



REGIONAL NODAL STATUS IN CARCINOMA BREAST - CLINICAL, SONOLOGICAL, CYTOLOGICAL AND PATHOLOGICAL CORRELATION

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ABSTRACT

Background Time immemorial axillary lymph node status has been established to be the single most important prognostic variable in the management of carcinoma breast. The relationship between axillary nodal spread and prognosis depends on the number of nodes involved, the level of the nodes affected, and the extent of disease within the nodes. **AIMS AND OBJECTIVES** To compare the features of malignant regional (axillary/ supraclavicular) nodes by clinical examination, ultrasound examination, and ultrasound-guided fine-needle aspiration cytology of regional nodes with postoperative pathological status in operable carcinoma breast. **Materials and Methods** This is a prospective study on 85 consecutive breast cancer patients who underwent clinical examination and presurgical axillary region ultrasound before surgery from august 2017 until December 2019. All operable carcinoma breast patients were included in the study and results were reviewed with definitive histopathology after surgery. **Results** Eighty-five cases were included in the analysis, of which thirty-three had evidence of metastatic nodal involvement at final histology. Of these 33 cases, ultrasound findings for 23 cases were positive. The overall positive predictive value of ultrasound for detecting metastatic nodal involvement measured 0.73. The negative predictive value was 0.83. The sensitivity was 71%; specificity 79%; and accuracy 80%. The ultrasound morphologic lymph node features with the greatest correlation with malignancy was the absence of a hyperechoic hilum ($p = 0.0001$). **Conclusion** Even though sonography cannot be used in isolation as a method for deciding whether to perform axillary lymph node dissection, high-frequency axillary USG as part of clinical examination in N0 and N+ patients will be definitely useful along with sentinel node biopsy in avoiding axillary dissection and there by its complication.

KEYWORDS : axillary, sentinel node, sonography

INTRODUCTION

Ultrasound examination as part of clinical examination of the axilla is becoming common practice in the presurgical assessment of breast cancer patients for staging purposes. Regional lymph node status is an important prognostic factor in the management of breast cancer. The current clinical pathway at many centers involves axillary ultrasound examination combined with fine-needle aspiration (FNA) cytology to identify malignant lymph nodes preoperatively before consideration of sentinel node biopsy.

If the fine needle aspiration cytology result shows no evidence of metastatic nodal involvement, patient may undergo sentinel lymph node biopsy (SLNB), if the cytologic result is positive for malignant involvement, axillary lymph node dissection (ALND) is recommended. The accuracy of ultrasound at identifying involved lymph nodes particularly in patients with early-stage breast cancer is less because of interobserver variability . Thus, many centers rely on ALND as the reference standard for staging disease. Better definition of nodal disease by USG appearance will see more and more patients undergoing sentinel node biopsy which will bring down the rates of post treatment lymphedema .

The aim of the study is to compare the features of malignant axillary nodes by clinical examination, ultrasound examination and ultrasound-guided fine-needle aspiration cytology of regional nodes with postoperative pathological status in operable carcinoma breast ,so that USG features of metastatic nodes are better evaluated.

Materials and Methods

Patient Population

This study was carried out at Government Royapettah Hospital , Chennai . Eighty five consecutive operable breast

cancer patients who underwent pre surgical axillary and supraclavicular region ultrasound before surgery from august 2017 until December 2019 . Results were collected and analysed . Ethical committee approval was received for this study.

Selection criteria

All operable breast cancer patients were included in study. Patient with locally advanced disease undergoing neo adjuvant chemotherapy before surgery and metastatic disease were excluded from study.

Ultrasound Analysis

Axillary and supraclavicular examinations were performed using a 7 to 13.5 -MHz linear-array transducer on an ultrasound scanner. Axillary lymph nodes were reported at the time of examination as normal /abnormal based on morphology-(figure 1 and 2)

- i) round shape
- ii) absence of the fatty hilum.

Histology

The histologic details including the size, and type of primary breast cancer, number of lymph nodes removed, and the number of lymph nodes with evidence of metastatic involvement were collected from the final pathologic reports. Cytology FNA cytologic analysis was carried out in all cases. Ultrasound-guided FNA was performed with a 23-gauge needle attached to a 10-mL disposable plastic syringe and an aspirator. Aspirated material was smeared and fixed in 70% ethanol for H and E staining.

Statistical Analysis

The final pathologic results from SLNB and ALND were

correlated with the clinical examination and axillary ultrasound reports. Data about specific ultrasound features were collected. Statistics were based on a description of variable results and the assessment of sensitivity, specificity, and predictive values. Comparisons between variables were performed using the chi-square test and Fisher exact test to assess the relationship between these features and the results of the ultrasound examination findings.

(In our study, ultrasound examination has been used as an extension of clinical examination. The finding of ultrasound examination or guided biopsy did not affect the treatment protocol of our institution.)

RESULTS

Patient Data

The median age of patients in this study was 53 years (range 32-85years). The histologic reports showed that 82 cases were infiltrating ductal carcinoma (IDC), 2 cases were mucinous carcinoma and one case was metaplastic carcinoma. Eight cases were T1 tumors, sixty-five cases were T2 tumours, ten cases were T3 tumour and two cases were T4 tumours. (table I) Clinical examination results Any clinically palpable node in axilla (hard and more than 1.5 cm approximately) is considered positive in the study .When results were analyzed according to the histologic findings, sensitivity was 43.0 %, specificity was 53.9%, positive predictive value was 36.8%, negative predictive value was 59.6%, the accuracy of the finding was 49.4 %.

Histologic Results

Final postoperative ALND histologic results showed that 52 (61%) cases had no evidence of metastatic nodal involvement and 33 (39 %) cases had metastatic nodal involvement. Of the 33 with metastatic nodal involvement, 9 cases (10%) had only one lymph node involved; 13 cases (17%) two lymph nodes involved; 2 cases (2%), three lymph nodes involved; and 9 cases (10%) four or more lymph nodes involved (Table I).

There is no significant association between T Status or molecular subtype status with relation to the positivity of ultrasound examination results. (table II)

Cytologic Results

Out of 85 cases. 9 cases had preoperative FNAC of node-positive, 23 patients had a false negative result. In this study, the sensitivity of ultrasound-guided FNAC was very low around 25 %.

Ultrasound Data

Histologic data after axillary node dissection were analyzed and compared against the results of the clinical examination and axillary ultrasound reports. Two important morphological features of malignant axillary nodes in axilla were taken for analysis.

- i) round nodes,
- ii) absent fatty hilum.

Round nodes were found in 33 cases, of which 11 cases were falsely positive. When results were analyzed according to the histologic findings, sensitivity was 68.7%, specificity was 79%, positive predictive value was 66%, negative predictive value was 81.2%, the accuracy of the finding was 75.36%.(table III)

The loss of the hyperechoic hilum with histologically confirmed nodal involvement was seen in 23 cases (27%) of cases compared with 45 cases (52.9%) of true-negative cases with neither metastatic spread nor absence of a hyperechoic hilum (chi-square, 27.7; p = 0.0001). When results were analyzed according to the histologic findings, sensitivity was 71%, specificity was 84 %, positive predictive value was 73 %,

negative predictive value was 83 %, the accuracy of the finding was 80 %.(table III)

Table I: Patient and Disease Characteristics

Characteristic	Value
1)Patient age (years)	
Median age	53
range	32-85
2)menopausal status	
premenopausal	39(45%)
postmenopausal	46(55%)
3)Pathologic stage, no. (%) of cases	
T1	8(9%)
T2	65(76%)
T3	10(12%)
T4	2(3%)
4)Tumor type, no. (%) of patients	
Invasive ductal nos	82(97%)
mucinous	2(2%)
metaplastic	1(1%)
5) grade of tumour	
Grade 1	14(16%)
Grade 2	61(72%)
Grade3	10(12%)
6)No. of lymph node metastases per patient, no. (%) of patients	
0	52(61%)
1	9(10%)
2	13(17%)
3	2(2%)
>4	9(10%)
7) Type of surgery	
Modified radical mastectomy	73(86%)
Total mastectomy with sentinel node biopsy	5(7%)
Breast conservation surgery with axillary dissection	3(3%)
Breast conservation surgery with sentinel node biopsy	4(4%)

Table II: Differences in Clinicopathologic Factors Between False-Positive and True-Positive Groups based on axillary ultrasound features

variables	False positive n (%)	True positive n(%)	p
T status			
T1	0	1(1%)	0.463
T2	8(9%)	18(22%)	
T3	3(4%)	3(4%)	
T4	0	1(1%)	
Molecular subtypes			
Luminal A	3(4%)	6(7%)	0.973
Luminal B	3(4%)	8(9%)	
Triple negative	3(4%)	5(6%)	
Her2 enriched	2(2%)	4(5%)	

Table III: Correlation of results of Clinical examination, Axillary ultrasound features, Ultrasound-guided fnac of the nodes with final histopathology report.

	specificity	sensitivity	NPV	NPV	accuracy
Clinical examination	53.9 %	43 .0%	36.8%	59.6%	49.4%
Axillary ultrasound features					
a)Round nodes	79%	68.7%	66%	81.2%	75.36%
b)Absent fatty hilum	84%	71%	73%	83%	80%
Ultrasound guided fnac of nodes	100%	25%	100%	69.2%	72%

DISCUSSION

The current clinical guidelines recommend that the preoperative workup for all patients scheduled to undergo surgery includes a breast ultrasound examination followed by an axillary ultrasound examination. The existence of palpable axillary nodes is often used to decide whether to perform a sentinel node biopsy or an axillary lymph node dissection, although axillary palpation has low sensitivity and specificity[1]. In our study, clinical examinations had very low sensitivity and specificity in detecting malignant axillary nodes.

The combination of percutaneous cytology of axillary nodes with axillary ultrasound can improve the accuracy of this procedure. A 40–50% identification rate for node-positive patients by percutaneous biopsy of axillary nodes has been reported [2]. In our study, the identification rate was less than 15%. Inclusions of USG guided FNAC results in the analysis in the study, did not alter the final results of the correlation between final histopathology and ultrasound features of axillary nodes.

Based on the results of ACOSOG Z0011 (Alliance) Randomized Clinical Trial, women with early breast cancer (T1 or T2), no palpable axillary adenopathy, and 1 or 2 sentinel lymph nodes containing metastases, 10-year overall survival for patients treated with sentinel lymph node dissection alone was non inferior to overall survival for those treated with axillary lymph node dissection [3]. Similarly, the B04 Study, which randomized breast cancer patients with negative clinical findings for nodal involvement into three treatment arms—radical mastectomy, total mastectomy, and nodal irradiation, or total mastectomy and delayed ALND if nodal recurrence occurred—showed no significant difference in any of the groups at 25-year follow-up [4]. So an accurate preoperative staging of the axilla is required for the selection of type axillary dissection.

Table IV: Diagnostic Accuracy of Axillary ultrasound in Patients with Breast Carcinoma based on morphological criteria

study	year	True positive	True negative	False positive	False negative	sensitivity %	Specificity %
Lam et al[5]	1996	8	19	1	3	72.7	95.0
Yang et al. [6]	1996	35	68	2	9	79.5	97.1
Sapino et al. [7]	2003	60	144	35	28	68.2	80.4
Damera et al. [8]	2003	35	83	19	29	54.7	81.4
Lee et al.[9]	2013	66	86	15	57	53.7	85.0
Hu et al[10]	2018	45	108	30	31	59.2	78.3
Our study		23	42	11	9	71.88	79.25

Various morphologic or structural criteria for the node were applied (a rounded shape, hypoechogenicity, cortical thickening, obliteration of the hilum, lobulation) to label a node malignant but the size of the axillary lymph nodes has limited utility for determining the likelihood of metastatic disease and was therefore not used as a criterion[11]. In our study, the size of nodes showed marked variability and could not be applied in statistical analysis. We took two important morphological features rounded nodes and loss of fatty hilum for evaluation in the study. In our study based on morphological criteria (rounded nodes and loss of fatty hilum) sensitivity and specificity for detecting malignant node was

71.88% and 79.25% respectively, which is comparable with other studies done in various institutions (table IV). The ultrasound morphologic lymph node feature with the greatest correlation with malignancy was the absence of a hyperechoic hilum (p = 0.0001).

CONCLUSION

Even though sonography cannot be used in isolation as a method for deciding whether to perform or not to perform axillary lymph node dissection, high-frequency axillary USG as part of clinical examination in N0 and N+ patients will be definitely useful along with sentinel node biopsy in avoiding axillary dissection and thereby its complications. Considering the subjective variation of USG examination further development of computer based algorithms and artificial intelligence may throw more light.

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figure -1 -benign node : oval with preserved fatty hilum

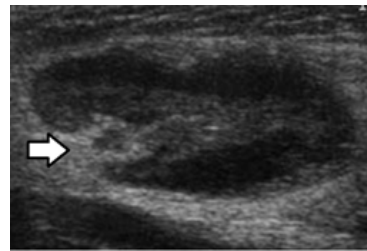
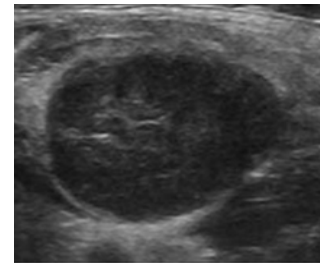


figure -2- malignant node: round with loss of fatty hilum



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