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Original Research Article

A prospective study to evaluate the axilla in cases of breast carcinoma to exclude axillary lymph node dissection in sentinel lymph node negative cases

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ABSTRACT

Introduction: Sentinel lymph node biopsy (SLNB) has become standard to stage the axilla in cases of clinically and Ultrasound negative axilla avoiding unnecessary axillary Lymph node dissection which is associated with higher morbidity in patients

Objective: 1. The Primary objective is to preoperatively detect axillary metastasis in USG confirmed node negative axilla and perform Sentinel Lymph node Biopsy, 2. To negate the need for axillary lymph node dissection and biopsy in the treatment of breast cancer patients with sentinel node negative

Materials and Methods: A total number of 80 patients with core needle biopsy proved were subjected to USG of Breast and axilla. The patients who had suspicious features in USG axilla were subjected to USG Guided FNAC. The patient having positive (metastasis) over USG guided FNAC were subjected to ALND and those patients with USG guided FNAC Negative and Normal USG Axilla i.e. No suspicious over USG were subjected to SLNB using blue dye. The SLNB negative cases were followed up with Adjuvant Chemotherapy and every 3months in combination with sonography of the breast and the axilla. Mammograms, X-ray and abdominal sonography performed annually.

Results: All 80 biopsy proven patients were subjected to USG. From which 32 patients had suspicious of metastatic deposits which were subjected to USG Guided FNAC. Rest 48 patients Normal Axilla. From 32 suspicious patients undergone USG Guided FNAC 15 showed deposits in Axilla which were subjected to ALND. Rest 17 Negative under USG guided FNAC along with 48 Normal Axilla patients were subjected to blue dye SLNB i.e., Total of 65 cases. i). From these 65 cases which undergone SLNB 4 cases (23.5%) showed metastatic deposit in USG guided FNAC Negative cases (17 total cases) and 8 cases (16.6%) showed metastatic deposit in USG Normal Axilla (48 Total cases) in frozen section. Which brings total SLNB of 18.4% (12 out of 65 cases). ii). These 12 cases were subjected to Axillary Lymph node dissection. The Final HPE study showed 100% metastatic deposits. iii). Remaining 53 cases were followed up for a period of 12 months. No local or Axillary recurrence could be observed in 53 patients who underwent SLNB without ALND.

Conclusion: Short term results were very promising with combination of USG along with SLNB without ALND in SLNB negative cases and holds a strong future perspective.

1. Introduction

Breast cancer next to lung cancer is leading cause of cancer related deaths, annually. Its impact on global health problem, with more than 2 million cases of breast

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cancer diagnosed worldwide each year. With evolving, breast cancer surgery from radical mastectomies to more conservative techniques of breast conserving surgery (BCS) and axillary sentinel lymph node (SLN) biopsy along with its association for least complication.[1]

Preoperative ultrasound of axilla done routinely can reduce the false positivity associated with clinical examination and help in avoiding axillary dissection and help selecting patients for sentinel node biopsy.[2]

Sentinel Lymph node has become standard of care for axillary nodal staging in early breast cancer without clinical evidence of Axillary lymph node metastasis.[3]

As ALND had many morbidities associated with it like lymphedema, numbness, pain, and shoulder impairment less invasive method using SNLB was developed as to replace the more debilitating ALND for breast carcinoma with negative clinically axilla owing to less false negative rate associated with SNLB ranging from 5%-10% without impacting the outcomes.[4]

The American College of Surgeons Oncology Group (ACOSOG) Z0011 trial set off a benchmark in the field which reported no benefit in clearing axillary nodes when there was involvement of up to two SLNs, and there was a very low axillary recurrence rate in patients not receiving completion ALND (0.9% after 6.3 years of follow-up).[5]

Recently, SLNB can also be done in selected patients with nodal positivity with neo adjuvant treatment by substantially down staging the nodal involvement. Currently, combined use of a radioisotope with blue dye is a standard SLNB method. But the radioisotope guided SNLB comes with intrinsic drawback especially in resource poor regions due to its cost along with radiation exposure which makes single blue dye technique a common method in SLNB.[6]

Sentinel lymph node biopsy has become a part in staging workup indicated in early-stage breast cancers of epithelial origin, such as ductal and lobular carcinomas, due to these tumours having higher chances to metastasize to lymph nodes. In cancer variants like invasive ductal and lobular carcinomas, T1 and T2 lesions, are considered for sentinel lymph node biopsy.[7]

2. Materials and Methods

2.1. Study design

Prospective study was performed:

1. The Primary objective is to preoperatively detect axillary metastasis in USG confirmed node negative axilla and perform Sentinel Lymph node Biopsy
2. To negate the need for axillary lymph node dissection and biopsy in the treatment of breast cancer patients with sentinel node negative.

A total of 80 cases with core needle biopsy proven carcinoma breast were included in the prospective study between July 2019 - December 2020.

2.2. Inclusion criteria

Female patients of all age groups with histopathological evidence on core needle biopsy for breast carcinoma with clinically node negative axilla will be included in the study.

2.3. Exclusion criteria

1. Clinically node positive axilla.
2. Patients on chemotherapy or radiotherapy.
3. Patients with prior breast surgery and axillary intervention.
4. Pregnant and lactating women.
5. Patient of previous breast surgery.
6. Locally Advanced disease.

A total number of 80 patients with core needle biopsy proved were subjected to USG of Breast and axilla. The patients who had suspicious features in USG axilla were subjected to USG Guided FNAC. The patient having positive (metastasis) over USG guided FNAC were subjected to ALND and those patients with USG guided FNAC Negative and Normal USG Axilla i.e. No suspicious over USG were subjected to SLNB using blue dye.

For the identification of SLNs, blue dye was injected peritoumorally 16–18 before surgery at a dose of 2.5ml if the tumour was palpable. Subareolar subcutaneous injection of 2.5 ml of blue dye (Methylene blue) was performed in the operating room after draping of the patient, and exactly 5 min after injection of the blue dye the axillary incision was given near mammary crease. Adequate haemostasis was maintained to identify the blue lymphatic channels leading to the blue SLN. Followed by excision of blue nodes and frozen section. Subsequently, breast surgery was performed as indicated. Axillary lymph node dissection was indicated in the same setting if SLNs were unidentified, or if SLNs were positive for mets in frozen sections. Complete axillary clearance was avoided, if SLNs were negative in frozen sections. If negative SLNs converted positive in permanent haematoxylin and eosin (H&E)-stained sections, a secondary ALND had to be performed. Sentinel lymph node biopsy alone, without ALND, was indicated in cases where SLNs were negative in frozen sections and in H&E-stained slides. The histopathologic examination of SLNs was performed according to the Austrian Pathology Society's consensus conference statement. SLNs of size 2–3mm were cut to slices, to obtain 2–3 frozen sections. Slices were finally paraffin embedded and serially cut down to 250 mm levels. From each level, one H&E-stained were examined if the H&E-stained slide was negative for metastases. All patients who did not undergone ALND with negative SLNB were subjected to Adjuvant chemotherapy

and patients that underwent BCS with negative SLNB underwent post op Adjuvant Radiotherapy. Postsurgical follow-up consisted of clinical controls every 3months in combination with sonography of the breast and the axilla. Mammograms, X-ray and abdominal sonography performed annually.

3. Results

Mean age of incidence of carcinoma of breast was found to be 42 years with the lowest being 32 years and highest being 69 years.Table 1

Table 1: Age ofincidence

Age in year	No. of cases
10-20	0
20-30	0
30-40	6
40-50	55
50-60	14
60-70	5
70-80	0

Around 65% of cases the tumor mass was found in upper outer quadrant. Of the cases studied around 91.25% were found to be Invasive ductal carcinoma, 6.25% of invasive lobular carcinoma and 2.5% others.Table 2

Table 2: Histopathological distribution of excised breast lump

Total No.	Invasive Ductal	Invasive Lobular	Other
80	73	5	2
100%	91.25	6.25%	2.5%

In majority of the cases with fine needle aspiration cytology positive i.e., showing malignancy were with tumor size >5cm. i.e., 44.8 % (26 out of 58), with 32.7 % (19 out of 58) of tumor with 2-5cm size and 22.4 % (13 out of 58) with tumor <2cm size.Table 3

Table 3: Showing correlation between tumor size and FNAC

Tumor Size	FNAC Positive	FNAC Negative	Total
<2 cm	13	11	24
2-5 cm	19	8	27
>5 cm	26	3	29
Total	58	22	80

In 32 cases with axillary ultrasound positive or suspicious, majority i.e., 62.5 % (20 out of 32) were of tumor size >5cm, around 25 % (8 out of 32) were of size 2-5 cm and around 12.5% (4 out of 32) were of size <2 cm.Table 4

In total 32 cases that were with Axillary ultrasound (AUS) positive the majority i.e. around 93.75% (30 out of 32) were with Invasive Ductal carcinoma & 6.25% (2 out of 32) were with Invasive lobular carcinoma.

Table 4: Showing correlation of tumor size and axillary USG finding

Tumor Size	AUS Positive	AUS Negative	Total
<2 cm	4	20	24
2-5 cm	8	19	27
>5 cm	20	9	29
Total	32	48	80

From the Axillary ultrasound (AUS) negative cases were also majority with Invasive ductal carcinoma i.e around 89.5 % (43 out of 48) with only 6.25% (3 out of 48) with Invasive lobular carcinoma and 4.25% with other types.Table 5

Table 5: Showing correlation between the histopathological type of carcinoma of breast and its AUS detection

	AUS Positive	AUS Negative	Total
Invasive Ductal	30	43	73
Invasive Lobular	2	3	5
Other	0	2	2
Total	32	48	80

Ultrasound guided fine needle aspiration cytology was also positive in 15 out of 32 axillary ultrasound suspicious cases which were also found truly positive after final axillary nodal dissection.

Ultrasound guided fine needle aspiration cytology of axilla in ultrasound suspicious cases was found to be 88.23% sensitive, 100% specific, with Positive predictive value 100% and Negatives predictive value 70%.

FNAC in patient with positive Axillary ultrasound

True Positive - FNAC +, HP +

False Positive - FNAC+, HP-

True Negative - FNAC-, HP-

False Negative - FNAC-, HP+

$Sensitivity - \frac{TP}{TP+FN} \times 100$

$Specificity - \frac{TN}{TN+FP} x100$

Positive Predictive Value -$\frac{TP}{TP+FP} x100$ TP $TP + FP$ x 100

Negative Predictive Value -$\frac{TN}{TN+FN} x100$ TN

Accuracy - $\frac{TN+TP}{TN+FN+TP+FP} x100$

TP-True positive

FP=False positive

TN=True negative

FN=False negative

Overall accuracy of ultrasound guided fine needle aspiration cytology in ultrasound suspicious cases was found to be 84.37%.

A total of 80 patients were included in the study. All 80 biopsy proven patients were subjected to USG. From which 32 patients had suspicious of metastatic deposits which were

subjected to USG Guided FNAC. Rest 48 patients Normal Axilla. From 32 suspicious patients undergone USG Guided FNAC 15 showed deposits in Axilla which were subjected to ALND. Rest 17 Negative under USG guided FNAC along with 48 Normal Axilla patients were subjected to blue dye SLNB i.e., Total of 65 cases.

From these 65 cases which undergone SLNB 4 cases (23.5%) showed metastatic deposit in USG guided FNAC Negative cases (17 total cases) and 8 cases (16.6%) showed metastatic deposit in USG Normal Axilla (48 Total cases) in frozen section. Which brings total SLNB of 18.4% (12 out of 65 cases).Table 6

Table 6: Mapping of sentinel lymphnode with methylene blue dye in AUS negative cases

Total no of AUS Negative cases	SLN Postive	SLN Negative
48	8	40
100%	16.66%	83.34%

Table 7: Mapping of SLN in AUS suspicious and FNAC negative cases

Total no of AUS (+) & FNAC (-) cases	SLN Positive	SLN Negative
17	4	13
100%	23.5%	76.5%

These 12 cases were subjected to Axillary Lymph node dissection. The Final HPE study showed 100% metastatic deposits.

Remaining 53 cases were followed up for a period of 12 months. No local or Axillary recurrence could be observed in 53 patients who underwent SLNB without ALND.

4. Discussion

Currently standard of care for early breast cancer extends from MRM and ALND of Levels I and II and occasionally Level III to BCS with radiotherapy with ALND. Patients with positive axillary Lymph nodes vary from 30%-40%. The remaining patients with Negative for metastatic deposits in Axilla are usually overtreated with complete axillary clearance which has negative deleterious early and late complications such as seroma, pain, restricted arm mobility, numbness or Lymph edema (Kuehn et al, 2000).[8]

Sentinel Lymph node biopsy as compared to ALND is a minimally invasive technique with less morbidity (Peintinger et al, 2003; Schijven et al,2003).[9,10] The accuracy of SLNB for staging axilla has been proven in many studies (Krag et al, 1993; Giuliano et al, 1994; Krag et al, 1998; O'Hea et al, 1998; Nieweg et al, 2001).[11–15] Data regarding local control of SLNB and only a few reports on SLNB alone without further ALND to date (Giuliano et al, 2000; Schrenk et al, 2001; Chung et al, 2002).[16–18] As reported in those studies, Axillary recurrence range between 0 and 1.4% and follow-up periods range between 22 and 39 months.

A study conducted that (Chung et al, 2002)[18] reported 208 patients who undergone SLNB alone with a median follow-up of 26 months. In this study, reported three axillary recurrences after a Negative SLNB, estimating a false-negative rate of 1.4%. 60% of patients received adjuvant systemic therapy in this study. As nearly all of our patients received adjuvant systemic treatment and all patients with breast-conserving surgery and radiotherapy to the whole breast. In our study, we have a median follow-up period of 12 months and no axillary recurrence could be observed. This may be a rather short follow-up period, but in a study conducted on outcome of axillary recurrences after ALND (Newman et al, 2000)[19] a median time interval of 19 months for local recurrence after ALND is reported.

Axillary recurrence after ALND ranges between 0 and 3% (Recht and Houlihan, 1995).[20] With 53 patients in our series there was no axillary recurrence with a median follow up of 12 months after SLNB only. In our study if we had missed the true positive SLN then axillary recurrence would range from 2-12% of patients (Kjaergaard et al, 1985; Senofsky et al, 1991)[21,22] which would have been in our study 1-6 patients. All of our patients were

SLN negative in frozen sections and H&E. As the impact of micrometastases identified by IHC is still controversial, we excluded IHC as a guide to ALND in our study. With ongoing research and improved diagnostic modalities ACOSOG Z0010 is working on answering the question of micrometastases in SLNs and its definite management.

The results of our study is to confirm the accuracy of both USG along with USG guided FNAC and SLNB in relation to no risk of axillary recurrences in cases of SLNB Negative cases in short term follow up.

The results of our study confirm the accuracy of SLNB and SLN negative patients with SLNB alone are not at risk for axillary recurrences in a short-term follow-up.

5. Conclusion

Carcinoma of breast is a global problem in today's world. Axillary lymph node mapping continues to be an important component for its staging and for planning proper treatment modality. After its discovery sentinel lymph node mapping has become a standard protocol in most of the institution in early breast cancer with clinically negative lymph node in the axilla. In the coming years ultrasound examination of axillary lymph nodes and missed cases or cases that undergo undetected in Ultrasound axilla can be detected on SNLB thus can avoid much higher debilitating and morbidity associated with ALND.

6. Conflict of Interest

None.

7. Conflict of Interest

None.

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