UK national survey of management of breast lobular carcinoma in situ

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ABSTRACT

INTRODUCTION There is no national standard treatment for patients with breast lobular carcinoma in situ (LCIS). Association of Breast Surgery guidelines for the management of breast cancer suggest that lesions containing LCIS should be excised for definitive diagnosis and recommend close surveillance after excision biopsy. The aim of this study was to form a picture of the current management of LCIS by UK breast surgeons.

METHODS A questionnaire about the management of LCIS was sent to 490 UK breast surgeons.

RESULTS Of 490 questionnaires sent out, 173 (35%) were returned. When LCIS is present in a core biopsy, 61% of breast surgeons perform surgical excision, 22% would not excise but would continue follow-up and the remainder perform neither or set no clear management plan. Over half (54%) follow patients up with five years of annual mammography. If classic LCIS were found at the margins of wide local excision, 92% would not re-excise. Conversely, if pleomorphic LCIS were found, 71% would achieve clear margins. Respondents were split evenly regarding management of classic LCIS with a family history as 54% would not alter management whereas 43% would treat the disease more aggressively.

CONCLUSION Our survey has shown that in cases where LCIS is found at core biopsy, most surgeons follow Association of Breast Surgery guidance, obtaining further histological samples to exclude pleomorphic LCIS, ductal carcinoma in situ or invasive cancer, whereas others opt for annual surveillance and some discharge the patient. This study highlighted the huge variability in LCIS management, and the need for randomised controlled trials and input into national audits such as the Sloane Project to establish evidence-based national standard guidelines.

KEYWORDS

Breast – Lobular carcinoma in situ – Lobular neoplasia

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Lobular carcinoma in situ (LCIS) is a breast lesion that is usually detected incidentally on biopsy for other indications¹ as lesions often have no clinically or mammographically recognisable signs. LCIS has been reported in 0.5–8% of breast biopsies,² with a greater than 50% increase in incidence having been observed over a 25-year period, from 1.2 per 100,000 women in the 1970s to 2.8 per 100,000 women between 1993 and 1995.³ LCIS has been shown to be associated with an increased risk of future malignancy in both the ipsilateral and contralateral breast, and for this reason and its growing incidence, its detection and subsequent management have become increasingly important.

There are currently three options for the management of LCIS: lifelong surveillance with the goal of early detection of subsequent malignancy; chemoprevention, for which compelling supporting evidence for its indication currently exists; or surgical excision and, historically, prophylactic mastectomy.⁴ Initially considered a precancerous lesion, the evidence reflects a cumulative risk for ipsilateral invasive carcinoma of 18% after the diagnosis of LCIS

and 14% for the contralateral breast.⁵ This resulted in the adoption of less invasive forms of management, with surveillance being the most common strategy used. Evidence in the literature suggests 10–20% of patients identified with LCIS develop breast carcinoma in the 15–25 years after initial diagnosis,⁶ raising the question as to whether greater risk reducing approaches are needed.

The Association of Breast Surgery (ABS) produced guidelines in 2009 for the surgical management of breast cancer, which included surgery for lobular in situ neoplasia (otherwise known as LCIS).⁷ Their guidelines state that owing to level 3 evidence showing an approximately sevenfold increase in the future risk of invasive breast cancer in both breasts, lesions containing LCIS should be excised for definitive diagnosis to exclude coexisting invasive malignancy. They suggest, however, that clear resection margins are not required and a policy of close surveillance afterwards should be followed.^{7,8}

There is currently no agreed national standard treatment for patients with breast LCIS. There are a variety of

different treatments and follow-up policies ranging from surgical excision to annual follow-up appointments with mammography or no treatment at all with no routine follow-up review. As a result, a national survey was undertaken with the aim of collating the different LCIS management policies used by UK breast surgeons, and establishing a national consensus of the best treatment and management of LCIS.

Methods

A survey with 7 questions was sent (together with a free-post envelope for responses) to 490 breast surgeons in the UK in conjunction with the ABS. The questionnaire is shown in Appendix 1 (available online). Overall, 173 questionnaires (35%) were returned to Medway Maritime Hospital’s clinical audit department. The results were collated and analysed, along with free text comments from the responses.

Results

The questionnaire identified that out of the 173 responding breast surgeons, 162 (94%) deal with screen detected breast cancer in patients. The annual caseload for these surgeons ranged from 0 to 900 with the mode number of cases treated annually being 101–200 ($n=66$, 38%).

The participants were asked their current method of management on finding LCIS (without invasive cancer or ductal carcinoma in situ [DCIS]) on core biopsy. Over half of the respondents ($n=101$, 58%) perform diagnostic excision as per ABS guidance, with a further six surgeons (3%) performing therapeutic excision (Table 1). A third ($n=56$, 32%) do not perform excision but two-thirds of these ($n=38$, 68%) proceed to follow-up whereas 18 do not. A few gave other management methods or chose to expand on the options given (eg waiting for multidisciplinary team decisions, performing vacuum assisted biopsies, differentiating between classical LCIS and pleomorphic LCIS lesions, and considering further follow-up after risk assessment).

Table 1 Results for question: ‘If you find lobular carcinoma in situ (without invasive cancer or ductal carcinoma in situ) on core biopsies, do you: ...’	
	Respondents
Perform diagnostic excision	101 (58%)
Perform therapeutic excision	6 (3%)
Not perform excision but follow up patient	38 (22%)
Not perform excision and no follow-up review	18 (10%)
Other	9 (5%)
Not recorded	1 (<1%)
Total	173 (100%)

In terms of surveillance, 134 respondents (77%) arrange annual mammography. Of these, over half ($n=72$, 54%) opt for 5 years of follow-up, with only 17 (12%) continuing for 10 years. Two surgeons declared that they continue annual mammography indefinitely. Five respondents (3%) arrange annual magnetic resonance imaging (MRI) instead.

Participants were also asked what their management plan would be if they were to find classic LCIS at the margins of wide local excision for an invasive cancer or DCIS. The majority ($n=160$, 92%) would perform no further excision. Regarding finding pleomorphic LCIS at the surgical margins, over two-thirds ($n=123$, 71%) expressed that they would perform re-excision to achieve clear margins.

Finally, participants were asked whether they manage patients with pure cases of LCIS and a family history of breast cancer differently. The responses showed an approximately even split with 74 (43%) saying yes and 94 (54%) stating they would not alter their practice. They expanded on this answer with many offering annual mammography for five years or more to such patients, or discussing prophylactic surgery with those who had a very strong family history. A number of surgeons involve their colleagues in clinical genetics to help inform their management decisions, and several mentioned referring to National Institute for Health and Care Excellence guidelines, which suggest using tamoxifen, which has been approved recently as a prophylactic agent for women with a moderate to high risk of subsequent breast cancer determined by their family history.⁹

Discussion

Attempts have been made to develop the ‘gold standard’ LCIS management algorithm. This was believed to depend ultimately on whether LCIS is a non-malignant lesion requiring conservative management¹ or, conversely, whether it is a pre-cancerous lesion warranting surgical excision.⁸

Surveillance

A literature search showed that surveillance is the most common management strategy for LCIS and such practice is in keeping with recommendations by organising bodies such as the National Comprehensive Cancer Network (NCCN).⁴ These clinical practice guidelines recommend annual mammographic screening and clinical breast examinations every 6–12 months in addition to MRI.¹⁰ Although LCIS lesions are characteristically undetectable on mammography,² the basis for surveillance is with the aim of detecting malignancy at the earliest point for intervention. MRI has a greater sensitivity for detecting LCIS than mammography and for this reason, many have advocated for the use of MRI in women with LCIS.^{11,12} However, the impact on survival rate using MRI screening is in need of further investigation as there have been too few randomised controlled trials for evidence to be conclusive.¹³

Chemoprevention

There is good founding evidence for the use of chemoprevention in LCIS and such measures may be of greatest

benefit to women with other risk factors including family history as well as testing positive for *BRCA1/BRCA2* and other associated risk alleles.¹⁴ September 1998 saw the results of the Breast Cancer Prevention Trial conducted under the National Surgical Adjuvant Breast and Bowel Project.¹⁴ Among a patient cohort of 13,338, 862 (6.2%) women were diagnosed with LCIS and the chemotherapeutic agent tamoxifen was found to reduce the risk of breast cancer by 56%.

Surgery

When LCIS was first described, it was treated as a malignancy necessitating mastectomy, like all breast carcinomas at the time.¹⁵ This remained the standard approach until studies demonstrated that the actual risk of breast cancer was lower than expected and that women with LCIS were equally likely to be diagnosed with contralateral as with ipsilateral breast cancer.⁵ The most recent NCCN guidelines recommend surgical excision in all patients diagnosed with a lobular neoplasia on core needle biopsy so as to rule out an associated malignancy.²

Although a number of clinicians are known to carry out these recommendations, the overall approach varies significantly from centre to centre owing to a perceived lack of prospective studies presenting evidence for such interventions.^{1,16,17} Other suggestions include the implementation of certain criteria for surgical excision of LCIS lesions on the basis of having more aggressive cell morphologies and histopathological features overlapping with those of malignancy, such as is observed with subvariants like pleomorphic LCIS.¹⁸ These suggestions perhaps recommend a further subdivision of LCIS management strategy based on core histological and polymorphic features; this is certainly a possibility with the identification of distinguishing markers that are assayable via immunohistochemistry and/or genotyping.^{18,19}

While routine surgical excision following a core biopsy diagnosis of LCIS is employed by some clinicians, a review of the reported rates of upstaging to malignancy demonstrates a wide range of findings, causing difficulty in defining the true rate of cancer at excision. It is a known fact that not all patients with LCIS on core biopsy proceed to excision. There could be an inherent selection bias for excision in certain cases, such as those with discordance between radiology and pathology, which may be the factor that has increased the likelihood of finding an associated malignancy, reflected in the current literature.^{1,20,21}

Current research and practice

The NHS Breast Screening Programme funded the Sloane Project to improve the quality of care for women with screen detected DCIS, and other non-invasive breast cancers such as LCIS and atypical hyperplasia.²² The national audit was launched in 2003 with the aim to produce the largest database in the world, and, ultimately, what might be the optimal treatment for DCIS and other non-invasive breast cancers. To date, over 85% of UK breast screening units are participating and have entered data on over 10,000 patients. The project has already helped guide

management of DCIS but results on LCIS and its management are still awaited.

In our study, in the scenario where a patient has had a core biopsy and only LCIS is found (ie no invasive carcinoma or DCIS), the majority of the breast surgeons surveyed opted to perform diagnostic excision. Some argued that they have had cases where LCIS was left without intervention and there had been a focus of invasive carcinoma or DCIS that had then spread. This result correlates well with the guidance from the ABS.⁷

LCIS shares great similarities in terms of cell morphology with malignant low grade DCIS.²³ The clear distinction between LCIS and DCIS therefore has important therapeutic implications, particularly when considering the significant variance in clinical approach to the two diagnoses. Histologically, LCIS (especially its pleomorphic subtype) appears very similar to DCIS. On the other hand, immunohistochemically and genomically, it is similar to invasive lobular carcinoma. This is supported by the fact that approximately 50–70% of breast carcinomas that have developed in individuals with LCIS are of the invasive lobular type.²⁴ Pleomorphic LCIS in particular is more likely to be associated with malignancy (up to 67% in one series).²⁵ It has been suggested that pleomorphic LCIS, a distinct variant from LCIS, should be treated more aggressively, with surgical excision and clear margins.^{26,27}

It follows that the clearest consensus among the surgeons in the national survey was shown when LCIS was separated into its two subtypes: classic and pleomorphic. The majority of respondents would not proceed to therapeutic excision if biopsy showed classic LCIS but they may perform further diagnostic excision or vacuum assisted biopsy to exclude missed pleomorphic LCIS, DCIS or invasive cancer. In contrast, they would proceed with further surgery until clear margins were achieved if the sample showed pleomorphic LCIS.

There is currently a limited degree of data in the literature reflective of the difference in protocol for the management of LCIS. Once diagnosed, conservative management predominates but only a minority of women pursue chemoprevention, highlighting the need for improved patient education and counselling. The use of chemoprevention in LCIS and its ability to reduce malignancy risk by 56% suggests that chemoprevention provides a viable option owing to its perceived benefits over the 'watchful waiting' of surveillance and the invasive methods of surgical intervention.

There are, however, no randomised controlled trials on the topic of LCIS management, which would help us to better understand the risks of conservative management as well as the efficacy of chemoprevention and surgical resection. The Sloane Project is attempting to address the many ambiguities in the management of LCIS and the results will be influential in the production of standard guidelines for the UK.

Study limitations

Our study was limited by its small sample size with only 35% of surveys returned. Consequently, the findings may not be reflective of the whole of UK practice. Nevertheless,

the study offers an interesting snapshot of current practice and shows the variability in practice among those surveyed.

Conclusions

Regardless of what may ultimately be deemed the most beneficial algorithm, a degree of agreement is required in terms of the guidelines presented to clinicians by the different advisory bodies. Our survey on the management of LCIS has shown a large variation in practice among UK consultant breast surgeons, which adds weight to the argument that a standardised practice needs to be implemented. There is still much ambiguity around the 'correct' management of LCIS. Our study received positive feedback from the responding surgeons, who said that a clear evidence-based consensus on the subject is both needed and greatly encouraged.

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