

A Longitudinal Study on Lymphedema in Patients Undergoing Axillary Dissection for Carcinoma Breast

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Abstract

Background: This study was conducted to evaluate the occurrence of lymphedema in patients undergoing axillary dissection and/or irradiation for breast cancer and also to determine the risk factors associated with the occurrence of lymphedema in these patients.

Methods: This was a hospital-based prospective study conducted among 198 patients who presented with carcinoma breast to the Department of General Surgery, Government, Medical College, Thrissur over a period of one year after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

Results: Out of 198 patients with a mean age of 53.8 years, a modified radical mastectomy was performed in 193 patients (97.5%), and 5 patients underwent breast conservation surgery (2.5%). 65.2% patients were diagnosed with stage II disease. 18.2 % of participants had post-operative wound infection or seroma. Of the 198 participants, 18 (9.1%) had ≥ 10 lymph nodes that tested positive for malignant cells on HPE. The incidence of lymphedema was 8.1 %.

Conclusion: Approximately 8% of breast cancer patients in our study developed clinically significant lymphedema. Non-dominant side malignancy, advanced stage of disease, post-operative wound infection, seroma, large nodal burden and systemic therapy are significant risk factors for lymphedema development. Irradiation had no significant effect on the development of lymphedema.

Keywords: Carcinoma Breast, Lymphedema (LE)

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Introduction

Breast cancer is by far the most commonly diagnosed cancer in women worldwide, accounting for 21% of all cancers diagnosed in women. [1] In India, breast cancer incidence is on the rise and has now become the most common cancer among women, having overtaken cervix in all the cancer registries, rural or urban. [2] Quality of life and long-term effects of

treatment have become increasingly important for breast cancer patients due to improved survival outcomes. [3,4,5]

A potential side effect of breast cancer surgery is lymphedema (LE), a chronic condition characterized by swelling of the arm, hand, breast, or trunk, which may develop from the accumulation of lymphatic fluid in the interstitial tissues.

Lymphedema is known to have detrimental effects on quality of life due to changes in body image, alterations in arm function, and increased complications such as infection and cellulitis. [6,7,8,9] Upper extremity LE is one of the most common complications after breast cancer surgery with a reported incidence of 6% to 30%. [10]

Lymphedema may present with different signs and symptoms including a feeling of heaviness or tightness in the limb, pain or discomfort, restricted range of motion, and swelling in a part or entire limb. With the early identification and management of lymphedema, we can help patients to maintain their quality of life by minimizing cosmetic, functional, psycho emotional, and potentially life-threatening complications. Risk factors for lymphedema development that are described in the literature include age, presence of co-morbid conditions, wound infection, obesity, stage of disease, axillary dissection, radiation and systemic therapy. [11,12,13] Univariate analysis of risk factors in the current study showed a correlation between increased lymphedema rates and advanced stage of disease, presence of co-morbid conditions, body surface area > 1.5 m and postoperative anthracycline-based chemotherapy and locoregional radiotherapy. However, only axillary irradiation and presence of co-morbid conditions have emerged as significant risk factors for lymphedema development in multivariate analysis. The aim of this study is to assess the risk of upper limb lymphedema in patients who underwent axillary dissection and to clarify the clinical, oncologic and therapeutic factors that could possibly influence this morbidity.

Aims and Objectives

- To find out the occurrence of lymphedema in patients undergoing

axillary dissection and/or irradiation for breast cancer.

- To determine the risk factors associated with the occurrence of lymphedema in these patients.

Materials & methods

This was a hospital-based prospective study conducted among 198 patients who presented with carcinoma breast to the Department of General Surgery, Government, Medical College, Thrissur, over a period of one year after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

Inclusion Criteria

Patients above 18 years of age who are diagnosed with carcinoma breast and underwent axillary dissection during the study period.

Exclusion Criteria

- i) Not willing to participate,
- ii) Presented with lymphedema itself (without neoadjuvant therapy)

Sample Size

Using formula $n = 4 pq/d^2$ for 5% level of significance where P is prevalence of lymphedema,

$$q = 100 - p \text{ and } d = 20\% \text{ of } p$$

$$\text{We have } P = 33.5\%^{[14]}$$

$$\text{Using above formula, sample size } (n) = 4 \times 33.5 \times 66.5 / (6.7)^2$$

$$\text{Which is } = 198.50$$

Therefore, my sample size = 198.

198 patients who underwent axillary dissection for carcinoma breast were studied.

Study Procedure

Every patient (satisfying the inclusion & exclusion criteria) who gets admitted to General Surgery Department, Government Medical College, Thrissur, with carcinoma breast, (from one year following ethical

clearance) were included in the study. Informed consent was obtained from all subjects. Data was collected from the patient according to the proforma. Patients were taken for surgery (modified radical mastectomy/ breast conservation surgery) after clearing the pre anesthetic checkups. The patient's bilateral upper limb sizes were measured prior to the procedure. Specimen was sent for HPE and later followed up. Upper limb sizes and adjuvant therapy data were later collected at 6 months and 1 year following surgery either through digital platform or in person.

Statistical Methods

Collected data coded, entered into excel sheet, analysed using SPSS software and

expressed as percentages, means and standard deviation. The continuous variables like age, lymph nodes positive were summarised as mean and standard deviation and median and IQR. Categorical variables like age, BMI category, diabetes mellitus, and other clinical features, and types of treatment were summarised as frequency and proportions.

Association of development of lymphedema with continuous variables were analysed using unpaired t-test and categorical variables using Chi-square test or Fisher's exact test depending on distribution.

Results

Table 1: Association between Side of Disease and Incidence of Lymphedema (N = 198)

Feature		No. of Patients	No Lymphoedema n = 182 (n, %)	Lymphoedema Present n = 16 (n, %)	P-Value
Side of Disease	Left	92	80, 87.0	12, 13.0	0.02*
	Right	106	102, 96.2	4, 3.8	
Dominant Hand	Left	4	4, 100.0	0, 0	1.0*
	Right	194	178, 91.8	16, 8.1	

* - Fisher's exact p-value

Incidence of lymphedema was higher among those who had disease on the left side (p-value 0.02). In this study, the majority were right handed persons. Patients who were right-handed with carcinoma on left side had more incidence of lymphedema, which suggests that active movements of the limb play a significant role in reduction of post-operative lymphoedema.

Table 2: Association between Stage of Disease and Incidence of Lymphedema (N = 198)

Feature		No. of Patients	No Lymphedema n = 182 (n, %)	Lymphedema Present n = 16 (n, %)	P-Value
Stage of disease	I	36	36, 100.0	0, 0	0.002*
	II	129	121, 93.8	8, 6.2	
	III	31	23, 74.2	8, 25.8	
	IV	2	2, 100	0, 0	

* - Fisher's exact p-value

Majority of patients belonged to stage II & III of disease.

Incidence of lymphedema was higher among those who had the disease diagnosed at stage III followed by stage II.

Table 3: Association between Post-Op Surgical Site Infection and Incidence of Lymphedema (N = 198)

Feature		No. of Patients	No Lymphedema n = 182 (n, %)	Lymphedema Present n = 16 (n, %)	P-Value
Post-op Surgical Site Infection/ Seroma	Yes	36	26, 72.2	10, 27.8	<.001 [#]
	No	162	156, 96.3	6, 3.7	

- Chi Square P-Value

Incidence of lymphedema was higher among those who had post-op surgical site infection/seroma (p-value <.001).

Table 4: Association between Number of Lymph Nodes and Incidence of Lymphedema (N = 198)

Feature		No. of Patients	No Lymphedema n = 182 (n, %)	Lymphedema Present n = 16 (n, %)	P-Value
No. of Lymph Nodes	< 10	180	175, 97.2	5, 2.8	<.001 [*]
	>= 10	18	7, 38.9	11, 61.1	

* - Fisher's exact p-value

Incidence of lymphedema was higher among those who had more than 10 positive lymph nodes (p-value <.001).

Table 5: Association between Neoadjuvant Chemotherapy and Incidence of Lymphedema (N = 198)

Feature	No. of Patients	No Lymphedema n = 182 (n, %)	Lymphedema Present n = 16 (n, %)	P-Value
Neoadjuvant Chemotherapy	Yes 36	29, 80.6	7, 19.4	0.006 [#]
	No 162	153, 94.4	9, 5.6	

- Chi Square P-Value

Neoadjuvant chemotherapy was significantly associated with the development of lymphedema, with a higher incidence among those who received neoadjuvant chemotherapy (p-value = .006).

The mean age of participants was 53.8 years, which was not statistically significant.

179 participants had a BMI of 30 kg/m², while the rest had a BMI greater than or equal to 30 kg/m². BMI was not significantly associated with the incidence of lymphedema (p-value 0.19).

Modified Radical Mastectomy (MRM) was done in 193 patients, and 5 patients underwent Breast Conservation Surgery (BCS), which, when compared, came out

to be not significant with incidence of lymphedema.

Radiotherapy (p value - 0.63) & hormonal therapy (p value - 0.73) were not statistically associated with the incidence of lymphedema.

Discussion

The majority of breast cancer patients in developing nations, including India, continue to present with locally advanced stages that demand a thorough axillary dissection. Our study shows that nearly 65% of patients present with locally advanced disease.

Lymphedema following breast cancer treatment continues to be a significant long-term morbidity in the current era. Lymphedema is difficult to cure once it develops. Although there is no definite

recognized or established strategy of preventing the onset of this dreaded consequence, prevention through proper surgical technique, arm care after surgery, exercises, and massage therapy may help reduce the incidence and/or severity. [14]

This study should help us generate some more information on the incidence of lymphedema in the patients operated here, so that we can base our future strategies for the management of lymphedema more effectively.

Thus, we at the “Department of Surgery, Government Medical College, Thrissur” have made a sincere attempt to find out the incidence of lymphedema in carcinoma breast following axillary dissection and the possible risk factors for the same. We have also compared our studies with other studies done previously. A brief outline of the studies compared is given below. In the present study, the overall incidence of lymphedema was 16 out of 198 patients (8.1%), which is comparable to some other studies. [9]

Participant’s age, BMI (kg/m²), radiotherapy and hormonal therapy were not significantly associated with the incidence of lymphedema, whereas previous studies showed a positive association of lymphedema with age, BMI and radiotherapy. [11,12,13]

In our study, lymphedema was more common in patients who had carcinoma in their non-dominant hand, which indirectly implies that post-operative limb usage and arm exercises play a significant role in reducing the chances and severity of lymphedema. Similar inferences was earlier noted in Sandra C. Hayes et al. study. [7]

Axillary dissection in an advanced stage of the disease can predispose to the development of lymphedema as per our study. In this study, it showed a significant p value of 0.002. Similarly, Pramod R. Pillai et al. conducted a study in 2011 on “Incidence of Lymphedema in Indian

Patients Undergoing Axillary Dissection for Breast Cancer” at Amrita Institute of Medical Sciences, Kochi and found a correlation between increased lymphedema rates and advanced stages of the disease. [15]

In the present study, postoperative wound infection and/or seroma formation increases the risk of lymphedema with a significant p value of <0.001. This is in accordance with the study results of Segerstorm K et al. [13]

In our study, 18 (9.1 %) out of the 198 participants had 10 or more lymph nodes that tested positive for malignant cells in histopathology. Of which 11 patients developed lymphedema among the total 16 cases of lymphedema. It implies pathological nodal status have a significant role in lymphedema formation. [15]

A study conducted by Sandra A. Norman et al. showed that ALND [HR, 2.61; 95% confidence interval (95% CI), 1.77-3.84] and chemotherapy, specifically multi agent therapies with anthracycline (HR, 1.46; 95% CI, 1.04-2.04), were the only treatments significantly associated with increased lymphedema risk in standard multivariable analyses.[16] In the present study, there was also a significant relationship between chemotherapy and lymphedema especially neoadjuvant chemotherapy (anthracycline based regimen) with a p-value of 0.006 (15 out of 16 cases of lymphedema patients had undergone neoadjuvant chemotherapy).

Conclusion

Approximately 8% of breast cancer patients in our study developed clinically significant lymphedema.

Non-dominant side malignancy, advanced stage of disease, post-operative wound infection/ seroma, large nodal burden and systemic therapy were significant risk factors for lymphedema development as per our study.

Prevention by means of diagnosis at an early stage of the disease, refined technique to minimize wound infection/seroma, post-operative arm care and exercises can reduce the development and severity of lymphedema.

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