



The sensitivity of pre-operative axillary staging in breast cancer: Comparison of invasive lobular and ductal carcinoma

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Accepted 26 March 2014
Available online 4 April 2014

Abstract

Introduction: Axillary ultrasound (AUS) with fine-needle aspiration (FNA) biopsy of abnormal lymph nodes is important for pre-operative staging and planning the surgical management of the axilla. Invasive lobular carcinoma (ILC) metastases are thought to be difficult to detect because the cells are small and on cytology resemble lymphocytes. To investigate this we directly compared the sensitivity of pre-operative axillary staging between ILC and invasive ductal carcinoma (IDC).

Method: Consecutive patients that presented in a single breast unit with pure IDC between April 2005 and December 2006 and pure ILC between January 2008 and December 2012 were retrospectively identified from pathology records. Pre-operative axillary ultrasound and FNA biopsy results were compared with post-operative histopathology from the sentinel node biopsy (SNB) or axillary lymph node dissection (ALND).

Results: A total of 275 and 142 axillae were identified in the IDC and ILC groups respectively. In the node positive patients there was no significant difference in the sensitivity of AUS (IDC vs. ILC; 58.7% vs. 52.8%). However, there was a significant difference in the sensitivity of ultrasound-guided FNA biopsy of abnormal nodes (IDC vs. ILC; 98.4% vs. 53.6%; $p < 0.001$).

Conclusion: AUS has comparative sensitivities between IDC and ILC populations. In contrast, FNA biopsy of abnormal axillary nodes is clearly less sensitive in the ILC group. In these patients, who have abnormal AUS, we suggest that a core biopsy is required to improve the pre-operative staging and prevent unnecessary surgical procedures.

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Keywords: Carcinoma; Ductal; Carcinoma; Lobular; Axilla; Sensitivity and specificity; Neoplasm staging; Biopsy; Fine-needle

Introduction

Pre-operative axillary staging in breast cancer consists of an axillary ultrasound (AUS) followed by ultrasound-guided (US-guided) needle sampling if morphologically abnormal lymph nodes are identified.¹ It provides important prognostic information and influences decisions on neoadjuvant chemotherapy and the need for more extensive staging. Furthermore, confirmation of axillary metastatic disease pre-operatively can allow a surgeon to proceed directly to axillary lymph node dissection (ALND) and avoid an additional sentinel node biopsy (SNB).

Invasive ductal cancer (IDC) and invasive lobular cancer (ILC) account for 70–80%² and 5–15%,^{3,4} respectively, of all invasive breast cancers. When compared with IDC, ILC has distinct features and is associated with older age, larger tumour size and is more frequently hormone receptor positive.^{5,6} ILC also has a different pattern of metastatic spread with spread to the gastrointestinal tract and ovary more common.⁷ Loss of expression of the intercellular adhesion molecule E-cadherin is characteristic of ILC.⁸

Of relevance to this study are the different histological appearances of ILC. Lobular carcinoma is characterised by its small, uniform cells with oval or rounded nuclei that may infiltrate tissues without architectural distortion.⁹ Classically, the cells infiltrate the stroma in a single or “Indian file” pattern.¹⁰ ILC may spread diffusely or between

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the collagen fibres in the breast to produce little desmoplastic response.¹¹ These pathological features may account for the higher false negative rate on mammography in diagnosing ILC when compared to other invasive cancers.¹²

The cells in the nodal metastases from ILC are small, resemble lymphocytes and are scattered throughout the lymph node which is thought to make them difficult to detect.¹³ It is with this diagnostic difficulty in mind that we compared the sensitivity of pre-operative axillary staging between ILC and IDC. Two previous studies designed to address this question have shown no difference^{14,15} but a more recent study has shown decreased sensitivity of axillary staging in ILC.¹⁶ Due to the comparative rarity of ILC there are only limited previous studies.

Patients with axillary metastatic disease do not gain any benefit from undergoing an SNB with its associated risks.^{17–19} Moreover, it is time consuming and gives the patient false hope. Therefore, the ability to pre-operatively diagnose as many of these women as possible is clinically important and any difference in the sensitivity of pre-operative axillary staging between ILC and IDC is highly relevant.

Methods

Consecutive patients that presented in a large tertiary level breast unit with pure IDC between April 2005 and December 2006 and pure ILC between January 2008 and December 2012 were retrospectively identified from pathology records. See Table 1 for tumour characteristics. Both symptomatic and screen-detected cancers were studied. Patients with recurrent tumours, previous axillary

surgery, any part of their investigation or treatment at another unit and those patients that did not proceed to surgery were excluded.

Axillary ultrasound was performed by an experienced breast radiologist or breast physician using a 11–15 MHz small parts probe of the GE Voluson 730 Expert system (GE Healthcare, Wauwatosa, WI 53226 U.S.A.). Lymph nodes were assessed for suspicious features, defined as; longitudinal:transverse ratio <2, maximal cortical thickness >2.3 mm, loss of fatty hilum, eccentric or nodular cortical thickening and non hilar blood flow. US-guided FNA was performed on any nodes with suspicious or indeterminate features. Patients with axillary metastases confirmed pre-operatively proceeded directly to ALND. The rest underwent standard dual technique SNB with Patent Blue V dye and technetium (99mTc)–albumin colloid. In accordance with the current Association of Breast Surgery recommendations,²⁰ when isolated tumour cells only were found in axillary nodes they were regarded as node negative.

A database was created from existing computer records to compare pre-operative AUS and fine-needle aspiration (FNA) biopsy results with post-operative histopathology from the SNB or ALND. Invasive tumour size and receptor status were included on the database. Four breast pathologists with at least five years specialist experience in breast pathology had assessed the cytology and histology of the lymph nodes and primary tumours. For oestrogen and progesterone receptors, a positive cut off with a quick score of ≥ 3 was used.

Unless stated otherwise, statistical analysis was performed using Pearson's chi-squared test (SPSS 17.0; Chicago, U.S.A.). $p < 0.05$ was considered statistically significant. Inadequate cytology (detailed in the results) was included in the analysis and counted as negative because a diagnosis of axillary metastases could not be made.

Results

Characteristics of sample populations

A total of 275 IDC and 139 ILC patients (3 ILC patients had bilateral breast cancer) were included in the study. Patient and tumour characteristics are shown in Table 1. In comparison with IDC, ILC was associated with older age, larger tumour size and a higher frequency of receptor positivity. There was no difference in the proportion of patients with node positive disease although of those patients with node positive disease the ILC population had a higher number of positive nodes ($p = 0.002$, N2/3 vs. N1).

Results of axillary staging

The results of the axillary staging for the node positive patients are shown in Figs. 1 and 2. In the node positive

Table 1
Patient and tumour characteristics of the sample populations.

	Invasive ductal cancer ($n = 275$)	Invasive lobular cancer ($n = 142$)	<i>P</i> value
<i>Age</i>			
Mean	61.1	64.4	0.004 ^a
Range	38–89	36–92	
<i>Pathological tumour size</i>			
Mean (mm)	16.2	32.8	<0.001 ^a
Node positive	104 (37.7%)	53 (37.3%)	N.S.
<i>Pathological node stage</i>			
N1	80	28	0.002 ^b
N2	20	16	
N3	4	9	
<i>Oestrogen receptor</i>			
Positive	224	138	<0.001 ^c
Negative	47	2	
Not done	4	2	
<i>Progesterone receptor</i>			
Positive	195	128	<0.001
Negative	75	11	
Not done	5	3	

^a Student's *t*-test.

^b N1 vs. N2/3.

^c Fisher's exact test.

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