International Journal of Cancer and Oncology

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Research Article

Contralateral Prophylactic Mastectomy: Characteristics Influencing Utilization

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Abstract:

Purpose: Breast conservation has been shown to have similar mortality rates as compared to mastectomy. We hypothesized that variables involving the patient, tumor and surgeon influence the treatment a patient may choose.

Methods: Retrospective review of a prospectively maintained database of all patients who underwent surgical treatment for breast cancer between 2000 and 2009 was performed. Multivariate logistic regression models were used to compare characteristics associated with breast conservation therapy (BCT) and contralateral prophylactic mastectomy (CPM).

Results: Of 1826 patients, 806 underwent BCT and 207 underwent CPM. Exclusion criteria included unilateral mastectomy (n=761), bilateral disease, stage IV disease, and incomplete records. Larger average tumor size and number of lymph nodes examined were associated with CPM (both $p<0.0001$). There were higher odds of patients who underwent CPM when younger than 40 (OR=3.1), less than 50 years of age (OR=2.5), with a history of breast cancer (OR=4.7), lobular histology (OR=2.3), invasive histology (OR=2.1), and multi-centric (OR=8.2). Patients treated by surgeons with greater than 10 years of experience were less than half as likely to undergo CPM (OR=0.4), however when treated by a surgeon not subspecialty trained in surgical oncology the patient was more likely to undergo CPM (OR=3.4). Conclusions: Our study is one of the first to evaluate patient comorbidities, personal history of breast cancer, and length of surgeon experience and the influence each may have on usage of CPM. Our data also suggest that there may be a training gap to bridge for general surgeons, because more surgery is becoming subspecialized.

Keywords: Contralateral prophylactic mastectomy, Breast conservation therapy, Breast cancer surgery, Breast cancer.

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Received Date: June 8, 2014 **Accepted Date: July 11, 2014** **Published Date: July 17, 2014**

Citation: Valerie G. Sams. et al. Contralateral Prophylactic Mastectomy: Characteristics Influencing Utilization (2014) Int J Cancer Oncol 1(1):1-5

Introduction

With continued advances in breast cancer screening practices and multimodal therapy, the medical community anticipated more conservative choices in management, such as partial mastectomy or lumpectomy with lymph node evaluation[1]. However, patients continue to undergo more aggressive treatment, such as total mastectomy, with increasing frequency[2]. Although breast conservation therapy (BCT) has been shown to be similar to total mastectomy in terms of mortality for invasive breast cancer[3], women are choosing not just total mastectomy, but contralateral prophylactic mastectomies (CPM). Thus, a large percentage of patients who are good candidates for BCT are still choosing mastectomy. Two population based studies using the Surveillance, Epidemiology, and End Results (SEER) database found that CPM rates for invasive breast cancer and ductal carcinoma *in situ* (DCIS) have increased 150% over the past decade[4,5]. Therefore, many health care institutions have attempted to assess their rates of mastectomy, and clarify the factors associated with treatment choice. Previous studies have examined the use of MRI[6-8], genetic testing[9], availability of immediate reconstruction in order to achieve a more symmetric cosmetic outcome[10-11], tumor characteristics[12-13], and surgeon subspecialty[14] as they related to mastectomy rates. Clinicians and epidemiologists alike are curious as to why women are choosing more aggressive treatment.

While there has been a national trend in women undergoing mastectomy for breast cancer treatment[2], regional variation in treatment selection has also been assessed[15-16]. However, there has been no previous examination of treatment choice in our patient population, which includes southeastern United States and Appalachian cultures. Therefore, our aim here was to

explore patient, tumor and surgeon characteristics that allowed us to look at a wide range of variables influencing the decision to undergo BCT versus CPM patients at the University of Tennessee Medical Center in Knoxville, Tennessee (UTMCK). Specifically, we hypothesized that recency of surgeon training and subspecialty training in surgical oncology both were associated with lower use of CPM, whereas younger age, personal history of breast cancer and unmarried status were all patient characteristics associated with increased use of CPM. Also, we hypothesized that tumor characteristics such as diagnostic use of MRI, higher stage and grade, lobular morphology, invasive histology, hormone receptor negativity, multi-centricity, and lymph node positivity were associated with higher use of CPM.

Methods:

After obtaining approval from the UTMCK Institutional Review Board (IRB), we performed a retrospective review of a prospectively maintained database of all patients who were evaluated, diagnosed and underwent surgical treatment for breast cancer at a university affiliated tertiary referral center between 2000 and 2009. We collected data involving patient characteristics to include age, BMI, race, marital status, occupation, health care related worker, type of insurance, comorbid conditions (diabetes, coronary artery disease, chronic obstructive pulmonary disease, psychiatric disorders, pain disorders, other cancers, personal history of breast cancer, benign breast disease), family history of cancer, and tobacco use. We also collected data regarding tumor characteristics including imaging used (mammography, ultrasound, MRI), multi-centric, multifocal, neoadjuvant chemotherapy, TNM classification, stage, size, grade, hormone receptor status, Nottingham score, number of lymph nodes examined, number of lymph nodes positive, angiolymphatic invasion, and morphology. Surgeon characteristics considered in this study include whether the surgeon had less than or greater than 10 years of experience at the time of operation, and whether the surgeon was subspecialty trained in surgical oncology.

Of the 1826 patients who underwent breast surgery at the UTMCK from 2000 through 2009, 807 underwent BCT and 207 underwent CPM. Eligible patients were greater than 18 years of age who underwent breast cancer surgery for unilateral invasive breast cancer or DCIS between 2000 and 2009. We excluded those patients who had unilateral therapeutic mastectomy (n=761) (did not choose to undergo a more aggressive choice of CPM), bilateral disease (ineligible for BCT), stage IV disease (ineligible for BCT), and incomplete records. The rate of CPM increased from 10% of all breast procedures (partial, unilateral, and contralateral) in 2000 to 25% in 2009.

We used T-tests to compare CMP and BCT according to the mean values of continuous variables in our data. Multivariate logistic regression models were used to estimate odds ratios (OR) and 95% confidence intervals (CI). Statistical analyses were performed using SAS software version 9.2 (SAS Institute., Cary North Carolina). All statistical tests were 2-sided.

Results:

Patient demographics are shown in Table 1.

	CPM (n=207)	BCT (n=807)
Age (year) <30	5 (2%)	3 (<1%)
30-49	86 (41%)	177 (22%)
50-59	60 (29%)	228 (28%)
>60	56 (28%)	398 (49%)
BMI[1] >30	47 (23%)	109 (13%)
25-29.9	34 (16%)	123 (15%)
<24.9	28 (14%)	78 (10%)
Unknown	98 (47%)	496 (62%)
Marital status Married	145 (70%)	549 (68%)
Not Married	62 (30%)	258 (31%)
Occupation Professional	55 (27%)	162 (20%)
Unknown	91 (44%)	439 (54%)
Health Care	27 (13%)	54 (7%)
Unknown	72 (35%)	370 (46%)
Insurance Public	60(29%)	332 (41%)
Private	145 (70%)	468 (58%)
Uninsured	2 (1%)	16 (<1%)
Smoking Current	32 (15%)	107 (13%)
Previous	35 (17%)	138 (17%)
Unknown	30 (15%)	147 (18%)
Family history Cancer Yes	126 (61%)	484 (60%)
Unknown	35 (17%)	153 (19%)
Comorbidities unknown	48 (23%)	169 (21%)
Diabetes	26 (12.5%)	93 (11.5%)
CAD[2]	8 (4%)	60 (7.5%)
COPD[3]	18 (9%)	60 (7.5%)
Psych disorder	52 (25%)	89 (11%)
Pain disorder	16 (8%)	64 (8%)
Other Cancer	14 (7%)	72 (9%)
Breast cancer	16 (8%)	24 (3%)
Benign breast disease	16 (8%)	113 (14%)
Imaging (MRI) Yes	72 (35%)	177 (22%)
Unknown	37 (18%)	80 (10%)
Stage 0	32 (16%)	185 (23%)
I	69 (33%)	409 (51%)
>II	106 (51%)	212 (26%)
Grade Well differentiated	26 (13%)	168 (21%)
Moderately differentiated	80 (38%)	242 (30%)
Poorly/undifferentiated	74 (36%)	189 (23%)
Unknown	27 (13%)	207 (26%)
Morphology DCIS[4]	27 (13%)	146 (18%)
IDC[5]	151 (73%)	557 (69%)
LCIS[6]	3 (1.4%)	16 (2%)
ILC[7]	29 (14%)	47 (5.8%)
Other	6 (2.8%)	40 (4.9%)
Invasive on histology	66 (32%)	97 (12%)
Estrogen receptor +	126 (61%)	533 (66%)
Herceptin receptor 2 +	27 (13%)	73 (9%)
Multi-centric Yes	19 (9%)	14 (1.7%)
Unknown	35 (17%)	89 (11%)

Lymph node +	79 (38%)	129 (16%)
Surgeon Experience >10yrs	112 (54%)	613 (76%)
Unknown	52 (25%)	69 (8.5%)
Surgeon subspecialty	157 (76%)	565 (70%)

[1]body mass index, [2]coronary artery disease, [3]chronic obstructive pulmonary disease, [4]ductal carcinoma in situ, [5]infiltrative ductal carcinoma, [6]lobular carcinoma in situ, [7]infiltrating lobular carcinoma.

The average tumor size in patients undergoing CPM was 25.1mm versus BCT 16.1 ($p<0.0001$). Patients undergoing CPM had an average of 10.6 lymph nodes total examined while BCT patients had 5.1 ($p<0.0001$).

Multivariate-adjusted analysis of patient characteristics when comparing BCT to CPM revealed patients who underwent CPM was significant for those less than 40 years of age (OR 3.1, CI 1.4-6.9) and 40-49 years of age (OR 2.5, CI 1.4-4.5) compared with those >60 years of age. Patients with a personal history of breast cancer were nearly five times more likely to undergo CPM (OR 4.7, CI 2.1-10.6). Marital status was not associated with an increase use of CPM.

When examining tumor characteristics, patients with lobular carcinoma were over two times more likely to undergo CPM (OR 2.3, CI 1.2-4.2) than those with all types of infiltrating ductal carcinoma. Patients with invasive histology were over twice as likely to undergo CPM (OR 2.1, CI 1.2-3.6). Patients with multi-centric disease were eight times more likely to undergo CPM (OR 8.2, CI 3.0-22.7).Diagnostic use of MRI, tumor stage and grade, estrogen receptor status, and lymph node positivity were not associated with increased use of CPM. (Table 2).

	CPM Age-Adjusted OR (CI)	CPM Multivariate-Adjusted OR (CI)
Age (year) <40	3.5 (1.9-6.5)*	3.1 (1.4-6.9)*
40-49	2.2 (1.4-3.4)*	2.5 (1.4-4.5)*
50-59	1.4 (0.9-2.1)	1.3 (0.8-2.3)
>60	1.0 †	1.0 †
Marital status Single	1.8 (1.1-3.0)*	1.3 (0.7-2.5)
Not Single	1.0 †	1.0 †
Personal H/o Breast Ca	3.6 (1.8-7.4)*	4.7 (2.1-10.6)*
MRI obtained	2.0 (1.4-2.9)*	1.3 (0.8-2.1)
Stage 0	1.0 †	1.0 †
I	1.3 (0.8-2.2)	0.7 (0.1-3.5)
>II	3.4 (2.0-5.7)*	1.0 (0.2-5.6)
Grade well diff	1.0 †	1.0 †
mod diff	2.9 (1.6-5.1)*	2.0 (1.0-4.2)
Poor/undiff	2.6 (1.4-4.7)*	1.7 (0.8-3.9)
Unknown	1.0 (0.5-2.0)	0.8 (0.3-2.3)
Morphology DCIS	0.6 (0.4-1.0)	1.0 (0.2-6.0)
IDC	1.0 †	1.0 †
ILC	2.3 (1.4-3.7)*	2.3 (1.2-4.2)*
Other	0.7 (0.3-1.6)	1.9 (0.5-7.0)
Invasive on histology	3.4 (2.3-5.1)*	2.1 (1.2-3.6)*
ER +	0.7 (0.4-1.0)	0.6 (0.3-1.2)
Multicentric	6.9 (3.3-14.5)*	8.2 (3.0-22.7)*
Lymph node +	2.9 (2.0 – 2.3)*	1.2 (0.6-2.3)
Surgeon Experience >10 years	0.6 (0.4-0.9)*	0.4 (0.2-0.7)*
General Surgeons (not Surgical Oncologist)	2.1 (1.3-3.4)*	3.4 (1.7-6.6)*

* Statistically significant ($p<0.05$); † Referent category
Note: All variables shown in multivariate models were mutually adjusted.

Finally, patients under the care of surgeons with greater than 10 years of experience were less than half as likely to undergo CPM (OR 0.4, CI 0.2-0.7) than those treated by a surgeon with less than 10 years of experience. Patients of surgeons not subspecialty trained were over three times more likely to undergo CPM (OR 3.4, CI 1.7-6.6) than patients treated by surgeons subspecialty trained in surgical oncology. There were a total of 12 surgeons who were all either general surgeons or surgical oncologists in our analysis.

Discussion:

At UTMCK, we use a multidisciplinary approach for all cases of breast cancer. Our surgeons all provide the same data and options to patients when considering BCT or therapeutic mastectomy (TM) with or without contralateral prophylactic mastectomy (CPM). We explain to our patients that survival outcomes are no different, only local recurrence is slightly higher in BCT and document this in dictated counseling office notes. Patients are also offered consultation with plastics and reconstructive surgeon to discuss all of their cosmetic concerns. Because there is an increased risk of a second contralateral breast cancer, patients are counseled on the National Cancer Center Network (NCCN) guidelines to continue screening for recurrence as well as cancer in the contralateral breast to include physical exam and mammography.

The 1991 consensus statement by the National Cancer institute supported breast conserving surgery as the preferred treatment for early stage breast cancers[17]. However, we have seen an increase in patients with documented early stage disease electing to undergo CPM when diagnosed with unilateral breast cancer from 1.8 to 4.5% from 1997 to 2003[2]. There have been many theories on why this is occurring, such as increased use of preoperative MRI, genetic testing, and demand for surgery due to availability of immediate reconstruction[18-26]. Multiple studies were reviewed by Cochrane and found that whereas CPM decreases the risk of contralateral breast cancer, it did not impact overall survival[27]. A 20-year follow up demonstrated an overall survival of 46% and 47% for breast conservation and mastectomy respectively and local recurrence was 8.8% and 2.3% respectively[3]. Analysis of the SEER database over ten years for patients with unilateral breast cancer found that young age, white race, lobular histology, recent year of diagnosis and large tumor size were associated with increased CPM rates[4,5]. A large cancer center retrospective review from 1994-1998 found that age younger than 40, large tumor size and lymphovascular invasion were all predictors of mastectomy[28]. One study from Los Angeles found that women younger than 40 years of age were less likely to choose BCT[14]. Neff and colleagues found

that at 5 years, women younger than 40 years of age had a local recurrence rate of 24% versus 6% in women over 40 after BCT[29]. Another study found that local recurrence in women younger than 35 years of age undergoing BCT was 46% versus 27% in those treated with mastectomy[23]. Several studies have demonstrated that fear of recurrence as a major contributor to selection of mastectomy over BCT[10,30,31]. With regard to patient characteristics, patients undergoing CPM at UTMCK were significantly younger than those choosing BCT as previously reported in other studies. This may imply that younger women are more aggressive in their treatment choice, which may relate to the number of years remaining that they face risk of developing a recurrence or new breast cancer. In this study, it was observed also that a personal history of breast cancer influences the decision to undergo CPM.

Several tumor characteristics have been associated with increased bilateral mastectomy rates. Tumor size[14,18], regional disease[14], lymphovascular invasion[28], lobular histology[32], and regional or distant lymph node involvement[14] have all been reported as increased association with mastectomy over BCT. Our study demonstrated similar findings with tumor size, lobular histology, invasiveness on histology, and multi-centricity.

There have been multiple studies evaluating the effect of the use of MRI in the decision to undergo CPM One institution found that patients who underwent a preoperative MRI with early stage breast cancer were more likely to undergo CPM[6]. This may be related to the patients undergoing MRI being younger with denser breast tissue and more specific findings. Furman and colleagues found that 13.2% of patients chose a different surgical management option based on MRI findings and underwent more aggressive surgical management[8]. Yet, another study found no significant association in preoperative MRI and CPM rates[7]. We did not find preoperative MRI to be a statistically significant factor in patients who underwent CPM.

Surgeon influence on treatment for breast cancer has been examined in multiple studies[2,10,14,33]. One study found that of patients undergoing mastectomy, the primary influencing factor was the surgeons' recommendation[10]. Another study found that patients treated by a surgical oncologist were more likely to undergo BCT[14]. In addition, patients treated at specialized cancer centers were less likely to undergo BCT[14], however this is likely due to the number of advanced stage cases seen at specialty centers[2,33]. Our study found that the longer the surgeon had been in practice and subspecialty training in surgical oncology each had an association with lower rates of CPM. The predominant thought at our institution prior to performing this data analysis was that newly trained and subspecialty trained surgeons were associated with increased BCT rates. Ours is the first study to demonstrate an effect of surgeon length of operative experience and type of surgical training on CPM and BCT rates. These findings have profound implications in how we counsel our patients in terms of the confidence in delivery of the different options. If less experience and lack of subspecialty training are associated with higher rates of CPM, is this due to experience and confidence alone as it relates to BCT modalities? Is there a deficiency in general surgery training such that surgeons feel less comfortable with more conservative options? Whereas specialty training has been demonstrated previously to be associated with higher rates of BCT, the bigger issue to address is that some general surgeons and surgeons early in their practice are performing less BCT. Because a large number of general surgeons perform breast surgery, these are areas that warrant further study.

There are several limitations to our study. Our sample size did not provide us the statistical power to evaluate interactions among the predictor variables. Furthermore, missing values for several of the variables resulted in a reduced sample size in the multivariate-adjusted models. Hence, the multivariate analyses may not be generalizable to the entire study population if individuals with missing values were substantially different from those without missing values. In addition, our data were obtained from a prospectively maintained database and medical records, one that did not provide the specific reason for a patient's choice for CPM. We also had a fairly homogenous group of Caucasian females with reasonable access to reconstructive surgery and insurance coverage, which may have influenced the higher usage of CPM in our study population.

Despite these limitations, our study is one of the first to evaluate patient comorbidities, personal history of breast cancer, and length of surgeon experience and the influence each may have on usage of CPM. Personal history of breast cancer may be an obvious patient demographic one would expect when evaluating why a patient chose CPM over BCT. This is a patient characteristic that should be considered when counseling patients on treatment options as it may influence their decision. Our data also suggest that there may be a training gap to bridge for general surgeons, because more surgery is becoming subspecialized. One factor we were unable to evaluate is that of BRCA results and how that may have influenced decisions. This data was not available through the registry until 2010. Breast cancer is a vast field of study and surgeons must expend tremendous effort to keep current on the latest treatment modalities. The amount of research and clinical study results in breast disease being a specialized field and may lead to a significant lack of confidence in the general surgeon in terms of performing more BCT and adjuvant treatment.

When it comes to treatment, there is no one "right" choice for every woman with breast cancer. Clearly, treatment decisions should be appropriate for each individual patient, based on all of the information necessary to make informed decisions. What constitutes sufficient information in any individual patient is key; we believe that improved understanding of medical and personal factors related to treatment choice will ultimately help to ensure appropriate decisions are being made with consistency across surgeon training and sub-specialty.

We declare that we have no conflict of interest in relation to this article.

Acknowledgement:

We would like to acknowledge the University of Tennessee Medical Center Knoxville Cancer Center staff and medical records department for their assistance with the data collection.

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