

Evaluation of the role of preservation of the intercostobrachial nerve on the post-mastectomy pain syndrome in breast cancer patients of North India

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Abstract

Background: Post-mastectomy pain syndrome (PMPS) is experienced by 20-65% of the patients who undergo breast surgery for cancer. The etiology of this chronic neuropathic pain syndrome is still poorly understood and supposed to be multi-factorial. Intercostobrachial (ICB) nerve injury is supposed to be the main cause of the PMPS. **Objectives:** This retrospective study was designed to evaluate the role of preservation of the intercostobrachial nerve and post-mastectomy pain syndrome and also to evaluate various anatomical variations of the intercostobrachial nerve in our breast cancer patients. **Method:** The assessment was done subjectively by specific pain questionnaire and objectively by neurological examination for neuropathic pain and sensitivity alternations. Ninety-one patients were included in this retrospective study. Later on, 22 patients were excluded, mainly because of advanced stage of breast cancer. Forty-two patients were included into the ICB nerve preservation group A. In Group B, 27 patients were included where this nerve was sectioned. In all the cases, it was tried to identify the nerve and its course at the best to assess various variations. The subjective and objective pain evaluations were performed on the 2nd day, after 1 month and after 3 months post-operatively. **Results:** After 3 months, 76.2% of the patients were asymptomatic in Group A (ICB nerve preservation group) and 51.9% in the nerve section group (Group B) ($p < .01$). Although there was a slight increase in the total time of surgery in group A, it was not significant ($p = 0.62$) and there was also no significant difference in the numbers of axillary lymph nodes dissected between the two groups. At surgical dissection, we found that 69.6% of patients (48/69) were having Type 1 variation, followed by Type 2 (18.8%) and Type 3 (5.8%). We didn't find any variation of Type 5 in the course of the ICB nerve during axillary dissection. **Conclusion:** So it is concluded that the preservation of ICB nerve leads to significant decrease in the occurrence of post-mastectomy pain syndrome. To preserve the ICB nerve, the knowledge of the variations of this nerve is very important for the surgeons.

INTRODUCTION

Incidence of chronic pain following various surgeries for breast cancer is now thought to occur in more than 50%^{1,2}. Post-mastectomy pain syndrome is a neuropathic pain condition that can follow surgical treatment for breast cancer, including radical mastectomy, modified radical mastectomy and segmental mastectomy (lumpectomy)^{2,3,4}. The cause of PMPS probably has multi-factorial origin. ICB nerve injury is supposed to be the main cause⁴. Post-operative sensations reported by patients can be transient or long lasting and can include pain, phantom sensations and sensory loss changes. The pain characteristics include paroxysms of lancinating pain against a background of burning, aching and tightening sensations^{5,22,28,29,30}. Chronic pain can be a source of considerable disability and

psychological distress. Chemotherapy and radiotherapy can be additional sources of pain and related symptoms and make diagnosis difficult.

ANATOMICAL CONSIDERATIONS

The innervation of the cutaneous and subcutaneous (adipose, lactiferous) structures of the breast is simple with somatic and preganglionic sympathetic innervation being supplied through the medial and lateral cutaneous branches of the ventral ramus of the third through sixth intercostal ramus.

The lateral cutaneous branch of the 2nd intercostals nerve (T2) (intercostobrachial nerve) crosses the axilla to innervate the upper medial portion of the arm, axilla, and part of the anterior chest wall. T3 innervates the skin of the axilla and

the anterior branches innervate the anterior and posterior torso. Axillary dissection for breast cancer poses risks to the ICBN from stretches as well as from frank transection.

CLASSIFICATION OF THE PAIN AFTER BREAST SURGERY

Jung et al.⁶ distinguished four different types of chronic neuropathic pain following breast cancer due to surgical trauma.

1 Phantom Breast Pain is pain experienced in the area of the removed breast.

2 Intercostobrachial Neuralgia is pain often accompanied with sensory changes in the distribution of the intercostobrachial nerve following breast cancer surgery with or without axillary dissection. Cunck et al. revealed a wide variation of size, location and branching of the intercostobrachial nerve which may explain the high risk of damage to these nerves irrespective of surgical approach⁷.

Post-mastectomy pain syndrome consists of pain and sensory changes localized to the axilla, medial arm, and/or anterior chest wall on the ipsilateral side of the surgery. Damage to the intercostobrachial nerve has been identified as the most common cause of the PMPS^{5,6}.

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. A neuroma is formed from masses of tangled axons formed at the end of severed peripheral nerves. Neuroma trapped in scar tissue has been shown to cause chronic neuropathic pain, spontaneous pain and sever sensitivity to pressure on the breast surgery area. Excision to enable relocation of the neuroma to a protected site may be beneficial, but may risk an increase in neuropathic pain.

4 Other nerve injury pain results from damage to the medial/lateral pectoral, long thoracic or thoracodorsal nerve.

Reduction in the axillary morbidity by preserving the intercostobrachial nerve during axillary node clearance for breast cancer has been claimed in several non-randomized studies. The only prospective randomized study to have examined this relationship found no difference in symptoms between both groups (ICB nerve preserved and sectioned groups) three months postoperatively, but the sensory deficit remained larger when the ICB nerve was divided⁸.

Several factors can be hypothesized to increase the risk of developing PMPS after breast cancer surgery, including, younger age at diagnosis, a larger tumor size, axillary node invasion and use of chemotherapy and/or radiation therapy. Post-operative complications such as bleeding, infection or seroma formation may increase the risk of developing PMPS. Surgical techniques also play an important role in PMPS, particularly those that routinely remove the intercostobrachial nerves^{4,9}.

Despite increasing interest in the issue of post-mastectomy pain syndrome, this has not been studied in our country yet. So, aim and objectives of this study are to assess the incidence of PMPS in a developing country like ours, to evaluate various risk factors leading to PMPS and to assess the impact of the preservation of the ICB nerve on post-mastectomy pain syndrome. One of the very important aims is also to evaluate various anatomical variations of the intercostobrachial nerve.

PATIENTS AND METHODS

This is a retrospective study of 91 patients of breast cancer from January 2007 to October 2009 admitted in our institute. Twenty-two patients were excluded from this study because of advanced cancer (16/91), some left in follow-up (4/91) or died (2/91).

In the main study, 69 breast cancer patients were included. Sixty breast cancer patients were treated with modified radical mastectomy and nine patients with quadrantectomy with axillary lymphadenectomy at our institute from January 2007 to October 2009.

The Inclusion Criteria were: unilateral; early cancers (I, IIA, IIB-T2N1), and patients neither receiving neo-adjuvant chemotherapy/radiotherapy nor having previous axillary surgery. The Exclusion Criteria were: advanced diseases, bilateral, and recurrent diseases, or lost in follow up (22/91).

The 69 patients were retrospectively divided into two groups: with and without intercostobrachial nerve (ICB) preservation. In the ICB preservation Group (A) there were 42 patients and 27 patients were in the ICB section group (B).

Pain & Altered Sensations Evaluation Subjective Assessment: Post-operative pain was assessed by Specific Neuropathic Pain Questionnaire^{25,26,27} & Objective Assessment by neurological examinations¹⁵.

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Definition of post-mastectomy syndrome: The definition used in this study was based on three criteria: character, location, and timing of the pain. The pain should be typical of neuropathic pain as described above with unpleasant and peculiar sensations described in the categories of numbness, hypoesthesia, hyperesthesia/paresthesia; it should be located in the axilla, arm, shoulder, or chest wall of the side of the surgery; and should persist beyond the normal healing time of three months.

The anatomy of the nerve was described in the patients of both groups. The nerve trunk was identified medially where it emerged from the intercostal spaces. The intercostal spaces from which nerves arose were obtained by counting down from the 2nd rib which was an easily palpable landmark.

After surgery, the patients were evaluated for pain subjectively and objectively on the 2nd day, 1 month and in the 3rd month post-operatively. The last evaluation in the 3rd month was based on studies showing that alternations of pain sensitivity in the arm at this time are persistent and don't present significant differences as compared to 15, 18, or 24 months^{13,14,15}.

Statistical analysis: Continuous parametric data were compared using Student's t-test, categorical data were compared using Fisher's exact test, and $p < 0.05$ was considered statistically significant. Normally distributed data are reported as mean and range. Percentage was also used.

Results: The clinical and operative characteristics of the patients ($n=69$) are summarized in the tables 1&2. The mean age (\pm SD) was 51.5 ± 11.4 in the preservation group and 52.7 ± 12.5 in the ICB nerve section group ($p=0.72$). The body mass index (kg/m^2) (mean) was slightly higher in group B (24.5) than Group A (23.1) but without any statistical significance ($p=0.67$) (Table 1). In Group A 34/42 and in group B 23/27 were unemployed women. The mean operative time was 81.2 ± 25.5 minutes in Group A and 78.4 ± 31.4 minutes in Group B ($p=0.76$). So, operative time was marginally longer in Group B, i.e. 5-9 minutes.

The axillary lymph node dissection was done up to level 2 and nodes dissected (median (range)) were 12 (8-20) in Group A and 14 (9-22) in Group B ($p > 0.05$). Seroma collection was found more often in Group B as compared to Group A, but still statistically insignificant ($p=0.44$).

Reasons for division of the nerve in group B (section)

included accidental division ($n = 8$), large fixed lymph nodes with no attempt to preserve the nerve ($n = 12$) and facilitating access to the axilla ($n = 7$). All accidental divisions occurred within the first eleven cases.

In the three evaluations for pain and sensitivity in the IBN area, we found significant differences in the occurrence of sensitivity alterations between the groups, both subjectively and objectively. It was 47.6% in the section group and 24.5% in the preservation group ($p > 0.01$).

The character of the pain was mostly burning or dull aching in both groups. The Visual Analog score (mean \pm SD) was 3.1 ± 1.4 in the preservation group and 4.5 ± 2.1 in the section group ($p=0.34$). Hypoesthesia was the commonest (42.5%) sensitivity alteration observed along with the pain followed by hyperesthesia/paresthesia (37.4%) (Table 3).

As far as anatomical variations are concerned (classification as proposed by Cunnick et al.), the majority of the patients in both groups had Type 1 variation. We have not found any Type 5 variation of the intercostobrachial nerve in the axilla (Table 4).

Figure 1

Table 1: Demographic Features

Characteristics	Group A (Preservation)	Group B (Section)	P-Value
Age (Mean) (Range)	51.5 (31-70)*	52.8 (34-78)	NS
Body Mass Index (BMI) (kg/m^2)	23.1	24.5	0.76
Occupation			
Employed	8 (19.0)	4 (18.5)	NS
House wife/Retired	34 (81.0)	23 (81.5)	
Menopausal Status			
Pre/peri	19 (45.2)	13 (48.1)	NS
Post	23 (54.8)	14 (51.9)	

*Features in parentheses are in percentage, NS - statistically not significant

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Figure 2

Table 2: Features related to the operations

Characteristics	Group A (n=42)	Group B (n=27)
Type of Surgery		
Modified radical mastectomy	38 (90.9)	25 (94.4)
Quadrantectomy with axillary clearance	4 (9.2)	2 (5.6)
Time of surgery (mean±SD) (minutes)	81.8 ±25	77.4 ±20
Serum collection	4 (13.5)	3 (11.2)
Number of nodes dissected (median) (range)	13 (8-22)	15 (9-25)
Follow-up treatment		
Adjuvant chemotherapy	11 (26.2)	10 (37.3)
Adjuvant hormonal treatment	39 (92.1)	24 (89.9)
Follow-up duration	7-27 months	8-27 months

*Features in parentheses are in percentage

Figure 3

Table3: Evaluation of Pain/Sensitivity

Post-operative time	Alterations observed	Group A (n=42)	Group B (n=27)	P-Value
2 nd Day	Pain +			
	Hyperesthesia/paresthesia	7 (16.7)	6 (22.2)	
	Hypoesthesia	11 (26.2)	9 (33.4)	
	Anesthesia	2 (4.8)	2 (7.4)	
1 month	Pain +			
	Hyperesthesia/paresthesia	8 (19.0)	6 (22.2)	
	Hypoesthesia	10 (23.8)	8 (29.6)	
	Anesthesia	1 (2.4)	4 (14.8)	
3 months	Pain +			
	Hyperesthesia/paresthesia	5 (11.9)	5 (18.5)	
	Hypoesthesia	5 (11.9)	7 (25.9)	
	Anesthesia	0	1 (7.7)	
	None	32 (76.2)	14 (51.9)	<0.05

P according to Fisher's exact test

Figure 4

Table 4: Anatomical Variations of Intercostobrachial Nerve Observed During Operation

*Anatomical variations observed.	Group A (n=42)	Group B (n=27)
Type 1	30/42 (71.4)	18/27 (66.6)
Type 2	8/42 (19.4)	5/27 (18.5)
Type 3	2/42 (4.7)	2/27 (7.4)
Type 4	0/42	1/27 (3.7)
Type 5	0/42	0/27
Type 6	2/42 (4.7)	1/27 (3.7)

*Type 1 – arises from T2 alone and does not give off any branches

Type 2 – arises from T2 alone and divides into a large main trunk and a much smaller branch

Type3 – arises T2 alone and divides equally into two branches

Type 4 – formed by two equal-sized branches from T1 and T2 nerves. No significant branches during its course through the axilla

Type5 – arises from two separate T2 radicals to form a single nerve which does not give off branches in the axilla

Type 6 – arises from T2 alone and divides into a large main trunk and at least two smaller branches (range: 2-5 branches).²³

DISCUSSION

There is no such study conducted in India as far as our searches are concerned. Initially, we had planned to evaluate the impact of intercostobrachial nerve preservation on post-mastectomy pain syndrome in our breast cancer patients. Later on, we also included the study of various preoperative factors leading to PMPS and the evaluation of various variations of the intercostobrachial nerve in the axilla.

The reported incidence of PMPS is 20% to 65% and suggests that many women suffer from this syndrom^{4,30,31}. The main etiology is supposed to be the damage to the ICB nerve during axillary dissection. The majority of surgeons routinely sacrifice the ICB nerve because of their concern with thoroughness of clearance, technical difficulty involved, and partly because of their underestimation of the clinical benefit of preserving it. Benefits from preserving the ICB nerve have been identified in several non-randomized

studies^{13,14,16}.

The medial portion of the ICBN is encountered during exposure of the long thoracic and thoracodorsal nerves. Identification of these nerves is therefore essential to its preservation^{16,24}. Freeman et al.²⁰ reported that preservation of ICB nerve only marginally increases the duration of surgery and significantly decreases patient sensory deficits. Considering the increasing awareness of post-operative deficits resulting from ICB nerve sacrifice, there is now a trend toward preservation of ICBN during axillary surgery²³. In our study also, the operative time was slightly (5-9 minutes) longer in the nerve preservation group.

Since the axillary status is considered the most important isolated prognostic factor of breast cancer, any procedure that would interfere with this evaluation could have a negative impact on disease treatment. In the present study, no significant differences were found regarding the number of nodes¹⁵.

Evaluation of function following axillary dissection in the treatment of breast cancer is a matter under discussion^{12,13}.

In this study, 10/42(23.5 %) in the ICB nerve preservation group and 13/27 (48.1 %) in the ICB section group were having post-mastectomy pain syndrome 3 months post-operatively. They remained symptomatic in the further follow-up of 7-26 months although pain intensity decreased. In our study, we also found significantly more symptomatic patients in the nerve section Group but we also had 10/42 (23.5%) patients in the nerve preservation group. A possible explanation could be neuropathy in the region of the intercostobrachial nerve following its conservation possibly as a result of an operatively traumatized nerve^{14,15}, although it is said that neuropathy following intercostobrachial nerve conservation is transitional and found in the majority of the studies¹³.

The etiology of PMPS is very complex and multifactorial. Indeed, no recent study was able to identify any specific risk factors when examining the cause of post-mastectomy pain and this is a highly complicated phenomenon^{21,22,23,24}.

The various risk factors are younger age, increased body mass index, pre-operative pain, depression, anxiety, post-operative chemotherapy, radiotherapy, post-operative hematoma, and seroma formation, apart from ICB nerve injury²⁰. In our study, we found that PMPS was more common in patients of high body mass index and with

unemployment in both groups. There are no clear associations observed with chemotherapy, radiotherapy or the use of tamoxifen. The age effect could be due to a greater sensitivity to nerve damage in the younger age groups or to more extensive efforts at axillary dissection and clearance in younger women; it could also be a reaction to the nature of breast and associated anxiety⁴. We had already excluded the patients with neo-adjuvant chemotherapy or any axillary/breast surgery. Post-operative treatment policies were the same in both groups to keep this parameter constant.

A benefit of preservation of the ICB nerve has been reported in several descriptive studies and includes a reduction in postoperative pain, improved sensation and reduced arm stiffness^{14,18,19,20}.

The course of the nerve is important for the surgeon. It is important to identify this nerve during surgical dissection if preservation is being contemplated. We have observed four types of variations in the course of the ICBN.

Some authors criticize the excessive manipulation of the perineural lymphoadipose tissue in trying to preserve the ICB nerve, saying that it could lead to higher rates of local relapse. However, evaluations carried out after periods of 18 months to 5 years of follow-up between the groups with and without preservation of the ICB nerve did not find significant differences in the local-regional relapses between the groups^{14,20}. In this study, after 32 months of follow-up, no local recurrences in both groups were observed.

Cunnick et al.²³ described that the anatomy of the ICB nerve in the axilla is highly variable. He has grouped it into the six variants as mentioned above. We have also found these variants - except type 5 - in this study.

In conclusion, this study shows that pain and altered sensations are common complications of breast/axillary surgery. Whether this PMPS improves with long follow-up is still debatable and difficult to determine. The patients must be informed about this risk before the surgery.

This study has shown that preservation of intercostobrachial nerve is a feasible and wise way to decrease post-mastectomy pain syndrome in breast cancer patients without compromising operative time. The knowledge of various variations of this nerve is very important for the operating surgeons.

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