AUCTORES
Globalize your Research

Journal of Surgical Case Reports and Images

Anil Heroor *

Open Access

Case Report

Clinical Value of Size, quadrant, and Hormonal Status in Predicting Axillary Node Metastasis in Early Clinico-Radiologically Negative Indian Breast Cancer- A Hospital Based Prospective Observational Study

Yadhukrishnan T.P.[2], Aysha Khan [2], Ziaul Rahman [2], Arul Vanan [1], Hitesh Singhavi [1], Anil Heroor [1*]

[1] Consultant, Department of Surgical Oncology, Fortis Hospital, Mulund, Mumbai, India.

[2] Registrar, Department of Surgical Oncology, Fortis Hospital, Mulund, Mumbai, India.

***Corresponding Author:** Anil Heroor, Head of Department, Surgical Oncology, Fortis Hospital, Mulund, Mumbai, India.

Received date: May 27, 2021; Accepted date: August 10, 2021; Published date: October 23, 2021

Citation: Yadhukrishnan T.P., Aysha Khan, Ziaul Rahman, Arul Vanan, Hitesh Singhavi, Anil Heroor (2021) Clinical Value of Size, quadrant, and Hormonal Status in Predicting Axillary Node Metastasis in Early Clinico-Radiologically Negative Indian Breast Cancer- A Hospital Based Prospective Observational Study. *J, Surgical Case Reports and Images* 4(8); DOI: 10.31579/2690-1897/082

Abstract

Background: Sentinel lymph node biopsy (SLNB) is standard of care in clinico- radiologically negative axilla in early breast cancer case. It's an oncologically safe alternative to Axillary lymph node dissection (ALND), however factors predicting sentinel node metastasis in Indian population is lacking.

Methods: A prospective observational study which recruited 80 patients with breast cancer who underwent SLNB with or without ALND, with evaluation of predictive factors including size, type and quadrant , hormonal status of breast this characteristics were prospectively analyzed to predict the axillary metastasis and need of SLNB .

Result: Mean age of the patients included in our study was 52.4 years. On univariate analysis, size ($p<0.013$), upper outer quadrant (UOQ) ($p<0.038$), central quadrant (CQ) (0.07) were significantly associated with axillary node metastasis in T2 tumors. While on multivariate analysis, UOQ ($P<0.009$), CQ ($p<0.02$) metastasis were associated with axillary node metastasis in T2 tumors. Overall sensitivity, specificity, positive predictive valve (PPV) and negative predictive valve (NPV) of SLNB in predicting axillary node status was 77.59%, 100%, 100% and 62.86% respectively. The overall accuracy was 83.7%.

Conclusion: Upper outer quadrant, central quadrant and size of the tumors are important prognostic factors to predict axillary node metastasis without the need of sentinel node biopsy in early breast cancers.

Keywords: sentinel node biopsy, breast cancer, axillary node metastasis, sentinel node metastasis

Introduction

Sentinel lymph node (SLNB) mapping and dissection is a sensitive and accurate technique for nodal evaluation and has been applied to staging of axillary lymph nodes in patients with breast cancer [1]. It has prognostic value, least invasive and less surgical morbidity than with axillary lymph node dissection (ALND), it's also important prognostic indicator of overall survival in patients with breast cancer. However, SNB has its own limitation. Its false negative rate is 5% according to Amersi et al, there is increase the risk of recurrence and its controversial in pregnancy, vital blue dye is contraindicated in pregnant patients, or use of radioactive colloid alone to map this subgroup of patients [2].Similarly other relative disadvantages of SNB includes its implication of finding micro metastases in the sentinel nodes, and its effectiveness after neo adjuvant therapy, and in staging of axilla in locally recurrent breast cancer following breast surgery with or without prior axillary surgery. The British journal on cancer, published a study which show the model estimated that SLNB results in 1.1 more axillary recurrences per 1000 patients at 5 years, and 1.9 more axillary recurrences per 1000 patients at 20 years than ALND [3, 4].

We need to find out usefulness of SLNB in a patient with high risk of axillary metastasis. Patients at high risk for nodal involvement based on clinical characteristics may remain at unacceptably higher incidence of axillary disease. There are many studies around the globe regarding the controversies of axillary lymph node dissection and sentinel lymph node

biopsy However data of Indian population with respect to site (quadrant) of breast cancer influencing axillary metastasis and axillary dissection without sentinel lymph node biopsy in early breast cancer is scarce.

In those specific high risk cases of early stage, usefulness of SNB may be questionable. Therefore, we decided to study those specific cases in which axillary node dissection can be performed in resource constrain settings. We also aimed to find out site and size-specific incidence of ALNM depending on the quadrant of the breast involved.

Methods

This is a prospective observational study done in our tertiary care center from January 2019 – January 2020. Early stage, clinic-radiological negative patients with Fine needle aspiration cytology or true cut biopsy positive patients were included in the study. Patient receiving any definitive prior treatment were excluded. All patients underwent surgery as a definitive treatment. They underwent breast conservative therapy or modified radical mastectomy with sentinel node biopsy followed by Axillary node dissection. A pretested proform was used to collect relevant information (patient data, detailed history, clinical examination, FNAC/Trucut biopsy, USG breast and axilla, mammography and chest x-ray, lab investigations, etc.) from all selected patient was assessed. All patient underwent required preoperative investigations, informed consent from all participating patients and after ensuring fitness for surgery, these patients were taken for SLNB along with wide local excision with axillary clearance or modified radical mastectomy. Methylene blue dye was injected in sub areolar region 2 minutes prior to surgery. Intra operatively, sentinel lymph node was searched after raising superior flap. Axillary node dissection was done to detect stained node. All blue nodes and any node receiving a blue lymphatic channel was considered as sentinel nodes. After excising the stained lymph nodes, nodes were sent for frozen section examination and complete axillary clearance was done. In node positive, removal of breast tissue was done. Further histopathological examination and pathological data including histopathological type, size of the tumor, ER/PR status, HeR2Neu status, and lymph node status in sentinel and non-sentinel lymph nodes was collected. SLNs were routinely examined by serial sectioning with two sections of 200 microns each were stained, one with routine hematoxylin and eosin (H&E) and one by IHC using cytokeratin. Lymph nodes were examined by H&E staining. Negative lymph node was additionally stained with IHC.

Statistical analysis:

Demographic, histopathological data was categorically. To analyze the effect of presence of breast cancer (site), size, ER, PR and HER's-2 status on the presence of ALNM and SNLM. Univariate analysis was done using chi-square test. Multivariate analysis was performed using logistic regression analysis for those factors which were significant on Univariate analysis. Odds ratios and *p*-values were calculated with 95% confidence intervals (CI). All *p*-values less than 0.05 were used for statistical significance. Statistical analyses for evaluating sensitivity, specificity, accuracy, and positive and negative predictive values of SLNB were performed in comparison to ALND. False-negative sentinel lymph nodes localization was defined as negative sentinel lymph nodes with other nodes in the basin positive for metastatic breast cancer. Sensitivity was calculated by the number of patients in whom the histological characteristics of the sentinel lymph nodes reflected the histological characteristics of the rest of the nodes in the basin. All analyses were performed using SPSS software version 20.0 (IBM Corp., Armonk, NY, USA).

Results

The study included 80 cases of early breast cancer, of which 44 (55 %) showed axillary metastasis. Mean age of the patient at the time of surgery was 52.84 years which ranged from 30-70 years. 32 patients were below 50 years of age. The tumor size was T2 (2–5 cm) in 65 patients and T1 (<2 cm) in 15 (Table 1). No correlation was observed between tumor size and patient's age with ALNM. On histological typing of breast cancer, 68 (71.57%) cases were infiltrating duct carcinoma (IDC). Correlation was noted between histological type of tumor and axillary metastasis (p <, 0.046). Tumors like DCIS, lobular carcinoma and mucinous carcinoma showed less tendency for ALNM compared to IDC.

39 patients (48.75%) had grade II tumors which were the most common. ER was positive in 54 patients while PR was positive in 42 patients. On ER and PR immunohistochemistry, it was not significantly associated with low risk of ALNM ($p < 0.002$ Table 2). Quadrant- wise location of breast cancer is presented in Table 1. To identify the clinical traits affecting SNLM, Univariate analysis was performed on all candidate predictors. The results showed that T2 has higher significance on SLNM (p<0.013) and ALNM (p<0.028),parts of Quadrants including upper outer , upper inner, lower outer, were significantly correlated with SLNM with p value of 0.038, 0.01 and 0.12 respectively (Table 2). Features statistically significant in the Univariate logistic regression model were included in the multivariable logistic regression model. The results showed that size, UO and central quadrant were independent risk factors of SLNM. (P<0.038).

Factors			SLNM	ALNM
Age	30 - 40	(14)17.5%	9	9
	41-50	(18)22.5%	8	9
	51-60	(25)31.25%	14	16
	61-70	(23)28.75%	13	12
Tumor Location:				
Upper outer	46	57.5%	31	33
Upper inner	5	6.25%	0	1
Lower outer	15	18.75%	13	12
Lower inner	8	10%	0	0
Central quadrant	6	7.5%	1	1
Tumor Size:				
Less than or equal 2 cm	15	17.5%	4	6
2-5	42	52.5%	23	41
DCIS	2	1.25%	0	1
IDC	73	91.25%	69	46
ILC	2	2.5%	0	0

ER	54	67.5 %	28	31
PR	42	52.5%	24	28
Her 2 neu	20	25%	14	13

Table 1:

Demographic data and characteristic of breast cancer

Factors	SLNB yes	SLNB NO	P VALUE	ALND YES	ALND NO	P VALUE	MULTIVARIATE	Odds ratio
UOQ	31	15	0.038	33	13	0.008	0.009	6.85
UIQ	0	5	0.12	1	4	0.15	0.063	3.25
LO	13	2	0.01	12	3	0.08	0.072	3.23
LI	0	7	0.002	0	7	0.001	-	-
CQ	1	5	0.07	1	5	0.03	0.026	4.94
T1	5	12	0.013	6	11	0.028	0.022	5.26
T2	40	22	-	41	21	-	-	-
ER	28	26	0.225	31	23	0.629	-	-
PR	24	18	0.1	28	14	0.178	-	-
HER 2 NEU	14	6	0.382	13	7	0.59	-	-

UOQ= Upper outer quadrant

UIQ= Upper outer quadrant

LO=Lower outer

LI=Lower inner

CQ=Central quadrant

T1 = tumor less than or equal to 2 cm

T2=size 2cm-5cm

ER=Estrogen receptor

PR=Progesterone receptor

Her 2 neu=Human epidermal receptor

Table 2: *Univariate and Multivariate analysis of factors influencing sentinel and axillary node metastasis*

To identify the clinical traits affecting ALNM, Univariate logistic regression was performed on all clinical factors influencing ALNM. The results showed that T2 ($P < 0.028$), parts of Quadrants including upper outer (P value 0.008), upper inner (p value =0.015), lower outer (n p value =0.08), were significantly correlated with ALNM (Table 2). Features statistically significant in the univariate analysis model were included in the multivariable logistic regression model. The results showed that size, UOQ, and CQ were independent risk factors of ALNM. ($p<0.022$, $p<0.009$, $p<0.026$ respectively) (Table 2). After analyzing the data, overall sensitivity, specificity, positive predictive valve (PPV) and negative predictive valve (NPV) of SLNB in predicting axillary node status was 77.59%, 100%, 100% and 62.86% respectively. The overall accuracy was 83.7%.

Discussion

The presence of axillary disease is the most important prognostic factor in breast cancer. Axillary metastasis indicates biological aggressiveness and extent of tumor involvement, often with systemic spread [18]. SNB has replaced axillary lymph node dissection (ALND) in clinically node negative axilla. Multiple randomized trials have demonstrated that when the SLN is tumor-free, observation alone confers similar regional control and survival compared to SNB followed by ALND [5-8] .Women with operable breast cancer and multicentric tumors, with ductal carcinoma in situ, and planned for mastectomy, with previous breast and/or axillary surgery, or who received preoperative/neoadjuvant systemic therapy may be offered SNB, however SNB is thought to be safer before chemotherapy due to its systemic therapy induced lymphatic changes. Also,SNB for patients with ductal carcinoma in situ (DCIS) is controversial. While women with large or locally advanced invasive breast cancer (tumor size T3/T4), inflammatory breast cancer, or ductal carcinoma in situ (when breast-conserving surgery is planned) or are pregnant should not undergo SNLB [9]. In NSABP-B32, pathologically negative SLNs, 99.9% on follow-up at 95.6 months, there was no statistically significant difference between the SNB plus ALND group and the SNB-only group with respect to regional recurrence (RR) , 8-year overall survival (OS) and 8-year disease-free survival (DFS) [10] Gary H et al suggested that SNB is associated with less morbidity than ALND, but the comparative effects of these two approaches on tumor recurrence or patient survival are unknown [11]. Meanwhile, high-frequency ultrasonography, the first-line imaging modality in breast cancer diagnosis, can show the rich morphological features of breast tumor, associated with ALNM. [13-20]. Previous studies have shown that clinico-pathological features such as size, age at diagnosis, palpable mass or not, body mass index (BMI) and hormone receptors are related to ALNM [21-22]. However, in our study, we aimed to compare the incidence of SLNM and ALNM based on the quadrant of breast and size of tumor in breast cancer. We found that different quadrant of breast involvement had differential incidence of SLNM and ALNM.In our study Upper outer quadrant had significantly higher incidence of breast cancer. We also found that incidence of SLNM and ALNM was significantly

higher for this specific quadrant. It was interesting to note that there was no significant difference between the SLNM and ALNM. Thus, axillary node can be addressed in the patient having disease in the outer upper quadrant without the need of sentinel node biopsy especially in low resource settings. Another study led by Franco et al has shown that USG guided FNAC can be an effective alternative to SLNB with frozen section of nodes [23]. It concluded that USG guided FNAC had better specificity, cost reduction and reduction in false positive results. Lee et al in 2002 published a study stated that tumor size and Lymphovascular invasion LVI were the only variables independently predictive of positive SLNB results [22].

In our study, we found that T2 breast lesion had significantly higher number of SNM and ALNM.Similar results were concluded in the study led by Jong Hong Lee et al. [12]. Thus according to our study, quadrant of breast and size of tumor can be consider as a clinically valuable marker for axillary metastasis and reducing the use of SLNB. This can not only help us in cost reduction avoiding the use of radioactive tracer but also in reducing intraoperative timing and need for second surgery. This algorithm will help us in reducing the false negative cases improving overall survival without compromising oncological safety. Indian study led by Nandu [23] showed the Sensitivity of SLNB is 90.48%, specificity is 85.71%, PPV of is 90.48%, NPV is 85.71%, and accuracy is 88.57% comparable to our sensitivity, specificity, PPV, NPV and accuracy of 77.59%, 100%,100%, 62.86% ,83.7% respectively.

Limitation: Lymphovascular invasion, perineural invasion were not taken into consideration for SLNM and ALNM as our study limited to clinical factors influencing the metastasis. Our study is first of its kind Indian study to state the importance of site of early breast cancer in influencing SLNM and ALNM.

Conclusion

Upper outer quadrant, central quadrant and size of the tumors are important prognostic factors to predict axillary node metastasis without the need of sentinel node biopsy in early breast cancers.

Conflict of interest

None

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

References

1. Amersi F, Hansen NM. (2006) The benefits and limitations of sentinel lymph node biopsy. Curr Treat Options Oncol. 7(2):141-151. doi:10.1007/s11864-006-0049-y
2. Nano MT, Kollias J, Farshid G, Gill PG, Bochner M. (2002) Clinical impact of false-negative sentinel node biopsy in primary breast cancer. Br J Surg. 89(11):1430-1434. doi:10.1046/j.1365-2168.2002.02233.x
3. Verry H, Lord SJ, Martin A, et al. (2012) Effectiveness and cost-effectiveness of sentinel lymph node biopsy compared with axillary node dissection in patients with early-stage breast cancer: a decision model analysis. Br J Cancer. 106(6):1045-1052. doi:10.1038/bjc.2012.62
4. Songtish D, Praditsitthikorn N, Teerawattananon Y. (2014) A Cost-Utility Analysis Comparing Standard Axillary Lymph Node Dissection with Sentinel Lymph Node Biopsy in Patients with Early Stage Breast Cancer in Thailand. Value Health Reg Issues. 3:59-66. doi: 10.1016/j.vhri.2014.01.003
5. Krag DN, Anderson SJ, Julian TB, et al. (2010) Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol. 11(10):927-933. doi:10.1016/S1470-2045(10)70207-2
6. Veronesi U, Viale G, Paganelli G, Zurrida S, Luini A, et al. (2010) Sentinel lymph node biopsy in breast cancer: ten-year results of a randomized controlled study. Ann Surg. 251(4):595-600. doi: 10.1097/SLA.0b013e3181c0e92a. PMID: 20195151.
7. Canavese G, Catturich A, Vecchio C, et al. (2009) Sentinel node biopsy compared with complete axillary dissection for staging early breast cancer with clinically negative lymph nodes: results of randomized trial. Ann Oncol. 20(6):1001-1007. doi:10.1093/annonc/mdn746
8. Zavagno G, De Salvo GL, Scalco G, et al. (2008) A Randomized clinical trial on sentinel lymph node biopsy versus axillary lymph node dissection in breast cancer: results of the Sentinella/GIVOM trial. Ann Surg. 247(2):207-213.
9. Lyman GH, Somerfield MR, Bosserman LD, Perkins CL, Weaver DL, Giuliano AE. (2017) Sentinel Lymph Node Biopsy for Patients With Early-Stage Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 35(5):561-564. doi:10.1200/JCO.2016.71.0947
10. Krag DN, Anderson SJ, Julian TB, et al. (2010) Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol. 11(10):927-933. doi:10.1016/S1470-2045(10)70207-2
11. Lyman GH, Giuliano AE, Somerfield MR, Benson AB, Bodurka DC, Burstein HJ, et al. (2005) American Society of Clinical Oncology. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol. 23(30):7703-20. doi: 10.1200/JCO.2005.08.001. Epub 2005 Sep 12. PMID: 16157938.
12. Lee JH, Kim SH, Suh YJ, Shim BY, Kim HK. (2010) Predictors of axillary lymph node metastases (ALNM) in a Korean population with T1-2 breast carcinoma: triple negative breast cancer has a high incidence of ALNM irrespective of the tumor size. Cancer Res Treat. 42(1):30-36. doi:10.4143/crt.2010.42.1.30
13. Houssami N, Irwig L, Simpson JM et al. (2003) Sydney breast imaging accuracy study: comparative sensitivity and specificity of mammography and sonography in young women with symptoms. Am J Roentgenol, 180: 935–940. [PubMed] [Google Scholar]
14. Kolb TM, Lichy J, Newhouse JH. (2002) Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology, 225: 165–175. [PubMed] [Google Scholar]
15. Osako T, Iwase T, Takahashi K et al. (2007) Diagnostic mammography and ultrasonography for palpable and nonpalpable breast cancer in women aged 30 to 39 years. Breast Cancer, 14: 255–259. [PubMed] [Google Scholar]
16. Devolli-Disha E, Manxhuka-Kërliu S, Ymeri H, Kutllovci A. (2009) Comparative accuracy of mammography and ultrasound in women with breast symptoms according to age and breast density. Bosn J Basic Med Sci, 9: 131–136. [PMC free article] [PubMed] [Google Scholar]
17. Royal College of Radiologists. Guidance on Screening and Symptomatic Breast Imaging. 2nd edn. London: RCR; 2003. [Google Scholar]
18. Kolb TM, Lichy J, Newhouse JH. (1998) Occult cancer in

women with dense breasts: detection with screening US – diagnostic yield and tumor characteristics. Radiology, 207: 191–199. [PubMed] [Google Scholar]

19. Buchberger W, DeKoekkoek-Doll P, Springer P et al. (1999) Incidental findings on sonography of the breast: clinical significance and diagnostic workup. Am J Roentgenol, 173: 921–927. [PubMed] [Google Scholar]
20. Kaplan SS. (2001) Clinical utility of bilateral whole-breast US in the evaluation of women with dense breast tissue. Radiology, 221: 641–649. [PubMed] [Google Scholar].
21. Wang J, Cai Y, Yu F, Ping Z, Liu L. (2020) Body mass index increases the lymph node metastasis risk of breast cancer: a dose-response meta-analysis with 52904 subjects from 20 cohort studies. BMC Cancer. 20(1):601. Published 2020 Jun 29. doi:10.1186/s12885-020-07064-0
22. Zhang, W., Xu, J., Wang, K. et al. (2020) Independent risk factors for axillary lymph node metastasis in breast cancer patients with one or two positive sentinel lymph nodes. BMC Women's Health, 20, 143.

DOI: 10.31579/2690-1897/082