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Original article

Pre-operative staging of the axilla in primary breast cancer. By redefining the abnormal appearing node can we reduce investigations without affecting overall treatment?

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ABSTRACT

Primary axillary clearance (ANC) is currently performed based on cytology from abnormal appearing node(s) without considering extent of involvement. We assessed correlation between nodal burden and nodal appearance.

439 invasive breast cancer cases underwent axillary ultrasound (AUSS) with nodal scoring [UN2-normal ($n = 293$), UN3-indeterminate ($n = 84$), UN4-suspicious ($n = 29$), and UN5-replaced ($n = 34$)]. Fine needle aspiration cytology (FNAC) of all UN3, UN4 & UN5 nodes was performed.

64 cases had nodal metastases identified pre-operatively, proceeding to primary ANC. 375 cases underwent sentinel lymph node biopsy (SLNB), 64 of whom were found to have nodal metastases. Likelihood of metastases and nodal burden was related to AUSS score. >50% of malignant UN4 & UN5 scored nodes had ≥4 metastases compared to 19% of UN3 nodes.

Most UN3 nodes are either not involved or have low metastatic burden which may be better served by SLNB alone. Redefining our FNAC nodal threshold could potentially avoid additional ANC morbidity and reduce pre-operative workload.

Introduction

Axillary lymph node status remains the key prognostic factor in invasive breast cancer [1,2], with the presence of metastatic disease in the nodes guiding decisions both on adjuvant therapy and surgery. Experience in the technique of axillary ultrasonography (AUSS), guided fine needle aspiration biopsy and wide bore needle biopsy has resulted in a greater proportion of those cases with nodal metastases at presentation being identified pre-operatively [3]. Current UK practice is for these to proceed directly to axillary node clearance (ANC). As a result of breast cancer screening programmes, improved imaging technology and heightened public awareness breast cancer is presenting at an earlier stage and the proportion of cases with lymph node involvement is correspondingly less [4,5]. Furthermore, there is ongoing debate about the need for aggressive surgical treatment of the axilla in those with limited axillary involvement. Several randomised trials have failed to show any survival benefit from axillary clearance [6,7] while others have confirmed increased morbidity [8,9] compared with sentinel lymph node biopsy (SLNB).

SLNB is now accepted as the preferred method for the surgical staging of the axilla in patients with a clinically and radiologically normal axilla pre-operatively [10,11]. The American College of Surgeons Oncology Group (ACOSOG) Z0011 trial [7] has questioned the need for completion axillary lymph node dissection (cALND) in a select group of patients who had less than 3 positive sentinel lymph nodes (SLN), however in this study there were no formal radiology guidelines for imaging the axilla pre-operatively. The majority of patients in Z0011 in fact had no pre-operative axillary imaging but despite this there was no detriment to survival or local control in the group that did not proceed to cALND. It could be argued, therefore, that patients with clinically N0 disease do not need AUSS at all but clinical assessment of the axilla is notoriously inaccurate and in this respect it may not be appropriate to translate the experience of Z0011 into routine practice. On the other hand, if the safety of leaving potentially involved non-sentinel nodes after a positive SLNB is accepted it is important to address the question of whether the axilla should be cleared on the basis of pre-operative axillary assessment without clarifying the extent of involvement.

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This prospective audit has aimed to assess whether there is a correlation between nodal burden and pre-operative axillary assessment with ultrasound.

Materials and methods

From June 2011 to August 2012, non-randomised consecutive patients with newly diagnosed invasive breast cancer were prospectively audited. All patients underwent pre-operative axillary ultrasound scanning with abnormal appearing nodes having image guided fine needle aspiration cytology (FNAC) performed as per our protocol. This was performed directly after biopsy of the primary breast lesion. If more than one node was identified, the most morphologically abnormal node was selected for FNAC. All invasive cancers that had an axillary surgical procedure were included in the study. Invasive cancer status was confirmed on final histology by haematoxylin-eosin (H&E) pathological analysis. Cases of pure Ductal Carcinoma in Situ were excluded as were cases where distant metastatic disease was evident at initial presentation.

Throughout the study period, there was a fixed team of six consultant breast radiologists, four consultant surgeons with consistent cytology and histopathology staff. Sentinel nodes underwent intra-operative nodal analysis with Touch Imprint Cytology (TIC). Patients with positive intra-operative nodal analysis proceeded to an immediate axillary clearance (cALND). Cases where TIC was negative but metastases confirmed on H&E analysis were discussed, the majority undergoing completion axillary lymph node dissection within 4 weeks of initial surgery.

Axillary ultrasound was performed by a consultant breast radiologist in all cases, the ipsilateral axilla being assessed at the same time as the newly diagnosed cancer. The patient was positioned supine with the arm raised above the head to facilitate scanning in orthogonal directions which included the breast axillary tail. AUSS was performed with 8–14 MHz linear array transducer with a Toshiba Aplio (Toshiba Medical Systems Corporation, Tochigi, Japan) ultrasound platform. Colour Doppler flow was also utilised. Axillary nodes were scored using the criteria shown in Table 1. Where abnormal appearing nodes were visualised FNAC was performed using multiple passes with a 21G needle.

Those patients with nodal metastases identified pre-operatively by malignant cytology proceeded direct to axillary clearance. Those with indeterminate or suspicious appearing nodes (AUSS scores UN3 & UN4) but normal lymphoid cells seen on FNAC underwent SLNB. Where cytology samples were inadequate for analysis or there was a lack of concordance between suspicious nodal appearance and cytological findings the procedure was repeated.

Results

Four hundred and thirty nine newly diagnosed invasive cancers in 433 patients were prospectively studied. Median age at diagnosis was 62.4 (range 27.7–91.1) years, two patients were male. During the study period, 18 separate cases were excluded from analysis, 4 because there was evidence of distant metastases at first presentation and 14 because they did not undergo an axillary procedure due to advanced age or co-morbidity (all had normal AUSS pre-operatively).

Sixty four patients had metastatic nodes identified pre-operatively and proceeded directly to ANC, 2 patients undergoing neo-adjuvant treatment prior to surgery. The remaining 375 cases proceeded to SLNB, 7 of whom had a four node axillary sample (1.9%) due to failure of sentinel node localisation. The median number of localising sentinel nodes was 2 (range 1–6). Sixty four of the 375 sentinel node biopsies were positive, 2 of which had failed SLNB localisation. Overall 29.2% (128) cases had nodal metastases, half of which were identified pre-operatively. Complete pathological analysis was obtained for all cases; invasive tumour characteristics are shown in Table 2. Sixty two cancers were multifocal. In such cases the largest invasive tumour foci and the highest tumour grade was recorded, 17 separate cases also had a significant non-invasive component which resulted in overall tumour size being >50 mm.

Pre-operatively normal appearing axillary nodes (UN2) were recorded in 293 cases (66.7%) seven of which had FNAC performed as multiple nodes were seen. Indeterminate appearing nodes (UN3) were seen in 83 cases (18.9%), suspicious nodes (UN4) were found in 29 cases (6.6%), and completely replaced nodes (UN5) being identified in 34 cases (7.8%). Sixty four cases (11-UN3, 19-UN4, 34-UN5) with nodal metastases confirmed pre-operatively proceeded to ANC, 2 patients receiving neo-adjuvant therapy prior to surgery. The median ANC nodal harvest was 15 (range 5–36). The nodal burden for these cases is shown in Table 3.

Table 1
Allocated nodal score according to morphological features on ultrasound.

Nodal score	Morphological feature(s)
UN2 (normal)	Uniform cortex <2.3 mm and centrally placed fatty hilum
UN3 (indeterminate)	≥2.3 mm cortex with uniform cortical thickness
UN4 (suspicious)	Localised bulge of cortex >2.3 mm, eccentric displacement of fatty hilum, small vessels entering cortex of node (colour flow ultrasound)
UN5 (replaced)	Enlarged node with no fatty hilum

Table 2
Comparison of tumour characteristics on final histology for all cases according to method of confirming metastatic nodal involvement (*IBR – Immediate Breast Reconstruction, LVI – Lymphovascular Invasion).

	Involved nodes identified pre-operatively $n = 64$	Involved nodes identified intra/post-operatively $n = 64$	No nodal involvement $n = 311$
Screen detected	28 (43.8%)	33 (51.6%)	234 (75.2%)
Breast conserving surgery	20 (31.2%)	31(48.4%)	227 (73.0%)
Mastectomy ± IBR*	44 (68.8%)	33 (51.6%)	84 (27.0%)
Cancer type:			
Ductal (NST)	57 (89.1%)	54 (84.4%)	246 (79.1%)
Lobular	4 (6.2%)	7 (10.9%)	34 (10.9%)
Mixed	2 (3.1%)	1 (1.6%)	2 (0.7%)
Specific type	1 (1.6%)	2 (3.1%)	29 (9.3%)
Tumour size:			
T1	18 (28.1%)	20 (31.3%)	209 (67.2%)
T2	30 (46.9%)	39 (60.9%)	98 (31.5%)
T3	11 (17.2%)	4 (6.2%)	4 (1.3%)
T4	5 (7.8%)	1 (1.6%)	0
Tumour grade:			
1	0	2 (3.1%)	53 (17.0%)
2	16 (25%)	36 (56.3%)	156 (50.2%)
3	48 (75%)	26 (40.6%)	102 (32.8%)
ER status			
Positive	46 (71.9%)	60 (93.8%)	265 (85.2%)
Negative	18 (28.1%)	4 (6.2%)	46 (14.8%)
HER2 status			
Positive	12 (18.8%)	7 (10.9%)	37 (11.9%)
Negative	52 (81.2%)	57 (89.1%)	274 (88.1%)
LVI presence			
Yes	32 (50%)	26 (40.6%)	28 (9.0%)
No	32 (50%)	38 (59.4%)	283 (91.0%)
Nodal involvement			
Macrometastases	63	51	n/a
Micrometastases	1	13	