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Research Article

A Hospital-Based Observational Study of Association of Various Factors with Axillary Metastasis in Operable Breast Carcinoma Patient

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Abstract: This study was carried out to find out association between various histopathological and clinical feature of tumor and axillary lymph nodes metastasis. So we can found various profile of patient in which there is high incidence of ALNM(axillary axillary lymph nodes metastasis).and patient in which very low or none chances of having ALNM preoperatively by this we can minimize or avoid any kind of axillary dissection in favorable profile `s patients and prevent dreaded complication of axillary LN dissection without compromising onchological principle. Factors like patient's age, tumor size, histopathological type, histological grade; lymphovascular invasion (LVI)and estrogen and progesterone receptor status were correlated with the axillary metastases. Out of 10231 patient shows ALNM(29.4%incidence of ALNM).there was no association found between age,type of tumor and ALNM(P-value >.05).association was found between size of tumor and ALNM(P-value 0.001). Association was found between grade of tumor and ALNM (P-value0.006). Association was found between LVI and ALNM (P-value 0.000). association was found between ER/PR status of tumor and ALNM(P-value .015). By this study we can conclude that in favorable profile of patient(conclusion that small tumor and with histopathological feature of medullary or mucinous ca ,low grade tumor, absent LVI ,ER+/PR+ on IHC staining) are associated with low risk of ALNM in patient of such profile we can minimize or avoid axillary dissection and by this we can avoid most of its complication (Paresthesias, shoulder pain, weakness, lymphedema, seroma and axillary web syndrome are recognized morbidities of ALND).
Keywords: Breast cancer, Axillary metastases, Histological, Grade LVI

INTRODUCTION

The Halsted radical mastectomy included an en bloc resection of axillary contents. Now, more than a century later, there is little controversy about the use of breast-conserving surgical treatments in place of mastectomy, while the routine use of axillary dissection, or at least axillary sampling, has persisted despite the fact that it is the greatest source of morbidity from breast surgery. Is it time to abandon this procedure all together, at least in some patients?

Axillary lymph node status is one of the most important prognostic indicators in breast cancer and detection of nodal metastasis is a key factor in recommending adjuvant chemotherapy after surgery [1]. Widespread use of mammography has resulted in marked increase in early detection of breast cancer, improvement in therapy and declining mortality

The positive yield of axillary LN dissection and node negative patient do not benefit from axillary dissection but may suffer from its complication. Axillary dissection is now no longer considered to be the standard treatment in all patients with invasive breast cancer. This study is undertaken to find out predictors of axillary LN metastasis in breast cancer which will help to select the group of patient in whom axillary dissection can be avoided.

MATERIAL AND METHODS

It is an anterograde observational analytical study. Eligible patients admitted in Dept. of General Surgery and Oncosurgery unit, SMS Medical College Jaipur is selected for study on the basis of inclusion and exclusion criteria. Each patient will be explained about the study and consent for participation is taken in their native language.

Clinical assessment was carried out .All routine investigation is done for PAC work up. Sonography and Chest x-ray will be done for metastatic work up.

Any suspicious lesion will be evaluated further by higher investigation. Trucut biopsy is taken if required(in undiagnosed patient) and sent for histopathological examination and ER/ PR study.

Patient was undergo breast conservation surgery or modified radical mastectomyand specimens are sent for histopathological examination and hormonal study.

Histopathological Type, Histological Grade, Lvi, Er/Pr Status

The Nottingham modification of the Bloom-Richardson Grading system was used for histological grading of cancers[3] . Immunohistochemical staining for estrogen receptor (ER) and progesterone receptor (PR) was performed using the Streptavidin- Biotin Immunoperoxidase procedure, % of +ve lymph node and –ve lymph node is calculated.% of patient with +ve node is calculated. Statistical Analysis-chi-square test was used as test of significance.

Inclusion Criteria:

- Operable breast cancer patients admitted in Department of General Surgery and Oncosurgery unit.

Exclusion Criteria:

- Inoperable breast cancer patients.
- Patients with breast cancer refusing surgery.
- Systemic metastatic cancer.
- Patients who have taken neo-adjuvant chemotherapy.
- Patient having palpable axillary lymph node.

OBSERVATION & RESULTS

In our study 102 cases is assessed who have clinically negative axilla and up to T3 and N0M0 tumor.in our study age of the patient is from 23 to 80 year and mean age 49 year. 54 /102 (53%) <50 year of age and 45/102 (44.11%) is in 50 – 70 year of age and only 3/102(2.9%) in >70 year of age . In our study patient mainly (75/102) belong to group who have lump size 2-5cm in size. 11/102 patient in <2cm size and16 patient in>5cm size group. we observed if the lump size is bigger there is more chance of having metastasis to axillary LN we found 1 patient with positive ALNM in 11 patient in T1 (<2cm) group.19 out of 75 in T2(2-5cm) group and 11 out of 16 in T3 (>5cm)group And more important the p value of this distribution by chi square test came to be .001 which is highly significant. In our study out of 102, 21(20.5%) are of grade 1 tumor 35(34.3%) of GRADE II and 46 (45%) of GRADE III. we found 20 positive ALNM out of 46 patient of grade III tumor which is more than grade I and II and distribution of patients with ALNM in these group by chi square test came to be .006 which is highly significant .it shows there is increase chance of positive ALNM with poor differentiation of tumor. 93(91.1%) patient is of IDC and only 4 patient of ILD and 2 patient of medullary and 1 of mucinous ca. We found 29 patient of positive ALNM in IDC and 2 in ILC 0mucinous ca. p value of distribution of patient having ALNM came to be .401 which is not significant. We divide the patient according to combination of ER/PR status as shown in table and p value came to be .015 which is significant.

Table-1: Correlation between various factors and axillary lymphnode metastasis in breast cancer

Fector	**NO. OF CASES**	**Axillary lymph node metastasis**		**P-VALUE**
		Positive	Negative	
Patient's Age				.203(NS)
<50 years	54(52.94%)	20	34	
50–70 years	45(44.11%)	11	34	
>70 years	3(2.9%)	0	3	
SIZE OF LUMP				.001(Highly Significant)
T1	11(10.7%)	1	10	
T2	75(73.5%)	19	56	
T3	16(15.6%)	11	5	
TYPE		Positive	Negative	
Infiltrating duct carcinoma	93(91.1%)	29	64	.401(NS)
Infiltrating lobular carcinoma	4(3.9%)	2	2	
Medullary carcinoma	2(1.9%)	0	2	
Mucinous carcinoma	3(2.9%)	0	3	
GRADE		Positive	Negative	
GRADE I	21(20.5%)	1	20	.006(Highly Significant)
GRADE II	35(34.3%)	10	25	
GRADE III	46(45%)	20	26	
LVI				.000(Highly Significant)
ABSENT	84(82.3%)	15	69	
PRESENT	18(17.6%)	16	2	
Hormonal Status				.015(Significant)
ER + & PR +	40(39.2%)	5	35	
ER + & PR −	9(8.8%)	3	6	
ER-& PR +	4(3.9%)	2	2	
ER-& PR −	49(48%)	21	28	

DISCUSSION

A common first route of spread for breast carcinoma is through the axillary lymph nodes .Nodal status is the most powerful independent prognostic factor in breast cancer and remains the most important feature for defining risk category[1]. There is evidence that overall survival decreases as the number of positive node increases ALNB remains the gold standard in determining prognosis, adjuvant therapy and loco-regional control. However, as mammography screening for breast cancer becomes more prevalent, breast tumors are being found at smaller sizes than before. With this, the positive yield of axillary lymph node dissection also decreases. Node negative patients do not benefit from ALNB but may suffer its dreaded complications. This has led to calls for more conservative management of the axilla in early breast cancer

In our study we took 102 cases of operable breast cancer patient who have not taken neoadjuvant chemotherapy and do not have systemic metastasis and they do not have clinically palpable LN so we took all patient f T1, T2, T3 with N0 M0.

In our study incidence of ALNM is 29.4% (31/102)as compare to 41% (207/501) in Chua B *et al*,[5] this decrease in incidence is due to exclusion of patient who have clinically palpable ALN we excluded these patients because there is more chances of positive ALNM in whom the axillary LN is palpable. We also exclude patients who had T4 stage because they had to take neoadjuvant chemotherapy and after chemotherapy there is decrease tendency to axillary LN to come positive and that will distort our results.

The peak occurrence of breast cancer in developed countries is above the age of 50 whereas in India it is above the age of 40(Population based cancer registries consolidated report 1990-96). in our study mean age of patient having ca breast is 49 year mostly the patient in our study is in 40 t0 60 year 54 /102 (53%) <50 year of age and 45/102(44.11%) is in 50 – 70 year of age and only 3/102(2.9%) in >70 year of age .in developing country like India prevalence of ca breast is more in younger patient as compare to western world.

In India, the average age of developing a breast cancer has undergone a significant shift over last few decades. In our study 20 patient out of 31 patient (+ve ALNM) present in <50 year age group ,11/31/31 patient(+ve ALNM) present in 50-70 year age group and 0 /31 patient(+ve ALNM) present in >70 year age group which shows if the ca breast patient is young there is more chances to have positive ALNM. but p value is came in this distribution is .203 which is stasticaly not significant. In study of Csaba *et al*[6] thirty-seven percent of the 63 women younger than age 40 had lymph node involvement compared with 25% of the 787 women older than age 40.which show same results as ours.

In our study patient mainly (75/102) belong to group who have lump size 2-5cm in 11/102 patient in <2cm size and16 patient in>5cm size group. This is due to because mammography is not widely available as screening for ca breast and peoples of rural area are still not very aware for the ca breast. That is why we do not found many cases of smaller tumor. We also have less patient having tumor of >5cm because bigger tumor are usually infiltrated the skin or chest wall or systemic metastasis was present in these patients and these patient was excluded from study. We observed if the lump size is bigger there is more chance of having metastasis to axillary LN we found 1 patient with positive ALNM in 11 patient in T1 (<2cm) group.19 out of 75 in T2(2-5cm) group and 11 out of 16 in T3 (>5cm) group. And more important the p value of this distribution by chi square test came to be .001 which is highly significant.

If we compare our result with recent studies there are also same results of Csaba *et al*[6] thirty-five percent of the 470 patients with tumors >1 cm had nodal involvement compared with 13% of the 380 patients with smaller cancers.

Giuseppe *et al*[7] univariate analysis, the likelihood of additional metastases to axillary LN was significantly higher for patients with primary tumors larger than 2 cm ($P = 0.0029$),

In our study out of 102, 21(20.5%) are of grde 1 tumor 35(34.3%) of GRADE II and 46 (45%) of GRADE III. We found 20 positive ALNM out of 46 patient of grade III tumor which is more than grade I and II and distribution of patients with ALNM in these group by chi square test came to be .006 which is highly significant. It shows there is increase chance of positive ALNM with poor differentiation of tumor. Yip CH *et al* [4] some 23.9% of grade 1 cancers were node positive, compared to 42.9% of grade 2/3 cancers

In the study of Amrut V *et al* [2], there was strong association between histological grade and presence of axillary metastasis (p<0.001). Iwasaki Y *et al* [8] found 13% of grade 1 ,25% of 2 and 32 % of grade 3 shows ALNM (P value.01)

LVI

In our study LVI was found in 18 cases out of 102 .in that 18 patients 16 patient show ALNM .and there were 84 patients who do not show LVI in their tumor and only 15 of this group shows ALNM and p value of this distribution came to be .000 which is highly significant .it shows there is strong association between LVI in tumor and ALNM.

In LVI positive group 23.1 % dissected LN show metastasis and in LVI negative group only 2.2% dissected LN show metastasis. it show that there is more chance of having increased no. positive LN in axilla if the tumor show LVI.

In most of the study on LVI in ca breast show that LVI is strong predictor of ALNM and carrying poor prognosis as observed in our study

Giuseppe Viale *et al*[7], in univariate analysis, the likelihood of additional metastases was significantly higher for patients with primary tumors exhibiting peritumoral vascular invasion (*P* <0.0001) and Csaba Gajdos *et al*[6] lymphatic invasion was significantly related to nodal involvement because the majority (51%) of patients with lymphatic invasion had axillary lymph node metastases, compared with 19% of patients without identifiable lymphatic invasion ($p < 0.001$)

In our study 93(91.1%) patient is of IDC and only 4 patient of ILD and 2 patient of medullary and 1 of mucinous ca. We found 29 patient of positive ALNM in IDC and 2 in ILC 0mucinous ca. p value of distribution of patient having ALNM came to be .401 which ih not significant.

This is limitation of our study that we could not found any case of ductal ca in situ .and found few cases of ILC, medullary and mucinous ca that is why we could not found any correlation between type of tumor and ALNM.

In the study of Amrut V. Ashturkar *et al* [2] 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, tubular carcinoma and mucinous carcinoma showed less tendency for axillary metastasis compared to IDC.

In most of study they observed that IDC has poor prognosis and more associate with ALNM as observed in our study. tubular , mucinous and medullary ca has good prognosis and has favorable outcome because it shows less association to ALNM.

Amrut V. Ashturkar *et al* [2] 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, tubular carcinoma and mucinous carcinoma showed less tendency for axillary metastasis compared to IDC and Iwasaki Y *et al* [8] found 27% of IDL ,20% of ILC 12% of mucinous ,1% of tubular and 0% of mucinous tumor shows ALNM(p value .01).

In our study IHC typing (ER/PR status of tumor) significantly correlated with ALNM. In our study we divide the patient according to combination of ER/PR status as shown in table and p value came to be .015 which is significant.

ER-/PR+ and ER-/PR- group show more tendency to have ALNM as compare to ER+/PR+ and ER+/PR- group.

10.9 % dissected LN show metastasis in ER-&PR+ group which maximum followed by ER-&PR-(7.1%), ER+&PR-(5.7%), and least in ER+&PR+(4%).it shows there is less chances to have ALNM in ER+&PR+ and %), ER+&PR- group and in ER-&PR+ and ER-&PR- group there is more chances to have many no. of LN positive for metastasis.

Amrut V. Ashturkar *et al* [2] found on ER and PR immunohistochemistry, ER and PR-negative status was significantly associated with low risk of axillary node metastasis (p<0.002).this results are opposite in our study .in our study as mention above inER+&PR+ is associated with low risk of ALNM and ER-&PR+ and ER-&PR- is associated with high risk of ALNM. Most of the study shows ER+&PR+ associated with more incidence of ALNM. And few study show there is no association between IHC and ALNM.

CONCLUSION

On the basis of results of our study we can reach to a conclusion that small tumor and with following histopathological feature (medullary or mucinous ca, low grade tumor, absent LVI ,ER+/PR+ on IHC staining) are associated with low risk of ALNM in patient of such profile we can avoid axillary dissection and by this we can avoid most of its complication(Paresthesias, shoulder pain, weakness, lymphedema, and axillary web syndrome are recognized morbidities of ALND. As previously reported, the rate of wound infections, axillary seromas, and paresthesias among patients in the Z0011 trial was higher for theALND group than for the SLND-alone group (70% vs 25%, *P*_.001). Lymphedema in the ALND group was significantly more common by subjective report (*P*_.001))

Results from Z0011(The American College of Surgeons Oncology Group

Z0011 trial, a phase 3 noninferiority trial conducted at 115 sites and enrolling patients from May 1999 to December 2004.) indicate that women with a positive SLN and clinical T1-T2 tumors undergoing lumpectomy with radiation therapy followed by systemic therapy do not benefit from the addition of ALND in terms of local control, disease-free survival, or overall survival. The only additional information gained from ALND is the number of nodes containing metastases. This prognostic information is unlikely to

change systemic therapy decisions and is obtained at the cost of a significant increase in morbidity.

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