

Differences between Breast Conservation-Eligible Patients and Unilateral Mastectomy Patients in Choosing Contralateral Prophylactic Mastectomies

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■ **Abstract:** There has been an increasing use of bilateral mastectomy (BM) for breast cancer. We sought to examine our trends among breast conservation (BCT) candidates and women recommended for unilateral mastectomy (UM). Our prospective breast cancer database was queried for women with a first-time, unilateral breast cancer. Patient and histologic factors and surgical treatment, including reconstruction, were evaluated. A detailed chart review was performed among patients from two representative time periods as to the reasons the patient underwent mastectomy. We identified 3,892 women between 2000 and 2012 of whom 60% underwent BCT, 1092 (28%) had UM and 12% underwent BM. BM rose from 4% in 2000 to a high of 19% in 2011, increasing around 2002 for women <40. BCT was less likely with decreasing age ($p < 0.0001$), lobular histology ($p < 0.0001$), higher stage ($p < 0.0001$) and decreasing BMI ($p < 0.0001$). Among mastectomy patients, contralateral mastectomy was associated with decreasing age ($p < 0.0001$), Caucasian race ($p < 0.0001$), and lower stage ($p = 0.005$). Over time, indications for mastectomy decreased while patients deemed BCT-eligible opting for UM or BM increased dramatically. Increases in the use of BM are in large part among women who were otherwise BCT-eligible. Factors associated with BM use are different for BCT-eligible patients and those recommended for UM. A better understanding of the factors driving individual patient choices is needed. ■

Key Words: breast cancer, breast conservation, contralateral prophylactic mastectomy, reconstruction

Over the same period that we have seen a shift toward less aggressive axillary surgery in breast cancer, we have seen a parallel shift toward more aggressive breast surgery, with a significant increase in the rate of contralateral prophylactic mastectomy (CPM). This has been demonstrated in both single institution studies (1,2), and in data from national databases (3–5). These trends occur despite the lack of evidence regarding the impact of CPM on survival, particularly among patients without a known increased risk for contralateral disease (6).

These trends have not occurred in a bubble. Over this same time period we have seen the increasing sensitivity of breast imaging, improvements in breast reconstruction, and our understanding of family history, genetics and risk. This information is not only available to clinicians, but is increasingly available to our patients via mass media, the internet and through social media. The institutional studies to date have primarily focused on patients undergoing mastectomy who then opted to also undergo CPM (1,2). However, the threshold to undergo bilateral mastectomy (BM) when a unilateral mastectomy (UM) is necessary, is substantially different than opting for CPM when breast conservation (BCT) is an option. This study was performed to document trends in surgical therapies for all women with operable breast cancer, and identify those factors associated with both the decision to forego BCT as well as the decision to undergo BM.

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METHODS

All biopsy-proven breast cancer patients seen at the University of Michigan Comprehensive Cancer clinic are presented at a multidisciplinary tumor board composed of surgical, medical, radiation oncologists, radiologists, pathologists and associated support staff. Once the patient has undergone surgery, the data from these discussions and the patient treatment records are entered into our breast cancer database. With Institutional Review Board approval, our prospective breast cancer database was queried for all adult female patients 21 years of age and older who underwent surgery for a unilateral, primary stage I, II, or III breast cancer at the University of Michigan Comprehensive Cancer Center between January 1, 2000 and December 31, 2012. Women with bilateral cancers and women with a prior history of breast cancer were excluded from this study. The database was queried to obtain information regarding age at diagnoses, race/ethnicity, height and weight at diagnosis, and smoking history. Details of surgical treatment, including reconstruction, and tumor pathologic characteristics (tumor size, nodal status, grade, estrogen and progesterone receptor and HER2 status) were also collected. BMI was calculated using the Quetelet Index.

For select time-periods, a detailed review of the multidisciplinary visit was conducted to determine the tumor board recommendations, whether the patient opted for mastectomy, or the reason the patient was recommended to undergo mastectomy by the surgeon. For the purposes of this study, patient choice was defined as a clinical situation where the surgeon informed the patient that either BCT or mastectomy was an option, as documented at the initial multidisciplinary tumor board visit, and the patient chose to undergo mastectomy, either unilateral or bilateral. Tumor size, as a reason for recommending mastectomy, was defined as any situation where the size of the tumor (including surrounding calcifications), compared to the size of the breast was such that the surgeon felt the cosmesis would be poor, and thus mastectomy was a better option. This also included patients for whom neoadjuvant chemotherapy wasn't an option, or the tumor failed to decrease with neoadjuvant chemotherapy. BCT failure included any patient where BCT was attempted, but ultimately a mastectomy was performed, even if patients had an option for a re-excision lumpectomy. Multicentric disease was defined as more than one site of documented

disease that could not be incorporated into a single lumpectomy. This did not include patients with suspicious areas on imaging who opted not to undergo biopsy, as they had opted for mastectomy. Additional reasons for mastectomy included patients with diffuse calcifications and those who could not undergo radiation, either secondary to prior nonbreast cancer radiation (as prior breast cancers were excluded), pregnancy, or collagen-vascular disease. Specific BRCA mutation status was not available in our database for analysis as part of this study.

The distribution of categories was compared using the chi-squared test statistic between lumpectomy and mastectomy groups, and between unilateral and bilateral groups within those having mastectomies. P-values at or below 0.05 were considered significant.

RESULTS

After excluding patients with a prior history of breast cancer or bilateral cancers, we identified 3,892 women with primary, unilateral breast cancer treated between 2000 and 2012. During this time period, 2,325 (60%) underwent BCT, 1,092 (28%) had a UM and 475 (12%) underwent a BM. Table 1 shows the demographics and tumor characteristics and their association with undergoing BCT, UM, and BM. Younger age was a highly significant predictor of undergoing not only mastectomy, but also opting for CPM ($p < 0.0001$ for both). This was particularly true among women under age 40, where only one-third of women opted for BCT. The proportion rose to over one-half of women age 40–49, and continued to rise as women aged. Race was not a factor significantly associated with BCT rates ($p = 0.09$). A similar percentage of white and African-American patients underwent BCT. However, race was strongly associated with undergoing BM as opposed to UM, with white women having CPM at a significantly higher rate (33%) than African American (18%), Asian (10%), or other races (22%) ($p < 0.0001$).

Overall, there was no difference in BCT rates or CPM usage for patients with in situ disease versus invasive disease. Among patients with invasive cancer, there was a significantly lower rate of BCT in patients with lobular carcinoma compared with ductal carcinoma (48% versus 61%). Patients with “ductal with lobular features” and other histologies had a similar BCT rate to ductal carcinoma. Even though patients with lobular carcinoma were more likely to undergo

Table 1. Factors Associated with Surgical Decisions among Patients with First-Time, Primary, Unilateral Breast Cancer

	Breast conservation		Unilateral mastectomy		Bilateral mastectomy		% of mastectomies
	N	% of total	N	% of total	N	% of total	
Age							
<40	120	34	118	33	117	33	50
40–49	520	53	306	31	161	16	34
50–59	720	62	305	26	129	11	30
60–69	570	67	219	26	60	7	22
70–79	299	73	110	27	3	1	3
>80	95	71	34	25	5	4	13
p-value						<0.0001	<0.0001
Race							
White	1,970	60	867	27	429	13	33
African American	173	59	97	33	22	8	18
Asian	79	50	70	45	8	5	10
Other	103	58	58	33	16	9	22
p-value						0.0915	<0.0001
Invasive versus in situ							
In situ	478	61	205	26	102	13	33
Invasive	1,847	59	887	29	373	12	30
	2,325		1,092		475		
p-value						0.4607	0.2157
Histology							
Ductal	1,401	61	617	27	264	12	30
Lobular	174	48	135	37	53	15	28
Ductal with lobular features	146	59	76	31	26	10	25
Other	112	61	49	27	23	13	32
p-value						<0.0001	0.7430
T-stage							
T1mic	42	62	25	37	1	1	4
T1a	174	64	67	24	33	12	33
T1b	421	74	90	16	55	10	38
T1c	716	67	246	23	107	10	30
T2	399	50	290	36	111	14	28
T3	24	16	95	64	30	20	24
p-value						<0.0001	0.0058
Node positivity							
No	1,380	68	442	22	208	10	32
Yes	460	43	446	42	165	15	27
	1,840		888		373		
p-value						<0.0001	0.0521
BMI							
<20	66	46	51	35	27	19	35
20–24.9	514	55	265	28	155	17	37
25–29.9	559	58	283	30	114	12	29
30–34.9	343	63	147	27	57	10	28
35–39.9	194	66	67	23	31	11	32
40–44.9	83	66	26	21	17	13	40
>45	77	68	26	23	10	9	28
	1,836		865		411		
p-value						<0.0001	0.1349
Tobacco use							
Yes	590	62	267	28	96	10	26
No	1,586	59	757	28	347	13	31
Unknown	127	60	59	28	25	12	30
p-value						0.2773	0.1990

mastectomy, this was not a factor associated with choosing to undergo BM, with a similar fraction to other invasive histologies ($p = 0.734$).

Among patients with invasive disease, tumor size was, as expected, associated with decreasing use of

BCT, but not removal of the contralateral breast. In fact, increasing T-stage was associated with a decreased likelihood of undergoing contralateral mastectomy ($p = 0.006$). A similar pattern was seen with nodal involvement. Patients with node positive disease

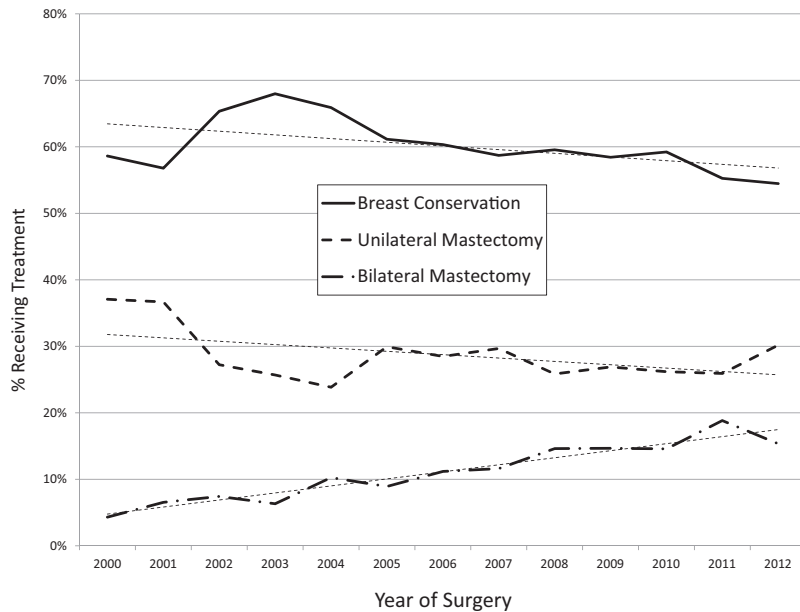


Figure 1. Trends in breast conservation, unilateral and bilateral mastectomy among patients with unilateral, primary breast cancer.

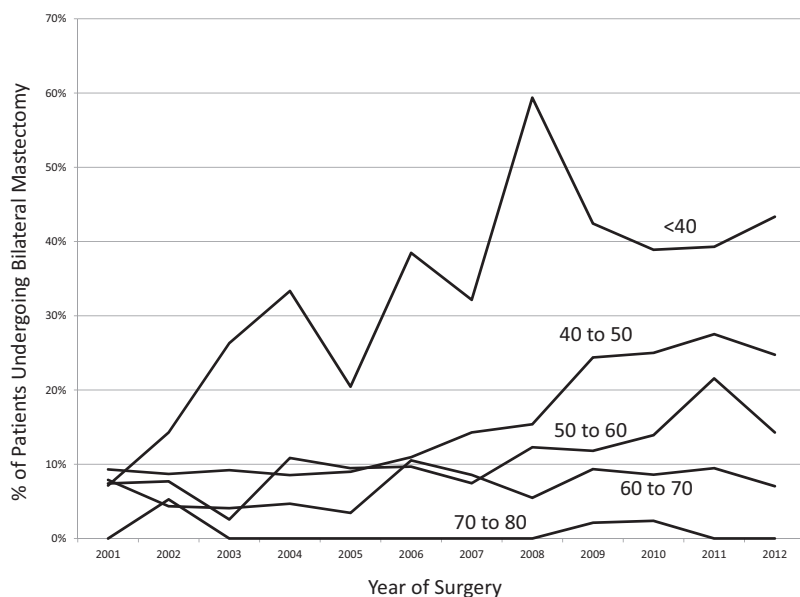


Figure 2. Trends in patients with unilateral, primary breast cancer undergoing bilateral mastectomy by decade. While bilateral mastectomy has risen among women <40 since 2002, it began increasing for women between 40 and 60 around 2008.

were less likely to have BCT (43% versus 68%, $p < 0.0001$), but less likely to have contralateral mastectomies (27% versus 32%, $p = 0.05$).

The year of treatment was strongly associated with surgical decision making (Fig. 1). Over the period from 2000 through 2012, we saw a decrease in the BCT rate, ranging from a high of 68% in 2003 to a low of 54% in 2012. During this time period, the UM rate remained relatively constant while the BM increased, from a low of 4% in 2000 to a high of 19% in 2011. The rise in bilateral mastectomies was most significant among women less than age 40

(Fig. 2), however there were also rises among women in their forties and fifties. These appear to have increased at several years later, with the increase in women <40 starting around 2002, but not increasing for women 40–60 until around 2007 or 2008.

RECONSTRUCTION

As improved reconstruction options have been implicated as a reason women increasingly opt to undergo BM, we examined these trends. Over this entire time period, patients undergoing mastectomy

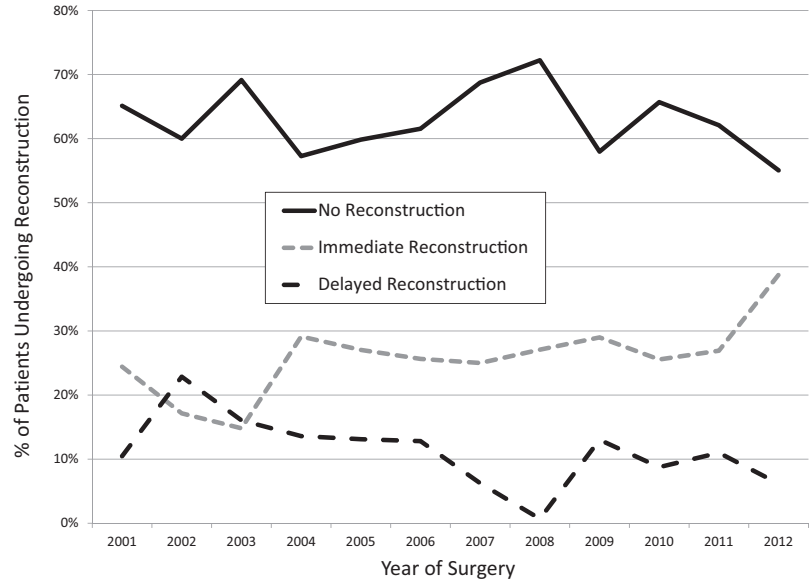


Figure 3. Trends in immediate or delayed reconstruction after mastectomy.

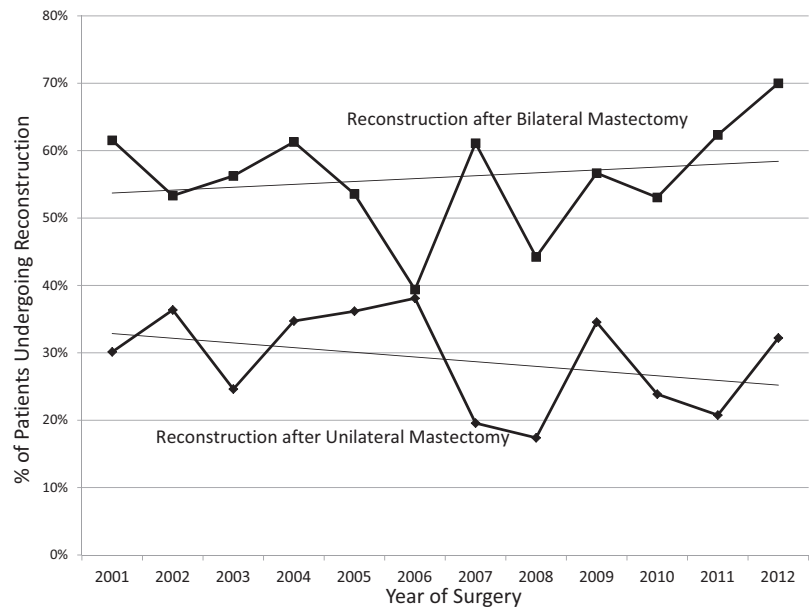


Figure 4. Trends in patients undergoing reconstruction after unilateral or bilateral mastectomy.

were offered consultation with plastic surgery to discuss reconstructive options. Among the 1,565 patients undergoing unilateral or BM, 428 (27%) opted to have immediate reconstruction and another 161 (10%) underwent delayed reconstruction. The most common form of reconstruction was with implants, with or without expanders (71%), while autologous reconstruction represented 29%, with the most common technique being a pedicled transverse rectus abdominis myocutaneous (TRAM) flap (17%).

Overall, from 2000 through 2012, although mastectomy rates increased, we did not see an overall

change in the percentage of mastectomy patients who opted for reconstruction, fluctuating between 24% and 31% of patients undergoing either unilateral or BM ($p = NS$). Over this time period, however, we did see a shift from delayed reconstruction to immediate reconstruction (Fig. 3). While throughout the years of this study the ratio of allogeneic versus autologous reconstruction remained constant, the type of autologous reconstruction changed, with pedicled TRAM flaps dropping to a smaller percentage of autologous reconstructions in favor of muscle sparing TRAMs and deep inferior epigastric perforator flaps.

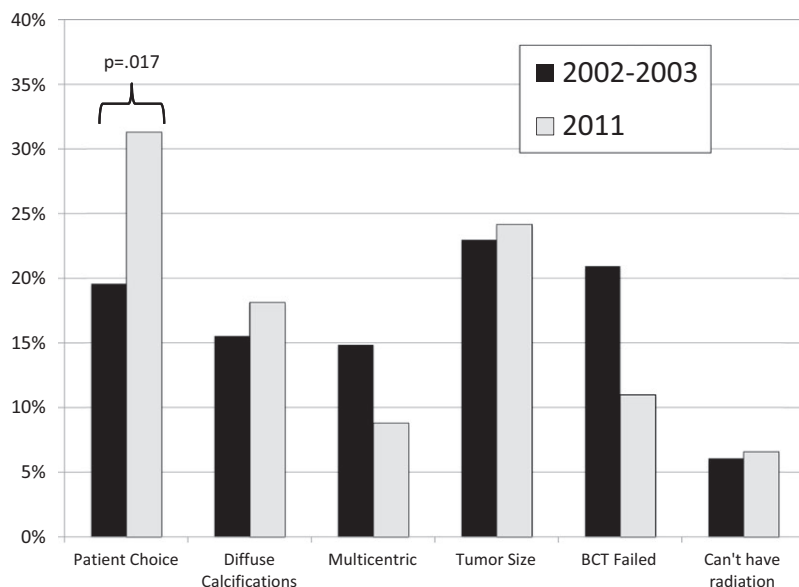


Figure 5. Reasons for undergoing mastectomy in 2002–2003 and 2011. Patient choice includes all patients for whom breast conservation was an option but the patient chose unilateral or bilateral mastectomy.

Breaking down mastectomy patients by unilateral versus bilateral, there has also been no change over time in the fraction of patients undergoing reconstruction over time for either group. Reconstruction was consistently more common among women undergoing BM than unilateral reconstruction (Fig. 4).

We also examined additional factors that may impact a woman's suitability to undergo reconstruction, and hence their decision to undergo mastectomy, including tobacco use and BMI. These data are shown in Table 1. Patients with a current or recent smoking history (37% of patients), did not have a higher rate of mastectomy compared with nonsmokers, and there was no impact of smoking history on bilateral versus unilateral mastectomies ($p = 0.27$ and 0.19 respectively). Increasing BMI did impact surgical decision making, with BCT increasing as BMI increased ($p < 0.0001$). However, among women undergoing mastectomy, there was no correlation between BMI and the decision to undergo bilateral versus UM ($p = 0.13$).

REASONS FOR MASTECTOMY

As the threshold for undergoing BM is lower when a UM is recommended, we examined whether the rise in CPM may be related to increased indications for UM. To do this, we reviewed the charts for the 452 patients treated in 2002–2003, when the BCT rate was at its highest (67%), and the 408 patients treated in the year 2011 (when BCT was at 55%). Using

medical record data as described above, we differentiated between those situations where the surgeon recommended mastectomy and those situations where the patient was felt to be a candidate for BCT by the surgeon (and was offered both choices), and opted to pursue mastectomy (unilateral or bilateral). Figure 5 shows the differences between these two time periods. Over this time period, there were minimal differences in the reasons women were recommended to undergo mastectomy, with no statistically significant difference between diffuse calcifications, tumor size, multicentricity or inability to have radiation. In fact, there was a small decrease in the percentage of patients recommended to undergo mastectomy, specifically after a failed attempt at BCT, secondary to our incorporation of intraoperative margin analysis in 2009 (7).

In contrast, there was a dramatic and statistically significant increase in the number of patients who were eligible for BCT, but instead opted to undergo mastectomy, rising from 19.6% in 2002–2003 to 31.3% in 2011 ($p = 0.0169$). The addition of a CPM among these patients also rose, both for patients requiring mastectomy (13–33%) and for patients opting for mastectomy, which was nearly half (45%) of patients in 2002–2003, and rose to nearly 2/3rds (63%) in 2011.

DISCUSSION

At the University of Michigan we have witnessed a similar increasing trend in the use of the CPM as has

been described nationally. This is not, however, an increasing use of CPM among patients recommended to undergo mastectomy, but rather is associated with a corresponding drop in BCT rates. This is despite a strong institutional bias toward BCT. The use of bilateral mastectomies rose from 4% to a high of 19% and was strongly associated with young age, as only one-third of patients under the age of 40 and one-half of patients between 40 and 49 opted for BCT. The trend is not explained by changes in the ages of our patient population, as neither the median age nor the proportion of patients under 40 has changed over this time period.

Several articles have described the increased popularity of the contralateral mastectomy, both at single institutions and in national databases (1–5). When simply tracking whether a patient had a CPM or not, it can sometimes be difficult to discern whether this represents women who are undergoing a UM and have opted to remove the other breast (for reasons that might not be related to risk reduction), or these are women who were excellent candidates for BCT, and opted for the more radical procedure primarily for prophylaxis. Examining the CPM rate in the context of all surgical decision making during this time period, and excluding patients with bilateral cancer and prior breast cancers (as this might influence decision making), we note both a slight decrease in the number of patients undergoing UM, and a decrease in the number of patients undergoing BCT. Although this may reflect a change in referral patterns, it suggests that this pattern is not just women undergoing mastectomy opting to have both breasts removed. Instead, a substantial component of women undergoing BM today were patients who 10 years ago would have undergone BCT (8). This is confirmed by recent data from the National Cancer Database which shows a small decrease in lumpectomy rates between 2003 and 2010 (5).

Several factors have been associated with a higher likelihood of undergoing a CPM. Our results suggest there is a difference between those factors that may be associated choosing BM among all patients, and those factors associated with opting for a contralateral mastectomy when committed to a UM. For example, race has been strongly associated with surgical decision making, with minorities less often getting CPM (2,9,10). Our data show that overall, BCT rates were extremely similar among the races, however, white women, compared with other races, were more likely to undergo BM compared with UM, a finding

consistent with other studies of CPM in different samples/settings (11,12). Histology showed the opposite trend. There was no difference in BCT or BM rates between in situ and invasive disease. Lobular histology was associated with a significantly lower BCT rate (potentially due to tumor size or failure to achieve negative margins) Women with lobular histology undergoing mastectomy were not more likely to undergo BM, despite the perceived association with an increased risk of contralateral disease, and in contrast with studies showing increased CPM among women with lobular histology (9,10). Increasing tumor size expectedly correlates with mastectomy over BCT. However, larger tumors are associated with a decreased likelihood of BM. In a similar vein, nodal positivity has a positive association with mastectomy, but a negative association with BM. As any potential benefit of prophylactic surgery decreases as the risk of recurrence of the known cancer rises, these trends may reflect appropriate counseling.

Age is by far the most significant factor for both, in our study and others (1–3,9,10,13). Younger individuals may have more anxiety regarding recurrence and second primary tumors in their lifetime, and are more likely to harbor a genetic predisposition. Genetic testing, and the increased identification of patients carrying the BRCA1 and BRCA2 mutations, has certainly contributed to this trend. In 2002, the turnaround time for obtaining genetic testing results dropped significantly, allowing for preoperative counseling and shifting genetic testing from survivors to newly diagnosed patients. This may explain a jump in prophylactic mastectomies prior to 2002, but over this time period, and in the two specific time periods chosen for comparison (2002–2003 and 2011), BRCA testing was readily available. Though we were not able to identify BRCA mutation status in our patients, we do know that testing became easier for patients to obtain, and the guidelines for genetic testing were broadened, potentially identifying a slightly larger subset of patients harboring a genetic predisposition. Thus we may assume that more patients were tested and this may have contributed to a fraction of CPM. However, the analysis examining the reason for choosing mastectomy was abstracted from the initial conversation with the surgeon after multidisciplinary presentation, at which point BRCA mutation status was rarely known. Most patients informed the surgeon of their decision to proceed with BM before referral to the genetic counselor or testing.

Breast imaging has changed considerably over this time period with the introduction of digital mammography and breast MRI. At the University of Michigan, we do not recommend routine breast MRI for BCT eligible patients, although an increasing number of patients arrive with MRIs obtained by outside physicians (radiologists, primary care physicians) prior to their initial consultation. Despite this, when one examines the reasons for patients undergoing mastectomy, diffuse calcifications, tumor size and multicentric disease (factors associated with sensitivity of imaging), did not significantly change.

In addition to increasing rates of CPM, there have been increasing rates of reconstruction and it has been hypothesized that the availability of reconstruction may be driving the mastectomy and BM rate (14,15). Certainly, there may be some cases where mastectomy and reconstruction can achieve a better cosmetic outcome than BCT, and potentially avoid the complications of radiation. However, while reconstruction has been statistically linked to CPM rates, this does not necessarily translate to a causative relationship. At the University of Michigan, we have offered consultation with plastic surgery for any patient considering mastectomy for all the years included in this study. Although we have seen dramatic changes (more free flaps, a shift to more immediate reconstruction), we have not seen a rise in reconstruction rates among women undergoing either unilateral or bilateral reconstruction. In addition, factors that may impact the ability to undergo reconstruction, such as obesity and tobacco use, were not associated with the surgical decision making. These data suggest that while reconstruction rates may be increasing, changes in availability or morbidity are not, in large measure, driving BCT-eligible women toward either mastectomy or BM. Rather, women opting for mastectomy and CPM are doing so for other reasons, and then choosing whether to have reconstruction.

This of course begs the question why women are choosing more extensive surgery despite increased recovery time, complications and no clear benefit to survival (16). Although retrospective in nature, this single institution study does benefit from a consistency in practice over the time period being examined. Despite a pro-BCT approach, consistent use of genetic counseling/testing, consistent discussion of reconstruction options and referral to plastic surgery, avoidance of breast MRI and no significant change in patient age, BMI or presenting tumor stage, we too have seen

the same concerning increase in bilateral mastectomies, particularly among younger women and even when limited to BCT-eligible patients.

What has increased over this time period, for which we have little control, is the public perception regarding the risk of a second cancer, the importance of family history, and the availability of prophylactic surgery. Surveys of women opting for CPM have identified a substantial fear of recurrence and a desire to prevent metastases and improve survival as quoted reasons (11,12). However, many of these patients overestimate their risk for either dying of disease or developing a 2nd primary cancer, or misinterpret the benefit of BM (11,17–19). The perceived benefit of BM may be, to some degree, media driven. This has often been referred to as the “Angelina Jolie effect,” a fear that interest in genetic testing and bilateral mastectomies would rise after the actress announced publicly that she had undergone risk reduction surgery. However, Angelina Jolie’s announcement was in May of 2013, and the rise in bilateral mastectomies clearly began at least a decade prior to this. More importantly, the news coverage regarding Angelina Jolie’s breast cancer centered on her family history and her BRCA status. In contrast, there have been many media reports of celebrities with breast cancer undergoing BM and immediate reconstruction, without explaining the decision making process or discussing alternative options.

In addition to this media attention, there is likely increased word of mouth as there are more breast cancer survivors and an increased willingness (if not encouragement) to talk about it. And while the risk of a contralateral cancer is low, estimated to be no more than 4–5% over 10 years (20,21), given the prevalence of breast cancer, may be a large number of BCT patients who reply, “if I had to do it all over again, I’d have bilateral mastectomies,” when queried about their decision; more when one includes patients dissatisfied with their cosmetic outcome.

While we clearly need better patient education regarding risk and the true benefits and complications of BM, the fact that higher education level seems to correlate with opting for CPM suggests that education alone may not be sufficient (22). It is clear that we need additional studies addressing the reasons why women choose BM, particularly those who are seemingly excellent candidates for BCT. A more nuanced approach to identifying and addressing patient fears and other motivating factors may be needed to

counter the preconceived notions and mixed messages originating from outside sources.

DISCLOSURE

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