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Research Article

Original Article: Diagnostic Accuracy of Ultrasound-Guided FNAC in Carcinoma Breast Patient Taking Histopathology as a Gold Standard

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ABSTRACT

Background: Ultrasound is a sensitive tool for detecting axillary metastasis in breast cancer patients in the absence of palpable lymph nodes. FNA (Fine Needle Aspiration) of these suspicious nodes can help in accurate preoperative staging of the axilla.

Materials and Methods: This descriptive cross-sectional study was conducted at Department of Surgery, Unit 1 at Holy Family Hospital, Rawalpindi from 20th February 2017 to 19th August 2017. A total number of 100 patient of biopsy-proven breast cancer with no palpable lymph nodes in axilla were included. All underwent axillary ultrasound. FNA was performed in all cases having suspicious lymph node characteristics. Those having malignant cells in FNA report had axillary dissection without undergoing per-operative sentinel lymph node biopsies. In rest, per-operative SLNB (Sentinel Lymph Node Biopsy) was performed. Postoperative all dissected axillary specimens were reviewed by a pathologist for final diagnosis.

Results: Ultrasonography guided FNA supported the diagnosis of malignant breast lesions in 60 (60.0%) patients. Histopathology confirmed malignancy in 62 (62.0%) cases. In 60 ultrasonography-guided FNA positive patients, 58 (true positive) had malignant breast lesions and 02 (false positive) had benign on histopathology findings. Among, 40 ultrasonography-guided FNA negative patients, 04 (false negative) had malignant breast lesions on histopathology whereas 36 (true negative) had benign lesions on histopathology. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasound-guided FNA for diagnosis of carcinoma breast taking histopathology as the gold standard was 93.55%, 94.74%, 96.67%, 90.0% and 94.0% respectively.

Conclusion: Ultrasound-guided fine-needle aspiration is a highly sensitive and accurate modality for diagnosing carcinoma breast.

Keywords: Breast cancer; Axillary staging; Ultrasound-guided fine-needle aspiration; Sensitivity

INTRODUCTION

Cancer of the breast is the most common cancer affecting women worldwide. Its the second most common cause of cancer-related deaths next to lung cancer. The triple assessment now forms the cornerstone for a reliable diagnosis. Most common presenting type is invasive ductal carcinoma which just like other carcinomas tends to early spread to lymph nodes. Several studies show axillary lymph node status to be an absolute and most important predictor of breast cancer survival [1]. In fact, all node-positive patients should be suspected for occult metastasis even in presence of negative workup. These hence become candidates of systemic therapy. In past, all and sundry presentations of breast cancer were treated by standard modified radical mastectomy. This conventionally included clearance of axilla uptil level two lymph nodes [2]. Recent times saw an increase in popularity of breast-conserving surgery as it yielded a similar survival rate but better cosmesis [3]. Adequate axillary staging forms an integral part of breast conservation. This is usually done by a separate incision. Sentinel lymph node biopsy using patent blue V dye or radioisotope labelled isotope can be done. The specimen is then usually sent for frozen section depending upon whose result formal level 2 dissection should or should not performed [4]. This protocol, however, requires trained staff and sophisticated gadgets for its implementation. In our indigenous setup, specialized breast cancer clinics are sparse and general surgical teams bear the major brunt of this disease.

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Therefore, routine SLNB and frozen section for staging axilla become impractical. In such situations, preoperative axillary ultrasound can be of help in more than one way. Increase in size, architectural distortion, loss of fatty hilum and changes in doppler flow are sonographic features of metastatic lymph nodes [5]. Fine needle biopsy of such suspicious nodes followed by cytology can help in preoperative axillary staging. This then aids in making decisions regarding the need for neoadjuvant therapy as well as axillary dissection.

STUDY DESIGN

This descriptive, cross-sectional validation study was performed at surgical unit 1 of holy family hospital Rawalpindi from 20th February 2017 to 19th August 2017. Prior permission from the institutional research forum was taken. Non-probability, consecutive sampling was done. The sample size was calculated to be 100 patients. All patients presenting to breast clinic were examined by a qualified general surgeon with more than one-year work experience in the breast clinic. Histopathological evidence of malignancy was achieved in all cases using trust biopsy method. Those with benign lesions on biopsy were excluded from the study. Patients with palpable axillary nodes were also excluded as their involvement was evident even without performing the ultrasound. After examination in the breast clinic, all patients who met the inclusion criteria were sent to the in-hospital radiology department. All axillary ultrasounds were performed by a single qualified radiologist. Increase in lymph node size, spherical diameter, hypoechogenicity, loss of fatty hilum, increased cortical thickness and distorted architecture all were considered as suspicious signs of axillary lymph node metastasis. Fine needle aspiration biopsy was performed in all such cases. Each time procedure was performed by a trained surgical resident after obtaining informed consent. The sample was taken through several passes of a 5-cc syringe under image guidance. Slides were made at the same time, fixed in alcohol and air-dried. Later they were submitted for histopathology review in hospitals lab. Patients in whom axillary lymph node FNA showed malignant cells directly underwent axillary dissection while skipping the step of SLNB and frozen section. Axillae who were reported negative by FNAC was evaluated on the table through SLNB. These axillae were either dissected or preserved depending upon results of SLNB. All specimens were submitted to the pathology lab for histopathological review. Report of histopathology was considered the gold standard against which results of FNA were compared.

Data analysis procedure

The data collected was entered and analyzed using the Statistical Package of Social Sciences (SPSS version 21). For quantitative variables like age of patients, duration of signs of symptoms and size of the tumour in millimetres, mean ± SD were calculated. For qualitative variables like the involvement of lymph nodes based on ultrasonography and histopathology (as per operational definition), frequencies and percentages were calculated. They were then tabulated in the form of 2 × 2 table shown in Table 1 and formulae mentioned below were applied to calculate sensitivity, specificity, predictive values for the positive, negative value and diagnostic accuracy of each of both scores taking results of histopathology as the gold standard. Roc and likelihood ratio were calculated. Effect modifiers like age and BMI were controlled through stratification and post-stratification diagnostic accuracy was calculated.

Diagnostic accuracy will be calculated as follows:

$$Sensitivity = \frac{TP}{TP + FN} \times 100$$

$$Specificity = \frac{TN}{FP + TN} \times 100$$

$$Positive\ predictive\ value = \frac{TP}{TP + FP} \times 100$$

$$Negative\ predictive\ value = \frac{TN}{FN + TN} \times 100$$

$$Diagnostic\ accuracy = \frac{(TP + TN)}{(TP + FP + FN + TN)}$$

Table 1: Comparison between histopathology and ultrasound.

		Histopathology	
		+	-
Ultrasound-guided FNAB	+	39	0
	-	8	49

RESULTS

The age range in this study was from 15-75 years with a mean age of 44.98 ± 12.76 years. Majority of the patients 58 (58.0%) were between 15 to 45 years of age as shown in Table 2. Mean duration of disease was 6.29 ± 2.61 months (Table 3). Mean size of the lesion was 3.73 ± 0.66 cm (Table 4). Mean BMI was 29.55 ± 3.53 kg/m^2 (Table 5).

Table 2: Distribution of patients according to age.

Age (years)	No. of patients	%age
15-45	58	58.0
46-75	42	42.0
Total	100	100.0
Mean ± SD=44.98 ± 12.76 years		

Table 3: Distribution of patients according to the duration of disease (n=100).

Duration of disease	No. of patients	%age
≤ 6 months	60	60.0
>6 month	40	40.0
Mean ± SD=6.29 ± 2.61 months		

Table 4: Distribution of patients according to the duration of disease (n=100).

Size (cm)	No. of patients	%age
≤ 3	39	39.0
>3	61	61.0
Mean ± SD=3.73 ± 0.66 cm		

Table 5: Distribution of patients according to the duration of disease (n=100).

Bmi (kg/m^2)	No. of patients	%age
≤ 27	32	32.0
>27	68	68.0
Mean ± SD=29.55 ± 3.53 kg/m^2		

Ultrasonography guided FNA was performed in all patients. FNA report supported the diagnosis of malignant breast lesions in 60 (60.0%) patients. Axillary lymph node dissection was performed on all these. Samples were submitted for histopathology. This confirmed malignancy in 58 cases (true positives). Two patients who had a positive FNA were found negative on axillary dissection sample s review (false positive). Among, 40 ultrasonography-guided FNAB negative patients, 04 (false negative) had malignant breast lesions on histopathology whereas 36 (true negative) had benign lesions on histopathology as shown in Table 6.

Table 6: Diagnostic accuracy of ultrasound-guided FNAB for diagnosis of carcinoma breast taking histopathology as the gold standard.

	A positive result on histopathology	A negative result on histopathology	p-value
Positive on ultrasound guided FNAB	58 (tp)*	02 (fp)***	0.0001
Negative on ultrasound guided FNAB	04 (fn)**	36 (tn)****	
*-tp=true positive **-fp=false positive ***-fn=false negative ****-tn=true negative Sensitivity: 93.55% Specificity: 94.74% Positive predictive value (ppv): 96.67% Negative predictive value (npv): 90.0% The likelihood ratio for positive results: 17.77 The likelihood ratio for negative results: 0.07 Diagnostic accuracy: 94.0%			

Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasound-guided FNA for diagnosis of carcinoma breast taking histopathology as the gold standard was 93.55%, 94.74%, 96.67%, 90.0% and 94.0% respectively. ROC curve is shown in Figure 1.

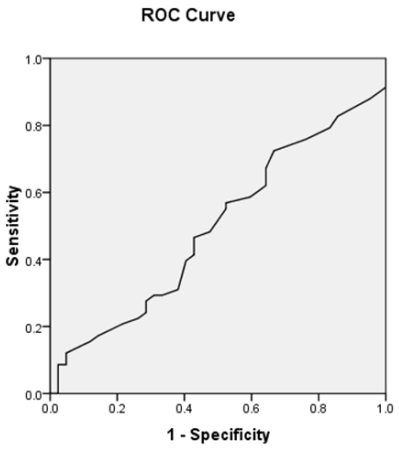

Figure 1: ROC curve.

Stratification of diagnostic accuracy with respect to age groups is shown in Tables 7 and 8. Stratification of diagnostic accuracy with respect BMI is shown in Tables 9 and 10.

Table 7: Stratification of diagnostic accuracy with respect to age 15-45 years (n=58).

	A positive result on histopathology	A negative result on histopathology	p-value
Positive on ultrasound guided FNAB	34 (tp)	01 (fp)	0.001
Negative on ultrasound guided FNAB	04 (fn)	19 (tn)	
Sensitivity: 89.47% Specificity: 95.0% Positive predictive value (ppv): 97.14% Negative predictive value (npv): 82.61% Diagnostic accuracy: 91.38%			

Table 8: Stratification of diagnostic accuracy with respect to age 46-75 years (n=42).

	A positive result on histopathology	A negative result on histopathology	p-value
Positive on ultrasound guided FNAB	24 (tp)	01 (fp)	0.001
Negative on ultrasound guided FNAB	00 (fn)	17 (tn)	
Sensitivity: 100.0% Specificity: 94.44% Positive predictive value (ppv): 96.0% Negative predictive value (npv): 100.0% Diagnostic accuracy: 97.62%			

Table 9: Stratification of diagnostic accuracy with respect to bmi ≤ 27 kg/m^2 (n=32).

	A positive result on histopathology	A negative result on histopathology	p-value
Positive on ultrasound guided FNAB	19 (tp)	01 (fp)	0.001
Negative on ultrasound guided FNAB	00 (fn)	12 (tn)	
Sensitivity: 100.0% Specificity: 92.31% Positive predictive value (ppv): 95.0% Negative predictive value (npv): 100.0% Diagnostic accuracy: 96.88%			

Table 10: Stratification of diagnostic accuracy with respect to BMI >27 kg/m^2 (n=68).

	A positive result on histopathology	A negative result on histopathology	p-value
Positive on ultrasound guided FNAB	39 (tp)	01 (fp)	0.001
Negative on ultrasound guided FNAB	04 (fn)	24 (tn)	
Sensitivity: 90.70%			
Specificity: 96.0%			
Positive predictive value (ppv): 97.50%			
Negative predictive value (npv): 85.71%			
Diagnostic accuracy: 92.65%			

DISCUSSION

Last few decades have witnessed a radical change in treatment strategies of breast cancer. Especially obvious is the paradigm shift in Breast surgeons approach regarding staging and treating axilla [6]. Presence of axillary lymph nodes continues to be the single most important prognostic factor for survival [7]. Traditionally TNM staging depended on the presence of palpable lymph nodes for considering axillary involvement. However now American Joint Committee on Cancer classifies sentinel lymph node involvement into three stages ranging from micro-metastasis (less than 2 mm) to macro-metastasis (more than 2 mm). All these categories are rarely palpable and mostly diagnosed as either suspicious lymph nodes on ultrasound or on pathological review of sentinel lymph node [8,9]. Staging axilla up to this minute level helps in decisions regarding systemic adjuvant therapy [10]. MIRROR trial established that systemic therapy in cases of micro-metastasis helped in reducing adverse event rate [11].

Currently, per-operative sentinel lymph node biopsy is the standard of care for staging axilla in the absence of palpable lymph nodes. This method has a sensitivity approaching 93% with blue dye and 96% with radioisotope tracer [12]. Despite its benefits, the procedure cannot be performed in the majority of our hospitals locally due to unavailability of radio-isotopes and their detecting gamma probes. Therefore, while performing breast conservation procedure most surgeon's clear axilla to adequate stage it. This approach can lead to considerable morbidity in terms of wound complications, shoulder dysfunction and lymphedema of the arm. Preoperative ultrasound-guided FNAC can be especially useful in staging axilla in such situations [13].

A recent metanalysis showed sensitivity and specify of ultrasound-guided FNAB in the detection of lymph node metastasis to be 79.6% and 98.3% respectively [14].

In our study, FNAB supported the diagnosis of malignant breast lesions in 60 (60.0%) patients. Histopathology confirmed malignancy in 62 (62.0%) cases. In 60 ultrasonography-guided FNAB positive patients, 58 (true positive) had malignant breast lesions and 02 (false positive) had benign on histopathology findings. Among, 40 ultrasonography-guided FNAB negative patients, 04 (false negative) had malignant breast lesions on histopathology whereas 36 (true negative) had benign lesions on histopathology. Thus, the overall sensitivity and specificity of ultrasound-guided FNA was 93.55% and 94.74% respectively. The positive predictive, negative predictive value and diagnostic accuracy were 96.67%, 90.0% and 94.0% respectively. The ultrasound had the highest sensitivity (87%) when length >5 mm was taken as a criterion for malignancy.

A recent study conducted in Iran also found ultrasound-guided FNAC to be 88.46% sensitive and 100% specific technique that was also safe and significantly cost-effective [15]. Previously Koelliker et al. had drawn a similar conclusion [16]. They also noted that the sensitivity of detecting axillary nodes increased with an increase in primary tumour size [17]. Choy et al. discussed the novel concept of tattooing the lymph nodes while performing ultrasound-guided FNA. They found that tattooed lymph nodes corresponded with sentinel lymph nodes in all patients (n=26) with or without a history of neoadjuvant chemotherapy. This can further obviate the need for intraoperative SLNB hence shortening procedure time [18].

The major hitch in this technique was that FNAC is an operator-dependent procedure. Detection of both suspicious lymph nodes and hitting them with needle require expertise. Inadequate sampling might lead to falsely negative reports. Houssami et al. found rate of yielding an insufficient sample of about 4.1% [14]. This can be further reduced by possible utilization of the newer concept of ultrasound-guided core needle biopsy. In 2018, a study reported US-CNB to be superior to USG-FNA with respect to sensitivity, (88% versus 74%). However, the former was tecnically more challenging and resulted in higher complication rates were (7.1% vs 1.3%; p <0.001). Need for repeat biopsy was found more in US-FNA (4.0% vs 0.5% for USG-CNB; p <0.001). Both procedures had a specificity of 100% [19].

CONCLUSION

Ultrasound-guided FNA is a highly sensitive and accurate modality for preoperative adequate staging of the axilla in diagnosed cases of breast cancer having clinically negative axilla on examination.

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