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Selection for axillary clearance in breast cancer (ultrasound negative, sentinel node positive patients have low rates of further metastases)

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Abstract

Background: The aim of this study was to determine whether we could identify a subset of axillary clearance patients in whom the procedure yielded negative nodes and was therefore of no therapeutic benefit.
Methods: Over a three year period 138 patients underwent axillary clearance at our unit. The axillae of all patients were assessed preoperatively with clinical examination, ultrasound (USS) and FNAC if suspicious nodes identified. Patients with clinically malignant nodes or positive FNAC underwent axillary node clearance where appropriate, whilst completion axillary node clearance was performed in those who had no preoperative evidence of metastatic axillary disease but positive sentinel node biopsy (SNB)/axillary node sample (ANS).
Results: Of the 138 patients, the indications for axillary clearance were positive FNAC or clinically malignant nodes in 89 and positive SNB/ANS in the remaining 49. Patients with preoperative evidence of axillary metastases had significantly more positive nodes compared to those who underwent SNB and completion ANC 4.6 vs. 3.1 $p = 0.037$. Of the patients with ultrasonographically normal axillae but positive SNB, 8.7% had further nodal metastases at completion ANC. This was significantly less than in those with abnormal USS (negative FNAC) and positive SNB (41.7%); $p = 0.033$.
Conclusions: Preoperative ultrasound in conjunction with FNAC and clinical judgement identifies most patients with positive axillary nodes and such patients have more widespread disease. The additional value of completion axillary ANC in patients with ultrasonographically normal axillae but positive SNB appears small as sentinel node 'biopsy' serves to clear the axilla of metastases in most of these patients.

Keywords: Sentinel node; Breast cancer; Axillary node clearance; Ultrasound

Introduction

Sentinel lymph Node Biopsy (SNB) can be used to accurately identify women with invasive breast cancer who have axillary nodal metastases[1] and patients with clear sentinel nodes need no further axillary treatment.[2–4] Completion Axillary Node Clearance (ANC) remains the standard treatment for patients with positive sentinel nodes[5] although axillary radiotherapy can be used alternatively with proponents highlighting similar survival and local recurrence rates.[6] However, both treatments have a high incidence of morbidity including lymphoedema, seroma, shoulder weakness and neuromuscular problems.[7,8] The incidence of further nodal metastases at completion clearance has been reported as 45–63%.[9–11] Given the potentially disabling side effects of treatment, several authors have aimed to identify a subgroup of patients in whom further nodal metastases is unlikely and thus spare them unnecessary surgery. Mathematical models produced by Sloan–Kettering,[12] Stanford[13] and Cambridge[14] centres are examples of these, including parameters such as tumour grade, size, number and size of lymph nodes involved. However, a recent study sought to independently verify these models and found that the predictive accuracy of each model was not as good as reported by the original studies (AUC 0.63–0.72) and such models are not used routinely to determine which patients should be offered completion clearance.[15]

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Axillary ultrasound can be used to accurately assess the morphology of axillary lymph nodes. Fine Needle Aspiration Cytology (FNAC) can be performed at the time of axillary USS and patients with positive axillary node cytology can proceed to axillary clearance without undergoing further axillary staging such as sentinel node biopsy. Previous studies have shown that USS with FNAC can identify the majority of patients with positive axillary nodes.[16–18] It is our impression that since the advent of routine preoperative axillary USS ± FNAC, the proportion of patients with positive SNB who have further metastases present at completion ANC has decreased. The existing algorithms for predicting further axillary lymph node metastases after positive SNB do not include axillary USS and FNAC.[12–14]

The aim of this study was to determine whether we could identify a subset of axillary clearance patients in whom the procedure yielded negative nodes and was therefore of no therapeutic benefit.

Patients and methods

Consecutive women with histologically proven primary invasive breast cancer undergoing axillary node clearance at The County Hospital, Hereford between Jan 2008 and Jan 2011 were included. All patients were discussed in a multi-disciplinary meeting and those with no clinical or radiological evidence of irresectable local or metastatic disease were offered attempted curative resections with neoadjuvant chemoradiotherapy where appropriate, subject to performance status, co-morbid disease and patient wishes. Indication for axillary node clearance included clinical or cytological evidence of axillary metastases or positive sentinel node biopsy/axillary node sample. Patients not suitable for axillary node clearance were offered axillary radiotherapy where appropriate.

Axillary ultrasound (Toshiba-Nemio machine, Toshiba medical systems Ltd, West Sussex, UK) was performed as a routine preoperative staging procedure by either of two consultant breast surgeons with FNAC performed if enlarged (≥1.0 cm) or suspicious nodes present. Suspicious features included loss of corticomedullary distinction, increased cortical thickness >2 mm or hypoechoic cortex. Cytology specimens were analysed by one of two consultant cytopathologists, and patients were deemed to have positive cytology if the slides unequivocally demonstrated the presence of malignant cells. Indeterminate findings did not result in review by the other observer.

Patients without clinical evidence of nodal metastases, normal axillary ultrasound imaging or negative FNAC underwent surgical axillary staging at the time of definitive breast surgery. This was usually in the form of Sentinel lymph Node Biopsy (SNB) although Axillary Node Sample (ANS) of at least four nodes was performed if isotope was unavailable. Sentinel nodes were identified using dual blue dye and radioisotope localisation.

Patient details including age, sex, date of diagnosis, clinical findings, cytology status and tumour histology were collected in a contemporaneously maintained database. Axillary nodes were deemed to be positive if the diameter of tumour involvement was >2 mm (macrometastases).

Statistical analysis

All analyses were carried out by the authors and values given as median (range). Categorical variables were compared by means of Fisher's exact test. Statistical analysis was performed using standard software package (SPSS 17.0; Chicago, U.S.A.). Statistical significance was defined as p-values of less than 0.05.

Results

During the three year study period, 138 patients with clinical, cytological or histological evidence of axillary metastases underwent ANC (median age 57 yrs, range 27–94 yrs). Of these, 89/138 underwent primary ANC as they either had clinical suspicion of axillary metastases[21] or had positive axillary node FNAC (68). The respective positive predictive values for detection of nodal metastases was 66/68 (97.1%) for positive FNAC and 14/21 (66.7%) for clinical suspicion. $P < 0.001$. The remaining 49 patients underwent axillary clearance following positive ANS 12 or SNB 37. (Table 1). The rate of further metastases at completion ANC was 6/12 for ANS and 9/37 for SNB $p = 0.148$.

Of the 89 patients who underwent primary ANC, 80 had nodal metastases. Of the 49 patients undergoing completion ANC, 15 had further metastases present $p < 0.001$. Patients undergoing primary ANC had significantly more positive nodes compared to those who underwent SNB/ANS and completion ANC 4.6 vs. 3.1 $p = 0.037$. The median total number of nodes removed in both groups was fifteen.

Overall, 37 patients with positive SNB underwent ANC. In two patients the tumour had breached the resected node and both had further nodal disease. Of the remaining 35 patients with macrometastases but no nodal breach, 7 had further nodal metastases at ANC. Patients with ultrasonographically normal axillae and positive SNB were significantly less likely to have further positive nodes at completion clearance compared to those with abnormal USS but negative preoperative FNAC 2/23 vs. 5/12 $p = 0.033$ (Table 2). There

Table 1
Axillary metastases detected at ANC based upon indication for surgery.

	Nodal mets	No nodal mets	Overall
Median age (range)	61 (27–94)	56 (37–83)	57(27–94)
Clinical suspicion	14	7	21
USS+ and FNAC+	66	2	68
ANS	6	6	12
SNB	9	28	37
Total	95	43[a]	138

[a] Including 34 patients with positive nodes at ANS or SNB.