Chronic pain evaluation in breast cancer patients using the Self-Report Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS): a single center cross-sectional retrospective study

Original article

Dhiraj Daga[1], Narender Singh Shah[1], Sanchit Jain[2], Gaurav Sharma[3], Harsh Goel[4], Sooyun Caroline Tavolacci [5], Boski Gupta[6], Kiran Gulia[7], Tabish H Khan[8], Darksha Usmani[9], Akash Gujral[10], Naoshad Muhammad[11], Sandeep Mittan[11], Poonam Banthia[3]

[1]Department of Radiation Oncology, JLN Medical College and Hospital, Ajmer, India
[2]Department of General Surgery, RUHS College of Medical Sciences, Jaipur, India
[3]School of Applied Science, Suresh Gyan Vihar University, Jagatpura, Jaipur, India
[4]Department of Laboratory, All India Institute of Medical Sciences, New Delhi, India
[5]Department of Hematology and Medical Oncology, Center for Thoracic Oncology, Tisch Cancer Institute and Icahn School of Medicine, Mount Sinai, New York, United States
[6]Department of Dentistry, GMERS Medical College, Gandhinagar, Gujarat, India
[7]Department of Materials and Manufacturing School of Engineering University of Wolverhampton England, United Kingdom
[8]Department of Pathology and Immunology, Washington University School of Medicine, St Louis, Missouri, United States
[9]Department of Ophthalmology, Washington University School of Medicine, St Louis, Missouri, United States
[10]Department of Medicine, NYU Grossman School of Medicine, New York, United States
[11]Montefiore Medical Center, The University Hospital for Albert Einstein College of Medicine, New York, United States

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Abstract

Background: Breast cancer is the most common cancer in India, and the number of survivors has increased over the last few years. Pain is one of the most common symptoms during cancer treatment due to either the disease itself or the adverse effects of treatment. The available data suggests that breast cancer patients have a high prevalence of neuropathic pain.

Patients and methods: A cross-sectional observational study was done at the Department of Radiation Oncology, between November 2021 to June 2022. The patients were admitted and screened for participation, non-metastatic post-operative breast cancer on regular follow-up for 2 years after their last chemotherapy or radiotherapy and not having any chronic neuropathy disease and the Self-Report Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) pain scale was used to assess the neuropathy pain status of patients. Patients' demographics, clinical characteristics, and treatment of surgery, radiation therapy, and chemotherapy were collected and the comparison of the pain scores between the patients was analysed.

Address for correspondence:
Poonam Banthia
School of Applied Science, Suresh Gyan Vihar University, Jagatpura, 302017 Jaipur, India
e-mail: poonam14banthia@gmail.com

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Results: A total of 149 patients were included in the study. S-LANSS score was calculated in the study population and more than 61% of participants reported a score equal to or greater than 12, suggesting a predominant neuropathic pain component. Autonomic dysfunction, thermal pain, and allodynia were more prevalent in patients who underwent mastectomies compared to breast-conserving surgery. Whereas the dysesthesia and autonomic dysfunction score was higher in only the anthracycline group.
Conclusions: The most important index for quality of life in cancer patients is the presence of persistent chronic pain and it is important to classify it accordingly in order to provide the best management. Using the S-LANSS score, the pattern of neuropathic pain can be determined early which leads to early intervention.

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Keywords: neuropathic pain, S-LANSS, chronic pain, breast cancer, pain measurement

Introduction

Breast cancer is the most common cancer diagnosed in the world, including India. The incidence of breast cancer is on the rise, and this increase is highest in developing countries in Southeast Asia, Africa, and South America. According to GLOBOCAN 2020, a total of 178 361 cases were diagnosed with a 5-year prevalence of 459 271 cases in India [1]. With increasing incidence as well as the availability of early detection and better modalities of treatment, the number of breast cancer survivors has increased over the last few years [1].

Pain is one of the most common symptoms reported by cancer patients during the disease trajectory. 39–66% of cancer patients suffer from pain during the course of the disease and treatment, which can either be nociceptive, neuropathic, or mixed type [2]. The International Association for the Study of Pain introduced the term "neuropathic pain", defined as pain initiated or caused by a primary lesion or dysfunction in the nervous system [3]. There are multiple aetiologies for both nociceptive and neuropathic pain in cancer patients. It can be due to either the disease itself or the adverse effects of treatment [4]. Neuropathic pain can further be divided into radiculopathy, peripheral neuropathy, spinal cord compressions, and leptomeningeal metastasis, whereas treatment-related causes of neuropathic pain can be post-surgical complications, post radiotherapy, and chemotherapy agents [5]. The treatment of neuropathic pain is different from nociceptive pain and is often challenging while simultaneously negatively affecting the patient's treatment outcomes, and physical, social and cognitive functions, as well as degrading the quality of life of the patient.

A systematic review of pain among cancer patients showed the prevalence of neuropathic pain in the range of 19% to 39% [6]. Similarly, a multi-centric observational study conducted in India showed that 54% of patients had pain with predominantly neuropathic components [2], which is relatively high when compared to the systemic review data. However, in a retrospective study conducted at a tertiary cancer centre in India, the burden of neuropathic pain was far lower than the global data of 11.8% [7]. Thus, despite the widespread recognition of cancer-related neuropathy, there is a paucity of multi-centre studies to determine the burden of neuropathic cancer pain in Indian patients [2].

The systematic review conducted by Ilhan et al. [8] reported the pooled prevalence estimate of neuropathic pain as 32.6–58.2% in breast cancer patients using screening questionnaires, which was significantly higher when compared to other cancer sites. Given the many causes that lead to neuropathic pain, several patient-reported measures have been developed for evaluation, including the Neuropathic Pain Scale [9], the Leeds Assessment of Neuropathic Symptoms and Signs [10], the Self-Report Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) [11], ID pain [12].

The available data suggests that patients with breast cancer have a high prevalence of neuropathic pain when compared to other cancers [13]. Additionally, in the context of India, they have a higher prevalence of neuropathic pain than Western nations. The purpose of the present study is to investigate the prevalence of neuropathic pain in breast cancer patients who underwent surgical resection and received adjuvant chemotherapy.

Patients and methods

A cross-sectional observational study was conducted at the Department of Radiation Oncology, between November 2021 to June 2022. The inclusion criteria consisted of patients with breast carcinoma who underwent surgery of either a mastectomy or breast-conserving surgery, were HER2/neu negative, on regular follow-up for 2 years after their last

chemotherapy or radiotherapy session and aged between 18 years to 60 years. Patients who have metastatic disease or any chronic neuropathy disease at the time of diagnosis were excluded. The patients were screened for participation during their follow-up and were included in the study after obtaining informed consent. Institutional ethical committee approval was taken before starting the study.

Demographic and clinical characteristics of the disease and treatment were obtained from patients and their medical records. The self-reported version of the Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) [11] was used to assess the neuropathy pain status of the patient. This self-reported version is a simpler tool that eliminates the necessity of clinical examination and consists of 7 questionnaires indicating different pain subtypes (dysesthesia, autonomic dysfunction, evoked pain, paroxysmal, thermal, allodynia, and altered pinprick), which can be self-completed or completed through a basic interview. The range of the S-LANSS total score is from 0–24 and differentiates the patient's pain status between two ends of a pain spectrum: "pain of predominant neuropathic" or "pain of predominant nociceptive". Scores of 12 or greater suggest pain of predominantly neuropathic origin while a score of 10 or lower suggests predominantly nociceptive pain [4, 14]. S-LANSS pain scale is an established score system with Cronbach's alpha ranges from 0.6 to 0.74 demonstrating internal consistency and has been validated in diverse sets of populations across the world [4, 14]. This S-LANSS pain scale is not adapted as per the place of study, only extemporary translation was done at the patient's bedside during an interview.

Patients' demographics, clinical characteristics and surgery treatment data — either mastectomy or breast-conserving surgery (BCS), radiation therapy, and chemotherapy (either anthracycline-based regimen or anthracycline- and taxane-based regimen) were collected. The comparison of pain scores based on the S-LANSS test among patients was analysed. The normality of data was checked by the Shapiro–Wilk test with a score between +1.96 and −1.96. If data is found to be normally distributed, Continuous variables were presented as mean and standard deviation (SD) and categorical variables were summarized with frequency. If any continuous data is not found normally distributed, medians and interquartile ranges will be described as necessary. Student's t-test and logistic regression were used to compare the outcome and a p-value of less than 0.05 was considered to be statistically significant. Statistical analysis was done using IBM-SPSS software version 20 and SAS 9.4.

Results

A total of 149 patients with surgically resected breast cancer, who were screened based on the inclusion and exclusion criteria, were included in the study. The mean age was 53.1 ± 9.9 years with a maximum age of 75 years (Table 1). Nearly all (98.66%) of the patients were female and only two male patients were enrolled in the study. In the socioeconomic context, more than 84.6% of patients were married and importantly, 81.88% had an education level below 10th standard, for which 16.1% were uneducated. Stage 2 (46.98%) was the most common followed by stage 3 (33.56%) and 77.18%. Nearly 86.58% of patients underwent a mastectomy and 77.18% of patients had a positive lymph node status. Radiotherapy was not given in 22.15% of patients. Anthracycline and taxane combination chemotherapy was used more than anthracycline alone, about 83.2%. 71.14% of patients underwent hormonal treatment with oestrogen/progesterone (ER/PR) positive status (Table 1). S-LANSS pain scores were calculated as a sum of 7 pain subtype components (Supplementary file 1). Analysing the S-LANSS score in the study population, 61.07% of patients reported an S-LASS score greater than or equal to 12 (Supplementary file 1), suggesting a predominant neuropathic pain component, whereas 33.56% of patients reported nociceptive pain. In the investigation of treatment effects on neuropathic pain, 65.89%, 53.45%, and 57.26% of patients, respectively, who underwent mastectomy, radiotherapy, and anthracycline- and taxane- (TA) based chemotherapy reported neuropathic pain, respectively. All 33 patients who did not receive radiotherapy underwent mastectomies and 87.88% had neuropathic pain (Figure 1). Among 91 patients with neuropathic pain, treatment-related risk factors associated were mastectomy, radiotherapy and TA-based chemotherapy (Figure 2). The risk associated was 14.2-fold in patients who underwent mastectomy compared to BCS and 3.6-fold in patients who received TA-based chemotherapy compared to anthracycline-based chemotherapy.

Logistic regression was built to assess the effects of mastectomies on neuropathic pain. Within the patients who received radiotherapy and TA-based chemotherapy, patients with mastectomies had 4.5 times more risk of neuropathic pain when compared with BCS: odds ratio (OR) 4.507, 95% CI 1.62–12.54; $p = 0.004$. Mastectomies were a significant independent risk factor for neuropathic pain, suggesting that 430% and 327% more risk of having neuropathic pain than BCS in all patients (OR 4.3, 95% CI 1.3–14.24, $p = 0.017$) and a group of patients who received radiotherapy (OR 3.27, 95% CI 1.16–9.23, $p = 0.026$).

Table 1. Characteristics of the study population

Characteristics	Number of patients [%]
Age (years)	
18–30	2 (1.34%)
31–45	41 (27.51%)
46–60	74 (49.66%)
61 and above	32 (21.48%)
Sex	
Male	2 (1.34%)
Female	147 (98.66%)
Marital status	
Unmarried	02 (1.34%)
Married	126 (84.6%)
Widow	21 (14.09%)
Educational qualifications	
Uneducated	24 (16.11%)
Elementary school	50 (33.56%)
Middle/Junior high school	48 (32.21%)
Senior high school	12 (8.05%)
Higher education	15 (10.07%)
Family history of malignancy	
Yes	12 (8.05%)
No	137 (91.95%)
Cancer stage	
Stage 1	21 (14.09%)
Stage 2	70 (46.98%)
Stage 3	50 (33.56%)
Stage 4 (4a–4c)	8 (5.37%)
Lymph node involvement	
Yes	115 (77.18%)
No	34 (23.82%)
ER/PR status positive	106 (71.14%)
Anti-oestrogens	46 (43.4%)
Aromatase inhibitors	60 (56.6%)
Surgery	
Breast-conserving surgery	20 (13.42%)
Mastectomy	129 (86.58%)
Radiotherapy	
Yes	116 (77.85%)
Chemotherapy regimen	
Anthracycline-based	25 (16.78%)
Anthracycline and taxane-based	124 (83.22%)

ER — oestrogen receptor; PR — progesterone receptor

When comparing the various components of S-LANSS based on surgical procedures performed, dysesthesia and autonomic dysfunction scores were significantly higher in patients who underwent breast-conserving surgery compared to mastectomies (Table 2). In the comparison of S-LANSS scores by chemotherapy group, Autonomic dysfunction and thermal and allodynia components were significantly predominant in the anthracycline and taxane combination chemotherapy group. All other components except evoked pain and paroxysmal showed a higher S-LASS mean score in this group. The evoked pain component score had a higher mean in the anthracycline-based chemotherapy group and the paroxysmal component score was the same in the two groups (Table 3).

Additionally, the socioeconomic status regarding education was used to assess the association between education level and having neuropathic pain, given that S-LANSS is a self-reporting pain scale. Uneducated (66.67%) and elementary educated (68%) patients reported more neuropathic pain than the high-school and higher-educated patients. The two groups were divided into patients who received equal or below elementary education ($n = 74$) and those who received above elementary education ($n = 75$). Education level was not significantly associated with neuropathic pain (logistic regression, $p = 0.11$).

Discussion

Breast cancer is a major cause of morbidity and mortality among females in developing countries and is a leading cause of cancer-related deaths worldwide. With the advancement of diagnostic techniques and the availability of effective treatment modalities, the life expectancy of breast cancer patients has increased. In such scenarios, the focus has shifted to the quality of life. Among the most important indices for quality of life in cancer patients is the presence of persistent chronic pain. Though there may be multiple causes, cancer pain is under-assessed and undertreated in tertiary care hospitals in India [2]. The present study attempts to evaluate cancer-related pain through the utilization of patient-reported questionnaires i.e., S-LANSS.

The maximum patients were above the age of 46––60 years, similar to the disease peaks of 40–50 years in Indian women [15, 16]. Most of the patients were from rural backgrounds, where females get married at a comparatively younger age. More than 84% of the study population was married. Breast cancer is considered to be diagnosed at an earlier stage and more likely to be treatable in urban populations, the

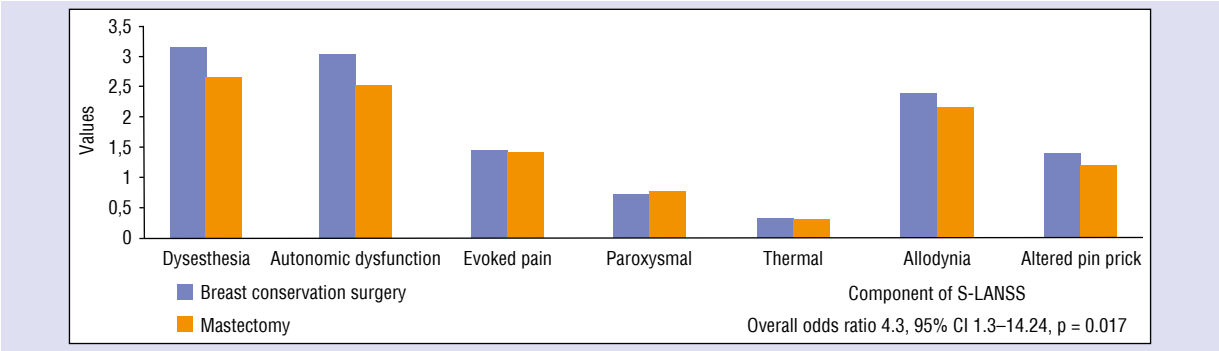

Figure 1. Patterns of pain according to type of surgery

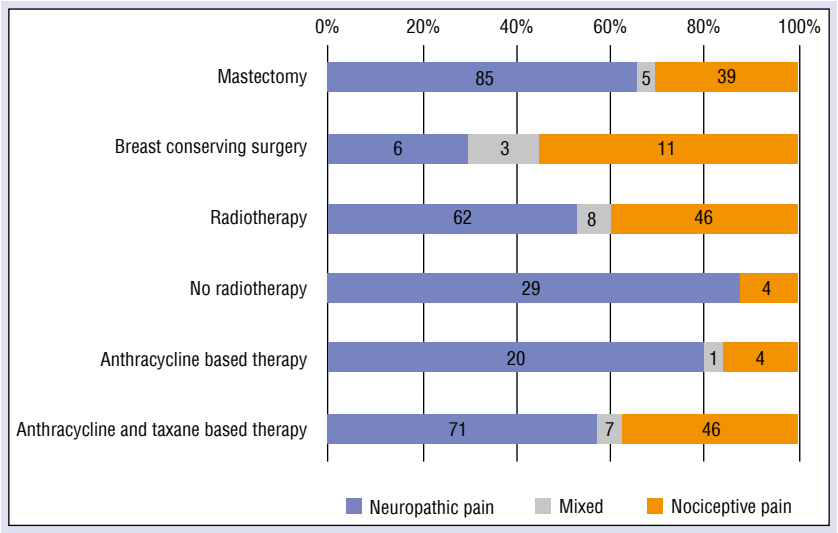

Figure 2. Neuropathic pain by treatment

Table 2. S-LANSS score comparison on the basis of surgery

	Breast conservation surgery	Mastectomy	p-value (t-test)
Dysesthesia	3.16 ± 0.8	2.66 ± 1.0	**0.02**
Autonomic dysfunction	3.04 ± 0.79	2.52 ± 0.97	**0.01**
Evoked pain	1.44 ± 0.51	1.42 ± 0.71	0.9
Paroxysmal	0.72 ± 0.46	0.76 ± 0.68	0.8
Thermal	0.32 ± 0.48	0.31 ± 0.46	0.9
Allodynia	2.4 ± 0.82	2.17 ± 0.86	0.2
Altered pin prick	1.4 ± 0.91	1.22 ± 0.78	0.3

S-LANSS — Self-Report Leeds Assessment of Neuropathic Symptoms and Signs

reasons include the availability of better healthcare facilities and a higher level of education in cities [17]. Around 50% of patients had an education below the primary level and 16% were uneducated. This is in contrast to other studies where more than 60% had an education level above secondary [16, 17]. In the study population, 86.6% underwent either modified radical or total mastectomies. In comparison to a study conducted in 2010, the mastectomy percentage was 57%. It should, however, be noted that the study was conducted in the USA [12]. Similarly, more patients required radiotherapy (77.8%) compared to Western data [12]. It is known that patients undergoing axillary lymph node dissection and radiotherapy have a significantly higher incidence of chronic pain [18]. Whenever there is a presence of chronic pain, it is important to classify the pain into the neuropathic or the nociceptive variety. One of the reasons for this

Table 3. S-LANSS score comparison on the basis of chemotherapy

	Anthracycline-based	Anthracycline- and taxane-based	p-value (t-test)
Dysesthesia	2.6 ± 0.94	2.77 ± 1.0	0.5
Autonomic dysfunction	2.15 ± 0.81	2.68 ± 0.96	0.02
Evoked pain	1.45 ± 0.76	1.42 ± 0.67	0.9
Paroxysmal	0.75 ± 0.72	0.75 ± 0.64	1.0
Thermal	0.0	0.36 ± 0.48	0.001
Allodynia	1.85 ± 0.67	2.26 ± 0.87	0.05
Altered pin prick	1.0 ± 0.73	1.29 ± 0.81	0.1

S-LANSS — Self-Report Leeds Assessment of Neuropathic Symptoms and Signs

distinction is to clarify that while nociceptive pain is sensitive to opioids, neuropathic pain shows a weak response to opioids [19].

One of the main purposes of the study is to identify the burden of neuropathic pain in post-surgical breast cancer patients. S-LANSS is easy to comprehend, can quickly be completed by the patient, and can be used by non-specialists [2]. Our study reports a significant percentage (61.07%) of patients with a score of 12 or more, suggesting a neuropathic origin of pain. This derivation contrasts the study conducted by Reyes-Gibby et al. [12], where only 12% of patients reported a score of 12 or higher. It is important to mention that in breast cancer patients, it is difficult to discriminate surgically induced neuropathy from other types of neuropathy e.g. taxane induced [20].

The above study is one of the first studies where an S-LANSS components score comparison was utilized based on conducted surgery and chemotherapy. A significant difference in autonomic dysfunction and dysesthesia, components were found in patients undergoing breast conservative surgery as compared to mastectomy, which can be attributed to residual breast tissue having inflammatory changes, open nerve endings and post-radiotherapy fibrotic changes. The autonomic dysfunction, thermal and allodynia score was higher in the anthracycline and taxane group, which can be attributed to the use of multiple chemotherapeutic agents and a higher number of chemotherapy cycles along neuropathic side effects of taxane drugs.

Limitations to our study include a single-centre study and a small sample size. A prospective study can be done in the future to remove the recall bias which is often found in retrospective studies. With the development of treatment for breast cancer, new HER2/neu studies and their treatment options are essential parts of treatment, which acted as exclusion criteria for our retrospective study.

Conclusions

Pain is one of the major symptoms which affect patients' quality of life during and after cancer treatment. Patients with breast cancer have higher chances of suffering from chronic neuropathic pain. Thus, appropriate management is critically needed to improve quality of life. S-LANSS is an efficient and user-friendly tool and can be used to prematurely detect neuropathic pain and investigate the underlying cause of the pain.

Article information and declarations

Data availability statement

The data used to support the findings of this study are included in the article.

Ethics statement

Ethics Committee approval number 659/ACAD-III/ /MCA/2021 S.No 12 has been obtained.

Author contributions

DD, NSSh, SJ, GS and HG have contributed to the conception, design and data collection. BG, CSL, PB, KG, TK, DU, AG, NM and SM have contributed to the data analysis and interpretation. All authors reviewed and approved the final manuscript.

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Conflict of interest

The authors do not have any conflict of interest to declare.

Supplementary material

The Supplementary material for this article can be found online at https://journals.viamedica.pl/palliative_medicine_in_practice/article/view/PMPI.a2023.0027.

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