



### Original Research Article

## Distribution of Early-Stage Lymphedema and Risk Factors in Postoperative Patients with Breast Cancer: A Hospital Based Study

Authors

**Dr Swodeep Mohanty<sup>1</sup>, Dr Krupa Sindhu Panda<sup>2</sup>**

<sup>1</sup>MS, FMAS, FAIS, Assistant Professor, Department of Surgical Oncology

Email: [swodeep@gmail.com](mailto:swodeep@gmail.com)

<sup>2</sup>Chief and Head, Department of Surgical Oncology

<sup>1</sup>Acharya Harihar Regional Cancer Centre, Cuttack, Odisha, India

<sup>1,2</sup>Panda Medical Centre, Bepari Sahi, Cuttack, Odisha, India

### Abstracts

*Lymphedema is a highly prevalent condition in women who have undergone treatment for breast cancer. Lymphedema negatively affects the quality of life. Lymphedema development, which affects the quality of life negatively, is defined as interstitial tissue effusion rich in protein as a result of failure in the lymphatic system in patients who undergo surgical treatment and radiotherapy (RT) for breast cancer. In the routine follow-up of the cases, the clinical and histopathological data and the data relating to the surgical procedure assessed at the 12th month were examined retrospectively, and arm measurements were made for lymphedema evaluation. In this study, we determining the early-stage postoperative lymphedema distribution and specifying the risk factors in its development.*

**Key words:** Breast cancer, Lymphedema, & Risk Factor

### Introduction

The increase in the survival time of breast cancer cases in the last 2 decades has brought health problems in the long term relating to treatment.<sup>1</sup> Lymphedema development, which affects the quality of life negatively, is defined as interstitial tissue effusion rich in protein as a result of failure in the lymphatic system in patients who undergo surgical treatment and radiotherapy (RT) for breast cancer.<sup>2</sup> Even though the lymphedema development rates are given as 30% in the literature, there are many studies which that it in a large range of 2%-83%.<sup>3-5</sup> Breast cancer continues to be the most frequently occurring cancer in women. With the advent of multimodality

treatment and early detection methods, there is an overall improvement in survival. With this transformation of the disease into a chronic condition the focus of attention is recently being directed towards late post treatment sequelae like lymphedema. Complications of varying magnitude occur in up to 8 to 63% of patients following breast cancer treatment.<sup>6-9</sup> The incidence of upper extremity lymphedema varies from 2% to 40% in women with breast cancer who have been treated with surgery, radiation, or both.<sup>10,11</sup> The reasons for the wide range of reported prevalence rates of lymphedema are related to lack of standard diagnostic and universal assessment criteria, insidious nature of

onset, prolonged clinical course and limited physician knowledge. The overall treatment approach towards breast cancer has changed in the recent past and there is a trend towards less radical surgical procedures. In our study, we aimed to determine the early-stage postoperative lymphedema distribution and specifying the risk factors in its development.

### Material and Methods

This study was conducted in the DEPARTMENT OF SURGICAL ONCOLOGY, PANDA MEDICAL CENTRE (PMC) BEPARI SAHI CUTTACK, ODISHA, INDIA. A total 45 patients diagnosed having one-sided breast cancer who had surgical intervention to the breast and axilla between January, 2014 to December, 2015 were included in the study. In the routine follow-up of the cases, the clinical and histopathological data and the data relating to the surgical procedure assessed at the 12th month were examined retrospectively, and arm measurements were made for lymphedema evaluation. Among the factors relating to the patient envisioned as risk factors, age (<45 or ≥45), BMI (<25 kg/m<sup>2</sup>, ≥25 kg/m<sup>2</sup>), smoking status, arm dominance (present or not), the surgery of breast [mastectomy/breast-conserving surgery (BCS) and axilla (axillary dissection (AD)] applied, dissected number of LN, LN positivity, postoperative seroma and infection development (present or not), CT or RT treatment, grade (1,2,3) relating to the T, size (T1, T2, T3), and parameters of histopathological type were evaluated (Table 1,2,3).

### Arm Lymphedema Measurement Method

The circumferential measurement method was used. Circumferential measurements were made in four regions of both upper extremities: the metacarpophalangeal joint, wrist, and 10 cm distal and 15 cm proximal to the lateral epicondyle. A diameter difference of more than 2 cm in the measurements made at the four regions compared to the healthy side was evaluated as lymphedema presence.<sup>12</sup>

All of the cases were informed of lymphedema and protective measures after the clinical evaluation. The cases in which lymphedema development was determined were taken into a treatment program by the Physical Treatment and Rehabilitation Clinic, and written informed consent was obtained from patients who participated in this study.

### Statistical Analysis

We used student t-test and Pearson's correlation coefficient to find the statistical significance. A P-value <0.05 was to be considered statistically significant.

### Results and Discussion

Our study enrolled total 45 patients and their distribution of parameters in the case groups shown in Table-1,2,3. With the transformation of breast cancer into a chronic disease, there is a greater emphasis on quality of life and long-term post treatment sequelae. There is an expectation on the part of patients, their families and caregivers that the patient should lead a near normal life style. One problematic condition for women following breast cancer treatment is lymphedema. Except for breast cancer recurrence, no event is more dreaded than the development of lymphedema. Lymphedema can cause severe physical and psychological morbidity in breast cancer survivors and measurable reduction in quality of life in respect to functional, emotional, physical and social wellbeing.<sup>13,14</sup>

Apart from surgical oncologists more and more general surgeons are doing breast surgery. So more technical aspects are not followed and results in lymphoedema post operatively. Brachial fascia not to be removed. Level III nodes done only in FNAC positive case. Post operative exercises after 15 days, circular massages and shoulder moment (all 7 moments of joint physiotherapy) should be done. Dynamic compression device can be used. Radiation induced lymphoedema occurs late and should one should be careful from the beginning to follow the preventive patterns as it appears late.

**Table 1.** The distribution of parameters in the case groups:

Parameters		All case groups (N=45)%	Lymphedema (+ve) (N=5)%	p- value
Age	>45	22(48.9%)	3(60%)	0.001
	<45	23(51.%)	2(40%)	
BMI	>25	15(33.3%)	1(20%)	1.10
	<25	30(66.7%)	4(80%)	
Smoking status		2(4.4%)	0	
Arm dominance		24(53.33%)	1(20%)	0.71
Mastectomy/BCS	Mastectomy	29(64.4%)	2(40%)	0.12
	BCS	16(35.5%)	3(60%)	
AD	AD	25(55.5%)	5(100%)	0.001
The number of LN dissected in cases to whom AD has been applied		6(7-16)	13(20-32)	0.07
LN positivity		1(0-4)	4(5-25)	0.012
Cases with 7≤LN dissection		23(51.11%)	5(100%)	0.011
Seroma development		14(31.11%)	4(80%)	0.71
Infection development		3(6.7%)	1(20%)	1.20
RT treatment (+)		28(62.22%)	5(100%)	0.05
CT treatment (+)		22(48.9%)	5(100%)	1.01

**Table 2:** shows the tumor grade and tumor size.

Parameters		All case groups (N=45)%	Lymphedema (+ve) (N=5)%
Tumor Grade	1	2(4.4%)	0
	2	40(88.9%)	5(100%)
	3	3(6.7%)	0
Tumor Size (T)	T1	10(22.22%)	1(20%)
	T2	33(73.33%)	3(60%)
	T3	2(4.4%)	1(20%)

**Table 3:** shows the Histopathological type

Histopathological type	All case groups (N=45)%	Lymphedema (+ve) (N=5)%
Invasive ductal carcinoma	36(80%)	4(80%)
Tubular carcinoma	2(4.44%)	0
Papillary carcinoma	2(4.44%)	0
Medullary carcinoma	1(2.22%)	0
Invasive lobular carcinoma	1(2.22%)	0
Apocrine carcinoma	2(4.44%)	0

The most important reason of such a large range of lymphedema incidence is the timing differences in detection and evaluation.<sup>15</sup> In the evaluation of lymphedema, volumetric measurement, circumferential measurement, tissue tonometer, or imaging techniques are used. While it is known that volumetric measurement techniques give

more accurate results, the circumferential measurement technique is used more frequently because of its higher practicability.<sup>16</sup> For this reason, we used the circumferential measurement technique in our study. The 6th postoperative month is envisioned as the best time for the evaluation, when the adjuvant CT and RT are

usually completed and the lymphedema symptoms became measurable.<sup>17</sup> In our study, lymphedema development was found in 5 (11.11%) cases at the assessment at the 12th month.

When the risk factors were assessed in patients with lymphedema development, no statistically significant difference was found between the cases aged over 45 and under 45 in terms of lymphedema development. Geller et al.<sup>21</sup> reported a significant increase in lymphedema development risk in women aged under 45. In many studies where age is assessed in the literature, similar to the results we obtained, this factor did not show a significant effect on lymphedema development.<sup>5, 18, 20, 21, 22</sup>

When BMI was assessed as a risk factor, it was seen that there was no statistically significant difference between the BMI values of  $>25$  or  $\leq 25$  on lymphedema development. In the studies, lymphedema development risk shows a 2-fold increase in cases where BMI is over 30. Even though its etiology is unclear, it is thought to occur because of increased fat and the subcutaneous tissue's role as a lymphatic fluid resource or the increase in lymphatic damage as a result of the need for more ecartation in axillary intervention.<sup>19</sup>

In many studies present in the literature where smoking status and arm dominance are assessed, they are not found to be potent risk factors in lymphedema development, similar to our findings.<sup>20, 23, 24</sup>

It is reported that the range of surgery of the breast and axilla and adjuvant treatments, such as RT, may increase the risk of lymphedema.<sup>25</sup> Schunemann and Willich et al.<sup>26</sup> reported lymphedema development rates after radical mastectomy without postoperative RT, modified radical mastectomy (MRM), and BCS of 22.3%, 19.1%, and 6.7%, respectively. In most of the studies in the literature, it is reported that there is a relation between AD range and lymphedema incidence. Siegel et al.<sup>27</sup> reported that the lymphedema incidence of 37% with level I, II, and III dissection reduces to 8% when only level I and II dissection is applied. Moreover, in a study

where BCS was applied, the lymphedema rate of 15% in the cases in which lumpectomy and AD were performed reduced to 3% in cases with only lumpectomy.<sup>28</sup> In many studies, the LN number dissected was found to increase the lymphedema risk.<sup>17, 29, 30</sup> It is reported that the lymphedema frequency, which is recommended to be performed in axilla-negative cases today compared to AD.<sup>31-38</sup>

In our study, RT treatment seemed to be one of the major factors that increased the lymphedema incidence. In the literature, even cases without surgical intervention with RT to the axilla showed increased lymphedema incidence; moreover, with the combination of AD, it is reported to increase the lymphedema risk even more by showing a synergistic effect.<sup>39</sup> In similar studies, the lymphedema incidence in patients to whom RT was applied in addition to surgery was 41%, while this ratio was 17% in patients in whom surgery was performed alone.<sup>40, 41</sup>

It is reported in the literature that infection and seroma development with adjuvant CT treatment do not increase the lymphedema incidence. No significant difference in these parameters in terms of lymphedema development was found in our study.

In all 5 (11.11%) cases in which lymphedema development was found, the T grade was 2. T histopathology revealed invasive ductal carcinoma in 4(80%) cases and inflammatory carcinoma in 1 (20%) case.

When the relationship between the T value and lymphedema incidence was assessed, T1 was seen in 1(20%) T2 was determined in 3 (40%), and T3 was determined in 1(20%) cases. When compared to the whole case group, a significant difference was determined between T size and lymphedema incidence. In many studies, T diameter was found to be a potent factor in lymphedema development.<sup>20, 42, 43</sup>

As a result, a statistically significant relationship has been determined with the range of the AD ( $7 \leq$  LN), dissected positive LN number, RT, and T and early-stage lymphedema incidence. The wide-spread prevalence of cases with early-stage breast

cancer diagnosis, small T sizes, and absence of application of RT to the axilla (as the axillary involvement is lower), as well as where the axilla is clinically negative, are the basic reasons of the low lymphedema rates in our study group.

Conclusion:

We conclude that lymphedema is a preventable morbidity. The planning of health programs and services appropriate to the immediate postoperative treatment of women with breast cancer, and increasing the awareness of health professionals regarding the early diagnosis of lymphedema, can help minimize morbidity. Understanding and improved definitions of the associated factors could be important tools for treatment of this condition.

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#### Author Profile



**Dr Swodeep Mohanty** MS, FMAS, FAIS, Assistant Professor, Dept of Surgical Oncology Acharya Harihar Regional Cancer Centre, Cuttack, Odisha, India  
Panda Medical Centre, Bepari Sahi, Cuttack, Odisha, India  
Email: [swodeep@gmail.com](mailto:swodeep@gmail.com)