Contralateral prophylactic mastectomy and its impact on quality of life

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Does contralateral prophylactic mastectomy (CPM) improve quality of life (QOL)? That is a key question and central to the current debate about the growing trend for CPM among women with unilateral breast cancer. Over the last several decades there has been a steady increase in the choice for CPM by these patients and there is no sign of this trend reversing (1,2). This trend is amplified in women undergoing mastectomy with immediate breast reconstruction (IBR) (3-5).

Discussions related to CPM have focused both on the oncologic outcomes (risk of contralateral breast cancer, risk reduction with CPM, lack of impact on survival) and on factors impacting patients decisions to pursue CPM (anxiety, symmetry). However, patient data on QOL outcomes have been lacking. To put it another way, we have clearly studied and documented that women diagnosed with unilateral breast cancer are frequently interested in pursuing CPM; however the long term patient reported outcomes after the decision are less well understood.

Hwang and colleagues report on patient reported outcomes after CPM in women self-enrolled in the Dr. Susan Love Research Foundation Love/AVON Army of Women volunteer program, which is open to adults interested in breast cancer research study participation (6). The investigators recruited nearly 4,000 women who had undergone mastectomy for breast cancer, 40% of whom also underwent a CPM, and the women completed a webbased survey using the BREAST-Q, a validated instrument to assess patient reported outcomes including psychosocial well-being, physical well-being, sexual well-being, and breast satisfaction. The women who completed the survey were on average 4.6 years out from their therapeutic mastectomy. On multivariable analysis of QOL domains, the women who had CPM reported higher breast satisfaction and psychosocial well-being, but no differences in physical or sexual well-being. Patients undergoing reconstruction with or without CPM had better overall QOL and patients undergoing radiation had worse overall QOL.

Whether and how CPM impacts QOL is a key factor when evaluating the cost effectiveness of CPM as a procedure. In an initial study, CPM was shown to be cost-effective compared to surveillance for women under 70. However, results were highly sensitive to QOL assumptions (7). A subsequent study that assumed CPM was associated with a lower QOL found CPM was cost-saving in women under 50 but also reduced health and thus concluded that the savings for health lost were insufficient to be considered cost-effective (8). With the current survey providing data indicating that CPM improves QOL, then, at least for those women who elect to pursue it, CPM may indeed be costeffective.

The CPM debate is ongoing at both professional meetings and in the media. Are women pursing CPM appropriately or based on misinformation? Should physicians be talking their patients out of considering CPM? One aspect of the current controversy around CPM centers around whether women who undergo CPM are wholly informed in an appropriate fashion about the risks and benefits of this surgical option or whether they are coerced by peers, the media or physicians into removing a healthy breast. Will removal of a healthy breast be a potential cause for future regret or is this the best option for women who seek peace of mind and better symmetry? With increased counselling and shared decision making, will rates of CPM

decrease again, or will they increase further?

Critics of the increasing rates of CPM have emphasized that there is little evidence to support a survival advantage for CPM among average risk women and that many women overestimate their risk of a new primary cancer while discounting the risk conveyed by their index cancer (9). CPM effectively lowers the relative risk of contralateral breast cancer by approximately 95% although it does not eliminate it (10-12). However, for women without a genetic predisposition to cancer, the absolute risk reduction is small and thus there is little data supporting a survival benefit to CPM (13). It is logical to assume that women most likely to benefit are those with a favorable index tumor who also have a higher than average risk of subsequent contralateral breast cancer and limited comorbidities otherwise affecting life expectancy. For women with a pathogenic BRCA1 or 2 mutation, overall survival appears to be improved with CPM (14,15). There is a lack of data on the efficacy of CPM for women with other mutations associated with elevated breast cancer risk, such as PALB2, CHEK2 and ATM, or prior thoracic radiation, and the survival benefit for these high risk women will be dependent on the penetrance of the mutation and likelihood of contralateral breast cancer, which is not clearly known. In addition, contralateral breast cancer is not always diagnosed at an early stage. Two studies report that approximately one third of patients with contralateral breast cancer were diagnosed with nodepositive disease, often of higher stage than the index tumor (10,16). For women who do undergo CPM, the rate of clinical and imaging occult contralateral breast cancer found on pathology from the CPM is low, about 5% in the largest studies published to date, with the majority being in situ disease (17-20). An additional 10% to 15% of patients are identified as having a high-risk lesion [such as atypical ductal hyperplasia, atypical lobular hyperplasia and lobular carcinoma in situ (LCIS)] in the CPM tissue (19).

We endorse discussion about an individual's risk factors for contralateral breast cancer as well as how their risk will be mitigated by therapy for the index tumor. For example, endocrine therapy for estrogen receptorpositive breast cancer appears to be a strong contributing factor to the overall decline in contralateral breast cancer incidence over the past several decades (21). The Society of Surgical Oncology guidelines from 2007 suggest that discussion of CPM is reasonable for women with diffuse microcalcifications, LCIS in the remaining breast, invasive cancer after surveillance for LCIS, atypical hyperplasia, multi-centric index tumor, and for women < age 40 at diagnosis or with dense or difficult to screen breasts, or large, ptotic or disproportionately-sized breasts (9).

There are factors other than future breast cancer risk that may enter into a woman's decision for CPM. These include the burdens and limitations of screening and consideration of symmetry in appearance, regardless of whether or what type of reconstruction is performed. Potential benefits include improved balance as well as symmetry, and the elimination of the need for screening for a new primary breast cancer. It is not infrequent that patients indicate that avoiding future mammograms and the potential for call backs and biopsies is a significant factor in weighing the decision for CPM.

A key component of informed individualized collaborative patient decision-making also must include discussion of expected survival from the index tumor (dependent on tumor biology, stage and response to therapy) and comorbid health along with the complications of CPM to fully discuss the goals and expectations of bilateral mastectomy. For women with more advanced disease and those with aggressive tumor biology the risks from the index tumor generally greatly outweigh any reduction in the potential risk of development of contralateral disease. In the same way that management of the primary tumor is increasingly individualized based on stage and biology, the option of CPM should also take these features into account.

So what then are the risks of CPM? Breast cancer surgery is quite safe and overall morbidity is low. Most complications are attributable to a second surgical site and possibly the longer operative time. It is well-documented that side-specific complications, mainly bleeding, infectious and wound-related, are approximately doubled with bilateral versus unilateral mastectomy (22-24). In fact the surgical complications on the CPM side have similar rates to the cancer side. Systemic complications such as thromboembolic events are rare overall and do not appear to be significantly increased when a bilateral procedure is performed (22,24). It is well known that after CPM, even with IBR, the chest wall/reconstructed breast is insensate. Although this is usually mentioned in pre-operative discussions, it remains an area where women may appear dissatisfied in the long run, indicating that we either do not discuss this well enough, or that women indicate they understand this pre-operatively at the time of decision making (often at the time of navigating their new cancer diagnosis) and yet are disappointed in the degree of loss of sensation in the long term. Further information on QOL and satisfaction of women with CPM is important for both physicians and patients to increase

understanding and aid counselling and decision making. With mastectomy, the nipple is frequently lost, although with increasing use of nipple-sparing mastectomy, both for cancer and for risk reduction, it may be preserved (25). However, even with preservation of the nipple-areola complex, sensation is not preserved.

It seems that the discussion with patients swings from breast conservation to bilateral mastectomy, with unilateral mastectomy glossed over as an option by many women. The impact of the increased availability and increased use of breast reconstruction on the rates of CPM have been documented in multiple studies (3-5). This was also seen in the current study as women who reported CPM were more likely to have had reconstruction than women without CPM (OR, 1.72). What is the benefit of reconstruction after unilateral mastectomy when the result is asymmetrical and often requires a symmetrization procedure on the other breast? A previous report by the same authors from BREAST-Q data from the Army of Women showed that women undergoing mastectomy without reconstruction had the lowest satisfaction and that out of those that pursued reconstruction the lowest satisfaction was seen in women undergoing unilateral mastectomy with implant reconstruction (26). Often the desire for optimal cosmetic outcomes, together with 'peace of mind', secures the final decision for women considering CPM, regardless of data related to oncologic outcomes and survival. As breast surgeons we are good at counselling patients regarding oncologic outcomes; however, data on QOL outcomes are harder to provide. This survey of Army of Women volunteers related to OOL after mastectomy with or without CPM provides information to share with our patients considering CPM. However the question remains as to whether the improvements in breast satisfaction and psychosocial well-being seen in those women pursuing CPM are clinically meaningful. In many ways, this can help affirm a decision made for CPM, however probably should not be used to encourage a women to pursue CPM. Ultimately, the patient's preference has always been and remains the key driver of surgical choice. This is often not a decision driven by data, but a personal decision which varies based on individual preferences and goals. We should remember that CPM is irreversible, may not be necessary and the potential for regret and psychological sequelae do exist. CPM is never an emergency and if there is any doubt, the decision for CPM can be delayed to a later time after completion of oncologic therapy.

Several older studies with longer follow-up have shown that most women are satisfied with their choice for CPM. The perception of informed decision-making for CPM is high and associated with QOL. When dissatisfaction occurs, it is most often related to high levels of psychological distress, poor body image or cosmetic outcome and diminished sexuality (27-29). Ultimately, we need more information on long term patient reported outcomes using robust methodologies to share with our patients. Ultimately the decision regarding CPM is best made by respectful attention to the delicate balance between patient autonomy and physician advice based on the best available estimates of the risk of contralateral breast cancer, limitations of current screening methods, prognosis of the index cancer and life expectancy based on patient general health status. The duty of breast oncologic surgeons is to provide knowledge that permits patients to make an informed choice, allays fear and anxiety and respects patient preferences.

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Footnote

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