

Occult breast carcinoma in breast reduction specimens in European women

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Abstract Breast reduction is a common surgical procedure performed by plastic and oncoplastic breast surgeons. The authors report on the incidence and management of cancer and atypical hyperplasia in breast reduction specimens from one institution over a 10-year period. All patients who underwent breast reduction surgery at Northern General Hospital, Sheffield were identified from an electronic prospective database. The histopathology reports were analyzed. Case records of all patients with significant abnormalities were retrieved and examined to identify their management and follow-up. Between October 1999 and April 2010, 1,588 patients underwent breast reduction. Nine specimens showed atypical hyperplasia (0.57%). Five cancers were detected (0.31%). Four of the five patients had normal screening mammograms 1–3 years before the reduction operation. Of these cancers, four were invasive (three lobular, one ductal) (0.25%) and one was DCIS (0.06%). A lump was felt macroscopically by the pathologist in two of the four patients with invasive cancer. The patients with DCIS did not undergo further surgery,

whereas those with invasive disease underwent mastectomy (three patients) and axillary nodal staging (four patients). None of the patients with normal post-reduction breast imaging had residual cancer on histology. The incidence of occult carcinoma in breast reduction specimens is low. Patients should be counseled with regards to the possible consequences preoperatively.

Keywords Breast cancer · Breast reduction · Mammography · Reduction mammoplasty · Screening

Introduction

Breast reduction is a common procedure performed by plastic and oncoplastic breast surgeons in women with macromastia for relief of associated back and neck pain, kyphosis, deep furrows from bra straps, and intertrigo in the skin folds underneath the breasts. Breast reduction is also performed as a symmetrisation procedure in patients with congenital breast asymmetry and after an operation for breast cancer. The procedure effectively alleviates physical and psychological symptoms and improves health related quality of life [1].

The excised breast tissue is commonly sent for pathological examination though this is of 'limited or no clinical value' according to the Royal College of Pathologists [2]. There is a wide variation in the reported incidence of occult breast carcinoma in breast reduction specimens from 0.06 to 0.96% [3–8]. The differences may be attributed to the increased use of screening mammography, differences in patient populations and pathological processing of specimens, reporting on invasive cancers alone, or combined with in situ breast cancer. In addition to breast carcinoma, pathologists may identify atypical breast lesions in breast

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reduction specimens [9]. Sampling of grossly abnormal areas is justified but the value of random sampling for histology is questionable whilst adding to the workload of the pathologist [2].

There are few data on the management of breast cancer found incidentally in the breast reduction specimens. Completion mastectomy is frequently performed in patients where cancer is identified as margin assessment is difficult as specimens are often received in multiple pieces with no orientation.

More evidence is needed to clarify the role of histology in breast reductions and develop clinical practice guidelines for management of these patients. Very little information pertaining to European women is available [2]. The authors report on the incidence and management of cancer and atypical hyperplasia in breast reduction specimens from one institution over a 10-year period.

Methods

All patients who underwent breast reduction surgery at Northern General Hospital, Sheffield over a 10-year period were identified from an electronic prospective database. The histopathology reports were analyzed. Patient demographics, diagnosis, laterality of reduction (bilateral vs. unilateral), specimen weight, macroscopic findings, and microscopic diagnosis were recorded. Case records of all patients with significant abnormalities were retrieved and examined to identify their management and follow-up.

Preoperative evaluation included history and breast examination. Breast size and degree of ptosis determined the technique of reduction. Breast reductions were performed by plastic surgeons using standard breast reduction techniques. All operative specimens were submitted for histopathology examination.

Mammography

The NHS (National Health Service, UK) breast screening programme recommends screening mammography for women starting at 47 years of age every 3 years. Patients with significant risk of familial breast cancer are offered annual mammographic surveillance [10]. Patients diagnosed with early breast cancer including ductal carcinoma in situ, undergo annual mammography for 5 years or until they enter the NHS breast screening programme [11]. However, there are no formal guidelines for surgeons on the use of mammography before breast reduction in the UK. Patients undergoing breast reduction were not offered mammography prior to surgery unless indicated by findings on physical examination.

Pathological assessment

The specimens were received as multiple fragments and were not orientated. The protocol for examination of the reduction specimens was to slice all at 1 cm intervals and examine macroscopically. At least three random blocks per breast were examined microscopically in addition to sampling of any grossly abnormal tissue. All suspicious areas were sectioned and examined microscopically. A macroscopic abnormality was defined as the presence of pronounced irregular fibrosis, discrete mass or defined nodule. Microscopically typical fibrocystic disease and skin lesions were not included in this definition. No specimen radiographs were routinely obtained during this study period. All breast tissue was processed and examined by a single pathology department.

Statistical analyses

PASW Statistics 18.0 was used for data entry and analyses. 95% confidence intervals are reported for proportions.

Results

Between October 1999 and April 2010, 1,588 patients underwent breast reduction. Their clinico-pathological characteristics are summarized in Table 1. 341 underwent unilateral reduction (21.5%) and 1,247 underwent bilateral reduction (78.5%). Indications for surgery were macromastia in 1,194 (75.2%), congenital asymmetry in 182 (11.5%) and contralateral symmetry procedure post breast

Table 1 Patient characteristics

Variable	<i>n</i> = 1,588
Indication for breast reduction	
Macromastia	1,194 (75.2%)
Congenital breast asymmetry	182 (11.5%)
Contralateral cancer	178 (11.2%)
Age at date of surgery (years), mean (SD)	39 years (13)
Macromastia	38 years (11)
Congenital breast asymmetry	32 years (14)
Contralateral cancer	54 years (9)
Unilateral versus bilateral	
Unilateral	341 (21.5%)
Bilateral	1,247 (78.5%)
Specimen weight (grams), mean (SD)	
Left	607.6 (401.9)
Right	595.4 (346.8)

cancer surgery in 178 (11.2%). Congenital asymmetry patients were younger than other groups.

14 patients were found to have a lump, two a nodule and two a warty brown growth on macroscopic examination. Of the 14 patients with a lump, microscopic examination revealed that two had invasive carcinoma, one intraductal papilloma, five fibroadenoma, four fibrocystic changes and two duct ectasia. Intraductal papilloma was found in one patient with a warty growth while microscopic examination was normal in the remaining three patients.

Findings on microscopic examination are listed in Table 2. Nine specimens had atypical hyperplasia (0.57, 95 CI 0.30 to 1.07%). These women were referred to the breast surgeons to have a discussion about their risk and institute a plan for breast surveillance based on their risk estimates.

Five cancers were detected (0.31, 95 CI 0.13 to 0.73%) (macromastia-3/1,194 (0.25, 95 CI 0.09 to 0.74%), asymmetry-0/182 (0, 95 CI 0 to 2.07%), contralateral cancer-2/178 (1.12, 95 CI 0.31 to 4.0%)).

Clinical follow up with the breast surgeons was arranged for all patients with a diagnosis of DCIS or invasive malignancy. Four of the five patients had normal screening mammograms 1–3 years before the reduction operation (not done in one). Of these cancers, four were invasive (three invasive lobular, 1 invasive ductal) (0.25, 95 CI 0.10 to 0.65%) and one was DCIS (0.06, 95 CI 0.01 to 0.36%) (Table 3). A lump was felt macroscopically by the pathologist in two of the four patients with invasive cancer. Margin assessment was difficult as the specimens were received in multiple pieces without orientation. Three of the four invasive cancers were ER positive and all were HER-2 negative. The patient found to have DCIS did not undergo

further surgery while three of the four with invasive disease underwent mastectomy. Of the four patients with invasive disease, one was found to have nodal metastasis. None of the patients with benign/normal post-reduction breast imaging had residual breast cancer on histology. The two patients who did not undergo mastectomy remain disease free. One patient was found to have residual disease on post-operative mammogram and this was confirmed on histopathological assessment of the completion mastectomy specimen. In addition, this patient was found to be node positive, developed distant metastases on follow-up and died 6 years after diagnosis (Table 3).

Discussion

This study defines the incidence of occult breast carcinoma and spectrum of pathology identified in a large cohort of consecutive, non-selected breast reduction specimens. This largest single-centre European study shows a 0.31 percent incidence of occult breast carcinoma, similar to some North American studies with overlapping confidence intervals [3, 4]. Other studies have found a lower [5] or higher [12] incidence and this is attributable to marked variations in specimen processing, patient populations, preoperative workup, disparities in data collection, and reporting. Women with a primary breast cancer are at a twofold to sixfold higher risk of contralateral breast cancer [13, 14]. Similar to previous studies, the rate of occult carcinoma was higher in those with unilateral cancer who underwent a contralateral breast reduction (1.12%). No cancer was detected in the congenital asymmetry group. It was observed that all cancers were found in women older than 45 years consistent with the breast cancer risk in the general population.

Histological examination of the entire breast reduction specimen would be labor intensive and not practical whereas random selection of two or three blocks of tissue means less than one percent of tissue submitted is examined under the microscope. Sampling error might underestimate the true incidence of occult carcinoma in reduction specimens. The findings of a lump in two of the four invasive cancers on macroscopic examination support the importance of palpation of the tissue to identify suspicious areas and target microscopic examination. The surgeon should mark these areas before sending the tissue for histopathology evaluation, particularly since fixation may harden tissue and make later palpation more difficult. An alternative strategy would be to perform specimen radiography on all breast reduction specimens and restrict microscopic examination to those with radiological or gross abnormality, although this would be expensive and has not been investigated in this study.

Table 2 Histopathological findings in breast reduction specimens

Histology	Number of patients (<i>n</i> = 1,588)
Atypical hyperplasia	8
Atypical hyperplasia and LCIS	1
DCIS	1
Invasive carcinoma	3
Invasive carcinoma and LCIS	1
Intraductal papilloma	11
Papillomatosis	3
Fibroadenoma	30
Adenomyoepithelioma	2
Hamartoma	1
Lipoma	1
Radial scar	1
Other benign/normal	1,525

DCIS ductal carcinoma in situ, LCIS lobular carcinoma in situ

Table 3 Characteristics and management of patients found to have occult carcinoma

Variable	Patients with occult carcinoma in breast reduction specimens				
	1	2	3	4	5
Age (years)	68	57	47	55	65
Breast reduction					
Indication	Macromastia	Contralateral cancer	Macromastia	Macromastia	Contralateral cancer
Unilateral or Bilateral	Bilateral	Unilateral	Bilateral	Bilateral	Unilateral
Preoperative mammogram (years before surgery)	2 years	1 years	Not done	3 years	3 years
Gross inspection	Lump	NS	Lump	NS	NS
Histology	Invasive lobular	Invasive lobular	Invasive ductal	Invasive lobular	Comedo DCIS
Total size, mm	12	4	18	2	4
Invasive size, mm	12	4	18	2	NA
Grade	3	2	3	2	High
Microcalcification	No	No	No	No	No
ER/HER-2	+/-	+/-	-/-	+/-	Not done
Unifocal or multifocal	Unifocal	Unifocal	Unifocal	Unifocal	Unifocal
Excision margins	Not assessable	Not assessable	Not assessable	Not assessable	Not assessable
Residual cancer on post breast reduction imaging					
MRI	No	Not done	Not done	No	Not done
Mammogram	No	Yes	No	No	No
Ultrasound	Not done	Not done	Not done	No	Not done
Treatment					
Mastectomy	Yes	Yes	Yes	No	No
Residual tumor	No	Yes	No	NA	NA
Axillary nodal staging	SNB	ALND	ALND	FNS	No
Nodal metastases	No	1/27	No	No	NA
RT	No	No	No	Yes	No
Chemotherapy	No	Yes	Yes	No	No
Endocrine treatment	Yes	Yes	No	Yes	No
Follow-up (months)	16	71	125	8	79
Recurrence/distant metastasis	No	Distant metastases	No	No	No
Outcome	Alive	Dead	Alive	Alive	Alive

ALND axillary lymph node dissection, ER estrogen receptor, FNS four node sampling, HER-2 human epidermal growth factor receptor, NA not applicable, NS nil significant, RT radiotherapy, SNB sentinel node biopsy

Routine mammography prior to surgery was not performed in this study and therefore no comment is possible on the usefulness of routine mammography prior to breast reduction surgery. A survey of breast and plastic surgeons in the UK published recently showed that 92% breast surgeons and 41% plastic surgeons routinely perform mammography prior to breast reduction [15]. In the United States, mammograms are performed routinely in all patients over 40 [16] but multiple North American studies have failed to demonstrate its usefulness in identification of early breast cancer [6, 17, 18].

Margin assessment is imprecise as the tissue is typically removed in several pieces and not oriented before sending to histopathology. This complicates subsequent treatment if

cancer is present in multiple pieces, or if the tumor is close to a margin. Re-excision of the entire breast reduction margins is impractical as this will remove a large amount of breast tissue causing significant deformity. Mastectomy is usually performed and is justified in patients with multifocal tumors, scattered in multiple pieces from the breast reduction. It may be performed through the previous Wise-pattern incision including scar excision.

Patients found to have invasive carcinoma should undergo nodal staging. Breast reduction involves extensive gland mobilization and lymphatic disruption. However, there is increasing evidence to support the use of sentinel lymph node biopsy in this setting with less than 5% failure rate [19, 20]. However, the published series have a small

sample size and further follow-up data are needed on local axillary recurrence as data on false-negative rate are lacking.

In conclusion, histopathological examination of breast reduction specimens may reveal occult carcinoma and lesions that increase the risk of developing breast carcinoma. Patients should be counseled with regards to the possible consequences preoperatively. Surgeons should orientate clinically abnormal breast tissue before sending it for histopathological examination to aid margin assessment.

Conflict of interest None.

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