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Could Using of Ultrasonic Grading for Axillary Lymph Nodes Improve Management of Early Stage Breast Cancer?

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Abstract

Purpose: Nowadays several studies suggested that needle biopsy of axillary suspicious nodes is more accessible than Sentinel Lymph Node Biopsy (SLNB); and thus, it is financially more beneficial. In this study, we compared using ultrasonographic features of lymph nodes alone, core needle biopsy, and SLNB for staging early breast cancers.

Methods: Participants included 50 patients who underwent axillary Ultra Sound-Guided Core Needle Biopsy (USG-CNB) from node/s larger than 10 millimeter (mm). Without considering the results of needle biopsy, SLNB, and if necessary axillary dissection were performed in all patients and the final results were compared.

Results: In all 38 (76%) cases with positive SLNB, final histology reports confirmed the diagnosis. In 24 of these patients, metastasis was diagnosed preoperatively by USG-CNB. Although only in 4 out 12 patients with normal lymph node characteristic in ultrasound, final histology revealed no metastasis. In patients with intermediate or suspicious feature, the test accuracy was more reliable. The total positive and negative predictive value of lymph node characteristic in ultrasonography were 95.7% and 40.7%, respectively.

Conclusion: Although ultrasonographic features of normal and metastatic lymph nodes can be helpful in accurate diagnosis of them, the accuracy of this modality alone is not enough to manage cancer patients with early stage breast cancer.

Keywords: Early Detection of Cancer; Breast Neoplasms; Axilla; Neoplasm Staging; Needle Biopsy; Lymph Nodes; Ultrasonography

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Introduction

Axillary lymph node metastasis is the most significant prognostic factor in breast cancer, so it is necessary to determine the axillary lymph node status before operation. Nowadays, one of the basic principles of breast cancer management is using noninvasive methods for evaluation of the axillary lymph nodes [1]. Because of low negative predictive value of lymph node metastasis by clinical examination, today, Axillary Ultrasound Scan (AUS) is used as a good choice modality in preoperative staging of breast cancer, and if in the AUS no suspected lymph node is detected, then Sentinel Lymph Node Biopsy (SLNB) is performed [2]. Although using SLNB can reduce the complications related to axillary dissection, its cost and accessibility are two important challenges with this method. In this study, we compared using ultrasonographic features of lymph nodes alone, core needle biopsy, and SLNB for staging early breast cancers.

Materials and Methods

The study was conducted after ethics committee approval (Mashhad University of Medical Sciences, Iran) from March 2013 to February 2014. The participants included 50 females with stage I

Table 1: Distribution of lymph nodes (LNs) characteristics in the Ultra Sonographic (US) examination of the axilla.

LNs characteristics in US	Mean	Number	Std. Deviation
Reactive < 5mm	1.4000	15	0.50709
Reactive ≥ 5mm (G1)	2.7500	12	0.62158
Intermediate (G2)	3.1250	8	1.12599
Suspicious (G3)	2.8000	15	0.77460
Total	2.4200	50	0.99160

breast cancer with clinically negative axilla. The patients with a tumor size of more than 2 cm according to the radiologic report, patients with documented genetic risk factors (such as BRCA1 and 2), and those who had received neoadjuvant chemotherapy were excluded from the study. All patients underwent a preoperative staging AUS and lymph nodes were graded to reactive lymph node with size ≥5 mm (G1), indeterminate (G2) and suspicious (G3). Regardless of the grading system, reactive lymph nodes with size less than 5 mm were included in the study. All patients in G1-3 underwent ultrasound-guided 14-gauge core-needle biopsy. In patients with more than one node, needle biopsy was done from the node with higher radiologic grade. Without considering the pathological report of these biopsies, sentinel lymph node biopsy was performed in all participants. All SLNB positive patients underwent axillary lymph node dissection (ALND). In accordance with previous studies, the criteria for grading of the lymph nodes were focal or diffuse cortical thickening (3 mm in thickness), compressed hilum of lymph nodes, round shape (rather than oval) and/or loss of the echogenic fatty hilum [3-9]. The final axillary lymph node status was categorized as either negative when all lymph nodes were negative for metastasis or positive when there was evidence of metastasis in one or more lymph nodes. The complications of the needle biopsy were documented. After data collection, results from AUS and US-guided core-needle biopsy were compared with final pathologic results from sentinel lymph node biopsy or axillary lymph node dissection and the sensitivity, specificity, diagnostic accuracy, and false-negative rate of ultrasound-guided core-needle biopsy in detecting the axillary lymph node metastasis were calculated.

Results and Discussion

Our study patients were 50 women with invasive ductal carcinoma of the breast and no axillary node involvement in physical examination. The mean age was 48 (range, 39-57) years. Breast conservative surgery and mastectomy were done in 28 (56%) and 22 (44%) patients, respectively. Axillary Ultra Sonography (US) and needle biopsy lasted 10.47 ± 1.12 (range, 8-13) minutes. In 15 patients, axillary US examination revealed reactive lymph node with size less than 5 mm, and thus in this group we did not perform needle biopsy. In the other patients, the ultrasonic evaluation realized G1 (≥ 5 mm), G2 and G3 lymph nodes or combination of them (G1=2.75 ± 0.62, G2=3.12 ± 1.12, and G3=2.80 ± 0.77) (Table 1). SLNB was performed in all 50 patients. As (Table 2) demonstrates, in 38 (76%) cases, SLNB was positive for malignant cells and final histologic reports of axillary dissection confirmed metastatic axillary lymph nodes (sensitivity: 94.7%, specificity: 100.00%, Positive Predictive Value (PPV): 100.00%, Negative Predictive Value (NPV): 85.7% and accuracy: 96%). Out of these 38 patients, in 24 cases, metastatic axillary lymph node was diagnosed preoperatively by US-guided core-needle biopsy (sensitivity: 85.7%, specificity: 100%). In addition, all patients who were tumor free in final histologic examination, the USG-CNB specimens had no metastasis too, which yields an overall negative predictive value and accuracy of 42.9% and 68%, respectively for US-guided core-needle biopsy. Based on (Table 3), of 15 patients who had reactive lymph node appearance (<5 mm) in ultrasound evaluation of axillary region, only 7 (46.7%) had normal lymph node in final histologic evaluation. In G1 group who had normal US appearance but with size ≥ 5 mm, only 4 out of 12 (33.3%) patients had reactive nodes in final histologic examination. In G2 and G3 groups, the metastatic nodes in permanent pathology were 7 out of 8 (87.5%), and 15 out of 15 (100.0%), respectively. In this study, the total positive and negative predictive value of lymph node appearance in ultrasonography was 95.7% and 40.7%, respectively. In 4 out of 35 cases with USG-CNB, due to unsuccessful sampling, histologic evaluation revealed only some fibro-fatty tissue. There was no false positive (metastatic) USG-CNB case in our study. No hematoma, vessels puncture or other complications were observed during or after the needle biopsy procedure. One of the important issues in determining of the stage and designing of treatment plan in breast cancer patients is evaluation of the presence of axillary node metastases [10]. Historically, classic Axillary Lymph Node Dissection (ALND) was done in all patients, but with the aim of preventing its complications, recently, there has been a major departure from ALND to SLNB. Sentinel lymph node biopsy is the method of choice to exclude axillary metastases in patients with no lymphadenopathy in physical examination. In practice, a large number of patients who are node negative in physical examination have pathologic node(s) in axillary imaging [11]. Among several modalities, it seems that ultrasonography is the best imaging modality for axillary evaluation because it is easily accessible, sensitive, and reliable in detection of pathologic nodes and also has the superiority regarding cost/benefit considerations [12,13]. Today, ultrasound-guided fine needle aspiration or core-needle biopsy has been used in patients with negative node in physical examination whose node(s) is/are suspicious in ultrasonography [7,14-16].

Table 3: Cross tabulation of Lymph Nodes (LNs) characteristics in axillary Ultra Sonography (US) with final histologic examination.

LNs characteristics in US	Final histologic examination				Total	
	Metastatic		Reactive			
Reactive < 5 mm	8	53.30%	7	46.70%	15	100.00%
Reactive ≥ 5mm (G1)	8	66.70%	4	33.30%	12	100.00%
Intermediate (G2)	7	87.50%	1	12.50%	8	100.00%
Suspicious (G3)	15	100.00%	0	0.00%	15	100.00%
Total	38	76.00%	12	24.00%	50	100.00%

Table 2: Diagnostic value of Ultra Sonography (US), Ultra Sound-Guided Core Needle Biopsy (US-CNB) and Sentinel Lymph Node Biopsy (SLNB) in axillary Lymph Node (LN) metastasis detection.

	Sensitivity	Specificity	PPV*	NPV†	Accuracy
US-CNB	85.70%	100%	100%	42.90%	68%
LN characteristics in US	57.90%	91.7.%	95.70%	40.70%	66%
SLNB	94.70%	100%	100%	85.70%	96%

*PPV= Positive Predictive Value; † NPV= Negative Predictive Value

Using SLNB in approximately 40% of patients who have suspicious node in axillary ultrasonography examination can be avoided [17-19]. Although US-guided core needle biopsy is a simple and safe procedure to perform, it requires experience and special equipment which may not be worldwide accessible. So, having a simpler method such as ultrasonic axillary grading can be helpful for a large number of patients in developing areas. According to our findings, 53.3% and 66.7% of patients with reactive lymph node appearance in US (< 5 mm and ≥ 5 mm, respectively) had metastatic cell in final histologic examination, which is not consistent with some studies that all reactive nodes in US were non-metastatic in microscopic examination [20]. These data strongly verify that the small size of lymph node cannot be a reliable parameter for ruling out of metastasis and nodes by size less than 5 mm may be metastatic, even though with lower incidence. In addition, some researchers realized that size more than 10 mm was an unreliable predictor of malignancy, and although it had high sensitivity (81.8%), its specificity (16.6%) rate was low (20, 21). Benign reactive enlargement of the lymph nodes can be seen in response to fibrocystic changes, infections, and any process such as a recent biopsy. Based on these data, it cannot be suggested that ultra sonographically benign node(s) of axilla are reliable enough to spare from further evaluation by another modality. It is known that the rate of axillary lymph node metastasis is very low in patients diagnosed at an early stage [22,23]. So, it is especially desirable to be able to observe the axilla using the "watch and wait" technique in patients with early stage breast cancer and low ultrasonic grading for axillary nodes without axillary intervention (CNB or SLNB). It seems that, in order to have more accurate scale for distinction of reactive nodes from suspicious ones, we need more accurate criteria than those available. For example, recently evaluation of newer parameters, such as non-hilar cortical vascular flow by Color Doppler has been reported to be a very sensitive descriptor [24]. In G2 and G3 groups, metastatic nodes were 87.5% and 100%, respectively. These data confirmed that in line with some other studies, in G2 and G3, ultrasonographic characterization of lymph nodes was more accurate in predicting positive findings at final histologic examination [2,8]. Our data suggest that, although detecting nodes with reactive characteristics in US are not reliable enough to avoid evaluation of axillary nodes with SLNB, when US detects axillary node(s) with grade 3, ALND can be performed without SLNB. Although this claim was supported by some studies, several others believed that due to unreliability of ultrasonography in predicting metastatic nodes, axillary dissection based on ultrasonographic features of metastatic nodes, would lead to overtreatment due to unnecessary axillary dissection in approximately 40% of patients [2,10,11,20,25-26]. Finally, according to our data, overall sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of ultrasonography for diagnosis of lymph node metastasis were 57.9%, 91.7%, 95.7%, 40.7% and 66%, respectively which are similar to other studies with larger sample size [14,20,27,28]. In general, the sensitivity of US in detecting metastatic involvement of axillary nodes has been reported to vary between 35% and 82%, while the specificity is between 73% and 98%; our data was within this range [29,30]. Based on Table 2 data, these figures for USG-CNB were higher and thus it was more reliable than ultrasonographic features alone in the evaluation of axillary nodes.

Conclusion

Although ultrasonographic features of normal and metastatic axillary lymph nodes can be helpful in their diagnosis -especially in the ultrasonographic suspicious feature-however, the accuracy of this modality alone is not enough to manage patients with early stage breast cancer. The worldwide accessibility and cost benefit superiority of ultra-sonography encourage us to improve its sensitivity and reliability in detection of pathologic nodes and also to create a specific grading system to prevent unnecessary use of core needle biopsy and or sentinel lymph node biopsy in early stage breast cancer managements.

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