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Contralateral Prophylactic Mastectomy in Breast Cancer: What to Discuss With Patients?

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Abstract

Introduction—The contralateral prophylactic mastectomy (CPM) rate in the U.S. has been steadily increasing. This is of particular concern because many women who undergo this procedure are candidates for breast-conserving surgery.

Areas covered—CPM's medical benefit is related to the risk of contralateral cancer development and whether CPM provides a survival benefit. Contralateral cancer rates have decreased, and CPM does not provide a survival benefit. Other potential benefits of the procedure may be improved quality of life; these data are reviewed. Research efforts have been undertaken to better understand the decision-making process of patients who consider, and ultimately undergo, this procedure.

Expert opinion—Decisional traits, personal values, the desire for peace of mind, and the desire to obtain breast symmetry are important factors that drive a woman's decision to undergo CPM. Additionally, many patients lack knowledge on how different types of breast surgery impact outcomes. To improve the shared decision-making process, a stepwise approach to address possible misconceptions, and clarify the real risks/benefits of this procedure should be utilized. A clear recommendation (for/against) should be made for every patient with newly diagnosed breast cancer who considers CPM. Communication tools to assist patients and surgeons in this process are sorely needed.

Keywords

Contralateral prophylactic mastectomy; harms; benefits; shared decision making; patient education

1.0 Introduction

Although the majority of women with unilateral breast cancer (BC) will obtain no oncologic benefit from contralateral prophylactic mastectomy (CPM), its use in the United States for both invasive and in situ disease has increased markedly over the last two decades (Figure 1) [1–9]. The proportion of women with stage I–III BC who underwent CPM increased from 1.8% in 1998 to 12.7% in 2012 [8,9]. This trend, although most pronounced among young women (where the rate of CPM is as high as 35%) [3,9–12], is seen across all age ranges [8,9] and has not yet reached a plateau [8,13]. Geographic variations in both rates of CPM

and the magnitude of increase in its use have been observed [14]. The role of providers and patients in the choice of CPM is complex. Although initially thought to be a provider-driven decision, recent studies have shown that the providers' contribution is marginal, accounting for only 20% of the variability in CPM rates [15], and this is largely a patient-driven decision [16–19]. The reasons why women opt to undergo more radical surgery are multifactorial. Desire to reduce the risk of contralateral breast cancer (CBC), obtain peace of mind, and improve survival are among the most commonly reported reasons for undergoing CPM [16,17,19–22]. New approaches to patient education about the real risk of developing CBC, the risks associated with CPM, and the lack of survival benefit are needed to help reverse this trend. This review will focus on patients with sporadic BC without a history of prior mantle radiation (i.e., patients who do not have an increased risk of developing CBC). We will discuss the potential benefits and harms of CPM, the psychosocial factors that drive the decision to undergo CPM, and the shared decision-making process necessary to help women make the best decision regarding this surgical procedure.

2.0 Potential Benefits and Harms of Contralateral Prophylactic Mastectomy

2.1 Contralateral breast cancer

After unilateral sporadic BC, the risk of developing a new malignancy in the contralateral breast varies based on tumor biology, age at diagnosis, and family history [23]. Due to the widespread use of adjuvant endocrine therapy for early stage BC [24], the rate of CBC in the United States has been decreasing since 1985 [25]. Currently, after primary BC, the risk of developing CBC ranges from 0.25–0.4%/year for patients with estrogen receptor (ER) positive tumors treated with tamoxifen, and between 0.45–0.6%/year for ER negative tumors [24,26]. The reduction in CBC with endocrine therapy is seen across all age groups, so that even among women in their early 30s at diagnosis, the absolute risk of CBC at 10 years ranges between 3–8 % according to the ER status of the first tumor [24]. Cytotoxic chemotherapy has been shown to reduce the risk of CBC by 30% [27], and newer targeted therapies such as anti-HER2 treatment also appear to lower the incidence of CBC [28]. A population-based study from the Netherlands reported a 43% CBC risk reduction with the combination of trastuzumab and polychemotherapy compared to no adjuvant therapy [27]. Although CPM is extremely effective at reducing the risk of CBC, with a relative risk reduction of 96% [29–31], in a population with a low risk of developing CBC, the absolute benefit is very low (e.g., for women with an ER positive tumor and a 20-year risk of CBC of 5–8%, CPM would avoid the development of 2–3 CBCs per 1000 treated) [30].

2.2 Survival benefit

In order to have a survival benefit from CPM, patients would need to survive their index cancer, and then develop and succumb to CBC [32]. Retrospective studies have shown contradictory results in terms of survival [3,33–36]. However, in the studies suggesting a survival benefit for CBC, the magnitude of the survival benefit was greater than the incidence of CBC in the control group, indicating the selection of healthier, lower-risk women for the procedure [37]. For example, Bedrosian et al. found a 4.8% absolute

reduction in BC mortality with CPM in women 18–49 years of age with stage I-II ER negative cancer, even though the incidence of CBC in the control group was only 0.9% [38]. To eliminate potential selection bias, Portschy et al. developed a Markov model to estimate the survival benefit of CPM. Among women with stage I and II sporadic BC, the absolute 20-year survival benefit from CPM was < 1% among all age, ER status, and cancer stage groups [39], and a Cochrane Review concluded that, currently, there is insufficient evidence that CPM improves survival [40].

2.3 Psychosocial outcomes

Parker et al. reported psychological outcomes among 288 women who underwent surgery for non-hereditary unilateral BC. Before surgery, those who underwent CPM (n = 50), had greater cancer worry, more cancer distress, and more body image concerns than those who underwent unilateral mastectomy (UM). At 6, 12, and 18 months after surgery, CPM recipients still had higher cancer distress and body image concerns than their counterparts, and also had lower quality of life (QoL) [41].

Cancer worry is a well-known psychological factor that influences the decision to undergo CPM [18,22,42]. Parker et al. found that cancer worry level decreased over time among CPM recipients and became similar to that of those who did not have CPM, indicating that CPM is effective in reducing cancer worry [41]. However, women who received CPM had greater body image concerns that persisted 1.5 years after surgery [41], and studies with longer follow-up have shown that body image concerns after CPM persist over time [43].

In the study of Parker et al., women who underwent CPM had decreased physical, social, emotional, and functional well-being [41]. In contrast, in a large cross-sectional study that evaluated QoL with the BREAST-Q questionnaire at a median of 4.6 years after surgery, Hwang et al. found that women who had CPM with reconstruction had higher satisfaction with their breasts and higher psychological well-being than women who had UM [44]. However, the differences between the groups were small and likely not clinically significant [44,45]. Koslow et al. compared BREAST-Q data at a median of 51.9 months postoperatively between women who had CPM and UM, (both with implant-based reconstruction) and also found that women with CPM had higher breast satisfaction, but no differences in other QoL domains were found [46]. Other studies have reported an adverse effect of CPM on feelings of femininity [43,47–49]. Frost et al. found that with long-term follow-up, approximately one-quarter of CPM recipients had difficulty looking at themselves naked and felt physically less attractive [43]. The degree of impact on sexuality and body image varies with age. Rosenberg et al. reported that among a cohort of young (age < 40 years) BC survivors who underwent CPM, 42% had a worse sense of sexuality than they expected, and 31% had more self-consciousness about their appearance than they expected [22]. Interestingly, a prospective study conducted in Sweden reported high rates of dissatisfaction with body appearance and femininity, but no impact on sexuality [50]. This study, however, had no control group. Although CPM with reconstruction increases symmetry and breast satisfaction, its impact on QoL is not fully understood, and patients should be informed of this.

2.4 Decisional satisfaction

Many studies have shown that women who choose to undergo CPM tend to be satisfied and have no decisional regret [19,21,22,51,52]. Frost et al. reported that among 583 women who had CPM (72% with reconstruction), at a mean time after surgery of 10.3 years, 83% were satisfied and would have chosen CPM again [48]. At 20.2 years after surgery, satisfaction increased (90%) as did the proportion of women who would have chosen CPM again (92%) [43]. Diminished sexual relationships and feelings of femininity, lack of information at the time of surgery, and increased level of stress after CPM, are factors associated with decreased satisfaction and with being less likely to choose CPM again [43,48,52].

2.5 Surgical complications

In a series of 600 patients undergoing surgery for unilateral BC, Miller et al. found that after adjusting for covariates (including reconstruction), patients undergoing CPM were 2.7 times more likely to have major complications compared with patients who underwent UM [53]. These findings were confirmed in a large study by the American College of Surgeons National Surgery Quality Improvement Program (ACS NSQIP) that found higher rates of wound, infectious, and overall complications among patients who received CPM compared to UM (5.8%, 2.2%, and 7.6% versus 2.9%, 0.8%, and 4.2% respectively) [54]. In the study of Rosenberg and colleagues, 33% of patients reported that the number of surgeries/procedures needed was higher than they initially thought, 25% stated that pain at the surgical site was worse than expected, and 28% reported that numbness and tingling in the chest was also worse than expected [22]. Because more surgery is associated with more complications, patients should be clearly informed about the increased operative risks of CPM.

2.6 Delay in treatment

Using data from the National Cancer Database, Sharpe et al. have demonstrated that CPM is associated with longer time to surgery compared to UM (median number of days from diagnosis to surgery: 40 versus 33, respectively) irrespective of reconstruction. If reconstruction was performed, patients were twice as likely to experience delay. Time to adjuvant chemotherapy was also longer (69 days versus 66 days). Notably, both delays increased from 2003 to 2010 [55]. Although, individually, these delays are of no clinical consequence, major surgical complications following CPM could result in further treatment delay that could impact oncologic outcomes, especially in high-risk patients [56].

2.7 Financial hardship

Greenup et al. investigated the financial harm after breast cancer surgery among 607 women with stage 0-III BC and found that 35% of participants reported financial hardship as a result of their cancer treatment. In multivariable analysis, the receipt of bilateral mastectomy (with or without reconstruction) was associated with a greater likelihood of reporting financial burden compared to breast conservation (OR 1.89, 95% CI 1.07–3.33) [57]. This is explained by the cost of bilateral mastectomy with reconstruction being \$6'400 to \$27'000 higher than the cost of lumpectomy with whole breast irradiation, due to both the cost of intervention and cost of complications [58].

3.0 Sociodemographic, Clinical, and Psychological Predictors of Contralateral Prophylactic Mastectomy

The sociodemographic and clinical predictors of CPM are well known and include younger age [6,10,12,59,60], white race [2,20,59], higher education [19,20,59], private insurance [59,61], positive family history [20,62], in situ disease [4,6], genetic testing (with a positive or negative result) [20], preoperative MRI [20], and availability of reconstructive surgery [10,19,63].

The decision-making process and personal values associated with the consideration of CPM have been investigated in a large (n = 2362) population-based survey. Women who preferred to make their own treatment decision (versus those who preferred the physician tell them what to do), and those who valued the possibility of avoiding radiation exposure and reducing cancer worry were more likely to strongly consider CPM [64]. Two recent, prospective (with pre- and post- surgical assessment) studies have further explored psychosocial factors associated with CPM uptake. Parker et al. reported that among 117 women diagnosed with early BC, less BC knowledge and greater cancer worry were associated with interest in CPM before the surgical visit, but only cancer worry predicted CPM uptake [18]. Metcalfe et al. evaluated 506 women diagnosed with unilateral BC for level of anxiety, depression, and psychological and sexual well-being, and found no differences between women who opted for CPM and those who did not. In their study, the only presurgical psychological factors associated with choosing CPM were lower breast satisfaction and lower level of optimism [60]. These findings are consistent with other retrospective studies that found the most common reasons for selecting CPM were cancer worry (fear of the cancer coming back and fear of harboring an occult malignancy), wanting peace of mind, and the desire for better cosmetic outcomes [19,20,22,59,65].

4.0 Patient Education

4.1 Giving recommendations on contralateral prophylactic mastectomy as part of the decision-making process

The proportion of patients reporting a recommendation from their surgeon against CPM is low: approximately 30% [59,66]. This may be due to many factors, such as the fear of generating misunderstanding, further complicating the treatment decision process, and a willingness to respect patient autonomy and values [66–68]. A population-based study demonstrated that a surgeon recommendation against CPM did not substantively increase patient dissatisfaction, use of second opinion, or loss of patient to a second surgeon [66]. Physicians should therefore feel comfortable in both addressing CPM and actively recommending against it if not clinically indicated. This is of major importance because women who do not receive recommendations (for or against) are more likely to undergo the procedure. This was clearly shown in a population-based study that analyzed the influence of surgeons' recommendation on treatment receipt, finding that CPM rates were 10 times higher among women who did not receive a recommendation versus those who received one against it (1.9% versus 19%, respectively) [59].

4.2 Addressing possible misconceptions

Patients with newly diagnosed BC tend to overestimate their risk of CBC [69]. Additionally, Jagsi et al. recently reported that of patients who consider CPM, only 38.1% are aware that CPM does not improve survival in all BC patients, and that only 43.5% have adequate knowledge about the effect of CPM on BC recurrence. Additionally, 37.3% of CPM recipients in this study believed that CPM improves survival for all BC patients [59]. These data underline the importance of addressing misconceptions that patients may have about potential outcome benefits of CPM [59], and of clearly and simply stating what the procedure will and will not accomplish. Surgeons should also point out that other therapeutic interventions such as endocrine therapy do improve survival, and decrease the risk of recurrence and new primary BCs [26,70]. Although satisfaction rates among CPM recipients are high, poor information at the time of surgery is a predictor of increased regret. Therefore, enhancing the decision-making process may decrease regret after surgery [18,52].

4.3 Addressing potential benefits, harms, and psychological issues

Figure 2 shows an algorithm for a stepwise informed discussion with patients with a pre-existing desire for CPM. Possible harms, benefits, and psychological factors associated with cancer diagnosis, such as cancer worry, should be properly addressed [18]. Communication with patients about CPM is particularly challenging because the motivation behind wanting more extensive surgery is based on complex reactions. It is important to reassure patients that the majority of women with unilateral BC do not undergo CPM since the internet is rife with advice that this is the “safest” approach. The fact that the contralateral breast will be carefully screened and any abnormalities promptly evaluated should also be discussed. Although not a comfortable conversation for many physicians, the risk of death from the index cancer is often higher than the risk of developing a second BC, and emphasizing the need to avoid unnecessary surgery which may delay prompt and appropriate treatment of the index cancer may also be helpful. Many authors have suggested the development of a dynamic decision aid to guide the shared decision-making process for practitioners and patients [71]. Results from a pilot study have shown that in-visit decision aids are effective at improving knowledge about how surgical procedures affect outcomes [72]. An online decision support tool is currently being evaluated in a multi-institutional randomized trial; the primary outcomes of the study are acceptability, changes in patient knowledge, and reductions in decisional conflicts about CPM [73]. The questions and concerns of family and friends should be thoroughly addressed since their opinions have been shown to influence patient surgical choices [19,74].

5.0 Expert opinion

Physicians should actively advise patients against extensive surgical procedures that do not impact oncological outcomes [75,76]. When surgeons provide a recommendation, patients are likely to follow it [15,59,77]. Yet, only 30% of patients at average risk of CBC receive a recommendation regarding CPM from a surgeon [59]. This likely reflects the current emphasis on shared decision making and incorporation of patient values into treatment decisions, but unlike the choice between breast conservation and mastectomy in a cancer patient, CPM is a medically unnecessary procedure. Since 2005 there has been a decrease in

the rate of breast conservation, with a concomitant 14% annual increase in the rate of CPM and stable rates of UM [63]. Katz et al. have shown that the estimated rate of CPM for surgeons who favored BCS the most and who were reluctant to perform CPM was only 4% versus 34% for those surgeons who favored BCS the least and were the least reluctant to perform CPM [15]. Additionally, recent surveys of surgeons performing breast surgery have found great variability in their knowledge of CBC risk, and current rates of local recurrence after BCS and mastectomy [78,79]. This means that patients with similar CBC risk may receive different information and undergo different procedures based on their surgeon's preferences or misinformation.

Great effort was expended by the surgical community to show that decreasing BC surgery was oncologically safe [80–83], but, paradoxically, surgical trends have reversed in the last 15 years [84–86]. This is particularly troublesome, since we now understand that local recurrence is usually a function of tumor biology, and that bigger surgery does not cure bad biology. The findings discussed in this article indicate a clear need for better education of both patients and surgeons to decrease the use of CPM in women who are unlikely to benefit from the procedure.

Considering improvements in breast reconstruction—particularly the enthusiasm for nipple-sparing mastectomy [87]—and the lack of effective strategies to address the emotional aspects of patient CPM choice, we believe that CPM rates will continue to rise over the next five years. Nevertheless, educational tools will help surgeons enhance the shared CPM decision-making process based on data while incorporating patient wants. Research in this area will help determine if improved knowledge of CPM outcomes will affect treatment decisions. If proven effective, the use of such tools should be endorsed by national guidelines. Since surgeon beliefs have been shown to influence the variation in CPM use, understanding the reasons for different attitudes between surgeons should also be the focus of future research.

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Article highlights/Main findings

- Contralateral prophylactic mastectomy does not improve cancer outcomes, and it increases the rate of surgical complications
- It is unclear if contralateral prophylactic mastectomy improves quality of life
- Knowledge of the possible harms and benefits of contralateral prophylactic mastectomy among breast cancer patients is low
- Addressing possible misconceptions is crucial to helping patients make the best decision
- Surgeon recommendations against contralateral prophylactic mastectomy are effective in decreasing its rate, but are only reported by a small percentage of patients
- Educational aids may enhance the shared decision-making process

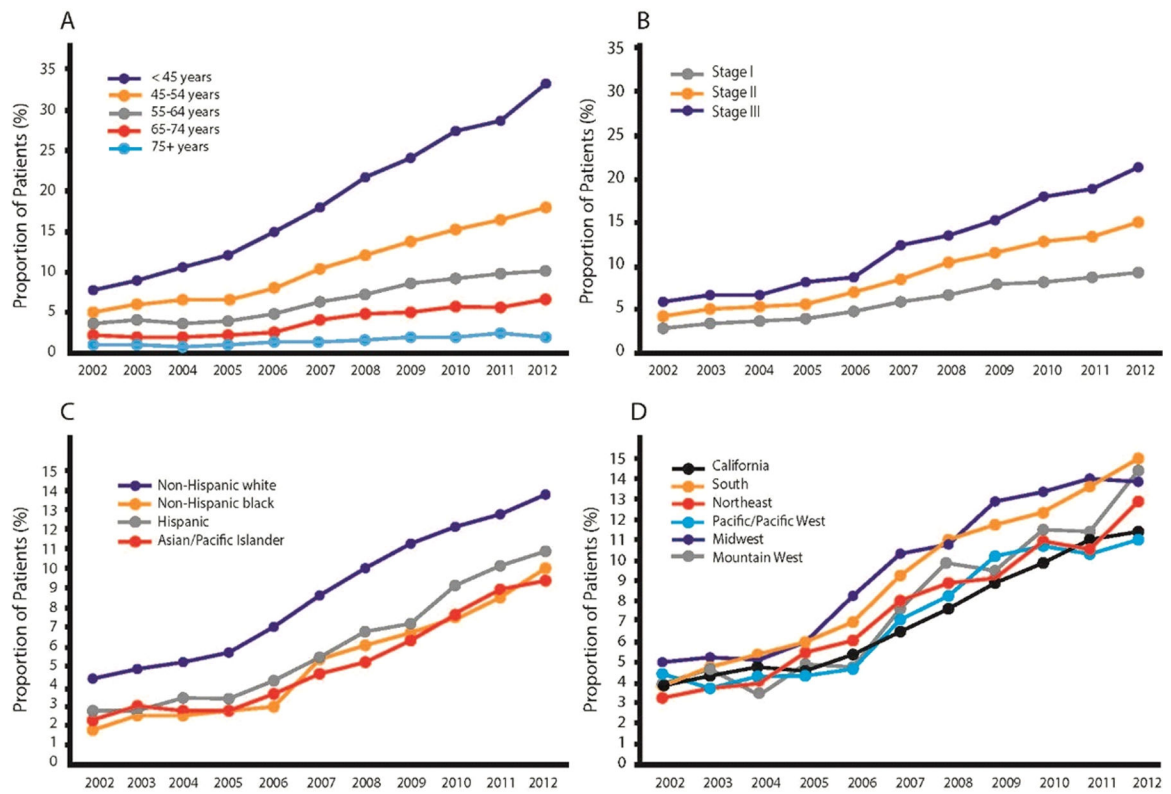


Figure 1. Annual trends (2002–2012) in type of surgery for women diagnosed with stage I-III breast cancer according to: A) age at diagnosis; B) American Joint Committee on Cancer stage; C) racial group; D) geographic (Surveillance, Epidemiology, and End Results) region. (Adapted with permission from Wong SM, Freedman RA, Sagara Y, Aydogan F, Barry WT, Golshan M. Growing Use of Contralateral Prophylactic Mastectomy Despite no Improvement in Long-term Survival for Invasive Breast Cancer. *Ann Surg.* 2017;265(3):581–589.). Abbreviations: AJCC: American Joint Committee on Cancer; SEER: Surveillance, Epidemiology, and End Results

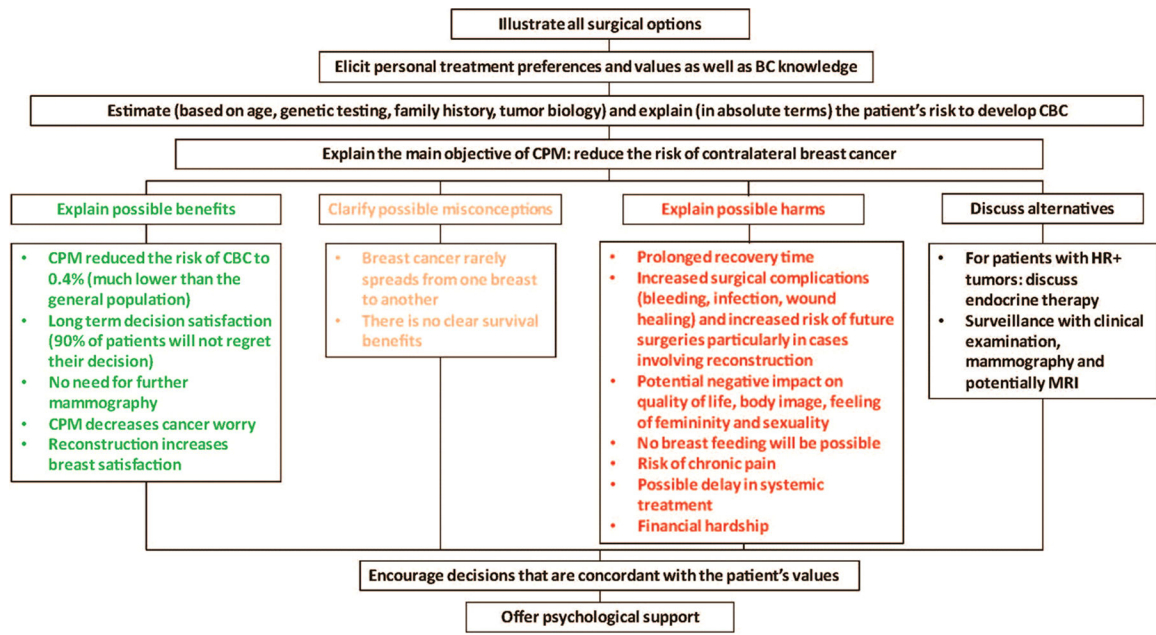


Figure 2. Framework for a stepwise informed discussion with patients with sporadic unilateral breast cancer who are considering CPM. Abbreviations: BC: breast cancer, CBC: contralateral breast cancer, CPM: contralateral prophylactic mastectomy