

Original Research Article

Correlation between tumor size and site with axillary lymph node metastasis in breast cancer

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ABSTRACT

Background: Breast cancer remains significant health concern across the world and the leading cause of cancer related mortality and morbidity among females. Various trials have been performed to evaluate the chances of less extensive surgery in both breast and axilla, even omission of axillary surgery. So, it is paramount to identify the prognostic and predictive factors that may fulfill the goal in the future.

Methods: This was a cross-sectional observational study which took place in the Department of Surgical Oncology, National Institute of Cancer Research and Hospital (NICRH), Mohakhali, Dhaka from January 2023 to December 2023 over a period of 12 months. A $p < 0.05$ was considered statistically significant.

Results: A total number of 76 patients were enrolled in the current study after fulfilling the inclusion and exclusion criteria. Mean age of the study population was 42.37 ± 9.87 years. There is statistically significant relationship between tumor size and ALNM ($p < 0.05$) where majority of the patients ($n=47$) presented with T2 lesion (61.84%). Results of the study also showed involved site of breast by cancer was significantly related to axillary lymph node metastasis (ALNM). The number of patients presented with upper and outer quadrant, Upper and Inner quadrant and lower and inner quadrant were 48 (63.2%), 13 (17.1%) and 6 (7.9%) respectively. Lower and outer quadrant was involved by 8 (10.5%) patients which was not significantly related with ALNM ($p > 0.05$).

Conclusions: The current study demonstrated quadrant involvement can emerge as a clinically useful prognostic factor in breast cancer as there is a higher incidence of lymph node positivity with increasing size of the breast tumor and for tumors located at the outer quadrants of the breast. So, the site of primary tumor and size may be an important characteristic finding affecting the prognosis and treatment of patients with breast cancer.

Keywords: Tumor size, Tumor site, Axillary lymph, Node metastasis

INTRODUCTION

With an estimated 2.3 million new cases, or 11.7% of all cancer cases, in 2020, breast cancer (BC) has already overtaken lung cancer as primary cause of cancer worldwide.¹ The prevalence of breast cancer is progressively rising worldwide. The precise situation in relation to Bangladesh is unknown, although frequency is progressively increasing. According to a recent study, the prevalence of breast cancer in women is highest and has been roughly 32.8% over the past five years.

The size of the tumor and the nodal status are the two most significant prognostic markers mentioned in the American Joint Committee on Cancer (AJCC) TNM staging for breast cancer. Nottingham prognostic index is another widely used prognostic approach that is based on tumor size, lymph node status, and tumor grade.² Prognostic indicators have a major role in clinical decision making, the development of management protocols, and outcome prediction. Therefore, decision to avoid sentinel lymph node biopsy (SLNB), a suitable predictive nomogram is needed to separate BC patients who were at a reduced preoperative risk of SLN metastases from those who were at a higher risk. Histological grade, lympho-vascular invasion (LVI), and molecular indices are linked to ALNM of BC that have been identified in a number of earlier investigations.³ It is unclear, yet, if these indicators are accurate enough to omit SLNB. Furthermore, the potential for non-invasive or preoperative uses of these prognostic models is limited because they rely on postoperative histological findings. Therefore, the creation of a nomogram for preoperative use can assist medical professionals in reaching more customized treatment recommendations.

Large breast tumour (>2 cm) had axillary lymph node metastases about 30%-35%, which suggested a dismal prognosis.⁴ A statistically significant link appears to exist between the initial size of the tumor and the metastasis of lymph nodes.⁵ The original tumor's size may be used as a reliable indicator of ALNM, which is cause of concern because individuals with small tumors (less than 2 cm) have a low risk of ALNM.⁶ The breast lymphatic system has a dense network of lymph vessels in the dermis, indicating that cancers that are positioned more superficially may have a higher chance of spreading through the lymphatics to the axillary nodes than tumors that are located deeper. Primary tumor location has yet to be adopted as a standard of prognosis although there have been multiple studies suggesting a substantial prognostic utility. The challenge of including the tumor site as a prognostic factor, there is lack of consensus regarding the existence of biological variations among malignancies of different sites. Breast cancers are more frequently found in the upper outer quadrant of breast. Studies done in Asia, however, have also highlighted the significance of site of tumor in breast, concurring that cancers located in the inner quadrants of the breast typically have a worse prognosis.⁷ The mortality rises dramatically (up to 21%)

as the tumor's distance from the axilla is increasing. Compared to malignancies elsewhere in the breast, women with an upper lateral quadrant tumor have a much higher chance of survival. The development and occurrence of early invasive breast cancer may be accompanied by axillary lymph node metastases. Therefore, precise axillary lymph node staging is crucial in guiding decisions regarding the choice of local treatment strategy, systemic comprehensive treatment, and prognostic assessment.⁸

Axillary lymph node dissection and SLNB are currently the gold standards for the diagnosis of axillary lymph node metastases in breast cancer.⁹ A number of studies have recently developed protocols to predict axillary lymph node (ALN) status, indicating that the clinical data and primary tumor characteristics may be able to estimate the ALN status. Additionally, some research has attempted to predict ALN status using primary tumor imaging characteristics. Moon et al. demonstrating the usefulness of peritumoral tissue imaging features in providing information about ALN status.¹⁰ Additionally, according to some earlier research, imaging characteristics of the underlying tumor may help distinguish between ALN status differentiation whether involved by tumor or not. Therefore, ALNM assessment, in addition to tumor morphology and several histological features, has become a crucial component of the breast cancer treatment plan.

Current study's aim is to establish a correlation between the size and location of the tumor with the ALNM in cases with early and locally advanced breast cancer.

METHODS

This cross-sectional observational study took place in the Department of Surgical Oncology, National Institute of Cancer Research and Hospital (NICRH), Mohakhali, Dhaka from January 2023 to December 2023. Female patient of breast carcinoma admitted in the indoor and visited at outdoor in the department of Surgical Oncology (Breast Unit), National Institute of Cancer Research and Hospital during the period of study after fulfilling the inclusion and exclusion criteria were enrolled in the study. A purposive sampling technique was used. An ethical clearance was taken from ethical clearance committee of NICRH to conduct the study. An informed written consent was obtained from all the participants regarding the study procedure.

Inclusion criteria

Female patient with clinically palpable breast carcinoma proven by histological examination were included.

Exclusion criteria

Recurrent breast cancer, multifocal, multi centric and bilateral breast tumor, patient who received neo-adjuvant

therapy, *in-situ* carcinoma, metastatic breast cancer, pregnancy associated breast cancer, inflammatory breast cancer and patient with previous breast surgery for benign breast diseases with excluded from the study.

Data regarding socio-demographic characteristic including age, occupation, socioeconomic status and level of education was recorded by interviewer administered questionnaire. Data regarding clinical morphology of breast tumor was recorded under proper screening in the presence of female attendant. Tumor location according to quadrant was assessed on lying position by palpation. Tumor size was assessed by USG and mammography of breast. Size was measured in mm, later on categories in chronologic different group at interval of 1 cm and divided into 6 groups: group A (0.1-≤1cm), B (1.1-≤2 cm), C (2.1-≤3 cm), D (3.1-≤4 cm), E (4.1-≤5 cm), F (>5 cm). Chest wall fixity and overlying skin fixity accessed by clinical examination. Information regarding tumor location, size and fixity noted in data collection sheet.

Axillary lymph node status was accessed clinically from front except posterior group that was accessed from behind, USG and mammographic features, axillary lymph node FNAC, SLNB, ALND and post-operative histopathology report. Information regarding location, number, size and fixity was noted in data collection sheet.

Tumor histological information like tumor type, grade and histochemical information like receptor status was collected from core biopsy/ postop specimen histopathological and immunohistochemistry analysis.

Data analysis was done with SPSS for Windows (IBM SPSS statistics for Windows, version 26.0; Armonk, NY, IBM Corp.) software. Continuous variables were express in term of frequency and standard deviations. Qualitative variables were tested by Chi-square test& Fisher exact test accordingly. A p value less than 0.05 was considered as statistically significant.

RESULTS

A total number of 76 patients were included in the current study after fulfilling the inclusion and exclusion criteria. Mean age was 42.37±9.878 years. Minimum and maximum ages were 22 years and 70 years respectively (Table 1). Most of the patients, 71 (93.4%) had no family history of breast cancer. Only 5 (6.6%) patients had positive family history.

Table 1: Age distribution of the patients.

Age (in years)	N	Percentage (%)
21-30	3	3.95
31-40	12	15.8
41-50	24	31.58
51-60	28	36.84
61-70	9	11.84
Total	76	100

The 41 (53.9%) participants had tumor on right breast. On the contrary, 35 (46.1%) participants had tumor on left breast. We found that 6 (7.9%) patients had tenderness during ALN examination and 3 (3.9%) patients had fixed ALN during clinical examination. The 14 (18.42%) patients presented with peau d'orange and all of them had ALNM. Most of the patients presented with unilateral palpable axillary LN, 57 (75%) and among them 42 patients have ALNM followed by 13 patients had no palpable ALN, but after USG of axilla with FNAC of suspicious ALN revealed that 8 patients had ALNM (Table 3). most patients presented with stage T2N1M0, 29 (38.2%) followed by 14 (18.4%) patients presented with stage T1N0M0 (Table 3).

Table 2: Distribution of patients according clinically palpable ALN with ALNM.

ALN	N	Percentage (%)	ALNM
Unilateral palpable	57	75.00	42
Bilateral palpable	6	7.89	4
Not palpable	13	17.11	8
Total	76	100	54

Table 3: Distribution of patients by TNM stage, (n=76).

TNM stage	N	Percentage (%)
T1N0M0	14	18.4
T1N1M0	10	13.2
T2N0M0	8	10.5
T2N1M0	29	38.2
T3N1M0	1	1.3
T4N1M0	11	14.5
T4N2M0	3	3.9
Total	76	100

Most of the patients, 55 (72.4%) have grade-II tumors, among them ALNM occur in 35 patients. Second most common histologic grade is grade-III, accounting for 23.7% of all study population (n=18), among them ALNM occur in 17 patients (Table 4). Only 3 (3.9%) patients have grade-I disease, out of which 2 patients had ALNM. The relationship between tumor grade and ALNM was statistically significant, (p<0.05) (Table 4).

There were only two histologic subtypes found in this study, among them 73 (96.1%) were ductal carcinoma, out of which 52 patients had ALNM and 2 (3.9%) were lobular carcinoma, out of which 2 patients had ALNM. Majority of the patients, 44 (57.9%) belong to luminal A and among them 30 patients had ALNM, followed by 14 (18.4%) patients had TNBC and among them 9 patients had ALNM (Table 4).

Table 4: Distribution of patients according to histological type, grade and molecular subtype.

Variables	N	Percentage (%)	ALNM	P value
Receptor status				
Luminal-A	44	57.9	30	0.676
Luminal-B	10	13.2	8	
TNBC	14	18.4	9	
Her-2 enriched	8	10.5	7	
Histologic type				
Ductal	73	96.1	52	0.647
Lobular	3	3.9	2	
Total	76	100	54	
Grade				
Grade-I	3	3.9	2	0.029
Grade-II	55	72.4	35	
Grade-III	18	23.7	17	
Total	76	100	54	

There was statistically significant relationship between tumor size and ALNM ($p < 0.05$). Patients presented with tumor size < 1 cm was 3 (3.9%) and 1.1-2 cm was 21 (27.6%). Total 24 (31.5%) represents T1 tumor according to AJCC staging system. Patients presented with T2 lesion was 47 (61.84%). Patients represent as $\geq T3$ lesion according to AJCC staging system is 5(6.6%) (Table 4).

The most involved site of breast by cancer is upper outer quadrant (UOQ), 48 (63.2%) and among them 38 showed ALNM. On the other hand, upper inner quadrant (UIQ) involvement occurred in 13 (17.1%) patients with 6 of them showing ALNM. Lower inner quadrant (LIQ) was involved by 6(7.9%) patients with 2 of them had ALNM. The ALNM is significantly ($p < 0.05$) related with tumor site involving UOQ, UIQ and LIQ (Table 4). There was no significant relationship between lower outer quadrant (LOQ) involvement and ALNM.

Table 4: Distribution of patients according to tumor site and size with ALNM.

Variables	N (%)	ALNM	P value
Site			
UOQ	48 (63.2)	38	0.041
UIQ	13 (17.1)	6	0.030
LOQ	8 (10.5)	7	0.278
LIQ	6 (7.9)	2	0.034
Central (behind nipple areolar complex)	1 (1.32)	1	
Tumor size (cm)			
< 1	3(3.9)	1	
1.1-2	21(27.6)	9	
2.1-3	21(27.6)	17	
3.1-4	17(22.4)	13	0.04
4.1-5	9(11.8)	9	
> 5	5(6.6)	5	

DISCUSSION

As there is rising incidence of breast cancer worldwide, so a clear knowledge about the disease biological pattern and mode of dissemination is very important to combat with this tumor. Management and prognosis of breast cancer depends on multiple factors, among them involvement of axillary lymph node is the most important prognostic marker. Tumor size, site and histological features are also important prognostic indicators.¹¹ As breast cancer has biological diversity among different area, so through this study the clinical pattern and histological features of breast tumor in our locality can be assessed.

According to the current study, 61% of cases of the disease occur in people between the ages of 35 and 50 years. The youngest patient is 22 years old, while the most senior patient is 70 years old. The mean age of patients affected by breast cancer is 42.37 (SD \pm 9.88). The mean age of the 100 patients in research by Chopra et al with histopathologically confirmed breast cancer was 51 years (SD \pm 10.48).¹² It is necessary to investigate potential environmental factors that may be causing variations in the mean age.

The present study revealed a significant correlation between tumor grade and axillary lymph node metastasis ($p < 0.05$), this result aligns with result found by Garg et al.¹³ So, tumor grade is an important predictive factor for ALNM and can be used as a prognostic factor as well. Following a histological analysis of breast cancer cases, we discovered that 73 patients (96.1%) had ductal carcinoma and 3 patients (3.9%) had lobular carcinoma. These histological variations do not substantially relate to ALNM ($p > 0.05$). This result is in contrast to the study conducted by Feig et al which found that ductal carcinoma and lobular carcinoma account for 75% and 15% of all cases of breast cancer, respectively.¹⁴

The current study demonstrated a close relationship between tumor size and ALNM ($p=0.04$). Larger tumor size was found to be an independent predictor of node positive disease in our study, coincide with result from several other centers.^{15,16} Legha et al found that as the average size of the breast tumor increases, so does the average number of lymph nodes, both clinically as well as histopathologically positive for metastasis to the axillary lymph node.¹⁷

According to our study, the percentages of hormone receptor-positive cancer are 71.1%, TNBC is 18.4%, and Her-2 enriched cancer is 10.5%. Receptor status is not significantly ($p>0.05$) associated with ALNM which is disparate with the findings of Tseng et al.¹⁸ They discovered that Her-2 enriched tumors had a propensity to spread in ALN and have high grade tumor biology. So, Her-2 status would therefore be a significant predictor in the assessment of axillary nodal status.

According to our findings, the upper and outer quadrants of the breast (63.2%) are the most affected area of breast by cancer. These findings are consistent with large-scale studies of national breast cancer statistics from other nations. Chand et al also discovered that 62% of patients showed involvement of the upper and outer quadrant of the breast.¹⁹ Upper and inner quadrant accounted for the second highest frequency (16%), with lower outer quadrant coming in second with 6% and diffuse instances (including more than two quadrants) with 12%. This could be explained by the fact that the upper and outer quadrant of the breast has more breast tissue than other areas of breast. We note following comparable outcome, which is in descending order of most involved quadrant: UOQ>UIQ>LOQ>LIQ. Significantly, the tumors in the upper and outer quadrants were linked to ALNM ($p=0.041$), which is consistent with other studies.^{20,21}

The current study had some limitations. This study was conducted in a single center in short period of time. So, result may not reflect the actual scenario of the whole country. Besides, sample size was small that can reduce the statistical power of the study, making it difficult to detect significant correlations.

CONCLUSION

Study demonstrated both tumor size, site along with lymph node status are independent prognostic indicators. There was significant relationship between increasing size and tumor located in outer quadrants with ALNM. Thus, size and nodal status form basis for TNM system, and remain as crux parameters for making management decisions and estimating prognosis of patients with invasive breast cancer in developing countries.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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