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Research Article

Evaluation of Occurrence of Arm Lymphedema After Breast Cancer Treatment

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Abstract

Introduction: Breast cancer related lymphedema is a chronic and recurrent condition involving the lymphatic and blood systems.

Objective: Objective is to determine, within our survey, the incidence of breast cancer related lymphedema as well as to a study the different risk factors relating to the occurrence of arm lymphedema.

Materials and Methods: Sectional study carried out over a period of two years from January 1, 2018 to December 31, 2019 covering all women treated for breast cancer in the obstetrics and gynecology department of University Hospital center MOHAMED VI in Marrakesh.

Results: The incidence of BCRL is 26.5% (22/83 patients), after a median follow up of 48 months. 64% of them have minimal disability according Dash score; 36% of patients with lymphedema had rehabilitation. However, improvement of lymphedema was observed by patient in 7 cases. Parameters predicting lymphedema were studied. Significant risk factors were higher BMI, diabetes and the long time to treatment initiation between diagnosis of BC and treatment, the type of surgery, ALND, RLNR, CT did not predict lymphedema.

Conclusion: The development of arm lymphedema is an unpredictable occurrence that can happen years after axillary surgery, findings from this study can help health professionals in educating breast cancer survivors about lymphedema risk factors, as well as early detection and management of it by use of circumferential arm measurements to evaluate limb evolution during follow-up care.

Keywords: *Arm Lymphedema; Incidence; Risk Factors; Breast Cancer*

Abbreviations

ALND: Axillary Lymph Node Dissection; BC: Breast Cancer; BCLR: Breast Cancer Related Lymphedema; BMI: Body Mass Index; CT: Chemotherapy; RNLR: Regional Lymph Node Radiation

Introduction

Breast cancer occurs when cells in the breast begin to grow out of control, it became the most commonly diagnosed cancer type since 2020, beside the most common cause of cancer death in women and the fifth most common cause of cancer death overall. In Morocco, breast cancer represents a serious public health disease, it's the first cancer among women and the third one of all registered cancer

cases, with the increase of incidence the last decade. In the region of Marrakech-Safi in Morocco, through a retrospective study in 2020 spread over 10 years from January 1, 2007 to December 31, 2017 on all women treated for breast cancer in the obstetric gynecology service of the University hospital center MOHAMED VI in Marrakech, 1790 cases of breast cancer were identified [1,2]. Lymphedema secondary to the treatment of breast cancer is a chronic and recurrent condition involving the lymphatic and blood systems [2,3]. The dysfunctional lymphatic system becomes less capable of performing the complete resorption of large protein molecules, and these remain in the interstitial space. The consequent tissue fibrosis and the increasing accumulation of fluid and proteins in this space can trigger neurological alterations such as pain or paresthesia, distortion in the shape of the limb, and increased risks of related complications [4,5]. Chronic lymphedema causes physical deficiencies and psychological stress, which worsens with the progression of the dysfunction, to reduce the discomfort of the patient and improve the quality of life, an accurate diagnosis of lymphedema is essential for prognosis and treatment planning [6].

Objective of the Study

Is to determine, within our survey, the incidence of breast cancer related lymphedema as well as to a study the different risk factors relating to the occurrence of arm lymphedema.

Materials and Methods

This is a cross sectional study carried out over a period of two years from January 1, 2018 to December 31, 2019 covering all women treated for breast cancer in the obstetrics and gynecology department of University Cadi Ayad, Hospital center MOHAMED VI in Marrakesh. We used medical files from the department 's archives; we collected all the informations from the files including the phone number of patients. Selected women with breast cancer treatment were invited to participate in this study, the Research Ethics Committee of the Faculty of Medicine and Pharmacy of Marrakesh approved the study. The data collected was strictly confidential. The research protocol did not affect the patient's health, safety, or privacy. Reference photos (Figures 1-3).

Results

During the period of our study, spanning 2 years, the total number of breast cancer files that we were able to explore was 254. Among 254 (100%) selected patients, 83 (32%) were included, 36 (14.17%) patient refused due to the distance from Marrakech and the lack of financial means, 55 patients died (21%) and 64 (25%) patients were inaccessible due to telephone unreachability. The incidence of lymphedema was 26.5% after a median follow-up time of 4 years with minimum and maximum were 3 to 5 years.

Among the patients diagnosed with arm lymphedema the mean age was around 48 years; the extremes were 29 and 66 years. The mean of body mass index was 30 among patients with lymphedema and the minimum and maximum were 23,8 and 34,4. Over 50% of our patients were in the obesity range. While the mean of Body mass index in patients without lymphedema was 27 and the minimum and the maximum were 18,7 and 34,7, over 40% of them were in the overweight range.

About 36.4% (8 cases) were diabetic among patients with arm lymphedema, while only 14.8% (9 cases) were diabetic in patients without lymphedema. We observed only two cases 9.1% of high blood pressure in patients with arm lymphedema.

The invasive ductal carcinoma was the most frequent type in this study in both categories, 72.7% among patients with arm lymphedema vs 86.9% of patients without arm lymphedema, followed by the invasive lobular carcinoma type respectively with 22.7% vs 8.2%. The bivariate analysis wasn't applicable due to the large categorization and the small sample included in this study.

Among the patients with lymphedema T4, N0, and M0 are the most frequent whereas, T1/T2, N0 and M0 are the most represented among the patients without lymphedema the bivariate analysis cannot be applicated due to the small sample compared to the categorization, also

it was limited due to the absence of the exact numbers of lymph nodes removed in the anatomic pathology reports of the patients. During this study, more than 3 of 4 carcinoma (75%) was diagnosed in grade II in both categories of patients.

The therapeutic tools were: surgery, chemotherapy, radiation therapy, hormone therapy and physiotherapy. The mastectomy with axillary lymph node dissection was the most surgery type practiced during our study in both categories of patients. All patients (N = 83) had undergone axillary lymph nodes dissection. All patients with arm lymphedema 22 (100%) had chemotherapy, whereas 54 (88.5%) of patients without arm lymphedema underwent chemotherapy treatment. More than 50% of patients with arm lymphedema had neoadjuvant chemotherapy vs 37% in patients without arm lymphedema while 63% of patients without lymphedema had adjuvant chemotherapy vs 40.9 in patients with arm lymphedema. 77.3% of patients with arm lymphedema were radiated during this survey, while 55.7% of patients without arm lymphedema had undergone radiotherapy. Around 86.4% of patients with arm lymphedema received hormonotherapy. Lymphedema occurred in 22 patients (26.5%), and only 8 (36,4%) patients who had physiotherapy during this study.

Lymphedema was defined as being present when the volume of the ipsilateral arm was 200 cm^3/ml or greater than that of the contralateral arm. Most patients with arm lymphedema were in stage I of arm lymphedema 17 (77.4%) with minimum and maximum of arm volume difference were 234 ml and 382.3 ml respectively.

Most of patients with arm lymphedema 64% have minimal disability, 27% have moderate disability and only 9% of them have severe disability. Whereas all the patients without arm lymphedema have minimal disability with minimum and maximum were 0% and 8.3% (Figure 1).

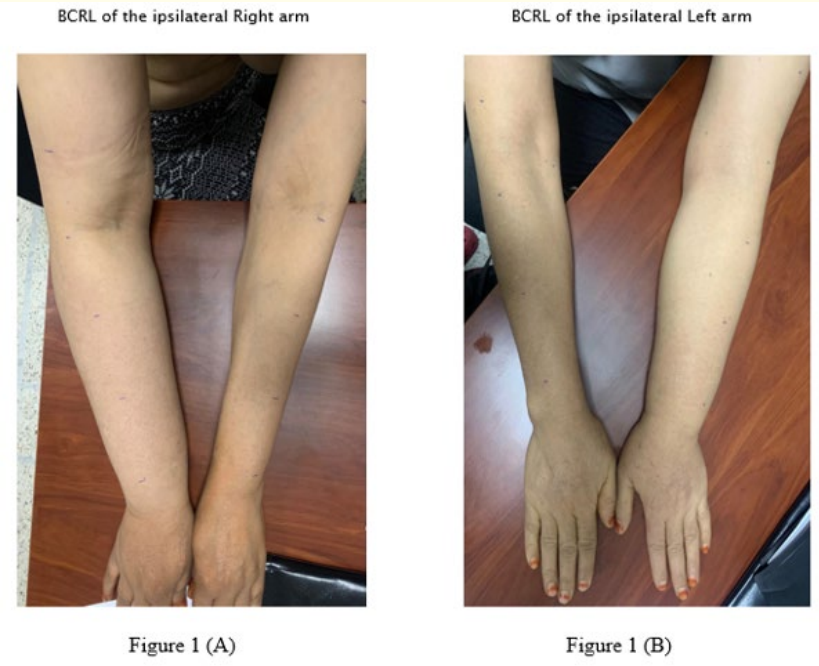

Figure 1: *Images of arm lymphedema of two of our patients demonstrating the edema in ipsilateral arm compared to the contralateral arm.*

Most of patients with arm lymphedema 64% have minimal disability, 27% have moderate disability and only 9% of them severe disability (Figure 2).

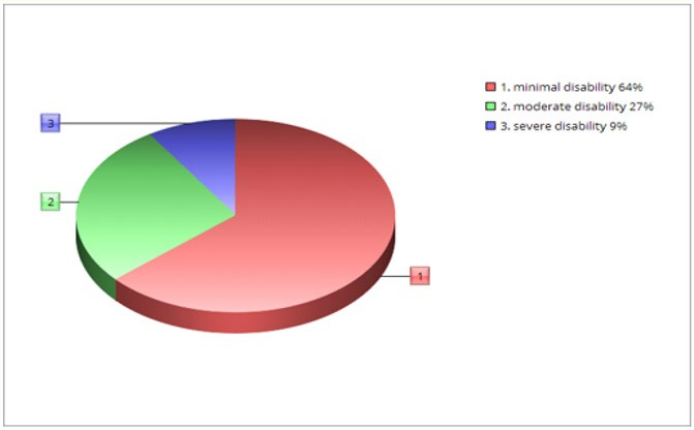

Figure 2: *Distribution of dash score among patients with lymphedema.*

Whereas all the patients without arm lymphedema have minimal disability with minimum and maximum were 0% and 8.3%.

Associated factors	Lymphedema n(%)		P value
	No	Yes	
Diabete n (%)			
Yes	9 (53.00)	8 (47.00)	0.03
No	51 (78.5)	14 (21.5)	
BMI (mean)	27.00	30.00	0.04
TTI (mean number of day)	95.00	125.23	0.02
Chemotherapy n (%)			
Yes	54(71%)	22(29%)	0.10
No	7(100%)	0(0%)	
Radiotherapy n(%)			
Axillary	40(70%)	17(30%)	0.37
breast	21(81%)	5(19%)	
Chemotherapy type n(%)			
Neoadjuvant	37(71%)	15(29%)	0.06
Adjuvant	17(71%)	7(29%)	
Age (mean)	50	48	0.42
Site (%)			
Right	38(74.5%)	13(25.5%)	0.80
Left	23(72%)	9(28%)	

Figure 3: *Associated risk factors of BCLR according to bivariate analysis.*

Discussion

Breast cancer (BC) is a leading health concern among women due to its high mortality and morbidity rate. The five-year survival rate in metastatic breast cancer is less than 30% [7]. In Morocco, the BC new cases in 2020 are estimated at 11,747 and 3,695 deaths [8]. The edema can be considered as a palpable swelling resulted from the increase of fluid in the interstitium, due to an imbalance between capillary filtration and lymph drainage no matter the underlying cause. Given the variation of criteria used to define lymphedema and the variety of assessment methods, we have wide variation in the reported incidence of lymphedema following breast cancer treatment. Lymphedema rates of 6% to 70% among patients with breast cancer have been described [9-11]. In our research the incidence was 26.5%, more than the ones of the studies lead by Rupp., *et al*. and Pereira., *et al*. [10,12] who reported respectively 13.5 and 20.7%. The means age of patients included in the studies of Pereira., *et al*. (55 ± 13 years) and Haen., *et al*. (61.3 ± 9.9 years) [9,10]. But, the mean age of our participants was older than the participants mean age of the study carried. The mean of the body mass index was in the study reported by Haen was (29.4 ± 5.67 kg/m^2). The body mass index means of the patients (24.52 ± 3.54 kg/m^2) in the study conducted by Lee., *et al*. which was lower than the BMI in our study 30 kg/m^2. The invasives ductal carcinoma and lobular carcinoma were the most observed during our study like the studies conducted by Hassan and QABA, but the cancer was diagnosed more often at grade III in study carried out by Pereira [13].

We have also the questionnaire of DASH (Disabilities of the arm, shoulder and hand) [14,15]: It's an upper-extremity specific outcome measure tool introduced by the American Academy of Orthopedic Surgeons in collaboration with a number of other organizations. One of the main concepts behind developing the DASH was to facilitate comparisons among different upper-extremity conditions in terms of health burden. The DASH outcome measure is a 30 items patient self-report questionnaire. In our study, most of patients with arm lymphedema 64% have minimal disability, 27% have moderate disability and only 9% of them have severe disability. Whereas all the patients without arm lymphedema have minimal disability with minimum and maximum were 0% and 8.3%.

The main treatment-related risk factors for BCRL literature include axillary lymph node dissection (ALND) and regional lymph node radiation (RLNR). There is strong evidence that both ALND and RLNR are independent risk factors for BCRL. In a meta-analysis, Disipio., *et al*. analysed 72 studies and found, 9 studies, including at least two prospective cohort studies and two randomized clinical trials, provided strong evidence that ALND is a risk factor for BCRL, in the study of Kilbreath., *et al*. 18.2% of patients with ≥ 5 axillary LNs removed developed BCRL compared to 3.3% of patients with < 5 nodes removed. In our study all patients had surgery with axillary lymph node dissection (ALND), and 26.5% of them had developed BCRL, but it was not applicable in bivariate analysis. Some studies indicate adjuvant chemotherapy as a potential risk factor for BCRL whereas other studies do not, in our survey. The comparison between patients undergoing neoadjuvant CT and patients undergoing adjuvant CT was not statistically significant. In many studies radiotherapy to the regional nodes, or RLNR, has been shown to be a significant risk factor for lymphedema development, in our survey. Despite the fact that patients who received RLNR had a higher BCRL risk compared with those who received chest/breast radiation (30% v 5%, respectively), this difference was not significant. Tamoxifen treatment leads to lymphatic dysfunction and aggravates lymphedema besides in our study type of hormone therapy is not associated to risk factors of BCRL.

Conclusion

The development of arm lymphedema is an unpredictable occurrence that can happen years after axillary surgery. Findings from this study can help health professionals in educating breast cancer survivors about lymphedema risk factors, as well as early detection and management of it by use of circumferential arm measurements to evaluate limb evolution during follow-up care.

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