Counseling Breast Cancer Patients on Contralateral Prophylactic Mastectomy: The Physician's Role

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CPM may be a rational choice for patients with known BRCA mutations, patients who have received therapeutic chest radiation, and some mastectomy patients.

Using the Surveillance, Epidemiology and End Results (SEER) cancer registry, we recently reported that the rate of contralateral prophylactic mastectomy (CPM) for stage I–III unilateral breast cancer increased by 150% from 1998 to 2003 in the United States.[1] We found that the CPM rate increased through the end of our study period with no diminution in the incline of the curve. Based on 2003 data, we estimate that about 10,000 breast cancer patients with unilateral breast cancer undergo CPM in the United States each year. In our study, young patient age, non-Hispanic white race, lobular histology, and previous cancer diagnosis were associated with significantly higher CPM rates.

Since the majority of patients with unilateral breast cancer will not develop cancer in the opposite breast, CPM is unnecessary for preventing contralateral breast cancer in most patients. Moreover, since the risk of systemic metastases often exceeds the risk of contralateral breast cancer, most patients will not experience any survival benefit from CPM. Still, many women choose CPM despite potential risks, complications, and irreversibility of the operation. Presently, controversy exists about whether physicians or patients should initiate the discussion of CPM and whether physicians should actively discourage patients who desire CPM. For the purposes of this article, this author contends that physicians should initiate the discussion regarding CPM and should not discourage appropriately selected patients who desire CPM.

Risk of Contralateral Breast Cancer
For women with unilateral breast cancer, the annual risk of clinically detected metachronous contralateral breast cancer is about 0.7%.[2-6] This risk is constant and shows no trend of either increasing or decreasing with follow-up. In contrast, the peak hazard of systemic recurrence of unilateral breast cancer is about 1 to 2 years after treatment; the risk decreases consistently after 2 to 5 years.[7] Thus, occurrence of contralateral breast cancer is clinically more significant for patients who are likely to survive for a long time.

Some breast cancer patients have an increased risk of developing contralateral breast cancer. Multiple studies have reported that young age at the time of diagnosis of the first breast cancer is associated with a significantly increased risk.[3,5,8] Patients with at least one first-degree relative with breast cancer also have an increased risk of contralateral breast cancer.[8] Moreover, patients with unilateral breast cancer who also have BRCA1 or BRCA2 genetic mutations have a markedly increased risk of developing contralateral breast cancer.[9,10] Verhoog et al reported that contralateral breast cancer was four to five times more frequent in patients with BRCA1 mutations compared with a sporadic group of breast cancer patients.[10] Survivors of Hodgkin's disease treated with mantle radiation have a significantly increased risk of bilateral breast cancer.[11] Invasive lobular carcinoma is associated with an increased risk of contralateral breast cancer as compared with other histologic types.[2,8,12] Multicentric unilateral breast cancer is also associated with a significantly increased risk of contralateral breast cancer.[2]

Benefits of CPM
Several studies have demonstrated the effectiveness of CPM in preventing contralateral breast cancer.[13-17] In a study of 745 breast cancer patients with a family history of breast cancer, McDonnell et al reported that CPM reduced the incidence of contralateral breast cancer by more than 90%.[14] In a retrospective study of 239 patients, Goldflam et al reported that only 1 (0.4%) contralateral breast cancer developed after CPM.[17] In a cohort of patients with unilateral breast cancer and BRCA1 or BRCA2 mutations, van Sprundel et al reported that CPM reduced the risk of contralateral breast cancer by 91%.[16]

Clearly, CPM is an effective strategy to reduce the risk of contralateral breast cancer, a desired outcome to avoid further breast cancer treatment and anxiety. However, the effectiveness of CPM in
preventing breast cancer mortality is not as clear. A recent Cochrane review of eight studies included 1,708 patients who underwent CPM; the authors concluded that CPM decreased the incidence of contralateral breast cancer, but was not associated with any survival improvement.[18] Yet, in a retrospective cohort study of 1,072 patients from the Cancer Research Network, Herrinton et al reported that CPM was associated with a significant decrease in the breast cancer mortality rate (hazard ratio [HR] = 0.57; 95% confidence interval [CI] = 0.45–0.72) and overall mortality rate (HR = 0.6; 95% CI = 0.5–0.72).[15] In this study, women who underwent CPM were less likely to die from non-breast cancer-related causes, thus emphasizing the selection bias that healthier patients undergo CPM more frequently.

In a retrospective case-control study, Peralta et al reported that CPM was associated with a significantly increased disease-free survival rate (CPM, 55%; no CPM, 28%; P = .01), but not an increased overall survival rate (CPM, 64%; no CPM, 49%; P = .26).[13] Finally, using a Markov state transition model, Schrag et al estimated that a 30-year old patient with early-stage breast cancer and a BRCA mutation would gain an additional 0.6 to 2.1 years in life expectancy after CPM.[19]

**Complications of CPM**

Despite the potential benefits of CPM, the surgery is not risk-free. Severe complications after CPM may potentially delay recommended chemotherapy or radiation therapy after surgery. In a series of 239 patients undergoing CPM (most received immediate reconstruction), Goldflam et al reported a 16.3% complication rate (ipsilateral breast, 8.4%; contralateral breast, 6.3%; both breasts, 1.7%).[17] Barton et al reported that the most common complications after bilateral prophylactic mastectomy were pain (35%), infection (17%), and seroma (17%).[20]

The performance of CPM generally doubles the complication rate for patients undergoing mastectomy. However, life-threatening side effects are very rare. Bilateral mastectomy with immediate breast reconstruction usually requires about 5 hours of surgery; even without complications, patients are typically hospitalized 2 to 3 days after surgery.

**CPM Operations**

In the past, many CPMs were subcutaneous mastectomies that left behind a substantial amount of breast tissue. Total mastectomy, including removal of the nipple-areolar complex, is recommended for prophylactic surgery today. Skin-sparing total mastectomies are oncologically equivalent procedures that preserve the skin envelope and improve the cosmetic outcomes in conjunction with reconstructive breast surgery. Some investigators have also performed nipple- and areolar-sparing mastectomies in highly selected patients.[21,22] Improvements of mastectomy and reconstruction techniques in recent years probably account for some of the increased use of CPM in the United States. Nevertheless, no mastectomy can remove all breast tissue and completely eliminate the risk of breast cancer.

**Alternatives to CPM**

Patients with unilateral breast cancer may consider other options to reduce the risk of contralateral breast cancer. Surveillance with clinical breast examination, mammography, and breast magnetic resonance imaging (MRI) may detect cancers at earlier stages.[23,24] Studies have shown that patients with unilateral breast cancer who were closely monitored developed significantly smaller tumors in the contralateral breast and had lower rates of axillary lymph node metastasis compared with their unscreened counterparts.[23,25] Because the annual risk of contralateral breast cancer is relatively constant, surveillance should continue indefinitely or until age- or other health-related issues significantly impair life expectancy.

Several prospective randomized trials demonstrated that tamoxifen, given as adjuvant therapy for estrogen-receptor–positive breast cancer, significantly reduces the rate of malignancy in the contralateral breast.[26-28] In the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-14 study, 2,892 women with node-negative, estrogen-receptor–positive breast tumors were randomly assigned to either tamoxifen (20 mg/d) or placebo for at least 5 years.[26] After an average follow-up of 53 months, 55 contralateral breast tumors occurred in placebo-treated women and 28 occurred in tamoxifen-treated women (P = .001). Aromatase inhibitors may reduce the risk of contralateral breast cancer as much as, or even more than, tamoxifen.[29] The Arimidex, Tamoxifen Alone or in Combination (ATAC) Trial demonstrated that anastrozole (Arimidex) was superior to tamoxifen in preventing contralateral breast cancer in postmenopausal women.

**Patient Satisfaction**

Despite potential risks and complications, most patients are satisfied with their decision to undergo CPM.[30-32] Frost et al reported that 83% of patients were either satisfied or very satisfied with their decision to undergo CPM at a mean of 10 years after surgery.[30] Montgomery et al reported that...
the most common reasons for regret after CPM were poor cosmetic outcome and diminished sense of sexuality. Gieger et al found that patients who underwent CPM were less likely to express breast cancer concern, as compared with patients who did not undergo CPM.

Since our study was published in the Journal of Clinical Oncology, this author has received more than 100 e-mails from breast cancer patients explaining their choice of CPM. Many women wrote that they underwent CPM to reduce the risk of recurrence: "I chose CPM because I want to ensure that I did everything I could to prevent a recurrence." Another wrote, "I sleep very well knowing that I have eradicated breast cancer from my body." For others, symmetry and body image were important: "I chose bilateral mastectomy to prevent being lopsided and off balance." Another wrote, "I felt my breasts would look more alike if they were both replaced rather than having one real and one reconstructed."

Many women wanted to avoid any further treatment: "I have been through a hell of a lot of treatment and don't want to do any of it again." Others voiced concerns regarding the limitations of surveillance of the contralateral breast: "I chose double mastectomy because a mammogram didn't detect my cancer." The patient correspondence that this author has received is consistent with the findings reported by Frost and colleagues. One patient commented: "I had bilateral mastectomy 5 years ago and haven't regretted it since."

**Future Research**

To date, no study has prospectively evaluated the decision-making processes that lead to CPM in the general population of patients with breast cancer. The only prospective study evaluating these processes was reported by Schwartz and colleagues in a selected cohort of patients referred for genetic counseling and BRCA testing. The BRCA test results, the number of first-degree relatives with breast cancer, disease stage, and physician recommendation were associated with the choice to have CPM.

Future research in this area should focus on the development of unique models and instruments to elucidate the decision-making processes for patients with breast cancer. No research has prospectively evaluated the surgeon's influence on the decision to undergo CPM. Perhaps the age, training, type of practice, and sex of the surgeon influences CPM use. Timely decision-analysis research is important because it may ultimately provide decision aids for patients and physicians.

**Recommendations**

The patient-physician interaction strongly influences breast cancer decision-making processes. In a review of the National Prophylactic Mastectomy Registry, Montgomery et al reported that the most common reason for CPM, as cited by patients, was physicians' advice regarding the high risk of contralateral breast cancer. Since some patients may grossly overestimate their risk of contralateral breast cancer, physicians must provide accurate and understandable information so patients can make informed decisions. Genetic counseling and selective testing may also guide rational decision-making.

For newly diagnosed breast cancer patients, immediate treatment decisions should focus on the known potentially life-threatening malignancy. If a patient with an average risk of contralateral breast cancer appropriately chooses breast-conserving treatment, then CPM is not a relevant treatment option. Likewise, the benefits of CPM are unclear for most patients with advanced breast cancer because the risk of systemic metastases exceeds the risk of contralateral breast cancer. In addition, these patients will likely require months of cytotoxic chemotherapy and radiation therapy; complications from CPM may delay the delivery of such therapies. However, even if CPM is not being considered, the method and frequency of surveillance of the remaining breast and the role of chemoprevention should be discussed.

For selected patients with early breast cancer, physicians should initiate discussions regarding CPM. For example, CPM may be a rational choice for patients with known BRCA mutations or patients who have received therapeutic chest radiation (Hodgkin's disease) because of the marked increased risk of contralateral breast cancer. Moreover, many patients have contraindications for breast-conserving treatment (tumor size, multiple tumors, or contraindications for breast radiotherapy) and require mastectomy. For some mastectomy patients, CPM may be appropriate especially if the contralateral breast is large, creating balance and symmetry difficulties after unilateral mastectomy. Also, a large remaining breast after unilateral mastectomy complicates symmetric reconstructive techniques. Finally, the presence of dense breast tissue on mammography, strong family history without an identified genetic mutation, lobular carcinoma in situ, and atypical hyperplasia may also be considered in the decision-making process.

Many patients request bilateral mastectomy (with CPM) even if breast-conserving treatment is feasible. "I just want to be done with it" is a common mantra. Although these preferences may seem
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Illogical, physicians should try to understand patient concerns and priorities and should not immediately discourage patient preference. For example, if a breast cancer patient desires CPM because she believes that the procedure will allow her to live longer, then her physician must counsel her that CPM probably will not improve her chances of long-term survival. In addition to reducing the risk of contralateral breast cancer, CPM may also improve symmetry and balance for many patients, avoid future surveillance (mammography, MRI, biopsies), reduce breast cancer anxiety, and prevent future breast cancer treatment. For some breast cancer patients, CPM is preferable to yearly surveillance (with or without MRI) and chemoprevention strategies. More than ever, physicians must provide their patients with accurate information on the benefits, limitations, and potential risks of both CPM and alternative strategies (surveillance, chemoprevention).

—Todd M. Tuttle, MD

For the CON Perspective, see Dr. Wood’s commentary here:
Increasing Use of Contralateral Prophylactic Mastectomy: A Counterintuitive Trend

References:


13. Peralta EA, Ellenhorn JD, Wagman LD, et al: Contralateral prophylactic mastectomy improves the


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