

The Role of Combined Assessment in Preoperative Axillary Staging

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ABSTRACT

Background: Axillary lymph node status is the most significant single prognostic factor in breast cancer, and preoperative axillary staging is essential in determining lymph node status. Axillary ultrasound scan (AUS) is the gold standard modality in preoperative staging. However, triple assessment—including clinical examination and radiological assessment with fine needle aspiration (FNA) with or without core biopsy—ensures high sensitivity.

Methods: Our study included 219 women diagnosed with invasive breast cancer between 2009 and 2010. All patients underwent a preoperative staging AUS that was graded from normal (U1) to malignant (U5). All patients with ultrasound scans graded U3 (indeterminate) and above underwent FNA that was graded from C1 (inadequate for diagnosis) to C5 (malignant). Patients diagnosed preoperatively with metastatic lymph nodes were offered axillary lymph node clearance. The rest of the patients were offered sentinel lymph node biopsy.

Results: The 219 women were diagnosed with 228 invasive breast cancers. The mean age was 60 years (range 29–90 years). The final histology report showed metastatic axillary lymph nodes in 49 (21.5%) cases. Of these 49 cases, 22 were diagnosed preoperatively with metastatic axillary lymph node and were elected for axillary lymph node clearance, and 27 were elected for sentinel lymph node biopsy that revealed metastatic lymph nodes. AUS showed abnormal (U3/U4/U5)

axillary lymph nodes in 30 of 49 (61.2%) cancer cases with an overall accuracy of 91.6%.

Conclusion: Combined triple assessment increases the sensitivity, negative predictive value, and overall accuracy of preoperative staging of the axilla.

INTRODUCTION

Axillary lymph node status is the single most significant prognostic factor in breast cancer,¹ and during the last decade, sentinel lymph node biopsy has become the gold standard procedure to determine lymph node status.² This approach allows selection of patients who should directly undergo axillary lymph node clearance, sparing a second surgical procedure.³ Sentinel lymph node biopsy is indicated for patients with normal preoperative axillary lymph nodes. Imaging assessment of axillary lymph nodes involves preoperative staging with axillary ultrasound scan (AUS). Although many studies report the use of positron emission tomography (PET) and magnetic resonance imaging (MRI) in preoperative staging, AUS remains the standard imaging modality in the preoperative staging of axillary lymph nodes in the United Kingdom.⁴ We report our experience with the use of AUS in detecting metastatic lymph nodes preoperatively.

METHODS

Our study included 219 consecutive patients diagnosed with breast cancer from January 2009 until November 2010. All patients were clinically assessed for axillary lymph node involvement and underwent a preoperative AUS. Axillary lymph nodes were assessed by Philips iU22 ultrasound (Royal Philips, Amsterdam, The Netherlands) scan with high frequency 12–17 MHz probe. Thickening of the cortex of more than 2 mm and absence of the hilum were considered key diagnostic features of an abnormal lymph node. A simple 5-point classification system recommended by the European Society of Breast Cancer Specialists (EUSOMA) was used to describe

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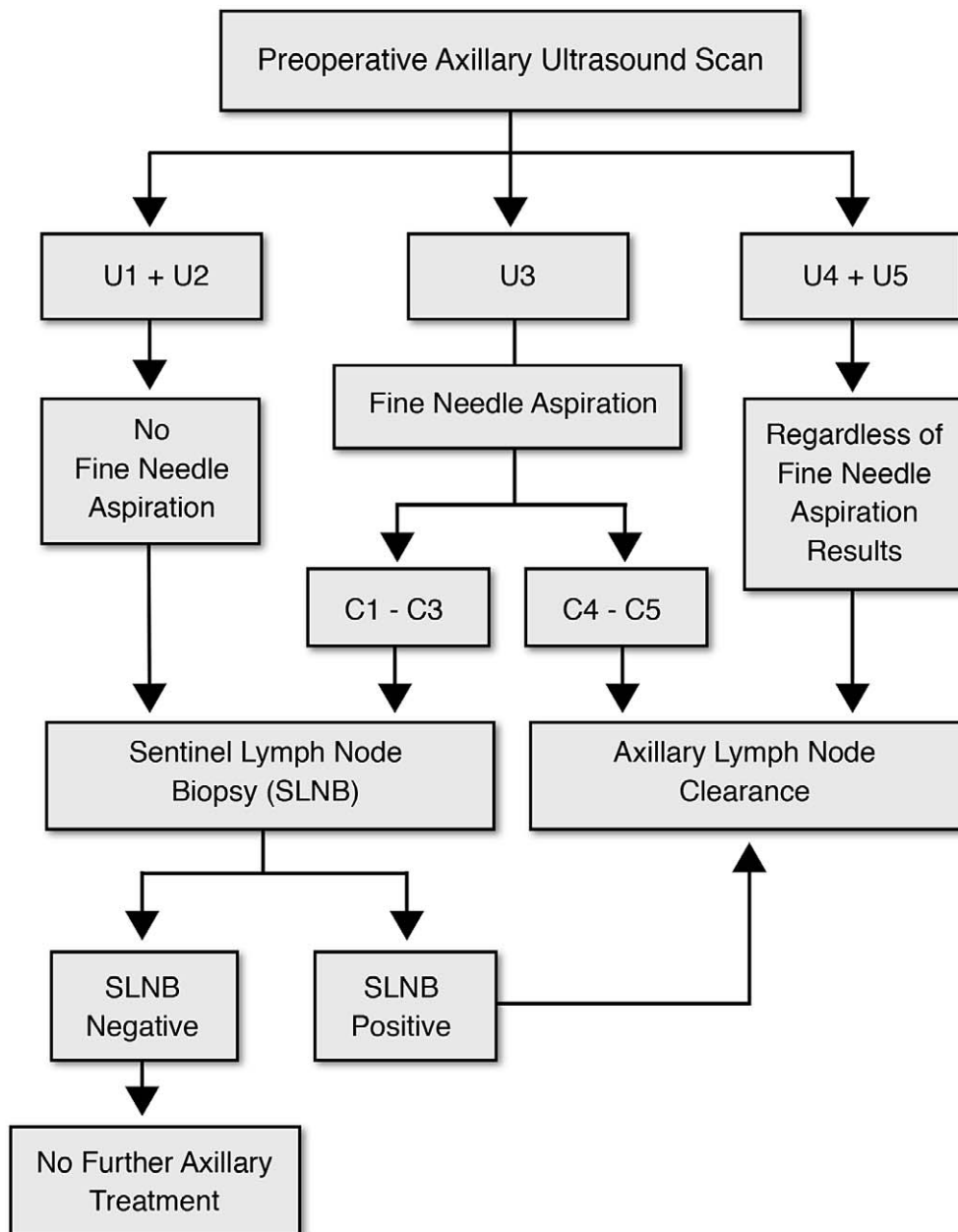


Figure. The protocol used for preoperative axillary staging.

Table 1. Preoperative Axillary Staging of Cancer Cases With Metastatic Axillary Lymph Nodes

Cancer Cases With Metastatic Axillary Lymph Nodes n=49	AUS Grade / (FNA Grade)	n
Detected preoperatively (n=22)	U4 +U5	16
	U3 (FNA C4, C5)	6
Detected following SLNB (n=27)	U3 (FNA C1,C2,C3)	8
	U1+U2 (no FNA)	19

AUS, axillary ultrasound scan; FNA, fine needle aspiration; SLNB, sentinel lymph node biopsy.

AUS grades: U1 (normal), U2 (benign), U3 (indeterminate), U4 (suspicious), U5 (malignant).

FNA grades: C1 (inadequate for diagnosis), C2 (benign), C3 (indeterminate [probably benign]), C4 (suspicious of malignancy), C5 (malignant).

Table 2. FNA Results for Cancer Cases With U3 (Indeterminate) Preoperative AUS

Cancer Cases With U3 (Indeterminate) AUS n=14	FNA Results
6	C4, C5
8	C1, C2, C3

AUS, axillary ultrasound scan; FNA, fine needle aspiration. FNA grades: C1 (inadequate for diagnosis), C2 (benign), C3 (indeterminate [probably benign]), C4 (suspicious of malignancy), C5 (malignant).

the appearance of the lymph nodes. Scans were graded U1 (normal), U2 (benign), U3 (indeterminate), U4 (suspicious of cancer), or U5 (malignant).

A 21-gauge fine needle aspiration (FNA) was performed on U3-U5 lymph nodes. The FNA aspirates were studied using Papanicolaou staining and were classified as recommended by EUSOMA: C1 (inadequate for diagnosis), C2 (benign), C3 (indeterminate [probably benign]), C4 (suspicious of malignancy), and C5 (malignant).

All patients with preoperative AUS graded U1 (normal) and U2 (benign) had no FNA performed and underwent sentinel lymph node biopsy. All patients with scans graded U4 (suspicious) and U5 (malignant) underwent FNA. These patients were offered axillary lymph node clearance irrespective of FNA findings. All patients with a U3 (indeterminate) scan underwent FNA and were then offered sentinel lymph node biopsy if the FNA results were C1-C3 or axillary lymph node clearance if the FNA results were C4-C5 (Figure).

Data were analyzed to determine the sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of preoperative AUS with and without FNA cytology.

RESULTS

In the 219 women included in the study, 228 invasive breast cancers were diagnosed; 9 patients

Table 4. Distribution of Cancer Cases According to the Preoperative AUS and Axillary Node Status on the Final Pathology Result

Preoperative AUS	Metastatic Axillary Lymph Node on Final Pathology	
	Positive	Negative
AUS showed abnormal lymph nodes: U3/U4/U5 (n=30)	30 ^a	0 ^b
AUS did not show abnormal lymph nodes: U1/U2 (n=198)	19 ^c	179 ^d

AUS, axillary ultrasound scan. AUS grades: U1 (normal), U2 (benign), U3 (indeterminate), U4 (suspicious), U5 (malignant).

FNA grades: C1 (inadequate for diagnosis), C2 (benign), C3 (indeterminate [probably benign]), C4 (suspicious of malignancy), C5 (malignant).

^aCancer cases with positive metastatic axillary lymph node and abnormal lymph node on AUS.

^bCancer cases with negative metastatic axillary lymph node and abnormal lymph node on AUS.

^cCancer cases with positive metastatic axillary lymph node and no abnormal lymph node on AUS.

^dCancer cases with negative metastatic axillary lymph node and no abnormal lymph node on AUS.

had bilateral breast cancer. The patients' mean age was 60 years (range 29-90 years).

The final histology report revealed 49 (21.5%) cases with metastatic axillary lymph nodes. Of the 49, preoperative axillary staging detected metastatic axillary lymph nodes in 22 cases. Patients with these cancer cases were primarily offered axillary lymph node clearance. Preoperative axillary staging failed to detect metastatic axillary lymph nodes in 27 of the 49 cases. These cancer cases were elected initially for sentinel lymph node biopsy that revealed the metastatic lymph nodes (Table 1).

Preoperative AUS was reported as U1/U2, U3, and U4/U5 in 19 (38.8%), 14 (28.6%), and 16 (32.7%) cancer cases, respectively (Table 1).

Table 3. Metastatic Lymph Nodes in Cancer Cases With U3 (Indeterminate) AUS and C1-C3 FNA

Number of Metastatic Lymph Nodes on Final Pathology Report	Cancer Cases With U3 (Indeterminate) AUS and C1-C3 FNA n=8		
	C1	C2	C3
1	1	2	1
1-3	1	1	1
>3	0	1	0

AUS, axillary ultrasound scan; FNA, fine needle aspiration. FNA grades: C1 (inadequate for diagnosis), C2 (benign), C3 (indeterminate [probably benign]), C4 (suspicious of malignancy), C5 (malignant).

Table 5. Diagnostic Accuracy for Detecting Abnormal Lymph Nodes

Diagnostic Criteria	Combined Assessment (AUS + FNA)
Sensitivity: A/A+C	61.2%
Specificity: D/B+D	100%
Positive predictive value: A/A+B	100%
Negative predictive value: D/C+D	90.4%
Overall accuracy: A+D/A+B=C=D	91.6%

AUS, axillary ultrasound scan; FNA, fine needle aspiration.

A: Cancer cases with positive metastatic axillary lymph node and abnormal lymph node on AUS.

B: Cancer cases with negative metastatic axillary lymph node and abnormal lymph node on AUS.

C: Cancer cases with positive metastatic axillary lymph node and no abnormal lymph node on AUS.

D: Cancer cases with negative metastatic axillary lymph node and no abnormal lymph node on AUS.

Patients With AUS U4/U5

FNA was performed for all 16 cancer cases with U4/U5. One patient with U4 was found to have C1; one case with U5 had C2. The rest of the cases in this group had C4/C5. The multidisciplinary meeting decision for cancer cases in the C4/C5 group was to proceed to axillary lymph node clearance regardless of the FNA results.

Patients With AUS U3

In all 14 cancer cases with an indeterminate U3 stage, FNA was used to assist the preoperative staging. Six cases with U3 had either suspicious or malignant cytology C4/C5 and were therefore considered not suitable for sentinel lymph node biopsy. These 6 cases underwent axillary lymph node clearance (Table 2).

Eight cases with C1, C2, and C3 FNA results were found to have lymph node metastasis on sentinel lymph node biopsy. These cancer cases underwent further surgery in the form of axillary lymph node clearance. The number of cancer cases and the total number of nodes in the clearance specimens are shown in Table 3.

Patients With AUS U1/U2

The total number of cancer cases graded as U1/U2 preoperatively was 198. Nineteen of 198 (9.6%) cancer cases were found to have metastatic sentinel lymph nodes and were elected to have axillary lymph node clearance.

Of these 19 cases with U1/U2 found to have lymph node metastasis on histology, 12 cases had only 1 metastatic lymph node involved, 5 cases had 2 metastatic lymph nodes, and 2 cases had 3 nodes involved with tumor.

Sensitivity of AUS

Preoperative AUS detected abnormal axillary lymph nodes U3/U4/U5 in 30 of 228 cases. AUS did not detect an abnormality in 198 of 228 cases, but these patients were elected for sentinel lymph node biopsy. Unfortunately, 19 of the 198 (9.6%) cancer cases had metastatic sentinel lymph node biopsy and underwent axillary lymph node clearance (Table 4).

The overall sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of AUS with and without FNA cytology are shown in Table 5.

Table 6. Comparison of Our Study With Other Published Results

Study	Staging Method	Total Number of Cancers	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Accuracy
Podkrajsek et al ³	AUS + FNA	165	84%	91%	97%	62%	N/A
Tahir et al ⁷	AUS + FNA	197	47.1%	100%	100%	70%	76.3%
Mainiero et al ⁸	AUS + FNA	224	59%	100%	N/A	N/A	N/A
Nori et al ⁹	AUS	132	45.2%	86.6%	61.3%	77.2%	73.5%
Sato et al ¹⁰	AUS	262	89.2%	100%	N/A	94.3%	96.1%
Our Study	AUS + FNA	228	61.2%	100%	100%	90.4%	91.6%

AUS, axillary ultrasound scan; FNA, fine needle aspiration; N/A, not available.

DISCUSSION

In the last 3 decades, the management of axillary lymph nodes in patients with breast cancer has changed remarkably. More recently, the ACOSOG Z0011 trial has been described as practice changing.^{5,6} More emphasis is placed on accurate preoperative axillary staging to determine lymph node status and to plan surgery accordingly.

AUS is the gold standard method for preoperative staging in the United Kingdom because of its high sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy.³ The results of various studies are shown in Table 6.

Although ultrasound is the best evaluated modality, centers around the world have used other imaging modalities such as MRI,¹¹ computed tomography,¹² duplex sonography,¹¹ 99mTc-sestamibi scintimammography^{11,12} and PET.¹¹⁻¹³ These methods have not been routinely adopted because they are not uniformly available.¹⁴ Scan of the axilla is noninvasive and fast¹⁵ although the technique is operator and equipment dependent.⁷

Combining clinical examination, AUS, and FNA increases the accuracy of diagnosing metastatic lymph nodes and reduces the number of sentinel lymph node biopsies.^{1,16} The diagnostic features of AUS suggesting malignancy are thickening of cortex and absence of hilum.¹⁴ These 2 findings carried a positive predictive value of 100% in the Torres Sousa et al 2011 study.¹⁷

Many studies emphasize the importance of combined assessment in determining lymph node status. Gruber et al estimated that 40% of patients with breast cancer received overtreatment with unnecessary axillary lymph node clearance if preoperative staging included clinical examination and/or imaging (AUS) only.¹⁸ Some studies show that performing an ultrasound-guided FNA on 2 or more lymph nodes will increase the sensitivity 47.1%-80% and negative predictability 70%-93.3%.⁴

Some studies now recommend core biopsy for suspicious-looking axillary lymph nodes to increase the predictability of metastatic lymph nodes.¹⁷ Gruber et al stressed the importance of ultrasound-guided core biopsy in patients who had equivocal FNA results.¹⁸

In our study, the overall accuracy of the preoperative AUS was 91.6%, and the sensitivity of AUS was 61.2%. Our results verify the importance of combined assessment for preoperative staging of the axilla. Consequently, we have introduced new protocols in our unit, including performing regular core biopsy of all lymph nodes when FNA is equivocal or insufficient.

CONCLUSION

Combined triple assessment increases the sensitivity, negative predictive value, and overall accuracy of preoperative staging of the axilla. The use of core biopsy helps when FNA result is equivocal or insufficient.

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