EVALUATING THE ROLE OF ULTRASOUND ELASTOGRAPHY, COLOR DOPPLER, AND GREYSCALE ULTRASOUND IN ASSESSING AUXILIARY LYMPH NODES IN SUBJECTS WITH PRIMARY BREAST CANCER

Dr Akshaya Shivaram,[1] Dr Sumukhi Shankar BS[2*]

[1]MBBS MD, Associate Professor, Department of Radio-Diagnosis
Sridevi Institue of medical sciences, Lingapura, Tumakuru, Karnataka
email id: akshaydr82@gmail.com
[2*]MBBS DCP, Consulting Pathologist, Dhanvantri scan centre, Nagasandra, Bangalore
sumukhishankar@gmail.com

Corresponding author

Dr Sumukhi Shankar BS
Dhanvantri scan centre, No1 Shibra farms, Nagasandra, Bangalore
Email id: sumukhishankar@gmail.com

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ABSTRACT

Introduction: Most common metastasis site for breast carcinoma in axillary lymph nodes. Lymph nodes of the axilla metastasis are one of the reliable and vital prognostic factors in subjects with breast cancer. Early and accurate differentiation of benign axillary lymph nodes from malignant lymph nodes is vital to prevent the conversion of treatable lesions to an incurable one and for improved survival and outcomes.

Aims: The present study was conducted to assess axillary lymph nodes in subjects with breast carcinoma on strain wave elastography, color doppler, and greyscale ultrasound and to correlate them histopathologically. Also, the present study compared the negative and positive predictive values, specificity, and sensitivity of combined greyscale ultrasound and elastography findings to findings of greyscale ultrasound.

Materials and Methods: In 68 subjects with a confirmed diagnosis of carcinoma breast on histopathology were evaluated for axillary lymph nodes assessed for cortical thickness/fatty hilum thickness ratio (C/F ratio), cortical thickness, long /short axis ratio (L/S ratio), presence/absence of hilum, shape, and size on color doppler for vascularity, greyscale ultrasound, and elastography. The diagnosis was made and was confirmed on histopathology.

Results: It was seen that malignancy was favored by increased C/F ratio, decreased L/S ratio, increased cortical thickness, eccentric/compressed or absent hilum, irregular nodular margins, and round shape in morphology. Differentiation from benign to malignant lymph nodes was done based on peak systolic velocity/end-diastolic velocity ratio, resistivity index, and vascular flow pattern type. In malignant lymph nodes, the mean strain ratio was higher than benign lymph nodes.

Conclusions: The present study concludes that ultrasound including strain elastography, color Doppler, and greyscale ultrasound should be routinely included in the initial screening of subjects with breast carcinoma owing to its advantages of being accurate, easy accessibility, radiation-free nature, and cost-effectiveness.

Key Words: Axillary lymph nodes, Colour Doppler, Elastography, Grayscale ultrasound, Primary breast cancer, Prospective study

INTRODUCTION

Carcinoma of the breast is one of the most common malignancies affecting females in large proportion globally. Carcinoma breast usually spread via intraductal growth and local invasion to the lymphatics in the predictable and step-wise from before the occurrence of distant metastasis occurring via hematogenous spread.[1]

The most common site of metastasis for carcinoma breast is axillary lymph nodes. Lymph nodes of the axilla metastasis are one of the reliable and vital prognostic factors in subjects with breast cancer. Early and accurate differentiation of benign axillary lymph nodes from malignant lymph nodes is vital to prevent the conversion of treatable lesions to an incurable one and for improved survival and outcomes. Differentiation of benign axillary lymph nodes from malignant nodes is vital allowing better survival and outcomes.[2]

The lymph node to get earliest lymphatic drainage from carcinoma breast is sentinel lymph node (SLN) and helps in accurate prediction of lymph node status for remaining axillary lymph nodes. Biopsy of the sentinel lymph node is not openly accepted in developing countries owing to its high cost, the need for nuclear medicine, false-negative rate, weakness of the arm, limited shoulder movements, pain, lymphedema,post-procedure complications, waiting time, and frozen section facilities. Hence, the application and use of non-invasive procedures like strain wave elastography, Colour Doppler, and ultrasonography are vital in differentiating benign lymph nodes from malignant lymph nodes is efficacious and advantageous.[3]

Diagnosis and management of malignant axillary lymph nodes and breast carcinoma can decrease associated mortality, improve life quality, and better survival outcomes. The present study was conducted to assess axillary lymph nodes in subjects with breast carcinoma on strain wave elastography, color doppler, and greyscale ultrasound and to correlate them histopathologically. Also, the present study compared the negative and positive predictive values, specificity, and sensitivity of combined greyscale ultrasound and elastography findings to findings of greyscale ultrasound.

MATERIALS AND METHODS

The present prospective observational clinical study was conducted to assess axillary lymph nodes in subjects with breast carcinoma on strain wave elastography, color doppler, and greyscale ultrasound and to correlate them histopathologically. Also, the present study compared the negative and positive predictive values, specificity, and sensitivity of combined greyscale ultrasound and elastography findings to findings of greyscale ultrasound. The study was conducted atSridevi Institue of medical sciences, Lingapura, Tumakuru, Karnataka from

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June 2020 to June 2021after obtaining clearance from the concerned Ethical committee. After explaining the detailed study design, informed consent was taken from all the subjects in both written and verbal form. The study included a total of 68 subjects within the age range of 35-78 years and the mean age of 52.4±4,62 years.

The study included females with confirmed histopathologic diagnosis of breast carcinoma on histopathology and radiographic imaging showed the axis of axillary lymph nodes less than 5mm. Exclusion criteria for the study were subjects who had a history of prior axillary interventions, neoadjuvant chemotherapy, radiotherapy scheduled subjects who had undergone bilateral breast surgery affected by bilateral carcinoma breast.

Strain wave elastography, color doppler, and greyscale ultrasound were done in axillary lymph nodes of all the affected subjects using a multi-frequency linear array transducer. For the ipsilateral axilla, ultrasound was done in primary breast carcinoma subjects in 90-degree shoulder abduction and supine position. This was done for positioning the axillary levels following a straight course so that all axillary parts can be thoroughly assessed. Compression of the variable amount was applied with a transducer for thinning of axillary area, which further helps in improving the image quality and radiation penetration.

Morphology of the lymph nodes was also assessed, and in subjects with normal appearance of axillary lymph nodes, the most representative lymph node in the lower axilla was selected for further assessment. Greyscale ultrasound, color doppler ultrasound, and strain wave elastography were done for all the subjects using standard procedures. The parameters seen on greyscale ultrasound were cortical/fatty hilum thickness ratio(C/F), long axis/short axis ratio (L/S), focal thickening of the cortex, margins sharpness, present /absent fatty hilum, and oval or round appearance. Color doppler ultrasound assessed pulsatility index (PI) and systolic/diastolic (S/D) ratio and resistivity index (RI) where the highest value was recorded. Vascularity distribution of lymph nodes was done and described as mixed vascular patterns, peripheral non-hilar, central perihilar, and hilar nodes.

The results assessed were then correlated to the obtained histopathologic findings to confirm the diagnosis. For further analysis, the size and number of the largest lymph nodes were correlated histopathologically. Hence, 68 lymph nodes were assessed in 68 study subjects. Comparison of negative and positive predictive values, specificity and sensitivity of combined greyscale ultrasound and elastography findings to findings of greyscale ultrasound were performed.

The collected data were subjected to the statistical evaluation using SPSS software version 21 (Chicago, IL, USA) and one-way ANOVA and t-test for results formulation. The data were expressed in percentage and number, and mean and standard deviation. The level of significance was kept at $p<0.05$.

RESULTS

The present prospective observational clinical study was conducted to assess axillary lymph nodes in subjects with breast carcinoma on strain wave elastography, color doppler, and greyscale ultrasound and to correlate them histopathologically. Also, the present study compared the negative and positive predictive values, specificity, and sensitivity of combined greyscale ultrasound and elastography findings to findings of greyscale ultrasound. The study included a total of 68 subjects within the age range of 35-78 years and the mean age of 52.4±4,62 years. The study included 4 nulliparous females and 64 multiparous females with positive breast carcinoma family history seen in 6 study subjects. Right, and left-sided breast carcinoma was seen in 36 and 31 study subjects respectively.

Among 68 assessed lymph nodes, 46 lymph nodes showed metastasis and 22 nodes were benign. The disease characteristics are summarized in table 1. The results showed that for hilum localization, it was absent in 6.52% (n=3) subjects with malignant axillary lymph nodes, whereas, Compressed/Eccentric localization was seen in 9.09% (n=2) and 89.13% (n=41) subjects with benign and malignant lymph nodes. Central maintained hilum was seen in 90.09% (n=20) and 4.34% (n=2) subjects with benign and malignant lymph nodes respectively. The ovoid shape was seen in 94.45% (n=21) and 6.52%v (n=3) subjects with benign and malignant nodes respectively. In malignant nodes, irregular nodular margins were seen in 82.60% (n=38) subjects. The vascular pattern in benign nodes was majorly mixed with 45.45% (n=10) subjects, whereas, in malignant nodes, the hilar flow pattern was prominent and was seen in 58.82% (n=40) study subjects.

On assessing the vascular pattern, the mixed pattern was major in malignant axillary lymph nodes with 82.60% (n=38) subjects, whereas, in benign axillary lymph nodes most common pattern was hilar in 45.45% (n=10) study subjects followed by non-hilar in 31.81% (n=7) subjects. S/D ratio was 3.12±0.51 and 6.45±5.68 for benign and malignant nodes respectively, RI was 0.64±0.08 and 0.80±0.17, PI was 1.16±0.23 and 1.58±0.34, Cortical/fatty hilum thickness ratio(C/F) was 0.80±0.44 and 4.59±4.77, cortical thickness was 2.25±0.73 and 8.08±4.87, and long axis/short axis ratio (L/S) was 12.32±2.87 and 1.71±8.21 respectively. All these parameters were significantly raised in malignant axillary lymph nodes compared to benign axillary lymph nodes with $p<0.0001$ as shown in Table 2.

The findings are seen on greyscale ultrasound, color doppler, electrometry, and combined examination were assessed and correlated to histopathologic findings. The results showed that on greyscale ultrasound, benign tumors were 90% (n=18) confirmed on histopathology and 2 cases were false negative, whereas malignant tumors corrected to histopathology were 97.91% (n=47), whereas, 1case (2.08%) was negative. Color Doppler showed the histopathologic correlation in 15% (n=3) were false and 85% (n=17) correlated, and for malignant 97,91% (n=47) were histopathologic correlated and 4.16% (n=2) were false. Elastography showed similar results wherein 90% (n=18) cases histopathologic correlation was seen and in 0% (n=2) cases this correlation was not seen, whereas, in malignant tumors, 95.83% (n=46) subjects showed correlation on histopathologic assessment. Combined data showed that malignant tumors were 97.91% (n=47) correct and the false result was seen in only 1 case, whereas, benign tumors had 90% (n=18) positive histopathologic result and negative false values were seen in 10% (n=2) cases. This difference was statistically significant with $p<0.0001$ as shown in table 3.

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DISCUSSION

The present prospective observational clinical study was conducted to assess axillary lymph nodes in subjects with breast carcinoma on strain wave elastography, color doppler, and greyscale ultrasound and to correlate them histopathologically. Also, the present study compared the negative and positive predictive values, specificity, and sensitivity of combined greyscale ultrasound and elastography findings to findings of greyscale ultrasound. The study included a total of 68 subjects within the age range of 35-78 years and the mean age of 52.4±4,62 years. The study included 4 nulliparous females and 64 multiparous females with positive breast carcinoma family history seen in 6 study subjects. Right, and left-sided breast carcinoma was seen in 36 and 31 study subjects respectively. Among 68 assessed lymph nodes, 46 lymph nodes showed metastasis and 22 nodes were benign. The results showed that for hilum localization, it was absent in 6.52% (n=3) subjects with malignant axillary lymph nodes, whereas, Compressed/Eccentric localization was seen in 9.09% (n=2) and 89.13% (n=41) subjects with benign and malignant lymph nodes. Central maintained hilum was seen in 90.09% (n=20) and 4.34% (n=2) subjects with benign and malignant lymph nodes respectively. The ovoid shape was seen in 94.45% (n=21) and 6.52%v (n=3) subjects with benign and malignant nodes respectively. In malignant nodes, irregular nodular margins were seen in 82.60% (n=38) subjects. The vascular pattern in benign nodes was majorly mixed with 45.45% (n=10) subjects, whereas, in malignant nodes, the hilar flow pattern was prominent and was seen in 58.82% (n=40) study subjects. These results were consistent with the results of Latif MA et al[4] in 2016 and Chang W et al[5] in 2018 where similar disease characteristics were reported by the authors.

The assessment of the vascular pattern in the present study showed that mixed pattern was major in malignant axillary lymph nodes with 82.60% (n=38) subjects, whereas, in benign axillary lymph node most common pattern was hilar in 45.45% (n=10) study subjects followed by non-hilar in 31.81% (n=7) subjects. S/D ratio was 3.12±0.51 and 6.45±5.68 for benign and malignant nodes respectively, RI was 0.64±0.08 and 0.80±0.17, PI was 1.16±0.23 and 1.58±0.34, Cortical/fatty hilum thickness ratio(C/F) was 0.80±0.44 and 4.59±4.77, cortical thickness was 2.25±0.73 and 8.08±4.87, and long axis/short axis ratio (L/S) was 12.32±2.87 and 1.71±8.21 respectively. All these parameters were significantly raised in malignant axillary lymph nodes compared to benign axillary lymph nodes with $p<0.0001$. These results were in agreement with the studies of Liu H et al[6] in 2018 and Park Y et al[7] in 2014 where ultrasound parameters compared to the present study were reported by the authors.

The findings are seen on greyscale ultrasound, color doppler, electrometry, and combined examination were assessed and correlated to histopathologic findings. The results showed that on greyscale ultrasound, benign tumors were 90% (n=18) confirmed on histopathology and 2 cases were false negative, whereas malignant tumors corrected to histopathology were 97.91% (n=47), whereas, 1case (2.08%) was negative. Color Doppler showed the histopathologic correlation in 15% (n=3) were false and 85% (n=17) correlated, and for malignant 97,91% (n=47) were histopathologic correlated and 4.16% (n=2) were false. Elastography showed similar results wherein 90% (n=18) cases histopathologic correlation was seen and in 0% (n=2) cases this correlation was not seen, whereas, in malignant tumors, 95.83% (n=46) subjects showed correlation on histopathologic assessment. Combined data showed that malignant tumors were 97.91% (n=47) correct and the false result was seen in only 1 case, whereas, benign tumors had 90% (n=18) positive histopathologic result and negative false values were seen in 10% (n=2) cases. This difference was statistically significant with p<0.0001. These results were similar to the results of Maxwell F et al[8] in 2015 and Choudhary J et al[9] in 2017 where authors reported similar findings of axillary lymph nodes on the greyscale, color doppler, and elastography in axillary lymph nodes associated with breast carcinoma.

CONCLUSION

Within its limitations, the present study concludes thatultrasound including strain elastography, color Doppler, and greyscale ultrasound should be routinely included in the initial screening of subjects with breast carcinoma owing to its advantages of being accurate, easy accessibility, radiation-free nature, and cost-effectiveness.However, the present study had a few limitations including a small sample size, short monitoring time, and geographical area biases. Hence, more longitudinal studies with a larger sample size and longer monitoring period will help reach a definitive conclusion.

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TABLES

Characteristics	Benign % (n=22)	Malignant % (n=46)	p-value
Hilum Localization			
Absent	0	6.52 (3)	<0.0001
Compressed/Eccentric	9.09 (2)	89.13 (41)	
Central and maintained	90.09 (20)	4.34 (2)	
Shape type			
Irregular nodular margins	4.54 (1)	82.60 (38)	<0.0001
Round	0	10.86 (5)	
Ovoid	95.45 (21)	6.52 (3)	
Vascularity			
Mixed flow pattern	45.45 (10)	13.04 (6)	23.52 (16)
Peripheral non-hilarflow pattern	13.63 (3)	4.34 (2)	7.35 (5)
Central prehilar flow pattern	31.81 (7)	0	10.29 (7)
Hilar flow pattern	9.09 (2)	82.60 (38)	58.82 (40)

Table 1: Disease-related characteristics in the study subjects

Parameter	Benign % (n=22)	Malignant % (n=46)	Total
Vascular Pattern			
Mixed	9.09 (2)	82.60 (38)	40
Non-hilar	31.81 (7)	2.17 (1)	8
Prehilar	13.63 (3)	2.17 (1)	2
Hilar	45.45 (10)	13.04 (6)	16
Variables	**Mean± S.D**	**Mean± S.D**	p-value

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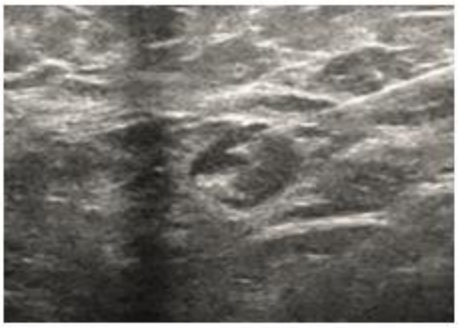
Systolic/diastolic ratio	3.12±0.51	6.45±5.68	<0.0001
Resistivity index (RI)	0.64±0.08	0.80±0.17	<0.0001
Pulsatility index (PI)	1.16±0.23	1.58±0.34	<0.0001
Cortical/fatty hilum thickness ratio(C/F),	0.80±0.44	4.59±4.77	<0.0001
Cortical thickness	2.25±0.73	8.08±4.87	<0.0001
Long axis/short axis ratio (L/S)	12.32±2.87	1.71±8.21	<0.0001

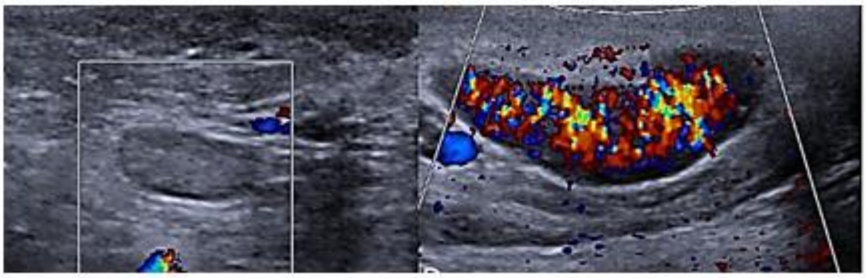
Table 2: Comparison of axillary lymph nodes and ultrasound parameters to histopathologic findings in the study subjects

Parameter	Benign % (n=22)	Malignant % (n=46)	Total
Combined			
Malignant	10 (2)	97.91 (47)	<0.0001
Benign	90 (18)	2.08 (1)	
Elastography			
Malignant	10 (2)	95.83 (46)	<0.0001
Benign	90 (18)	4.16 (2)	
Color Doppler			
Malignant	15 (3)	97.91 (47)	<0.0001
Benign	85 (17)	2.08 (1)	
Greyscale			
Malignant	10 (2)	97.91 (47)	<0.0001
Benign	90 (18)	2.08 (1)	

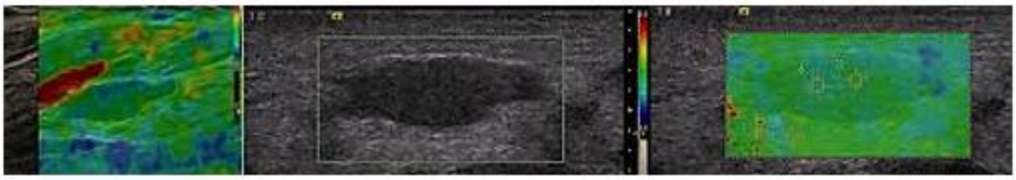
Table 3: Association of histopathologic findings to greyscale, elastography, color doppler, and combined results in the study subjects



a) Greyscale ultrasound



b) Color Doppler



c) Ultrasound Elastography

Figure 1: Greyscale ultrasound, color doppler, and ultrasound elastography seen in axillary lymph nodes of subjects with carcinoma breast