

Prevalence of Post-treatment Chronic Pain in Breast Cancer Patients and its Effect on their Quality of Life

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Abstract

Introduction: Post-mastectomy pain syndrome (PMPS) is typically a chronic neuropathic pain, which can develop shortly after, or up to several months after surgery (BCS and MRM) and can persist for years. There is some evidence that chronic pain and sensory abnormalities do decrease over time. The study was aimed to assess frequency and intensity of chronic pain in the breast area and ipsilateral arm in already treated breast cancer patients. To study the demographic and clinical characteristics affecting the development of chronic pain and to assess the effect of chronic pain on the quality of life in post-treatment breast cancer patients.

Materials and Methods: This was a cross-sectional study conducted at a tertiary institute in South India. The study included breast cancer patients older than 18 years attending the oncology clinic within the study period, who have undergone breast surgery and completed their treatments at least 6 months before and were free of disease at the time of interview. Pain

characteristics were assessed in detail using the Short Form McGill Pain Questionnaire (SF-MPQ). Quality of life was assessed using the Functional Assessment of Cancer Therapy-Breast (FACT-B) questionnaire (Tamil/English version). The comparisons of domain scores were carried out by using independent student's t test.

The comparison of domain scores and overall score of FACT-B in relation to histological grade was carried out by using one-way Analysis of Variance. The association of pain with menopausal status, post-treatment duration, comorbidities, age at diagnosis, clinical stage of disease, histological grade, type of surgery, quadrant involved and postoperative complications were assessed by using χ^2 test. All statistical analyses were carried out for two-tailed significance at 5% level of significance.

Results: A total of seventy post-treatment breast cancer patients participated in the study. Postoperative pain was experienced by the majority of women with a VAS score of 4 to 6. The character of chronic pain was assessed using Short Form McGill Pain Questionnaire. The intensity of chronic pain was VAS 4 to 6 in 30 out of 31 patients. On comparing patients with chronic pain, there was no association noted to age, menopause, comorbidities, type of tumor, type of procedure, postoperative complication, adjuvant received and post-treatment duration.

Quality of life scores in the subscales varied from 47 to 63% of their maximum scores. The mean Trial outcome index (TOI), FACT-G score and FACT-B overall score were 50%, 61% and 82% of their maximum scores respectively. On comparing women

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with and without chronic pain, the mean Breast Cancer Subscale (BCS) score was found to be higher and statistically significant in the latter. Though mean scores of FACT-B domains were higher in patients who underwent modified radical mastectomy, no statistically significant difference was found. On comparing quality of life scores and adjuvant therapy, it was found that all domain scores except SWB and BCS scores were significantly higher in patients who received both chemotherapy and radiotherapy than those who received radiotherapy alone.

Conclusion: This preliminary work suggests that the severity of acute postoperative pain may predict future chronic pain. Aggressive treatment of acute post-operative pain may therefore decrease the incidence of chronic pain. Surgeons should be aware that younger women may be at a higher risk of developing chronic pain syndromes after breast cancer surgery. Further studies are needed to determine whether more careful surgery and radiotherapy can diminish the incidence of these symptoms.

Keywords: Chronic pain, Breast cancer, Quality of life.

Introduction

The breast cancer is the second common cancer in India and its incidence is rising slowly. Chronic pain after surgery for breast cancer is a common problem with prevalence rates ranging from 20 to 68%.^{1,3} With increasing survival rates, improving the post-treatment quality of life assumes greater significance. In this context, chronic pain following breast cancer treatment is an under-recognized and under-treated problem. A study on chronic breast pain in the Indian population may help to increase current awareness, identify the predisposing factors and improve management approaches by treating surgeons and is more generalizable to Indian population.

Post-mastectomy pain syndrome (PMPS) is typically a chronic neuropathic pain, which can develop shortly after, or up to several months after surgery (BCS and MRM) and can persist for years. It is often located in the axilla, the shoulder, the arm or the chest wall. Jung *et al.* described four different types of chronic neuropathic pain following breast cancer surgery⁴.

1. Phantom Breast Pain is pain experienced in the area of a removed breast.
2. Intercostobrachial Neuralgia is pain often accompanied by sensory changes, in the distribution of the intercostobrachial nerve following breast cancer surgery with or without axillary dissection.

3. Neuroma pain (including scar pain) is pain in the region of a scar on the breast, chest, or arm that is provoked or exacerbated by percussion.
4. Other nerve injury pain may result from damage or traction to other intercostal nerves, the medial and lateral pectoral, long thoracic, or thoracodorsal nerves.

There is some evidence that chronic pain and sensory abnormalities do decrease over time. Ivens *et al.* found that the likelihood of chronic pain diminished from 31% at 1–2 years following breast cancer surgery to 20% after more than 4 years following surgery.

The study was aimed to assess frequency and intensity of chronic pain in the breast area and ipsilateral arm in already treated breast cancer patients. To study the demographic and clinical characteristics affecting the development of chronic pain and to assess the effect of chronic pain on the quality of life in post-treatment breast cancer patients.

Materials and Methods

This was a cross-sectional study conducted at a tertiary institute in South India from 1st November 2011 to 31st July 2012. The study included breast cancer patients older than 18 years attending the oncology clinic within the study period, who have undergone breast surgery and completed their treatments at least 6 months before and were free of disease at the time of interview. All patients with history of thoracotomy surgery, angina pectoris and other malignancies were excluded.

Chronic pain was defined as any kind of pain in ipsilateral breast, chest wall, shoulder, arm or axillary region, persisting for at least 3 months after termination of surgery and adjuvant therapy. Pain characteristics were assessed in detail using the Short Form McGill Pain Questionnaire (SF-MPQ). The SF-MPQ consists of 15 descriptors (11 sensory; 4 affective) which are rated on a 4-point intensity scale as 0 = none, 1 = mild, 2 = moderate or 3 = severe. Three pain scores are derived from the sum of the intensity rank values of the words chosen for sensory, affective and total descriptors. The SF-MPQ also includes the Present Pain Intensity (PPI) index of the standard MPQ and a visual analogue scale (VAS).

Quality of life was assessed using the Functional Assessment of Cancer Therapy- Breast (FACT - B) questionnaire (Tamil/English version). FACT-B is a 44-item self-report questionnaire and consists of the FACT-G plus additional items that make up the

breast cancer subscale (BCS). The FACT-G contains four subscales: physical (PWB), functional (FWB), social/family (SWB) and emotional well being (EWB). Each item is rated on a 5-point scale and summed so that a higher subscale score indicates higher well being or satisfaction. The Trial Outcome Index (TOI) of FACT-B is the sum of scores of PWB, FWB and BCS. The FACT-G total score is the sum of PWB, SWB, FWB and EWB scores. All ratings on the FACT-B are completed in terms of the past seven days.

Demographic and clinicopathological details of the patients were collected from each patient through individual pro forma. Both the questionnaires were administered to the study patients by the same interviewer at a single sitting.

The distributions of data related to all clinicopathological parameters were expressed as frequencies and percentages. The data on all domain scores and overall score of FACT-B was expressed as mean with Standard Deviation. The comparisons of domain scores and overall score in relation to pain, age group (≤ 40 years and > 40 years), post-treatment duration (≤ 3 years and > 3 years), menopausal status, the clinical stage at presentation, type of surgery and adjuvant therapy were carried out by using independent student's t test.

The comparison of domain scores and overall score of FACT-B in relation to histological grade was carried out by using one way analysis of variance. The association of pain with menopausal status, post-treatment duration, comorbidities, age at diagnosis, clinical stage of disease, histological grade, type of surgery, quadrant involved and

post-operative complications were assessed by using χ^2 test. All statistical analyses were carried out for two tailed significance at 5% level of significance.

Results

A total of seventy post-treatment breast cancer patients participated in the study. The mean age of patients was 51.9 years. Among them 56(80%) were post-menopausal and 14 (20%) were pre-menopausal women and 2 (3%) were nulliparous. Majority of the patients (53%) had Stage II disease at presentation. Except a single case of medullary carcinoma, all had infiltrating ductal carcinoma (IDC) of no special type. 48 patients (68.6%) were noted to have grade 2 IDC, 12 patients (17.1%) had grade 1 IDC and 10(14.3%) had grade 3 IDC. Receptor status was as given in Table 1.

Sixty-two patients (89%) had undergone modified radical mastectomy and 8 patients had had a wide local excision (WLE) with level II axillary lymph node dissection (ALND). As adjuvant therapy, majority of the women (78.5%) received both chemotherapy and radiotherapy (Table 2). Postoperative pain was experienced by the majority of women with a VAS score of 4 to 6. (Fig. 1) 31 patients had chronic pain, among whom most had pain confined to the axilla (13 women) followed by pain over chest wall, noted in 8 patients. The character of chronic pain was assessed using Short Form McGill Pain Questionnaire. The intensity of chronic pain was VAS 4 to 6 in 30 out of 31 patients (Fig. 2).

Table 1:

Parameters		N (%)		
Age (years)	25-35	3(4.39)		
	35-45	9(12.86)		
	45-55	29(41.43)		
	55-65	21(30)		
	>65	8(11.43)		
Parity	Nulliparous	2(3)		
	1	(8)		
	2	(33)		
	3 or more	37(59)		
Disease stage at diagnosis	1	1(1.4)		
	2a	20(28.6)		
	2b	17(24.3)		
	3a	22(31.4)		
	3b	10(14.3)		
Receptor status		Positive	Negative	N/A
	ER	38(54.3)	31(44.3)	1(1.4)
	PR	36(51.4)	33(47.1)	1(1.4)
	HER2	30(42.9)	33(47.1)	7(10)

Table 2:

Parameter		N (%)
Operative procedure	MRM	62(89)
	WLE+ level II	8(11)
	ALND	
Post op complications	None	55(78.57)
	Wound infection	10(14.29)
	Flap necrosis	2(2.86)
	Seroma	2(2.86)
	LRI	1(1.43)
Adjuvant treatment received	CT	3(4.3)
	RT	1(1.4)
	HT	3(4.3)
	CT, RT	40(57.1)
	RT, HT	8(11.5)
	CT, RT, HT	15(21.4)

The present pain intensity (PPI) was discomforting in the majority of patients (16 women). However, a few (3) reported horrible/excruciating pain. Majority (20) had a Short Form McGill Pain

Questionnaire sensory score of 2 out of a maximum sensory score of 33 (Table 3). On comparing patients with chronic pain, there was no association noted to age, menopause, comorbidities, type of tumor, type of procedure, postoperative complication, adjuvant received and post-treatment duration. Quality of life of the women included in the study was measured through different subscale scores and indices of the well validated FACT-B. The mean scores in the subscales varied from 47 to 63% of their maximum scores. The mean Trial Outcome Index (TOI), FACT-G score and FACT-B overall score were 50%, 61% and 82% of their maximum scores respectively. On comparing women with and without chronic pain, the mean Breast Cancer Subscale (BCS) score was found to be higher and statistically significant in the latter. The differences in mean scores of the other domains of FACT-B were not significant.

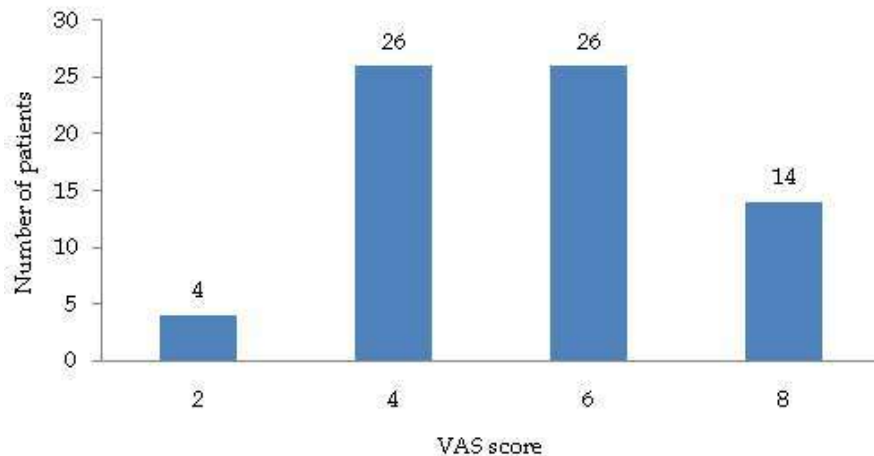


Fig 1: Post-operative pain

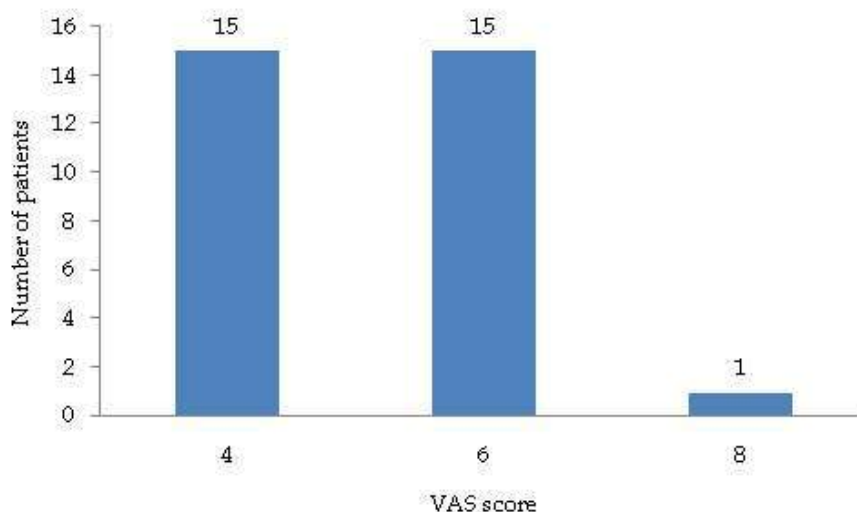


Fig. 2: Distribution of the intensity of chronic pain (N=31)

Table 3: Chronic pain (n=31)

		N (%)
Site of pain	Axilla	13(41.9)
	Chest	8(25.8)
	Arm	5(16.1)
	Scar site	1(3.2)
	Axilla and scar	2(6.5)
	Arm and scar	2(6.5)
Intensity of pain (PPI-Present pain intensity)	Mild	7(22.6)
	Discomforting	16(51.6)
	Distressing	5(16.1)
	Horrible	2(6.4)
SF-MPQ sensory score	1	7(22.6)
	2	20(64.5)
	3	2(6.5)
	4	2(6.5)

Physical well being score was higher in patients less than 40 years and was statistically significant. The mean scores of other domains were not found to be significantly different. FACT-B subscale scores were found to be higher in patients who had completed treatments more than 3 years ago, though none of the differences were statistically significant. Premenopausal women had a PWB score and FACT-G score which was significantly higher than post-menopausal women. The mean scores of other domains in premenopausal women were also higher. No significant difference was found in any of the quality of life measures between the different stages and histological grades. Though mean scores of FACT-B (Table 4) domains were higher in patients who underwent modified radical mastectomy, no statistically significant difference was found. On comparing quality of life scores and adjuvant therapy, it was found that all domain scores except SWB and BCS scores were significantly higher in patients who received both chemotherapy and radiotherapy than those who received radiotherapy alone.

Table 4: Comparison of FACT B parameters

	PWB	SWB	EWB	FWB	BCS	TOI	FACT G	FACT B
Age <40 yrs and >40 yrs	$p < 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$
Pre- and post-menopausal	$p < 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p < 0.05$	$p > 0.05$
Post-treatment duration <3 yrs or >3 yrs	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$
Presence of comorbidity	$p > 0.05$	$p < 0.05$	$p < 0.05$	$p < 0.05$	$p > 0.05$	$p > 0.05$	$p < 0.05$	$p < 0.05$
Clinical stages	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$
Grade of IDC	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$
Adjuvant therapy RT+CT and CT	$p < 0.05$	$p > 0.05$	$p < 0.05$	$p < 0.05$	$p > 0.05$	$p < 0.05$	$p < 0.05$	$p < 0.05$
Type of surgery	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$

Discussion

The point prevalence of chronic pain in this study was found to be 44.2%. In general, the prevalence estimates are in agreement with the estimates in literature varying between 25% and 60%.^{1-3,5} The wide range of pain prevalence in literature may be due to differing definitions of persistent pain, differing measurements of pain and its consequences, a varying mix of type of surgery and adjuvant treatment, and variations in time since surgery.

Jung *et al.* (2003) proposed four distinct pain syndromes: phantom breast pain, intercostobrachial neuralgia (ICN), neuroma pain and other nerve injury pain.⁴ It would not be possible to categorize the women in our study to these syndromes without detailed neurological assessment. Pain descriptors reported by most women in our study were stabbing, shooting, aching or hot-burning. Although our study sample is small, terms used by women to describe their pain are similar to adjectives reported in other studies.^{6,7}

In our study, younger women (≤ 40 years of age) were found to report chronic pain more often. According to similar studies, this may be caused by the more aggressive character of disease in this group of patients, requiring more invasive surgical procedures and chemotherapy.^{2,7-9} This is supported by objective evidence noted in our study that younger women more often have receptor negative, higher grade tumors.

Although other studies have found radiotherapy to be a risk factor for sensory disturbances, this was not confirmed in our study.¹⁰ Altogether, comparison of our results with the literature is difficult because no previous study has given detailed information about the exact dose and location of radiotherapy.

The incidence of breast pain was higher in the breast conservation therapy (BCT) group than in the MRM group ($p > 0.05$). This was in agreement with previous studies, which indicated that more than 1 year after surgery the incidence of breast pain was higher after BCT than MRM.^{2,11} There are other studies which have reported lesser incidence of pain after BCT than MRM, but these studies included patients on whom sentinel node dissection was done along with BCT, facilities for which were unavailable at our centre during the study period.

Two possible surgical risk factors, which have been considered previously, are the sectioning of the intercostobrachial nerve and axillary dissection. Most of the previous publications where the intercostobrachial nerve had been preserved during surgery showed a reduced incidence of complications in the ipsilateral arm.^{7,12} In our study group all patients were subject to level 2 axillary clearance limiting conclusions about axillary dissection being a significant risk factor. The limitation of our study is that none of the surgical records specifically documented the handling of the intercostobrachial nerve (preserving, tractioning, sacrificing) during the operation.

The remembered intensity of acute postoperative pain was noted to correlate with the development of chronic pain.¹³ This is in line with other studies indicating that acute postoperative pain is a predisposing factor for the development of chronic pain. Considering the probable role of central sensitization as a causal mechanism for chronic pain, this observation is not surprising. One drawback of our study was the recall bias brought in by retrospectively asking about the intensity of pain experienced in the early postoperative phase.

The FACT-B domain scores of the patients in our study ranged from 46% to 61% of maximum scores. Previous studies have noted that quality of life after adjuvant treatments was impaired and the physical performance poor as compared to general population.¹⁴ Younger patients were observed to have better mean scores in FACT domains than older patients, especially the physical well being score. This may be explained by better general health status noted in patients <40 years of age.¹⁵ Janz *et al.*, however, noted worse symptoms and quality of life scores in younger patients.¹⁶

No significant differences in quality of life scores were observed between patients undergoing MRM and BCT. This observation is in accordance with previous authors who have concluded that patients undergoing breast conservation therapy, especially younger patients, have psychological symptoms

that appear acutely worse in the short run and, in the end, are not significantly better than patients who elect to have mastectomies. Psychological issues related breast surgery at younger age, added burden of immediate radiation therapy, increased apprehension about recurrence in BCT patients may explain this observation to a degree.

After control for potential confounding factors, a few authors have observed that women with BCT reported better physical and role functioning, were sexually more active and more satisfied with their body image at 1 year after diagnosis.¹⁷ Surprisingly, patients in our study who received both chemotherapy and radiotherapy had better quality of life scores than those who received radiotherapy alone.¹⁸ This contradicts the previous studies. Our finding may be explained by the psychological significance attributed to chemotherapy by the patients.

In general, breast cancer patients showed significant improvement over time in the social, psychological, and social well-being domains, as well as overall quality of life. Age at diagnosis was inversely associated with quality of life changes in physical well-being score. Similar findings have been reported in literature. It has been reported that long-term survivors of breast cancer who had received diagnoses at an older age showed significantly worse quality of life outcomes in the physical domain, while those who were diagnosed at a younger age (27–44 years) showed worse quality of life outcomes in the social domain than other age groups. The confounding factors and certain cultural values which may influence the quality of life of these older patients must be evaluated before giving these results due importance.

There were no significant differences between quality of life scores of patients who received radiotherapy and those who did not. While some studies in literature report worse outcomes with radiotherapy, others do not. As mentioned earlier, no previous study on chronic post treatment pain has defined exactly the dose and location of radiotherapy given. This precludes comparison of our result with other studies.

Stage of disease and histological grade of disease had no influence on overall quality of life. Similar results were reported by some investigators.

In our study chronic pain was found to significantly influence the breast cancer subscale score of FACT-B. On the other hand, not much effect was observed on social, functional and emotional well-being in contrast to previous studies. This probably reflected the social and cultural fabric

of India where social and family support is very well provided when someone is in distress. Similar results have been reported by studies from other countries as well.

Conclusion

Persistent pain in the surgical area is a clinically significant problem in approximately 44% of post-treatment breast cancer patients. This preliminary work suggests that the women in this study who experienced chronic pain after breast cancer surgery had lower quality of life than those without pain. It seems that the severity of acute postoperative pain may predict future chronic pain. Aggressive treatment of acute postoperative pain may therefore decrease the incidence of chronic pain. Surgeons should be aware that younger women may be at a higher risk of developing chronic pain syndromes after breast cancer surgery. All women undergoing breast cancer surgery should be fully informed of the possibility of developing chronic neuropathic pain syndromes. Further studies are needed to determine whether more careful surgery and radiotherapy can diminish the incidence of these symptoms.

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