

Axillary Ultrasound as Preoperative Staging in Clinical Negative Axillary Lymph Node Breast Cancer Patient

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ABSTRACT

Objective: To determine the diagnostic accuracy of axillary US as a preoperative investigation by comparing it with the histology outcome of nodal status.

Methods: This validation analysis was conducted in Mater Misericordia university hospital, Dublin Ireland from Feb 2007 to Feb 2015. All female patients with palpable axillary lymph node and histology proven unifocal breast cancer between ages 18 to 75 years were included. Patients with the diagnosis of breast cancer were followed with Ultrasound imaging and results in Picture Archiving and communication system (PACS) and histology was confirmed using the patient center data base in both preoperative and postoperative course of breast cancer, including both sentinel lymph nodes and axillary lymph nodes.

Results: A total of 625 patients had axillary ultrasound (US) to assess the preoperative axillary nodal status with mean age of 56±12 years. cN0 was diagnosed in 469 (75%) cases, cN1 in 136 (21.8%) cases and cN2 in 20 (3.2%) cases. After negative axillary ultrasound cN0 pathology shows positive pN2 and pN3 disease in 14 (2.9%) cases with the NPV of 97.01%. Axillary ultrasound had shown cN1 disease in 136 cases with the pathology outcome of pN2 and pN3 in 41 (30.14%) cases with the negative predictive value (NPV) of 69.85%. The overall sensitivity and specificity of the axillary US in detection of the positive node was 51.6% and 92.8% with PPV of 82.69% and NPV of 74.2%.

Conclusion: Axillary US is a useful modality for screening of breast cancer patients. The negative US findings exclude the presence of advanced nodal disease. However, it cannot accurately distinguish between pN1 and pN2 or pN3 nodal disease.

Keywords: Axillary ultrasound, Axillary lymph nodes, Breast cancer.

INTRODUCTION

Breast cancer is the commonest malignancy in female population.¹ The survival in these patients depends on the presence of meta-stasis of the adjacent lymph nodes.² Sentinel lymph node biopsy (SLNB) is the standard diagnostic modality for diagnosis of metastasis, taking biopsy is an invasive procedure and is therefore associated with complications.³ Differentiating between the malignant and benign axillary lymph nodes using non-invasive methods is always challenging. Physical examination is the first line method for detection of lymph node metastasis with false negative rate of 30-45%.⁴

Recent European guidelines recommend to perform physical examination followed by ultrasound (US) of axilla to determine the presence of malignancy in all patients of newly diagnosed breast cancer. And in suspected cases of metastasis recommendation is to perform tissue sampling under US guidance.⁵

Lymph node dissection is the standard procedure in patients having positive SLN involvement.⁶ However, up-to 65% of the patients who have positive SNL involvement do not have meta-stasis of axillary LNs and performing the unnecessary axillary dissection in these patients significantly increases the risk of morbidity and mortality in these patients.^{7, 8}

Therefore, accurate diagnosis of axillary lymph nodes is very important in determining the extent of resection. Axillary US being the non-invasive tool can be easily utilized in pre-operative setting to determine the presence of meta-stasis and performing FNAB in US findings based suspected patients can help to reduce the need of biopsy analysis and can help to decide either to perform axillary

dissection or not.^{9, 10} Therefore, the present study is designed to determine the diagnostic accuracy of axillary US as a preoperative investigation by comparing it with the histology outcome of nodal status.

METHODS

This validation analysis was conducted in Mater Misericordia university hospital, Dublin Ireland from Feb 2007 to Feb 2015. All female patients with palpable axillary lymph node and histology proven unifocal breast cancer between ages 18 to 75 years were included in the study. Patients who had stage 4 breast cancer with palpable lymph nodes already received chemo radiotherapy and unsuitable for surgery with ASA 3 or 4 were excluded. Due to retrospective nature of the study, certified medical ethical committee waived the requirement of the consent.

All patients enrolled from outpatient department of breast center of hospital with the diagnosis of breast cancer were followed with Ultrasound imaging and results in Picture Archiving and communication system (PACS) and histology is confirmed using the patient center data base in both preoperative and postoperative course of breast cancer, sentinel lymph nodes and axillary lymph nodes. Data concerning age; sex; diagnostic work-up; surgical procedures; and pathology reporting of tumor type, grade, size, receptor status and lymph nodes will be collected using same data base.

Data was analyzed in SPSS v.23. Demography like age, size of lump, and duration of lump was presented as mean and standard deviation. Frequency and percentages for grade of breast cancer, receptor status, and

menopausal status, detection of lymph node involved in axillary ultrasound and on histology was calculated for these variables. A 2X2 table was drawn to calculate the sensitivity, specificity, positive predictive value, negative predictive value and test the diagnostic accuracy of Axillary ultrasound, taking histopathology as gold standard.

RESULTS

Mean Age of the patient included in this study was 56.43±12 years. Mean size of tumor was 22±11.47 mm. Mean duration of the lump before surgery was 6.56±5.39 weeks.

The commonest tumor presentation was invasive ductal carcinoma diagnosed in 480 (76.8%) cases, followed by invasive lobular in 94 (15%) cases, ducto-lobular in 5 (0.8%) cases, mucinous in 11 (1.8%) cases, tubular in 7 (1.1%) cases, papillary in 5 (0.8%) cases and other breast cancer like mixed, lymphoma etc in 23 cases (3.7%) cases. Grade 2 (moderately differentiation) tumors were diagnosed in 322(51.5%) cases and grade III tumors in 231 (37%) cases.

In total 366 (58.6%) cases are treated with Breast conserving surgery and 259 (41.4%) cases with mastectomy. On receptor status of tumor analyses, ER/PR positive and Her neu2 negative was found in 405 (64.8%) of total cases, variety of other combinations were seen in 97 cases (15.5%) (Table 1).

Axillary ultrasound finding showed 469 cases with cN0 (75%), 136 cases with cN1 (21.8%) and 20 cases with cN2 (3.2%). Postoperative histology of the tumor shows metastasis in 250 cases (40%) and 375 cases (60%) without the evidence of metastasis (Table 2).

Accuracy of Positive Axillary Ultrasound Finding:

Preoperative stage on the axillary ultrasound as cN1 (n= 136) on histology turns to be pN1 in 69. pN2 histology in 24 and pN3 histology in 17 of the axillae. Thus advance nodal disease (pN2-pN3) is present in 41 out of 136 axillae staged as cN1, resulting in the false percentage of 30.14% and NPV of 69.85% to exclude advance nodal disease if axillary ultrasound detect cN1. In axilla preoperatively stage as cN2 (n=20) ALN specimen revealed pN1 in 5 cases, pN2in 11 and pN3 in 3 cases (Table 3).

Table 1. Frequency and Percentage for Hormonal Receptor status.

Triple Negative	57 (9.1%)
ER/RP + Her2 Neu -	405 (64.8%)
ER/PR - Her2 Neu+	19 (3.0%)
Triple positive	47 (7.5%)
Others	97 (15.5%)

Table 2. Comparison of US Based Tumor Grading with Histopathology Tumor Grading.

US Based Tumor Grading	Histopathology Grading of Tumor				Total
	N0	N1	N2	N3	
cN0	348	107	9	5	469
cN1	26	69	24	17	136
cN2	1	5	11	3	20
Total	375	181	44	25	625

Accuracy of Negative Axillary Ultrasound Finding:

Preoperative stage on axillary ultrasound as cN0 (n=469), 348 cases are true negative, 107 cases have histology report c N1, 9 cases were pN2 and 5 cases having

histology of the pN3. Thus advance disease was present in 14 cases, resulting in the false percentage of 2.9% and NPV of 97.01%. This advance disease did not depend on the size of the tumour or type of breast cancer (Table 3).

Table 3. Comparison of Nodal Status with tumor size.

	pN0	pN1	pN2	pN3	Total
cNo					
pT1	173	37	2	-	212
pT2	150	69	6	2	227
pT3	23	2	2	3	30
pT4	-	-	-	-	-
cN1					
pT1	11	13	3	-	27
pT2	14	50	13	8	85
pT3	1	6	7	9	23
pT4	-	-	1	-	1
cN3					
pT1	-	2	1	-	3
pT2	1	3	7	2	13
pT3	-	-	3	1	4
pT4	-	-	-	-	-
Total					625

DISCUSSION

SLN biopsy is the standard diagnostic test for clinically axillary node negative breast cancer patient and is of great help in reducing the morbidity associated with arm and shoulder.^{6, 11} Imaging technology are using these days in almost all clinical negative breast cancer breast in conjunction with FNAC and even with the core biopsy of the suspicious lymph node to stage the patient and making the plan for axillary clearance in order to avoid surgeries in patient.¹²

There is now a huge controversy in performing ALND in patients with SLN meta-stasis having less disease burden. Because performing ALND in did not provide any survival benefits and systemic therapy is sufficient to eradicate the disease. Moreover, ALND also increases the risk of post-operative complications and even in some cases can cause mortality. Accurate assessment of axillary lymph nodes meta-stasis is very valuable in planning for chemotherapy extent and helps to decide surgical approach¹³. Therefore, in present study we determined the role of US axillary examination in predicting the presence of meta-stasis in breast cancer patients. We found that axillary US is 51.6% sensitive and 92.8% specific for the diagnosis of meta-stasis.

The study by Houssami et al. reported sensitivity of axillary ultrasound 79.6% and specificity 98.3% by taking biopsy diagnosis as gold standard.¹⁴ Whereas in present study the sensitivity was 51.6% and specificity 92.8%. Sensitivity is less in our case because of the better screening program and the diagnosis of the breast cancer at earlier phase. Metastasis in lymph node with early breast cancer and with only node positive is difficult to diagnose on axillary ultrasound.

Schipper and colleagues¹ found out the similar results showing that 43.8% of the pN1 were found as cN0 on axillary ultrasound staging.¹⁵ Stachs et al. also reported that the axillary US accuracy directly depends on the size of metastasis.¹⁶

In case of cN1 the NPV of the axillary US was 58.8% in the study done by Schipper and colleagues comparable with our NPV of 69.85% for cN1.¹⁵ This value seems to be reliable as pre-procedural distinction between cN1 and cN2 is always of prime importance. According to the guidelines by Dutch breast cancer society, adjuvant radiotherapy is designated after mastectomy in patient with pN2 –pN3 in comparison to pN1 patients. Immediate breast reconstruction is usually not offered to the patient who needs adjuvant radiotherapy because the results are less satisfied with poor cosmetic outcome.¹⁷ Some of the recent studies however offers satisfactory outcome with no related radiotherapy complications.¹⁸

Therefore, post mastectomy radiation is no longer contraindication for immediate breast reconstruction. So in our centre even if the nodes become pN2 –pN3 and needs radiation therapy keeping in view the wish of the patient reconstruction is offered to the patients. Delayed reconstruction after radiation therapy makes the procedure more difficult with poor cosmetic results.

In our set up usually there is the ultrasound staging done before any surgery. Patients with suspicious lymph node after having confirmation with FNAC undergo ALNC, not related to the kind of breast surgery. Those who turn positive on the sentinel lymph node biopsy may undergo radiation if reconstruction done or proceed to the axillary clearance if breast conserving surgery done. Patients with mastectomy are usually offered radiation therapy for metastatic disease.

Limitation: Firstly, this study is retrospective which may have cause selection bias. The slightly lower rate of advanced tumor stage in present study may be because of that we excluded patients who were treated with neo-adjuvant chemotherapy. The exclusion of these cases may have resulted in underestimation of NPV of axillary US to exclude advanced disease.

CONCLUSION

Axillary US is a useful modality for screening of breast cancer patients. The negative US findings exclude the presence of advanced nodal disease. However, it cannot accurately distinguish between pN1 and pN2 or pN3 nodal disease and is not much beneficial for patient having tumor size <2 cm.

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