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VALUE OF AXILLARY ULTRASONOGRAPHY IN DIAGNOSING AXILLARY LYMPH NODE METASTASIS OF BREAST CANCER

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Background:. *Metastatic invasion of axillary nodes is an important prognostic factor in breast cancer. Formal axillary dissection is an integral part of the surgical treatment, however, in many patients proved to have been unnecessary after histological node examination. Various imaging techniques failed to help. On the assumption that B-mode ultrasonography of the axilla using updated electronics and sensitive transducer and applying the criterion of combination of different sonographic features, this prospective study was done to evaluate the role of axillary ultrasonography in diagnosing axillary lymph node metastasis of breast cancer.*

Methods: *Forty consecutive patients with breast cancer who were treated within four weeks from the ultrasound examination of their ipsilateral axillae by formal axillary dissection with lumpectomy or mastectomy. The histopathological results were related to the ultrasonographic findings. Sensitivity and specificity of the examination were calculated.*

Results: *Abnormal lymph nodes were demonstrated in 19 axillae, only 10 of which were clinically detected. The sensitivity of sonogrpahy in detecting malignant nodes was 76% , the specificity 82.5% and the positive and negative predictive value 94.7% and 71.4% respectively.*

Conclusion:. *The present results demonstrated that, though axillary sonography allows the detection of abnormal lymph nodes which are clinically undetected, yet, with sensitivity and specificity less than 90%, Therefore ultrasongraphy may not be a sufficiently effective noninvasive method for diagnosing axillary lymph node metastasis in patients with breast carcinoma.*

Key words: Axillary nodes-Breast carcinoma- Axillary ultrasongoraphy

INTRODUCTION

Metastatic invasion of axillary nodes is an important prognostic factor in breast cancer[1]. Halsted's radical mastectomy with complete excision of axillary lymph nodes has been the most common operation in the past. However, in many patients, axillary dissection proved to have been unnecessary after histological node examination.[2]. The single most predictive factor for the 10- to 20- year survival is the number of lymph nodes found to contain metastatic tumor[3]. Unfortunately, clinical examination has only a sensitivity of 33% in detecting metastatic axillary nodes [4]. In the literature, the sensitivity of ultrasound in detecting metastatic involvement of axillary lymph nodes has been reported to be between 60% and 72.7% [4-7]. In contrast to the expectations of early, initially enthusiastic researchers, the sensitivity of ultrasound in detecting malignant axillary node involvement can be increased only marginally (70 % to 78%) by color doppler ultrasound[8]. Various imaging techniques including mammography, CT, MR imaging, lymphangiography, and scintigraphy have been investigated for assessing axillary lymph node metastasis of breast cancers. However these examinations have insufficient sensitivity and specificity. For example, the sensitivity of mammography ranged from 18 to 41% and the specificity ranged from 80 to 90%[9]. The sensitivity of CT was 50% and the specificity was 75%[10]. On the assumption that the sensitivity of ultrasound was higher than previously published indications, provided that optimal transducers, updated electronics and very experienced sonographers were used, therefore this prospective study was conducted.

PATIENTS AND METHODS

Between January 1999 and November 2002, forty female patients were treated for breast cancer. All cases were submitted to thorough clinical examination including palpation of both axillae, preoperative laboratory work and metastatic work up in the form of chest X-ray, abdominal U.S. and bone scan. An experienced sonographer performed axillary sonograms for all patients to determine the stage of the detected ipsilateral breast tumor.

High –resolution real-time Aloka instrument (Model SSD-650 CL. Aloka, Tokyo, Japan) was used with the probe consisting of a 10 MHz mechanical sector scanning transducer. The patients were examined in the supine position with the upper part of the body raised and the arm in 80^{o} 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, by putting various degrees of pressure on the axillary skin by means of the transducer. In all patients the pectoral region and the infraclavicular region around the subclavian vessels were also scanned with special attention to the interpectoral space looking for possible interpectoral lymph node metastasis (Rotter's).

For B-mode ultrasonographic diagnosis of metastatic lymph nodes four features of lymph nodes were assessed: size, shape, border demarcation and internal echo[11]. Size and shape were objectively and quantitatively measurable, while border demarcation and echo needed to be determined subjectively. To determine the best criteria for size and shape features, the sensitivity and specificity in diagnosing metastatic lymph nodes were calculated according to the change in an increment of size and shape. For the border demarcation, a lymph node was judged to be metastatic when the border was clear, smooth, or well-defined compared with surrounding fatty tissue. For internal echo, when the fatty hilum was obliterated with markedly hypoechoic internal texture in the majority of areas of a lymph node was the indication of a metastatic node.

All patients underwent formal axillary lymph node dissection together with or after lumpectomy or mastectomy. The interpectoral fat along with the pectoralis minor muscle are removed with the axillary contents sparing: the lateral pectoral nerve and blood vessels supplying the pectoralis major muscle, the long thoracic nerve which represents the extent of dissection posterolaterally and the thoraco dorsal nerve. The axillary dissection was done through a separate incision when it is coupled with lumpectomy.

The sonogrpahic findings were related to the histology of nodes resected during subsequent (within 1 month, maximum, after sonography) axillary node dissection. Sensitivity and specificity were calculated for every combination of the four ultrasonographic features. ROC (Receiver operating characteristic) curves [12], also were created to identify the best combination of features. The true positive fraction of the ROC curve abscissa corresponds to sensitivity, while the false, positive fraction of the ordinate corresponds to specificity. The area under the ROC Curve indicates diagnostic performance of a test; a perfect classifier produces an area of 1.0, while an entirely random classifier produces an area of 0.5.

RESULTS

Included into this prospective study were forty women with mean age of 45.9 years (Range from 30-72). Clinically palpable axillary lymph nodes were detected in ten patients (25%) and the metastatic work up including chest x-ray, abdominal ultrasound and bone scan revealed no distant spread in all patients. Abnormal ipsilateral axillary lymph nodes were detected by ultrasonography in ninteen patients. (47.5%). Histo-pathological examination of the operative specimens revealed: a-18 cases of invasive ductal carcinoma with pathological metastatic lymph nodes and 12 cases with negative lymph nodes. b-7cases of invasive lobular carcinoma with pathological metastatic lymph nodes and 3 cases with negative lymph nodes (Table 1).

Table (1): ***Patient Characteristics***

No. of patients	40
Age (years.)	
Mean	45.9
Range.	30-72
Clinical examination	
Positive axilla	10 (25)*
Negative axilla	30 (75)
Distant metastasis (Liver, Lung, Bone.)	0 (0)
Axillary ultrasound	
Abnormal lymph nodes	19 (47.5)
Histopathology examination	
Invasive ductal cancinoma	30 (75)
Invasive lobular carcinoma	10 (25)
Positive axilla	25 (62.5)
Negative axilla	15 (37.5)

** Numbers within parentheses denote percentages.*

The sensitivity and specificity for detecting axillary lymph node metastasis using size alone are summarized graphically in (Fig 1.)

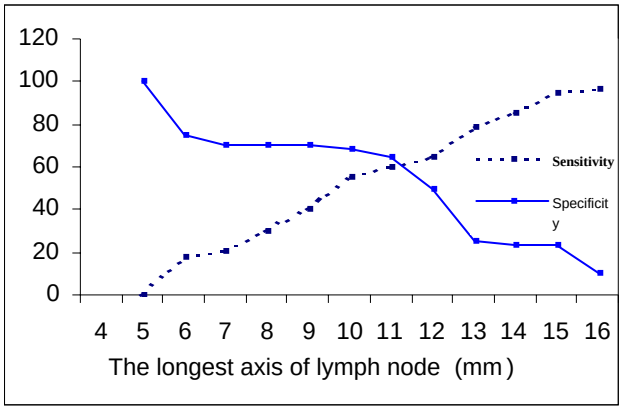

Fig. (1): The sensitivity and specificity for diagnosing axillary lymph node metastases based on size. The ordinate is the long axis of lymph node.

The sensitivity and specificity curves crossed each other between 10 and 11 mm. Therefore, a size of 10 mm or greater was considered to indicate a metastatic lymph node. The sensitivity and specificity for detecting axillary lymph node metastasis using shape alone are summarized graphically in (Fig 2.)

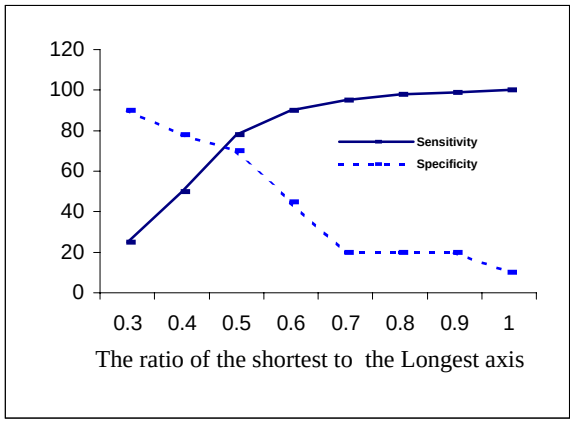

Fig. (2): The sensitivity and specificity for diagnosing axilary lymph node metastasis based on shape. The ordinate is the ratio of the shortest to the longest axis of lymph node

The sensitivity and specificity curves crossed each other between the ratios of 0.4 and 0.5. Therefore, a ratio of the shortest to the longest axis between 0.5 and 1.0 was considered to indicate a metastatic lymph node.

In summarizing all four ultrasonographic features, lymph node metastasis was indicated by 1- a large size (the longest axis) (10 mm or greater) ; 2- a circular shape (i.e., the ratio of the shortest axis to the longest axis between 0.5 and 1.0) ; 3- a sharply demarcated border; 4- a hypoechoic internal echo, with obliteration of the fatty hilum. (Figs 3a,b&c) display different combinations of positive ultrasonographic features.

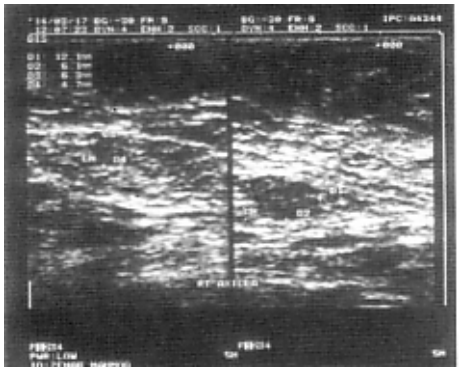

Fig 3 (A): characterization of lymph nodes on the basis of the number of positive B-mode ultrasonogrpahic features. A, the node was 3x14 mm in size, not circular in shape (the ratio of the shortest to longest axis was. 0.21), not sharply demarcated and not hypoechoic. Only one feature indicated metastasis. This node was histologically non metastatic.

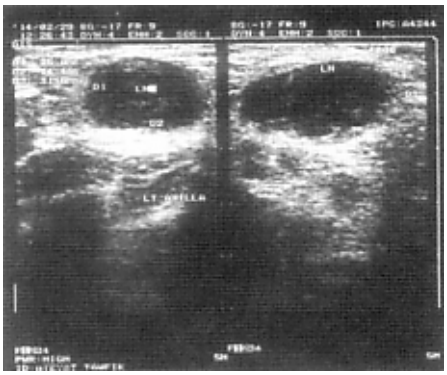

Fig 3 (B): the node was 8x20 mm in size, not circular in shape (the ratio of the shortest to longest axis was 0.40), sharply demarcated and hypoechoic. Three features indicated metastasis. This node was histologically metastatic.

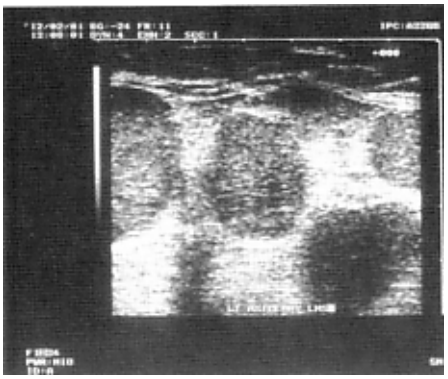

Fig 3(C): Nodes were more than 10mm in size, circular in shape (the ratio of the shortest to longest axis was 0.50), sharply demarcated and hypoechoic. All four features indicated metastasis. These nodes were histologically metastatic.

The sensitivity and specificity for detecting axillary lymph node metastasis using all four positive features to indicate metastasis was highly specific (97%) but not sensitive (30%). On the other hand, the criterion that used any three positive features to indicate metastasis provided both sensitivity and specificity higher than 70 %. (Table 2.)

Table (2)*: Diagnosing Axilary Lymph Node matastasis using different combinations of four. Features.*

	All four features *		*Three of the four features* ϕ	
Criteria	***Sensitivity (%)***	***Specificity (%)***	***Sensitivity (%)***	***Specificity (%)***
Size, shape, Border, echo	30	97	76	82.5

*

* Lymph nodes that demonstrated all four features were considered to be matastatic .

* Lymph nodes that demonstrated any three of the four features were considered to be matastatic.

Abnormal lymph nodes using any three positive features, were detected by ultrasound in 19 axillae, only ten of which (52.6%) had been clinically detected. The number of sonographically visualized nodes per axilla was: one or two nodes in 11 axillae; three or four nodes in 4 axillae; and more than four in 5 axillae.

In this group of 40 patients with ipsilateral breast carcinoma, the sonographic findings of the axilla were related to the intraoperative and subsequent histological findings in surgically resected nodes (Table 3).

Table (3): ***Correlation between Sonographic and Histological examination of Surgically resected Nodes***

	Sonography positive	*Sonography negative*
Histology positive	18	6
Histology negative	1	15

In all cases, the time delay between sonography and surgery was less than 4 weeks. Although the number of malignant nodes per axilla discovered by ultrasound was frequently lower than the number detected by formal axillary dissection, the sensitivity of ultrasound in detecting malignant lymph node invasion of the axilla nonetheless was 76% and the specificity 82.5%. Its positive predictive value was 49.7% and its negative predictive value 71.4%. The prevalence of lymph node involvement was 60%.

DISCUSSION

Axillary lymph node dissection with histologic examination is currently a standard procedure to determine the lymph node status of patients with invasive breast cancer[13]. Because of the 30 to 40% prevalence of lymph node metastasis in breast cancer, routine axillary operations result in dissections of nonmetastatic lymph nodes in 60 to 70% of patients [14]. In this study the prevalence of lymph node metastasis was 60% and this was attributed to the relative delayed discovery.

Axillary lymph node dissection is major surgery and is associated with operative morbidity. New surgical approaches, such as sentinel node dissection or selective node dissection, have been proposed to reduce the number of unnecessary axillary dissections and are under investigation. An accurate noninvasive diagnostic method to assess axillary lymph node status would reduce the need for axillary operations[15].

Ultrasonographic studies of axillary lymph nodes in breast cancer started in 1980s. various features of B-mode ultrasonographic images were investigated in attempts to distinguish metastatic from non metastatic nodes. In studies of the 1980s and the early 1990s, size, shape and internal echo were the features frequently evaluated using 3.5 to 7.5 MHz ultrasonography. "Rounded hypoechogenic lymph nodes with a diameter of 5mm or more" usually were considered to be metastatic[16-18]. The sensitivity of B-mode ultrasonography in these studies ranged from 56 to 75% and its specificity ranged from 70 to 98%. In 1996, Yang and colleagues[19] considered a lymph node to be metastatic when it was "rounded and hypoechoic with associated eccenteric cortical hypertrophy and obiteration of the fatty hilum", but they considered size to be unimportant. Based on their criteria, sensitivity was 73 to 84% and specificity

was 95 to 97%. In 1999, Tateishi and colleagues[15] used node by node analysis to evaluate criteria indicative of metastasis and had the advantage of precisely correlating ultrasonographic findings with histologic determinations. Their study showed that a circular shape was the best single feature for distinguishing metastatic from non metastatic lymph nodes and using the combination of four features they obtained sensitivity 85% and specificity 73% by considering a lymph node to be metastatic when at least three of the four features were present.

In the present study using 10 MHz mechanical sector scanning transducer, and considering 10mm or greater size, a circular shape, a sharply demarcated border and a hypoechoic internal echo one indicative of metastatic lymph node, the sensitivity obtained was 76% and specificity 82.5% by the criterion that used any three positive features.

In a prospective study by Verbanck and colleagues[20] of 144 consecutive patients, abnormal lymph nodes were sonographically demonstrated in 72 axillae. Only half of them (36 of 72) were clinically detected. In a subset of 47 patients with breast surgery and axillary dissection after ultrasound, the sensitivity of ultrasound in detecting malignant lymph nodes was 92%, its specificity 95% and its positive and negative predictive values 96% and 91% respectively. In this present study the sensitivity of ultrasound in detecting malignant lymph node invasion of the axilla was 76% and the specificity 82.5% Its positive predictive value was 94.7% and its negative predictive value 71.4%.

Twenty one patients had a negative axillary sonogram. Subsequent formal axillary dissection of these patients showed that in six of them the negative axillary sonogram was false. Those patients had one or two lymph nodes of less than 1.0 cm in diameter with microscopic invasion. The prognostic value of detecting microscopic metastasis in lymph nodes remains to be determined[21].

The sonogram of one patient showed one lymph node (8mm in diameter) which was thought to be malignant. However subsequent removal of axillary lymph nodes did not reveal any histologically malignant cells. The possible explanation for this false positive sonogram is that in contrast to what has been published, recently updated scanners using 10 MHz linear probes seem to allow the visualization of normal lymph nodes [15].

CONCLUSION

The present results demonstrated that, though, axillary sonography allows the detection of abnormal lymph nodes which are clinically undetected in many patients, yet the sensitivity and specificity of B-mode ultrasonography were lower than 90% even using the best criterion. Therefore, B-mode ultrasonography may not be a sufficiently effective noninvasive method for diagnosing axillary lymph node metastasis in patients with breast cancer. In addition, some B-mode ultrasonographic features (e.g., border demarcation, internal echogenicity and texture) were difficult to quantify; hence their assessment was subjective. The result of lymph node evaluation using B-mode ultrasonography was particulary dependant on the examiner. Formal axillary dissection remains, till now, an integral part with lumpectomy or mastectomy in treating breast cancer.

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