The Degree of Post-Mastectomy Upper Limb Lymphedema in Relation to the Extent of Axillary Lymph Nodes Involvement and Dissection

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ABSTRACT

Background: Lymphedema of the upper extremity is a serious consequence of breast cancer surgery. Postmastectomy lymphedema of the upper limb is usually related to many risk factors like axillary surgery, radiotherapy, venous obstruction, obesity, and infection.
Objectives: To identify the relationship between the extent of axillary lymph nodes involvement and dissection on the development of upper limb lymphedema.
Methods: One hundred and seventy patients managed by modified radical mastectomy with axillary dissection for mammary invasive adenocarcinoma between January 2009 and December 2016 in Al-Fayhaa Teaching Hospital. The patients were divided in to three groups according to the number of lymph nodes involvement by pathology. The patients had been followed up for a minimum of two years and assessed by standard lymphedema assessment, then categorized in to three groups according to the severity of lymphedema.
Results: After the analysis of patient parameters, the highest age group was 36-45 years. More than 60% of the patients had 4-9 lymph nodes involvement. Forty one patients from the 170 developed lymphedema postoperatively. Forty patients had seroma and twenty one patients had wound infection postoperatively.
Conclusion: Postmastectomy lymphedema is sequelae of disease process related to the extent of lymph nodes involvement and resection rather than operative fault.
Keywords: Breast cancer, Mastectomy, Lymphedema.

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Breast cancer still the most frequently occurring malignancy in women. Worldwide over the past three decades, breast cancer remained the number two leading cause of cancer death amongst woman[1]. With the benefit of early detection methods and multimodality surgical options and adjuvant therapy, the overall survival will be improved. Modified radical mastectomy with axillary dissection remains the most popular procedure for the management of breast cancer[2,3]. Axillary dissection is the integral part for the radical and conservative breast cancer surgeries for prognostic and curative purposes[4].

This procedure not free of complications, among these complications is the upper limb lymphedema which of the most common occurrence after breast cancer surgery with a registered incidence of 6% to 30%[5].

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Lymphedema is a clinical manifestation of lymphatic system inadequacy and lymph transport impairment[6]. It is a collection of lymphatic fluid as a result of inadequate drainage of lymphatic flow due to damage or obstruction of lymphatic vessels[7].

The lymphedema occurs when the transport capacity of lymphatic system below the lymphatic load. It is either primary lymphedema which is develop as a result of congenital underdevelopment and/or hereditary pathology, or secondary lymphedema usually caused by mechanical obstruction of the lymphatic channels and lymph nodes by radiation, surgery, trauma, infection, secondary involvement of lymph nodes or chemotherapy[8,9].

Postmastectomy lymphedema most commonly present as an obvious swelling of the upper arm on the side of mastectomy with gradual tightening of cloths or jewelries and impaired functionality of the affected limb[10,11]. Severe physical and

psychological insult can occur among the survivors with lymphedema after breast cancer surgery and causing reduction of quality of life under the esteem of physical, functional, social and emotional wellbeing[12]. After the diagnosis of breast cancer or following surgery the incidence of upper limb lymphedema apparently to increase up to 2 years[13,14].

This study was conducted to assess the effect of extent of lymph nodes involvement and dissection on the development of upper limb lymphedema after modified radical mastectomy in patients with breast carcinoma.

Methods

This is a prospective study includes a total number of one hundred and seventy patients with breast carcinoma, who were diagnosed and then operated on during the period between January 2009 and December 2016 in Al Fayhaa Teaching Hospital, Basrah, Iraq. Patient's demographics, past history, family history, recent history, drug history and accompanying systemic diseases were evaluated. All patients were underwent modified radical mastectomy with the excision of nodal level one, two and sometime three according to the extent of lymph node involvement. The patients were subdivided to three groups according to the number of lymph nodes involvement by the disease under the umbrella of TNM classification[3], which was subsequently removed by surgery and diagnosed postoperatively by histopathology; the first group those with (1-3) lymph nodes involvement, the second group (4-9) lymph nodes were involved, and third group those with ten and more lymph nodes involvement.

Nearly all patients in group one had have level one axillary lymph node dissection and in the second group the dissection involve the level one and two, while in the third group had farther more, a level three dissections. All cases of axillary recurrence will be excluded from this study because of their limited number (four patients, three of them in the second group and one in the third group) and two of them escape from the follow up. Patients were followed in the outpatient department and clinic two years after surgery.

Those patients who developed arm and/or hand swelling, feeling of tightness, heaviness, fullness, skin thickening and pain or redness, were subjected to standard lymphedema assessment method as described by Markowaski et al[15] and Margaret et al[16]. Measurements and comparing of both upper limbs circumference which taken at fixed five levels from the olecranon process, two above the process (11.5 and 21 cm) and three levels below it (7.5, 14 and 24 cm). Any difference in the circumferences between the two limbs at any level was regarded as lymphedema. The lymphedema was subdivided into mild were difference in the arms circumference less than 3 cm, moderate were between 3-5 cm and severe when exceeding 5 cm.

Results

The age distribution of breast cancer patients is summarized in table 1. This table shows that breast carcinoma was more common in patients of age group between 36-45 years.

Table 2 shows the extent of axillary lymph nodes involvement among patients with mastectomy; more than 67% (114 patients) had 4 to 9 lymph nodes involved by tumor (group two).

From the 170 cases, only 41 patients (24.11%) developed lymphedema at the side of mastectomy, 58.53% of them were mild, (Table 3).

More than 68% (28 patients) from those who developed lymphedema where from group two and more nearly three quarter of them (22/28) had mild lymphedema and all the patients of group three had moderate to severe lymphedema, (Table 4).

Twenty-one patients (12.35%) developed wound infection postoperatively

with more than 52% (11 out of 21) in group two, (Table 5).

Wound seroma developed postoperatively in 40 patients (23.52%) and it was more in the second group (25/40), (Table 6).

From the total 170 patients who operated on only twenty five patients received radiotherapy, 16 patients from group two and 9 patients from group three, (Table 7).

Table 1: Age distribution of patients undergoing surgery.

Age in years	No. of patients	Percentage %
Less than 25	0	0
25-35	11	6.47
36-45	73	42.94
46-55	43	25.3
56-65	31	18.24
Above 65	12	7.05
Total	170	100

Table 2: Extent of axillary lymph node involvement.

Group	No. of lymph node involvement	No. of patients	% of patients
One	1-3	45	26.47
Two	4-9	114	67.06
Three	>9	11	6.47
Total number		170	100

Table 3: Type of lymphedema developed postoperatively.

Lymphedema	No. of patients	% of patients
Mild	24	58.53
Moderate	11	26.83
Severe	6	14.64
Total	41	100

Table 4: The frequency and severity of lymphedema among the three groups.

Group	No. of patients developed lymphedema	% of patients developed lymphedema	Mild	Moderate	Severe
One	2	4.87	2		
Two	28	68.3	22	5	1
Three	11	26.83		6	5
Total	41	100			

Table 5: The number and percentage of wound infection among three groups.

Group	No. of patients develop wound infection	% of patients develop wound infection	No. of patients for each group	% of wound infection in each group
One	9	42.86	45	20
Two	11	52.38	114	9.6
Three	1	4.76	11	9.1
Total	21	100	170	

Table 6: The number and percentage of patient who develop seroma.

Group	No. of patients develop seroma	% of patients develop seroma	No. of patients for each group	% of patients in each group
One	11	27.5	45	24.44
Two	25	62.5	114	21.92
Three	4	10	11	36.36
Total	40	100	170	

Table 7: The number of patients receiving radiotherapy postoperatively.

Group	No. of patients	No. of patients for each group
One	0	45
Two	16	114
Three	9	11
Total	25	170

From the above tables we found that there is a significant increase in the incidence of lymphedema with the increase of lymph nodes involvement. As the number of removed lymph nodes by dissection increases, the risk of lymphedema development also increases. Only 4.4% (2/45) of patients from group one who have three lymph nodes involvement or less developed lymphedema postoperatively, while 24.5% (28/114) of the patients from group two who having 4-9 lymph nodes involvement developed lymphedema and all the patients 100% (11/11) in group three developed moderate and severe form of lymphedema (more than 10 lymph nodes involvement). Severe lymphedema was more in the third group.

Discussion

Many surgical options are adopted for the treatment of breast cancer. Modified radical mastectomy with axillary clearance is the most commonly procedure underwent[2,3]. Axillary lymph nodes dissection remains an integrative step of the conservative and radical breast cancer surgery for prognostic issue and curative purposes[3,4].

The morbidity issue is discussed in a variety of articles and has been categorized as early and late surgical complications. Early ones are seroma, wound infection, parasthesia, hematoma, hemorrhage, flap necrosis and muscle paralysis. Late complications include lymphedema, shoulder stiffness, brachial plexopathy and psychosexual disturbances.

In meta-analysis of 72 studies discussed by DiSipio et al in 2013, summed estimate of postmastectomy lymphedema incidence was 16.6%, and it was 21.4% when data restricted to prospective cohort studies[13]. The overall incidence of lymphedema varies from 8% to 56% at 2 years of follow-up after surgery[16]. The incidence of upper limb lymphedema have wide range limit between 2% to 40% among women having breast cancer surgery and/or radiotherapy[17,18]. In the current study, the incidence of lymphedema was 24.11%. The reasons of the reported wide range of prevalence of postmastectomy upper limb lymphedema are the lack of standard universal diagnostic and assessment criteria, slowly developed onset, clinically prolonged course and limited physician knowledge.

American Cancer Society and other references review the risk factors that mostly implemented in the development of lymphedema after breast cancer surgery are axillary radiation after axillary dissection, upper outer quadrant tumor location, infection, axillary trauma postoperatively, seroma and hematoma, axillary tumor recurrence, extent of axillary lymph nodes dissection, and large number

of axillary lymph nodes involvement by pathology[4,14,19].

As mentioned above, the incidence of lymphedema in the studied sample was 24.11%. It is higher in group three 100% (11/11) and more severe, while it is 24.5% (28/114) and less severe in the group two, and it is less and mild 4.4% (2/45) in the group one, that shows the incidence and severity of lymphedema became more with the extensive lymph nodes involvement and dissection.

The incidence of wound infection in this study is higher in the group one 20% (9/45) when compared with the other groups 9.6% (11/114) and 9% (1/11) in group two and three respectively, in which there is less lymph nodes involvement and dissection and less lymphedema development, that's why, cannot be regarded it as a major risk factor in the development of lymphedema in this patients sample.

The incidence of seroma formation is higher in group three and nearly convergent in the first and second groups. For the most patients in the second and third groups the draining volume become less than 30 ml/day within 8 to 9 days postoperatively, while it became less than 30 ml within 4 to 5 days in the first group, so the drain was removed after less than 7 days in the first group and nearly after 10 days in the second and third groups, that's why the percentage of seroma formation was nearly equal in the first and second groups but it is still higher in the third one in which there was extensive axillary lymph nodes dissection because of massive axillary lymph nodes involvement.

There are several factors implicated in the development of postoperative seroma formation, in addition to the number of positive nodes and extent of lymph node dissection (the most important factors), other factors are intraoperative lymphatic channel ligation, postoperative radiation, preoperative chemotherapy, unusual arm activity postoperatively, and extensive use of electrocautery and vascular disruption[3,20,21]. This also confirmed by Petrek et al, in a prospective randomized trial showed that the most significant factor that causing the seroma were the number and extent of axillary lymph node involvement and resection[22], so the lymphedema development share with the seroma formation in the same important causative and risk factors.

From the 170 patients only 25 patients receive radiotherapy 16 patients from group two and 9 patients from group three (because their limitation in the previous years). In all patients, the field of radiotherapy restricted only to the mastectomy bed excluding the axilla, that's why the effect of radiotherapy in the development of lymphedema in this patients sample is very limited and minimal.

For all three groups the site of tumor mostly in the upper outer quadrant.

No patients from the one hundred seventy develop postoperative hematoma. Only four patients have axillary tumor recurrence and two of them lost from fallow up. No case was subjected to postoperative axillary trauma by re-exploration due to postoperative bleeding, hematoma or abscess collection. So there are no great impact for the last four risks factors in the development of post mastectomy lymphedema and not interferes with the result of this study.

From these finding the study conducted that as the number of lymph nodes involvement and the degree of dissection of these lymph nodes increase, the risk of lymphedema development will be more and this finding supported by many literatures. The higher number of axillary lymph node dissection which proportional with the extent of lymph node involvement during axillary surgery is a predictor of lymphedema development[23,24,25].

Nowadays, most people have a less aggressive procedure which followed by low risk and less form of lymphedema like sentinel lymph node biopsy and breast conservative surgery (by removing fewer lymph nodes than wide axillary dissection)[26,27,28]. Breast cancer survivors

who have sentinel lymph node biopsy are about 4 times less likely to develop lymphedema than those who have an axillary dissection[14].

In conclusion; the present study concluded that the extent of axillary lymph node dissection which predicted and related to the number of lymph nodes involvement is the most important factor for lymphedema development.

The postmastectomy lymphedema is part of disease process because it was predicted by the extent of lymph nodes involvement and resection and not a complication or surgical fault of modified radical mastectomy.

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