International Surgery Journal
Masthi GK et al. Int Surg J. 2019 Aug;6(8):2889-2894
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20193337

Original Research Article

A simple scoring system to determine axillary lymph node metastasis in carcinoma breast

Greeshma K. Masthi, Rohit Krishnappa*, Rajagopalan S.

Department of General Surgery, Rajarajeswari Medical College and Hospital, Bangalore, Karnataka, India

Received: 22 March 2019
Revised: 20 June 2019
Accepted: 26 June 2019

***Correspondence:**
Dr. Rohit Krishnappa,
E-mail: rohitkrishappa@yahoo.co.in

ABSTRACT

Background: The aim of this study is to develop a scoring system wherein axillary lymph node metastasis in carcinoma breast can be predicted preoperatively using simple variables.
Methods: A prospective study carried out from December 2017-November 2018 at Rajarajeswari Medical College and Hospital. All clinically node negative cases were included. Data from clinical examination, histopathology report and immunohistochemistry (obtained from trucut biopsy preoperatively) is correlated with presence or absence of lymph node metastasis obtained after modified radical mastectomy. And a scoring system is proposed according to the results obtained.
Results: Out of 36 cases studied, 12 cases had score <10, 11 cases had score 11-13, 13 cases had score >14, indicating that more than 50% of cases were over treated with axillary lymph node dissection.
Conclusions: Lymph node metastasis in carcinoma breast can be predicted clinically using a scoring system. Further a recommendation for or against axillary node dissection can be made according to the respective scores.

Keywords: Axillary lymph node metastasis, Carcinoma breast, Sentinel lymph node biopsy

INTRODUCTION

Axillary lymph node metastasis (ALNM) is the single most independent prognostic factor in carcinoma breast.[1] Axillary lymph node dissection (ALND) is an overtreatment in majority of the cases, it reduces the quality of life, prolongs operating time and hospitalisation without therapeutic benefit in node negative cases.[2] Lymphedema(13%), sensory loss(31%), restricted shoulder mobility, weakness of shoulder, unnecessary axillary pain, increased risk of infection are seen after ALND.[1,2] To avoid ALND, sentinel lymph node biopsy(SLNB) has been widely used to determine ALNM. SLNB is invasive and can have complications such as lymphedema-5%, axillary paraesthesia-8.8%, anaphylaxis to dye-0.1%. SLNB has a false negative rate of 12%, it is contraindicated in pregnancy, lactation and in locally advanced breast cancer(LABC).[2-4] Role of SLNB in multicentric or extensive multifocal disease, previous breast or axillary surgery , prior neo adjuvant treatment is not known.[3-5] Predicting ALNM before SLNB using certain clinical, histopathological and IHC variables helps in decision making. Current treatment of breast cancer is guided by tumor behavior and staging. [4-7] Benefit of treatment would be greater if it is planned according to the spectrum of disease, thereby reducing morbidity from axillary surgery.[7]

ALND and SLNB have their own pitfalls as mentioned. Optimal approach to clinically node negative cases is still a matter of debate and there is scope for a clinico-pathological scoring system.

The Objective of this study was to develop a simple scoring system wherein axillary lymph node metastasis can be predicted preoperatively in order to decide the best treatment option namely:

- No axillary staging for patients with no probability of metastasis
- SLNB for patients with low probability of metastasis
- ALND for those with high probability of metastasis.

METHODS

The Study design is Prospective cohort study and Study period are July 2017- December 2018, The Sample size are taken 36 patients, Study place was Rajarajeswari Medical College and Hospital.

Inclusion criteria

All breast cancer patients with clinically node negative axilla.

Exclusion criteria

Local recurrence
Neoadjuvant chemotherapy
Bilateral tumors

Procedure

The baseline demographic data as per pro forma was collected. Breast and axilla were thoroughly examined. Investigations as per pro forma before and after surgery were sent. All patients underwent trucut biopsy and specimen was sent for HPE (Histopathological examination) to obtain details of variables mentioned in the outcome measures below.

Outcome measures include correlation of tumor size and data obtained from trucut biopsy {histological subtype, grade, Lymphovascular invasion (LVI), Estrogen receptor (ER), Progesterone receptor (PR), HER2(Human epidermal growth factor receptor 2), Ki-67 status} with ALND results obtained after MRM. The ethical approval was Institutional Ethical committee clearance obtained.

Statistical analysis

The assosciation between selected variables, subgroups and ALNM was determined using percentage of metastasis for each variable and importance of variable decided by odds ratio.

Based on the results obtained from statistical analysis-scoring system to predict lymph node metastasis is developed.

According to the results (percentage of lymph node metastasis and odds ratio), each variable was assigned a score and a scoring system was developed with total score of 17.

Table 1: Scores for each variable separately.

Variables	Score
TS (cm)	
<2	1
2-5	2
>5	3
NHG	
3-5	1
6-7	2
7-9	3
LVI	
Absent	0
Present	5
MS	
Triple negative	0
Lum A	1
Lum B Her 2 –	2
Her 2+	3
Lum B Her 2+	4
Ki-67	
<14%	0
14-45%	1
>45%	2

Table 2: Maximum score assigned to each variable.

Variables	Max. score
Tumor size(TS)	3
Nottinghamhistological grade (NHG)	3
Lympho-vascular invasion (LVI)	5
Molecular subtype (MS)	4
Ki-67 status	2
Total	17

To decide the probability of metastasis, scores was categorized into 3 groups- no metastasis, probable metastasis, highly probable metastasis. In author study there were 12 patients with score less than 10 ,11 patients with score 11-13, 13 patients with score 14-17.

RESULTS

Age distribution in carcinoma breast patients with clinically node negative axilla

There were 25 patients in the age group above 40 years and 11 patients with age group less than 40 years

6 patients in age group less than 40 years had lymph node metastasis, 14 patients in age group more than or equal to 40 years had lymph node metastasis.

Table 3: Age distribution.

Age (years)	No.	LNMx	No LNMx
<40	11	6	5
≥40	25	14	11
Total	36	20	16

LNMx- Lymph node metastasis, No. –Number

Correlation of size of tumor with lymph node metastasis

Size of tumor was categorised into 3 groups, and lymph node metastasis in each group was assessed

14.2% of patients with tumor size <2 cm had lymph node metastasis, 57.8% of patients with tumor size 2-5cm had lymph node metastasis, 80% of the patients with tumor size >5 cm had lymph node metastasis

As depicted in table below odds ratio is highest (4.67) for tumor size >5 cm, indicating five times higher chance of lymph node metastasis if tumor size >5 cm.

Table 4: Size of tumor and lymph node metastasis.

Size (cm)	No.	LNMx	No LNMx	%	Odds ratio
<2	7	1	6	14.2	0.08
2-5	19	11	8	57.8	1.23
>5	10	8	2	80	4.67
Total	36	20	16		

%- percentage of lymph node metastasis in each group

Correlation of lympho-vascular invasion with lymph node metastasis

Among 18 patients with lympho-vascular invasion, 17 patients constituting to 94.4% had lymph node metastasis.

Among 18 patients with no lympho-vascular invasion, only 3 patients constituting 16.6% had lymph node metastasis. Odds ratio is 85 for lympho-vascular invasion, highest among all variables, indicating eighty five times higher chances of lymph node metastasis if it is positive.

Table 5: LVI and lymph node metastasis.

LVI	No.	LNMx	No LNMx	%	Odds ratio
Present	18	17	1	94.4	85
Absent	18	3	15	16.6	0.01
Total	36	20	16		

LVI- Lymphovascular invasion.

Correlation of Nottingham histological grade with lymph node metastasis

According to Nottingham histological grade, tumour was divided into low, intermediate and high grades.

72.7% of high grade tumours, 55% of intermediate grade tumours and 20% of low grade tumours had lymph node metastasis. Odds ratio for high grade tumour is higher (2.2) as indicated in the table below.

Table 6: Nottingham histological grade and lymph node metastasis.

Grade	NO.	LNMx	No LNMx	%	Odds ratio
3-5 (low grade)	5	1	4	20	0.17
6-7 (intermediate grade)	20	11	9	55	1.4
8-9 (high grade)	11	8	3	72.7	2.2
Total	36	20	16		

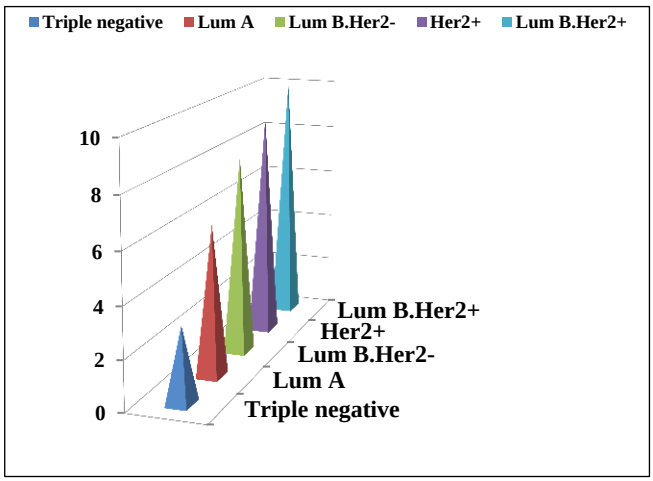

Figure 1: Molecular subtypes.
X-axis: Molecular subtype, Y-axis: Number of patients.

Correlation of molecular subtype with lymph node metastasis

According to St. Gallen molecular subtypes tumour was categorised into 5 molecular subtypes.

Luminal B Her2+ has the highest odds ratio of 4.6, hence this subtype possesses higher risk for lymph node metastasis.

Correlation of Ki-67 status with lymph node metastasis

Tumours were grouped into 3 sub-groups based on Ki-67 status.

30% of tumours with Ki-67 less than 14, 62.5% of the tumours with Ki-67 14-45, 75% of the tumours with Ki-67 more than 45 had lymph node metastasis.

Ki-67 >45% has odds ratio of 2.3, indicating 2.3 times higher chances of lymph node metastasis.

Table 7: Molecular subtype and lymph node metastasis.

MS	NO.	LNMx	No LNMx	%	Odds ratio
Triple negative	3	0	3	0	0
Lum A	6	2	4	30	0.3
Lum B. Her 2-	8	4	4	50	0.75
Her2+	9	6	3	66.6	1.8
Lum B. Her 2+	10	8	2	80	4.6
	36	20	16		

MS- Molecular subtype, Lum -Luminal, LNMx- Lymph node metastasis.

Table 8: Ki-67 proliferative index and lymph node metastasis.

Ki-67(%)	No.	LNMx	No LNMx	%	Odds ratio
<14	10	3	7	30	0.23
14-45	16	10	6	62.5	1.67
>45	10	7	3	75	2.34
Total	36	20	16		

Table 9: Proposed scoring system to assess lymph node metastasis.

Score	Probability of metastasis
<10	No metastasis
11-13	Probable metastasis
14-17	Highly probable metastasis

Table 10: Total score distribution in our study.

Score	No.
<10 (No metastasis)	12
11-13 (probable metastasis)	11
14-17 (highly probable metastasis)	13
	36

As shown in the Table 11, the NPV for score <10 is 100%, hence we can negate the possibility of lymph node metastasis and skip axillary treatment, NPV is 63.6% for score 11-13, hence SLNB is to be performed which if positive should proceed with ALND. But if the score is 14-17, which has NPV of 7.69, straightaway ALND is indicated.

Table 11: Scoring and findings from histopathological report obtained after MRM.

Score	No.	Post MRM results		Percentage of LNMx (%)	NPV (negative predictive value) (%)
<10	12	LNMx	0	0	100
		No LNMx	12		
11-13	11	LNMx	4	36.3	63.6
		No LNMx	7		
14-17	13	LNMx	12	92.3	7.69
		No LNMx	1		

DISCUSSION

ALN (axillary lymph node) status is an important factor in developing a individualised treatment plan for patients with breast cancer.[2,8,10]

Currently, SLNB is used as a standard tool to assess the risk of preoperative ALN in clinically node negative breast cancer patients.[6,9,12] This study has provided evidence of the independent impact of routine clinicopathological parameters, St Gallen molecular subtypes and tumour size on the lymphatic spread of breast cancer. This simple scoring system has been proposed based on comprehensive data, with the aim of allowing the clinician to evaluate the risk of axillary metastatic disease and the extent of lymph node involvement more accurately, as a tool for determining the appropriate method of axillary surgery if necessary.

ACOSOG Z0011 was a randomized trial (1999) which enrolled women with cT1-2N0 breast cancer undergoing breast-conserving therapy and adjuvant whole-breast radiotherapy. The initial results, with a median follow-up of 6·3 years, demonstrated no differences in overall or disease-free survival for patients with one to two metastatic sentinel nodes who had ALND versus those who had SLNB alone.[11] The updated report of the same trial, with a median follow-up of 9·25 years, supported the initial conclusion indicating no clinical benefit of completion axillary dissection for patients with one or two involved lymph nodes. The IBCSG trial 23-01 conducted from April 2001 to February 2010, was designed to determine whether omission of ALND was non-inferior to axillary dissection in patients with micrometastatic sentinel nodes and tumour no larger than 5 cm, irrespective of type of breast surgery.

The results supported the notion that axillary dissection can be safely avoided in patients with early breast cancer and micrometastatic sentinel node involvement.

Dihge et al, in their retrospective study (2016) titled "Nomograms for preoperative prediction of axillary lymph node metastasis in breast carcinoma" concluded that their pre-operative nomogram can be used to predict ALNM using variables such as vascular invasion, multifocality, tumor size, age, histologcal type and mode of detection of carcinoma breast.[13] Takada et al, proposed a decision tree based model in 2012 and emphasised that it can aid oncologists in decision making process before starting treatment in early breast carcinoma.[14]

There is a great advantage to develop a scoring system that accurately and non-invasively predicts ALN metastasis preoperatively. Establishing reliable tool with clinico-pathological factors is a feasible method to evaluate the likelihood of ALN metastasis.

In this study, we have proposed and validated a simple scoring system for prediction of ALN status in patients with breast cancer. By categorizing the endpoints into: No metastasis, Probable metastasis and Highly probable metastasis groups based on the clinico-pathological factors and not solely counting on sentinel node status as a benchmark, the present scoring system is able to identify patients at risk of axillary metastasis.

In the present study we found that increasing tumor size presence of lympho vascular invasion, higher Nottingham histological grade, LumB Her2+ St Gallen molecular subtype, higher Ki-67 proliferative index were all associated with increased risk of axillary lymph node metastasis. With this tool, patients with low risk of ALN metastasis can avoid ALND and SLNB.

This study has two limitations. First, ours was a small study population, a larger number of patients are needed to acquire more reliable evidence for clinical application. Second, the data of our scoring system established and validated were all from the same hospital, so we believe a multi-center study to carry out external validation for the scoring system will help.

Our simple scoring system seems a reliable and non-invasive tool for preoperative prediction of ALN status without any additional investigational burden and can be conveniently used to optimize current treatment strategy for breast cancer patients.

CONCLUSION

The scoring system presented facilitates preoperative decision making regarding the extent of axillary surgery. For patients with clinically node negative carcinoma breast, this scoring system predicts lymph node metastasis. Further, the necessity of performing SLNB or ALND can be decided based on the probability of metastasis according to the score.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA. 2011;305(6):569-75.
2. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Costantino JP, et al. 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. 2010;11(10):927-33.
3. Morrow M. Sentinel Lymph Node Biopsy: Benefits and Limitations. Zentralbl Gynakol. 2003;125(9):335-7.
4. Veronesi U, Paganelli G, Viale G, Luini A, Zurrida S, Galimberti V, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med. 2003;349(6):546-53.
5. Yoo SH, Park IA, Chung YR, Kim H, Lee K, Noh DY et al. A histomorphologic predictive model for axillary lymph node metastasis in preoperative breast cancer core needle biopsy according to intrinsic subtypes. Hum Pathol. 2015;46(2):246-54.
6. Lyman GH, Giuliano AE, Somerfield MR, Benson AB III, Bodurka DC, et al. 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. 2005;23(30):7703-20.
7. Smeets A, Ryckx A, Belmans A,Wildiers H, Neven P, Floris G, et al. Impact of tumor chronology and tumor biology on lymph node metastasis in breast cancer. Springerplus. 2013;2(1):480.
8. Cianfrocca M, Goldstein LJ. Prognostic and predictive factors in early-stage breast cancer. Oncologist. 2004;9(6):606-16.
9. Meretoja TJ, Heikkilä PS, Mansfield AS, Cserni G, Ambrozay E, Boross G, et al. A predictive tool to estimate the risk of axillary metastases in breast cancer patients with negative axillary ultrasound. Ann Surg Oncol. 2014;21(7):2229-36.
10. Denley H, Pinder SE, Elston CW, Lee AH, Ellis IO. Preoperative assessment of prognostic factors in breast cancer. J Clin Pathol. 2001;54(1):20-4.
11. Giuliano AE, Ballman K, McCall L, Beitsch P, Whitworth PW, Blumencranz P et al. Locoregional recurrence after sentinel lymph node dissection with

or without axillary dissection in patients with sentinel lymph node metastases: long-term follow-up from the American College of Surgeons Oncology Group (Alliance) ACOSOG Z0011 randomized trial. Ann Surg. 2016;264(3):413-20.
12. Dengel LT, Van Zee KJ, King TA, Stempel M, Cody HS, El-Tamer M et al. Axillary dissection can be avoided in the majority of clinically node-negative patients undergoing breast-conserving therapy. Ann Surg Oncol. 2014;21(1);22-7.
13. Dihge L, Bendahl PO, Rydén L: Nomograms for preoperative prediction of axillary nodal status in breast cancer. Br J Surg. 2017;104(11):1494-505.
14. Takada M, Sugimoto M, Naito Y, Moon HG, Han W, Noh DY, et al. Prediction of axillary lymph node metastasis in primary breast cancer patients using a decision tree-based model. BMC Medical Informatics and Decision Making. 2012;12(1):54.

Cite this article as: Masthi GK, Krishnappa R, Rajagopalan S. A simple scoring system to determine axillary lymph node metastasis in carcinoma breast. Int Surg J 2019;6:2889-94.