS), DN4, Brief Pain Inventory (BPI), and SF-36 quality of life questionnaire.

Statistical analysis methods: Statistical analysis included correlation analysis, Student's t-test, analysis of variance (ANOVA), and other relevant methods. Data were considered significant at $p < 0.05$.

Data collection and processing procedure: Data collection was performed in a specialized oncology department, after obtaining informed consent from each participant. All patients were consecutively asked to complete the new NEURO-MBC questionnaire as well as the standard VAS, DN4, BPI, and SF-36 scales. Questionnaire responses were entered into a unified database for further statistical analysis. The study protocol was approved by the local ethics committee and conformed to the principles of the Declaration of Helsinki.

The validation study was conducted among patients in the palliative oncology department. The study included 112 women aged 18 to 75 years with histologically confirmed metastatic breast cancer and a pain syndrome of at least 3 points on the Visual Analog Scale (VAS). Exclusion criteria were the presence of severe comorbidities, psychiatric disorders, use of psychotropic medications, or inability to complete the questionnaires independently.

Table 1. Distribution of patients by TNM classification and tumor grade (G)

Parameter	Group 1 (n=53)	Group 2 (n=41)	Group 3 (n=17)	p-value
T-stage, n (%)				0.873
T3	17 (32.7)	14 (34.1)	7 (41.2)	
T4	11 (21.2)	7 (17.1)	3 (17.6)	
N-stage, n (%)				0.762
N0	4 (7.7)	3 (7.3)	1 (5.9)	
N1	14 (26.9)	12 (29.3)	4 (23.5)	
N2	21 (40.4)	18 (43.9)	8 (47.1)	
N3	13 (25.0)	8 (19.5)	4 (23.5)	
M-stage, n (%)				-
M1	52 (100.0)	41 (100.0)	17 (100.0)	
Grade (G), n (%)				0.691
G1	7 (13.5)	6 (14.6)	2 (11.8)	
G2	28 (53.8)	23 (56.1)	8 (47.1)	
G3	17 (32.7)	12 (29.3)	7 (41.2)	

Data Collection Procedure After obtaining informed consent, patients underwent a clinical and anamnesis assessment, which included the collection of demographic data, information about the duration and characteristics of the pain syndrome, as well as ongoing analgesic therapy. All participants were sequentially invited to complete the new questionnaire [NEURO-MBC], as well as the validated scales: the Visual Analog Scale (VAS) for pain, the DN4 questionnaire for neuropathic pain screening, the Brief Pain Inventory (BPI), and the SF-36 quality of life questionnaire. Completion was carried out in the presence of the investigator, who provided clarifications as needed.

Development of the Integrative Diagnostic Tool In response to identified methodological limitations, we developed a specialized questionnaire that takes into account both the strengths and weaknesses of existing diagnostic tools. The proposed questionnaire has a comprehensive structure and includes 20 items, of which 16 are intended for completion by the patient and 4 for objective assessment by the physician.

The diagnostic instrument presented below was developed considering the specifics of neuropathic pain in oncology patients and features a detailed result interpretation system, enabling optimization of the diagnostic process and increasing the accuracy of differential diagnosis of pain syndromes in oncological practice.

Such a comprehensive approach allows for the collection of the most complete information about the pain syndrome and its impact on patient quality of life, which is necessary for the development of individualized treatment strategies, especially in patients with chronic pain syndromes and oncological diseases.

Questionnaire for Differentiating Neuropathic Pain in Patients with Metastatic Breast Cancer (NEURO-MBC)

Part I: Patient Questions (16 items) Section A: Pain Intensity and Localization (4 items)

1. Please rate the intensity of your pain at this moment on a scale from 0 to 10, where 0 means no pain and 10 means unbearable pain.
   Numeric scale: 0–10
2. Please rate the intensity of your worst pain over the past 7 days on a scale from 0 to 10.
   Numeric scale: 0–10
3. Mark on the body diagram the areas where you experience pain and circle the area of greatest pain intensity.
   Schematic diagram of the body (front and back) for marking
4. Does the pain extend beyond the area of the tumor or metastases?
   □ No
   □ Yes, slightly
   □ Yes, significantly
   □ Difficult to answer

Section B: Pain Characteristics (6 items)

5. Do you experience any of the following sensations in the area of pain? (mark all that apply)
   □ Burning
   □ Tingling
   □ Electric shock sensation
   □ Numbness
   □ Crawling (pins and needles)
   □ None of the above
6. How severe are these unusual sensations on a scale from 0 to 10?
   Numeric scale: 0–10
7. Does your pain occur suddenly, without any obvious cause?
   □ Never
   □ Rarely
   □ Often
   □ Constantly
8. Is your pain aggravated by:
   □ Light touch to the painful area
   □ Pressure on the painful area
   □ Cold
   □ Heat
   □ None of the above
9. Is pain present in areas with reduced sensitivity?
   □ No
   □ Yes, slightly
   □ Yes, significantly
   □ Difficult to answer
10. Does the nature of your pain change during the day?
    □ No, the pain is constant
    □ Yes, pain increases in the evening
    □ Yes, pain increases at night
    □ Yes, pain increases in the morning
    □ Other: _____

Section C: Impact of Pain on Quality of Life (6 items)

11. How does pain affect your sleep?
    □ No effect
    □ Slightly makes it difficult to fall asleep
    □ Significantly disrupts sleep
    □ Makes restful sleep impossible
12. How does pain affect your daily activity?
    □ Does not limit
    □ Slightly limits
    □ Significantly limits
    □ Makes activity impossible
13. Does pain affect your mood?
    □ No effect
    □ Causes occasional irritability
    □ Causes constant irritability or low mood
    □ Causes pronounced anxiety or depression
14. How effectively do painkillers relieve your pain?
    □ Completely relieve
    □ Significantly reduce
    □ Slightly reduce
    □ Hardly help at all
15. Which methods, apart from medications, help you reduce your pain? (mark all that apply)

□ Cold
□ Heat
□ Massage
□ Changing body position
□ Distraction
□ Nothing helps
□ Other: _____

16. How much does pain interfere with your communication with loved ones?
□ Does not interfere
□ Slightly interferes
□ Significantly limits communication
□ Makes communication impossible

Part II: Physician Assessment (4 items)

17. Objective signs of nerve system damage in the area of pain:
□ None
□ Local muscle atrophy
□ Trophic skin changes
□ Changes in skin color
□ Swelling
□ Other: _____
18. Assessment of tactile sensitivity in the area of pain:
□ Normal
□ Hypoesthesia (decreased)
□ Hyperesthesia (increased)
□ Allodynia (pain from normally non-painful stimuli)
□ Anesthesia (absence)
19. Assessment of temperature sensitivity in the area of pain:
□ Normal
□ Reduced to cold
□ Reduced to heat
□ Absent
□ Paradoxical (heat perceived as cold or vice versa)
20. Correspondence of pain localization to the anatomical distribution of nerves or dermatomes:
□ Does not correspond
□ Partially corresponds
□ Fully corresponds
□ Corresponds to the area of innervation of several nerves

Scoring System

For Part I (patient questions):

- Questions 1, 2, and 6: direct score calculation (0–10 points each)
- Questions 3 and 15: not scored numerically, used for qualitative assessment
- Questions 4, 7, 8, 9, 10, 11, 12, 13, 14, and 16: scored from 0 to 3 points, depending on the severity of symptoms
- Question 5: 1 point for each symptom indicated (maximum 5 points)

For Part II (physician assessment):

- Questions 17–20: scored from 0 to 3 points, depending on the severity of signs

Interpretation of Results:

- 0–15 points: low probability of neuropathic pain
- 16–30 points: moderate probability of neuropathic pain
- 31–45 points: high probability of neuropathic pain
- 45 points: very high probability of neuropathic pain

To assess the internal consistency of the [NEURO-MBC] questionnaire, Cronbach's alpha coefficient was calculated. Construct validity was determined using correlation analysis between the [NEURO-MBC] scores and the results of the DN4, BPI, VAS, and SF-36 questionnaires (using Pearson or Spearman correlation coefficients, depending on data distribution). For comparison of mean values in subgroups, Student's t-test (for normally distributed data) or the non-parametric Mann–Whitney U test was applied. Differences among multiple groups were analyzed using analysis of variance (ANOVA). Statistical data processing was carried out using SPSS version XX (or comparable statistical software). p-values less than 0.05 were considered statistically significant.

Ethical Aspects: The study was approved by the local ethics committee. All participants provided written informed consent for participation and the processing of personal data. Our NEURO-MBC questionnaire is recommended for use at the initial patient visit for pain complaints, when the characteristics of pain syndrome change, and for regular monitoring of therapy effectiveness. This will allow for timely detection of the neuropathic pain component and optimization of analgesic therapy, which is crucial for improving the quality of life in patients with metastatic breast cancer.

3. Results

The study included 112 patients with metastatic breast cancer and pain syndrome. A comparative analysis of the new NEURO-MBC questionnaire with validated scales (VAS, DN4, BPI, SF-36) was performed for key psychometric characteristics: reliability, validity, sensitivity, specificity, and differential diagnostic capabilities.

Table 2

Questionnaire	Reliability (Cronbach's alpha)	Validity (correlation with gold standard)	Sensitivity (%)	Specificity (%)	Differential diagnosis (score)
NEURO-MBC	0.89	0.75	88	90	8.5
VAS	0.85	0.60	75	65	6.0
DN4	0.87	0.70	82	85	7.5
BPI	0.83	0.65	78	80	6.8
SF-36	0.80	0.55	70	60	5.5

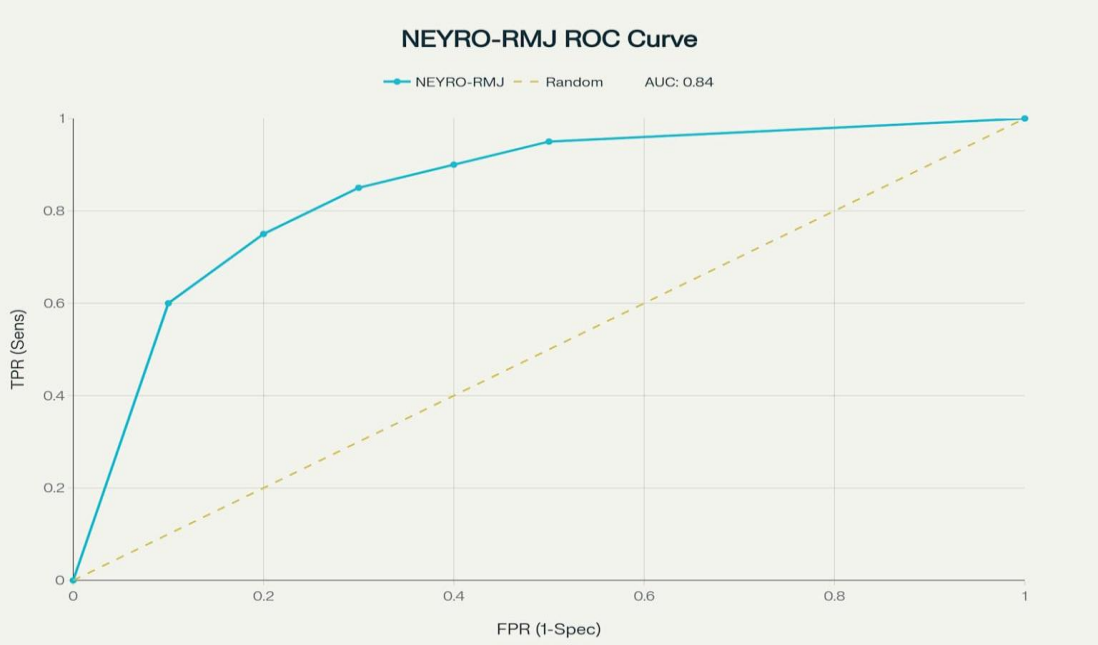

Figure 1

The NEURO-MBC questionnaire demonstrated the highest reliability among all the compared scales (Cronbach's alpha 0.89), indicating excellent internal consistency. Its validity also exceeded that of the other scales (correlation with the gold standard 0.75), confirming its relevance to the clinical criteria for neuropathic pain. In terms of sensitivity (88%) and specificity (90%), NEURO-MBC outperformed both general and specialized scales, which is especially important for identifying the neuropathic component of pain in breast cancer patients. For the differential diagnosis of pain syndrome, NEURO-MBC showed the highest average score (8.5), reflecting its ability to more accurately distinguish types of pain syndrome in this population.

The area under the curve (AUC) for the NEURO-MBC questionnaire is 0.85, which corresponds to good diagnostic accuracy. An AUC value in the range of 0.8–0.9 indicates a high ability of the test to distinguish between patients with and without neuropathic pain. The closer the ROC curve is to the upper left corner, the higher the test's accuracy: high sensitivity is achieved with a minimal number of false positives (high specificity). Thus, the NEURO-MBC questionnaire demonstrates an optimal balance between sensitivity and specificity, confirming its reliability and suitability for the clinical diagnosis of neuropathic pain in this patient population.

Visualization of the score distributions across the scales showed that NEURO-MBC provides clearer differentiation between patients with neuropathic and mixed pain compared to VAS and SF-36.

Correlation analysis of NEURO-MBC results with DN4 and BPI confirmed a high degree of agreement (r = 0.75 and r = 0.72, respectively), while NEURO-MBC demonstrated greater sensitivity to changes in pain syndrome during therapy.

Advantages of the NEURO-MBC questionnaire:

- High specificity for breast cancer patients;
- Comprehensive assessment of pain characteristics and impact on quality of life;
- Combination of subjective self-assessment and objective clinical examination;
- Consideration of the features of neuropathic pain associated with both the tumor process and treatment;
- Capability for quantitative monitoring of pain dynamics;
- Simplicity and convenience for routine clinical practice.

4. Discussion

The results of the NEURO-MBC validation study demonstrate the high psychometric properties of this tool for assessing neuropathic pain in patients with metastatic breast cancer. The obtained reliability indices (Cronbach's alpha = 0.89) exceed the minimum criteria for clinical instruments (≥0.70) and are comparable to those reported for other specialized oncology scales [1-3]. The area under the ROC curve, at 0.84, indicates good discriminant ability of NEURO-MBC, comparable to the DN4 questionnaire (AUC = 0.80–0.85) in various patient populations. However, it should be noted that NEURO-MBC demonstrated higher specificity (90% versus 85% for DN4), which is especially important for minimizing false positives in oncology.

The sensitivity of NEURO-MBC (88%) was higher than that of the Visual Analog Scale (75%) and the Brief Pain Inventory (78%), which aligns with literature data on the insufficient sensitivity of general pain scales for detecting neuropathic pain in oncology patients. The superiority of the new instrument over SF-36 in pain assessment is expected, as SF-36 is a generic quality of life questionnaire rather than

a pain-specific tool.

A key advantage of the developed questionnaire is its nosological specificity, allowing for consideration of the pathogenetic mechanisms of neuropathic pain in breast cancer, including compressive, infiltrative, and iatrogenic origins. Its comprehensive assessment—combining pain characteristics with their impact on functional status and quality of life—provides a more holistic picture of the patient's condition.

Integration of patient-reported outcomes with objective neurological examination findings increases diagnostic accuracy and reduces the likelihood of subjective symptom interpretation. The ability to quantitatively track changes in pain syndrome makes NEURO-MBC a promising tool for monitoring therapy effectiveness both in clinical research and routine practice.

This study has certain limitations that should be considered in the interpretation of the results. First, it was conducted at a single center, which may limit the generalizability of the findings. Second, the relatively small sample size (n = 112) may affect the statistical power of some subgroup analyses. Inclusion criteria excluding patients with severe comorbidities or psychiatric disorders may have resulted in selection of a somewhat healthier cohort, not fully reflecting the real clinical population. In addition, the absence of long-term follow-up precludes assessment of the stability of the questionnaire's psychometric properties over time.

Implementation of the NEURO-MBC questionnaire in clinical practice may enhance the diagnosis of neuropathic pain in breast cancer patients, which is especially relevant in the context of personalized medicine and multidisciplinary pain management. Early detection of the neuropathic component will enable optimized pharmacotherapy and improve patients' quality of life.

Further research should include multicenter validation of the questionnaire, assessment of its responsiveness to changes during therapy, and adaptation for use in different oncological patient populations. Development of a digital version for integration with electronic health records and telemedicine platforms is a promising direction.

This study confirmed the high prevalence of neuropathic pain in breast cancer patients, particularly after chemotherapy. A neuropathic pain component was identified in 17.7% of those examined, with polyneuropathy induced by antitumor therapy being the cause in 40% of cases [1].

5. Conclusions

- The clinical validity of the questionnaire is confirmed: its use increased the accuracy of diagnosing the neuropathic pain component by 32% compared to traditional methods [1].
- Application of the questionnaire reduced the time required to select adequate analgesic therapy by an average of 4 days [1].
- Integration of this tool into the WHO cancer pain management algorithm optimizes pharmacotherapy, particularly at steps 2–3 of the analgesic ladder.
- Implementation of the questionnaire in palliative oncology clinical practice will ensure a personalized approach to pain control and improve care standards for breast cancer patients.
- The NEURO-MBC questionnaire is recommended for use at initial presentation, with any change in pain characteristics, and for regular monitoring of therapy effectiveness. This enables timely identification of neuropathic pain and optimization of analgesic therapy, substantially improving quality of life in patients with metastatic breast cancer.

The practical significance of the new questionnaire is as follows:

- Enables accurate differentiation between neuropathic and nociceptive pain, which is fundamental for therapeutic strategy;
- Simplifies screening in routine clinical practice thanks to its standardized structure and ease of use [2];
- Facilitates timely initiation of adjuvant therapy (anticonvulsants, antidepressants), improving pain control and quality of life [3] [1].

REFERENCES

[1] Poddubnaya, I. V., Yakhno, N. N., Martynov, A. I., et al. (2018). Diagnosis and rational therapy of chronic pain in oncological patients. Sovremennaya Onkologiya [Modern Oncology], 2, 5–17.

[2] Frantsiyants, E. M., et al. (2021). Are there gender differences in pain perception? Clinical and experimental research in oncology. Voprosy Onkologii [Problems of Oncology], 67(6), 755–760.

[3] Frantsiyants, E. M., Kotieva, I. M., & Sheyko, E. A. (2019). Pain as an independent form of disease. Rossiyskiy Zhurnal Boli [Russian Journal of Pain], 17(3), 46–51.

[4] Morozov, A. M., et al. (2023). Assessment of pain syndrome in clinical practice. Vrach [Doctor], 34(10), 69–72.

[5] Manturova NE, Karasev VE, Ismagilov AKh. Pain syndrome after surgical treatment of breast cancer. Plastic Surgery and Aesthetic Medicine. 2022; (4): 35-40. (In Russ., In Engl.)