ROLE OF DOPPLER USG FOR EVALUATION OF AXILLARY LYMPH NODE STATUS IN CARCINOMA BREAST

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ABSTRACT

BACKGROUND

Axillary staging of patients with breast cancer is essential for treatment planning. It can be done by sentinel lymph node biopsy. However, Doppler ultrasound of axilla can be used, which is a non-invasive procedure and has less complication as compared to sentinel lymph node biopsy.

AIM AND OBJECTIVE

This prospective study was conducted to evaluate the use of Doppler ultrasound in preoperative evaluation of clinically node-negative axilla in breast cancer.

PATIENTS AND METHODS

Seventy histologically (core needle) proven cases of breast cancer with clinically negative axilla were evaluated using 7.5 MHz high frequency Doppler ultrasound. The Long axis/Short axis(L/S) ratio, Hilum/Long axis(H/L) ratio, flow pattern of lymph node, Resistivity Index (RI) and Pulsatility Index (PI) were recorded.

RESULTS

On the basis of the Doppler ultrasound findings, it is possible to identify the subset of patients at high-risk of harbouring nodal metastasis and these patients can be offered upfront axillary nodal dissection.

CONCLUSIONS

It can be concluded that USG and USG guided FNAC is the best tool to assess the axillary metastasis in cases of carcinoma breast especially in clinically axillary node-negative cases.

KEYWORDS

Carcinoma Breast, Doppler USG of Axilla, Axillary Node Evaluation.

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INTRODUCTION: A lump in the breast whether inflammatory, benign or malignant, is one of the most prevalent reasons for a woman to seek consultation with surgeon. Benign breast lesions are common and though not life threatening, but may be the cause of much concern till the possibility of a malignant process is excluded. Carcinoma of the breast is the second most common cancer among females in India. Significant numbers of malignant lesions are considered benign by clinical examination and mammography.[1] This appears to be a particular problem in patient below 50 yrs. of age where 40% of carcinomas are considered benign or normal by clinical examination.[2] Thus, clinical diagnosis calls for further investigation for confirmation of diagnosis. To overcome this difficulty, many more accurate and sophisticated diagnostic modalities like mammography, ultrasonography, have been advocated and evaluated to arrive at an accurate preoperative diagnosis. Each modality of investigation has certain advantages like sensitivity, specificity, etc. in adding to the diagnosis of different breast pathologies with the evaluation of advanced investigation modalities, breast cancers are now detected in early stage and the patients are undergoing less radical surgery like breast conservation surgery.[3] Axillary lymph node is one of important predictor of prognosis in patients with breast cancer. It can be assessed with various methods, but histopathological study is most accurate. But non-invasive study like USG and USG guided FNAC of axillary lymph node preoperatively, in clinically node-negative axilla, can help to avoid more invasive method like sentinel lymph node biopsy which has its own complication like pain, lymphoedema, shoulder joint stiffness.[4] Preoperative axillary staging in breast cancer is saving time and resource.[5] Moreover facility for sentinel lymph node biopsy, gamma probe and gamma camera not available at all centres. Given

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the limitation of sentinel lymph node biopsy, it was decided to evaluate the efficacy of Doppler USG and USG guided FNAC in differentiating metastatic and non-metastatic axillary lymph nodes in clinically node-negative breast cancer.[6]

AIMS & OBJECTIVES: To assess the accuracy of USG and USG guided FNAC of axillary lymph node in carcinoma breast in clinically node-negative cases.

MATERIALS:

Inclusion Criteria: The study included all consecutive female and male patients from all age groups presenting with confirmed cases of carcinoma breast and clinically impalpable and insignificant axillary nodes admitted and undergone elective breast surgeries with removal of axillary nodes in the Department of Surgery, M.K.C.G. Medical College Hospital, Berhampur, Odisha.

Exclusion Criteria:

1. Previously undergone any treatment for carcinoma breast.
2. Clinically node positive case.

METHODS: All cases satisfying the inclusion criteria were selected for the study. Informed consent was obtained from them. Then they were subjected to ultrasonography and ultrasonography guided FNAC of the axillary lymph nodes and the report were obtained from the pathologist regarding the status of the axillary nodes. These were compared with the histopathological examination of the operative specimen, regarding the status of the nodes after axillary dissection and the accuracy of USG (Fig. 1) and USG guided FNAC (Fig. 2) were assessed by appropriate statistical methods.

Doppler ultrasound evaluation of the ipsilateral axilla was done using high resolution real time Siemens Sonoline G50 compact ultrasound device with a high frequency linear array probe of 7.5 MHz. The patients were examined in supine position with the arm in 90 degree abduction and external rotation. In this position, the axillary vessels have a nearly straight course facilitating orientation and all parts of the axilla can be thoroughly examined. The pectoral and infraclavicular region around the subclavian vessels were also scanned. The following parameters were recorded:

- L/S ratio: Long axis/ short axis of lymph node.
- H/L ratio: Long axis of Hilum/ long axis of Lymph node.
- Flow pattern of lymph node: Central or peripheral.
- Resistivity Index (RI): Peak systolic velocity – End diastolic velocity/ Peak systolic velocity.
- Pulsatility Index (PI): Peak systolic velocity – End diastolic velocity/ Mean velocity.

Long axis/Short axis Ratio (L/S Ratio): The size of the lymph node is considered to be an important parameter to distinguish benign from malignant nodes. But lymph node enlargement could be malignant or benign. Therefore it is not just the long axis of lymph nodes but their globular shape which helps to distinguish benign from malignant nodes. The globular shape can be assessed by the L/S ratio. In this study, we had taken L/S ratio < 2.[6]

Hilum axis/Long axis Ratio (H/L Ratio): The hilum of a normal lymph node constitutes the central part of the lymph node and appears homogeneously hyper echoic on Doppler ultrasound. Metastatic deposit leads to shrinkage of hilar area and loss of echogenicity on sonography. Hilar diameter to long axis ratio has been used to distinguish benign from malignant nodes. In this study we had taken H/L ratio <0.3.[6]

Resistivity Index (RI): The principle of RI is that in a lymph node, the high resistance of distal vessels produces a low diastolic flow in the feeding artery increasing the difference between peak systolic and end diastolic velocity. In this study we had taken RI index >0.8.[6]

Pulsatility Index (PI): This is a measure of the variability of blood flow in a vessel and is equal to the difference between peak systolic and minimal diastolic velocity divided by the mean velocity during the cardiac cycle. in this study we had taken PI index >2.[6]

Arterial Flow Pattern: The normal blood flow to lymph nodes is through the hilum which gets intensified during inflammation. In case of metastatic deposits the hilum is disrupted and the flow gradually shifts to the periphery.[6]

Morphology of lymph node: Usually, a benign lymph node is ovoid, with a hypoechogenic cortex, extremely thin or even invisible at ultrasonography with hyperechogenic hilum due to connective tissue trabeculae, lymphatic tissue cords and medullary sinusoids. Changes such as cortical thickening, hilum decrease or absence, changes in shape or vascular pattern, are considered suspicious. The metastatic lymph node are having hypo echoic cortex, round shape, loss of fatty hilum, cortical lobulation. Metastatic cells in the lymph reach the lymph nodes through afferent lymphatic vessels on the convex aspect of the organ. Then, the lymph is filtered through the cortex, paracortex and finally the hilum. Metastatic deposits accumulate in the lymph node peripheral area, causing enlargement of the cortex, usually focal (at early stages), or uniform.[6]

All the nodes were assessed on the above parameters. In axilla with multiple nodes, the node with minimum L/S ratio, H/L ratio and maximum RI and PI were taken into account. These nodes were subjected to FNAC.

All the patients were subjected to surgical removal of breast lesion and axillary nodes, either by BCT+ALND or MRM depending on the stage of the disease as per the individual need of the case. The results of Doppler ultrasound were correlated with the result of the histopathology of the lymph nodes harvested from the axilla along with breast specimen. Then True +ve, True –ve, False +ve and False –ve cases were recorded.

RESULTS: A total of 70 consecutive patients confirmed diagnosis of breast cancer by core needle biopsy with clinically insignificant axillary node, during the period from September, 2013 to August, 2015 were included in this study, for evaluation of status of axillary node, with respect to Doppler ultrasound evaluation.

Table 1 shows the number of positive cases (metastatic axillary node) in USG of axilla. Forty three (61.42%) cases were positive for nodal metastasis in USG of axilla. Out of which true positive cases were 41(95.34%) and false positive were 2 (4.65%). Total node-negative cases were 27(38.57%), out of which true negative were 22(81.48%) and false negative were 5(18.52%). USG guided FNAC of axillary node detected metastases in 44(62.8 5%) cases, out of which 43(97.72%) cases were true positive and 1(2.28%) case was false positive. Similarly this method detected 26(37.15%) cases of negative axillary lymph nodes, out of which 23(88.46%) were true negative and 3(11.54%) were false negative the above result was obtained after histopathological examination of all remove axillary nodes.

Role of USG in Assessing Axillary Metastasis: Taking these into consideration the sensitivity, specificity and positive predictive value of USG of axilla examination in breast lumps were calculate as follows:

True +ve	=	41(58.57%).
False +ve	=	02(2.87%).
True –ve	=	22(31.42%).
False –ve	=	05(7.14%).

$$\text{Sensitivity} = \frac{\text{true positive}}{\text{true positive} + \text{false negative}} x100 = \frac{41}{41+05} X100 = 89\%$$

$$\text{Specificity} = \frac{\text{true negetive}}{\text{true negative} + \text{false positive}} x100 = \frac{22}{22+02} X100 = 91.66\%$$

$$\text{Positive predictive value} = \frac{\text{true positive}}{\text{total positive}} x100 = \frac{41}{41+02} X100 = 95.35\%$$

$$\text{Negative predictive value} = \frac{\text{true negative}}{\text{total negative}} x100 = \frac{22}{22+05} X100 = 81.48\%$$

$$\text{Overall accuracy} = \frac{\text{true positive} + \text{true negative}}{\text{total no. ofcases}} x100 = \frac{41+22}{70} X100 = 90\%$$

Role of USG guided FNAC in Assessing Metastasis: Out of 44(62.85%) positive cases, true positive cases were 43(97.72%), false positive case was 01(2.28%). Out of 26(37.15%) negative cases, true negative cases were 23(88.46%), false negative cases were 03(11.54%).

$$\text{Sensitivity} = \frac{\text{true positive}}{\text{true positive} + \text{false negative}} x100 = \frac{43}{43+03} X100 = 93.47\%$$

$$\text{Specificity} = \frac{\text{true negative}}{\text{true negative} + \text{false positive}} x100 = \frac{23}{23+01} X100 = 95.83\%$$

$$\text{Positive predictive value} = \frac{\text{true positive}}{\text{total positive}} x100 = \frac{43}{44} X100 = 97.72\%$$

$$\text{Negative predictive value} = \frac{\text{true negative}}{\text{total negative}} x100 = \frac{23}{23+06} x100 = 79.31\ \%$$

$$\text{Overall accuracy} = \frac{\text{true positive} + \text{truenegative}}{\text{total no. of cases}} x100 = \frac{43+23}{70} X100 = 94\%.$$

DISCUSSION: In this study, 70 patients having carcinoma breast were included for evaluation. These patients were having clinically insignificant axillary lymph nodes. Out of 70 patients, 97% were female and 3% were male.

In this study, it is found that, sensitivity, specificity, positive predictive value, and negative predictive value and overall accuracy of USG axilla is 89%, 92%, 95%, 81%, and 90% respectively.

Altomare V et al, in their study, presented a preliminary result regarding the efficacy of fine-needle aspiration cytology (FNAC) to identify metastatic axillary lymph nodes in the preoperative phase. It was possible to avoid a sentinel lymph node biopsy in 30% of the cases; the sensitivity was 68%, specificity 100%, PPV 100%, and NPV 65%. Echo-guided FNAC of the axillary lymph nodes should thus be included among the regular diagnostic procedures of pre-surgical staging.[7] Van Rijk MC et al, evaluated the sensitivity of preoperative ultrasonography and fine-needle aspiration cytology for detecting axillary metastases and to assess how often sentinel node biopsy could be avoided. They found that ultrasound and fine-needle aspiration cytology established axillary metastases in 58 (8%) of the 726 patients. These 58 cases constituted 21% of the total of 271 patients who were proven to have axillary metastasis at the end of ultrasonography and FNAC was 21%, and unnecessary sentinel node biopsy was avoided in 8% of the patients.[8]

Holwitt DM et al did study to determine the accuracy of axillary ultrasound (AUS) and fine-needle aspiration biopsy (FNAB)/needle core biopsy in axillary breast cancer staging. They conclude that AUS-guided FNAB/needle core biopsy is accurate in predicting the status of the axilla in 70% of clinically node-negative breast cancer patients. This technique is minimally invasive with a low complication rate and can obviate the need for staged lymph node procedures.[9]

De Kanter AY, et al had done a multicentre study of ultrasonographically guided axillary node biopsy in patients with breast cancer. This study investigated whether ultrasonographically guided fine-needle aspiration cytology (FNAC) of the axillary lymph nodes in clinically node-negative patients was an accurate staging procedure to select patients for sentinel node biopsy or not. They conclude that Ultrasonography was sensitive in patients with extensive nodal involvement.[10]

Jung et al did study the Accuracy of preoperative ultrasound and ultrasound-guided fine needle aspiration cytology for axillary staging in breast cancer. The aims of this study were to evaluate the accuracy of preoperative ultrasound and ultrasound-guided fine needle aspiration (FNA) cytology (US-FNAC) for detecting axillary metastases, and to assess how often sentinel node biopsy could be avoided. The sensitivity, specificity and positive and negative predictive values of the ultrasound alone of axillary lymph nodes for metastatic breast cancer were 54%, 91%, 75% and 81%, respectively. For the US-FNAC, the respective values were 80%, 98%, 97% and 84 and concluded that Preoperative axillary ultrasound in combination with US-FNAC provides a simple, minimally invasive and reliable approach to the initial determination of the axillary lymph nodes status.[11]

Brancato et al studied 'Role of ultrasound-guided fine needle cytology of axillary lymph nodes in breast carcinoma' staging. And evaluate the efficacy of cytology on axillary lymph node ultrasound-guided aspiration biopsy in the reduction of inappropriate surgery, such as the sentinel node (SN) procedure if positive, or axillary dissection if negative.[12] Cowher MS et al correlated the use of axillary ultrasound and lymph node needle biopsy with surgical lymph node pathology in patients with invasive breast cancer. The sensitivity of AUS both with and without biopsy was 54%, and specificity was 96%. The positive predictive value was 91%, and the negative predictive value was 71%. They conclude that Preoperative AUS should be included in the preoperative workup of clinically node-negative patients.[13]

Davis et al studied Ultrasound-guided fine-needle aspiration of clinically negative lymph nodes versus sentinel node mapping in patients at high risk for axillary metastasis. Radiographic, cytological, and histological diagnostic data on breast primary tumours from 114 consecutive SN candidates were prospectively assessed for clinicopathologic variables associated with an increased incidence of axillary metastases. They conclude that patients at increased risk for axillary metastases, the use of sonographic evaluation of the axilla in combination with fine-needle aspiration is not only clinically justified, but also cost effective.[14]

USG guided FNAC shows sensitivity, specificity, positive predictive value and negative predictive value, overall accuracy is 93%, 95%, 97%,79%, and 94% respectively. This observation is similar to the study by A Das et al,[6] Altemore et al,[7] VanRajik et al,[8] DM Holwitt et al,[9] AY Kanter et al,[10] J Jung et al,[11] B Brantco et al,[12] and MS Cower et al,[13] JT Davis et al.[14]

CONCLUSION: For evaluation of axillary lymph node in cases of carcinoma breast, Doppler USG alone is having the sensitivity, specificity, positive predictive value, negative predictive value, overall accuracy of 89%, 92%, 95%, 81% and 90%, respectively. USG guided FNAC is having sensitivity, specificity, positive predictive value, negative predictive value, overall accuracy of 93%, 96%, 98%, 79%, and 94% respectively. Therefore, USG guided FNAC is possibly the most valuable preoperative diagnostic tool to assess the axillary nodal metastasis in cases of carcinoma breast with clinically node-negative axilla.

Finally, it can be concluded that USG guided FNAC in cases of carcinoma breast is the best tool to assess the axillary metastasis in carcinoma breast, irrespective of the clinically axillary nodal status.

	Only USG axilla	**USG guided FNAC**	**Histopathology of axillary nodes**
Positive for metastasis	43(61.42%)	44(62.85%)	45(64.28%)
Negative for metastasis	27(38.58%)	26(37.15%)	25(35.72%)
Total	**70(100%)**	**70(100%)**	**70(100%)**

Table 1: Results of the observation

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Fig. 1: Photograph During Doppler Ultrasound of Right Axilla

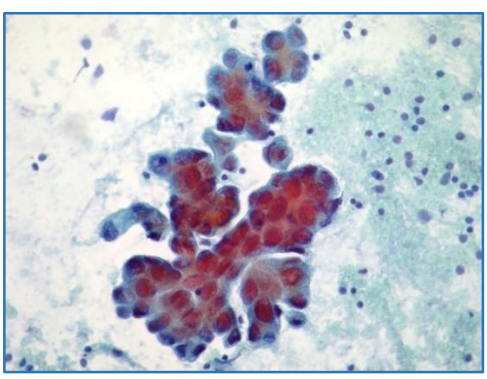

Fig. 2: FNAC. Aspirate From Axillary Node in A Case of Ductal Breast Carcinoma Showing Clusters of Malignant Epithelial Cells Associated with Lymphocytes

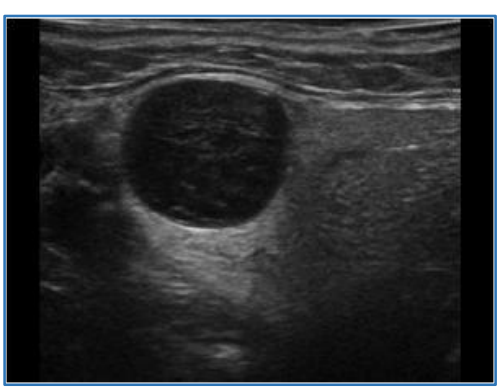

Fig. 3: Benign Axillary Lymph Node

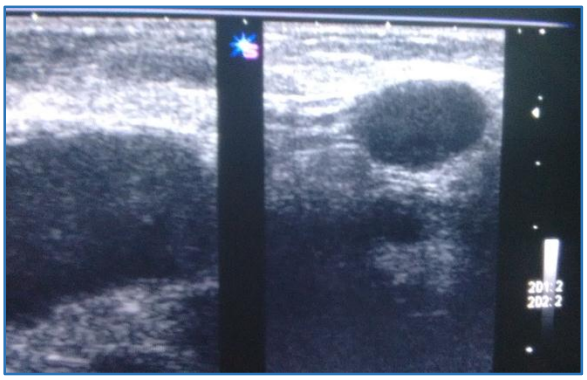

Fig. 4: Malignant Lymph Node

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