

Original Research Article

The predictors and the prognostic significance of axillary lymph nodes involvement in breast cancer

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ABSTRACT

Background: Breast cancer is the most common cancer among women worldwide. The presence of axillary lymph node metastases in breast cancer is an important factor in assessing prognosis and determines management after surgery. The study aimed at identification of the factors that predict axillary lymph node involvement in CA breast. Addressing the prognostic effect of axillary lymph node involvement in turn of predicting the recurrence of CA breast.

Methods: This is a prospective review of one hundred cases of Ca breast who have underwent modified radical mastectomy and axillary clearance at Al-Karama Teaching Hospital during the period from January 2014 to December 2018.

Results: Positive axillary involvement was found in (74/100, 74%). The highest occurrence of positive axilla was found in (less than 30 and 30-39 years) age groups (27/74, 36%) with the outer quadrants (upper and lower) constituting the majority (50/74, 68%). Positive axillary involvement was mostly notified in tumor grade T4 (39/74, 53%) and in poorly differentiated lesions (47/74, 64%). The highest recurrence rate was found in patients with positive axillary metastases (12/74, 16%), nodal involvement of ten or more nodes (9/41, 22%), nodes with extracapsular extension (10/51, 20%) and in patients who have not taken and/or completed their chemo-radiation sessions (9/11, 82%).

Conclusions: Positive axillary lymph node involvement was seen mostly in: young age patients, outer quadrant lesions, tumors with skin involvement, and poorly differentiated lesions.

Keywords: Axillary lymph nodes, Breast cancer, Prognosis

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among women and the leading cause of cancer death in females worldwide. It accounts for 30% of all female cancers and 15% of all cancer related death among women.¹

The involvement of axillary lymph nodes (LNs) is the most important prognostic factor in operable primary

breast cancer and is strongly associated with both disease-free and overall survival. The absolute number of nodes involved is also considered when deciding on the use of radiotherapy according to current guidelines based on the tumor-node-metastasis system.²

Anatomically, the protuberant part of the human breast is generally described as overlying the 2nd to the 6th ribs, and extending from the lateral border of the sternum to the anterior axillary line.³

In regard to the lymphatic drainage, surgeons identify seven primary groups: (1) the axillary vein group or lateral group; (2) the external mammary group (anterior or pectoral group); (3) the scapular group (posterior or subscapular); (4) the central group; (5) the subclavicular group (apical) of pectoralis minor; (6) interpectoral (Rotter's group) consists of 1-4 nodes interposed between the pectoralis minor and major muscles; (7) the internal mammary nodes are fewer in number in lie along the internal mammary vessels deep to the plane of the costal cartilages.³

More than 75% of lymph from the breast passes to the axillary lymph nodes, the remainder of the lymph flows into parasternal lymphatics. Both the axillary and parasternal groups receive lymph from all quadrants of the breast.⁴

Staging of breast cancer provides an overall perspective of the disease as it relates to prognosis. It includes data on the status of potential sites of regional metastasis (lymph nodes) and distant sites (lung, bone, liver, etc). For the former, axillary sampling, dissection or clearance have been employed. Sentinel node biopsy following lymphatic mapping (with dye or isotope) as an alternative to axillary dissection is still under clinical investigation.⁵

Bone scan, computed tomography (CT) and magnetic resonance imaging (MRI) as staging tools are used commonly, even though they have poor specificity.

Hormonal receptors, genetic information, C-erb B2 oncogene evaluation, and other biologic parameters are profiled in clinical practice not only for prognosis and staging but also for therapeutic planning.

Surgery is one of the cardinal therapeutic options for this clinical problem. It was believed that early Greco-Roman and Egyptian surgeons practiced some form of mastectomy.⁶

More than century ago Halsted and Meyer reported a new operation for treatment of breast cancer.⁷ At that time it was truly an appropriate solution to the problem, it showed dramatic improvement in decreasing the local recurrence, but long term cure rate did not change. Some surgeons believe in more radical surgery for cure, so extended radical mastectomy and supraradical mastectomy became useful clinical tools.⁸⁻¹²

Dr. H. DH Patey of middlesex hospital in London was credited with demonstration of the worth of modified radical mastectomy technique which involve in continuity removal of the breast and axillary content with preservation of pectoralis major muscle. Madden and Auchincloss advocated the preservation of both pectoralis major and minor muscles.¹³

Postoperatively, adjuvant therapy should be given in the form of locoregional radiotherapy (in patients under 25

years old, patients with positive resection margins or multifocal disease) and systemic therapy which is constituted of chemotherapy (CMF) (C: Cyclophosphamide, M: Methotrexate, F: 5 – Flurouracil) given in case of positive axillary involvement (2) and hormonal therapy (Tamoxifen) which has been used widely in both pre and post-menopausal females.

As lymph nodes are shown to be an important factor to determine type of surgery, we undertook this study to explore the importance of lymph node involvement as predictor and prognostic factor.

METHODS

In this prospective study of one hundred cases of Ca breast who have underwent modified radical mastectomy and axillary clearance at Al-Karama Teaching Hospital during the period from January 2014 to December 2018.

This 100 cases which were diagnosed to have CA breast, and assessed preoperatively by thorough clinical examination and investigated by hematological, biochemical, radiological and cytopathological investigations. The diagnosis was documented by fine needle aspiration cytology and/or excisional biopsy.

All of the patients were free of distant metastases and they have undergone modified radical mastectomy and axillary clearance. The samples were sent for histopathological study.

Certain variables were correlated with the positive axillary lymph nodes involvement namely the age, site and size of the primary lesion and its grade.

Four criteria related to the lymph nodes were correlated to the risk of recurrence and these are positive axillary metastases, number of the involved nodes, extracapsular extension and postoperative adjuvant chemo-radiation.

Patients included if the meet inclusion criteria which are, aged 18 and above, consented to participate in the study, and has been diagnosed with breast AC for more than a year. Exclusion criteria included, patients who are suffering from other malignant diseases or having serious heart disease that affect outcome of surgery. All data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 22.

RESULTS

In regard to the age distribution of the patients with positive axillary lymph nodes involvement, it was shown that (27/74, 36%) of patients were found in (<30 and 30-39 years) age groups. While in patients within the (40-59 years) age group, (24/74, 32.5%) of cases were found. The least occurrence of positive axillary lymph node involvement was reported in patients (≥60 years old) [23/74, 31.5%].

Considering the site distribution of malignant breast lesions and axillary lymph nodes involvement, it is shown that lesions which were located in the upper and lower outer quadrants constituted (50/74, 68%) of cases with positive axillary lymph nodes involvement. On the other hand, centrally located lesions were found in (14/74, 19%) of positively involved axillae. The least incidence of axillary lymph node involvement was found in medially located (inner quadrants) lesions (10/74, 13%). In regards to the correlation between axillary lymph nodes involvement and the clinical extent of the tumor, it is observable that lesions that were associated with skin involvement (Peu De Orange) (T4) constituted the majority of positively involved axillae (39/74, 53%), while the least incidence was found in tumors less than 2 cm (T1) (3/74, 4%). Concerning the association of histological grade of Ca breast with axillary lymph nodes involvement, it is observable that poorly differentiated tumors were associated with (47/74, 64%) of positive axillae, moderately differentiated lesions were found in (18/74, 24%) and well differentiated ones in (9/74, 12%) of cases with positive axillary lymph node involvement (Table 1).

Table 1: Distribution of lymph nodes involvement by selected variables.

Variable	Positive lymph nodes	
	No.	%
Age (in years)		
<30	12	16
30-39	15	20
40-49	14	19
50-59	10	13.5
60-69	13	18
≥70	10	13.5
Site		
Upper outer quadrants	31	42
Lower outer quadrants	19	26
Central (nipple and subareolar)	14	19
Upper inner quadrants	6	8
Lower inner quadrants	4	5
Clinical extent		
<2 cm (T1)	3	4
2-5 cm (T2)	11	5
>5 cm (T3)	21	28
Any size with skin involvement (T4)	39	53
Histological grade		
Well differentiated	9	12
Moderately differentiated	18	24
Poorly differentiated	47	64

Considering the relation the recurrence of breast CA with some clinical variable, it was shown that patients with positive axillae recorded recurrent in (12/74, 16%) of

them, while those with negative axillae had recurrence in (1/26, 4%) of them.

In cases of 3 or less involved lymph nodes, the recurrence was (1/12, 8%), in patients with 4-9 nodes the recurrence was (2/21, 10%), the highest recurrence rate was in patients with 10 or more positively involvement nodes (9/41, 22%).

In regard to the correlation between the extracapsular extension of the involved axillary lymph nodes and the loco-regional recurrence, presence of extracapsular extension was associated with recurrence in (10/51, 20%), while its absence reported a recurrence rate of (2/23, 9%).

Concerning the association between postoperative adjuvant chemotherapy and the locoregional radiotherapy with the risk of recurrence, it is observable that patients who have completed their courses expressed recurrence in (3/63, 5%) while those who have not completed their sessions had recurrence in (9/11, 82%) of them (Table 2).

Table 2: Distribution of cancer recurrence by selected variables.

Variable	No.	Recurrence	
		No.	%
Lymph node status			
Positive	74	12	16
Negative	26	1	4
Number of involved nodes			
1-3	12	1	8
4-9	21	2	10
≥10	41	9	22
Extracapsular extension			
Presence	51	10	20
Absence	23	2	9
Chemo-radiotherapy			
Completed course	63	3	5
Uncompleted course	11	9	82

DISCUSSION

In this prospective review of one hundred cases of CA breast who have underwent modified radical mastectomy and axillary clearance, (74/100, 74%) of patients were found to have positive axillary involvement, of whom (27/74, 36%) were below 39 years old, then the rate decreases to become (24/74, 32.5%) in the (40-59 years) age group and (23/74, 31.5%) in patients ≥ 60 years old. This result is in accord with that of: Tan et al who also found that as the age decreases the incidence of positive axillary involvement increases.¹⁴ This may be attributed to the more aggressiveness of the tumor in young age females and thus the more likelihood of regional lymph node metastasis.

In regard to the site distribution of Ca breast and its association with axillary lymph node involvement, we have conducted that upper and lower outer quadrants constituted the highest percentage of axillary lymph node involvement (50/74, 68%), next to it was the central area (nipple and areola complex) (14/74, 19%) and the least incidence was encountered in inner quadrant lesions (10/74, 13%). Similar results were conducted by:

Cutuli and Contesso who also found that axillary lymph node involvement was more frequent when the tumor was located externally or centrally than when located in an inner quadrant.^{15,16}

Considering the correlation between axillary lymph node metastasis and the clinical extent of the primary lesion, it was found that tumors with skin involvement (Peu de orange) "giving the tumor a grade of T4" had the highest prevalence of axillary lymph node involvement (39/74, 53%). The incidence declined as the tumor size decreased. This result concedes with that of Fein et al, Sinnett et al, Taylor et al and Barth et al who also recorded that larger tumor size is an independent predictor of axillary lymph node involvement.¹⁷⁻²⁰

In regard to the histological grade of the tumor and its correlation with axillary lymph node involvement, poorly differentiated lesions scored the most common association (47/74, 64%) and the incidence decreases as the degree of differentiation increases to become (9/74, 12%) in well differentiated lesions. This result is in agreement with that of Tan et al who also found that as the degree of differentiation decrease the incidence of positive axillary lymph node involvement increases.¹⁴

Considering the relation between the axillary lymph node status being positive or negative and the recurrence of Ca breast, patients with positive axillae had four times the risk of recurrence of those with negative axillae (16% in the former versus 4% in the latter). This result goes with that of Adami et al who also conducted that patients with axillary metastases carried higher risk of recurrence than those with negative axillary involvement.²¹

In regard to the association between the number of positively involved lymph nodes and the recurrence rate, we have reported that the risk of recurrence was escalating as the number of positively involved nodes increased. This result concedes with that of

Arriagada et al, Voogd et al, Le and Vinh – Hung et al who also found that the recurrence rate raises as the number of positively involved axillary lymph nodes increases.²²⁻²⁵

Considering the correlation between extracapsular extension of the positively involved axillary lymph nodes and risk of recurrence, patients with the presence of extracapsular extension carried about twice the risk of recurrence of those without extracapsular extension (20%

in the former versus 9% in the latter). Similar results were found by Tulay et al who also found that extracapsular extension had significant prognostic value in predicting the recurrence in Ca breast.²⁶

In regard to the impact of postoperative adjuvant chemotherapy and locoregional radiotherapy, patients who have taken and completed their sessions were facing a risk of recurrence that was about 16 times less than those who had incomplete courses (5% in the former versus 82% in the latter). This result is in concurrence with that of: Coles et al who conducted that postoperative adjuvant chemoradiation in CA breast is very important prognostic determinant of recurrence.²⁷

CONCLUSION

Positive axillary lymph node involvement was seen mostly in: young age patients, outer quadrant lesions, tumors with skin involvement, and poorly differentiated lesions. Recurrent Ca breast was mostly noted in Patients with positive axillary lymph node involvement; Lymph node involvement of 10 or more and Presence of nodal extracapsular extension.

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