VOLUME 29 · NUMBER 16 · JUNE 1 2011

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Clinical Management Factors Contribute to the Decision for Contralateral Prophylactic Mastectomy

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Submitted March 18, 2010; accepted November 1, 2010; published online ahead of print at www.jco.org on April 4, 2011.

Presented in part at the San Antonio Breast Symposium, December 9-13, 2009, San Antonio, TX.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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0732-183X/11/2916-2158/$20.00

DOI: 10.1200/JCO.2010.29.4041

ABSTRACT

Purpose
To determine whether increasing rates of contralateral prophylactic mastectomy (CPM) are due to recognition of risk factors for contralateral breast cancer (CBC) or treatment factors related to the index lesion.

Methods
From 1997 to 2005, 2,965 patients with stage 0 to III primary unilateral breast cancer underwent mastectomy at Memorial Sloan-Kettering Cancer Center. Patients who did and did not undergo CPM within 1 year of treatment for their index cancer were compared to identify independent predictors of CPM.

Results
The rate of CPM was 13.8% (n = 407), increasing from 6.7% in 1997 to 24.2% in 2005 ($P < .0001$). Patients with *BRCA* mutations or prior mantle radiation (n = 52) accounted for 13% of those having CPM. The rate of CPM by surgeon varied from 1% to 26%. Multivariate logistic regression adjusting for surgeon-identified white race (odds ratio [OR] = 3.3), immediate reconstruction (OR = 3.3), family history of breast cancer (OR = 2.9), magnetic resonance imaging (MRI) at diagnosis (OR = 2.8), age younger than 50 years (OR = 2.2), noninvasive histology (OR = 1.8), and prior attempt at breast conversation (OR = 1.7) to be independent predictors of CPM.

Conclusion
These data suggest that increasing use of CPM is not associated with increased recognition of patients at high risk for CBC. Treatment factors, such as immediate reconstruction, preoperative MRI, and unsuccessful attempts at breast conservation, are associated with increased rates of CPM. Efforts to optimize breast conservation, minimize unnecessary tests, and improve patient education about the low risk of CBC may help to curb this trend.

J Clin Oncol 29:2158-2164. © 2011 by American Society of Clinical Oncology

INTRODUCTION

Rates of contralateral prophylactic mastectomy (CPM) for both ductal carcinoma in situ (DCIS) and stage I to III invasive breast cancer in the United States have increased by approximately 150% since 1988.[1-4] Although prophylactic mastectomy is an established option for women with a genetic predisposition or otherwise significantly elevated breast cancer risk,[3,4] the role of CPM in the management of the average newly diagnosed patient with breast cancer remains controversial.

The incidence of contralateral breast cancer (CBC) has significantly decreased in the modern era of adjuvant therapies,[5-7] and the oft-quoted annual incidence of 0.50% to 0.75%[8-11] is likely outdated. For most patients, the risk of developing CBC remains substantially lower than the risk of recurrence from their index cancer. Even in subgroups thought to be at higher risk for CBC, such as those younger than 45 years and those with lobular histologies, the actuarial CBC rate at 10 years remains less than 7%.[12] Heightened awareness of increased risk of CBC in women with *BRCA* mutations may be a factor, yet these mutations occur in only 5% to 10% of newly diagnosed patients,[13] and data regarding mutation status among women undergoing CPM are limited.[1,14] Thus many patients undergoing CPM are unlikely to have a survival benefit.[15]

Previous studies have identified an association between CPM, young age, and family history of breast cancer[1-4,14]; however, it is likely that other factors are also contributing to this trend. Contemporaneous with increasing CPM rates has been an increase in breast magnetic resonance imaging (MRI) use at diagnosis. MRI is documented to be

associated with higher mastectomy rates for the index cancer,[16-18] yet little is known about the relationship between MRI use and CPM.[19] Advances in breast reconstruction may be contributing to a desire for bilateral surgery to achieve symmetry, and some have suggested that surgeon bias may influence the decision-making process.[1,2,20] We performed this analysis to determine the association between the use of CPM, CBC risk factors, and treatment factors related to the index lesion.

METHODS

Prospective institutional databases were retrospectively reviewed to identify patients with unilateral stage 0 to III breast cancer who underwent mastectomy with or without CPM within 1 year of treatment at Memorial Sloan-Kettering Cancer Center (MSKCC) from January 1, 1997 through December 31, 2005. This time interval included patients treated by 13 specialized breast surgeons. Patients with a personal history of breast cancer or metastatic disease and those receiving neoadjuvant chemotherapy were excluded. The study was approved by the institutional review board.

Tumor size, estrogen receptor (ER), progesterone receptor (PR), and *HER2/neu* status were recorded for invasive cancers only. Site of first event was classified as ipsilateral locoregional recurrence (LRR), CBC, and distant metastases.

CPM and MRI rates were examined by year of diagnosis and tested using the Cochran-Armitage test. χ^2 and *t* tests were used for bivariate comparisons. To identify independent predictors of CPM, multivariate models that adjust for surgeon variability were fit using generalized estimating equations. Surgeon was also entered into a multivariable logistic model as a fixed covariate. Factors evaluated in the model were chosen based on significant results from bivariate analyses. At MSKCC, ER, PR, nodal status, tumor size, and multicentricity are not recorded for DCIS. To build a model for both DCIS and patients with invasive cancer, these variables were not included. However, to assess the effect of these variables on use of CPM, we fit a separate model for patients with invasive cancer only. Care was taken so only one of a set of correlated variables was included (eg, family history was included, but number of first- or second-degree relatives was not).

Kaplan-Meier methods and Cox regression were used to analyze time from definitive breast surgery to first event or last date of follow-up. All analyses are based on complete data. All *P* values were two-tailed, and values of $P \leq .05$ were considered significant. All statistical analyses were completed using SAS software V9.1 (SAS Institute, Cary, NC).

RESULTS

From 1997 to 2005, 12,181 patients underwent breast cancer surgery and were entered into the database. The 2,979 patients (24%) with unilateral stage 0 to III breast cancer who underwent mastectomy for their index breast cancer formed our study cohort (Appendix Fig A1, online only). In this group, 407 patients (13.7%) underwent CPM (367 immediate, 40 $\leq$ 12 months) within 1 year of treatment. The CPM rate increased from 6.7% to 24.2% during the study period (Fig 1; $P < .0001$, Cochran-Armitage test).

Predictors of CPM

Patient characteristics and breast cancer risk factors are summarized in Table 1. Patients who underwent CPM were younger, primarily white, and more likely to have a family history of breast cancer than non-CPM patients. However, among those having CPM, only 58% of patients with a family history had a first-degree relative (FDR) with breast cancer, and only 8% had more than one affected FDR. Genetic testing was performed in 29% of patients having CPM; of those, 31% had a deleterious mutation in *BRCA1* or *BRCA2*. Fifteen patients (4%) in the CPM group had received mantle radiation. Overall, patients with *BRCA* mutations or prior mantle radiation (n = 52) accounted for 13% of those having CPM.

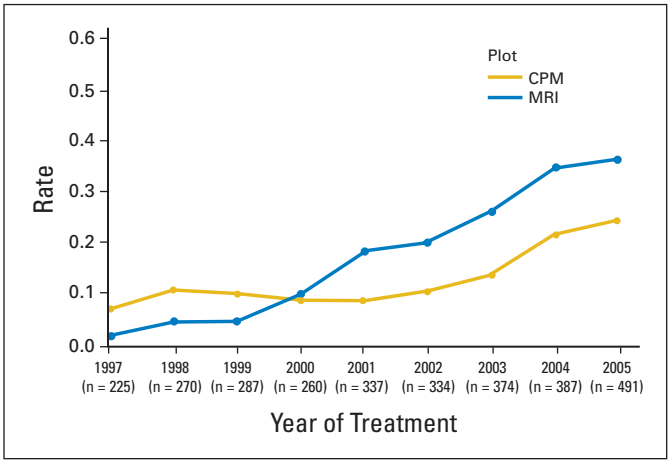

Fig 1. Rates of contralateral prophylactic mastectomy (CPM) and use of magnetic resonance imaging (MRI) at diagnosis by year of surgery.

Index tumor characteristics are summarized in Table 2. Among patients undergoing CPM, 22% had DCIS compared with 13% in the no-CPM group. Overall, in both groups, 21% of DCIS patients had CPM, whereas 24% of invasive cancer patients had CPM ($P = .001$). Patients who underwent CPM with invasive cancer had smaller tumors (1.2 cm *v* 1.8 cm; $P < .0001$). Fifty-three percent of patients who had CPM were node-negative, as compared with 43% of patients who did not undergo CPM. Overall, 15% of patients with node-negative disease had CPM, whereas 11% of node-positive patients had CPM ($P = .0001$). There were no differences in the frequencies of multicentricity/multifocality or ER, PR, or *HER2* status of the index carcinomas between the CPM and non-CPM groups. The rate of occult carcinoma among patients having CPM was 6% (24 of 407 patients); five (1.2%) were invasive, and the remainder were DCIS. Median patient age of those with CBC was 47.7 years; seven of 24 patients underwent genetic testing, and two patients were found to be mutation carriers.

Receipt of adjuvant treatment and clinical management factors are summarized in Table 3 and Appendix Table A1 (online only). MRI use at diagnosis increased from 1.3% in 1997 to 36.3% in 2005 ($P < .0001$; Cochran-Armitage test) and was more common among women having CPM (43% *v* 16%, $P < .0001$). Figure 1 demonstrates time trends in the use of MRI and CPM during the study period. Multicentric disease on MRI and recommendations for biopsies in the ipsilateral breast were both more common in the non-CPM group and may have contributed to the decision for mastectomy for the index breast cancer. In contrast, additional biopsies for MRI findings in the contralateral or bilateral breasts were more common among patients choosing CPM. Patients undergoing CPM were also more likely to have had a prior attempt at breast-conserving surgery (BCS) for the index cancer (28% *v* 16%; $P < .0001$), yet of those having a prior attempt, only 19% of patients undergoing CPM had more than one attempt at BCS as compared with 12% in the no-CPM group ($P = .11$). Immediate breast reconstruction was performed in 87% of

Table 1. Patient Characteristics*

Characteristic	No CPM (n = 2,572) No.	% of No CPM	% of Total With Characteristic	CPM (n = 407) No.	% of CPM	% of Total With Characteristic	P
Age at surgery, years							
Median			53.2			44.8	< .0001
Range			20-93			20-80	
Mean			54.7			45.6	
Age categorized							
< 50 years	1,061	41	78	291	71	22	< .0001
≥ 50 years	1,505	59	93	116	29	7	
Ethnicity							
Nonwhite/Hispanic	629	25	96	29	7	4	< .0001
White	1,924	75	84	378	93	16	
Missing	19			0			
Nulliparous							
No	2,039	79	86	334	82	14	.1815
Yes	530	21	88	73	18	12	
Missing	3			0			
Family history BC							
No	1,528	60	92	126	32	8	< .0001
Yes	1,023	40	79	278	68	21	
Missing	21			3			
No. of FDRs with BC							
0	559	55	83	118	43	17	.023
1	404	39	75	137	49	25	
≥ 2	60	6	72	23	8	28	
NA	1,528			126			
Missing	21			3			
No. of SDRs with BC							
0	313	31	82	71	25	18	< .0001
1	487	48	82	110	40	18	
≥ 2	223	22	70	97	35	30	
NA	1,528			126			
Missing	21			3			
Genetic testing							
No/not known	2,323	90.5	89	289	71	11	< .0001
Yes	249	9.5	68	118	29	32	
Mutation carrier (of tested)							
No	217	88	73	81	69	27	< .0001
Yes	32	12	46	37	31	54	

Abbreviations: CPM, contralateral prophylactic mastectomy; BC, breast cancer; FDR, first-degree relative; SDR, second-degree relative; NA, not applicable.
*Statistical tests are based on complete data.

patients in the CPM group as compared with 51% of patients in the non-CPM group ($P < .0001$), with implant reconstruction the predominant type in both groups (97% and 90%, respectively; $P < .0001$).

CPM rates by surgeon varied from 1% to 26%. In the multivariate logistic regression model adjusting for surgeon variability, age younger than age 50 years, white race, family history of breast cancer, noninvasive histology, MRI at diagnosis, prior attempt at BCS, and immediate reconstruction were significant independent predictors for CPM (Table 4). Multivariate modeling treating surgeon as a covariate and multivariate analysis of only patients with invasive cancer demonstrated similar findings (Appendix Tables A2 and A3, online only).

Outcomes

At median follow-up of 4.4 years (range, 0.18 to 11.70 years) for patients undergoing CPM and 6.8 years (range, 0.33 to 12.20 years) for patients not undergoing CPM, 14 patients (0.5%) not undergoing CPM developed CBC, and no contralateral events occurred in the CPM group. Distant metastases were the most common breast cancer event, developing in 7% of patients in the non-CPM group and 4% of patients in the CPM group at medians of 2.3 and 2.0 years, respectively (Table 5). At last follow-up, 91% of patients in the CPM group and 84% of patients in the non-CPM group were alive without disease. In a Kaplan-Meier analysis, CPM was associated with a lower probability of recurrence ($P = .02$). Multivariate Cox regression, adjusting for age and treatment factors (chemotherapy, radiotherapy, and MRI), demonstrated no difference in subsequent breast cancer event rates between groups ($P = .23$).

DISCUSSION

Consistent with other reports, CPM rates have increased three-fold at our institution since 1997, yet we observed that most patients undergoing CPM were not at significantly increased risk for CBC. Our study

Table 2. Tumor Characteristics*

Characteristic	No CPM (n = 2,572) No.	% of No CPM	% of Total With Characteristic	CPM (n = 407) No.	% of CPM	% of Total With Characteristic	*P*
Tumor size, cm							
Median			1.8			1.2	< .0001
Range			0.01 to 17			0.01 to 9.5	
Mean			2.16			1.53	
NA	339			89			
Unknown	60			2			
Index cancer pathology							
IFDC	1,942	76	87	281	69	13	< .0001
IFLC	291	11	89	37	9	11	
DCIS only	339	13	79	89	22	21	
Multicentric/multifocal							
No	1,290	58	87	188	60	13	.5232
Yes	943	42	88	127	40	12	
NA	339		79	89		21	
Unknown	0			3			
Nodal status							
Negative	958	43	85	168	53	15	.001
Positive	1,275	57	89	150	47	11	
NA	339		79	89		21	
ER							
Negative	532	25	87	80	27	13	.49
Positive	1,590	75	88	218	73	12	
NA	339		79	89		21	
Unknown	111		85	20		15	
PR							
Negative	961	45	88	128	43	12	.43
Positive	1,157	55	87	170	57	13	
NA	339		79	89		21	
Unknown	115		85	20		15	
HER2/neu (IHC and FISH)							
Negative	1,336	81	86	224	82	14	.71
Positive	304	19	86	48	18	14	
NA	845		87	123		13	
Unknown	87		88	12		12	

Abbreviations: CPM, contralateral prophylactic mastectomy; NA, not applicable; IFDC, infiltrating ductal carcinoma; IFLC, infiltrating lobular carcinoma; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; IHC, immunohistochemistry; FISH, fluorescent in situ hybridization.
*Statistical tests are based on complete data.

expands the observations of others[1-4] by providing detailed information on contralateral cancer risk factors. A greater awareness of genetic risk has been proposed as a factor responsible for increasing CPM rates, yet only 29% of our patients who underwent CPM underwent genetic testing despite a readily available, well-promoted genetic counseling service, and only one third of those tested were found to have a deleterious mutation. Overall, only 13% of our CPM population was documented to be at substantially increased risk due to gene mutation or history of mantle irradiation. The observation that our CPM group was not truly high risk is further supported by the low rate of unsuspected cancer found at time of CPM. The rate of occult invasive (1.2%) and noninvasive breast cancer (4.7%) among women in this series is consistent with that of other reports,[1,21,22] suggesting that most women choosing CPM are not at high risk for bilateral synchronous breast cancer. Collectively, these data suggest that factors other than breast cancer risk are contributing to the increasing use of CPM.

Patients may desire CPM as a result of concern about the impact of a second breast cancer on prognosis; however, studies examining CPM impact on overall survival show no benefit.[15] In our series, the incidence of CBC among women not having CPM (0.5%) was 17-fold less than the incidence of distant metastases (7%) and seven-fold less than the incidence of locoregional recurrence (3%). Although CPM does reduce the risk of CBC, distant metastases developed in 4% of patients in the CPM group at a median follow-up of only 4 years, supporting the view that prognosis for women with unilateral breast cancer is determined by the index lesion. A recent report suggests that patients younger than 50 years with early-stage, ER-negative breast cancer may have improved disease-specific survival with CPM, yet it is unclear how a 0.74% reduction in the rate of CBC leads to a 4.8% improvement in disease-specific survival.[23] Young age and family history of breast cancer were independent predictors for CPM in this series; however, only 8% of patients in the CPM group had more than one affected FDR, and only 29% pursued genetic testing. Among other

Table 3. Clinical Management Factors*

Factor	No CPM (n = 2,572) No.	% of No CPM	% of Total With Characteristic	CPM (n = 407) No.	% of CPM	% of Total With Characteristic	*P*
MRI at cancer diagnosis							
No	2,146	84	90	233	57	10	< .0001
Yes	414	16	70	174	43	30	
Missing	12			0			
Multicentric disease on MRI							
No	188	46	63	115	66	37	< .0001
Yes	226	54	79	59	34	21	
NA	2,146		90	233		10	
Missing	12			0			
Additional biopsy due to MRI finding							
No	165	39	71	66	38	29	.81
Yes	249	61	70	108	62	30	
NA	2,146		90	233		10	
Missing	12			0			
Site of additional biopsy/MRI finding							
No	165	39	71	66	38	29	< .0001
Ipsilateral breast	232	57	80	58	33	20	
Contralateral/bilateral	17	4	25	50	29	75	
NA	2,146		90	233		10	
Missing	12			0			
Prior attempt at BCS							
No	2,136	83	88	295	72	12	< .0001
Yes	424	17	79	112	28	21	
Missing	12			0			
No. of BCS attempts							
1	370	87	81	91	81	19	.11
2	48	11	71	20	18	29	
3	6	1	86	1	1	14	
NA	2,136		88	295		12	
Missing	12			0			
Immediate reconstruction							
No	1,253	49	96	53	13	4	< .0001
Yes	1,319	51	79	354	87	21	
Type of reconstruction							
Implant	1,181	90	77	344	97	23	< .0001
Autologous tissue	138	10	93	10	3	7	
NA	1253		96	53		4	

Abbreviations: CPM, contralateral prophylactic mastectomy; MRI, magnetic resonance imaging; NA, not applicable; BCS, breast-conserving surgery.
*Statistical tests are based on complete data.

reports citing an association between family history and CPM,[1,2,4,14] *BRCA* data are limited to two studies,[1,14] both of which note that many women who undergo genetic testing proceed to CPM regardless of the result. In subset analysis of single-institution data abstracted from the National Comprehensive Cancer Network database, Jones et al[2] compared detailed family history for 201 patients choosing CPM and 455 patients randomly selected from a group of 1,639 patients not having CPM. On bivariate analysis, higher CPM rates were seen in women whose mothers or sisters had breast cancer.

Socioeconomic factors, such as ethnicity, level of education, and employment, have also been cited as factors potentially associated with CPM. Our CPM population was predominantly white/non-Hispanic (93%), married (81%), and employed outside the home (67%). These characteristics parallel the general patient population at our institution; however, because of incomplete data for the non-CPM population, only ethnicity was included in our multivariate model and remained an independent predictor of CPM. This finding is consistent with Surveillance, Epidemiology, and End Results data set results.[3,4] In a study of CPM using New York State Hospital discharge and registry data from 1995 to 2005, McLaughlin et al[24] also demonstrated that women undergoing prophylactic mastectomies were more likely to be white (91%) than the general population of New York state patients with breast cancer (84%). In the same data set, among patients age $\leq$ 64 years of age, women undergoing prophylactic mastectomies were more likely to have private insurance than patients undergoing therapeutic mastectomy alone (88% *v* 77%). Jones et al[2] reported that level of education was associated with CPM, with larger proportions of more highly educated women choosing CPM over unilateral mastectomy. Although all socioeconomic factors have not been fully explored in adjusted analyses, these findings suggest that the decision to pursue CPM may be influenced by an individual's access to information, resources, and social networking.

Table 4. Predictors of Contralateral Prophylactic Mastectomy: Multivariate Logistic Regression Model Adjusted for Surgeon Variability

Variable	OR	95% CI	*P*
Ethnicity, white *v* other	3.31	2.40 to 4.57	< .0001
Family history of breast cancer	2.91	2.33 to 3.63	< .0001
MRI at diagnosis	2.79	2.17 to 3.60	< .0001
BCS attempted	1.69	1.21 to 2.36	.0002
Age, < 50 *v* ≥ 50 years	2.21	1.71 to 2.85	< .0001
DCIS only *v* IFDC	1.78	1.26 to 2.53	.0011
IFLC *v* IFDC	0.88	0.54 to 1.43	.6079
Immediate reconstruction, Y *v* N	3.27	2.31 to 4.63	< .0001

NOTE. Individual-specific *BRCA* mutation status was not available and could not be included in the model. This multivariate model is based on 2,924 patients who had complete data. Patients with incomplete data are excluded from the analysis. Final model assumes a compound symmetry covariance matrix.

Abbreviations: OR, odds ratio; MRI, magnetic resonance imaging; BCS, breast-conservation surgery; DCIS, ductal carcinoma in situ; IFDC, infiltrating ductal carcinoma; IFLC, infiltrating lobular carcinoma.

The lack of association of CPM with tumor characteristics and treatment characteristics that influence the risk of CBC also supports that patients may be choosing CPM for reasons other than increased risk, or alternatively, that patients have a limited understanding of their true CBC risk.[5] Adjuvant endocrine therapy is known to decrease CBC risk by 50%,[5] and the reduction is more pronounced among women receiving aromatase inhibitors.[6] Yet none of the reports to date have found an association between ER status of the index breast cancer and CPM use. Even cytotoxic chemotherapy reduces contralateral cancer events by 20%,[5] and early data from adjuvant trastuzumab trials suggest that it reduces contralateral cancer events as well.[7] Thus older data from time periods before widespread adjuvant therapy use may overestimate contralateral cancer risk and should not be used when counseling women about their risk.

Factors associated with clinical management of the index cancer were strongly associated with CPM use in our population, including preoperative MRI with the recommendation for additional biopsy of the contralateral breast, failed attempts at breast conservation, and breast reconstruction. Single-institution studies report conflicting results regarding the impact of MRI use and breast reconstruction on CPM. Preoperative MRI was not associated with CPM use in the series of Yi et al[14] or Arrington et al[1]; however, Sorbero et al[19] found that as use of preoperative MRI increased from 4.1% in 1998 to 2000 to 23.7% in 2003 to 2005, CPM use also increased by more than 50%, from 4.1% to 6.4% ($P < .002$). Although the association between MRI and CPM in the Sorbero study is limited by lack of detailed patient characteristics and tumor histology, our data, adjusted for potential confounders, support the finding that preoperative MRI is strongly associated with the decision to pursue CPM (odds ratio [OR] = 2.79; 905% CI, 2.17 to 3.60; $P < .0001$). In particular, there was a significant association between the recommendation for biopsy in the contralateral or bilateral breasts and CPM use ($P < .0001$), a variable that, to our knowledge, has not been previously reported. Others have documented that women with an abnormal MRI may choose to forgo biopsy and proceed with mastectomy for what is ultimately a benign finding.[25] Our data support this observation. Only 22 (44%) of 50 patients with a recommendation for contralateral or bilateral biopsy underwent a biopsy preoperatively, with the remainder proceeding directly to CPM. Proponents of MRI cite data that preoperative MRI will identify occult contralateral carcinoma in 3% of women.[26] Among the 24 patients with occult contralateral carcinoma identified in the CPM in this series, nine had preoperative MRI, leading to a recommendation for biopsy in four of nine cases. Although the study population does not include patients with a suspicious MRI who were diagnosed with a synchronous malignancy preoperatively, the low occult invasive carcinoma rate among women undergoing CPM in this series—five (1.2%) of 407—does not support routine use of MRI in the decision-making process for CPM. Although there was variation among surgeons in the use of CPM, there was no association with surgeon age, sex, or years of practice; some variation was secondary to a small number of surgeons who contributed patients only during the early years of the study when rates of CPM were lower.

Recent data indicate that mastectomy rates may be increasing. Katipamula et al[18] reported that although mastectomy rates at the Mayo Clinic decreased from 45% to 23% from 1997 to 2003, rates steadily increased over the next 4 years, reaching levels similar to 1997 in 2006. Concerns over persistent use of mastectomy led Morrow et al[27] to evaluate reasons for receipt of mastectomy in two large urban areas reporting to the Surveillance, Epidemiology, and End Results program registries. Among 1,984 patients with stage 0 to II breast cancer, only one third underwent mastectomy as final treatment. Among these women, 13.4% underwent initial mastectomy after physician recommendation; 8.8% had mastectomy on the basis of a patient-directed decision, and 8.8% had mastectomy after one or more unsuccessful attempts at BCS. These data suggest that patient preferences continue to play an important role in receipt of mastectomy. Although there was a low conversion rate to mastectomy (11.9%) when BCS was undertaken, the need for re-excision was a significant problem and was reported in 38% of patients in this series. Although concerns over high re-excision rates have been widely reported[28] and although the desire to complete therapy with a single surgical procedure may influence patient preference toward mastectomy, our study is the first to associate failed attempts at BCS with increased CPM use. Our observation that 81% of patients initially

Table 5. Contralateral Breast Cancers and Recurrences

Factor	No CPM (n = 2,572) No.	No CPM (n = 2,572) % of No CPM	CPM (n = 407) No.	CPM (n = 407) % of CPM
Follow-up, years*				
Median	6.8		4.4	
Range	0.33-12.2		0.18-11.7	
Site of first event				
None	2,297		383	
Contralateral breast cancer	14	0.5	0†	
Distant metastases	187	7	15	4
Ipsilateral locoregional	74	3	9	2
Chest wall	60		4	
Regional nodes	14		5	

Abbreviation: CPM, contralateral prophylactic mastectomy.

*Calculated for patients who did not experience recurrence.

†Occult carcinoma was identified in 24 (6%) of 407 of patients having contralateral prophylactic mastectomy.

attempting BCS converted to bilateral mastectomy after a single attempt at excision suggests that the need for multiple procedures has a significant impact on the surgical decision-making process.

Whether the availability of immediate reconstruction truly increases CPM rates is worthy of additional study. Although we found immediate reconstruction to be associated with CPM, Yi et al[14] reported the use of reconstruction to be associated with delayed, rather than immediate CPM, and others have observed lower rates of mastectomy in areas with high use of reconstruction[29] or decreasing use of reconstruction at a time when mastectomy rates were increasing.[30]

In summary, these data suggest that increasing CPM use is not associated with increased recognition of patients at high risk for CBC. Treatment factors, such as MRI use and unsuccessful attempts at BCS and immediate reconstruction, were associated with increased rates of CPM. Our findings indicate that patient education about the low absolute risk of CBC and the lack of survival benefit with CPM is needed. Avoidance of routine MRI use in the absence of a specific clinical problem to be addressed by the test and avoidance of routine re-excisions to achieve an arbitrary margin width greater than tumor not touching ink, may also be beneficial in decreasing patient demand for this procedure.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

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REFERENCES

1. Arrington AK, Jarosek SL, Virnig BA, et al: Patient and surgeon characteristics associated with increased use of contralateral prophylactic mastectomy in patients with breast cancer. Ann Surg Oncol 16:2697-2704, 2009
2. Jones NB, Wilson J, Kotur L, et al: Contralateral prophylactic mastectomy for unilateral breast cancer: An increasing trend at a single institution. Ann Surg Oncol 16:2691-2696, 2009
3. Tuttle TM, Habermann EB, Grund EH, et al: Increasing use of contralateral prophylactic mastectomy for breast cancer patients: A trend toward more aggressive surgical treatment. J Clin Oncol 25:5203-5209, 2007
4. Tuttle TM, Jarosek S, Habermann EB, et al: Increasing rates of contralateral prophylactic mastectomy among patients with ductal carcinoma in situ. J Clin Oncol 27:1362-1367, 2009
5. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: An overview of the randomised trials. Lancet 365:1687-1717, 2005
6. Forbes JF, Cuzick J, Buzdar A, et al: Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 100-month analysis of the ATAC trial. Lancet Oncol 9:45-53, 2008
7. Romond EH, Perez EA, Bryant J, et al: Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. N Engl J Med 353: 1673-1684, 2005
8. Hislop TG, Elwood JM, Coldman AJ, et al: Second primary cancers of the breast: Incidence and risk factors. Br J Cancer 49:79-85, 1984
9. Kollias J, Ellis IO, Elston CW, et al: Clinical and histological predictors of contralateral breast cancer. Eur J Surg Oncol 25:584-589, 1999
10. Rosen PP, Groshen S, Kinne DW, et al: Contralateral breast carcinoma: An assessment of risk and prognosis in stage I (T1N0M0) and stage II (T1N1M0) patients with 20-year follow-up. Surgery 106:904-910, 1989
11. Saphner T, Tormey DC, Gray R: Annual hazard rates of recurrence for breast cancer after primary therapy. J Clin Oncol 14:2738-2746, 1996
12. Gao X, Fisher SG, Emami B: Risk of second primary cancer in the contralateral breast in women treated for early-stage breast cancer: A population-based study. Int J Radiat Oncol Biol Phys 56:1038-1045, 2003
13. Nathanson KL, Wooster R, Weber BL: Breast cancer genetics: What we know and what we need. Nat Med 7:552-556, 2001
14. Yi M, Hunt KK, Arun BK, et al: Factors affecting the decision of breast cancer patients to undergo contralateral prophylactic mastectomy. Cancer Prev Res (Phila) 3:1026-1034, 2010
15. Lostumbo L, Carbine N, Wallace J, et al: Prophylactic mastectomy for the prevention of breast cancer. Cochrane Database Syst Rev 4:CD002748, 2004
16. Bleicher RJ, Ciocca RM, Egleston BL, et al: Association of routine pretreatment magnetic resonance imaging with time to surgery, mastectomy rate, and margin status. J Am Coll Surg 209:180-187, 2009
17. Houssami N, Ciatto S, Macaskill P, et al: Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: Systematic review and meta-analysis in detection of multifocal and multicentric cancer. J Clin Oncol 26:3248-3258, 2008
18. Katipamula R, Degnim AC, Hoskin T, et al: Trends in mastectomy rates at the Mayo Clinic Rochester: Effect of surgical year and preoperative magnetic resonance imaging. J Clin Oncol 27:4082-4088, 2009
19. Sorbero ME, Dick AW, Beckjord EB, et al: Diagnostic breast magnetic resonance imaging and contralateral prophylactic mastectomy. Ann Surg Oncol 16:1597-1605, 2009
20. Tuttle TM: Counseling breast cancer patients on contralateral prophylactic mastectomy: The physician's role. Oncology (Williston Park) 22:545-548, 2008
21. Dupont EL, Kuhn MA, McCann C, et al: The role of sentinel lymph node biopsy in women undergoing prophylactic mastectomy. Am J Surg 180:274-277, 2000
22. Yi M, Meric-Bernstam F, Middleton LP, et al: Predictors of contralateral breast cancer in patients with unilateral breast cancer undergoing contralateral prophylactic mastectomy. Cancer 115:962-971, 2009
23. Bedrosian I, Hu CY, Chang GJ: Population-based study of contralateral prophylactic mastectomy and survival outcomes of breast cancer patients. J Natl Cancer Inst 102:401-409, 2010
24. McLaughlin SA, Stempel M, Morris EA, et al: Can magnetic resonance imaging be used to select patients for sentinel lymph node biopsy in prophylactic mastectomy? Cancer 112:1214-1221, 2008
25. Berg WA, Gutierrez L, NessAiver MS, et al: Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology 233:830-849, 2004
26. Lehman CD, Gatsonis C, Kuhl CK, et al: MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. N Engl J Med 356:1295-1303, 2007
27. Morrow M, Jagsi R, Alderman AK, et al: Surgeon recommendations and receipt of mastectomy for treatment of breast cancer. JAMA 302: 1551-1556, 2009
28. Singletary SE: Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. Am J Surg 184:383-393, 2002
29. Ess S, Savidan A, Frick H, et al: Geographic variation in breast cancer care in Switzerland. Cancer Epidemiol 34:116-121, 2010
30. McGuire KP, Santillan AA, Kaur P, et al: Are mastectomies on the rise? A 13-year trend analysis of the selection of mastectomy versus breast conservation therapy in 5865 patients. Ann Surg Oncol 16:2682-2690, 2009

