

## Mastectomies on the Rise for Breast Cancer: “The Tide Is Changing”

Charles M. Balch, MD and Lisa K. Jacobs, MD

Johns Hopkins Departments of Surgery and Oncology and the Avon Foundation Breast Center, Johns Hopkins Medical Institutions, Baltimore, MD

In this issue of the *Annals* are three articles that describe a substantial increase in the number of therapeutic mastectomies for breast cancer and an increased rate of contralateral prophylactic mastectomies.<sup>1–3</sup> These publications reflect a national trend that is most likely the result of multiple factors. Of these, the major influence is a change in patient attitudes and their choices as they contemplate the benefits and risks of an increasing array of surgical options for breast cancer. Simultaneously, they are exposed to better information about future risks of contralateral disease and the increasing trend to have bilateral mastectomies to achieve a cancer treatment benefit, cancer prevention, cosmetically better symmetry of their breasts, and “peace of mind,” all in one surgical procedure. However, these approaches are not for everyone, and it is our burden of responsibility to ensure that patients are properly informed about all their options and know the relative risks and complications so they can be fully informed as we ask them to participate in these complex decisions.

The first of the three articles, by McGuire, Cox, and colleagues from the H. Lee Moffitt Cancer Center and University of South Florida in Tampa, describes a trend that many of us have seen in our breast cancer practice, i.e., that the proportion of women undergoing total mastectomies is on the rise.<sup>3</sup> They have documented a striking increase in total mastectomy (TM) rates at their institution during a 13-year period (1994–2007) from an extensive experience of 5,865 breast cancer patients. The rate of TM increased from 33% in the initial 5-year period (1994–1998) to 44% in the last 5-year period (2004–2007)

( $p < 0.01$ ). More striking, during this last time frame, TM rates increased from 35% in 2004 to a whopping 60% in 2007! This is a dramatic shift, for which the authors concluded that “the tide is changing in regard to the surgical management of breast cancer.” By logistic regression analysis, the significant predictors of women choosing to have a total mastectomy were: (1) age <40 years, (2) increase in tumor size, and (3) presence of lymphovascular invasion.

This trend occurred despite the fact that they helped establish an advocacy group of breast cancer survivors, which was formed for the purpose of educating women in Florida about the relative benefits of breast conservation treatment. Paradoxically, these efforts may have been one reason women coming to their Breast Center were choosing mastectomy after getting opinions from their peers. In discussions with Dr. Cox, he is convinced that this change is driven primarily by patient choice, because all of their patients are considered for lumpectomy as well as total mastectomy. Interestingly, this choice is not influenced as much by a desire for immediate breast reconstruction, even though reconstruction is discussed with all patients who undergo total mastectomy. Their rate of immediate breast reconstruction actually decreased during this time period, from 16% in the initial 5-year period (1994–1998) to 7% in the latest time period (2004–2007) ( $p < 0.01$ ).

During the past three decades, we have witnessed advances in the surgical management through a series of clinical trials comparing the Halsted radical mastectomy with modified radical mastectomy in the 1970s to the paradigm-changing surgical trials in the 1980s demonstrating the survival equivalency of breast conservation therapy (segmental mastectomy plus breast irradiation or BCT) and total mastectomy. There was a lot of “persuasion” that BCT was actually a superior treatment, because of the disfigurement and asymmetry of a total mastectomy,

especially in women with larger breasts. Surgeons were admonished to offer women BCT and some states even passed legislation to ensure the public that BCT would be offered to all women with breast cancer. In other words, the transition to performing more BCT was made by encouraging surgeons “to give women a choice from among treatment options.” Over time, surgeons responded and the rate of BCT did increase and the vast majority of women in the 1990s had BCT instead of total mastectomy. Indeed, a standard for accreditation by the National Accreditation Program for Breast Centers (NAPBC) is to demonstrate that 50% of patients with early-stage breast cancer are offered and/or treated with breast conservation surgery. But what happens if the women in your referral area are properly informed and still chose mastectomy over lumpectomy? We have all stated that “patients should have a choice” and made a presumption that lumpectomy was better. But in the absence of evidence that lumpectomy provides a medically superior treatment outcome, we must defer to the patients final decision when the choice between lumpectomy and mastectomy is based on differing quality-of-life perceptions and a varying risk-avoidance philosophy by patients about local recurrence rates after BCT.

During the past 10–15 years, there have been a number of influences that could have contributed to this increasing trend. The first is the increasing use of skin-sparing mastectomy along with immediate or delayed breast reconstruction surgery.<sup>4</sup> Second is a better understanding of risk factors that can identify women at higher risk for in-breast recurrences with breast conservation. Third, is the clearer picture of the late effects of breast irradiation and the continued incremental risk for developing a second breast cancer over time. Fourth and finally, women are increasingly proactive about their breast health and knowledgeable about their disease as well as the treatment options to consider from information they get from a network of breast cancer survivors, books about breast cancer, and the internet. In short, they better understand their role in choosing from among an array of breast treatment options and how each might differentially impact their quality of life. Each of these changes has brought about a “sea change” of activity for which the trends of increased mastectomy rates are driven largely by patient-driven decision-making.

We also have watched the tide turn once again in our breast oncology practice at the Johns Hopkins Avon Foundation Breast Center. Most notably, the availability of immediate breast reconstructive surgery has given women the choice to achieve breast symmetry with BCT or total mastectomy with breast reconstruction. This has been achieved with the advent of skin-sparing mastectomies as an essential component of immediate breast reconstruction, and its use has increased nationally during the past decade.<sup>4</sup>

This approach has been shown with long-term follow-up to be an oncologically safe operation, with local recurrence rates that are the same or even less than previously reported rates with prior total mastectomy approaches.<sup>5–7</sup>

Also, we have a better understanding of the natural history of breast cancer with regard to predicting in-breast failure rates with BCT and have better imaging tools to discern multicentric/multifocal breast tumors. Finally, public education and patient advocacy about breast cancer has made impressive strides and women with breast cancer come to the surgeon much more informed than they did only a decade ago. Many have made their decision even before seeing the surgeon. In other words, the change we are experiencing today is no doubt driven more by informed patients when there are choices among equivalent surgical outcomes with regard to 10-year survival rates. Isn't that what we wanted all along? If survival rates are equivalent and we are describing “personalized breast cancer therapies” to the public, wouldn't it be wrong to impose BCT as the “preferred treatment” as perceived by the physician?

The second and third articles describe the increasing trends of contralateral prophylactic mastectomies (CPM) in women with increased risk for opposite breast cancers. One study by Jones and colleagues focused on 201 patients who underwent CPM from among a total of 1,840 patients treated at the Ohio State Arthur James Cancer Center who had a total mastectomy for unilateral breast cancer.<sup>2</sup> In contrast to the experience at the Moffitt series, there was no trend of increased rate of total mastectomy, but the rate of CPM increased from 6.5% in 1999 to 16.1% in 2007. The 201 women who choose CPM were: (1) younger, (2) more highly educated, (3) had a lower stage of breast cancer, and (4) were more likely to have a family history of breast cancer.<sup>2</sup>

Similar results are reported in this issue by Arrington and colleagues from the University of Minnesota on 165 patients who had a total mastectomy plus contralateral prophylactic mastectomy treated at six hospitals in their healthcare system in the years 2006 and 2007.<sup>1</sup> Of the 571 patients, 48% underwent breast-conserving surgery, 23% underwent unilateral mastectomy, and 30% underwent mastectomy and CPM. Among all total mastectomy patients, 56% underwent CPM. Independent predictors of increased CPM rates were: (1) young age (<40 vs. >55 years), (2) large tumor size (>5 cm vs. <2 cm), (2) positive family history, (4) lobular histology, (5) multicentric disease, (6) presence of nodal metastases, and (7) surgeon gender (female). Interestingly, all patients who had BRCA testing, regardless of the results, underwent CPM. Occult contralateral breast cancer was found in 5.5% of patients and lobular carcinoma in situ (LCIS) or atypical ductal hyperplasia in an additional 2.4%—rates similar to a

previous study that found occult cancer in 5% of patients who had CPM.<sup>16</sup> Most patients (62.4%) who have CPM also chose immediate breast reconstruction.<sup>1</sup> These investigators had previously reported a national trend of increased CPM rates using SEER data.<sup>8,9</sup>

The justification for CPM is primarily one of reducing the risk of developing a second breast cancer, although it is controversial whether overall survival rates actually improve through preventative surgery. In another study, contralateral breast cancer developed in only 0.5% of 1,072 women with CPM compared with a 2.7% incidence of contralateral BC among a sample of 317 patients without CPM after a follow-up of 5.7 years; notably, there also was a decreased breast cancer mortality rate.<sup>10</sup> In some circumstances, a contralateral mastectomy is considered to achieve symmetry, especially in larger breasted women, for whom a substantial reduction mammoplasty would otherwise be required. Finally, the results from breast genetic testing have demonstrated a high risk of contralateral breast cancer in BRCA + patients. The Society of Surgical Oncology has published two position papers about the role of preventative surgery in this genetically determined high-risk group.<sup>11,12</sup>

Our ability to better understand the natural history of breast cancer and the availability of improved imaging and genetic testing has no doubt influenced this rate of CPM.<sup>13,14</sup> In addition, women are much better informed, educated, and proactive about their breast health. The list of factors associated with an increased rate of CPM reflects these confluent factors: (1) younger age, (2) multicentric tumors, lobular histology, LCIS, or extensive ductal carcinoma in situ in the ipsilateral breast, (3) BRCA + genes or genetic testing, (4) anxiety about cancer and desire to reduce the cancer risk, or (5) plans for immediate breast reconstruction.<sup>1,8,9,14-18</sup> After 1 to 2 years of follow-up, the majority of women who undergo CPM reported satisfaction with their decision and experienced psychosocial outcomes similar to breast cancer survivors without the procedure.<sup>19-21</sup>

The goal of making the final decision about surgical management of the breast cancer—in partnership with each patient—is to maximize the long-term results with regards to local disease control, symmetry of the breasts, cosmetic appearance, and emotional state. We are achieving this because many, if not most, women with breast cancer now are evaluated by a multidisciplinary team of breast specialists and patient advocates/survivors in a dedicated Breast Center. These women come prepared with a more informed and empowered ability to participate in decision-making with regard to their breast management. The teamwork and coordination between the breast imaging specialists, breast oncology surgeons, breast reconstruction surgeons, and breast radiation oncologists also have

resulted in better staging and consistent patient recommendations. Rather than being alarmed by this trend, we should acknowledge that the rising incidence of total mastectomy emanates from technological advances in our care and patient-driven choices. To ensure that all women have access to a range of surgical treatment options, we should continue to make improvements in BCT outcomes and availability of high-quality radiation therapy, especially in rural areas and inner cities. In addition, we need to ensure that all women have access to educational material that is evidence-based, understandable, and balanced.

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