Research Article

Prognostic significance of Lymph Node Ratio in breast cancer –A single institutional retrospective study

Sumana Maiti Das[1], Krishnangshu Bhanja Choudhury[2], Suvra Mondal[3], Rahi Das[4]

[1]Department of Radiotherapy, R.G.Kar Medical College and Hospital, Kolkata, West Bengal
[2]Department of Radiotherapy, Malda Medical College and Hospital,Malda, West Bengal
[3]Department of Radiotherapy, R.G.Kar Medical College and Hospital,Kolkata,West Bengal
[4]Department of Radiotherapy, R.G.Kar Medical College and Hospital, Kolkata, West Bengal

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Corresponding Author: ***Suvra Mondal***. Email: suvramondal1992@gmail.com

ABSTRACT

Introduction and Aim: Axillary lymph node metastasis is a significant prognostic indicator in breast cancer patients. Lymph Node Ratio (LNR) is a better predictor of survival in node positive patients. We aimed to evaluate the prognostic significance of LNR in breast cancer patients.

Materials and Methods: 643 breast cancer patients treated between January 2018 and December 2023 were analyzed retrospectively. LNR is calculated as ratio of number of positive lymph nodes and dissected nodes. Cut off value of LNR taken was 0.231 and patients were classified into low (=<0.231) and high (>0.231) LNR group. Survival outcomes were estimated by Kaplan Meier method while log rank test was used to assess the significance. Cox proportional hazard regression models were used for univariate and multivariate analysis of parameters associated with survival.

Results: 49.6%(319) patients were found in high risk group. Adequate lymph nodes dissection (≥ 10) was found in 417/501 (83.2%) patients with Modified Radical Mastectomy (MRM) and in 104/135 (77.0%) patients with simple mastectomy with axillary dissection. The median number of lymph nodes dissected in adequate arm (n=526) was 13 (mean ± SD 13.90 ± 2.69, range 10-26). N3 nodal disease was significantly associated with positive perineural invasion (PNI). Median Disease Free Survival (DFS) in high risk group was 84 months, while it was not reached in the low risk arm.

Conclusion: LNR is an independent predictive factor for the prognosis of DFS and OS for non-metastatic breast carcinoma. This observation should be tested in a larger study.

Keywords: Breast cancer, lymph node ratio, survival, prognosis

1. INTRODUCTION

The axillary lymph node metastasis remains a significant prognostic indicator of disease-free survival (DFS) and overall survival (OS) in breast cancer patients. A linear relationship has been found with nodal disease burden and breast cancer specific survival independent of tumor size [1].

According to American Joint Committee on Cancer(AJCC), absolute number of positive lymph nodes is a better prognostic marker than the total number of lymph nodes removed. The number of removed lymph nodes required for prognostication of breast cancer is controversial, although 8th version of AJCC proposes at least 6 nodes to be removed and examined [2]. While, according to Fisher et al. [3], at least 10 nodes needed to be dissected. Inadequate lymph nodes dissection, defined as less than 10 lymph nodes dissected, would result in underreporting of N3 stage. In patients with up to three positive nodes where decision of adjuvant RT in 1-3 positive nodes differs between physician, there lies the need for absolute number of positive nodes and the extent of nodal metastasis .

In this context, Lymph Node Ratio (LNR) may resolve this problem. The LNR is defined as the ratio of positive nodes and the total no of dissected lymph nodes. It additionally also provides information about the extent of lymph node dissection. Studies have shown LNR as a better predictor of survival compared to pN staging in node positive breast cancer patients

[4]. LNR reduces the discrepancy between clinical evaluation and actual status of lymph nodes [5]. It also has an independent prognostic value in other malignancies like lung, stomach and colorectal cancer [6].

Till date there has been no recommendation towards using the LNR as an alternative to current pathological nodal (pN) staging and as prognostic marker in breast cancer patients. Therefore, we conducted this study on prognostic role of LNR in predicting locoregional recurrence rate (LRR), OS and distant recurrence in non -metastatic breast cancer patients.

2. MATERIALS AND METHODS

This retrospective study was conducted in a tertiary care centre in Eastern India. Data of 643 biopsy proven patients between January 2018 and December 2023 were taken. Information recorded for each patient were epidemiological data, diagnostic modalities, histopathology, modality of treatment received and date of last follow-up visit, or local/distal recurrence or death. We selected patients who had undergone axillary node dissection and total number of nodes examined as mentioned in biopsy report. Patients excluded were those who had evidence of distant metastasis at the time of diagnosis, or with complete pathological response after Neoadjuvant-Chemotherapy (NACT), or whose tumor size was not mentioned in histo-pathological report. Data included were age, sex, tumor site, size, grade, TNM stages, Hormone (ER/PR) receptor status, Her-2-neu, chemotherapy, type of surgery, margin status, presence of lymphovascular invasion(LVSI), perineural invasion (PNI), total number of lymph nodes dissected, whether adequate or not, number of positive nodes, presence of extra-capsular extension(ECE)/ Extranodal Extension(ENE). Patients were followed up till date of death or date of last follow-up. The LNR was assessed by the ratio of number of positive lymph nodes to the total number of lymph nodes dissected. Based on LNR cutoff value (0.231) analyzed in previous studies [7], patients were categorized into low risk (LNR<=0.231) and high risk (LNR>0.231) group.

2.1 Statistical analysis

Student's t-test was used for continuous variables, and chi-square test was used for categorical variables. Disease free survival (DFS) in months was defined as the time from treatment initiation till disease progression, either locoregional or distant metastasis or both. The overall survival (OS) in months was calculated from treatment initiation till death due to disease. Kaplan Meier survival analysis was used to compare the survival parameters between low and high-risk groups, as previously defined. Cox proportional hazard regression models were used for univariate and multivariate analysis of factors associated with survival.

Statistical analysis was done using the Statistical Package for Social Sciences (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). P values of less than 0.05 were considered as statistically significant. The study was not registered with a publicly accessible clinical trials registry as it was a retrospective study. No funding was obtained for this study.

3. RESULTS

3.1 Baseline characteristics

Table 1: Baseline characteristics

Baseline characteristics		Count (N)	ColumnN %
Gender	Female	636	98.9%
	Male	7	1.1%
Symptoms of presentation	Breast lump	634	98.6%
	Pain	6	0.9%
	Nipple discharge	3	0.5%
Family history of malignancy	Yes	29	4.5%
	No	614	95.5%
Site	Left breast	348	54.1%
	Right breast	292	45.4%
	Bilateral synchronous breast	3	0.5%
Grade	Grade 1	27	4.2%
	Grade 2	476	74.0%
	Grade 3	140	21.8%
ER	Negative	335	52.1%
	Positive	308	47.9%
PR	Negative	389	60.5%
	Positive	254	39.5%
Her 2 neu	Negative	442	68.7%
	Positive	201	31.3%
Ki67%	<14%	441	68.6%
	>14%	202	31.4%
LUMINAL	LA	284	44.2%
	LB	47	7.3%
	Her 2 neu enriched	74	11.5%
	TNBC	238	37.0%
Tumour	1	32	5.0%
	2	312	48.5%
	3	183	28.5%
	4	116	18.0%
Node	0	141	21.9%
	1	254	39.5%
	2	178	27.7%
	3	70	10.9%
STAGE	Early Breast Cancer	240	37.3%
	Locally Advanced Breast Cancer	403	62.7%

LA-Luminal A, LB- Luminal B, TNBC-Triple Negative Breast Cancer

A total of 643 patients were included in the study. Almost all Locally Advanced Breast Cancer (LABC) (n=375) patients received neoadjuvant chemotherapy. Majority of the patients (77%) underwent Modified Radical Mastectomy.

The median number of lymph nodes dissected in adequate arm (n=526) was 13 (mean ± sd 13.90 ± 2.69, range 10-26) and in inadequate arm it was 8 (7.65 ± 1.06, range 5-9) (Table 4).

Table 2: Clinicopathological characteristics

Pathological parameters		Count	Column N %
Margin of surgical specimen	Negative	573	89.1%
	Positive	51	7.9%
	Unknown	19	3.0%
PNI	No	559	86.9%
	Yes	84	13.1%
LVI	Yes	292	45.4%
	No	351	54.6%

PNI-Perineural Invasion, LVI-Lymphovascular Invasion

Table 3: Lymph node adequacy according to stage and surgery type

Surgery, TNM parameters		LN adequacy				*p* value
		Adequate		Inadequate		
		Count	Column N %	Count	Column N %	
Surgery type	Modified Radical Mastectomy	417	79.3%	84	71.8%	0.196
	Simple Mastectomy with Axillary Dissection	104	19.8%	31	26.5%	
	Toilet Mastectomy	5	1.0%	2	1.7%	
Nodal staging (N)	0	137	26.0%	4	3.4%	< 0.001*
	1	191	36.3%	63	53.8%	
	2	128	24.3%	50	42.7%	
	3	70	13.3%	0	0.0%	
TNM stage	Early Breast Cancer	195	37.1%	45	38.5%	0.779
	Locally Advanced Breast Cancer	331	62.9%	72	61.5%	

*Statistically significant p value, LN-Lymph node

Table 4:Lymph node adequacy out of the dissected lymph nodes

Adequate lymph node dissection		Dissected lymph nodes	positive lymph nodes
Adequate	N	526	526
	Median	13.00	2.00
	Mean	13.90	3.87
	Std. Deviation	2.687	4.031
	Minimum	10	0
	Maximum	26	18
Inadequate	N	117	117
	Median	8.00	3.00
	Mean	7.65	3.81
	Std. Deviation	1.085	2.453
	Minimum	5	0
	Maximum	9	9
	p value	< 0.001*	0.884

*Statistically significant p value

Table 5: Extracapsular extension in positive lymph nodes

Extracapsular extension	N	Median	Mean	Std. Deviation
Yes	106	9.00	8.71	3.395
No	537	2.00	2.90	3.065
Total	643	3.00	3.86	3.792

Table 6: Perineural invasion according to nodal staging and lymph node positivity

		PNI lymph node				*p value*
		Yes		No		
		Count	Row N %	Count	Row N %	
Extracapsular extension	Yes	79	74.5%	27	25.5%	< 0.001*
	No	12	2.2%	525	97.8%	
Nodal staging (N)	0	0	0.0%	141	100.0%	< 0.001*
	1	0	0.0%	254	100.0%	
	2	51	28.7%	127	71.3%	
	3	40	57.1%	30	42.9%	

*Statistically significant p value, PNI-Perineural Invasion

Table 6b:PNI in positive lymph nodes

PNI lymph node	N	Median	Mean	Std. Deviation
Yes	91	9.00	8.98	3.211
No	552	2.00	3.01	3.166
Total	643	3.00	3.86	3.792
p value < 0.001*				

*Statistically significant p value

Patients with ECE/ENE positivity had a median lymph node positivity of 9, against 2 lymph nodes positive in ECE/ENE negative patients, p value 0.001.79 out of 91 patients (74.5%) with ENE/ECE patients had PNI positivity (p<0.001). Likewise, N3 higher burden of nodal disease was significantly associated with higher PNI positivity (40 out of 70 patients), p<0.001 (Table 6a).

3.2 Lymph node ratio parameters

Table 7: Lymph node ratio categorization

LNR	N	Median	Mean	Std. Deviation	Minimum	Maximum
≤ 0.231	324	.07143	.07923	.079194	.000	.231
> 0.231	319	.54545	.56255	.235061	.235	1.000
Total	643	.23077	.31901	.298347	.000	1.000

LNR-Lymph Node Ratio

Table 8: Comparsion of types of events between low and high risk Lymph Node Ratio category

		LN_RATIO				*p* value
		≤ 0.231 low risk		> 0.231 high risk		
		Count	Column N %	Count	Column N %	
Event for DFS analysis	Local recurrence only	5	13.2%	20	27.4%	0.063
	Distant Metastases	4	10.5%	14	19.2%	
	Both local recurrence and distant metastases	29	76.3%	39	53.4%	
Locoregional recurrences only	Chestwall only	3	60.0%	2	10.0 %	0.024*
	Lymph nodes only	0	0.0%	10	50.0 %	
	Both	2	40.0%	8	40.0 %	
Metastatic sites for DFS analysis	LUNG	4	12.1%	10	18.9%	0.921
	LIVER	11	33.3%	17	32.1%	
	BONE	6	18.2%	8	15.1%	
	BRAIN	2	6.1%	2	3.8%	
	MULTIPLE	10	30.3%	16	30.2%	

*Statistically significant p value, DFS-Disease Free Survival

Median value for lymph node ratio (LNR) in our study was 0.231. 50.3%(n=324) patients falls under low risk and rest 49.6% (n=319) patients under high risk.

3.3 Survival outcomes

3.3.1 DFS relation with LNR

DFS was significantly associated with LNR(p=0.000).The median DFS in months for patients with LNR > 0.231 (high risk group) was 84 months(95%CI,69.8-77.1), while it was not reached in the low risk arm (Figure 1). 3 out of 319 (77.1%) high risk patients had disease recurrence or progression unlike 30 individuals out of 324 patients in low risk group.

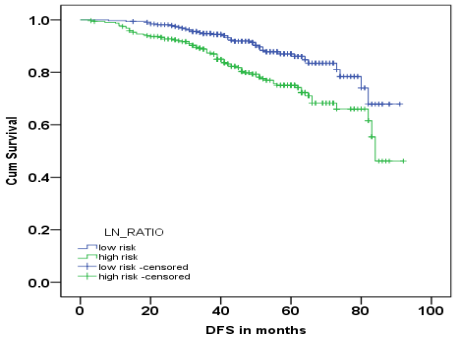

Figure 1:Disease free survival (DFS) of breast cancer patients in low risk(Lymph Node Ratio <=0.231) and high risk arm(Lymph Node Ratio>0.231) log rank p value <0.001.

3.3.2 Cox proportional hazard regression model for relation of different parameters with DFS

Initially univariate survival analysis was performed with the Cox proportional hazard regression for different groups (LN ratio, age groups, T and N staging, ER, PR, Her-2-neu and Ki 67%) for calculating the hazard ratio (HR) of disease progression (RR) with disease free survival parameters. Significant predictors in the univariate analysis were lymph node ratio, age group and T and N parameters which were further analysed by multivariate analysis. In multivariate analysis, age group, T and N parameters were statistically significant.

Table 9: Univariate Cox proportional hazard regression with DFS parameters

	HR (95% CI)	*p* value
Lymph Node Ratio		
≤0.231 (n=324)	1	
>0.231 (n=319)	2.101 (1.419-3.110)	0.001*
Age group		
<40 years (n=145)	1	
≥40 years (n=498)	0.556 (0.372-0.831)	0.004*
T stage		0.000*
1 (n=32)	1	
2 (n=312)	1.819 (0.438-7.560)	0.411
3 (n=183)	3.450 (0.829-14.362)	0.089
4 (n=116)	7.644 (1.840-31.760)	0.005
N stage		0.000*
N0 (n=141)	1	
N1 (n=254)	1.574 (0.830-2.983)	0.165
N2 (n=178)	3.109 (1.668-5.796)	0
N3 (n=70)	4.332 (2.180-8.609)	0
Histological Grade		0.796
Grade 1 (n=27)	1	
Grade 2 (n=476)	0.828 (0.335-2.047)	0.683
Grade 3 (n=140)	0.949 (0.363-2.482)	0.915
ER		
Negative (n=335)	1	
Positive (n=308)	1.046 (0.721-1.519)	0.813
PR		
Negative (n=389)		
Positive (n=254)	1.121 (0.770-1.632)	0.553
Her-2-neu		
Negative (n=442)	1	
Positive (n=201)	1.043 (0.701-1.553)	0.835
Ki 67%		
<14% (n=441)	1	
> 14% (n=202)	1.267 (0.857-1.874)	0.236

DFS-Disease Free Survival, T-Tumor stage, N-Nodal stage, ER-Estrogen Receptor, PR-Progesterone receptor, Her-2 neu-Human Epidermal Growth Factor Receptor 2 ,HR- Hazard Ratio, *statistically significant p value.

Table 10: Multivariate Cox proportional hazard regression with DFS parameters

	HR (95% CI)	*p* value
Lymph Node Ratio		
≤0.231 (n=324)	1	
>0.231 (n=319)	0.825 (0.402-1.689)	0.598
Age group		
<40 years (n=145)	1	
≥40 years (n=498)	0.600 (0.400-0.901)	0.014*
T stage		0.000*
1 (n=32)	1	
2 (n=312)	1.172 (0.275-4.994)	0.83
3 (n=183)	1.952 (0.455-8.378)	0.368
4 (n=116)	4.594 (1.078-19.588)	0.039*
N stage		0.015*
N0 (n=141)	1	
N1 (n=254)	1.296 (0.657-2.556)	0.455
N2 (n=178)	2.847 (1.100-7.364)	0.031*
N3 (n=70)	4.296 (1.580-11.679)	0.004*

DFS-Disease Free Survival ,T-Tumor stage, N-Nodal stage, HR- Hazard Ratio, *statistically significant p value

3.3.3 OS relation with LNR

At a median follow up of 52 months, it was found that patients with LNR<=0.23 had significantly greater overall surival(89.8% vs 83.7%) compared to patients with LNR>0.23 respectively(p<0.02) (Figure 2).

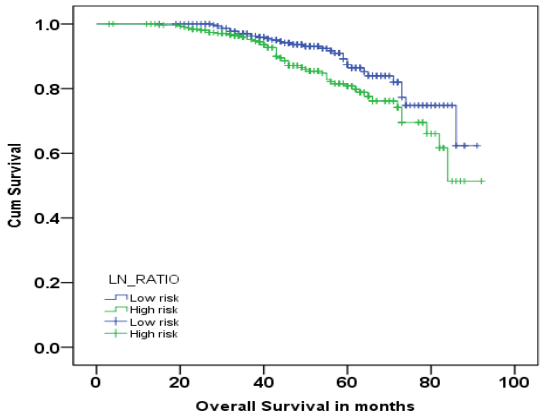

Figure 2:Overall survival (OS) of breast cancer patients in low risk(Lymph Node Ratio<=0.231) and high risk arm(Lymph Node Ratio >0.231) log rank test p value 0.02

3.3.4 Cox proportional hazard regression model for relation of different parameters with Overall survival

Table 11:Univariate Cox proportional hazard regression using OS parameters

	HR (95% CI)	*p* value
Lymph Node Ratio		
≤0.231 (n=324)	1	
>0.231 (n=319)	1.668 (1.078-2.581)	0.022*
Age group		
<40 years (n=145)	1	
≥40 years (n=498)	0.570 (0.358-0.906)	0.017*
T stage		0.000*
1 (n=32)	1	
2 (n=312)	1.203 (0.283-5.104)	0.803
3 (n=183)	2.595 (0.614-10.968)	0.195
4 (n=116)	6.857 (1.639-28.682)	0.008*
N stage		0.009*
N0 (n=141)	1	
N1 (n=254)	1.677 (0.840-3.348)	0.143
N2 (n=178)	2.762 (1.387-5.502)	0.004*
N3 (n=70)	3.054 (1.365-6.834)	0.007*
Histological Grade		0.25
Grade 1 (n=27)	1	
Grade 2 (n=476)	0.566 (0.227-1.415)	0.223
Grade 3 (n=140)	0.788 (0.296-2.094)	0.632
ER		
Negative (n=335)	1	
Positive (n=308)	1.024 (0.669-1.567)	0.914
PR		
Negative (n=389)		
Positive (n=254)	1.153 (0.751-1.771)	0.516
Her-2-neu		
Negative (n=442)	1	
Positive (n=201)	1.192 (0.765-1.855)	0.438
Ki 67%		
<14% (n=441)	1	
> 14% (n=202)	1.187 (0.758-1.860)	0.454

OS- Overall Survival, T-Tumor stage, N-Nodal stage, ER-Estrogen Receptor, PR-Progesterone receptor, Her-2 neu-Human Epidermal Growth Factor Receptor 2, HR- Hazard Ratio, *statistically significant p value

The same parameters used in DFS survival analysis were in OS cox proportional hazards model, first univariate followed multivariate analysis. Significant predictors in the univariate analysis were lymph node ratio, age group and T and N parameters which were further analysed by multivariate analysis. But in multivariate analysis, only Tumour staging (T) was significant predictor on overall survival but lymph node ratio along with nodal status (N) and age group variables had no statistically significant effect on overall survival.

Table 12: Multivariate Cox proportional hazard regression using OS parameters.

	HR (95% CI)	*p* value
Lymph Node Ratio		
≤0.231 (n=324)	1	
>0.231 (n=319)	0.750 (0.343-1.638)	0.471
Age group		
<40 years (n=145)	1	
≥40 years (n=498)	0.633 (0.394-1.017)	0.058
T stage		0.000*
1 (n=32)	1	
2 (n=312)	0.836 (0.191-3.659)	0.812
3 (n=183)	1.617 (0.369-7.088)	0.524
4 (n=116)	4.483 (1.038-19.363)	0.044*
N stage		0.176
N0 (n=141)	1	
N1 (n=254)	1.286 (0.613-2.696)	0.506
N2 (n=178)	2.667 (0.935-7.610)	0.067
N3 (n=70)	3.119 (1.002-9.706)	0.05

OS-Overall Survival, T-Tumor stage, N-Nodal stage, HR-Hazard Ratio, *statistically significant p value.

4. DISCUSSION

Adequate axillary lymph node dissection is very crucial for patients with breast cancer. In the N classification of current AJCC TNM staging system of breast cancer there are four prognostic nodal categories and they recommended dissection of at least 10 lymph nodes for adequate nodal staging [8]. But the technique and expertise of node dissection and to some extent variable effect of neo-adjuvant chemotherapy(NACT) on lymph node status does affect the number of lymph nodes detected after surgery. So, not only the number of nodes examined but also the number of positive nodes should be taken into account. Therefore, optimizing the methods for axillary lymph node

status assessment is essential. Here came the importance of LNR which provides both information regarding degree of lymph node metastasis as well as the extent of node dissection.

No consensus has been reached till date on the appropriate LNR cut off value.The cut off value is often set within a range of about 0.20-0.25 for low and high risk. Studies have shown [9] cut off values of LNR in between 0.20 and 0.65 could accurately predict prognosis than pathological nodal stage in breast cancer patients. We chose cut off value of 0.231 based on LNR cutoff values analyzed in previous study [7].

Till date most Indian studies [10] showed median age of disease occurrence ranging from 48-53 years. The median age of presentation in our study was 47 years (range 21-83 years), which also reinforced the fact of early occurrence of breast cancer in Indian woman than those in the West [11]. Median age of menarche and menopause was 13 and 45 years respectively which matched with data reported by Wu *et al.* [7]. There was left sided preponderance (54.1%). Majority of the patient (62.7 %) presented at locally advanced stage as shown in other study [12]. However, different observation was found by Kim *et al.* [13] where majority were of early stage. ER, PR positivity and Her 2 neu overexpression was seen in 47.9%, 39.5 and 31.3% cases respectively. We found a high incidence of TNBC (37.0%) which is comparable with Indian data [14] whereas in Western literature 10-20% of all breast cancer patients are of TNBC and it is the most aggressive type with poor outcome [15].

Almost all patients (n=375) with LABC received NACT. 501 (77%) patients underwent MRM and 20.9% patients had Simple Mastectomy with Axillary dissection. Incidence of surgery corroborates with other study [13] where 61.1% patients underwent total mastectomy and 38.9% partial mastectomy. Margin positivity rate is 7.9% while 13.1% patients showed PNI positivity and 45.4% had positive LVSI. Patients with ECE/ENE positivity had a median lymph node positivity of 9, against 2 lymph nodes positive in ECE/ENE negative patients, with significant p value 0.001. Similar findings were observed in another Indian study [16] with LVSI and ECE incidence of 45% (n=79) and 44% (n=78) respectively. Presence of LVSI has been found to be an important risk factor for axillary lymph node metastasis in another study [17] where they found similar incidence of LVSI (51.3%) and showed LVSI as (51.3% vs 30.3%; OR=2.07, 95% CI, 1.34-3.19) positive predictor of sentinel node metastasis. Another important finding of our study was higher burden of nodal disease (N3) which was also found to be associated with higher PNI positivity (40 out of 70 patients). Almost similar PNI incidence (14.1%) was seen in literature [18] where PNI positivity was also significantly associated with advanced T stage (p=0.005), lymph node positivity (p=0.001). Histologically, PNI is identified by the presence of malignant tumour cells adjacent to nerves in the tumour. It can predict regional and distant metastasis by virtue of its spread along the nerve pathways. Surgeons should reconsider extent of axillary lymph node dissection if PNI is detected on frozen section as PNI serves as poor prognostic factor with higher risk of disease. AJCC also recognizes PNI as a significant factor in staging breast cancer [8].

Studies had shown the number of lymph node dissected during axillary lymph node dissection was significantly lower in patients who received NACT than patients who did not [19]. There are possibilities of downstaging of axilla if less number of nodes are examined. Fisher *et al.* [3] showed that nodal status is most reliably assessed if at least 10 lymph nodes are retrieved. The predictability of prognosis by pN and LNR also depends on examination of at least 10 or more nodes [20]. We found adequate number of lymph nodes dissected ($\geq$ 10) in 417/ 501 (83.2%) patients with MRM and 104/135 (77.0%) patients with simple mastectomy with axillary dissection. 5 patients treated with toilet mastectomy had adequate lymph node dissection. The median number of lymph nodes dissected in adequate arm (n=526) was 13 (mean $\pm$ sd 13.90 $\pm$ 2.69, range 10-26) and in inadequate arm (n=117) it was 8 (7.65 $\pm$ 1.06, range 5-9). Similar incidence of adequacy in lymph node dissection (81%)was found in literature [9]. However the median number of involved node in

that study was 2 (range 1-32). Improved survival in patients with the increased number of total lymph node dissection and negative nodes was proved by Vinh-Hugh *et al* [21].

The median cut off value for lymph node ratio (LNR) taken was 0.231 which was previously validated as cut-off value of LNR by Wu *et al.* [7]. All values of LNR above 0.231 was considered as high risk for recurrence or disease progression and LNR ≤ 0.231 considered as low risk category. 50.3%(n=324) patients falls under low risk and rest 49.6%(n=319) patients under high risk.

Disease progression was observed more in high risk (22.8%) compared to low risk (11.7%). 61.2% patients had both locoregional failure and distant metastasis of which majority (57.3%) belongs to the high risk category. 80% patients in the high risk category had higher statistically significant (p<0.02) locoregional reccurence. 61.6% (n=53) of high risk category had distant metastasis. A study [13] with a median follow up period of 73.5 months (range 11-183 months) showed locoregional recurrence in 12.8% patients (n=30) and 5 year locoregional cotrol rate was 88.8%. They concluded significantly increased risk of locoregional recurrence in patients with high LNR (p=0.05).

We also found patients falling under high risk category had a median DFS of 84 months, while it was not reached in the low risk arm. OS was not reached in both the arms. Analysis also showed that patients whose LNR<=0.23 had significantly greater overall surival (89.8% vs 83.7%) compared to patients with LNR>0.23 respectively(p<0.02). A study [22] on 165 patients found inverse correlation of DFS with lymph node categories. They chose a LNR single value of 15% and showed decreased DFS was significantly associated with low LNR both in hormone receptor positive (p=0.04) or triple negative (p=0.001) patients. In another international study [19] more than 18% of high LNR patients had HR of -1.81(95% CI,1.34-2.45, p=0.0001) .Even in a recent meta-analysis[23], it was observed that there was a significant association between higher LNR and shorter OS (HR:4.74;95%CI:3.36-6.67;p<0.001) and DFS(HR:4.77; 95%CI:3.69-6.17; p<0.001) in breast cancer patients who received neoadjuvant chemotherapy.

Higher (76.7%) survival was also found in low risk group compared to 61.4% in high LNR group. Indian literature[16] also supports the same observation. They showed that with a median follow up period of 24 months, lower LRR (9% vs14%,p=0.25) was observed in patients with LNR <=20%, lower DR(13% vs27%, p=0.01) and also improved OS(89% vs 79%,p=0.02) compared to patients with LNR >20%. Although multivariate analysis in our study did not show any significant association of LNR with DFS and OS in contrast to a study[24] where LNR was a significant prognostic factor for DFS (p<0.001) and OS(p<0.001).

However this study had some limitations as well. First, this study was limited by its retrospective design and there were chances of selection bias as well as lack of medical record data. Also it is a single centre study, so the outcomes may not accurately reveal the results of the general population but accumulation of data from large prospective studies with a longer follow up periods will establish the importance of LNR based evaluation system.

5. CONCLUSION

Our study demonstrated high LNR associated with short OS and DFS in non-metastatic breast carcinoma. LNR based classification system is not used regularly. It may be an additional useful tool that can be implemented in clinical practice for better prognostications. However, a multicentric study with larger sample size is needed to establish the prognostic value of LNR in breast cancer patients.

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Conflicts of interest

The authors declare no conflict of interest in this work.

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Informed consent

Informed consent was not received due to the retrospective nature of the study

Ethical clearance

As treatment was already completed prior to this study and all patients received treatment as per standard protocol, Ethical Committee waived it.

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