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EPIDEMIOLOGY

Incidental breast carcinoma: incidence, management, and outcomes in 4804 bilateral reduction mammoplasties

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Abstract

Introduction Bilateral reduction mammoplasty is one of the most common plastic surgery procedures performed in the U.S. This study examines the incidence, management, and prognosis of incidental breast cancer identified in reduction specimens from a large cohort of reduction mammoplasty patients.

Methods Breast pathology reports were retrospectively reviewed for evidence of incidental cancers in bilateral reduction mammoplasty specimens from five institutions between 1990 and 2017.

Results A total of 4804 women met the inclusion criteria of this study; incidental cancer was identified in 45 breasts of 39 (0.8%) patients. Six patients (15%) had bilateral cancer. Overall, the maximum diagnosis by breast was 16 invasive cancers and 29 ductal carcinomas in situs. Thirty-three patients had unilateral cancer, 15 (45.5%) of which had high-risk lesions in the contralateral breast. Twenty-one patients underwent mastectomy (12 bilateral and nine unilateral), residual cancer was found in 10 in 25 (40%) therapeutic mastectomies. Seven patients did not undergo mastectomy received breast radiation. The median follow-up was 92 months. No local recurrences were observed in the patients undergoing mastectomy or radiation. Three of 11 (27%) patients who did not undergo mastectomy or radiation developed a local recurrence. The overall survival rate was 87.2% and disease-free survival was 82.1%.

Conclusions Patients undergoing reduction mammoplasty for macromastia have a small but definite risk of incidental breast cancer. The high rate of bilateral cancer, contralateral high-risk lesions, and residual disease at mastectomy mandates thorough pathologic evaluation and careful follow-up of these patients. Mastectomy or breast radiation is recommended for local control given the high likelihood of local recurrence without either.

Keywords Reduction mammoplasties · Incidental cancer · Breast cancer · High-risk breast lesions

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Introduction

Reduction mammoplasty is one of the most common plastic surgery procedures, with 109,000 such operations performed in the United States in 2016 [1]. The indications for reduction mammoplasty are macromastia, congenital asymmetry, and asymmetry due to contralateral breast cancer treatment. The prevalence of incidental cancer in reduction specimens ranges from 0.06 to 5.45%. The incidence is higher in older women and in patients with a history of contralateral breast cancer [2–8]. Studies of patients with a history of contralateral breast cancer report an incidence range of 1.2% to 4.5% [3–5], while papers excluding patients with prior cancer report an incidence range of 0.7% to 0.95% [4, 5]. The aforementioned studies are limited to small data sets; only three

papers contained more than 1000 reduction mammoplasty cases [7–9]. As a result, there are insufficient reduction mammoplasty data to fully understand the incidence, management, and prognosis of incidental breast cancer.

Theoretically, the electronic health record (EHR) should aid the execution of large cohort studies. Unfortunately, however, most medical information is recorded as free text, which limits the usefulness of the EHR for research. Manual curation is required to turn free text into structured data to fully access EHR data. Moreover, the difficulty, high cost, and significant time associated with manual extraction limits the size of the final data sets. Fortunately, the advent of natural language processing (NLP) has provided a plausible solution. NLP can be applied to decipher information locked in the EHR. Several previous studies have shown that NLP can extract medical information from the EHR with a satisfactory accuracy rate [10, 11].

In this study, we applied NLP to all electronically available breast specimen pathology reports from five institutions over a 27-year period. The NLP algorithm identified close to 5000 patients who underwent bilateral mammoplasty for macromastia without prior breast cancer. We identified those with incidental cancers using the NLP algorithm supplemented by manual chart review. Our goal was to better understand the incidence, management, and outcomes of cancers incidentally encountered in bilateral mammoplasty procedures.

Methods

With Institutional Review Board approval, we retrospectively collected electronically available breast pathology reports between 1990 and 2017 from five institutions within Partners® Healthcare system, including Massachusetts General Hospital, Brigham and Women's Hospital, Faulkner Hospital, North Shore Medical Center, and Newton-Wellesley Hospital. Mammoplasty specimen reports and any prior pathology reports were retrieved and reviewed for evidence of breast cancer and high-risk breast lesions.

NLP was used to identify and extract structured data from the pathology reports. The methods and details of this program have been previously reported [11]. In short, data from all reports of bilateral breast surgeries were categorized by side, thus representing two pathology reports (one for each side). The Machine Learning Model (MLM) was developed using an annotated training data set. When the model was developed, it was used to extract 20 pathologic entities from each pathology report and create a database [11]. For the purpose of this study, we included cancerous lesions, such as invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), ductal carcinoma in situ (DCIS), and high-risk breast cancer lesions, including atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), lobular carcinoma in situ (LCIS), and severe ADH bordering on DCIS. Each entity was recorded as either present or absent. All mammoplasty cases and their associated diagnoses were confirmed by manual review of each pathology report.

We included any female who underwent bilateral mammoplasty, including patients with a history of lesions with higher risk of breast cancer, but excluded those with history of breast cancer. Patients with incidental cancer (IDC, ILC, and DCIS) at the time of mammoplasty were identified and our patient cohort was created. A manual retrospective review of the EMR of this cohort was subsequently performed to collect patient and tumor characteristics, local and systemic treatments, follow-up and local, regional, and distant recurrences. Duration of follow-up was from the time of surgery to the time of last follow-up. If a patient experienced a recurrence and/or metastasis, the time of event was recorded.

Results

We identified 4804 women without prior breast cancer who underwent bilateral reduction mammoplasty procedures over a 27-year period. This amounted to 9608 individual breast pathology reports (by side). Overall, 45 breasts in 39 (0.81%) patients were found to have incidental cancer, including 16 invasive cancers and 29 DCIS.

The median patient age of the 4804 women was 40 (range 13–86) years [12]. The median patient age of those diagnosed with cancer was 53 (range 29–69) years. Three (7.7%) patients were under the age of 40, and 36 patients were over age 40. 17 of those 36 (47%) had a documented mammogram within a year of surgery, 6 (16.7%) had a mammogram report 13 to 36 months before surgery, and the remaining 13 patients had no mammogram results documented within 3 years of the mammoplasty.

Twenty-three women had mammogram results available within 3 years of mammoplasty. Twenty-one (91%) of the 23 was negative, while two identified calcifications that were biopsied with negative results. The first patient had a core biopsy demonstrating stromal calcifications which was concordant with the mammographic findings. She underwent bilateral mammoplasty 3 months later and DCIS was found in the same breast with stromal calcifications. The second patient's calcifications showed ADH on core biopsy and subsequent excisional biopsy showed biopsy site changes and ADH. DCIS was found in her bilateral breasts 1 year later at mammoplasty. Although both breasts with suspicious calcifications on mammogram eventually found DCIS at the time of mammoplasty, we found no evidence to suggest that the biopsied calcifications were related to the incidental cancer during mammoplasty.

Fifteen (38.5%) patients had a maximum diagnosis of invasive cancer (IC) and the remaining 24 (61.5%) patients had pure DCIS. Six patients (15%) had bilateral cancer, where three were bilateral DCIS, one was bilateral IC, and two were IC with contralateral DCIS. 33 patients had unilateral disease, of which 15 (45.5%) women had high-risk lesions in the contralateral breast. Overall, 45 breasts in this cohort contained cancer, including 16 invasive cancer and 29 DCIS. 14 of 16 invasive cancers and 21 of 29 DCIS were grade 1 or 2, and all sizes of invasive cancer were less than 2 cm, except one patient with 2 cm IDC at mammoplasty and 7 cm residual disease at mastectomy. The patient and tumor characteristics are shown in Table 1.

19 of 39 (48%) patients had breast MRI, after an incidental breast cancer diagnosis at mammoplasty, for further management planning. None of the patients had abnormal enhancement or MRI evidence of residual cancer. In the 19 patients, nine ended up having mastectomy and three actually had residual disease in mastectomy specimens, including two with residual DCIS and one with residual IDC (Table 2). In other words, MRI failed to identify all three patients with residual disease.

Twenty-one patients underwent mastectomy following their cancer diagnosed at mammoplasty. 12 patients had bilateral mastectomy and nine had unilateral mastectomy. In the 33 mastectomies, 25 were therapeutic and eight were prophylactic. Residual cancer was found in ten of the 25 (40%) therapeutic mastectomy specimens: six invasive and four DCIS only. No cancer was found in any of the eight prophylactic mastectomy specimens. Details of their management and outcomes are presented in Table 2.

Eighteen patients did not undergo mastectomy for incidental cancerous finding. Margins statuses for these patients were not available because margins were not typically evaluated for mammoplasty specimens in our system at that time. Among these patients, one had an 8-mm invasive lobular cancer and was found to have distant metastatic disease within 2 weeks after mammoplasty, before planned mastectomy. She received chemotherapy and hormonal therapy. Two patients with 5-mm and 9-mm invasive ductal cancers, respectively, elected to manage their cancer with whole breast radiation and hormonal therapy. The remaining 15 cases were pure DCIS: 4 managed with radiation only, three with hormonal therapy only, one with both radiation and hormonal therapy, and seven with active observation.

For the 21 women who underwent mastectomy, 13 patients had sentinel lymph node biopsy (SLNB) at the time of mastectomy, six SLNB for invasive cancer, and seven for DCIS. Eight patients with invasive cancers had axillary lymph node dissection (ALND). These patients were either treated before the sentinel node era, or had positive sentinel nodes, or had failed sentinel node mapping after mammoplasty. Overall, four patients had positive lymph nodes (number of positive lymph node(s): 1, 2, 5, and 6) (Table 2).

The median follow-up was 92 months for all patients. There was no local recurrence in all 21 patients who underwent mastectomy as their definitive treatment or in all seven patients who did not receive mastectomy but received breast radiation. Three of 11 (27%) without either mastectomy or RT had local recurrence/new cancer at 8, 22, and 27 months after mammoplasty, respectively. One of our patients had a very small focus of DCIS at mammoplasty without further treatment, but 22 months later was found to have invasive lobular carcinoma (ILC) in that breast with simultaneous distant metastasis. These patients had invasive local recurrences/new cancer that started with pure DCIS found at mammoplasty, and none received chemotherapy, only 1 received hormonal therapy at the time of found DCIS. One of the three patients died at 36 months and the other two survived without metastasis disease at 138 months and 176 months. We observed an overall recurrence rate of 7.7% (3/39). However, since there was no local recurrence observed in patients who received mastectomy or breast radiation, the local recurrence rate is 27% (3/11) in those did not receive either mastectomy nor breast radiation.

Five (13%) patients developed metastatic disease, including one who was found to have metastatic disease 2 weeks after mammoplasty (mentioned above). The remaining four included: two patients with IC, both managed with mastectomy and hormone therapy, were found to have metastatic disease at 30 and 38 months after mammoplasty, respectively. One patient with an initial diagnosis of DCIS that was upgraded to IDC with a positive node at mastectomy, who was subsequently treated with adjuvant hormonal therapy, was found to have metastatic disease in the 65th month after mammoplasty and the fourth patient was initially diagnosed with DCIS but did not receive any further local or systemic treatment due to comorbidities. That patient was found to have an in-breast invasive recurrence and metastatic disease both discovered in the 22nd month after mammoplasty. All five patients died of metastatic breast cancer. Outcomes and event times are described in Table 2.

The overall survival (OS) rate was 87.2%; disease-free survival (DFS) was 82.1% at a median follow-up of 92 months. OS and DFS for DCIS was 92% and 83%, respectively, while both OS and DFS for IC was 80%. In those patients who underwent completion mastectomy, OS and DSF were both 85%. Among the patients who did not undergo prophylactic contralateral mastectomy, 12 breasts had high-risk lesions and 13 did not. No new breast cancers were found in the contralateral breasts with high-risk lesions, but one new breast cancer developed in a breast without high-risk lesion identified at mammoplasty 122 months after surgery.

Table 1 Patient and tumor characteristics

Patients ($n=39$) characteristics	
Age (range)	53 (29–69) years
Menopause	
Pre	13
Post	22
NA	4
Mean BMI (range)	32 (23–45) kg/m^2
History of OCP	
Yes	15
No	6
NA	18
History of HRT	
Yes	11
No	11
NA	17
Family history of breast cancer	
Yes	14
No	19
NA	6
Median follow-up (range)	92 (2–230) months
Mean weight of removed tissue per breast at mammoplasty	720 (245 to 2035)
Maximum primary tumor type per patient	
IC	15
DCIS	24
Tumor ($n=45$) features	
Tumor type per breast	
IC	16
DCIS	29
Tumor grade for invasive	
1	5
2	9
3	2
Tumor grade for DCIS	
1	15
2	6
3	6
NA	2
Invasive cancer size	
≤ 0.5 cm	7
0.5 to ≤ 1 cm	3
1 to ≤ 2 cm	5
>2 cm	1 (7 cm)
ER for invasive	
Positive	11
Negative	1
NA	4
ER for DCIS	
Positive	14
Negative	3
NA	12
PR for invasive	
Positive	10
Negative	4
NA	2
PR for DCIS	
Positive	14
Negative	3
NA	12
HER2 for invasive cancer	
Positive	2
Negative	10
NA	4

BMI is body mass index, *DCIS* is ductal carcinoma in situ, *ER* is estrogen receptor, *HER2* is human epidermal growth factor receptor 2, *HRT* hormone replacement therapy, *IC* invasive carcinoma, *OCP* oral contraceptive pills, *PR* is progesterone receptor

Discussion

While EHRs contain vast amounts of clinical data, almost all of the critical medical information is recorded as free text. Manually extracting this information is time consuming and requires specialized knowledge, not only making it costly, but also limiting the size of the ultimate data set. The advent of NLP presents a unique opportunity to streamline this process. This paper exemplifies the utility of NLP for the autonomous extraction of data from EHRs in order to create databases large enough to answer clinical questions.

Bilateral reduction mammoplasty specimens present a small but unique opportunity to reveal incidental breast cancers in women without prior history of cancer. In this study, we utilized an NLP algorithm to identify a large cohort of patients (close to 5000) with no personal history of breast cancer undergoing bilateral mammoplasty for macromastia. Using this approach, the incidence of breast cancer in bilateral mammoplasty patients was 0.8%. Most cancers found at mammoplasty were DCIS, and if invasive, were low grade and small, making them difficult to detect on imaging. [4, 13] Indeed, 14 of 16 invasive cancers and 21 of 29 DCIS were grade 1 or 2, and 15 out of 16 (94%) invasive cancers were stage T1 (<2 cm), representing early disease (Table 1). The only exception is a patient had 2 cm IDC and 7 cm residual IDC at mastectomy, this patient did not have MRI after mammoplasty but did have 5/19 positive lymph nodes at axially node dissection, she was followed 213 months without recurrence or metastasis (Table 2).

Although some tumors are mammographically occult, preoperative mammogram remains the most practical and

Table 2 Management and outcomes of incidental breast cancer in reduction mammoplasties

Disease cohorts		Post-mammoplasty MRI	Management				Outcomes (follow-up time, mo = months)
			Mastectomy	Residual disease at mastectomy	Axillary surgery, and node status*	Other treatments**	
Bilateral disease ($n=6$)	Bilateral IC ($n=1$)	No	Bilateral	Yes, bilateral	ALND neg (B/L)	HT	No known recurrence or metastasis at 92 mo
	Bilateral DCIS ($n=3$)	Yes	Bilateral	No	SLNB neg (B/L)	No	No known recurrence or metastasis at 68 mo
		No	Unilateral***	Yes	None	XRT (side without mastectomy)	No known recurrence or metastasis at 151 mo
		Yes	None****	n/a	None	No	No known recurrence or metastasis at 103 mo
	IC with contralateral DCIS ($n=2$)	No	Bilateral	No	SLNB neg (B/L)	No	No known recurrence or metastasis at 70 mo
		No	Bilateral	Yes, invasive side	ALND neg (IC side only)	HT	No known recurrence or metastasis at 230 mo
Unilateral disease ($n=33$)	IC ($n=12$)	No	Bilateral	No	SLNB neg	HT	No known recurrence or metastasis at 66 mo
		Yes	Bilateral	No	SLNB neg	No	No known recurrence or metastasis at 135 mo
		Yes	Bilateral	No	ALND neg contralateral SLNB neg	No	No known recurrence or metastasis at 16 mo
		No	Bilateral	No	ALND, 2/17 pos	No	metastasis at 30 mo, deceased at 63 mo
		Yes	Unilateral	No	SLNB, neg	HT	metastasis at 38 mo, deceased at 95 mo
		No	Unilateral	Yes	ALND, 5/19 pos	XRT, chemo	No known recurrence or metastasis at 213 mo
		Yes	Unilateral	Yes	ALND, 6/20 pos	XRT, chemo	No known recurrence or metastasis at 110 mo
		Yes	Unilateral	Yes	ALND, neg	No	No known recurrence or metastasis at 80 mo
		No	Unilateral	No	None	HT	No known recurrence or metastasis at 126 mo
		Yes	None	n/a	SLNB, neg (B/L)	XRT	No known recurrence or metastasis at 2 mo
		No	None	n/a	None	XRT, HT	No known recurrence or metastasis at 68 mo
		Yes	None	n/a	None	HT, Chemo	Metastasis at 0 mo, deceased at 27 mo

Table 2 (continued)

Disease cohorts	Post-mammoplasty MRI	Management				Outcomes (follow-up time, mo = months)
		Mastectomy	Residual disease at mastectomy	Axillary surgery, and node status*	Other treatments**	
DCIS ($n=21$)	No	Bilateral	Yes (at cancer side)	SLNB, neg	No	No known recurrence or metastasis at 122 mo
	No	Bilateral	No	SLNB, neg	No	No known recurrence or metastasis at 95 mo
	Yes	Bilateral	Yes (cancer side)	ALND, 1/6 pos	HT	DCIS upgrade to IDC at mastectomy. ALND was done due to positive SLN. Metastasis at 65 mo, deceased at 94 mo
	Yes	Bilateral	No	None	HT	No known recurrence or metastasis at 60 mo
	No	Unilateral	No	SLNB, neg	No	No known recurrence or metastasis at 5 mo
	Yes	Unilateral	No	SLNB, neg	HT	No known recurrence or metastasis at 145 mo (developed contralateral breast cancer at 112 mo)
	No	Unilateral	Yes	None	No	No known recurrence or metastasis at 132 mo
	No: 7 Yes: 7	None ($n=14$)	n/a	None	See details at right	11 no known recurrence or metastasis at 7(HT), 10 ^{M}, 44 ^{M} (XRT), 47 ^{M}, 74(XRT), 74, 92 ^{M} (XRT, HT), 110 ^{M} (XRT), 116 ^{M} (HT), 164 ^{M} (XRT), 193 mo 1 in-breast invasive recurrence at 8 mo, no known metastasis at 138 mo(HT) 1 Ipsilateral new ILC and metastasis both at 22 mo, deceased at 36 mo 1 in-breast invasive recurrence at 27 months, no known metastasis at 176 mo

HT hormonal therapy, only patients finished 5 years of hormonal therapy was marked, *XRT* breast radiation therapy, only breast radiation to treat incidental cancer at mammoplasty marked, *ALND* axillary lymph node dissection, *SLND* sentinel lymph node biopsy, *DCIS* ductal carcinoma in situ, *IC* invasive cancer, *IDC* invasive ductal carcinoma, ^{M} patient had breast MRI to evaluate residual disease after incidental cancer at mammoplasty, *B/L* bilateral

*Axillary surgery at Cancer side only unless specified

**Only those treat incidental cancer at mammoplasty, not including treatment at recurrence or metastasis

***Contralateral radiation for single focus of Grade 1 DCIS

****Bilateral small and low-grade foci of DCIS thought to be associated with ADH

cost-effective method for screening prior to mammoplasty in those who are eligible. We found that incidental breast cancer in bilateral mammoplasty in women under 40 years was 0.16% compared to 1.47% in the older group [12], assuming that most women over 40 years had mammograms and those diagnosed with breast cancer were already excluded from our study. We did not study the efficacy of preoperative screening mammography in women under age 40, though the low incidence of cancer in this population would make that approach hard to justify. Other than routine mammogram, only the patient's family history and findings on physical examination in the preoperative setting might suggest the need for further investigation.

In our study, the mammoplasty surgeries were all performed by plastic surgeons, and only 47% of patients over 40 years had mammograms documented within 1 year before surgery. This finding is concordant with literature. There was a survey performed in the United Kingdom [14], published in 2009, regarding the use of preoperative mammogram in patients undergoing bilateral reduction mammoplasty. In this survey, among patients aged 40 to 50, only 53% of plastic surgeons offered radiological screening preoperatively. In patients over 50, 73% of plastic surgeons did so. However, plastic surgeons were reported to do radiological screening in patients with a family history of breast cancer (91%) and previous breast cancer (93%) [14]. We would suggest awareness should be raised among plastic surgeons to ensure appropriate breast imaging studies in patients over 40. For high-risk patients, including patients with a family history of breast cancer, personal history of high-risk breast lesion, or previous breast cancer, genetic testing and/or MRI should be considered.

We found that postoperative MRI had limited sensitivity to identify residual cancer after reduction mammoplasty in our cohort. This might be because rearrangement of breast tissue during the mammoplasty leads to significant postsurgical changes, which might have masked residual disease. Also, the initial tumor and residual disease were all small in this cohort, which would be harder to detect on imaging. If observation is opted over mastectomy or radiation, repeat bilateral breast MRI in 6 months when postoperative changes have resolved should be considered.

In our cohort, we found no local recurrence observed in 28 patients who were treated with either mastectomy and/or breast radiation in 92 months median follow-up. However, there was relatively high local recurrence (27%) in the patients without either mastectomy or breast radiation. In patients receiving therapeutic mastectomy, there was a high rate (40%) of residual disease. Considering the rate of residual disease and difficulties in mammoplasty specimen orientation, mastectomy is a reasonable choice for most patients. If mastectomy is not chosen as an option, our data, while limited, do suggest that radiation may be preferable to observation.

Is breast-conserving surgery a possible option for managing incidental cancer in mammoplasty? Margins are essential for breast-conservation surgery; however, mammoplasty specimens are usually made up of multiple unoriented pieces of tissue and it is therefore difficult to assess the margins or the location of the incidental cancer. In addition, plastic surgeons usually rearrange the breast tissue significantly during the procedure. Lack of orientation and difficulty determining location of the cancer in the reorganized breast makes targeted partial mastectomies nearly impossible [2, 5]. Slezak et al. [5] developed a special way of orienting the tissues for their pathologist to aid the identification of marginal status. In their cohort, there were ten cases of occult carcinoma among the 866 women (1.15 percent) who underwent reduction mammaplasty. Attempts were made to treat nine incidental cancers with breast-conserving therapy. Six were considered to have adequate resections at mammoplasty, thus only radiation and/or antiestrogens were offered, and three had additional margins taken (1 of which had a persistent positive margin and eventually underwent mastectomy). Over the 1 to 12 years of follow-up, one out of eight patients had in-breast recurrence 4 years after mammoplasty. Based on the small numbers of cancer found in this study, it is unclear whether implementing this orientation system is practical or effective.

In this current study, 45% of the 33 patients with unilateral breast cancer were found to have a high-risk lesion in the contralateral breast at mammoplasty. Freedman's study [15], which evaluated women with subsequent contralateral high-risk lesions in reduction mammoplasty, suggested an incidence rate of 21%, after being treated with unilateral breast cancer. This rate of high-risk lesion [15] discovery is lower than our study, possibly because their patients had prior breast cancer treatment, including hormonal therapy, for primary cancer management before mammoplasty.

Conclusion

In this study, we applied NLP in addition to manual chart review, to all electronically available breast specimen pathology reports from five institutions over a 27-year period. Using the semi-automated approach, we were able to identify close to 5000 patients who underwent bilateral mammoplasty for macromastia without prior breast cancer. We found that the risk of incidental breast cancer was 0.8%. Because of this, we recommended routine preoperative imaging for cancer screening as appropriate to age and risk level and thorough pathologic evaluation of the removed breast tissue. Patients treated without mastectomy or breast

radiation therapy appear to be a high risk for recurrence and need to be followed closely.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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