The importance of pre-operative axillary ultrasound and intra-operative sentinel lymph node frozen section analysis in patients with early breast cancer – a 3-year study

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ABSTRACT

INTRODUCTION To ensure appropriate axillary surgery is performed at a single operation, we have sought to identify patients with involved nodes who might progress directly to axillary dissection.

PATIENTS AND METHODS We evaluated pre-operative ultrasound of the axilla and intra-operative frozen section of sentinel lymph nodes over a 3-year period. Patients with clinical early breast cancer underwent axillary ultrasound. Abnormal nodes were defined as a cortex > 2.5 mm, loss of high echogenic medulla, and morphological changes. Any axilla containing a lymph node considered abnormal had ultrasound-directed fine needle aspiration (FNA) performed. Patients with positive cytology proceeded directly to axillary dissection. Patients with negative cytology and those with normal ultrasound proceeded to sentinel four-node biopsy using Patent Blue dye alone. A single sentinel node was evaluated by intra-operative frozen section.

RESULTS A total of 311 patients underwent pre-operative ultrasound successfully, identifying 115 (77%) patients of the total 150 who were found to have positive lymph nodes. Overall, 196 patients underwent sentinel lymph node biopsy analysis intra-operatively. Of the 11 false negative cases in which the lymph node was found to be positive postoperatively, eight cases showed the single tested sentinel node contained cancer that was recognised on postoperative staining but not frozen section. In six, the deposit in the sentinel node was a micrometastasis. Three cases were found to contain cancer in the 'non-sentinel' node; in all, this was micrometastatic disease.

CONCLUSIONS This study confirms the value of pre-operative ultrasound and intra-operative frozen section examination of axillary nodes. Only 3.5% of patients required two operations.

KEYWORDS

Ultrasound – Frozen section – Sentinel lymph node – Breast cancer

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Knowledge of axillary lymph node status is essential for the correct management of the patient with early breast cancer. Sentinel node biopsy (SNB) is an established treatment for the identification of axillary node status in patients with breast cancer.¹ Whilst SNB aims to minimise complications by avoiding the excesses of axillary dissection for node-negative patients, for patients with malignant nodes, a second operation, axillary dissection, remains standard treatment. We have evaluated two methods that attempt to identify patients with involved nodes that would allow appropriate axillary treatment to be undertaken as a single procedure.

First, the use of pre-operative axillary ultrasound. According to recent guidelines from the National Institute for Health and Clinical Excellence (NICE), pre-operative axillary ultrasound in patients with breast cancer is now

recommended to assess lymph node status.² In this technique, the ultrasonic appearances of ipsilateral axillary lymph nodes are evaluated; if there is suspicion, ultrasound-guided fine needle aspiration (FNA) is performed.

Second, a sentinel lymph node thought to be clear on pre-operative ultrasound is examined intra-operatively by frozen section analysis.

Patients and Methods

Over a 3-year period, we have evaluated pre-operative ultrasound of the axilla and intra-operative frozen section analysis of sentinel lymph nodes. Patients with clinical early breast cancer and negative staging for distant metastases first underwent axillary ultrasound. Abnormal axillary

lymph nodes were defined as a cortex greater than 2.5 mm, loss of high echogenic medulla, and morphological changes from kidney shape to spherical or eccentric. Any axilla containing a lymph node viewed as not entirely normal had ultrasound-directed FNA performed. Patients with positive cytology proceeded directly to axillary dissection. Patients with negative cytology and those with normal ultrasound appearances of their axillary nodes proceeded to sentinel four-node biopsy.

Sentinel node biopsy was performed using Patent Blue dye that was injected peri-areolarly in the quadrant of the primary tumour. The axilla was then explored and blue-stained afferent lymphatics from the breast were traced and dissected to the first blue stained sentinel node.⁵

Once received in the histopathology department, the sentinel node is stripped of fat, diameter is measured, and 5 µm slices are taken. All of the lymph node is then embedded for frozen section. After initial experience of the technique, the time between the node leaving the operating theatre and the receipt of the frozen section result is less than 25 min.

Results

Over the 3-year period, October 2005 to October 2008, Mayday University Hospital diagnosed 583 new breast

cancers. Figure 1 shows the pathway of pre- and intra-operative evaluation of these patients. Of patients with early breast cancer undergoing surgery, the tumour lay in the right breast in 54%. Overall, 30% of patients underwent mastectomy and 70% had breast-conserving surgery.

Pre-operative ultrasound of the axilla was used to evaluate the 311 patients with early breast cancer undergoing surgery. It successfully identified 115 (77%) patients pre-operatively of the total 150 who were found to have metastatic cancer in the lymph nodes (Table 1). These 115 patients proceeded directly to axillary dissection whilst the remaining 196 patients (aged, 34–86 years) underwent sentinel node biopsy. All 196 patients had a single sentinel lymph node analysed intra-operatively using frozen section and the findings are shown in Table 2.

Of the 11 false-negative cases in which the lymph node was found to be positive postoperatively, eight cases showed the single tested sentinel node contained cancer that was recognised on haematoxylin and eosin (H&E) staining but not frozen section. In six of these eight cases, the tumour deposit in the sentinel node was a micrometastasis. Three cases were found to contain cancer in the non-sentinel node and in all three cases this was micrometastatic disease.

Of the 11 postoperative node-positive patients, all went on to have an axillary node clearance following a full discussion of treatment options.

Table 1 Evaluation of pre-operative axillary ultrasound

	Pre-operative ultrasound lymph node positive	Pre-operative ultrasound lymph node negative	Total
Final histopathology positive	115	35	150
Final histopathology negative	0	161	161
Total	115	196	311

Positive Predictive Value (PPV) 100%; Negative Predictive Value (NPV) 82%; False positive rate 0; False negative rate 23%.

Table 2 Evaluation of intra-operative frozen section analysis

	Intra-operative sentinel lymph node frozen section positive	Intra-operative sentinel lymph node frozen section negative	Total
Final histopathology positive	24	11	35
Final histopathology negative	0	161	161
Total	24	172	196

Positive Predictive Value (PPV) 100%; Negative Predictive Value (NPV) 94%; False positive rate 0; False negative rate 6%.

Discussion

Axillary node status is essential for prognosis, treatment decision and to ensure optimal local control and survival of patients with early breast cancer. As more node-negative patients present, the importance of over-treatment by unnecessary axillary dissection and its accompanying morbidity has gained prominence. NICE has recommended pre-operative axillary ultrasound evaluation for all patients being investigated for early breast cancer.²

We have demonstrated the positive predictive value of pre-operative ultrasound of the axilla. Our figures of detection on pre-operative axillary ultrasound, 77% of node-positive patients, are favourable versus the quoted 40–50%.² However, 23% of patients with positive nodes were undetected by pre-operative ultrasound. Within this group, 13 out of 35 node-positive patients had only micrometastatic disease suggesting this figure may only have a limited potential for improvement with current technology.

Intra-operative examination of lymph nodes, by whatever method, will have its limitations particularly in the detection of micrometastatic disease.^{4,5} In our 11 false-negative patients, nine had micrometastatic disease, defined as tumour deposits ranging from 0.2–2.0 mm, and in only two patients was a macrometastasis missed on H&E examination of the first sentinel node.

Conclusions

This study confirms the value of pre-operative axillary ultrasound and intra-operative frozen section examination of nodes, in combination. We have avoided unnecessary axillary dissection appropriately for 89% of our patients with operable early breast cancer, and for the 35 (11%) in whom axillary dissection was required this was performed as a single operation in 24 patients, and only in 11 (3.5%) of our 311 patients with early breast cancer were two operations required.

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