Original Article

The value of Gray scale, color doppler and ultrasound guided- FNA in detection metastasis to the axillary lymph node in patient with primary breast cancer.

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Summary:

Background: Ultrasound guided fine needle aspiration (FNA) is a quick nonmorbid method of staging disease in the axilla,Color doppler ultrasound is used to differentiate benign lymph node from node that bears metastasis.

Objective: To evaluate the utility of ultrasound guided (FNA) of the axillary L.N depending on the size of the primary tumor and the appearance of the lymph node by ultrasound , and to document the difference in color Doppler flow features between benign and malignant lymph node in women with primary breast cancer.

Patients and methods: The total number of the patient in the study is (60). Data were collected about tumor size, lymph node appearance and color-power Doppler sonography compared to the result of ultrasound- guided FNA . Lymph node were classified as: Benign: if the cortex was even and measure < 3mm. Indeterminate : if the cortex was even but measure ≥ 3mm, or with focal cortical thickening but cortical thickness <3mm. Suspicious: if cortex focally thickened ≥ 3mm, or the fatty hilum was absent. Color-power Doppler evaluation was based on the morphologic pattern of vascularity (central, peripheral and mixed).

Results: of these (60) patients , ultrasound guided FNA was done to (42) lymph node .The sensitivity and specificity of ultrasound guided FNA to detect metastasis to axillary lymph node in correlation to the size of tumor was 50% in tumor (≤1cm), and 86% in tumor between (1 - 2cm), and 93% in tumor >2cm.The sensitivity and specificity of ultrasound guided FNA to detect metastasis to axillary lymph node was 67% for indeterminate lymph node, and 95% for suspicious lymph node. The sensitivity and specificity of ultrasound guided FNA to detect metastasis to axillary node in correlation to color Doppler flow was 100% for mixed vascularity and 100% for peripheral vascularity.

Conclusion: There is a strong significant correlation relationship between the presence of peripheral blood flow in addition to the morphological changes which include focal cortical thickening >3mm and loss of hilum ,and the size of the primary tumor with presence of malignancy in LN in patient with primary breast cancer.

Keywords: color doppler , lymph node , ultrasound guided FNA.

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Introduction:

Axillary lymph node staging is the most important prognostic indicator of outcome in patient with breast cancer(1).Ultrasound guided fine needle aspiration (FNA) is a quick non morbid method of staging disease in the axilla .Although percutaneous biopsy of breast lesion has largely supplanted surgery as a less costly and less invasive method of diagnosis, percutaneous evaluation of the axilla is still not routinely used in many centers despite growing body of evidence that it is very valuable in planning the appropriate management of patient and can spare some patients a surgical procedure(1). Traditionally axillary lymph node status has been an important prognostic factor in women with early stage breast cancer, and is critical in planning of systemic adjuvant therapy(2)In breast cancer patients axillary status continues to be the most powerful predictor of survival. Sentinel node mapping and complex axillary dissection are now considered the ,,standard of care,,for the evaluation of nodal disease in patients with clinically negative axillae(3).However axillary lymph node dissection is associated with substantial cost and morbidity including seroma formation and arm edema ,increasingly it is becoming recognized that not all patient need to undergo lymph node dissection especially those without nodal metastasis(2).High –frequency US probes with improved spatial and contrast resolution have been

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used to study both primary breast cancer and superficial nodes with encouraging results. To our knowledge, there is only one study in which color doppler flow have been addressed as adiagnostic criterion for axillary nodal metastasis.

Patients and Methods:

Data were collected about tumor size, lymph node appearance and color Doppler study and their site in the axilla and the result of ultrasound guided FNA at (NATIONAL CENTER FOR EARLY DETECTION OF CANCER IN BAGHDAD MEDICAL CITY) by a specialist breast radiologist from December 2010 to May , 2011 ,60 female patient were examined aged from (29-74)years, mean(49.6)years. All the patients were BIRAD V (8).

Lymph node were classified as: Benign: if the cortex was even and measure < 3mm , Indeterminate : if the cortex was even but measure ≥3mm fig(1), or with focal cortical thickening but cortical thickness <3mm .

Suspicious: if cortex focally thickened ≥3mm fig (2), or the fatty hilum was absent .

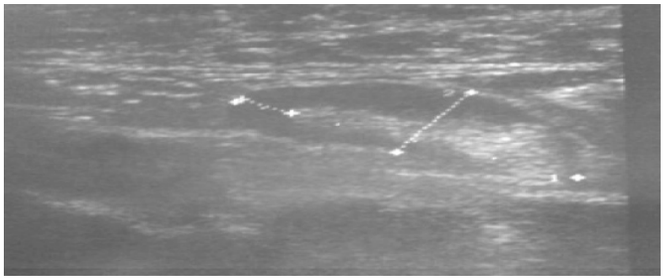
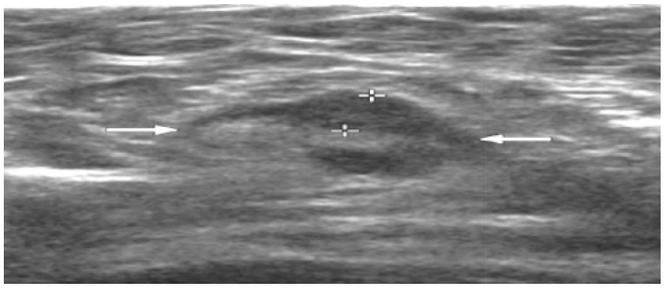


Fig (1) determinate lymph node



Fig(2) suspicious lymph node

Vascular Pattern:

The vascular pattern of each node was subjectively assessed according to the criteria by Na et al (2).Central perhilar vascularity was defined as a simple hilar signal or centrifugal branches that were either central or eccentric .Peripheral vascularity : was defined as circumferential linear vascularity along the periphery of the node.In lymph node where the hilum was absent , vascularity was described as either : central , peripheral , or mixed.The result of ultrasound guided FNA were analyzed in relation to sonographic appearance and color Doppler of axillary LN and the size of the primary tumor.

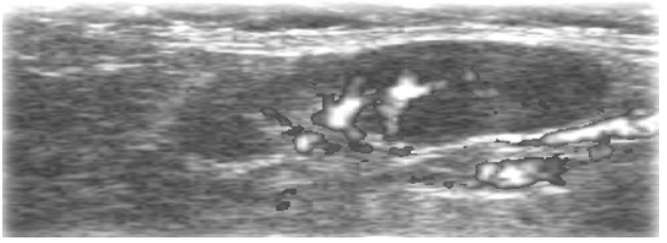


Fig (3) vascular pattern of lymph node.

All patients underwent FNA for the primary breast mass, one of them the cytology revealed invasive lobular carcinoma , One of them was lymphoma the rest were invasive ductal carcinoma . For most of suspicious and indeterminate axillary L.N, FNA and cytological analysis were performed.

Lymph Node Selection And Chracterization:

The axilla was scanned using(7.5-11.4 MHz electronically focused linear-array transducer) ultrasound equipment (SIEMENS Acuson x300) 2011.The pathologist performed FNA under ultrasound guide, the most suspicious node was selected for ultrasound guided FNA. Suspicious features were cortical thickening especially if thickening was focal , and the absence of fatty hilum, selected L.N was taken from the thicker portion of the cortex. The selection of which node to aspirate is guided by the radiologist ,the presence or absence of fatty hilum was noted, and the cortex was characterized as being even or focally thickened. Ultrasound Guided Fna Aspiration: A needle of 10ml syringe, gage (22G) was used to obtain a specimen for cytological examination.The routine practice at our center is to obtain at least two specimens from a selected lymph node while targeting the thickest portion of the cortex. The aspirate was placed in an alcohol solution (ethanol or methanol) for 20 minutes for fixation then send to cytological lab where it is processed and stained by papanicular stain. Cytological result were reported as satisfactory for cytological evaluation -ve for cytological evaluation ,+ve for malignancy, or insufficient for diagnosis.

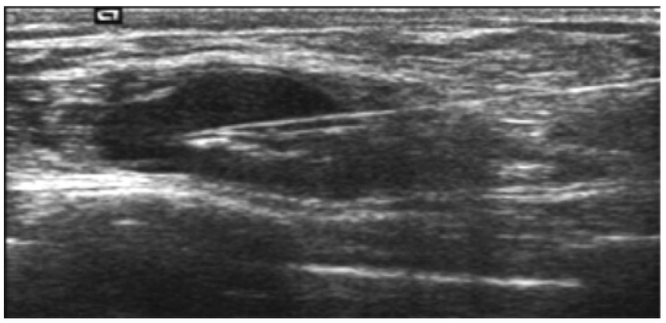


Fig (4) FNA of axillary lymph node

Results:

Patient and primary tumor characterstics: The total number of the patients in the study is (60) the mean mean age of them was (49.6)y . 58 of them presented a mass by ultrasound, two of them presented as speculated mass with microcalcification by mammography. The mean primary breast cancer tumor size 0f these cases was 1.97cm, 57 0f them were invasive ductal carcinoma, one was lobular carcinoma and one was lymphoma and one was inflammatory carcinoma. Two of them were bilateral single breast mass , and two of them were multiple masses in one breast. ultrasound guided FNA results: of these 60 patient FNA was done to 42 of lymph node , of these 42 FNA (35) which represent (58%) were positive for malignancy and (7) of them which represent (12%) were negative for malignancy and (18) of them were insufficient for cytological examination , all of the insufficient results were in either sonographically benign or indeterminate , there were no suspicious lymph node with cytology result of insufficient for diagnosis. Statistical analysis: Sensitivity and specificity of ultrasound guided FNA to detect metastasis to axillary lymph node in correlation to the size of primary breast cancer: The number of tumor size ≤ 1cm was(10)which represent (16.7%) , FNA was done to (6)lymph node (3) were positive and (3) were negative which reveal sensitivity and specificity of 50%.The number of tumor size 1-2 cm was (29) which represent(48.3%), FNA was done to (22) , (19)of them were positive and (3)negative , which reveal sensitivity and specificity of (86%).The number of tumor size >2cm was (21) which represent (35%), FNA was done to (14) of them (13)were positive and (1) was negative , which reveal sensitivity and specificity of (93%).

Table (1) Sensitivity and specificity of ultrasound guided FNA to detect metastasis to axillary LN in correlation to the size of Primary Breast Cancer.

Tumor size	No of axillary LN	No of FNA	SP ٪	SN ٪	PPV٪	NPV٪	P value	SIG
≤1cm	10	6(3)	50	50	50	50	0.007	S
1-2cm	29	22(19)	86	86	86	14	0.047	S
>2cm	21	14(13)	93	93	93	7	0.035	S
Total	60	42(35)	77	77	77	24	0.029	S

Sensitivity of ultrasound guided FNA to metstatic disease in correlation to the appearance of axillary lymph node: The number of benign appearing lymph node was (14) which represent (23.3%) ,FNA was done to (2) of them , both were negative by cytological examination. which mean sensitivity and specificity of (100%) of ultrasound criteria to detect benign lymph node .The number of indeterminate lymph node was (8) which represent (13.4%), FNA was done to (3)of them, (2) had mixed vascularity and were positive and (1)had central vascularity and was negative by cytological examination which reveal sensitivity and specificity of (67%).The number of suspicious lymph node was (38) which represent (63%),FNA was done to (37) of them (35) were positive and (2) were negative by cytological examination, these (2)nodes had central vascularity,so the sensitivity and specificity was (95%). The sensitivity and specificity of FNA guided ultrasound to detect metastatic disease in indeterminate and suspicious node was (81%).

Table (2)Sensitivity of ultrasound guided FNA to detect metastatic disease in correlation to the appearance of axillary lymph node.

Appearance	No of axill LN	No of FNA	SN٪	SP٪	PPV	NPV	P value	SIG
Benign	14	2(0)	0	0	0	100	0.004	S
Indeterminate	8	3(2)	67	67	67	33	0.027	S
Suspicious	38	37(35)	95	95	95	5	0.041	S
Total	60	42(37)	54	54	54	46	0.002	S

Correlation of color Doppler finding with the result of FNA of axillary lymph node of primary breast tumor:
The number of lymph node which had central vascularity was (21) which represent (35%), FNA was done to (7) of them , all were negative by cytolological examination .
The number of axillary lymph node which had mixed vascularity was (8) which represent (13.3%), FNA was done to (8) all were positive by cytological examination for malignancy, this reveal sensitivity and specificity of 100% .
The number of axillary lymph node which had peripheral vascularity was (31) which represent (51.7), FNA was done to (27) of them ,all were positive by cytological examination for malignancy this reveal sensitivity and specificity of (100%) for peripheral color Doppler to detect metastasis in axillary lymph node.

Table (3) Correlation of color Doppler finding with the result of FNA of axillary LN of primary breast tumor.

Color doppler	No of axill LN	No of FNA	SN٪	SP٪	PPV	NPV	P value	SIG
Central	21	7(0)	0	0	0	100	0.023	S
Mixed	8	8(8)	100	100	100	0	0.049	S
peripheral	31	27(27)	100	100	100	0	0.0043	S
Total	60	42(35)	67	67	67	33	0.025	S

Discussion:
Although axillary ultrasound and ultrasound guided FNA have the potential to spare the patient surgery by identifying many patient with metastatic disease preoperatively, the procedure is not yet of routine practice and the indication have not been clearly established.(1)In prior study of tumor (<or=2cm)cancers and sonographically normal appearing lymph node .Kuenen-Boumeester et al (4) recommended that ultrasound guided FNA be included in the preoperative staging of all primary breast cancer patient.Koelliker et al (6) found ultrasound guided FNA to be beneficial in selected population of patient with tumor ≤ 1cm including one with normal appearing lymph nodes, but they recommend a prospective study including a larger tumor to establish the indication in this group .the characterization of axillary lymph nodes by sonography has also been evolved in recent years , a cortical thickness of >or=3mm has been shown to be the most useful predictor of malignancy in clinical practice (1) , although the result of an in vitro study by Bedi et al (4) suggest that focal cortical thickening is most predictive of malignancy.
To maximize the percentage of ultrasound guided FNA that are positive ,one should select only the most abnormal appearing axillary lymph node , however one should perform ultrasound guided FNA in breast cancer patient with small tumors and nodes that appear less suspicious(1).Because ultrasound guided FNA is fast , inexpensive and not associated with any significant morbidity , we choose to optimize detection of as many positive axillae as possible preoperatively by including all patient for ultrasound guided FNA regardless of primary tumor size or axillary lymph node sonographic appearance.Color Doppler ultrasound provides information about flow and morphology , the use of high frequency transducer increases the detectability of low velocity signal from superficial structures with the increased sensitivity in flow detection permitted ,with advance in transducer and equipment technology , up to 85% of ultrasonographically normal axillary lymph nodes in women with no breast disease show the presence of color Doppler flow(2) .It is thus inappropriate to diagnose axillary lymph node metastasis on the bases of the presence of color Doppler flow signal alone (2).
Another study at 2003 (7) stated that gray scale sonography and color Doppler examination have the same overall accuracy for the differentiation of benign from malignant axillary lymph node spectral wave form analysis was proved to be statistically insignificant . the combined usage of both modalities would decrease the number of false negative cases .With increased primary tumor size we found the benefit of ultrasound and ultrasound guided FNA to detect metastasis in axillary lymph node(1) useful.Our study confirms that 3mm is a useful criteria for detecting whether a lymph node is suspicious enough to warrant ultrasound guided FNA with a high sensitivity and specificity in predicting ultrasound guided FNA procedure. Combining the 3mm cortical thickening threshold and the presence of cortical thickening , as we did in categorization of suspicious, indeterminate and benign , has a high sensitivity but lower specificity than using cortical thickness alone , therefore we have chosen to include indeterminate lymph nodes with a cortical thickness of< 3mm but with focal cortical thickening as an indicator for ultrasound guided FNA .(1) Combination of color Doppler study with the criteria of lymph node appearance was very helpful in our study especially for the patient in suspicious and indeterminate

lymph nodes depending on whether the vascularity was central which is found in benign appearing lymph node .mixed vascularity was found in 50% of indeterminate lymph nodes which were positive by ultrasound guided FNA and peripheral vascularity which is present in all suspicious lymph nodes.

Conclusion:

There is a strong significant correlation between the presence of peripheral blood flow in addition to the morphological changes which include focal cortical thickening >3mm and loss of hilum ,and the size of the primary tumor with presence of malignancy in LN in patient with primary breast cancer.

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