Research Article

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Correlation of clinical examination and ultrasonogram with histopathology in predicting the metastatic axillary lymph nodes in breast cancer

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ABSTRACT

Background: Examination of breast and axilla is an integral part of triple assessment of patient with suspected carcinoma breast. A retrospective study was conducted to compare the axillary lymph nodes in carcinoma breast based on clinical, ultrasonogram (USG) and post-operative histopathology (HPR).

Methods: One hundred patients with early breast cancer were included in the study. Clinical examination of axilla, followed by USG examination of all patients was done preoperatively. This was compared with the post-operative HPR of axillary lymph nodes (gold standard). The validity of the findings was evaluated by using sensitivity and

Results: There is a strong positive correlation for the detection of total number of lymph nodes (r=0.935) between USG and HPR which is statistically significant (p <0.05). The correlation between clinical detection and HPR detection of axillary lymph nodes was weak (r= 0.278). Accuracy of the USG findings was good (81%) compared to the HPR findings and this was statistically significant (p <0.05). The USG morphologic lymph node features with the greatest correlation with malignancy were loss of central fatty hilum (r= 0.953) and cortical thickness (r= 0.914). In HPR and USG, the number of positive lymph nodes was high in stage II.

Conclusions: The sensitivity for detecting malignancy by USG is only average. USG is more likely to detect an abnormal node if there is morphologic features of increased cortical thickening and loss of central fatty hilum. A multidisciplinary effort is needed to reduce unnecessary axillary dissections.

Keywords: Breast cancer, Ultrasonogram, Axillary lymph node, Fatty hilum, Lymphatic drainage, Elastography

INTRODUCTION

Breast cancer is the most commonly occurring female worldwide new cancer cases and cancer deaths were reported to be 14.1 million and 8.2 million in 2012. Breast cancer is a global health problem with more than 1 million cases of cases diagnosed worldwide each year. It is one of the leading causes of cancer related mortality.¹ In developing countries like India, inspite of wide

information conveyed through multimedia, women seek proper attention at late stages only this may probably explain the high rate of mortality. According to Indian Council of Medical Research (ICMR) registries of cancer in women, the incidence of breast cancer have steadily increased in India.² In Kerala, it accounts for 28.9% of all cancers in women. Every year 2200 to 2500 new cases are being reported in Kerala. Over the past 20 years a 12-13% increase has been registered by the cancer

registries.¹ A host of prognostic factors have been described in case of carcinoma breast. These include tumor size, lymph node status, tumor type standardized histological grading, lympho-vascular invasion, measures of tumor proliferation such as S-phase fraction and thymidine-labelling index, growth factor analysis and oncogene or oncogene product measurement. Yet, the single most important prognostic factor considered is the axillary lymph node status.

The breast lymphatic drainage occurs through a superficial and deep lymphatic plexus and more than 95% of the lymphatic drainage of the breast is through the axillary lymph nodes, with the remainder via the internal mammary nodes. Lymphatics from the medial edge of the breast pierce the pectoralis major and intercostal muscles to reach the internal mammary lymph nodes which account for 25% or less of lymph flow from the breast. The least important route is the posterior intercostals lymphatics to posterior intercostal lymph nodes, where ribs and vertebrae articulate. Clinical method of palpation of breast cancer for tumor size and axilla remains relevant even today in spite of the advances in technology. Examination of breast and axilla is an integral part of triple assessment of patient with suspected carcinoma breast; the other two being mammography ultrasonogram (USG) and Fine Needle Aspiration Cytology (FNAC) or core- cut biopsy. USG examination of the axilla has become common practice in the presurgical assessment of breast cancer patients for staging purpose. This study was carried out to compare the metastatic axillary lymph nodes in carcinoma breast based on clinical, USG and post-operative histopathology (HPR) (which is considered the gold standard).

METHODS

Patients admitted with carcinoma breast in Amala Institute of Medical Sciences, over a period of 18 months (from January 2013 to June 2014) were undertaken. Females with trucut or FNAC proven early breast carcinoma cases with only T1, T2 and T3 (operable) lesions and N0, N1 status were included in the study. Patients who have received neoadjuvant chemotherapy, locally advanced breast cancer patients such as T3 (inoperable), T4 leisons and N2, N3 status and patients with metastasis were excluded from the study. Written consent was obtained from the patient or their relatives and the study design was approved by the Institutional ethics committee for research, Amala Institute of Medical Sciences, Amala Nagar, Thrissur, India.

Clinical examination of the axilla of the affected breast was done. The five groups (anterior/pectoral, posterior/subscapular, lateral/brachial, central and apical) nodes were examined systematically with the patient in sitting position. Lymph nodes may or may not be palpable. If palpable, ascertain the number of nodes, whether the node is fixed or not. Clinical examination of axilla, followed by USG examination (12-17 MHz linear

transducer by an experienced radiologist) of all patients was done preoperatively. This was compared with the postoperative histopathologic status of axillary lymph nodes, which was taken as the gold standard.

Statistical Analysis

Analysis was done using statistical software SPSS Version.16. Independent sample t- test was used to find out whether there is any statistical difference between groups. For categorical data, Chi square test and Fisher exact test was used. The validity of the clinical examination and USG findings were evaluated by using sensitivity and specificity of the diagnostic test.

RESULTS

One hundred patients of age between 20-80 years with early breast cancer were included in the study. The median age of the study group was 47 years and the maximum number of cases was seen in 40-49 age groups (44%) (Figure 1). The number of cases was 4% between 20-29 and 3% between 70-79. There were no patients above 80 years and below 20 years, which shows that the prevalence of carcinoma breast is low in very young age group and very old age group. In our study group, 54 patients were post-menopausal, indicating that the incidence is higher in post-menopausal women.

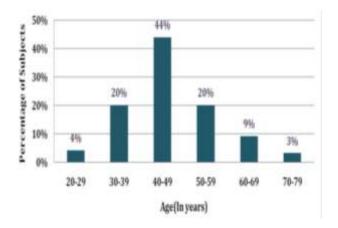


Figure 1: Distribution of age in patients with breast cancer.

The tumor size was divided into 4 groups (Table 1). In 26%, the tumor size was between 1.1-2 cm (T1 clinically) and the remaining 74% were between 2.1 -5 cm. Among the 74 patients, 41 patients were between 3.1-4 cm group (T2 clinically). The most common site of tumor was the upper outer quadrant (65%). The second commonest site was upper inner quadrant (28%). In 5% of the cases, there were skin changes in the form of dimpling or puckering. There were no peau dorange appearance, ulceration or satellite nodules. One of the 100 cases, there was fixity to pectoralis major muscle clinically, which was evident in the operation time as well. There was no fixity to chest wall clinically in any of the cases.

Table 1: Clinical tumor size.

Clinical tumor size (in cm)	Frequency	Percent
1.1-2	26	26
2.1-3	41	41
3.1-4	24	24
4.1-5	9	9
Total	100	100

Out of the 100 patients, 74 of them belonged to stage II clinically (T1, N1 or T2, N1 or T3, N0). Seventy patients had clinically palpable lymph nodes with 64% having 1 node and 6% having 2 nodes (Figure 2). All the palpable lymph nodes were freely mobile and discrete.

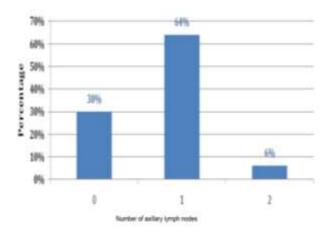


Figure 2: Clinically positive axillary lymph nodes.

Axillary lymph nodes were identified in all patients by USG. Twenty two of them had lymph nodes between 5-10, 43 had between 11-15, 30 had between 16-20 and 5 of them had nodes between 21-25 (Figure 3). In HPR, 39 of them had nodes in the range 11-15, 34 had between 16-20 and 18 had between 21-25. Only 9 had nodes between 5-10 (Figure 4). Twenty one patients who had clinically negative axilla had metastatic lymph nodes in HPR and 5 patients who had nodes clinically were negative pathologically.

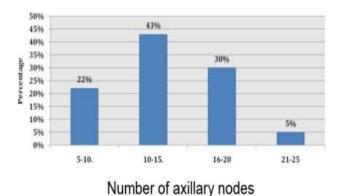
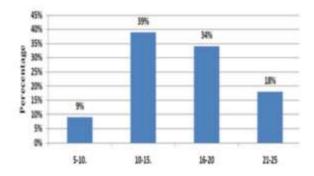


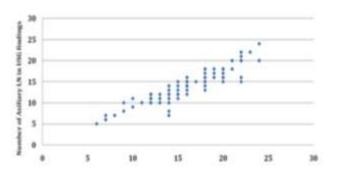
Figure 3: Number of axillary lymph nodes (LN) in ultrasonogram.



Number of axillary lymph nodes

Figure 4: Number of axillary lymph nodes in histopathology.

Scatter diagram showing correlation of total number of axillary nodes between HPR and USG findings is given in Figure 5. There is a strong positive correlation for the detection of total number of lymph nodes (r=0.935) between USG and HPR which is statistically significant (p<0.05). The correlation between clinical detection and HPR detection of axillary lymph nodes was weak (r=0.278).



Number of axillary lymph nodes in histopathological findings

Figure 5: Scatter diagram showing correlation of total number of axillary nodes between histopathology and ultrasonogram findings.

According to USG, 32 had zero positive lymph nodes and 68 had at least 1 lymph node positive. In HPR, 17 had 0 positive lymph node and 83 had at least 1 lymph node positive. Results of comparison between USG and HPR for positive axillary lymphnode are depicted in Table 2. Accuracy of the USG findings was good (81%) compared to the HPR findings and this was statistically significant (p<0.05). The USG morphologic lymph node features with the greatest correlation with malignancy were loss of central fatty hilum (r= 0.953) and cortical thickness (r= 0.914). Furthermore, in HPR and USG, the number of positive lymph nodes were high in stage II patients compared to stage I patients.

Table 2: Comparison between ultrasonogram and histopathology for positive axillary nodes.

Accuracy	81 5%	95% CI:73.32%-88.7%
Sensitivity	= 79.52%	95% CI:69.24%-87.59%
Specificity	= 88.24%	95% CI:63.52%-98.20%
Positive predictive value	= 97.06% (*)	95% CI:89.75%-99.56%
Negative predictive value	= 46.88% (*)	95% CI:29.11%-65.25%

^{*} P (Chi square) < 0.001

DISCUSSION

All the 100 patients included in this study were having early breast cancer (stage I and stage II) and underwent clinical examination of ipsilateral axilla followed by USG examination of axilla. In USG, the total number of lymph nodes was noted and, these nodes were labelled metastatic if they had 3 or more of the following four features: round shape, hypoechogenicity, loss of central fatty hilum and cortical thickening. The cortex was considered thick if the maximum thickness >1/2 of the transverse diameter of the hilum in the longitudinal plane. This was followed by Modified Radical Mastectomy (Auchincloss) and level I and II axillary dissection.

We found out that there is a strong positive correlation for the detection of total number of lymph nodes between USG and histopathology. The correlation coefficient is 0.935 between USG and HPR in detecting total number of lymph nodes which is statistically significant (p<0.001). But the correlation between clinical detection and HPR detection of axillary lymph nodes is only 0.278 which is not statistically significant. Twenty one patients who had clinically negative axilla, had metastatic lymph nodes in HPR and 5 patients who had nodes clinically were negative pathologically. In detecting metastatic lymph nodes, the accuracy of USG is good (81%) compared to HPR according to this study. The sensitivity is 79.52% and specificity is 88.24%. The positive predictive value is 97.06% and negative predictive value is 46.88%. This is statistically significant.

We found results of this study on parallel lines with the other studies. deFreitas et al reported the sensitivity of USG in detecting metastatic axillary lymph nodes to vary between 35% and 82% while the specificity to be between 73% and 98%. Some investigators reported that combined use of USG and FNAC could provide a highly accurate preoperative lymph node screening. Sousa et al. reported a 100% positive predictive value on finding of cortical thickness and non hilar cortical vascular flow. Verbanck et al. reported a sensitivity of 92% and specificity of 95% when using criteria of round or oval

hypoechoic lesions with 5mm diameter or more. Oz et al. used the criteria of cortical thickness >3 mm, increased size of lymph node, increased cortical hypoechogenicity, and nonhilar cortical flow and reported a sensitivity and specificity of 88.5% and 100% respectively and positive predictive value of 100% and negative predictive value of 66.6%.8 Altinyollar et al. used criteria of loss of central fatty hilum, rounded lymph nodes, decrease in echogenicity and presence of eccentric cortical hypertrophy. They reported a sensitivity of 47.5% and specificity of 98.3%. Bonnema et al. in their study of 148 patients showed that sensitivity and specificity of axillary USG for detection of abnormal nodes can be as high as 87% and 56%, if lymph node length was used as the criterion. In contrast, sensitivity and specificity were 36% and 95% respectively when echo pattern of lymph node was used. 10 Oruwari et al. demonstrated that ultrasound of the axilla was more accurate in staging the axilla than preoperative clinical examination and found the sensitivity of USG was 91%, specificity 100% and accuaracy 92%. 11 Sapino et al. recommended that preoperative evaluation of axilla by USG should be used because of low cost and high specificity.¹² He considered nodes suspicious when they had 2D enlargement imparting a rounded appearance, an echo-poor central hilus, and eccentricity of the nodal cortex.¹² Damera et al used nodal shape, including longitudinal to transverse axis ratio of less than 2, and abnormal morphology of cortex, particularly concentric or eccentric thickening to more than 2mm, as the most reliable criteria in predicting malignancy. 13 The following findings were used by Shetty et al to describe metastatic axillary node: size >20 mm, absence of a fatty hilum, abnormal sonographic appearance of cortex, hich included diffuse of focal thickening and round shape. 14

The ultrasound morphologic lymph node features with the greatest correlation with malignancy are loss of central fatty hilum (correlation coefficient-0.953) and cortical thickness (correlation coefficient-0.914). The other two morphologic features, roundedness and hypoechogenicity, were not statistically significant (P >0.05). The correlation coefficients of roundedness and hypoechogenicity are 0.087 and 0.048 respectively and their corresponding P values are 0.389 and 0.632 respectively. This study reports suggest that axillary ultrasound is at best moderately sensitive and fairly specific in diagnosing axillary nodal metastasis, but it has a low negative predictive value and negative ultrasound results cannot definitely exclude axillary node metastasis. More recently, the use of ultrasound elastography and microbubbles in detecting tumor activity has been investigated. This technique involves peritumoral rather than IV injections. 15 The contrast medium is taken up by the lymphatics in a matter of minutes and the sentinel node can be detected. Typically malignant involved lymph nodes will show areas of defect or will appear devoid of microbubbles, thus denoting tumor involvement. 16 The accuracy of assessing axillary lymph nodes using other technologies such as elastography or pulse wave imaging, may be more reproducible. However these studies are still investigational. ¹⁷

Metastatic involvement of axillary lymph nodes is the single most important prognostic factor in carcinoma breast. The presence of axillary involvement in breast cancer determines the patient's survival and staging of the disease and plays an important part in local control. In many situations, the axilla will be negative clinically, but on pathological examination, there may be positive nodes. USG has found an increasingly important place in the preoperative evaluation of clinically negative axilla. If USG detects axillary metastasis, the sentinel lymph node biopsy can be avoided and axillary lymph node dissection can be performed directly. The sentinel lymph node biopsy requires high setup, operating costs and complex techniques. This has limited the widespread application of this methodology. Furthermore, the interpretation of USG of axilla requires excellent skill and experience. There can be subjective variation in detection of abnormal lymph nodes. Also, the sonography was not able to resolve the pathologically detected and reported metastasis in the axillary lymph nodes that were less than 5mm in greatest dimension. The small sample size and short duration of study are the major limitations of this study.

CONCLUSION

Clinical examination is relevant in initial staging of carcinoma breast and thus plan further management. The sensitivity for detecting malignancy is only average and therefore the use of axillary ultrasound alone has not proved to be sufficiently accurate to justify its routine use in all preoperative breast cancer patients. Axillary ultrasound is more likely to detect an abnormal node if there is morphologic features of increased cortical thickening and loss of central fatty hilum. However a multidisciplinary effort is needed to reduce unnecessary axillary dissections and design a less invasive approach to accurately stage disease in patients with nodal metastasis.

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