

Factors Predicting Positive Axillary Lymph Nodes Metastasis in Primary Breast Cancer in Women

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Abstract

Objective: To predict factors which influence positive axillary lymph node metastasis (ALNM) in early stage of breast cancer in women.

Patients and Methods: A prospective study was carried out between the 1st of October 2002 and the 1st of October 2008 at Al-Ramadi Teaching Hospital. One hundred women in early stage of breast cancer with impalpable axillary lymph nodes were included. The breast lump and the axillary lymph nodes samples were histopathologically assessed.

Results: Analysis of axillary lymph nodes biopsies showed positive axillary lymph nodes metastasis in 34 (34%) of the patients. Four out of 30 patients (13.3%) were in stage I their mean age was (42±18.7 years) and 30 out of 70 patients (42.8%) were in stage II, their mean age was (45±16.9 years).

Conclusion: Tumor size, poor histological grade, lymph vascular invasion, age and, parity are significant predictors of axillary lymph nodes metastasis.

Key words: Axillary lymph nodes, breast cancer, metastasis, predictor.

Introduction:

Breast cancer constitutes a major economic and public health problem in the world due to the high morbidity and mortality rates. Worldwide, Breast cancer is the second most common type of cancer after lung cancer (10.4% of all cancer incidence, both sexes counted and it is found at all ages , but it is most prevalent in women between 40 and 60 of age, the risk of its development steadily increases up to age 60, then plateau and once again rises after the age of 55 ⁽¹⁾ Axillary lymph node metastasis (ALNM) is the most important prognostic factor and an important determinant for survival of patients with breast cancer.

The proportion of invasive breast carcinoma is increasing. The incidence and predictive factors associated with ALNM in patients with primary tumor, the role of axillary lymph node dissection has been controversial ⁽²⁾.

Axillary lymph node dissection has been the reference standard for establishing lymph node involvement, although 40%-70% of patients with breast cancer have histopathologically negative axillary lymph nodes ⁽³⁾.

To reduce the reported high morbidity associated with lymph node dissection, the less invasive surgical lymph node biopsy technique has been introduced as an alternative to complete axillary lymph node dissection ⁽⁴⁻⁵⁾.

Nevertheless, sentinel node biopsy is an invasive technique and is associated with radiation caused by a radioactive tracer-guided procedure that facilitates identification, removal, and pathological examination of the sentinel lymph node. Thus, a noninvasive technique that assists in the accurate identification of axillary lymph node metastases would be beneficial ⁽⁶⁾.

With the increase in routine screening mammography, the number of T1a and T1b breast cancer diagnoses has increased proportionally ⁽⁷⁾.

Several studies were reported on the predictive factors of ALNM in small, invasive breast cancers to determine whether ALN dissection could be avoided in this subset of patients. These studies also found that younger age, increasing tumor size, ad lymph vascular invasion (LVI) correlated with a higher incidence of ALNM ^(2,8-9).

Unfortunately, many patients with primary breast cancer present with advance stage which increase the possibility of positive axillary lymph node metastasis (ALNM). Therefore, this study was carried out to predict factors that may influence positive ALNM in early stage of breast cancer in women.

Materials and Methods:

A prospective study of one hundred women with breast cancer was carried out from the 1st of October, 2002 to the 1st of October, 2008 at Al-Ramadi Teaching Hospital.

All patients with early stage of breast cancer with clinically impalpable axillary lymph nodes and a positive fine needle aspiration (FNA) were selected randomly in the present study. Lobectomy done and axillary lymph nodes biopsy through separate small axillary incision at least five lymph nodes and mass were sent

for size, duct invasion, histological grade of tumor, lymph vascular invasion, estrogen and progesterone status.

Results:

Table (1) summarizes the predictor factors that influence positive axillary lymph nodes metastasis (ALNM) in early stage of breast cancer in one hundred patients.

Axillary lymph nodes were positive for metastasis disease in 34 patients (34%). Tumor size was between 0.7 – 4.7 cm with a mean of 2 cm.

Positive axillary lymph node were seen in 4 patients (13.3 %) out of 30 patients in stage I and in 30 patients (42.8%) out of 70 patients in stage- II.

Infiltrating ductal carcinoma were present in 82 out of 100 patient (82 %). The rest 18 had infiltrating lobular carcinoma. Positive ALNM were found in 24 out of 82 patients (29.3%) with infiltrating ductal carcinoma and in seven out of the 18 patient (33.8%) with infiltrating lobular carcinoma.

Lymph vascular invasion were present in 15 patients only. Out the 15 patients with lymph vascular invasion, ten patients (66.6%) had positive ALNM , of the rest 85 patients without lymph vascular invasion, 21 patients (24.7%) had positive ALNM .

Histological grading shows the following data, poorly differentiated tumor without tubular feature in 20 patients of 100, out the 20 patients, 13 patients 65% had positive ALNM. Moderately differentiated tumor in 70 (70%) of the patients , 19 patients (27.1%) of them had positive ALNM well differentiated tumor in ten patients (10%), in whom 2 patients (20%) had positive ALNM .

The ages of the patients were ranging from 28-72 years old. The cut-off age value was 50 years, only 20 patients (20%) were under 50 years with a mean

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age of 36 ± 13.5 years, in whom nine (40%) had positive ALNM, while 80 patients (80%) were above 50 years with a mean age of 55 ± 9.8 (60%), and a positive ALNM was found in 25 (31.2%) patients.

Parity shows increasing risk of ALNM in women with breast cancer, as 70% of 34 patients with ALNM were multipara (more than 5 children).

Estrogen receptor (ER) status: Out of 100 patients, 66 patients (66%) were with positive ER, in whom 18 patients (27%) had positive ALNM, the rest 48 patients (72.7%) had negative ALNM. Out of the 34 patients with negative ER, eight patients (23.5%) had positive ALNM, and the rest 26 patients (76.4%) had negative ALNM.

Table (1): Summary of ALNM by stage I & II breast cancer and the predicting factors.

Predicting factor <u>Tumor stage & size</u>	No. of Positive ALNM	%	No. of Negative ALNM	%
Stage 1 (< 2cm)	4 / 30	13.3	26 / 30	86.7
Stage 2 (> 2cm)	30 / 70	42.8	40 / 70	57.2
<u>Histological grading</u>				
Poorly differentiated	13 / 20	65	7 / 20	35
Moderately differentiated	19 / 70	27.1	42 / 70	72.9
Well differentiated	2 / 10	20	8 / 10	80
<u>Infiltrating lobular</u>	7 / 18	38.8	11 / 18	61.2
<u>Infiltrating ductal</u>	24 / 82	29.3	58 / 82	70.7
<u>Lymph vascular invasion</u>	10 / 15	66.7	5 / 15	33.3
<u>Non lymph vascular Invasion</u>	24 / 85	28.2	61 / 85	71.8
<u>Age</u>				
28 – 50	9 / 20	45	11 / 20	55
50 – 72	25 / 80	31.3	55 / 80	68.7
<u>Hormonal receptor</u>				
Estrogen receptor Positive	18 / 66	27.3	48 / 66	72.7
Estrogen receptor negative	8 / 34	23.3	26 / 34	76.7
<u>Multiparity</u>	24 / 34	69.6	10 / 34	29.4

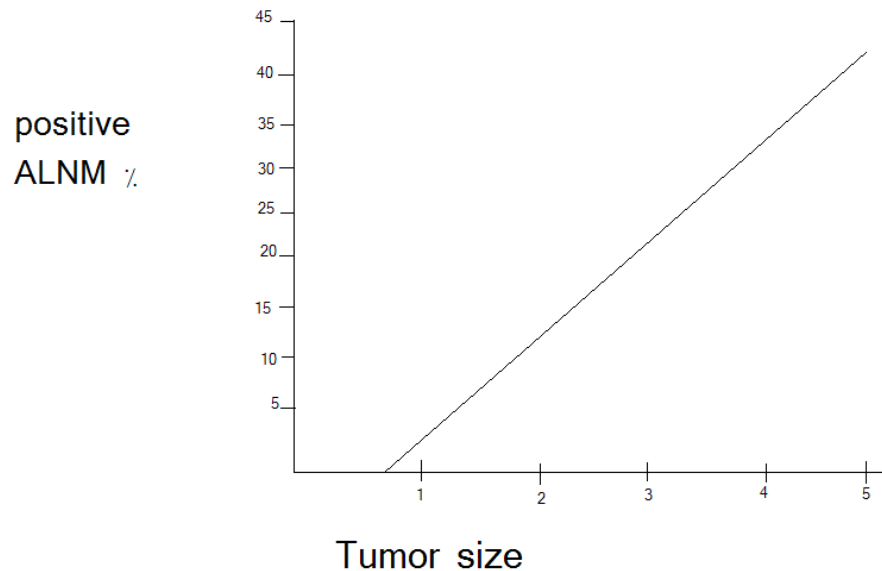


Figure (1): Relationship between positive axillary lymph nodes metastasis (ALNM) and tumor size.

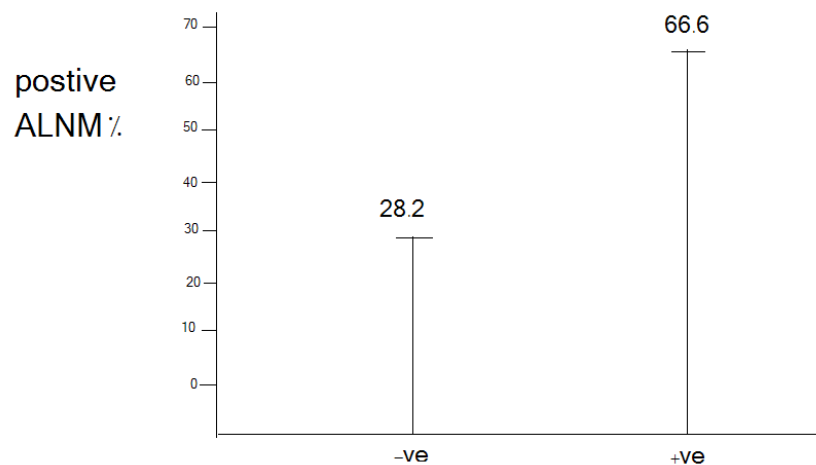


Figure (2): Percentages of positive and negative lymph vascular invasion in patients with positive ALNM.

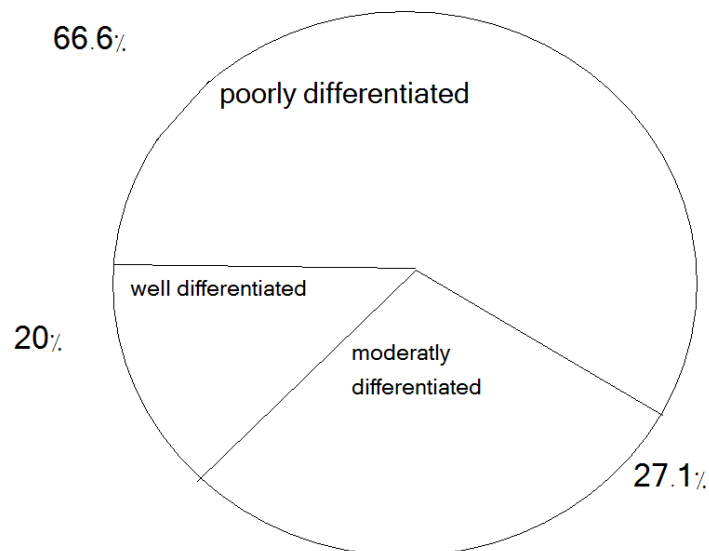


Figure (3): Percentages of positive ALNM according to histological grading

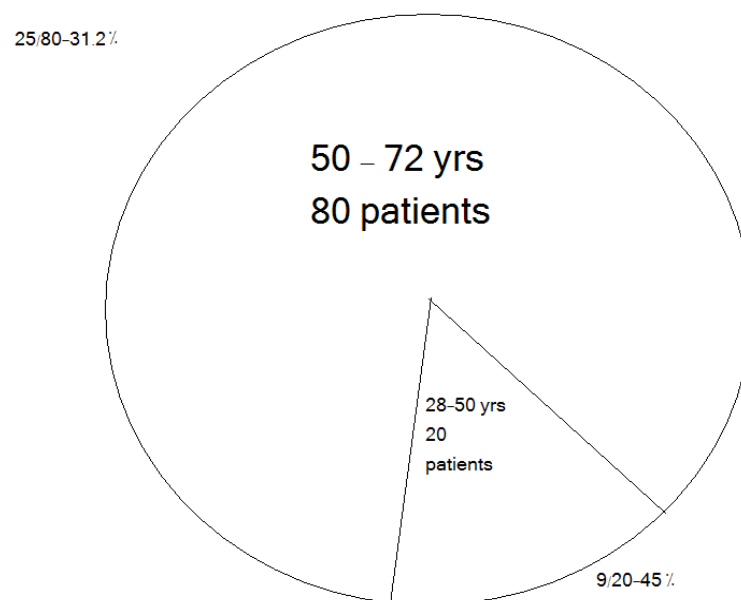


Figure (4): Age of patients & percentages of positive ALNM.**Discussion:**

ALNM is an important prognostic indicator which necessitate further management, for this reason, factors which predict it's involvement are important. In our study, tumor size was an important indicator of percentage of ALNM . Figure (1) shows clearly this relation of tumor size in centimeter to percentage ALNM. Other studies have shown the same relationship^(10,11,12). Lymph vascular invasion was a strong predictor of positive ALNM as shown in figure (2) as well as prognostic value, tumor-laden lymphatic which can be an important indicator of recurrence and have been found in 10% to 15% of patients without metastasis.

In one study of patients with stage I disease and lymphatic invasion, the recurrence rate was 32% compared with 10% no lymphatic tumor emboli⁽¹³⁾. In another study, 51% of the 181 patients with lymphatic invasion had ALNM compared with 19% of the 669 patients without lymphatic invasion⁽¹⁴⁾. Histological grading is an important predictor to ALNM as shown in figure (3) . Previous studies have shown poorly differentiated tumors which have more and earlier ALNM^(15,16). Age of patients predicted positive ALNM is shown in figure (4) . Another study shows 37% of the 63 women younger than age 40 had lymph node involvement compared with 25% of the 787 women with older than age 40⁽¹⁶⁾. Younger women tend to have a poorer prognosis than post - menopausal women due to several factors. Their breasts are active with their cycles, they may be nursing infants, large family size, and may be unaware of changes in their breast⁽¹⁷⁾. In the present study, estrogen status does not predict ALNM, but helps in

predicting method of treatment and recurrence and survival .

As patient with tumor that express ERs have a higher disease - free survival and overall survival than patients whose tumors are ER – negative^(18,19). These findings are most notable in patients with ALNM⁽²⁰⁾, but do not appear to indicate an advantage for those with tumor - free axillary nodes. ER finding may be useful, however; when combined with tumor size and oncogene expression⁽²¹⁾. Positive ERs also indicate improved survival after recurrence and an even better prognosis when both ERs and PRs are expressed⁽²²⁾. Parity shows increasing risk of ALNM in our study, another study shows same result⁽²³⁾.

Conclusions & Recommendations:

ALNM was mostly related to lymph vascular invasion in primary breast cancer, followed, in order of significance by histological grading, tumor size, age of patient and parity. The author of the present work recommends that patient with early primary breast cancer would have their axillary being assessed by either by a classical ALNM dissection or by intra operative lymph nodes biopsy. The used of more Advanced Super Paramagnetic Iron Oxide (USPIO) – enhanced Magnetic Resonance (MR) imaging⁽²⁴⁾ is also recommended.

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