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Original Article

Surgery Section

Lymphovascular Invasion and Ductal In-situ Components in Operable Infiltrating Duct Carcinoma of Breast- A Single Centre Experience

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ABSTRACT

Introduction: Lymphovascular Invasion (LVI) in carcinoma breast is a significant prognostic factor in invasive breast cancer, with respect to local and distant recurrence and poor survival. Infiltrating duct carcinoma with accompanying ductal carcinoma in-situ has shown significantly different expression patterns of Her2/neu, progesterone receptors and Ki67 than infiltrating duct carcinoma.

Aim: To associate the significance of LVI and concomitant in-situ component with the receptor status and clinicopathological characteristics of infiltrative duct carcinoma.

Materials and Methods: This retrospective study was conducted in a single unit in the Department Of General Surgery, Government Medical College, Thrissur, Kerala, India, for two months between June 2021 and July 2021 and data was analysed in August 2021. This study was conducted in a systematic manner to review all the operated infiltrative duct carcinoma patients from a single cohort in 100 patients based on surgical intervention. The collected data were entered in Microsoft Excel worksheet and the results were analysed statistically using Statistical Package of the Social Sciences (SPSS)-16. Chi-square test was used, considering p-value ≤0.05 as a significant.

Results: The mean age of the study population was 55.6±15 years with maximum number of patients above 60 years. In total 64% of the patients had tumour size of 2-5 cm (pT2) and 59% of the cases had no lymph nodal metastasis (pN0). 28 cases (28%) showed concomitant in-situ component and 37 cases showed lymphovascular invasion (37%). The presence of lymphovascular invasion, was found to be significantly associated with Her2 positivity (p=0.045). Concomitant in-situ component also seemed to increase the likelihood of lymphovascular invasion (p=0.0320). There was significant positive correlation observed between LVI and Her2 (r=0.238, p=0.045) and in-situ component (0.214; p=0.032). However, no significant association was observed between LVI and other clinicopathological variables.

Conclusion: The LVI is a significant prognostic factor in invasive breast cancer associated with poor survival and definitely carries a significant association with Her2 Status and also reflected on the concomitant in-situ carcinoma.

Keywords: Breast cancer, Hormone receptors, Recurrence, Surgical intervention

INTRODUCTION

According to Cancer statistics, 2020: report from National Cancer Registry Programme, India, carcinoma of breast is the most common cancer in Indian women. The lifetime risk of developing breast cancer was found to be an alarming 1 in 29 females [1]. The highest burden of breast cancer was observed in metropolitan cities and there is an increase in the trend of incidence of breast cancer [1]. Kerala shows a similar trend with a prevalence rate in rural areas of 19.8 per 100,000 and 30.5 per 100,000 in the urban areas [2]. The risk factors were found to be consistent with the established risk factors like nulliparity, history of previous breast biopsy, advancing age, first childbirth after 30 years of age, absence of breastfeeding, family history of breast cancer and history of irregular menstrual cycles [2].

Steroid hormone receptors are a predictive marker for endocrine therapy and a prognostic marker in the clinical management of breast cancer. The nuclear receptor for estrogen functions as a transcription factor controlling estrogen regulated genes and Progesterone receptor mediates progesterone action. Hormone Receptor (HR) negative tumours are more likely to be of higher grade and associated with a higher recurrence rate, decreased overall survival, and unresponsiveness to antiestrogens [3,4].

Several well-established tumour prognostic factors are used to guide the clinical management of patients with breast cancer. The presence of carcinoma cells in either lymphatic vessels (lymphatic invasion), blood vessels (vascular invasion) or both (lymphovascular invasion) is a significant prognostic factor in invasive breast cancer, with respect to local and distance recurrence and poorer survival [5]. LVI is also associated with other strong prognostic factors such as tumour size, grade and discuss- lymph node involvement [6].

Ductal Carcinoma In-situ (DCIS) is a proliferation of malignant cells which do not invade the basement membrane of the breast ducts. Being a non obligate precursor to Infiltrating Ductal Carcinoma (IDC) a substantial proportion of patients with IDC have accompanying DCIS component. The percentage of cases with DCIS associated with invasive cancer varies significantly. It is shown that IDC with accompanying DCIS tend to have a favorable biology and survival outcome [7]. Significantly different expression patterns of Her2/neu, PR and Ki67 were shown in IDC versus IDC/DCIS [6,7].

This study aimed to associate the significance of LVI and concomitant in-situ component with the receptor status and clinicopathological characteristics of operated infiltrative duct carcinoma patients from a single cohort.

MATERIALS AND METHODS

This retrospective study was conducted in a single unit in the Department of General Surgery, Thrissur Medical College, Kerala, India. Retrospectively data was collected between June 2021 and July 2021 and was analysed in August 2021. Institutional Ethical Committee clearance was obtained as IEC number: IEC/GMCTSR/167/2021.

Inclusion criteria: Carcinoma breast patients who underwent Modified Radical Mastectomy (MRM) or Breast Conservative Surgery (BCS) based on standardised protocol based surgical intervention were included. Hundreds cases of consecutive cases operated within the study period were enrolled in the study.

Exclusion criteria: The patients with lumpectomy and trucut biopsy specimens were excluded from the study.

Data Collection

Patient's clinical details of demographic profile, clinical symptoms and tumour size, Estrogen Receptor (ER) and Progesterone Receptor (PR) status, Her2 status, nodal status and grade of tumours were collected. The histopathological reports and immunohistochemistry reports were looked in for LVI and DCIS and tabulated. Tumours were staged according to the Tumour, Nodes, Metastases (TNM) staging [8]. Grading was done using Nottingham's modification of Bloom Richardson grading system [9]. Immunohistochemistry analysis was done to assess the ER, PR status and scored using Allred scoring system [10]. Human epidermal growth factor-2 expression was determined based on the membrane staining pattern and scored on a scale of 0-3+ as recommended by the American Society of Clinical Oncology (ASCO) guidelines [11].

STATISTICAL ANALYSIS

The collected data were entered in Microsoft Excel worksheet and the results were analysed statistically using SPSS-16. Chi-square test was used, considering p-value ≤0.05 as a significant. The 'r' value was calculated using Spearman correlation test to assess the correlation for the parameters which showed significant association.

RESULTS

The total number of patients were 100. The mean age of study population was 55.6±15 years with maximum number of patients 30 (30%) above 60 years. Most of the patients, 82 (82%) belonged to the postmenopausal age group [Table/Fig-1].

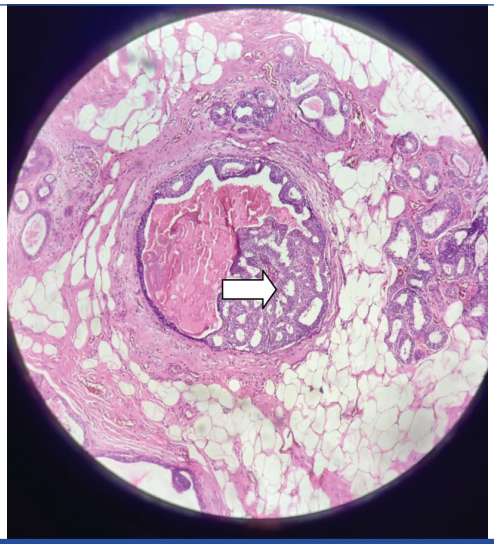
Clinicopathological characteristics	No. of patients (100)	LVI Present (37)	LVI Absent (63)	p-value
Age (years)				
<40	4	1	3	0.064
40-45	14	4	10	
46-50	14	4	10	
51-54	15	5	10	
55-60	23	15	8	
>60	30	8	22	
Size				
pT1 (less than 2 cm)	11	4	7	0.468
pT2 (2-5 cm)	64	23	41	
pT3 (More than 5 cm)	19	6	13	
pT4 (Tumours with skin/chest wall involvement)	6	4	2	
Modified bloom Richardson grade				
1	12	3	9	0.277
2	59	20	39	
3	29	14	15	
Lymph nodal status				
pN0	59	18	41	0.426
pN1	23	10	13	
pN2	6	3	3	
pN3	12	6	6	
Concomitant In-situ component				
Present	28	15	13	(r=0.214; p= **0.032**)
Absent	72	22	50	
ER positive	37	12	25	0.468
ER negative	63	25	38	
PR positive	21	7	14	0.695
PR negative	79	30	49	
Her2 positive	15	9	6	(r=0.238; p=**0.045**)
Her2 negative	85	28	57	

[Table/Fig-1]: Parameters with LVI.
Spearman's correlation test, Chi-square test was used to calculate the p-value; Level of significant p value <0.05

As a standard working protocol was followed for the management of carcinoma breast in a single unit 64 (64%) of the patients had tumour size of 2-5 cm (pT2). About 59 (59%) of the cases had no lymph nodal metastasis (pN0). Modified bloom Richardson grade 2 comprised of 59 (59%) of the specimens. About 37 (37%) cases were found to be ER positive and 21 (21%) were PR positive. In total 63 (63%) cases were triple negative (ER, PR and Her2) signifying a majority of tumours being aggressive and having prognostic negative significance [Table/Fig-1].

Out of the 100, 28 (28%) cases showed concomitant in-situ component and 37 (37%) cases showed LVI. Statistical significance was associated with Her2 negative tumours, in-situ component and lymphovascular invasion (p-value=0.045, r=0.238) and (p-value=0.032, r=0.214) respectively. However, no significant association was observed between LVI and other clinicopathological variables like tumour size, nodal status, ER, PR status. 96% cases had adequate margin clearance [Table/Fig-1].

Infiltrating Ductal Carcinoma-No Specific Type (IDC-NOS) was the most common type of malignancy detected occuring in 88 (88%). Other histologic subtypes detected were mucinous-2 (2%), medullary-3 (3%), cribriform-1 (1%), invasive lobular-1 (1%) and metaplastic carcinoma-4 (4%) [Table/Fig-2,3].



[Table/Fig-2]: Ductal carcinoma in-situ showing LVI [H&E stain, 40X].

Pathological type	Percentage
IDC-NOS	88
Metaplastic carcinoma	4
IDC-medullary	3
IDC-colloid/mucinous	2
Invasive lobular	1
Invasive cribriform	1
In-situ ductal	1

[Table/Fig-3]: Pathological types of carcinoma breast.

No significant association was observed between in-situ component and other clinicopathological variables like tumour size, nodal status, ER, PR and Her2 status [Table/Fig-4].

Clinicopathological characteristics	In-situ component present (28)	In-situ component absent (72)	p-value
Age			
<40	0	4	0.765
40-45	5	9	
46-50	4	10	
51-54	3	12	
55-60	7	16	
>60	9	21	
Size			
pT1	4	7	0.813
pT2	17	47	
pT3	6	13	
pT4	1	5	
Grade			
1	4	8	0.520
2	14	45	
3	10	19	
Lymph nodal status			
pN0	15	44	0.625
pN1	7	16	
pN2	3	3	
pN3	3	9	
ER positive	14	23	0.093
ER negative	14	49	
PR positive	8	13	0.246
PR negative	20	59	
Her2 positive	6	9	0.262
Her2 negative	22	63	

[Table/Fig-4]: Association of clinicopathological parameters with in-situ components. Chi-square test, level of significant p-value <0.05

DISCUSSION

In this study the age of patients varied from 34-78 with a mean age of 55.63. Most of the patients belonged to the postmenopausal age group similar to other studies. 88% of the cases belonged to no special type of invasive ductal carcinoma which was comparable to the studies done by Zhu X et al., (92.72%) and Thiygarajan M et al., (84.3%) [11,12]. Kang SW et al., showed that 69.8% of the patients had breast tumour size of T2 (2-5 cm) which is similar to the present study where 64% cases had T2 breast lesions [13]. The present study showed 37% ER positivity which was comparable to the findings of Kaur K et al., (36%) and Kaul R et al., (34.5%) [14,15]. 21% of the cases were PR positive which was less when compared to these studies by Kaur et al., (36%), Kaul R et al., (36.4%) [14,15]. ER and PR positivity was higher in postmenopausal group (67 and 57% respectively). A total of 15 cases were Her2 positive, but no significant statistical correlation was found between the hormone receptor status and the age of the patient. 51% were found to be triple negative. ER/PR and Her2neu expression demonstrated no significant correlation with the size or grade of the tumour in the present study. 63% of the cases did not show any lymphovascular invasion similar to study done by Cornwell LB et al., (60%) [16].

The LVI was found more in the postmenopausal age group but no statistical association could be established with the age, size or grade of the tumour. This contrasted with the study by Klingen TA et al., which showed that LVI is associated with aggressive tumour features, higher histological grade, lymph node positive tumours and higher Ki67 [17]. Her2 positivity was significantly associated with the presence of lymphovascular invasion (0.045) which was in contrast to the findings of Thiygarajan M et al., [12]. which showed no correlation ER/PR positive status showed no significant association with lymphovascular invasion in our study but Cornwell LB et al., and Gurleyik G et al., found that it was associated with a negative ER status [16,18]. There was no association between lymphovascular invasion, and the number of lymph nodes. Concomitant foci of in-situ component was present in 28% cases and incidence of lymphovascular invasion tend to increase with the presence of DCIS (p-value=0.032). This present study could not establish any significant association between the in-situ component and other clinicopathological characters of breast cancer like age, TNM staging, grade and receptor status.

Limitation(s)

This study was conducted in a cohort on consecutive 100 cases operated in a single unit retrospectively. Prospective design and larger sample size may through more light into the above factors in invasive carcinoma breast.

CONCLUSION(S)

The LVI is a significant prognostic factor in invasive breast cancer associated with poorer survival and carries a significant association with Her2 status and is also reflected on the concomitant in-situ carcinoma. However further studies are to be undertaken to probe the inverse relation in prognosis and disease free survival in IDC.

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