Mastectomy and Contralateral Prophylactic Mastectomy Rates: An Institutional Review

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ABSTRACT

Background. Breast conservation surgery (BCS) followed by radiation is as effective as mastectomy for long-term survival and is considered standard of care for early-stage breast cancer. An increasing number of patients are opting for cancer-side mastectomies (CM) and often contralateral prophylactic mastectomies (CPM). Our study investigates if there are increasing trends in our patient population toward CM and CPM and identifies common factors associated with those electing to have more extensive surgery.

Methods. A retrospective analysis was performed on 812 breast cancer surgeries between January 2001 and December 2009 at The George Washington University Breast Care Center. BCS-eligible patients who elected to have BCS were compared with those who chose CM. Patients who underwent CM were compared with patients undergoing CM and CPM.

Results. A personal or family history of breast cancer and larger tumor size were positively associated with choosing CM in BCS-eligible patients. A nonstatistically significant trend toward CM was seen in younger patients. Age, family history, fewer children, Caucasian race, and reconstructive surgery were positively associated with choosing CPM.

Conclusion. Mastectomy rates at this institution have not shown the recent sharp increase observed by some authors. The association of age, race, family history, and parity with

CPM has been corroborated in multiple studies. However, there is disagreement between statistically significant findings among investigators evaluating factors associated with CPM, and there is limited data in the literature characterizing BCS-eligible patients who chose CM. Larger prospective studies are necessary to further evaluate CM and CPM rates.

In 1991, The National Institutes of Health issued a consensus statement advocating breast conservation surgery (BCS) as the preferred surgical treatment for early-stage breast cancer.¹ Despite this long-standing recommendation, not all eligible patients receive this treatment. Furthermore, some institutions have noted an increasing trend in cancer-side mastectomy (CM) rates. In a 13-year institutional analysis of 5865 patients, McGuire and colleagues noted a rise in CM rates from 31% in 1997 to almost 60% in 2007. The authors cited possible reasons for this trend such as increased detection of additional foci, genetic testing, improved reconstruction techniques, and increased patient demand.²

Contralateral prophylactic mastectomy (CPM) reduces the risk of breast cancer by 91–96%.^{3,4} Although a significant improvement in survival has not been identified in most studies, a more recent study has demonstrated a modest survival benefit for women under 50.^{5,6} Prophylactic mastectomy is usually reserved for patients who are at high risk for developing a contralateral breast cancer. The Society of Surgical Oncology's Position Statement on prophylactic mastectomy reports that CPM is potentially indicated in women at higher risk, such as those with BRCA1–2 gene mutations, atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ, difficulty in following the contralateral breast radiologically or clinically, or for cosmesis.⁷ An argument against

routine CPM in patients without these risk factors is that the risk of systemic metastases is greater than the risk of developing a contralateral cancer. Additionally, treatment with Tamoxifen in patients with hormone receptor positive tumors reduces the incidence of contralateral breast cancer by approximately 50%.⁸

The purpose of this study was to identify specific characteristics among patients who chose to undergo CM or CPM. We also evaluated our mastectomy rates and identified trends in our patient population over the last 8 years.

METHODS

The charts of all patients who underwent breast cancer surgery between January 2002 and December 2009 at The George Washington University Breast Care Center were reviewed. Study protocols and design were approved by the Institutional Review Board at the George Washington University Office of Human Research. Surgeries were performed by general surgeons whose practices are dedicated exclusively to breast disease. Criteria for inclusion in the study included females of any race with unilateral breast cancer. All histologies and stages were included. Documentation of the rationale for CM versus BCS was required for inclusion in the study and was in 99.5% of reviewed charts. Patients were excluded if they had a mastectomy for a prior breast cancer. A new breast cancer in a patient with a previous history was included as a separate case as long as it was not a recurrence. Application of these criteria resulted in a total of 812 unique breast cancer cases that were divided into 3 groups for the purposes of analysis. The 1st group of cases included patients who underwent breast conservation for treatment of their cancer (498 cases). The 2nd group consisted of patients that underwent unilateral mastectomy regardless of eligibility for BCS (236 cases). The 3rd group included patients who had a CM with concurrent CPM (78 cases). These 3 groups were mutually exclusive. A 4th group, formed by taking patients from groups 2 and 3, represented patients who were eligible for BCS, but chose CM or CM with CPM (Fig. 1).

CM was recommended for patients with T4 lesions, a history of ipsilateral breast radiation or chest radiation (usually for Hodgkin's lymphoma), multicentric disease, large tumors relative to breast size, or persistently positive margins on re-excision. Patients without these contraindications were deemed candidates for BCS, including patients with strong personal or family histories of breast cancer, BRCA mutations, or multifocal disease confined to 1 quadrant. Patients with limited nipple or areola involvement were also offered breast conservation if they did not have any of the previously mentioned contraindications.

FIG. 1 Study design

Out of the 314 mastectomy patients, 68 patients chose CM or CM with CPM despite eligibility for BCS. Cases in which patients initially underwent breast conservation, but then chose to have a completion mastectomy over a re-excision were included in the “chose mastectomy” group as long as they were still eligible for BCS when they chose CM.

BCS-eligible patients who chose CM were compared as a group to patients who chose BCS. Similarly, patients who opted to have a CPM were compared with patients who elected to have CM only. Variables considered included age, race, initial presentation, biopsy technique, histopathology, tumor size, family history, history of contralateral breast cancer, number of children, reconstruction status, and use of neoadjuvant chemotherapy. Tumor size was determined from the final pathology report and considered the invasive component of the tumor only. In cases of patients who underwent neoadjuvant chemotherapy, prechemotherapy ultrasound measurements were substituted for pathologic measurements. With multifocal tumors, the largest focus was used as the measurement. A positive family history was defined as having any first- or second-degree family member diagnosed with breast cancer.

Two-sample *t* tests were used to test the equality of means for continuous variables and chi-square tests of independence were applied to categorical variables. In cases with counts less than 5 in any category, Fisher exact tests were used. Cochran-Armitage trend tests were used to assess trends in the degree of family history. Logistic regression was used to model the probability of choosing

CM among BSC eligible group. Similarly, a model was constructed to determine the probability of choosing CPM among all patients who underwent mastectomy. For each factor of interest, a reference category was chosen, usually the no-exposure or majority category and every other category was compared with the reference category. The ratio of the odds (OR) in each category versus the odds in the reference category are estimated. A multivariate model was fitted to adjust for potential confounding characteristics. The reported ORs from our multivariate analysis are conditional on holding all other adjustment factors the same.

Menopausal status and age could not be adjusted in the same model due to their high colinearity. When calculating ORs for age, menopausal status was eliminated from the model. Similarly, when calculating ORs for menopausal status, we omitted age. For all other factors, we used menopausal status rather than age in our final statistical model as menopause turned out to be a more significant predictor.

Statistical significance was defined as a *P* value less than .05. All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

The key characteristics of the patients in this study are summarized in Table 1. The mean age was 55.3 years (range 22–98). The overall mastectomy rate during the study was 39%, and 25% of patients who had CMs also had CPMs. The most common histology was invasive ductal carcinoma, followed by ductal carcinoma in situ. More than half the patients initially presented with a radiologic abnormality, most commonly mammographic, although many were also found by ultrasound, magnetic resonance imaging (MRI), or breast-specific gamma imaging (BSGI).

Patients who had BCS were compared with patients who were candidates for BCS but chose CM. The results of the multivariate analysis are presented in Table 2.

Patients who had CM were compared with those who elected to have a CM and CPM. The results from the multivariate analysis are presented in Table 3.

The overall trend in mastectomy rates from our institution is presented in Table 4 and Fig. 1. From 2002 to 2009, CPMs contributed to an increasing proportion of all mastectomies.

Tumor size and extent of disease were the most common factors associated with CM (Fig. 2). These included tumors too large or locally advanced for breast conservation (15.6%), extensive disease on preoperative imaging (15.9%), multicentric tumors (15.9%), and lesions with positive margins despite re-excisions (18.8%). A history of radiation to the breast or ipsilateral chest wall for previous

TABLE 1 Clinical and demographic data of the 812 breast cancer cases

Age	55.3 (± 12.8)
Procedure	
BCS	61% (498)
CM only	29% (236)
CM and CPM	10% (78)
Menopausal	
Yes	67% (543)
No	32% (261)
Unknown	1% (8)
Race	
Caucasian	46.3% (376)
African/African American	45.4% (369)
Asian/Asian Indian	4.3% (35)
Hispanic	3.5% (29)
Unknown	0.5% (3)
Preoperative pathology	
IDC	65.4% (531)
DCIS	21.7% (176)
ILC	3.9% (32)
Invasive mammary	2.6% (21)
Mucinous	1.2% (10)
Papillary	0.5% (4)
Metaplastic	0.5% (4)
Tubular	0.2% (2)
Medullary	0.1% (1)
Unknown	0.4% (3)
Atypia ^a	1.6% (13)
Personal history of breast cancer	
Yes	8% (69)
No	92% (743)
Family history of breast cancer	
Yes	39% (320)
No	60% (487)
Unknown	1% (5)
Presentation	
Abnormal imaging	53.9% (438)
Palpable mass	43.5% (353)
Nipple discharge	1.5% (12)
Erythema	1.0% (8)
Unknown	0.1% (1)
Parity	1.6 (± 1.5)
Size (invasive component)	1.92 cm (± 1.79)

IDC infiltrating ductal carcinoma, DCIS ductal carcinoma in situ, ILC invasive lobular carcinoma

^a The vast majority of patients with atypia on core biopsy first proceeded to excisional biopsy

malignancies such as breast cancer or lymphoma was present in 8.6% of patients. Women with breast implants (2.5%) were generally advised to undergo mastectomy.

TABLE 2 Multivariate analysis of patients who underwent BCS compared with those who were eligible for BCS but chose to have CM

Characteristic	BCS (<i>n</i> = 498)	Chose CM (<i>n</i> = 68)	Odds ratio for choosing CM	<i>P</i> value
Age	56.6 ± 12.4	53.5 ± 13.0		.06
Menopausal	72.2%	61.2%	0.6	.06
Race				.73
Caucasian	45.6%	52.9%	1.0	
African/African American	44.1%	41.2%	0.8	
Asian/Asian Indian	5.4%	2.9%	0.5	
Hispanic	4.8%	2.9%	0.5	
Personal history of breast cancer	6.4%	25.0%	4.9	<.01*
Family history	37.6%	55.9%	2.2	<.01*
Initial presentation				.67
Abnormal imaging	58.6%	57.3%	1.0	
Palpable mass	40.6%	35.3%	0.9	
Nipple discharge	<0.1%	4.4%	11.2	
Erythema	<0.1%	1.5%	7.5	
Biopsy technique				.69
Needle (core/stereotactic/fine)	88.4%	86.8%	1.0	
Excisional	11.6%	13.2%	1.6	
Preoperative Pathology				.72
IDC	66.3%	64.7%	1.0	
DCIS	22.3%	17.6%	0.7	
ILC	3.6%	8.8%	2.5	
Invasive mammary	2.2%	4.4%	2.0	
Tumor size (invasive component)	1.48 ± 0.97	1.81 ± 1.49		.05
Parity	1.6 ± 1.6	1.5 ± 1.8		.49
Nulliparous	32.7%	33.8%	1.1	.85
Definitive procedure was a re-excision	27.9%	32.3%	1.2	.47
Neoadjuvant chemo	3.8%	1.5%	0.4	.49

IDC infiltrating ductal carcinoma *DCIS* ductal carcinoma in situ, *ILC* invasive lobular carcinoma

* Statistically significant

DISCUSSION

The National Accreditation Center for Breast Cancer Standards Manual requires a BCS rate of at least 50%.⁹ Published mastectomy rates vary widely among centers and even in large studies, rates as low as 25% and as high as 90% have been reported.^{10,11} Breast conservation rates have been proposed as an objective measure of quality breast cancer care. Advocates for using BCS as a quality measure implicate physician treatment bias, inadequate counseling, and limited access to radiotherapy as reasons for variations in mastectomy rates with the assumption that most women would choose BCS over CM when presented with both options.^{11,12} Most CMs in our study were performed in patients who were not candidates for BCS. Our study found that institutional factors and patient preference were not the key factors in determining mastectomy rates (Fig. 2), which is similar to the findings by McCahill and colleagues.¹¹ Specialized centers such as ours often see more patients as second opinions, potentially have more advanced cases, and have patients seeking progressive

procedures such as nipple-sparing mastectomies with reconstruction. The increase in prophylactic mastectomy rates also contributes to an increased overall mastectomy rate in this study.

Our institution's overall mastectomy rate has not seen the recent dramatic increase reported by others.^{2,13} However, there was a steady rise between 2001 and 2006, with an additional spike in 2009. Additionally, the proportion of mastectomies performed because of patient choice has increased consistently, with twice as many patients choosing CM in 2006 than preceding years. CPMs have also increased almost 6-fold between 2002 and 2009. Some have speculated the liberal use of MRI has led to the increasing mastectomy rates at some institutions, as studies have shown that this modality affects surgical management.^{14,15} Our institution's increasing use of BSGI in place of MRI may in part counter the trends seen elsewhere by reducing the probability of overestimating extent of disease, as the sensitivity of BSGI is equal to MRI with superior specificity for cancer detection.¹⁶ In 2009, our institution performed more BSGIs than MRIs.

TABLE 3 Multivariate analysis of patients who underwent a unilateral mastectomy to those who underwent CM with a CPM

Characteristic	CM only (n = 236)	CM and CPM (n = 78)	Odds ratio for choosing CPM	P value
Age	54.7 ± 13.6	48.7 ± 10.9		<.01*
Menopausal	63.8%	46.8%	0.5	.01*
Race				.11
Caucasian	42.8%	57.7%	1.0	
African/African American	50.4%	37.9%	0.6	
Asian/Asian Indian	4.2%	1.3%	0.2	
Hispanic	2.5%	1.3%	0.4	
Minority status				.02*
Caucasian	42.8%	57.7%	1.8	
Non-Caucasian	57.2%	42.3%	1.0	
Personal history of breast cancer	11.4%	12.8%	1.1	.74
Family history	37.2%	59.7%	2.5	<.01*
Initial presentation				.19
Abnormal imaging	49.2%	38.5%	1.0	
Palpable mass	44.9%	57.7%	1.5	
Nipple discharge	3.8%	1.3%	0.4	
Erythema	1.9%	2.6%	1.6	
Biopsy technique				.38
Needle (core/stereotactic/fine)	85.2%	89.7%	1.0	
Excisional	14.8%	10.3%	0.7	
Preoperative pathology				.06
IDC	63.1%	66.7%	1.0	
DCIS	26.7%	17.9%	0.6	
ILC	3.0%	9.0%	<0.1	
Invasive mammary	3.8%	1.3%	0.3	
Tumor size (invasive component)	2.5 ± 2.3	2.2 ± 2.6		.41
Parity	1.7 ± 1.6	1.3 ± 1.5		.03*
Nulliparous	27.0%	35.9%	1.5	.14
CM was a re-excision	34.7%	19.2%	0.4	.01*
Reconstruction	48.3%	66.7%	2.1	0.01*
Neoadjuvant chemotherapy	11.9%	15.4%	1.4	0.42

* Statistically significant

The influence of neoadjuvant chemotherapy was not addressed in this study. Studies have shown that neoadjuvant chemotherapy increases rates of breast conservation in patients with locally advanced disease.^{17,18} Although there was no statistically significant difference in neoadjuvant chemotherapy use between BCS-eligible patients who chose BCS versus CM, it is unclear exactly how many patients were offered neoadjuvant chemotherapy purely as an option to avoid mastectomy and whether this would have shifted more CM patients into the BCS group.

Choice of CM

Larger studies have shown an association of CM with increasing age.¹⁹ Wang et al. speculate that the need for breast preservation is more important for young women,

perhaps because of body image issues.²⁰ However, most studies do not differentiate between patients who chose to undergo a CM versus those who were not candidates for breast conservation. A study that did account for patient choice was unable to show a significant age difference between patients who chose CM and those who chose BCS.²¹ Our study showed that women who *chose* mastectomy tended to be younger than their BCS counterparts, although the trend was not statistically significant.

Our population is almost entirely insured, and the majority of patients have private insurance, which has been shown to increase BCS rates 4-fold.²² Our patients are from a wide range of socioeconomic backgrounds, although our location in Washington DC may bias our sample to include more affluent and educated patients of all races. The metropolitan Washington, DC region is wealthiest urban

TABLE 4 Overall trend in mastectomy rates

Year	Institutional mastectomy rate ^a	Mastectomy patients that chose mastectomy ^b (%)	BCS-eligible patients that chose mastectomy ^c (%)	Prophylactic ^d (%)
2002	36% (31/85)	16% (5/31)	8% (5/59)	6% (2/31)
2003	35% (18/51)	11% (2/18)	6% (2/35)	11% (2/18)
2004	39% (34/86)	15% (5/34)	9% (5/57)	21% (7/34)
2005	41% (44/107)	18% (8/44)	13% (8/71)	14% (6/44)
2006	41% (46/112)	28% (13/46)	16% (13/79)	28% (13/46)
2007	35% (39/110)	20% (8/39)	10% (8/79)	36% (14/39)
2008	34% (34/101)	24% (8/34)	11% (8/75)	26% (9/34)
2009	43% (68/160)	28% (19/68)	17% (19/111)	37% (25/68)

^a Mastectomies divided by total number of cases for a given year

^b Of patients who underwent a mastectomy at our institution, percentage (regardless of BCS eligibility) who chose a mastectomy

^c Of patients who were BCS eligible, percentage who chose mastectomy

^d Percentage of mastectomies performed that were accompanied by a CPM

FIG. 2 Rationale for mastectomy in 314 mastectomy patients (236 CM + 78 CM with CPM) documented in patients' charts

area in the country.^{23,24} A geographic influence on BCS has also been reported with Mid-Atlantic and East Coast states having the highest rates.^{10,19,25}

We found that patients with a family history of breast cancer were twice as likely to choose CM, and those who had a previous diagnosis of breast cancer were 5 times as likely. Moreland and colleagues were unable to detect a difference in family history status, although their study was limited to 237 patients and did not differentiate between patients who chose CM and those for whom it was the only surgical option.²² A European study found that family history may be

associated with CM in patients with lower socioeconomic status, but the study did not address whether the CM was performed by patient choice or by medical necessity.²⁶

CM patients in our study had slightly larger tumors than BCS patients. There was also a nonstatistically significant increasing trend of invasive as opposed to in situ histologies in CPM patients ($P = .06$). It is possible that patients pursued CPM because of increased anxiety from having more advanced cancer, despite the known fact that patients with more advanced cancers benefit less from CPM because the probability of disease recurrence surpasses that of a new contralateral cancer.

The finding that more women underwent reconstruction when they chose to have CM may suggest the availability of a reconstructive surgeon factored into their choice. This has been corroborated by many authors and reflects that patients willing to undergo a more extensive procedure are also more inclined to accept the risks and benefits of reconstruction.^{27–29} Despite the younger age of this cohort, these differences were still statistically significant when accounted for by our logistic model. A weakness in this aspect of our study was that we only evaluated patients who underwent immediate reconstruction, which is often an option reserved for earlier-stage disease. We did not study patients who had delayed reconstructions.

The need for re-excision did not seem to influence patient choice, which suggests that patients who wanted to keep their breast were generally willing to continue attempts at breast conservation as long as it was an option.

Choice of CPM

Most studies are in agreement with our observation that younger age is a significant predictor of a patient choosing CPM.^{6,13,30} Previous studies examining CPM rates used

populations that are predominately Caucasian.³¹ Our study, which has equal numbers of Caucasian and African American patients, also showed increased rates of CPM in Caucasians compared with other races.^{3,32} Family history as a predictor of CPM is well documented in the literature.^{13,29,33} We also found that the closer the relative with breast cancer, the stronger impact it has on CPM. CPM patients had fewer children in this study, although the average age in this group was 49 with the majority presumably beyond childbearing. This observation was also noted in a study of BRCA positive patients with unilateral breast cancer, but the cohort in that study was almost 10 years younger than ours.³⁴ The reason for this association is unclear.

CONCLUSION

One of the greatest strengths of this study is that it is among the largest in the literature that accounts for patient choice as a factor for undergoing CM. Our data represent characteristics from the diverse patient population at our institution. Previous studies have considered mostly Caucasian populations. Additional considerations we did not discuss include surgeon influence on patient decision-making, psychological impact of mastectomy on patients, variation in mastectomy rates between surgeons, and the retrospective nature of the data available to us. The fact that there is disagreement between statistically significant findings CM and CPM rates from different institutions demonstrates the necessity for larger institutional studies.

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