



# Risk Factors for Lymphedema in Post Mastectomy Patients an Indian Scenario

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## Abstract

**Background:** Lymphedema (LE) is recognized as a common complication after Axillary Lymph Node Dissection (ALND). Numerous studies have attempted to identify risk factors for LE. However, it is difficult to predict the probability of LE for an individual patient. The purpose of this study was to construct a scoring system for predicting the probability of LE after ALND for Indian breast cancer patients.

**Patients and Methods:** 50 breast cancer patients were surveyed and followed for 90 days. LE was defined by circumferential measurement.

**Results:** The incidence rate of LE was 31.84%. Variables associated with LE and their corresponding score in the scoring system were: The level of ALND (level I=0, level II=1, level III=2), history of hypertension (yes =1, no =0), surgery on dominant arm (yes =1, no =0), radiotherapy (yes =2, no =0), and surgical infection/seroma/early edema (yes =2, no =0). The probability of LE was predicted according to the total risk scores.

**Conclusion:** Our scoring system could be a simple and easy tool for physicians to estimate the risk of LE.

**Aim:** To predict the risk factors of lymphedema in post modified radical mastectomy patients in Indian scenario.

**Keywords:** LE: Lymphedema; SLN: Sentinel Lymph Node; ALND: Axillary Lymph Node Dissection

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## Introduction

Breast cancer is the most common cancer among women worldwide with approximately 1.3 million people developing breast cancer each year [1,2]. At present, routine surgical treatments of breast cancer are either lumpectomy or mastectomy combined with Sentinel Lymph Node (SLN) surgery. Although the results of the ACOSOG Z0011 trial [3] suggest that women with clinically node negative T1-T2 tumors or fewer than 3 involved SLN cannot benefit from Axillary Lymph Node Dissection (ALND), for patients with positive SLN, ALND remains the standard practice. Complete ALND is associated with a nearly 3-fold increased risk of Lymphedema (LE) [4,5]. As breast cancer survival rate has increased dramatically, with 89% of these women surviving 5 years, LE will potentially impact more women [2]. LE is characterized by an abnormal accumulation of lymph in the interstitial spaces, leading to persistent swelling in the affected arm, shoulder, neck, breast, or thoracic region, or any combination of these [6]. LE has become a high-impact problem that profoundly impairs the quality of life in breast cancer survivors [7]. The reported prevalence of LE varies with the length of follow-up, the standardized definitions, measurement techniques, or other factors. Estimates for the incidence of LE in previous studies vary from 6.7% to 62.5% [8,9]. The onset of LE may occur at any time after breast cancer surgery, and there is no safe period after which an individual is no longer at risk for developing LE [6,10]. LE is a chronic, potentially disfiguring condition requiring early detection and management [11]. Therefore, identifying factors that place a breast cancer survivor at higher risk for developing LE is paramount. Studies have associated various risk factors with LE, such as the level of ALND, age, and radiotherapy [12]. While each of these factors contributes significantly and independently to LE, the combined effects of these factors on individual outcome have seldom been addressed. The aim of our study was to create a scoring system for predicting the individual probability of LE after ALND for Indian breast cancer patients.

## Patient and Methods

Retrospective study was done on a total number of 50 cases during a period of 180 days. Patients who had been diagnosed with breast cancer at integrated breast care center at All India Institute of Medical Sciences, Rishikesh and underwent ALND (level I, II, or III) were included in the study. Exclusion criteria included having history of any other cancer, previously operated in the same arm, bilateral breast cancer and synchronous breast cancer. Clinical data of patients were retrospectively collected. The data include: (a) age; (b) menopause; (c) BMI >25; (d) Hypertension; (e) number of lymph nodes involved; (f) type of surgery; (g) surgery in dominant hand; (h) surgical site infection; (i) number of lymph node dissected; (j) history of neoadjuvant chemotherapy; (k) patients on hormonal therapy. Grading of lymphedema was done taking all the above-mentioned factors in account. Lymphedema was categorized into four grades depending on the circumferential difference as compared to the opposite arm. All the patients who underwent mastectomy surgery and were in post-operative period were asked to mobilize their arms and were sent for adjuvant chemotherapy. Patients who underwent Breast conservation therapy underwent radiotherapy.

## Results and Observation

In our study conducted on 50 patients, 35 patients (70%) were in the age group more than 35 years and 15 patients (30%) were in the age group less than 15 years.

Peak age group was between 40 to 60 years. 24 patients out of 50 (48%) were in the post-menopausal age group while 26 patients (52%) were in premenopausal group.

35 patients (70%) were having Body mass index more than 25. 15 patients (30%) had body mass index less than 25. 46 patients out of 50 were hypertensive and 4 patients were normotensive. Most of the patients were brought to normotensive stage by oral medications before planning for surgery.

26 out of 50 patients were found negative for lympho-vascular invasion. 14 patients have <4 lymph nodes positive and 10 patients

were found to have more than 4 lymph nodes positive for invasion. Modified radical mastectomy was the preferred surgery in majority of patients. 46 out of 50 patients (92%) underwent Modified radical mastectomy, however only 4 patients (8%) consented for breast conservation surgery. 24 (48%) out of 50 patients had surgery done in dominant hand and 26 (52%) patients had surgery done in non-dominant hand. The incidence of surgical site infection was quite less in our set-up. Only 20% cases, that is 10 out of 50 patients had surgical site infection while 40 (80%) out of 50 patients were non-infected. More than 4 number of axillary lymph nodes were dissected in 42 patients (84%) and less than 4 axillary lymph nodes were dissected in 8 (16%) patients. 19 (38%) out of 50 patients received neoadjuvant chemotherapy. Hormonal chemotherapy was given in 35 (70%) patients after getting the immunohistochemistry done. Out of 50 patients, 92% i.e.; 46% were normotensive and rest 8% i.e.; were hypertensive. In the category of patients with grade 0 lymphedema, 33 (100%) were in normotensive group. No patient was hypertensive in Category of Grade 0 lymphedema. In Grade I lymphedema, 12 patients (100%) were normotensive. No patient was hypertensive in Category of Grade 1 lymphedema. Only 1 (20%) patient was in normotensive range with Grade 2 lymphedema and 4 (80%) were having hypertension. P value of clinical characteristic was significant -0.00.

## Statistical Analysis

All the statistical analysis was done using R × C contingency table test and p value was taken out. P value for all the clinical characteristics were calculated. Out of all the clinical characteristics, p value came out to be significant only for hypertension- 0.00. Degree of freedom was 2 in all.

## Discussion

The scoring system that we have developed is composed of 5 clinic pathological factors: the level of ALND, history of NACT, surgical infection/seroma/early edema, history of hypertension, BMI>25 and surgery on dominant arm. The 3 most heavily weighted factors were the level of ALND, BMI>25 and Hypertension.

**Table 1:** Grading of lymphedema.

A)

<b>Grade 0</b>	Circumferential difference of <10 % from opposite arm
<b>Grade 1</b>	Circumferential difference of 10% to 19 % from opposite arm
<b>Grade 2</b>	Circumferential difference of 20 to 29 % from opposite arm
<b>Grade 3</b>	Circumferential difference of 30% to 39 % from opposite arm
<b>Grade 4</b>	Circumferential difference of >40 % from opposite arm

B)

Age	Less than 60 years: - 35	More than 60 years: - 15
<b>Menopause</b>	Yes - 24	No - 26
<b>BMI&gt;25</b>	Yes - 35	No -15
<b>Hypertension</b>	Yes - 4	No - 46
<b>Number of lymph nodes involved</b>	Negative - 26	1-4: - 14
<b>Type of surgery</b>	MRM: - 46	BCS: - 4
<b>Surgery in dominant hand</b>	Yes: - 24	No: - 26
<b>Surgical site infection</b>	Yes: - 10	No: -40
<b>Number of lymph nodes dissected</b>	1-4: - 8	More than 4: - 42
<b>History of neoadjuvant chemotherapy</b>	Yes: - 19	No: - 31
<b>Patients on hormonal therapy</b>	Yes: - 35	No: - 15

C)

Clinical characteristics	Lymphedema grade 0	Lymphedema grade 1	Lymphedema grade 2	Total	P Value
<b>Age (in years)</b>					
age < 60	10 (31.25%)	3 (25%)	2 (28.57%)	15 (30%)	
age > 60	22 (68.75%)	9 (75%)	5 (71.42%)	35 (70%)	0.92
<b>Menopausal Status</b>					
Premenopausal	18 (54.54%)	6 (50%)	2 (40%)	26 (52%)	
Postmenopausal	15 (45.45%)	6 (50%)	3 (60%)	24 (48%)	0.821
<b>BMI status</b>					
BMI < 25	11 (33.33%)	4 (33.33%)	0 (0%)	15 (30%)	
BMI > 25	22 (66.66%)	8 (66.66%)	5 (100%)	35 (70%)	0.304
<b>Hypertension</b>					
Normotensive	33 (100%)	12 (100%)	1 (20%)	46 (92%)	
Hypertensive	0 (0%)	0 (0%)	4 (80%)	4 (8%)	0
<b>Lymph Nodes Involved</b>					
Negative	18 (54.54%)	6 (50%)	2 (40%)	26 (52%)	
1-4 Lymph nodes	11 (33.33%)	2 (16.66%)	1 (20%)	14 (28%)	0.793
>4 lymph nodes	4 (12.12%)	4 (33.33%)	2 (40%)	10 (20%)	
<b>Surgery in dominant Hand</b>					
Surgery in dominant Hand	16 (47.05)	4 (33.33%)	4 (80%)	24 (48%)	
Surgery in non - dominant Hand	18 (52.94%)	8 (66.66%)	1 (20%)	26 (52%)	0.214
<b>Surgical Site Infection</b>					
Surgical site infection	8 (24.24%)	1 (8.33%)	1 (20%)	10 (20%)	
No Surgical site infection	25 (75.75%)	11 (91.66%)	4 (80%)	40 (80%)	0.499
<b>Number of Lymph node dissected</b>					
01-Apr	7 (21.21%)	1 (8.33%)	0 (0%)	8 (16%)	
>4	26 (78.78%)	11 (91.66%)	5 (100%)	42 (84%)	0.342
<b>History of NACT</b>					
Patients received NACT	13 (39.39%)	4 (33.33%)	2 (40%)	19 (38%)	
Patient without NACT	20 (60.60%)	8 (66.66%)	3 (60%)	31 (62%)	0.929
<b>Hormonal Therapy</b>					
Received Hormonal Therapy	21 (63.63%)	11 (91.66%)	3 (60%)	35 (70%)	
Did not Received Hormonal therapy	12 (36.36%)	1 (8.33%)	2 (40%)	15 (30%)	0.169

The incidence of lymphedema of arm after axillary lymph node dissection is varying between 10% to 37% and increases with incidence of lymph nodes removed [1,2]. The cause of limb lymphedema after surgery may be fibrosis development after radiotherapy/NACT which induces lymphatic constriction, subsequently decreasing the filter function of lymph nodes. Another important risk factor is the number of lymph nodes [5,6]. NACT after modified radical mastectomy or breast conservation surgery with lymph nodal dissection is another important risk factor for lymphedema.

In our study, the incidence of arm lymphedema was more in the patients in whom more than 4 axillary lymph nodes were dissected. Grade 0 lymphedema cases were more in our study as predominantly level I axillary lymph nodal dissection was done. Only in few cases level II axillary dissection was done, while level III lymph nodal dissection was not done in any of the patients. Authors like Larson et al. [5], Kiel et al. [9], Senofsky et al. [10] found in their studies that the number of removed lymph nodes excised is another important risk factor for lymphedema occurrence. However, in our study, p value

for number of lymph node dissected came out to be 0.342 -which was clinically insignificant.

We had four cases of hypertension, all of which developed Grade 2 lymphedema. There is a documented association between lymphedema and hypertension. The reason owes to high capillary pressure that facilitates leakage of fluid into the tissues. Few studies have reported an association between lymphedema and hypertension. In the study conducted at our institution, P value of clinical characteristic was 0.00 -that was clinically significant.

35 patients in our study have BMI>25, who underwent surgery and developed Grade 0 and 1 lymphedema. Ozasalan et al. [1] found in their study that BMI>25 is an important independent risk factor for lymphedema. P value in the study conducted in patients of BMI was 0.304 -which was clinically insignificant.

Physical activities such as level of exercise and lymphedema risk reduction behavior were included in our study. All the patients irrespective of type of surgery were instructed about shoulder

exercises from post-operative day-one itself. Our explanation of this phenomenon is that the patients in our study were given sufficient education about prevention exercises, and thus they were able to handle the intensity of excise. Some variables have long been recognized as risk factors for LE, e.g. tumor size, tumor stage [13,14]. However, these factors were not found to be independent predictors in our study. Most of the patients underwent MRM and ALND. Few patients had BCS; none of the patients have undergone breast reconstruction surgery. Our scoring system might not be validated datasets. Further work is needed to validate our scoring system could be a simple and easy tool for both the physician and patients to estimate the risk of LE.

Hypertension was found to be a major clinically significant risk factor in patients developing lymphedema postoperatively. As our study was on a limited sample size, (50) patients; therefore, sample size has to be increased and further detailed study needs to be done for better results.

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