ORIGINAL RESEARCH PAPER

General Surgery

"LEVEL THREE NODAL INVOLVEMENT IN PATIENTS WITH EARLY BREAST CANCER –A CROSS SECTIONAL STUDY FROM A TERTIARY CARE INSTITUTION IN KERALA"

KEY WORDS: Level 3 nodal involvement, Early breast cancer (EBC), Breast Conservation Surgery(BCS). Modified Radical Mastectomy (MRM).

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ABSTRACT

Background Breast cancer is the most common cancer among humans. The mainstay of breast cancer treatment includes surgery followed by chemotherapy radiotherapy and targeted therapy. Aggressive axillary surgery increase morbidity and reduce the quality of life in terms of lymphedema which affects 20% of those who undergo axillary dissection2.The most important predictor for decreased survival and recurrence in patients with early breast cancer is the presence of axillary lymph node metastases. Axillary nodal involvement in breast cancer is unpredictable but once involved it starts from level 1and follow systematic order from level 1 to 2 to 3.

Objectives

1. To find the proportion of patients who turn out to have positive level three axillary nodal metastasis following axillary dissection for early breast cancer
2. To find out factors associated with level 3 node involvement in early breast cancer.

Methods Data was collected from 77 patients with early breast cancer. Axillary level 3 nodes were labelled separately during breast surgery and send to pathology for HPE and ER PR and her2neu status and results recorded. **Results And Discussion** Out of the 77 patients studied 3 of them turned out positive for level 3 nodal disease, even though 40 percent of patients were having clinically palpable nodes in the axilla. **Conclusion** Among 77 patients with early Breast cancer 3 (4 percent) were having level 3 nodal disease and the rest of them, 74 (96 percent) were free of level 3 nodal disease. Hence avoiding aggressive axillary dissection and limiting to levels 1 and 2 in EBC will be beneficial in preventing morbidity and for better quality of life.

INTRODUCTION

The female breast is a symbol of beauty, and femininity. But when diseased, it has always challenged clinicians. Surgery, which was the mainstay of cancer therapy, inevitably caused disfigurement which was born silently by women with Breast cancer. The history of breast cancer is a complex maze of attempts to understand the true nature of this hormone-responsive cancer and the will of physicians to control it by surgery, chemo-radiotherapy or biomodulation. It is also an event of intense exploration to find the tools to enable early diagnosis. The story of the domination of surgery over two millennia and its evolution from morbid procedures to minimal damage, surgeons worldwide are thinking to modify radical surgeries into modified radical and selective to reduce morbidity ,mortality and better quality of life .Keeping all mentioned above in mind this study intended to find out the proportion of patients presented with early breast cancer having level 3 nodal involvement.[10]

OBJECTIVES

1. To find the proportion of patients who turn out to have positive level three axillary nodal metastasis following axillary dissection for early breast cancer
2. To find out factors associated with level 3 node involvement in early breast cancer.

BACKGROUND

Breast cancer is the most common cancer among humans[1]. The mainstay of breast cancer treatment includes surgery followed by chemotherapy radiotherapy and targeted therapy. Early diagnosis of breast cancer and surgery still have major role in breast cancer treatment. Surgery is composed of two parts breast surgery and axillary dissection. Aggressive axillary surgery increase morbidity and reduce the quality of life in terms of lymphedema which affects 20% of those who undergone axillary dissection[2]. Some studies do not support routine axillary dissection in early breast cancers[4].

Early breast cancer is defined as disease confined to the breast with or without regional lymph node involvement, and the absence of distant metastatic disease. This is based on the fact that early-stage breast cancer is potentially curable, and patients with distant metastatic disease are not[3].

Early Breast cancer includes Stages1 and 2 (T1N1, T2N1andT3N0) T1-tumor size less than 2cm,T2-tumor size more than 2cm but not more than 5cm and T3-tumor more than 5cmin greatest dimension. N0-no regional node metastases and N1-metastases in ipsilateral level1and level2 axillary lymph nodes

The most important predictor for decreased survival and recurrence in patients with early breast cancer is the presence of axillary lymph node metastases. Traditionally, axillary lymph node dissection (ALND) was used to stage the axilla and was performed routinely. Axillary nodal involvement in breast cancer is unpredictable but once it involves it starts from level1 follow systematic order Level1 to Level2 to Level3. Studies based on 10 year survival do not support routine axillary dissection among women withT1or T2 invasive primary Breast cancer with no palpable axillary adenopathy, and 1or 2 sentinel lymph nodes positive for metastases.

This study focus on proportion of patients with level 3 node involvement if it is insignificant ,level3 nodes need not be addressed in early breast cancers so that morbidity can be limited without compromising disease free survival rates.

METHODOLOGY

(i)Study setting

Department of General Surgery, Govt.Medical College, Thrissur.

(ii)Study design

Cross-sectional study

(iii)Study population

Patients diagnosed with early breast cancer who underwent axillary dissection including level 3 nodes as a part of MRM/BCS in the department of surgery Govt. Medical College,Thrissur.

(iv)Inclusion criteria

Patients diagnosed with early breast cancer of female gender

in the age group of 20-70 yrs.

(v)Exclusion criteria
Patients who were not giving consent for study.

(vi)Sample size calculation
Samplesize-77(formula-4pq/d2)
WhereP=Prevalence(frompreviousstudies)5
Q=100-P
d= allowableerror(5-20 %ofP)
(zα)2pq
n=d2
(zα)2=(1.96)2=3.84
P=27.3q=72.7 d=10

(vii) Study procedure
Data collected from 77 patients with early breast cancer admitted in surgery department. Before data collection Informed consent obtained from patient. Data was collected based on a proforma which contains Socio-demographic details, clinical history, examination findings, relevant investigations surgical findings and histopathology. During surgery axillary level 3 nodes were labelled separately and send to pathology for HPE and ER PR and her2neu status report recorded.

(viii)Study tools
- Semi-structured questionnaire containing questions on socio-demographic details-age, gender, socio-economic status, clinical features of early breast cancer size, quadrant, dimpling and retraction of nipple etc.
- Histopathological examination of level 3 nodes.

(ix)Study period
One year from the date of Ethical Committee Clearance. From 21-10-2021 to 20-10-2022.

(x)Statistical analysis
Data collected from 77 patients coded entered in MS Excel and analyzed using SPSS version 25.50. For available qualitative variable proportion used .for available quantitative variable mean and standard deviation used.

Chisquare test used to find out association between quantitative variables.

Ethical concerns: NIL
RESULTS
Among77 patients 3 of them have level 3 nodal disease, even though 40 percent of patients were having clinically palpable nodes in axilla.

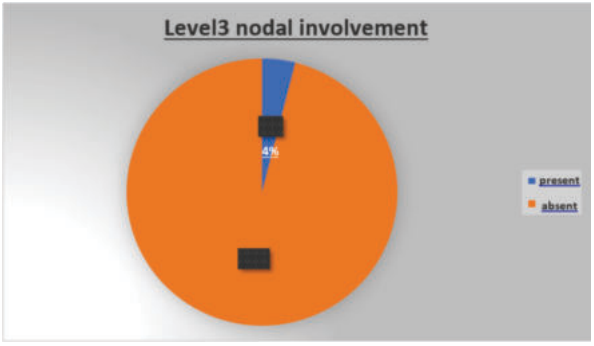

Fig 1. Level three nodal involvement Histologically in EBC

Among 77 patients only 3 of them having level 3 nodal involvement which corresponds to 4% of study population and rest of them74 (96 percent) free oflevel3 nodal disease

Table 1: Age Distribution Of Patients With Early Braest Cancer

Age group in years	Total no. of patients with EBC
<40	3
40-60	51
>60	23
Total	77

Patients between the age group 20 to 70 were studied for level 3 nodal involvement only 3 of them below the age of 40. Majority included in age group of 41 to 60 that is 51 patients and 23 patients above 60years of age.

In this study, 51 out of 77 patients (56 percent) were contributed by patients between age 41 to60, only 4 percent below 40 years and patients above 60 contributing 23 percent of study population.

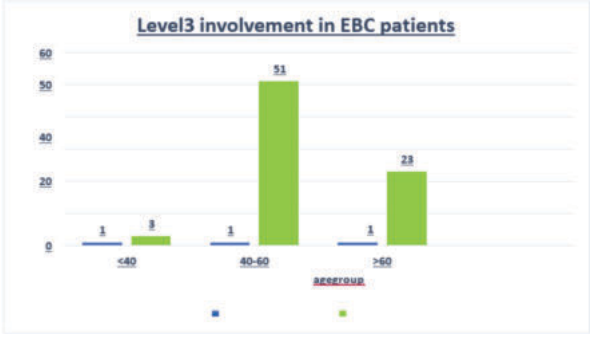

Figure2: Incidence Of Level 3 Involvement In Ebc Patients

Table2 : Tumour Size In Study Population

Tumour Size(in cm)	No. of patients
<2.0	25
2.0-5.0	52
Total	77

Even though early breast cancer includeT1N1,T2N1 and T3N0 (stage 1 and stage2).majority of patients lump size more than 2cm and not more than 5cm.among 77 patients 52havinglumpsize 2-5cm.22 patients with less than2cm.

Table.3 Size Of Lump And Level3 Nodal Involvement

TUMOR SIZE	LEVEL 3 NODE INVOLVED	LEVEL 3 NODE NOT INVOLVED
<2cm	0	25
2-5cm	3	49
Total	3	77

In this study all patient with level 3 nodal disease that is 3 patient having breast lump size 2to 5cm.

With a Pearson Chi-Square value :1.501andpvalue :0.221 Among 77 patients only 31 patients having palpable node in axilla and 46 do not have axillary nodes.

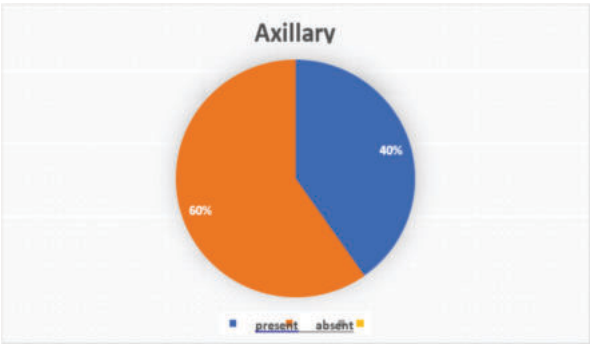

Figure 3 Palpable Axillary nodes in EBC

Only 40 percent of study population having palpable axillary node and 60 percent do not have palpable nodes

Table 4: axillary Nodal Status And Level3 Node Involvement

	Level 3 node involvement present	Level 3 node involvement absent
Axillary node present	3	28
Axillary node absent	0	46
total	3	74

All patient with level 3 disease having palpable nodes in axilla that is 3 patients with Pearson Chi-Square value :4.632 and p value p0.031

Table 5: showing Surgical Treatment Options In Ebc Patients

Surgical treatment options	No .of patients
MRM	70
BCS	7
Total	77

In this study70 patient underwent MRM and7patientBCS

DISCUSSION

Level3 Nodal Involvement In Ebc Patients

Among 77 patients only 3 of them were having level 3 nodal involvement by metastases which corresponds to 4% of study population and rest of them 74 (96percent) being free of level3 nodal disease.

Study conducted by Zhaoqing Fan etal investigated the incidence, associated factors and prognosis of levelIII node involvement for breast cancer with positive axillary lymphnodes after neoadjuvant chemotherapy. A consecutive series of 521 node positive T0-2 invasive breast cancer cases were included in this retrospective study. Axillary node metastases were proved by ultrasound guided needle biopsy (NB) if ultrasonographic abnormal node was detected or by sentinel node biopsy(SNB) if no abnormal node was detected. After 4 to 8 cycles of neoadjuvant chemotherapy (NCT), axillary lymph nodes dissection included level III lymph nodes were completed for each case. About 9% of node positive T0-2 breast cancer will have residual positive node in level III region after neoadjuvant chemotherapy. Node positivity proved by NB, large tumor size, and primary tumor non-response to neoadjuvant chemotherapy are independent predictors of level III lymph nodes positivity.8 In this study all patient with level 3 nodal disease that is 3 patients having breast lump sizem 2 to 5 cm. With a Pearson Chi-Square value:1.501 and p value :0.221. as size of lump increases there is a chance of level 3 nodal involvement.

Langer and colleagues demonstrate that patients with tumors of 3cm or more with micrometastatic foci 0.2–2mm on hematoxylin and eosin (H&E) stain or IHC have no worse 5 –year survival than the node-negative counterparts, despite the omission of a completion ALND. It is interesting to note that the authors found a 5-year disease-free survival advantage in patients who were found to have micrometastatic disease over node-negative patients. Colpaert and colleagues found that the primary tumor was an independent prognostic factor while axillary micrometastasis were not, and they proposed that micrometastatic disease somehow primes the immune system, allowing for a more robust response against further tumor invasion. The 5-year overall survival in the study by Langer and colleagues was equal in bothgroups.[7,9]

Axillary dissection is still the treatment of choice for mastectomy patients

With sentinel node involvement and for breast-conservation patients with > 2 metastatic nodes; however, the alternative of radiationtherapy is increasingly considered for patients with low nodal burden, as demonstrated in the AMAROS European trial.

Pilewskie etal reported on the likelihood of undergoing axillary dissection among patients with clinically N0 disease on the basis of treatment strategy. Among women with HER2-positive cancer, fewer women who received neoadjuvant chemotherapy required axillary lymph node dissection, Compared with women who received upfront mastectomy (oddsratio,0.19,p=0.001) for luminal cancers, the likelihood of axillary lymphnode dissection was not significantly different between women who underwent neoadjuvant chemotherapy, upfront mastectomy, or breast conserving surgery[11,12]

When we consider age distribution of patients with early breast cancer, Out of 77 patients 56 percent contributed by patients between age 41 to 60, only 4 percent below 40 years and patients above 60 contributing 23 percent of study population. There is a steep age gradient, with about a quarter of breast cancers occurring before age50, and <5%beforeage35.

Tumour Size In Study Population

Even though early breast cancer include T1N1 ,T2N1 and T3N0 (stage 1 and stage 2).majority of patients lump size more than 2cm and not more than5cm. among 77 patients 52(68 percent) having lump size 2-5cm.22(32) patients with less than 2cm.

In this study, it was observed that out of the two patients with tumor size <2 cm, none had the involvement of lymph nodes. While among 45 cases with size between 2 cm and 5 cm, 7 cases had no lymph nodes involved, 6 had 1–3, 22 had 3–9, and 10 cases had more than 10 lymph nodes involved. Of 3 patients with tumor size more than 5 cm, all had more than 10 lymph nodes involved. The observation was found to be highly significant. Thus, predicting that with an increase in tumor size, number of lymph nodes involved increases.

Presence Of Axillary Nodes In Ebc Patients

Only 31(40 percent) patients having palpable node in axilla and 46 (60percent)do not have axillary nodes. All patient with level 3 disease were having palpable nodes in axilla

Surgical Treatment Options In Ebc Patients

In this study 70 patient underwent MRM and 7 patient Among 77 patients only 9 percent thatis7 patients underwent BCS and 91 patients underwent MRM.

CONCLUSION

- Among77 patients 3 (4 percent) of them were having level 3 nodal disease. Rest of them, 74 (96 percent)were free of level 3 nodal disease
- Only 31(40 percent) patients were having palpable node in axilla and 46 (60 percent) did not have palpable axillary nodes. All patient with level 3 disease were having palpable nodes in axilla.
- In total 68 percents had tumour size of 2 to 5 cm(T2) .All patients with level 3 nodal disease comes under T2N1M0 showing increase size and axillary nodal status may be a predisposing factor for level3 nodal disease.
- In this study level 3 nodal disease was limited to 4 percent of ebc patients. Hence avoiding aggressive axillary dissection in early breast cancers may be beneficial in preventing morbidity and for better quality of life.

Limitation of this study: During analysis it is found that the sample size was inadequate to prove statistical significance of level 3 nodal involvement in early breast cancer. To obtain a statistically significant result study may be repeated with larger sample.

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