



Trend in Performing Mastectomy for Breast Cancer Treatment and Prevention

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Editorial

In recent years, a sharp increase in performing simple mastectomies of various types has been reported across the nation. Many patients who were traditionally treated by breast conserving surgery for early breast cancer or modified radical mastectomy for advanced primary cancer are now choosing simple mastectomy and sentinel lymph node biopsy. The trend of skipping modified radical mastectomy is no longer limited to those with clinically negative axilla with proven negative sentinel lymph nodes, and it has been extended to patients who have either limited metastatic sentinel lymph nodes or those who have pathologically proven metastasis but are converted to node negative disease by neoadjuvant chemotherapy.

ACOSOG Z0011 study [1,2] demonstrated that among patients with lumpectomy and limited positive sentinel lymph nodes who had postoperative whole breast radiation, there was no difference in overall survival and disease free survival rates between groups of patients with and without axillary lymph node dissection. The same approach has been extended into managing patients with mastectomy who had limited metastasis found in the sentinel lymph nodes. Fu et al. [3] recently reported that postmastectomy radiation without axillary lymph node dissection was as effective as those with axillary lymph node dissection in patients with mastectomy and limited metastasis in sentinel lymph nodes. Recently, we used the California State Tumor Registry's database to study the role of post-mastectomy radiation in patients with T1/2N1a breast cancer detected by sentinel lymph node biopsy [4]. We found that additional axillary lymph node dissection is not necessary for these patients if they underwent post-mastectomy radiation [4].

In addition, a recent ACOSOG Z1071 Allian study showed that 41% node positive patients became node negative after neoadjuvant chemotherapy [5] which further suggested this group of patients traditionally treated by axillary lymph node dissection now may have sentinel lymph node biopsy with simple mastectomy.

Parallel to the increasing use of simple mastectomy in treating invasive breast cancer, a growing trend of simple mastectomy is also observed in treating young women with Ductal Carcinoma In Situ (DCIS). It is well known that DCIS is associated with an excellent survival outcome after either breast conserving treatment or mastectomy. For many years, lumpectomy with radiation was preferred by most for treating DCIS. However, Rutter et al. [6] reported that the rate of using mastectomy in treating DCIS was rising after 2004.

In addition to the noticeable rise of using mastectomy in cancer treatment, an even more dramatic trend is choosing contralateral prophylactic mastectomy in women with unilateral breast cancer [7-9]. While it is not clear what are the reasons responsible for this change, Fu et al. [10] reported a retrospective analysis of 373 breast cancer patients treated by mastectomy between 2002 and 2010 in a single institution. Of the 373 patients, 55.5% had bilateral mastectomy and 44.5% had unilateral mastectomy. In this study, younger age, early stage breast cancer, family history of breast and/or ovarian breast, personal history of BRCA mutation, history of multiple breast biopsies, and preoperative MRI were found to be associated with having bilateral mastectomy when compared with the unilateral mastectomy group. Even after excluding those with bilateral breast cancer, the same predictors for choosing contralateral prophylactic mastectomy remained unchanged. Similar association factors with contralateral prophylactic mastectomy have also been reported by others [11-13]. Of the 151 patients reported by Fu et al. with unilateral breast cancer and bilateral mastectomy, 75% had immediate reconstruction. It is clear that the availability of immediate reconstruction and improved aesthetic options contribute to the trend of choosing contralateral prophylactic mastectomy in treating women with early breast cancer [14].

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In addition to an overall increase in choosing simple mastectomy either with or without axillary lymph node surgery for treating breast cancer, a trend of selecting contralateral prophylactic mastectomy has been observed across the nation. Many questions remain unanswered in the practice of contralateral prophylactic mastectomy. The first and foremost question is whether contralateral prophylactic mastectomy reduces a second breast cancer event and improves cancer specific survival. Kruper et al. [15] use SEER – the Surveillance, Epidemiology and End Results database to compare the outcomes of 26,562 cases of therapeutic mastectomy and contralateral prophylactic mastectomy with 138,826 cases of unilateral therapeutic mastectomy. After propensity score matched analysis, the authors found that contralateral prophylactic mastectomy was associated with better disease free and overall survival rates in all subset analysis including patients across all stages of disease and across ER positive and negative breast cancer groups. However, limitation of SEER database does not allow removing bias that may affect survival outcomes [16]. Similar observations were also reported by others but all had the same limitation in data analysis [17].

With contralateral prophylactic mastectomy rates continuing to rise and an unclear clinical benefit of the procedure, answers for other associated issues such as complication rate, short and long-term effects on patient satisfaction and issue of cost-effectiveness have been scrutinized to better inform patients regarding risks and benefits of this added procedure has become increasingly important.

Miller et al. [18] assessed complication rates associated with contralateral prophylactic mastectomy by comparing 209 cases of contralateral prophylactic mastectomy with 391 cases of unilateral mastectomy in cancer patients performed in a single institution between 2009 and 2012. The authors found that the contralateral mastectomy group was 1.5 times more likely to have any complication and 2.7 times more likely to have a major complication compared with unilateral mastectomy group. Other older studies [19,20] also cautioned the risks of surgical complications after bilateral mastectomy with or without reconstruction. A more recent study reported by Silva et al. [21] to compare the complication rates of the two groups however only showed a modest difference in postoperative complication rates – 8.8% after unilateral mastectomy and 10.1% after bilateral mastectomy in overall complication rate and 4.2 and 4.6% respectively for surgical site infection.

In addition to a potential increase in complications because of added contralateral prophylactic mastectomy, concern for delaying adjuvant therapy has been raised. Sharpe et al. [22] reported that bilateral mastectomy was associated with a delay to adjuvant chemotherapy; however, in multivariate analysis this association was not significant. There is no delay in receiving adjuvant radiation and hormonal therapy.

The added cost for contralateral prophylactic mastectomy is also a concern. According to recent data from a major private health insurer, the average cost of a bilateral mastectomy with reconstruction was \$30,500 and \$18,500 for unilateral mastectomy with reconstruction. A recent report by Edwards et al. [23] suggested that in high risk individuals, bilateral mastectomy is cost-effective compared with subsequent imaging screening based on Medicare reimbursement rates. The reported cost analysis did not include the costs for subsequent cancer diagnosis, treatment, and supportive care.

Beyond the concerns of surgical complications and cost

associated with added contralateral prophylactic mastectomy, it is also important to assess the long term effects of this procedure on women at the levels of body image, sexuality, and overall health. Studies were done to compare bilateral mastectomy with those in the general population, unilateral mastectomy and breast conserving therapy. Unukovych et al. [24] reported that no difference was found in health-related quality of life – including anxiety, depression, sexuality before and after contralateral prophylactic mastectomy and between women with contralateral prophylactic mastectomy and those in the general population, although more than half of the patients reported at least one body image issue at two years after surgery. When patients with reconstruction after contralateral prophylactic mastectomy and unilateral mastectomy were compared, the former group was associated with higher mean score for breast and outcome satisfaction [25]. Both groups had a similar health-related quality of life (HR-QoL). Sexual dysfunction was observed in both breast conserving therapy and mastectomy groups. However, postoperative sexual dysfunction was more significant in patients after mastectomy. Further subset comparisons between unilateral mastectomy and bilateral mastectomy with or without reconstruction was not performed in this study [26].

While mastectomy with or without reconstruction clearly affects women's body image and sexuality, Rosenberg et al reported that 80% patients who chose contralateral prophylactic mastectomy were confident in their decision and 90% would have made the same decision again [27]. As such, the trend of contralateral prophylactic mastectomy may continue to rise especially in young women with breast cancer.

After considering all concerns, a consensual statement from the American Society of Breast Surgeons recommended that contralateral prophylactic mastectomy should be discouraged in women with average-risk and unilateral breast cancer [28].

Historically, mastectomy was performed in women with breast cancer. However, in the recent decade, advances in molecular biology have played a key role in identifying women at increased risk for breast cancer. Although age and family history have always been recognized as the important factors in determining risk, the discovery of the *BRCA1* and *BRCA2* gene mutations associated with breast cancer risk has provided an objective means to identify women at high risk for developing breast cancer. These women not only carry a significantly increased risk of developing breast cancer but are also more likely to develop it at an early age [29-33]. Therefore, identification of these patients by genetic testing is critical if any aggressive measures to reduce the risk of developing breast cancer are to be considered. Currently, the most effective prevention for breast cancer is prophylactic mastectomy. However, prospective data are limited. Guidelines for considering prophylactic mastectomy have been proposed, but there is no absolute indication for this procedure [34,35]. These guidelines also recommend that prophylactic mastectomy may be considered in patients without a history of breast cancer but who are at increased risk of developing breast cancer or who have clinical conditions known to make evaluation of the breasts difficult [34]. Conditions recognized beyond a proven mutation include atypical hyperplasia with a high risk family history of breast cancer, lobular carcinoma in situ, history of a first-degree relative with premenopausal bilateral breast cancer, and dense breasts that are nodular which make evaluation exceptionally difficult.

A retrospective study of prophylactic mastectomy in women

with a family history of breast cancer was reported by Hartmann and associates [36] at the Mayo Clinic. This study demonstrated a significantly decreased incidence of breast cancer following prophylactic mastectomy after a mean follow-up of 14 years. Only 7 of 639 patients developed breast cancer after prophylactic mastectomy. All of whom developed breast cancer had a previous subcutaneous or incomplete mastectomy. None of the patients who underwent simple mastectomy developed breast cancer; however, the difference was not statistically significant. A similar retrospective study of 1500 patients by Pennisi and Capozzi [37] showed comparable results.

When genetic testing for inherited breast cancer becomes better understood and more available, many of these high-risk women may be attracted to the idea of risk reducing mastectomy. Studies have also shown that nipple-sparing mastectomy with reconstruction is safe feasible and preferable by most young women who choose to have risk reducing mastectomy [38-42]. Currently, BRCA1 or BRCA2 mutations and several other forms of hereditary breast cancer seem to be the only agreed upon indication for prophylactic mastectomy. Women should be thoroughly advised of available data on risk reduction, extent of surgery that is involved in prophylactic mastectomy and reconstruction, and the lack of long-term data from prospective studies before proceeding with this therapy.

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