

More Mastectomies: Is This What Patients Really Want?

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Breast-conserving therapy (BCT), consisting of breast-conserving surgery (BCS) followed by breast irradiation, is a notable success story in oncology. For nearly the entire first half of the 20th century, mastectomy was the standard of care in the United States. Remarkably, it took the mature results from six randomized clinical trials comparing BCT with mastectomy before a 1990 National Institutes of Health Consensus Development Panel concluded that BCS was the preferred method of primary surgical therapy for women with early-stage breast cancer.¹ From 1989 to 1995, the percentage of women undergoing BCT increased from 35% to 60% for stage 1 and from 19% to 29% for stage 2 breast cancer.^{2,3} BCT has been shown to be associated with improved body image and improved short-term physical functioning compared with mastectomy.⁴ In the era of sentinel node biopsy, BCS is an outpatient procedure that requires no drains, allowing a prompt return to full activity, although necessitating commitment to a course of radiation therapy. BCT also results in a sensate breast with an erectile nipple, an outcome that even the most elegant reconstruction cannot provide.

Local recurrence after BCT has been a concern of both patients and their physicians. Over time, improvements in preoperative breast imaging, pathologic evaluation of lumpectomy specimens, and routine use of adjuvant systemic therapy have resulted in a substantial decrease in the rates of local recurrence after BCT; these rates are now similar to those seen with mastectomy. In a recent series from one of our institutions, the 5-year rate of local recurrence after BCT was only 1.8%.⁵ Excellent outcomes have been achieved in a wide variety of clinical settings, with 10-year local recurrence rates of less than 8% reported in a series of NSABP (National Surgical Adjuvant Breast and Bowel Project) trials.⁶

The struggle for acceptance of BCT was long and occurred in response to patient demand for effective and safe alternatives to mastectomy. The excellent outcomes of BCT today, coupled with its strong scientific basis and initial patient advocacy for the procedure, make it particularly surprising that use of mastectomy in the United States seems to be increasing. In this issue of *Journal of Clinical Oncology*, Katipamula et al⁷ of the Mayo Clinic (Rochester, MN) report that after a decline from 1997 to 2003, the mastectomy rate increased from 31% to 43% between 2003 and 2006, a rate equivalent to that in 1997. This observation is not unique to this study. McGuire et al⁸ examined mastectomy rates at the Moffitt Cancer Center (Tampa, FL) between 1994 and 2007 and noted that the odds of mastectomy increased

1.8-fold in the period from 2004 to 2007 compared with the period from 1994 to 1998, after controlling for other variables. Additional support for the idea that increased use of mastectomy is not limited to a few tertiary care institutions comes from the Surveillance Epidemiology and End Results database on the use of contralateral prophylactic mastectomy in the United States. This nationwide database has demonstrated an increase in contralateral prophylactic mastectomy from 4.2% to 11% in women undergoing treatment with unilateral mastectomy between 1998 and 2003.⁹

The obvious question is: What has changed? Increased awareness of and testing for *BRCA1* and *BRCA2* mutations indicating breast cancer predisposition are often cited as factors that have appropriately increased use of mastectomy. But these mutations occur in only 5% to 10% of patients with breast cancer, and the proportion of women in the Mayo Clinic series⁷ with a first-degree relative with breast cancer did not increase over time, whereas the mastectomy rate did, making this an unlikely explanation for a large part of the effect observed in this and other studies.

Another potential reason for the increased rate of mastectomy is the increased use of breast magnetic resonance imaging (MRI) at time of diagnosis. On the basis of the superior performance characteristics of breast MRI relative to mammography (especially its high sensitivity¹⁰), it is being increasingly used at time of diagnosis to exclude the presence of multifocal or multicentric breast cancer in the ipsilateral breast. In a recent meta-analysis, MRI identified additional tumor foci in 16% (95% CI, 6% to 34%) of patients newly diagnosed with breast cancer and led to a change in surgical therapy in 8% to 33% of patients, most commonly resulting in mastectomy that would not otherwise have been performed. (It is worth noting that this incidence of additional cancer detected by MRI is considerably higher than the long-term local recurrence rates seen with BCT.) MRI also identifies mammographically occult contralateral breast cancers in approximately 3% of women who present with unilateral invasive breast cancer.¹¹ On the basis of these performance characteristics, it had been widely assumed that use of breast MRI for the selection of patients for BCT would reduce the need for re-excision, reduce local recurrence, and even improve long-term survival. At present, no studies have provided support for any of these improved clinical outcomes.¹²⁻¹⁴ However, breast MRI has been shown to result in additional biopsies and costs, increased patient anxiety, and delays in the start of definitive treatment. Although it is accepted that

MRI-detected abnormalities should be biopsied before altering surgical treatment plans, it has been documented that some patients have chosen to forgo these biopsies or additional work-ups and proceed with mastectomy because of concerns about delaying definitive therapy.¹⁵ A recent prospective randomized clinical trial¹⁶ demonstrated no reduction in the rate of re-excision in women randomly assigned to undergo preoperative MRI compared with those who were not.¹⁷ Despite these known disadvantages and the lack of established improvement in any clinical outcome, use of breast MRI at time of diagnosis has been—in our judgment, regrettably—increasing.

Against this backdrop, Katipamula et al⁷ provide a thoughtful retrospective analysis to assess whether the increased use of breast MRI is a factor in the increased use of mastectomy. They analyzed 5,405 patients who underwent definitive breast surgery at the Mayo Clinic between 1997 and 2006. Use of MRI increased from 10% in 2003 to 23% in 2006 ($P < .0001$). The key finding of this study is that patients who underwent MRI were more likely to undergo mastectomy than those who did not undergo MRI (54% v 36%; $P < .0001$). In a multivariable model, both MRI (odds ratio, 1.7; $P < .0001$) and year of surgery were independent predictors of mastectomy. Katipamula et al accurately note that this association does not necessarily imply a causal relationship, because confounding between use of MRI and mastectomy might explain some, although likely not all, of the association. The Mayo Clinic study is now part of the accumulating evidence that breast MRI at time of diagnosis increases the rate of mastectomy. In the COMICE (Comparative Effectiveness of Magnetic Resonance Imaging in Breast Cancer) trial,¹⁶ women randomly assigned to undergo MRI had a significantly higher mastectomy rate (7.1%) compared with those who did not undergo MRI (1.2%). In addition, Pengel et al¹⁴ of the Netherlands Cancer Institute (Amsterdam, the Netherlands) observed a doubling of the mastectomy rate from 5.1% in patients considered candidates for BCT and treated without MRI to 11.6% in those who underwent preoperative MRI. Bleicher et al¹³ examined the impact of MRI on mastectomy rates at the Fox Chase Cancer Center (Philadelphia, PA) between 2004 and 2006. Although the overall mastectomy rate did not increase during this interval, patients who underwent MRI had an odds ratio of mastectomy of 1.8, similar to the increased mastectomy rate seen at the Mayo Clinic.

Thus, despite the many intuitively obvious advantages of breast MRI in aiding surgical planning, there are no established benefits and several substantial disadvantages, one of which includes the needless increase in mastectomy rates. The history of breast cancer treatment is replete with interventions that seemed intuitively obvious but were eventually shown to be ineffective or harmful. The use of high-dose chemotherapy with bone marrow transplantation rescue is just one glaring recent example; an accumulating body of evidence suggests that use of MRI in selecting patients for surgical therapy is another.

Although the findings regarding use of MRI and increased mastectomy rates are troubling, they are only one piece of the puzzle, because mastectomy rates have also increased in women who did not undergo MRI. In many parts of the United States, patients are pushing their surgeons for mastectomy, even bilateral mastectomy, despite being told that such treatment will not improve prognosis. (Interestingly, this shift to mastectomy does not seem to be occurring in Europe.) Katz et al¹⁸ examined the role of patients in decision making regarding local therapy for breast cancer. In a population-based sample of white women without contraindications to BCT, the mastectomy rate increased from 5.3% when the patient identified the

surgeon as the primary decision maker to 16.8% when the decision was considered shared and to 27% when the patient felt that she had made the decision ($P < .001$). Patients articulated concern about cancer recurrence as the most important factor in the decision making process; an average of 6 months after diagnosis, only half were able to correctly answer a true-false question regarding lack of difference in survival between those undergoing BCT and mastectomy. These findings suggest that a desire to be safe, which is not founded in medical fact, is an important part of the observed increase in mastectomy rates.

The trends in choice of local therapy raise many questions. Individualized medicine and patient-centered decision making have been accepted as appropriate models of care. BCT rather than mastectomy for women with localized disease is a form of individualized care that provides local control and survival equal to those seen after mastectomy, and an increasing body of evidence suggests that it is the biology of the cancer rather than type of local therapy that determines risk of local recurrence, whether treated with mastectomy or BCT.^{5,19} Clearly we are not communicating this to our patients if they continue to choose mastectomy in the belief that it is a reasonable choice for decreasing risk of cancer recurrence. We agree with Katipamula et al⁷ that new studies are needed to evaluate whether these changes in surgical management lead to improvements in quality of life or patient satisfaction. More work is also clearly needed on how to effectively communicate complex treatment choices to women facing the stress of new cancer diagnosis. There are an increasing number of treatment decisions for patients with breast cancer today, ranging from the choice of BCT or mastectomy, type of breast reconstruction, and type and duration of radiation therapy to selection of adjuvant systemic therapy. As we move forward, treatment choices will be increasingly made on the basis of the outcomes of sophisticated molecular tests, the pros and cons of which are difficult to grasp for those without a scientific background. Unfortunately, if we are unable to convey to women the lack of an improved outcome with mastectomy compared with BCT despite a strong foundation of clinical trials and extensive experience with the procedure, the prospects for individualizing medical care and reducing unnecessary treatment on the basis of molecular profiling of tumors seem slim.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

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