Study of Lymphedema Risk Factors among Patients with Invasive Breast Cancer after the Initial Treatment

Saedi H[1], Taghizadeh Kermani A[2], Afzal Aghaee M[3], Mottaghi T[4], Moghadam S[5]

1- Assistant professor of radiation oncology, Gilan University of Medical Sciences, Rasht, Iran.
2- Assistant professor of radiation oncology, Mashhad University of Medical Science, Mashhad, Iran.
3- Community Medicine Specialist, Mashhad University of Medical Sciences, Mashhad, Iran.
4- General Practitioner, Mashhad University of Medical Sciences, Mashhad, Iran.
5- Radiation Oncologist, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Corresponding Author: Moghadam S
Email: moghadamshiva@yahoo.com

Abstract

Introduction: Upper limbs lymphedema is one of the rather common and debilitating sequels of breast cancer treatment. The incidence of this sequel has been reported in different sources to be from 25% to 38%. The purpose of this study was to evaluate the incidence and the risk factors of lymphedema following invasive breast carcinoma treatment.

Materials and methods: Recorded data of breast cancer patients referred to Mashhad Omid Hospital between 1997 and 2005 were evaluated for the incidence and risk factors of lymphedema. Univariate and multivariate analysis were performed to evaluate the risk factors using a logistic regression model.

Results: Out of 312 patients entering the study 101 patients (32.4%, 95% CI: 27.2-37.6) developed lymphedema. Univariate analysis did not show a statistically significant difference between the rates of lymphedema in radical mastectomy when compared to other types of surgery such as lumpectomy with axillary dissection. Obesity according to body mass index significantly affected the development of lymphedema (p=0.03). The average number of metastatic nodes was 4.56±4.05 in patients who had and 2.48 ± 3.19 in patients who did not have lymphedema (p<0.01). The average percentage of metastatic to excised nodes was %54.59 ± 37.48 in patients who had and %34.67 ± 34.84 in patients who did not have lymphedema (p<0.01). Age, the number of excised nodes, the stage of disease, hormonal therapy, adjuvant radiation therapy and chemotherapy had no correlations with lymphedema.

Conclusion: According to our findings, body mass index, the number of metastatic nodes and the percentage of metastatic to excised nodes were correlated with the development of lymphedema.

Key words: Breast carcinoma, surgery, lymph node, lymphedema, body mass index, radiotherapy, risk factor.

Introduction

Breast cancer continues to be the most frequently occurring cancer among women. With the advent of multimodality treatment and early detection methods, there is an overall improvement in survival [1]. 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 [2]. Upper limbs lymphedema is a common and debilitating sequel of breast cancer treatment [2]. The incidence of this sequel varies between % 25 and % 38 according to different studies [3]. Lymphedema in breast cancer patients is caused by interruption of the axillary lymphatic system by surgery or radiation therapy, leading to decreased distensibility of tissue around the joints and increased weight of the extremity[3]. Depending on its severity, this sequel can cause many problems for the affected patients including repeated infections, impaired daily activities, increased probability of limb angiosarcoma, and decreased quality of life [3]. Axillary lymph node dissection and axillary radiation therapy have been cited as the most important risk factors for lymphedema [4]. The purpose of this study was to evaluate the incidence of lymphedema in treated breast cancer patients and its relation to factors

like age, Body Mass Index (BMI), the number of resected and involved axillary lymph nodes, disease stage, surgical method, and receiving adjuvant treatments including chemotherapy, radiotherapy, and hormone therapy.

Materials and methods

In this cross sectional study, the oncologic files of 312 breast cancer patients who had been referred to Omid Hospital, Mashhad, Iran, between 1997 and 2005 were studied. The incidence rate of lymphedema was calculated and its relation with variables including age, Body Mass Index (BMI), the number of resected and involved axillary lymph nodes, disease stage, surgical method, and receiving adjuvant treatments including chemotherapy, radiotherapy, and hormone therapy was evaluated. All patients' data relating to this study including the demographic findings were recorded in a predesigned information sheet. SPSS version 11 was used for statistical analysis. Central indexes and data variations were used to report

the quantitative variables and frequency was calculated for qualitative variables. Then the effects of these factors on lymphedema were evaluated using logistic regression method.

Results

Of 312 patients who were included in the study, 101 (% 32.4, % 95 CI: 27.2-37.6) had lymphedema. The mean age of the study population was 47.6 ± 11.62 years. The demographic data of study participants is summarized in table 1.

The mean age of patients with and without lymphedema was 48.33 ± 10.53 and 47.6 ± 11.46 years, respectively and the difference between the two groups was not statistically insignificant (p = 0.6) (Table 2).

There was a statistically significant between patients BMI and the incidence of lymphedema (p = 0.03) (Table 2).

No statistically significant relation between the stage of disease and lymphedema was observed although this relation approached statistical

Table 1: Demographic findings among patients entering the study.

Parameter		Value
Age	Mean ± SD	47.6 ± 11.62
BMI	Low weight	12 (3.8%)
	Normal	113 (36.2%)
	Overweight	121 (38.8%)
	Obese	66 (21.2%)
Stage	I	15 (4.8%)
	II	172 (55.1%)
	III	103 (33.0%)
	IV	22 (7.1%)
The number of involved lymph nodes	Mean ± SD	3.4 ± 3.58
The number of resected lymph nodes	Mean ± SD	8.6 ± 4.87
Percentage of involved to resected lymph nodes	Mean ± SD	41.14 ± 36.86
Surgery	Radical mastectomy	16 (5.1%)
	MRM	286 (91.7%)
	Lumpectomy + axillary dissection	10 (3.2%)
Therapy	Radiotherapy	268 (85.9%)
	Chemotherapy	294 (94.2%)
	Hormone	204 (65.4%)

significance (p=0.06) (Table 2).

The mean number of involved lymph nodes in the study population was 3.4 ± 3.58. The mean number of involved lymph nodes was 2.84 ± 3.19 in patients without and 4.56 ± 4.05 in patients with lymphedema; the difference was statistically significant (P value <0.01) (Table 2).The mean number of the resected lymph nodes in the study population was 8.6 ± 4.87. The mean number of the resected lymph nodes was 8.68 ± 4.71 in patients without and 8.44 ± 5.21 in patients with lymphedema but the difference was not significant (p = 0.67) (Table 2). The mean percentage of involved to resected lymph nodes was % 41.14 ± 36.86 in the study population, % 34.67 ± 34.84 in patients without lymphedema and %54.59 ± 37.48 in lymphedematous patients. The difference between the two groups was statistically significant (p <0.01) (Table 2).

Modified Radical Mastectomy (MRM) was performed in % 91.7 of the study population of them 90 patients (%31.5) showed lymphedema. The percentage of lymphedema in other patients who underwent radical mastectomy and lumpectomy with axillary dissection was 56.3% and % 20, respectively. The difference between these three groups of surgery in univariate analysis was not significant (p = 0.08) (Table 2).

Overall, radiotherapy, chemotherapy and hormone therapy was performed in % 85.9, % 94.2, and 65.4% of the patients, respectively. There was not a statistically significant difference between these groups considering the number of patients with lymphedema (p = 0.43) (Table 2).

Of patients who received hormone therapy, 33.3% showed lymphedema and % 66.7 did not but the difference was not significant (p = 0.61) (Table 2).

In patients who received chemotherapy, % 68.5 had no lymphedema while % 31.5 showed lymphedema. This difference was not statistically significant, either (p = 0.59) (Table 2).

Discussion

According to our study, the prevalence of lymphedema was about 32.4%, which is almost

Table 2: Risk factors of lymphedema in breast cancer patients.

Parameter			With lymphedema (N=101)	Without lymphedema (N=212)	P*
Age	Mean ± SD		47.6 ± 11.46	48.33 ± 10.53	0.6
BMI	Low weight		2 (2.0%)	10 (4.7%)	0.03
	Normal		27 (26.7%)	86 (40.8%)	
	Overweight		45 (44.6%)	76 (36.0%)	
	Obese		27 (26.7%)	39 (18.5%)	
Stage	I		3 (3.0%)	12 (5.7%)	0.06
	II		51 (50.5%)	121 (57.3%)	
	III		37 (36.6%)	66 (31.3%)	
	IV		10 (9.9%)	12 (5.7%)	
Involved lymph nodes	Mean ± SD		4.56 ± 4.05	2.84 ± 3.19	<0.01
Resected lymph nodes	Mean ± SD		8.44 ± 5.21	8.68 ± 4.71	0.67
Percentage of involved to resected lymph nodes	Mean ± SD		54.59 ± 37.48	34.67 ± 34.84	<0.01
Surgery	Radical mastectomy		9 (8.9%)	7 (3.3%)	0.08
	MRM		90 (89.1%)	196 (92.9%)	
	Lumpectomy + axillary dissection		2 (2%)	8 (3.8%)	
Therapy	Radiotherapy		86 (85.1%)	165 (78.2%)	0.43
	Chemotherapy		98 (97.0%)	196 (92.9%)	0.61
	Hormone		64 (63.4%)	140 (66.4%)	0.59

* Based on logistic regression

similar to other reports [1, 5, 6]. We did not notice any statistically significant correlation between the disease stage and development of lymphedema, while some other studies, such as a study on 300 breast cancer patients in Rotari Hospital, India, concluded that the development of lymphedema was related to disease stage through single variable analysis [1].

In the present study, adjuvant radiotherapy was not related to the development of lymphedema; however, some studies have reported positive correlation using single variable and multiple variable analysis [1, 5, 7, 8, 9, 10]. Of various treatment factors which we evaluated, the method of surgery did not show a significant correlation with lymphedema.

Also, the prevalence of developing lymphedema was significantly higher in overweight and obese patients, which is similar to other studies [1, 6, 11, 12].

In some studies, developing pain, motion restriction, and other lymphedema signs were higher in younger ages [13]. However, in our study, the mean age was similar in patients with and without lymphedema.

The mean number of involved lymph nodes in the patients without lymphedema and in patients with lymphedema showed a statistically significant difference.

Many similar researches have also found a significant correlation between developing lymphedema and the number of involved lymph nodes [7, 9, 14, 15].

In contrast in a study performed by Purushotham et al., the number of positive nodes was inversely associated with arm volume. These results were counterintuitive to the conventional understanding of the pathophysiology of breast cancer related lymphedema. A possible explanation is that patients who develop disease in axillary lymph nodes and subsequently undergo axillary lymph nodes dissection have more time and ability to develop lymphatic collaterals, which may provide adequate lymphatic drainage following surgery, thereby reducing the risk of developing lymphedema [16].

In multivariate analysis, factors such as BMI, the number of involved lymph nodes, and type of surgery were associated with developing lymphedema. An increase in BMI and the number of involved lymph nodes raised the possibility of developing lymphedema, while lumpectomy + axillary dissection lowered this possibility. These findings were similar to other studies in this subject [1, 7, 11, 12, 15].

Conclusion

According to our study, body mass index, metastatic nodes and metastatic to excised nodes were correlated with the development of lymphedema.

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