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Original Article

Characterization of Axillary Lymph Nodes as Normal, Reactive and Benign Using Conventional Ultrasonography

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Abstract

Background: Detection of abnormalities of axillary lymph nodes is important for the diagnosis of different pathologies. **Objective:** The purpose of this present study was to see the accuracy of conventional USG for the differential diagnosis of axillary lymph nodes. **Methodology:** This cross sectional study was carried out in the Department of Radiology & Imaging at Bangabandhu Sheikh Mujib Medical University, Dhaka from July 2012 to June 2013 for a period of one year. Normal healthy woman who came for screening of breast disease without any symptoms and did not have any abnormality on USG was included as normal patient. Axillary lymph nodes from these normal patients were categorized as benign lymph nodes. Patients, who came with the complaints of mastalgia with normal breast findings, were included as patients with mastalgia. The lymph nodes from the patients of mastalgia were considered as reactive lymph nodes and patients with known breast cancer and lymph node metastasis were included as malignant patients. Metastatic lymph nodes from breast cancer patients were included. **Result:** In benign vs reactive the area under curve for long axis diameter was 0.534 (p=0.307), short axis diameter was 0.589 (p=0.007), sinus length 0.492 (p=0.798), cortical thickness was 0.684 (p=0.0001) short long ratio was 0.570 (p=0.033), sinus long ratio 0.445 (p=0.095) cortex short axis ratio 0.641 (p=0.0001). **Conclusion:** The accuracy of conventional USG is good diagnostic modalities for the differential diagnosis of axillary lymph nodes**.** [*Journal of Science Foundation, January 2016;14(1):8-16*]

Keywords: Axillary; lymph nodes; conventional; ultrasonography

Introduction

Breast is the female reproductive organ which undergoes changes in every menstrual cycle, in every pregnancy (Rokutanda et al., 2007). The diseases of breast are ranging from mastalgia through abscess, benign tumor to malignant tumor. Lymphatic drainage from breasts goes mainly to axillary lymph nodes. In Bangladesh female are used Boti which is a special type of knife used in Indian subcontinent in house hold works and use to cut fish, meat, vegetables and other things which may cut their fingers specially thumb and cause infection draining to axillary nodes. These nodes may appear as enlarged and can be confused with metastatic lymph nodes. If there is a fibroadenoma in breast with incidental axillary lymphadenopathy, differential diagnosis of malignant tumor with axillary metastasis may arise, leading to unnecessary lymph

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node FNAC or biopsy (Stavros et al., 2004). Thus differentiation between benign, reactive, and metastatic nodes is also important. The detection of metastasis in lymph nodes is critical for tumor staging and preoperative planning in patients with breast cancer (Damera et al., 2003). Many women undergo sentinel node biopsy and proceed to axillary node dissection if the sentinel node or nodes show malignancy. Sonography and ultrasound guided fine needle aspiration have increasingly been used to evaluate suspicious lymph nodes prior to sentinel node procedure. If a malignant node is diagnosed by ultrasono guided fine needle aspiration, then the patient can avoid the sentinel node procedure and can proceed to full axillary node dissection at the time of primary tumor surgical resection. However in many centers lack of sentinel node procedure, axillary lymph node dissection (ALND) is performed routinely in cases of invasive breast cancer (Cho et al., 2009). Axillary lymph node dissection is a costly procedure associated with various side effects such as paresthesia, hematoma, seroma, restricted shoulder motion and lymphedema.

Ultrasonography is a cheap, easily available and hazardless imaging modality which can easily appreciate axillary lymph nodes. A number of studies have been done on USG features of axillary lymph nodes. Multiple USG features were evaluated to make a differentiation between benign and metastatic lymph nodes. The purpose of this present study was to see the accuracy of conventional USG for the differential diagnosis of axillary lymph nodes.

Methodology

This cross sectional study was carried out in the Department of Radiology & Imaging at Bangabandhu Sheikh Mujib Medical University, Dhakafrom July 2012 to June 2013 for a period of one year and was approved by institutional review board of Bangabandhu Shiekh Mujib Medical University, Dhaka, Bangladesh. Women, who underwent USG of both axilla and breast, were included in this study. In this study normal healthy woman who came for screening of breast disease without any symptoms and did not have any abnormality on USG was included and were categorized as normal patient. Axillary lymph nodes from the normal patients were categorized as benign lymph nodes. Patients, who came with the complaints of mastalgia with normal breast findings, were included as patients with mastalgia. The lymph nodes from the patients of mastalgia were considered as reactive lymph nodes and patients with known breast cancer and lymph node metastasis were included as malignant patients. Metastatic lymph nodes from breast cancer patients were included diagnosed by cytopathology or histopathology as metastatic lymph nodes. Female in the age group of 16 years and below was excluded. Patients having malignancy other than breast, lymphoma, TB, other diseases like granulomatous mastitis and patients having history of premenstrual mastalgia were excluded. USG examinations and biopsies were performed with a Linear Matrix 13-MHz transducer on a General Electric Voluson 730 US system. Patients were first informed and written consent was taken. Ensuring all the privacy USG exam was done by expert female radiologists. Long axis diameter was taken as longest diameter in long axis. Short axis diameter was taken as longest diameter perpendicular to the long axis. Cortical thickness was taken as maximum thickness along the sort axis diameter. Sinus length was taken at the largest sinus section. Short axis / long axis (S/L ratio) was the ratio of transverse to longitudinal diameter. Sinus / long axis ratio was calculated as ratio of length of hilum and long axis diameter. Cortex / short axis diameter was calculated as the ratio of cortical thickness to short axis diameter. Data on focal cortical thickness, color flow and power Doppler could not be taken accurately in all lymph nodes. Thus these parameters were not evaluated. Data was entered into SPSS 16.0 software and calculation was done. Receiver operating curve (ROC) for long axis diameter, short axis diameter, cortical thickness, sinus length, short/long ratio, sinus/long axis ratio, and cortex/short axis ratio was prepared to differentiate between benign and reactive, benign and metastatic and reactive and metastatic LNs. All participants were volunteered. Informed written consent was taken from the participants after explaining in Bengali about the facts to the subjects in case of primary data collection. Information was taken with structured questioner. Images were saved as both soft copy and hard copy. And measurement of the variables was done off line. The asymptotic significance is less than 0.05.

Results

Three hundred and eighty nine lymph nodes from 365 women, who underwent USG of both axilla and breast, were included in this study from. In this study 158 normal healthy women who came for screening of breast disease without any symptoms and did not have any abnormality on USG was included and

werecategorized as normal patient. Axillary lymph nodes from the normal patients werecategorized as benign lymph nodes. 137 patients, who came with the complaints of mastalgia with normal breast findings, were included as patients with mastalgia. The lymph nodes from the patients of mastalgia were considered as reactive lymph nodes and 70 patients with known breast cancer and lymph node metastasis were included as malignant patients.

Table 1: Area under the Curve for Benign Vs Reactive

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% CI	
				Lower Bound	Upper Bound
Long Axis Diameter	0.534	0.034	0.307	0.466	0.601
Short Axis Diameter	0.589	0.032	0.007	0.526	0.652
Sinus Length	0.492	0.033	0.798	0.426	0.557
Cortex	0.684	0.030	0.000	0.626	0.743
Short Long Ratio	0.570	0.033	0.033	0.505	0.635
Sinus Long Ratio	0.445	0.032	0.095	0.382	0.509
Cortex Short Ratio	0.641	0.032	0.000	0.578	0.704

Benign Vs Reactive (Table1; Figure1)

Receiver operating curve was drawn to evaluate the performance of long axis diameter, short axis diameter, cortical thickness, short long ratio, sinus long axis ratio, cortex short axis ratio. The area under curve for long axis diameter was 0.534 (asymptotic significance 0.307), short axis diameter was 0.589 (asymptotic significance 0.007), sinus length 0.492 (asymptotic significance 0.798), cortical thickness was 0.684 (asymptotic significance 0.000) short long ratio was 0.570 (asymptotic significance 0.033), sinus long ratio 0.445 (asymptotic significance 0.095) cortex short axis ratio .641 (asymptotic significance 0.0001).The cut off for cortical thickness was 0.28 and that for cortex short axis diameter was 0.5.

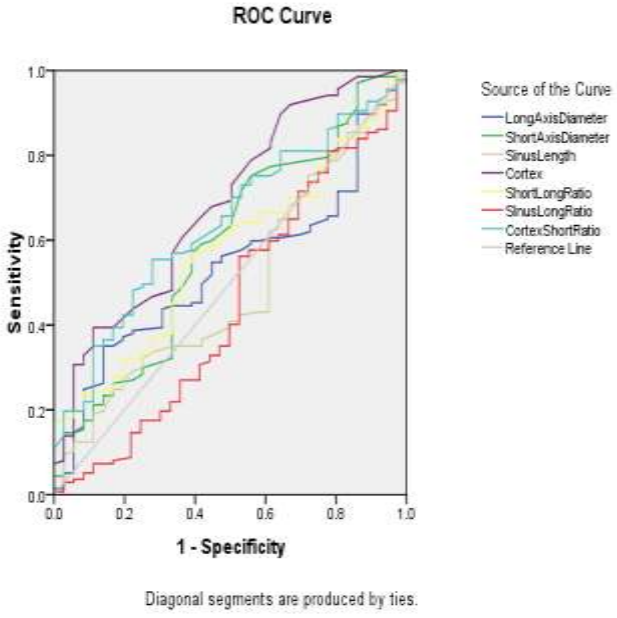

Figure 1:ROC for Benign Vs Reactive

Reactive Vs Metastatic (Table 2; Figure 2)

Table 2: Area under the Curve for Reactive Vs Metastatic

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% CI	
				Lower Bound	Upper Bound
Long Axis Diameter	0.464	0.040	0.391	0.384	0.543
Short Axis Diameter	0.741	0.039	0.000	0.665	0.817
Sinus Length	0.257	0.037	0.000	0.186	0.329
Cortex	0.625	0.044	0.003	0.539	0.712
Short Long Ratio	0.791	0.036	0.000	0.720	0.862
Sinus Long Ratio	0.279	0.040	0.000	0.200	0.357
Cortex Short Ratio	0.516	0.041	0.708	0.435	0.597

Receiver operating curve was drawn to evaluate the performance of long axis diameter, short axis diameter, cortical thickness, short long ratio, sinus long axis ratio, cortex short axis ratio to differentiate between reactive and metastatic. The area under curve for long axis diameter was 0.464 (asymptotic significance 0.391), short axis diameter was 0.741 (asymptotic significance 0.000), sinus length 0.257 (asymptotic significance 0.037), cortical thickness was 0.625 (asymptotic significance 0.003) short long ratio was 0.791 (asymptotic significance 0.000), sinus long ratio 0.279 (asymptotic significance 0.040) cortex short axis ratio .516 (asymptotic significance 0.708).The cut off for short-long axis diameter ratio was 0.43, for short axis was 0.66cm and for cortical thickness 0.37cm.

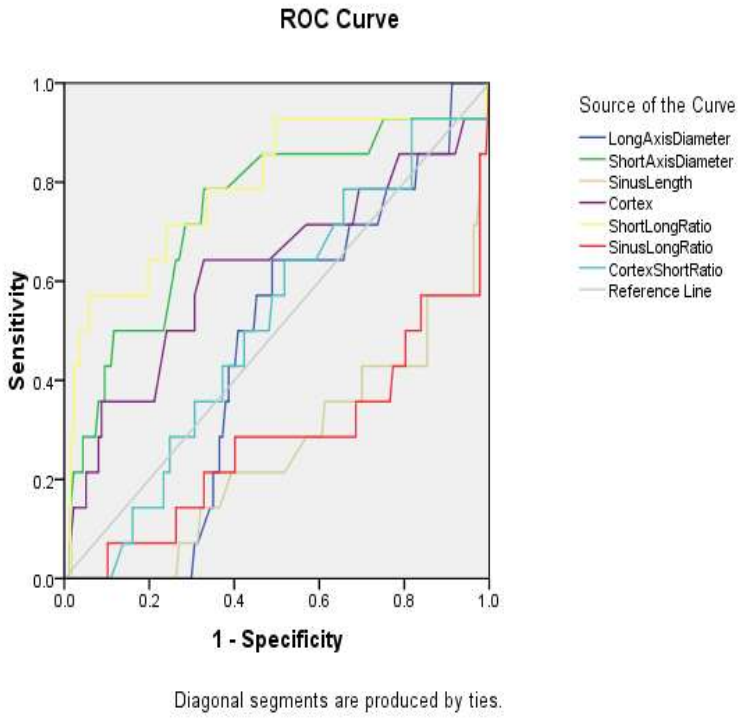

Figure 2: ROC for Reactive Vs Metastatic

Benign Vs Metastasis: (Table 3, Figure 3)

Receiver operating curve was, drawn to evaluate the performance of long axis diameter, short axis diameter, cortical thickness, short long ratio, sinus long axis ratio, cortex short axis ratio. The area under curve for long axis diameter was 0.533 (asymptotic significance 0.417), short axis diameter was 0.797 (asymptotic significance 0.000), sinus length 0.254 (asymptotic significance 0.000), cortical thickness was 0.757 (asymptotic significance 0.000) short long ratio was 0.847 (asymptotic significance 0.000), sinus long ratio 0.241 (asymptotic significance 0.000) cortex short axis ratio .661 (asymptotic significance 0.000).

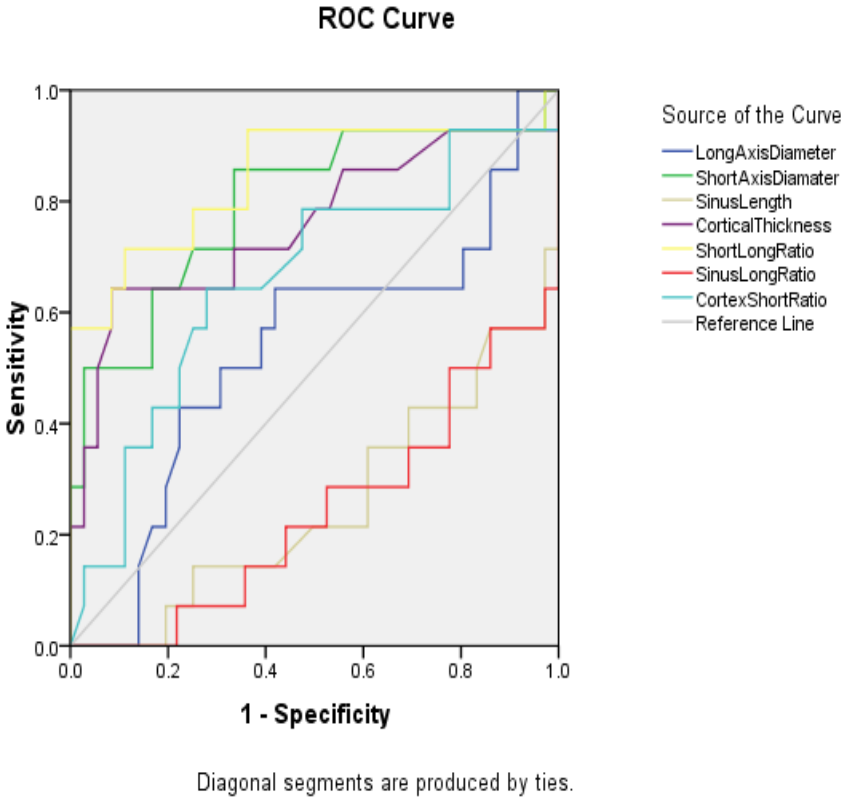

Figure 3: ROC for Metastatic Vs Benign

Table 3: Area under the Curve for Metastatic Vs Benign

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	95% CI	
				Lower Bound	Upper Bound
Long Axis Diameter	0.533	0.043	0.417	0.449	0.617
Short Axis Diameter	0.797	0.035	0.000	0.729	0.865
Sinus Length	0.254	0.036	0.000	0.183	0.325
Cortical Thickness	0.757	0.039	0.000	0.680	0.834
Short Long Ratio	0.847	0.033	0.000	0.783	0.911
Sinus Long Ratio	0.241	0.035	0.000	0.173	0.310
Cortex Short Ratio	0.661	0.041	0.000	0.582	0.741

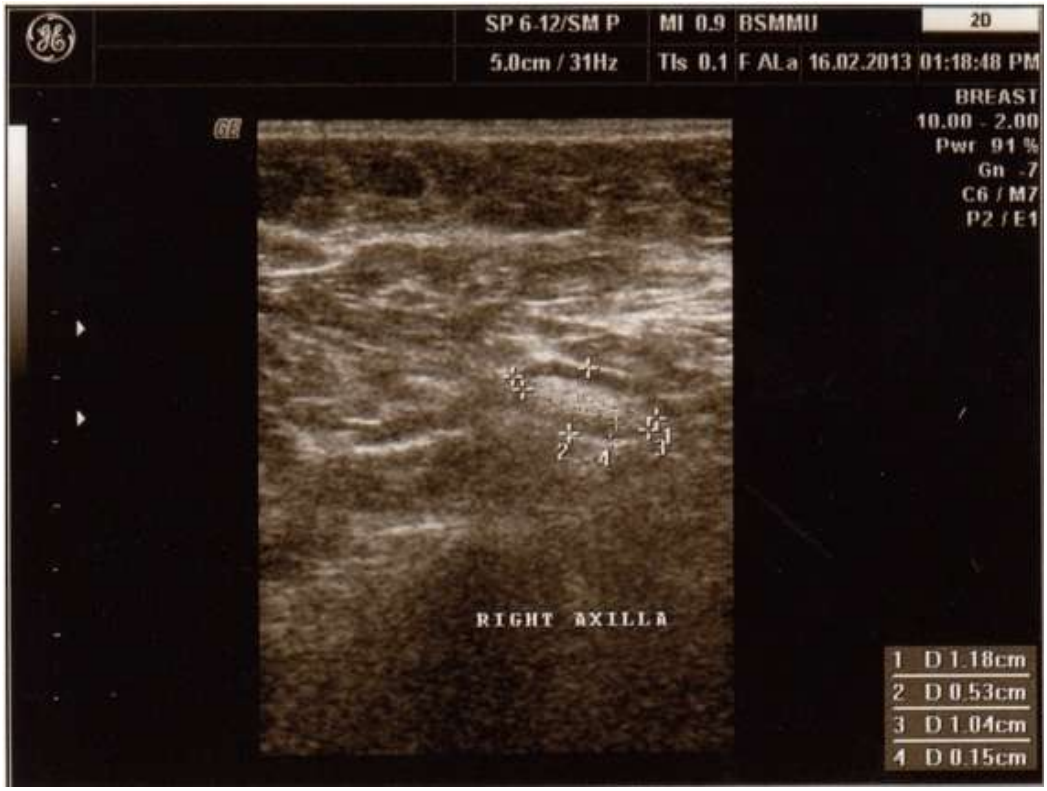

Figure 1: USG finding of Normal Lymph Node

Discussion

This retrospective study was conducted in a tertiary care hospital serving an urban and suburban population in Dhaka. Three hundred sixty five patients were scanned for the study at Bangabandhu Sheikh Mujib Medical University, Dhaka, during period of eleven months from July 2012 to May 2013.

Figure 2: USG finding of Benign Lymph Node

Benign Vs Reactive (Table1; Figure1)

One hundred and seventy nine benign and 137 reactive lymph nodes were evaluated. ROC curve was drawn for the seven differentiating parameters. The largest area under the curve (with asymptotic significance below 0.05) was shown by cortical thickness (area 0.684 with asymptotic significance 0.0001), cortex-short axis diameter ratio (area 0.641 with asymptotic significance 0.0001), short axis diameter (0.59 with asymptotic significance 0.007) and for short-long ratio (area 0.570 with asymptotic significance 0.033).The cut off for cortical thickness was 0.28 and that for cortex short axis diameter was 0.5. Area for long axis diameter (0.534) was above 0.5 but the asymptotic significance (0.307) above 0.05. Sinus length and sinus-long axis ratio and showed two smallest are under the curve 0.492 (with asymptotic significance 0.798) and 0.45 (p=0.095) respectively.

Figure 3: USG finding of Metastatic Lymph Node

Study on ultrasonographic differentiation between benign and reactive lymph node is not reported. In this present study differentiation between benign and reactive lymph nodes has been made because of a large number of patients present in this outpatient department with the complaints of mastalgia. In conventional practice it has been used to report lymphadenopathy if the long axis diameter is more than 1.5 cm. Sometimes incidental fibroadenomas are also found in patients of mastalgia. In these cases the surgeons send the patient for FNAC of axillary lymph node which is unnecessary. Re-evaluation of the parameters of differentiating benign and reactive lymph nodes has been performed in this present study.

The cortical thickness, cortex-short axis ratio, short axis diameter and short-long ratio have been appeared as the useful parameters for the differentiation between benign and reactive lymph nodes. The cut off for cortical thickness is 2.8 mm at the level of sensitivity and specificity 65% and 63% indicating that lymph nodes having cortical thickness less than 2.8 mm can be considered as benign lymph node. Deruloo et al (2003) also found that normal cortical thickness of 1 to 2 mm, and abnormal lymph node generally has a thickness greater than 2.3 mm. They reported a sensitivity of 95% and a specificity of 44%. The second useful parameter in this study is the cortex short axis diameter ratio, with cutoff 0.5 at the level of sensitivity and specificity 63% and 61% respectively. It indicates that if the cortex-short axis diameter ratio is less than 0.5 it may be considered as benign lymph node.

Here it has been found that long axis diameter is not a useful parameter for benign reactive differentiation. In studies during 1980-1990s long axis diameter is evaluated and it has been being proved to be an insensitive parameter for differentiating lymph node status. And now-a-days long axis diameter is not being evaluated

in the studies on lymph node. More over the lymph nodes in different locations of body have different lengths. Rather sort axis diameter and short-long ratio was third and fourth important parameters.

Reactive Vs Metastatic (Table 2; Figure2)

The larger area under the curve (with asymptotic significance below 0.05) was shown by Short-long ratio, short axis diameter and cortical thickness. The best cut off for short-long axis diameter ratio was 0.43, for short axis was 6.6 mm and for cortical thickness 3.7 mm. The area under the curve for cortex-short axis ratio was above 0.5 but the asymptotic ratio was more than 0.05. Next large area was shown by long axis diameter (0.464) was below 0.5 and the asymptotic significance (0.391) above 0.05. Sinus-long axis ratio and sinus length showed two smallest are under the curve 0.279 (with asymptotic significance 0.040) and 0.257 (with asymptotic significance .037) respectively. According to our result short-long axis diameter ratio more than 0.43 (i.e. shape rounder than oval) can be considered as metastatic. Reports are not found which has been differentiating between reactive and metastatic. However, several studies have evaluated short-long or long-short diameter of benign and metastatic lymph nodes. Damera et al (2003) performed a careful scan of the lower axilla posterior to where the pectoralis major muscle crosses the cranial edge of the breast disc, which is the common location of sentinel node. They measured the longitudinal and transverse dimensions to determine the axis ratio of a lymph node. If longitudinal-transverse axis ratio (we measured transverse-longitudinal ratio) was <2, then the lymph node was considered suspicious. In this study short axis diameter 6.6mm was considered as cut off for differentiating reactive and metastatic, i.e. larger than 6.6 mm in short axis can be considered as metastatic and smaller than that can be considered reactive. The cutoff cortical thickness has been found in 3.7 mm at sensitivity and specificity 64% and 65% respectively. Other studies were between benign and metastatic. Damera et al (2003) considered cutoff cortical thickness 2mm, Deruloo et al (2003) considered 2.3 mm and reported sensitivity & specificity of about 55% & 82%; 95% and 44% respectively. To select cutoff it has been considered the level where sensitivity and specificity are nearest. Moreover it has been evaluated reactive lymph nodes and they evaluated benign lymph nodes which may be the cause behind the difference between previous cut offs and the present study cut off values.

Benign Vs Metastasis (Table3, Figure3)

The larger area under the curve (with asymptotic significance below 0.05) was shown by Short-long ratio (area 0.847 with asymptotic significance 0.000), short axis diameter (area 0.797 with asymptotic significance 0.000) and cortical thickness (0.757 with asymptotic significance 0.000). The best cut off for short-long axis diameter ratio was 0.41, for short axis was 6.4 mm and for cortical thickness 3 mm. The area under the curve for cortex-short axis ratio (0.661) was above 0.5 with the asymptotic ratio 0.0001. Sensitivity and specificity of cortical thickness at 3 mm was 70% and 66% respectively. Area under the curve for cortical thickness was almost same as that of shape 0.829 indicating cortical thickness as a strong predictor of metastatic lymph node. This criterion was also evaluated by Rokutandaet al (2007) where they evaluated lymph nodes from breast cancer patients. In their study the cortical layer of LN was thicker in positive for malignant group of lymph node than the negative group (3.11mm vs 2.12mm, $p<0.05$). Damera et al (2003) also evaluated these criteria and got the same result. Deurlooet al (2003) used maximum cortex thickness as the main feature to predict metastatic disease in lymph node. The normal cortical thickness of a lymph node is 1 to 2 mm, and an abnormal lymph node generally has a thickness greater than 2.3 mm. They reported a sensitivity of 95% and a specificity of 44% using this criterion. In our study cortical thickness cutoff at 2.3 mm gives sensitivity and specificity of 86% and 47%. Cortical thickness has been evaluated by Cho et al (2009) and has evaluated 191 lymph nodes from breast cancer patients. When the cutoff point of a cortical thickness of 2.5 mm was used, sonographic classification showed 85% (35/41) sensitivity, 78% (117/150) specificity. Cortical morphology was also evaluated by Bedi et al (2008) an in vitro study of cortical morphologic features of axillary lymph nodes from patients having infiltrating breast cancer. They reported sensitivity and specificity of about 77% and 80%. Both the above studies have reported better sensitivity and specificity than the present study results. They evaluated lymph nodes from patients having invasive carcinoma of breast. And in this study it has been considered lymph nodes from both normal people and patients having breast cancer. Area for long axis diameter (0.533) was above 0.5; however, the asymptotic significance (0.417) above 0.05. Sinus length and sinus-long axis ratio and showed two smallest are under the curve 0.254 (with asymptotic significance 0.0001) and 0.241 (with asymptotic significance 0.0001) respectively. Above data indicate that long axis diameter as well as sinus length and sinus-long axis

ratio are not useful parameter for differentiation of metastatic and reactive lymph nodes. The study was a retrospective study and has its inherent weakness. Further prospective studies are warranted to improve the characterization between benign, reactive and metastatic lymph nodes.

Conclusion

The accuracy of conventional USG is good diagnostic modalities for the differential diagnosis of axillary lymph nodes**.** To differentiate benign, reactive and metastatic lymph node, cortical thickness and shape are the important parameters. Long axis diameter should not be considered as important parameter.

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