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Factors impacting the decision of breast cancer patients to undergo contralateral prophylactic mastectomy

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Abstract

Background—Increasing numbers of women with breast cancer are electing for contralateral prophylactic mastectomy (CPM) to reduce the risk of developing contralateral breast cancer. The objective of this study was to identify factors that may impact a patient's decision to undergo CPM.

Methods—We identified 2504 women with stage 0–III unilateral primary breast cancer who underwent breast surgery at our institution from January 2000 to August 2006 from a prospectively maintained database. We performed logistic regression analyses to determine which factors were associated with undergoing CPM.

Results—Of 2504 breast cancer patients, 1223 (48.8%) underwent total mastectomy. Of the 1223 patients who underwent mastectomy, 284 (23.2%) underwent immediate or delayed CPM. There were 33 patients (1.3%) who had genetic testing before the surgery; with the use of testing increasing in the latter years of the study (0.1% in 2000–2002 vs. 2.0% in 2003–2006, P<0.0001). Multivariable analysis revealed several factors that were associated with a patient undergoing CPM: age younger than 50 years, white ethnicity, family history of breast cancer, *BRCA1/2* mutation testing, invasive lobular histology, clinical stage and use of reconstruction.

Conclusions—We identified specific patient and tumor characteristics associated with the use of CPM. Although genetic testing is increasing, most women undergoing CPM did not have a known genetic predisposition to breast cancer. Evidence-driven models are needed to better inform women of their absolute risk of contralateral breast cancer as well as their competing risk of recurrence from the primary breast cancer to empower them in their active decision making.

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Keywords

contralateral breast cancer; breast cancer prevention; contralateral prophylactic mastectomy; risk-reducing mastectomy

INTRODUCTION

Women diagnosed with breast cancer have a significantly increased lifetime risk of developing contralateral breast cancer (CBC) over the general population [1–4]. Gao et al. evaluated the incidence of CBC in 134,501 patients previously diagnosed with breast cancer identified from the Surveillance, Epidemiology, and End Results (SEER) database and found that the actuarial incidence of CBC at 5, 10, 15, and 20 years was 3%, 6.1%, 9.1%, and 12%, respectively, or approximately 0.6% per year [5]. Patients with unilateral breast cancer who have germline mutations in *BRCA1*/2 have a markedly increased risk of developing CBC [6, 7]. Specific clinical and pathologic factors that have been associated with an increased risk of developing CBC include age younger than 50 years old, a family history of breast cancer, lobular type histology, multicentric cancer, and previous chest irradiation [4, 8–12]. Additional risk factors for CBC that have been identified in other studies include African American ethnicity [5], body mass index > 30 kg/m^2 [13] medullary carcinoma histology [5], and HER2-positive tumors [13].

To reduce their risk of developing CBC, some breast cancer patients choose to undergo contralateral prophylactic mastectomy (CPM). However, the surgeon's decision to perform and the patient's decision to undergo CPM are complex. The decision making process should include assessing the patient's risk of CBC, which can vary according to age, genetic factors such as *BRCA1/2* mutation status, tumor histology and multicentricity. Other issues to consider include available reconstructive options, the ability to achieve symmetry if a unilateral procedure is performed and the projected oncologic outcome from the known ipsilateral breast cancer [14].

In a previous study, we identified the clinicopathologic factors that predicted the presence of an unsuspected CBC at the time of CPM: a 5-year Gail risk ≥ 1.67%, additional ipsilateral moderate- to high-risk pathology, an ipsilateral multicentric tumor, or an ipsilateral tumor of invasive lobular histology [12]. These findings may impact the decision-making process regarding CPM in patients with a diagnosis of unilateral breast cancer. The clinicopathologic characteristics associated with a patient's decision to undergo CPM are less well defined. In the current study, we sought to identify factors that may impact the patients' decision regarding CPM in women faced with a diagnosis of unilateral breast cancer.

MATERIALS AND METHODS

Patient Selection and Data Collection

We used the prospectively maintained Surgical Breast Oncology Database at The University of Texas M. D. Anderson Cancer Center for patient selection. We retrospectively identified patients with unilateral breast cancer who underwent breast-conserving surgery and/or mastectomy between January 2000 and August 2006. We included patients with unilateral

stage 0–III primary breast cancer who had no clinical or radiographic evidence of a contralateral breast malignancy. Patients known to have had bilateral breast cancer prior to CPM were excluded from analysis. Some patients who underwent CPM were included in previous reports from our institution [9, 12]. The M. D. Anderson Institutional Review Board approved this study and the need for informed consent was waived.

We reviewed patient charts for demographics, disease, and treatment characteristics, including year of surgery, age at the time of diagnosis, ethnicity, marital status, use of hormone replacement therapy, family history of breast cancer, clinical tumor stage, use of pretreatment magnetic resonance imaging (MRI), type of surgery for primary tumor, performance and timing of CPM, reported reasons for undergoing CPM, surgeon characteristics (gender, age), use and type of reconstructive surgery, genetic testing for *BRCA 1/2* mutations and results, histology of the primary tumor (invasive lobular carcinoma versus other histology), estrogen receptor (ER) status, and progesterone receptor (PR) status of the primary tumor.

Breast-conserving surgery or mastectomy was performed on the ipsilateral side with or without lymph node staging as considered appropriate based on diagnostic biopsy findings. In patients who chose to undergo CPM, synchronous or delayed CPM was performed with or without sentinel lymph node biopsy at the discretion of the operating surgeon.

Statistical Analysis

For statistical analyses, patients who underwent surgery for breast cancer were separated into two groups—patients who underwent CPM and patients who did not undergo CPM. Clinicopathologic data were tabulated for each of these groups. Student's t test with appropriate normality checks was used to compare the means of all continuous variables. For univariable comparisons of all categorical variables, Chi squared analysis or Fisher's exact test (when sample sizes are small) was used. We performed univariable and multivariable analyses, and used a stepwise multiple logistic regression analysis to identify variables that were associated with undergoing CPM in patients who underwent surgery for breast cancer (breast-conserving surgery and/or mastectomy) and separately in those who underwent mastectomy as the primary procedure for their breast cancer. All *P* values were 2-tailed, and we considered *P* values ≤ 0.05 to be significant. Stata statistical software (StataSE 10, StataCorp LP, College Station, TX) was used for all statistical analyses.

RESULTS

Patient, Tumor, and Treatment Characteristics

A total of 2504 women with stage 0–III unilateral primary breast cancer who underwent surgical treatment at the University of Texas M. D. Anderson Cancer Center were included in this study. The median age of the patients was 54 years (range, 22–97 years); 1861 (74.3%) were white, and 643 (25.7%) were of other ethnicities (African American, Asian, Hispanic). The clinical stage of the primary tumor at diagnosis was 0, I, II, and III in 16.2%, 37.8%, 32.2%, and 13.8% of the patients, respectively. A total of 304 (12.1%) patients had primary tumors of invasive lobular histology. Of the 2504 patients, 1223 (48.8%) underwent

total mastectomy for their known ipsilateral cancer. Of the 284 patients (23.2% of those undergoing ipsilateral mastectomy) who had CPM, 246 underwent CPM at the time of treatment for their ipsilateral breast cancer (immediate) and 38 had CPM at a later time (delayed). Eight patients (2.8%) had an occult malignancy in their CPM specimen, and 50 patients (17.6%) had ADH, ALH, and LCIS histologic findings in the CPM specimen.

Figure 1 shows the proportion of patients who underwent CPM over time from 2000 to 2006. The CPM rate increased significantly from 6.8% in 2000 to 14.0% in 2006 (a 105% increase, P<0.0001). The CPM rate was also significantly increased when only patients undergoing mastectomy for treatment of their primary tumor were considered. This increased, from 15.5% in 2000 to 29.8% in 2006 (a 92% increase, P<0.0001).

Factors Associated with CPM

The demographics, tumor, pathologic and treatment characteristics of the patients who did and did not undergo CPM are summarized in Table 1. Univariable analyses revealed that patient age <50, white ethnicity, marital status, family history of breast cancer, use of hormone replacement therapy, undergoing *BRCA1/2* genetic testing before surgery, higher clinical tumor stage, multicentric primary tumor, invasive lobular histology, and use of reconstructive surgery were significantly associated with undergoing CPM.

MRI was performed only selectively in this series. Patients who underwent CPM were more likely to have undergone an MRI of either breast compared with patients who had a unilateral mastectomy without a CPM (9.9% vs. 5.4%, p<0.0001), however, of the 28 CPM patients who underwent an MRI, 18 only had imaging of the ipsilateral breast, and 7 had imaging of the contralateral breast, and 3 had bilateral imaging. Review of the medical records suggested that none of the 28 CPM patients who had an MRI of either breast decided to pursue a CPM due to MRI findings.

Multivariable logistic regression analysis with backward variable selection (Table 2) revealed that younger patients (< 50 years of age) were significantly more likely to undergo CPM (odds ratio (OR) 1.78, 95% confidence interval (CI): 1.33–2.39): 17.6% of patients < 50 years underwent CPM compared with only 8.0% of women ≥ 50 years. Patients were also significantly more likely to undergo CPM if they were white (OR 2.54, 95% CI: 1.73–3.74), had a family history of breast cancer (OR 1.57, 95% CI: 1.19–2.09), had stage II tumors (OR 2.25, 95% CI: 1.46–3.46) or stage III tumors (OR 2.44, 95%CI: 1.44–4.15), underwent *BRCA1/2* genetic testing before surgery(OR 4.51, 95% CI: 1.98–10.25), had reconstructive surgery (OR 8.82, 95% CI: 6.59–11.80), or had invasive lobular histology (OR 1.89, 95% CI: 1.30–2.74). Neither ER/PR status of the primary tumor nor surgeon characteristics (gender, age) was associated with the use of CPM.

When only patients who underwent total mastectomy for treatment of their primary tumor were included in the analysis, univariable analysis (Table 1) revealed that patient age, ethnicity, marital status, family history of breast cancer, undergoing *BRCA1/2* genetic testing before surgery, higher clinical tumor stage, invasive lobular histology, and use of reconstructive surgery were significantly associated with undergoing CPM. Multivariable logistic regression analysis (Table 2) revealed that younger patients (< 50 years of age) were

significantly more likely to undergo CPM (OR 1.72, 95% CI: 1.26–2.25): 30.6% of patients < 50 years of age underwent CPM compared with only 18.2% of women ≥ 50 years of age. Patients were also significantly more likely to undergo CPM if they were white (OR 2.51, 95% CI: 1.70–3.71), had a family history of breast cancer (OR 1.45, 95% CI: 1.08–1.94), had stage II tumors (OR 1.76, 95% CI: 1.11–2.79), underwent *BRCA1/2* genetic testing (OR 3.92, 95% CI: 2.30–6.67), underwent reconstructive surgery (OR 2.70, 95% CI: 1.95–3.74), or had invasive lobular histology (OR 1.63, 95% CI: 1.11–2.39).

Factors Associated with Timing of CPM

The demographics, tumor, and treatment characteristics of the patients who underwent immediate CPM as compared with delayed CPM are summarized in Table 3. Patients with younger age, other ethnicity, single status, who had *BRCA1/2* genetic testing before surgery, higher clinical tumor stage, and use of reconstructive surgery were more likely to undergo delayed CPM instead of immediate CPM.

Patients' Decision-Making Regarding the Use of CPM

The patients' reasons for undergoing CPM (as attributed by the surgical team and prospectively collected in the database) are summarized in Table 4. Most patients (87%) chose to undergo CPM because of a family history of breast cancer, a psychological fear of developing another breast cancer, or perceived difficulty in surveillance for CBC because of clinically and mammographically dense breast tissue or diffuse microcalcifications in the contralateral breast.

Genetic Testing for Germline Mutations in *BRCA1/2*

Table 5 summarizes the impact of genetic testing on the decision to undergo CPM. Thirty-three patients had genetic testing prior to surgery. Eight of these patients had a deleterious *BRCA1/2* mutation identified and then proceeded to undergo CPM. Interestingly, 10 patients who underwent genetic testing and were found not to carry a deleterious *BRCA1/2* mutation still chose to undergo CPM.

DISCUSSION

Over the past decade, increasing numbers of women with breast cancer have been electing to undergo CPM to reduce the risk of contralateral breast cancer [15]. In this study, we sought to identify factors that were associated with the decision to undergo CPM. Of 2504 women with stage 0–III unilateral breast cancer who underwent breast-conserving surgery or mastectomy for their primary tumor at our institution, we found that 11.3% underwent CPM. Several patient and tumor characteristics were associated with patients undergoing CPM including patient age, ethnicity, family history of breast cancer, undergoing *BRCA1/2* genetic testing, higher clinical tumor stage, invasive lobular histology, and use of reconstructive surgery.

We found that the proportion of patients who chose to undergo CPM at our institution doubled between 2000 and 2006. Similarly, Tuttle et al. found that the rate of CPM in patients with stage I–III unilateral breast cancer increased by 150% from 1998 to 2003 [16]

and that the rate of CPM in patients with ductal carcinoma in situ increased by 148% in the United States from 1998 to 2005 [17]. There are many factors that may have contributed to the increased use of CPM over this timeframe, including an increased patient interest in cancer prevention, the availability of genetic counseling and *BRCA 1/2* testing, and the increased utilization of skin-sparing mastectomy and availability of breast reconstruction.

MRI is increasingly used in the preoperative assessment of both the ipsilateral and contralateral breasts of women with newly diagnosed breast cancer[18, 19]. Katipamula and colleagues recently reported that among women treated for early-stage breast cancer at the Mayo Clinic between 1997 and 2006, 52% of those who had a breast MRI underwent mastectomy compared with 38% of women who did not receive an MRI[20]. Sorbero and colleagues reported that women who underwent MRI were nearly twice as likely to have CPM[21]. In this study, the overall use of MRI is low, with MRI being used selectively. Although more of the patients that underwent CPM had a MRI, only 3.5% underwent a contralateral MRI, and a retrospective review of the medical records of the CPM patients who had an MRI of either breast suggested that the MRI results did not lead to the decision for CPM in our patients. Thus the trend of increasing CPMs in our institution appears to not be driven by the use of MRI. However, in our institution, more recently, the contralateral breast is also imaged when an ipsilateral MRI is ordered. How this change in practice will affect CPM rates will need to be followed.

At our institution, several patient variables were associated with the decision to undergo CPM. For example, in all patients who underwent surgery for breast cancer and in those who underwent mastectomy for treatment of their primary tumor, Caucasian race was associated with significantly higher CPM rates. Ethnicity was also found to be an important predictor of CPM in studies examining the SEER database by Tuttle et al. [16, 17]. Race and ethnicity are known to effect the delivery of definitive local therapy [22], choice of breast-conserving surgery versus mastectomy [23], and utilization of immediate breast reconstruction in patients undergoing mastectomy [24]. In our study, Caucasian race was a predictor for patients undergoing CPM independent of tumor stage and use of reconstruction. Further study is warranted to evaluate both the patient and heath care provider variables that may contribute to this ethnic disparity.

Age younger than 50 years and invasive lobular histology were both significantly associated with patients undergoing CPM in our study. Using data from the SEER registry and the Connecticut Tumor Registry, Tuttle et al. [16] and Polednak [25] also reported that young age and lobular histology were associated with higher CPM rates. The increased utilization of CPM in younger patients is not surprising, as patients who are younger in age at breast cancer onset are more likely to have a hereditary breast cancer. In addition, among *BRCA1/2* mutation carriers, younger age at diagnosis of the first breast cancer predicts a higher risk of CBC [26]. Furthermore, even among women without a recognized genetic predisposition to breast cancer, younger women would still be expected to derive more benefit from CPM owing to their longer life expectancy and subsequently higher expected lifetime risk of developing another primary breast cancer.

The increased utilization of CPM that we and others found in patients with invasive lobular carcinoma is of particular interest. Although patients with invasive lobular carcinoma have been reported to be at a significantly increased risk of CBC [4, 9–12], many of these studies were performed more than twenty years ago when there was still controversy regarding the diagnoses of lobular carcinoma in situ and invasive lobular histology. Others, such as our recent study, have determined predictors of incidental CBC on CPM specimens [12], and found that ipsilateral lobular histology increased the likelihood of identifying a CBC on CPM. However, these studies do not truly answer the question of whether patients with invasive lobular carcinoma undergoing current standard-of-care treatments for unilateral cancer are more likely to develop a clinically significant CBC in the future. In fact, Gao et al. [5] did not observe a higher rate of CBC in patients with invasive lobular cancer compared with invasive ductal cancers. Similarly, in our previous work, we have found no difference in the CBC rates of patients undergoing breast conservation for invasive lobular carcinoma compared with those with ductal carcinoma. [27] As most lobular carcinomas are ER positive, it is likely that even if there is a propensity for CBC development, it may be overcome by the chemopreventive effect of current adjuvant endocrine therapy regimens.

When considering CPM, it is important to weigh the absolute risk of CBC against the risk of the proposed surgery, patient comorbidities, and competing risk of recurrence from the primary tumor. The absolute risk of CBC varies not only with the factors discussed above but also with the treatment of the primary tumor. An overview of randomized polychemotherapy trials demonstrated that adjuvant chemotherapy was associated with a 20% reduction in CBC risk and that the use of tamoxifen was associated with a 47% risk reduction [28]. In considering the risk of the proposed surgery, one must also consider how the surgery will effect adjuvant therapy; even minor wound complications may potentially delay recommended chemotherapy or radiation therapy for the primary cancer after surgery. Indeed, in a previous study, we found that bilateral mastectomy for unilateral cancer conferred a higher risk of complications than unilateral mastectomy, with 8.4% of the complications occurring on the primary side, 6.3% occurring on the contralateral side, and 1.7% occurring bilaterally; thus, CPM does increase the complexity of the surgical procedure and may increase the complications incurred [1].

Breast cancer patients with deleterious *BRCA1/2* mutations have a significantly increased risk of developing CBC [6, 7]. Thus, it is important to pursue genetic risk stratification for patients with a family history of breast or ovarian cancer or those who are at a young age at breast cancer onset. We found that genetic testing for the *BRCA1/2* mutation has increased in recent years at our institution. This may reflect increased awareness and acceptance of genetic testing by patients and physicians, or it may reflect a more recent restructuring of the medical cancer genetics services at our institution. In our study, genetic testing for *BRCA1/2* mutations was associated with patients choosing to undergo CPM. Interestingly, several patients who underwent testing and were negative for any deleterious mutations in the *BRCA* genes still chose to undergo CPM. In fact, patients who had pursued genetic testing were more likely to undergo CPM regardless of results of *BRCA* testing.

Although there is evidence that CPM does in fact decrease CBC risk [2, 29–31], the impact of CPM on survival has been more controversial. If there is indeed a survival benefit from

CPM, it could be hypothesized that the benefit would be greatest in patients with early-stage cancer, who have the lowest risk of death from the primary cancer. Shrag et al. reported that in *BRCA1/2* mutation carriers, patients with early-stage node-negative breast cancer would be expected to have the greatest gains in life expectancy after CPM [32]. Interestingly, among all patients who underwent surgery for breast cancer in our study, patients who had higher-stage disease (stage II or III) were more likely to choose to undergo CPM; however, this was no longer true when only patients who underwent mastectomy for treatment of their primary tumor were considered. Whether our findings reflect the greater psychologic fear of patients who have a more aggressive primary tumor at diagnosis or whether it reflects that patients with larger tumors that necessitate mastectomy are more likely to elect a contralateral procedure remains unclear. However, it emphasizes that we need better tools to inform women of their absolute risk of CBC as well as the competing risk of recurrence from their primary breast cancer to assist them in their decision-making process.

Although absolute indications for CPM have not been established, the Society of Surgical Oncology has published criteria for considering the use of CPM, listing reconstructive issues, such as symmetry and/or balance as a consideration [33]. Also, in a study of breast cancer patients from the National Cancer Institute-funded Cancer Research Network between 1979 and 1999, Geiger et al. reported that patients who underwent CPM were more likely to undergo breast reconstruction than patients who did not undergo CPM [34]. In our study, use of reconstructive surgery was the strongest factor associated with patients undergoing CPM on multivariable analysis. Some patients may pursue CPM for reconstructive issues, such as the desire to achieve symmetry (especially a concern with implant reconstructions) or the ability to undergo autologous abdominal tissue-based reconstruction only once. Alternatively, there may be other variables driving the decision to pursue reconstruction and/or CPM.

Our study had several possible limitations, including those inherent to any single-institution, retrospective study. One limitation is that we did not evaluate patient satisfaction with and psychosocial outcomes after CPM. Given the retrospective nature of the study, we were also unable to discern the role of the patient’s choice versus the surgeon’s influence on the decision to pursue CPM. Furthermore, this study reflects the patterns of care at a major cancer center. The CPM rates may have been influenced by an increased number of informed patients seeking out certain treatments, the ready availability of genetic counseling, and the patients’ desire and ability to undergo immediate reconstruction. Regardless, results of this study may be valuable to other institutions with respect to their own recommendations on the use of CPM in patients with unilateral breast cancer. Our study opens this subject up to further critical analysis and debate among patients and clinicians who treat women with breast cancer.

In conclusion, we found that various patient and tumor characteristics were associated with the decision to undergo CPM. Evidence-driven models are needed to better inform women of their absolute risk of CBC and the competing risk of recurrence from their primary breast cancer in order to empower these women during the active decision-making process. Genetic counseling and selective use of genetic testing may also guide rational decision making.

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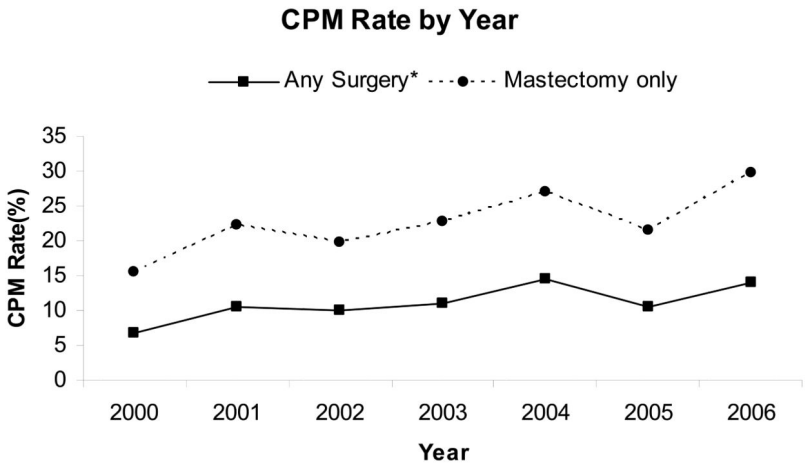

Figure 1.

Patients with unilateral breast cancer who underwent contralateral prophylactic mastectomy.

Abbreviation: CPM, contralateral prophylactic mastectomy.

* Breast-conserving surgery and/or mastectomy for treatment of the patient's primary tumor.

Table 1

Demographic, tumor, pathologic and treatment characteristics of breast cancer patients who underwent CPM compared with those who did not.

Characteristics	CPM, (n=284)	No CPM, Any surgery* (n=2220)	P†	No CPM, Mastectomy (n=939)	P†
Median age (range) year	49.6 (22–85)	55.8 (26–97)	<0.0001	54.3 (26–88)	<0.0001
Age			<0.0001		<0.0001
<50 year	152 (53.5)	711 (32.0)		345 (36.7)	
>=50 year	132 (46.5)	1509 (68.0)		594 (63.3)	
Ethnicity			<0.0001		<0.0001
White	244 (85.9)	1617 (72.8)		646 (68.8)	
Others	40 (14.1)	603 (27.2)		293 (31.2)	
Marital status			<0.0001		<0.0001
Married	221 (77.8)	1466 (66.0)		611 (65.1)	
Single	24 (8.5)	252 (11.4)		114 (12.1)	
Others	39 (13.7)	502 (22.6)		214 (22.8)	
Family history of breast cancer			<0.0001		<0.0001
Yes	161 (56.7)	939 (42.3)		401 (42.7)	
No	123 (43.3)	1281 (57.7)		538 (57.3)	
Family history of breast cancer			0.001		0.002
In a first-degree relative	75 (26.4)	399 (18.0)		169 (18)	
Not in first-degree relatives	209 (73.6)	1821 (82.0)		770 (82.0)	
Hormone replacement therapy			0.001‡		0.1‡
Yes	95 (33.5)	977 (44.0)		366 (39.0)	
No	179 (63.0)	1192 (53.7)		547 (58.2)	
Unknown	10 (3.5)	51 (2.3)		26 (2.8)	
BRCA1/2 genetic testing before surgery			<0.0001		<.0001
Yes	18 (6.3)	15 (0.7)		9 (1.0)	
No	266 (93.7)	2205 (99.3)		930 (99.0)	
Breast MRI			<0.0001*		0.001*
None or after surgery	256 (90.1)	2121 (95.5)		888 (94.6)	
Primary side	21 (7.4)	94 (4.2)		48 (5.1)	
Contralateral side	7 (2.5)	5 (0.3)		3 (0.3)	

Characteristics	CPM, (n=284)	No CPM, Any surgery* (n=2220)	P†	No CPM, Mastectomy (n=939)	P†
Clinical tumor stage			<0.0001		0.003
0	39 (13.7)	367 (16.5)		142 (15.1)	
I	81 (28.5)	865 (39.0)		238 (25.4)	
II	122 (43.0)	684 (30.8)		330 (35.1)	
III	42 (14.8)	304 (13.7)		229 (24.4)	
Multicentric tumor			<0.0001		0.46
No	231 (81.3)	1981 (89.2)		745 (79.3)	
Yes	53 (18.7)	239 (10.8)		194 (20.7)	
Histology of primary tumor		<0.0001		0.02	
Invasive lobular	56 (19.7)	248 (11.2)		132 (14.1)	
Others	228 (80.3)	1972 (88.8)		807 (85.9)	
Estrogen receptor status			0.098‡		0.64‡
Positive	184 (64.8)	1530 (68.9)		614 (65.4)	
Negative	88 (31.0)	582 (26.2)		274 (29.2)	
Unknown	12 (4.2)	108 (4.9)		51 (5.4)	
Progesterone receptor status			0.16‡		0.80‡
Positive	142 (50)	1197 (53.9)		471 (50.2)	
Negative	129 (45.4)	906 (40.8)		413 (44.0)	
Unknown	13 (4.6)	117 (5.3)		55 (5.8)	
Surgery for primary tumor			<0.0001		
Breast-conserving surgery	0	1281 (57.7)			
Mastectomy	284	939 (42.3)			
Reconstruction					<.0001
Yes	184 (64.8)			348 (37.1)	
No	100 (35.2)			591 (62.9)	

Abbreviation: CPM, contralateral prophylactic mastectomy.

Note: Data are presented as the number (%) of patients, unless otherwise specified.

*Breast-conserving surgery or mastectomy for treatment of the patients' primary tumor.

†Compared to patients who underwent CPM. P-values correspond to t-tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables

‡Excluding the unknown category.

Table 2

Multivariable analysis of the factors associated with undergoing contralateral prophylactic mastectomy.

	Any surgery*			Mastectomy only		
Variable	**OR**	**95 % CI**	**P**	**OR**	**95 % CI**	**P**
Age						
≥50 (referent)	-	-	-	-	-	-
<50	1.78	1.33–2.39	0.001	1.84	1.35–2.50	<0.0001
Race						
Others (referent)	-	-	-	-	-	-
White	2.54	1.73–3.74	<0.0001	2.63	1.78–3.88	<0.0001
Marital status						
Single (referent)	-	-	-	-	-	-
Married	1.62	0.99–2.64	0.055	1.66	1.002–2.73	0.049
Other	1.16	0.64–2.09	0.62	1.16	0.63–2.11	0.63
Family history of breast cancer						
No (referent)	-	-	-	-	-	-
Yes	1.57	1.19–2.09	0.001	1.58	1.17–2.11	0.002
BRCA1/2 genetic testing						
No test before surgery (referent)	-	-	-	-	-	-
Test before surgery	4.51	1.98–10.25	<0.0001	5.16	2.15–12.35	<0.0001
Clinical tumor stage						
0 (referent)	-	-	-	-	-	-
I	1.07	0.68–1.67	0.83	1.37	0.85–2.19	0.195
II	2.25	1.46–3.46	<0.0001	1.82	1.11–2.79	0.011
III	2.44	1.44–4.15	0.001	1.15	0.85–2.19	0.622
Invasive lobular histology						
No (referent)	-	-	-	-	-	-
Yes	1.89	1.30–2.74	0.001	1.58	1.07–2.31	0.019
Reconstruction						
No (referent)	-	-	-	-	-	-
Yes	8.82	6.59–11.80	<0.0001	2.72	1.97–3.76	<0.0001

Abbreviation: CI, confidence interval; OR, Odds Ratio

*Breast-conserving surgery and/or mastectomy for treatment of the patient's primary tumor.

Multivariable analysis was done with logistic regression with backward variable selection

Table 3

Demographic, tumor, pathologic and treatment characteristics of breast cancer patients who underwent immediate CPM as compared with delayed CPM.

Characteristics	Immediate CPM N=246	Delayed CPM N=38	P value
Median age (range) year	49 (22–85)	43.5 (29–68)	0.005
Age			0.055*
<50 year	120 (48.8)	12 (31.6)	
>=50 year	126 (51.2)	26 (68.4)	
Ethnicity			0.01*
White	217 (88.2)	27 (71.1)	
Others	29 (11.8)	11 (28.9)	
Marital status			0.03
Married	197 (80.1)	24 (63.2)	
Single	17 (6.9)	7 (18.4)	
Others	32 (13.0)	7 (18.4)	
Clinical tumor stage			0.012*
0	37 (15.0)	2 (5.2)	
I	76 (30.9)	5 (13.2)	
II	100 (40.8)	22 (57.9)	
III	33 (13.5)	9 (23.7)	
Family history of breast cancer			0.6
Yes	141 (57.3)	20 (52.6)	
No	105 (42.7)	18 (47.4)	
BRCA1/2 genetic testing before surgery			<0.0001
Yes	9 (3.7)	9 (23.7)	
No	237 (96.3)	29 (76.3)	
Reconstruction			0.027*
Yes	153 (62.0)	31 (81.6)	
No	93 (37.8)	7 (18.4)	

Abbreviation: CPM, contralateral prophylactic mastectomy.

* P-values correspond to t-tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables

Table 4

Factors influencing a patient's decision to undergo contralateral prophylactic mastectomy (as documented in the patients' records)

Factors	Number of patients* (%)
Family history of breast cancer	85 (30)
Difficult surveillance	91 (32)
Psychological fear	135 (48)
Family history of other cancer	66 (23)
Multicentric/multifocal primary breast cancer	50 (18)
Reconstructive issue	30 (11)
Unknown	17 (6.0)

*Some factors were listed more than once in an individual patient's medical records

Table 5

Incidence and results of genetic testing in patients who did and did not undergo CPM

Characteristics	Number of patients (%)		P*
	No CPM	CPM	
Genetic testing before surgery(n=33)	(n=15)	(n=18)	0.003
BRCA1/2 mutation	0	8	
No *BRCA1/2* mutation	15	10	

Abbreviation: CPM, contralateral prophylactic mastectomy.

* Fisher's exact tests