World J Surg (2012) 36:1475–1479
DOI 10.1007/s00268-012-1469-4

World Journal of Surgery

United States Trends in the Surgical Treatment of Primary Breast Cancer

Todd M. Tuttle · Natasha M. Rueth · Andrea Abbott · Beth A. Virnig

Published online: 18 February 2012

Introduction

Before the publication of National Surgical Adjuvant Breast Project Trial (NSABP) B-06, most breast cancer patients in the United States were treated with mastectomy [1, 2]. After the publication of NSABP-B06 in 1985, the rates of breast-conserving surgery (BCS) increased, but only slightly. After the 1990 National Institutes of Health Consensus Statement concluded that BCS plus radiation therapy (RT) was "preferred" for early-stage breast cancer, BCS rates markedly increased throughout the 1990s and early 2000s [2, 3]. However, during the past decade, several trends in the local treatment of breast cancer have been observed that are counter-intuitive to the findings from prospective randomized trials.

The objective of this review is to evaluate recent patterns in the local treatment of breast cancer in the United States. This review will concentrate on three specific trends: (1) mastectomy/BCS rates; (2) contralateral prophylactic mastectomy (CPM) rates; and (3) use of RT after BCS. We will also discuss potential consequences of these trends and strategies to ensure appropriate local treatment for most breast cancer patients.

T. M. Tuttle (✉) · N. M. Rueth · A. Abbott
Department of Surgery, Division of Surgical Oncology, University of Minnesota, 420 Delaware St. SE, Minneapolis, Minnesota 55455, USA
e-mail: tuttl006@umn.edu

B. A. Virnig
Division of Health Policy and Management, University of Minnesota, 420 Delaware St. SE, Minneapolis, Minnesota 55455, USA

Mastectomy/BCS rates

After the NIH Consensus Statement was released in 1990, the rates of BCS markedly increased in the United States throughout the 1990s and into the 2000s [2, 3]. However, in 2009, two single-institutional studies reported that mastectomy rates had markedly increased with a corresponding decrease in BCS rates [4, 5]. In a study of 5,865 patients treated at the Moffitt Cancer Center, McGuire et al. reported that the mastectomy rates increased from 35% in 2004 to 60% in 2007; young age (<40 years), larger tumor size, and lymphovascular invasion were independent predictors of mastectomy [4]. In another study of 5,405 patients treated at the Mayo Clinic, Katipamula et al. [5] reported that mastectomy rates increased from 31% in 2003 to 43% in 2006; young age (<50), TNM stage, lobular histology, breast density, concurrent or prior contralateral breast cancer, laterality, family history, and use of magnetic resonance imaging (MRI) were independent predictors of mastectomy. These studies received considerable attention in the lay press and led to the publication of several prominent editorials [6, 7].

Habermann et al. [8] recently evaluated mastectomy/BCS trends in the United States using the Surveillance Epidemiology and End Results (SEER) database to determine if the findings from single-institutional studies reflected national trends. A total of 233,754 patients with ductal carcinoma in situ or stage I–III breast cancer were identified in the SEER database from 2000 to 2006. The proportion of women treated with mastectomy significantly decreased from 41% in 2000 to 37% in 2006. Mastectomy rates decreased over time for patients with all tumor sizes, grades, and stages. In this study, patient age ≤40 years, stage I or II breast cancer, low-grade tumors, estrogen-receptor positive tumors, negative lymph nodes, nonlobular

histology were associated with lower mastectomy rates. Significant geographic variation in mastectomy rates was observed (Louisiana, 51%; Connecticut, 27%). Interestingly, the mastectomy rates slightly increased from 2005 to 2006, perhaps indicating future trends in the United States.

Several factors have also been associated with mastectomy rates. Nattinger et al. [9] reported that the middle Atlantic and New England regions had the lowest mastectomy rates, while the south central regions had the highest rates. Al-Refaie et al. [10] reported that widow status was a significant predictor of mastectomy treatment. Using a population-based data set, Hershman et al. [11] reported that patients who underwent BCS were more likely to have a female surgeon. Low patient socioeconomic status has also been associated with low use of BCS [12].

Variations in referral patterns and patient selection are potential explanations for the reported differences between single institutional and population-based studies. Patients may select larger institutions to undergo more aggressive surgery (mastectomy). Likewise, physicians may be more likely to refer patients with a strong family history of breast cancer or a documented BRCA gene mutation to a large institution for unilateral or bilateral mastectomy. In addition, patients may seek large institutions to receive breast reconstructive surgery. As significant geographic variations in mastectomy rates have been observed in the United States, the results from a large single-institutional study may simply reflect practice patterns of a particular geographic region. Because race and ethnicity are associated with surgical treatment of breast cancer [13], patient demographic characteristics at a particular institution may affect reported mastectomy rates. Nevertheless, we cannot exclude the possibility that national trends trail the findings reported from single institutional studies, and that mastectomy rates in the United States may increase in the future.

Contralateral prophylactic mastectomy (CPM) rates

While the use of BCS has increased or remained stable during the past decade, the CPM rates among patients with unilateral breast cancer have markedly increased. In an analysis of the SEER database, the CPM rate among all surgically treated patients with invasive breast cancer increased 150% from 1998 to 2003 in the United States [14]. These trends were observed for all cancer stages and continued to increase at the end of the study period, with no plateau. Similar findings were observed among patients with ductal carcinoma in situ [15]. Other studies using different databases confirmed these findings. In a study using the New York State Cancer Registry, McLaughlin et al. reported that CPM use more than doubled from 1995 to 2005 [16]. Single-institutional studies have also demonstrated marked increases in CPM rates [17, 18]. Young patient age, lobular histology, white race, higher education, and BRCA mutation, as well as family history of breast cancer, have been associated with higher CPM rates [14–20]. So, CPM rates have markedly increased during the past decade, while BCS rates have remained stable or slightly increased. Conversely, the rates of unilateral mastectomy have significantly decreased in the United States [14].

The CPM rates outside the United States have not been well documented. In an international registry of women with unilateral breast cancer and BRCA mutation, Metcalfe et al. reported that 49% of women with breast cancer in the United States underwent CPM [19]. In contrast, the CPM rates from Europe and Israel were only about 5%. Presumably, the CPM rates for patients without the BRCA mutation are much lower among patients treated outside the United States.

This trend toward more aggressive surgery is curious and counterintuitive in the modern era of minimally invasive surgery. Many factors probably contribute to increased CPM use. Public awareness of genetic breast cancer and increased BRCA testing may partially explain these observations. Improvements in mastectomy (including skin-sparing and nipple-sparing mastectomy) and reconstruction techniques, as well as improved access to breast reconstruction, probably contribute to increased CPM rates. A recent prospective survey study from Abbott et al. found that breast cancer patients substantially overestimate their risk of developing contralateral breast cancer [21]. Other studies have demonstrated that healthy women substantially overestimate their risk of breast cancer events [22, 23], and patients with early breast cancer substantially overestimate their risk of breast cancer recurrence [24, 25]. Since young patient age is consistently associated with higher CPM rates, generational differences in the value of breast-conserving treatment (including radiation) may partially explain these trends. Finally, some investigators have suggested that the use of breast MRI is associated with increased CPM rates [17]. However, in the SEER study, the sharp increase in CPM use preceded the widespread utilization of breast MRI in the United States [14]. Determining the precise rationale for choosing a particular breast cancer treatment is probably not possible from retrospective or database studies.

Most patients report being satisfied with their decision to undergo CPM [26–29]. In a study of 572 women, Frost and colleagues reported that, at a mean follow-up of 14.5 years after surgery, 70% were satisfied with their decision to undergo CPM [26]. The greatest reported benefit contributing to patient satisfaction is a reduction in breast cancer related concerns [28, 29]. Some patients, however, may

overestimate the cancer risk-reducing effectiveness of CPM. In a review of open-ended comments from women who underwent CPM, Altschuler et al. [29] recorded comments such as "I do not worry about recurrence," and I am "free of worries about breast cancer". Such comments suggest a lack of understanding of the benefits of CPM. Although a retrospective cancer registry study found that CPM was associated with lower breast cancer mortality, patients who underwent CPM had a lower risk of death from other causes, suggesting selection bias [30]. In fact, CPM probably does not improve breast cancer mortality among patients without BRCA mutations. To date, no prospective study has examined the factors that influence women to choose CPM; future studies should focus on the decision-making processes that lead to the choice of irreversible risk-reducing surgery.

Use of radiation therapy after BCS

Several randomized trials have demonstrated that local recurrence rates are significantly higher if radiation therapy (RT) is omitted after BCS [1, 31–33]. In the overview analysis, the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) estimated that the absolute 5-year local recurrence rate was 7% after BCS plus RT as compared with 26% after BCS without RT [33]. Although individual randomized trials have not demonstrated a survival difference between BCS alone and BCS plus RT, the EBCTCG analysis demonstrated a significantly increased risk of breast cancer death for patients who did not receive RT (BCS plus RT, 30.5%; BCS alone, 35.9%).

Despite the effectiveness of RT after BCS, an increasing number of patients are not receiving RT. In a study using the SEER database, Freedman et al. [34] determined treatment trends of patients with stage I and II breast cancer diagnosed from 1988 to 2004. Definitive local treatment was defined as either mastectomy or BCS plus RT. The authors found that the rates of definitive local therapy significantly decreased during the study period (1988, 95.2%; 2004, 79.2%; $p < 0.01$). Among women who underwent BCS, rates of RT significantly decreased over time (1988, 79.4%; 2004, 66.4%; $p < 0.0001$). Omission of RT was unexpectedly associated with unfavorable prognostic features including Black and Hispanic race (versus white), estrogen receptor-negative tumors, and young patients. Because of concerns about potential under ascertainment of RT in cancer registry data [35], Malin et al. conducted an additional analysis using Medicare claims data and found excellent agreement between the two sources of data. In another recent study using the American College of Surgeons National Cancer Data Base, Daroui et al. [36] reported the only 66.6 and 63.0% of patients with stage I and II breast cancer, respectively, received RT after BCS from 2000 to 2006. Although randomized trials have suggested that RT may be safely avoided in selected patients 70 years or older [37], recent trends suggest that RT is increasingly omitted in younger patients [38].

The reasons for omission of RT after BCS are not entirely clear. The daily requirement of RT for 6 weeks probably contributes to the observed trends. Transportation may be difficult for some patients, particularly elderly or employed women. Patients who live far distances from RT centers are less likely to receive RT after BCS [39]. Because of the complex multidisciplinary nature of breast cancer treatment, patient handoffs between surgeons, medical oncologists, and radiation oncologists may not occur smoothly. Finally, many patients may simply overestimate the frequency and severity of radiation therapy side effects and decline to have it on that basis.

Accelerated partial breast irradiation (APBI) is increasing used as an alternative to whole breast radiation after BCS. In a recent analysis of the SEER registry, Abbott et al. evaluated the use of APBI after BCS among patients with ductal carcinoma in situ or early invasive breast cancer [40]. The APBI rates increased by 1,600% from 2000 through 2007 in the United States. These trends were observed for all age groups, but especially among older patients. Independent predictors of APBI use included recent year of diagnosis, white race, older age, and early breast cancer stage. In 2007, about 7% of patients in the United States were treated with APBI after BCS. In fact, one manufacturer claims on its website that over 50,000 patients have now been treated with their balloon-catheter device [41]. Clearly, most patients undergoing APBI are not being enrolled in prospective trials.

Consequences

One potential consequence of these trends is that many patients are overtreated with CPM. Although CPM is an effective risk-reducing strategy for some patients, the 10-year cumulative risk of contralateral breast cancer is only about 5–6% among patients without an identified BRCA mutation [42]. Recent studies suggest that the risk is significantly less today with increased used of endocrine therapies [43]. Bilateral mastectomy (including CPM) with reconstruction frequently requires 5–6 h of surgery, use of multiple drainage tubes, prolonged hospital stay, and long recovery. As result, patients may develop complications that may require additional treatments that may delay recommended adjuvant therapies. Additionally, CPM is not associated with an improved breast cancer survival rate [44].

Another potential consequence of these trends is that many patients may be undertreated by the omission of RT

after BCS. As a result, increased local recurrence rates may be observed in the future. Ultimately, more women may require mastectomy or systemic therapy to treat breast cancer local recurrences. Breast cancer mortality rates may also increase in the future with the omission of RT. In addition, the widespread adoption of APBI has preceded the results of the NSAPB B39/Radiation Therapy Oncology Group (RTOG) 0413 randomized trial. If APBI is associated with higher local recurrences or long-term complications, then a large number of patients may be harmed.

Strategies

Perhaps the simplest strategy to reverse these potentially harmful trends is to provide patients with accurate and easily understood information. For example, patients with unilateral breast cancer who are considering bilateral mastectomy (CPM) should understand the risk of systemic metastases from the known cancer, the cumulative incidence of contralateral breast cancer, the potential risks and benefits of CPM, and alternative strategies to CPM. Decision aids have been developed to educate patients about the outcomes of various oncologic treatments [45]. The web-based program IBTR! provides quantitative estimates of the risk of local recurrence with and without the use of radiation therapy after BCS [46].

Strategies have been initiated to reduce the likelihood of fumbled handoffs between different breast cancer specialists. For example, Bickell et al. [47] described a prospective tracking system to ensure multidisciplinary care for breast cancer patients in New York City. In this program, the tracking system alerted the surgeon and oncologist if an oncology appointment was missed after surgical treatment. In addition, patient navigators assist women through the complex maze of modern multidisciplinary breast cancer care, particularly among nonaffiliated physicians and practices.

Alternative strategies to deliver radiation therapy may ensure adequate local treatment after BCS. Hypofractionated radiation therapy delivered over 3 weeks, as compared with 6 weeks, represents an attractive alternative method for radiation therapy after BCS. Whelan et al. reported the results of a clinical trial in which women with node negative breast cancer were randomized to traditional radiation therapy (50 Gy in 25 fractions over 35 days) or hypofractioned radiation (42.5 Gy in 16 fractions over 22 days) after BCS; local recurrence rates at 10 years were not significantly different between the two groups [48]. Moreover, if the NSABP/RTOG trial demonstrates equivalency between APBI and standard whole breast irradiation, then more patients may receive RT after BCS.

References

1. Fisher B, Bauer M, Margolese R et al (1985) Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. N Engl J Med 312:665–673
2. Lazovich D, Solomon CC, Thomas DB et al (2000) Breast conservation therapy in the United States following the 1990 National Institutes of Health Consensus Development Conference on the treatment of patients with early stage invasive breast carcinoma. Cancer 86:628–637
3. National Institutes of Health consensus conference (1991) Treatment of early-stage breast cancer. JAMA 265:391–395
4. McGuire KP, Santillan AA, Kaur P et al (2009) Are mastectomies on the rise? A 13-year trend analysis of the selection of mastectomy versus breast conservation therapy in 5,685 patients. Ann Surg Oncol 16:2682–2690
5. Katipamula R, Degnim AC, Hoskin T et al (2009) Trends in mastectomy rates at the Mayo Clinic Rochester: effect of surgical year and preoperative magnetic resonance imaging. J Clin Oncol 27:4082–4088
6. Morrow M (2009) More mastectomies: is this what patients really want? J Clin Oncol 27:4038–4040
7. Balch CM, Jacobs LK (2009) Mastectomies on the rise for breast cancer: the tide is changing. Ann Surg Oncol 16:2669–2672
8. Habermann EB, Abbott A, Parsons HM et al (2010) Are mastectomy rates really increasing in the United States? J Clin Oncol 28:3437–3441
9. Nattinger AB, Gottlieb MS, Veum J et al (1992) Geographic variation in the use of breast-conserving treatment for breast cancer. N Engl J Med 326:1102–1107
10. Al-Refaie W, Kuerer HM, Khuwaja A et al (2005) Determinants of mastectomy in breast conservation therapy candidates. Am J Surg 190:602–605
11. Hershman DL, Buono D, Jacobson J et al (2009) Surgeon characteristics and use of breast conservation surgery in women with early stage breast cancer. Ann Surg 249:828–833
12. Gilligan MA, Kneusel RT, Hoffmann RG et al (2002) Persistent differences in sociodemographic determinants of breast conserving treatment despite overall increased adoption. Med Care 40:181–189
13. Hawley ST, Griggs JJ, Hamilton AS et al (2009) Decision involvement and receipt of mastectomy among racially and ethnically diverse breast cancer patients. J Natl Cancer Inst 101: 1337–1347
14. Tuttle TM, Habermann EB, Grund EH et al (2007) Increasing use of contralateral prophylactic mastectomy for breast cancer patients: a trend toward more aggressive surgical treatment. J Clin Oncol 25:5203–5209
15. Tuttle TM, Jarosek S, Habermann EB et al (2009) Increasing rates of contralateral prophylactic mastectomy among patients with ductal carcinoma in situ. J Clin Oncol 27:1362–1367
16. McLaughlin CC, Lillquist PP, Edge SB (2005) Surveillance of prophylactic mastectomy: trends in use from 1995 through 2005. Cancer 115:5404–5412
17. Sobero ME, Dick AW, Beckjord EB et al (2009) Diagnostic breast magnetic resonance imaging and contralateral prophylactic mastectomy. Ann Surg Oncol 16:1597–1605
18. Jones NB, Wilson J, Kotur L et al (2009) Contralateral prophylactic mastectomy for unilateral breast cancer: an increasing trend at a single institution. Ann Surg Oncol 16:2691–2696
19. Metcalfe KA, Lubinski J, Ghadirian P et al (2008) Predictors of contralateral prophylactic mastectomy in women with a BRCA1 or BRCA2 mutation: the Hereditary Breast Cancer Clinical Study Group. J Clin Oncol 26:1093–1097

20. Arrington AK, Jarosek SL, Virnig BA et al (2009) Patient and surgeon characteristics associated with increased use of contralateral prophylactic mastectomy in patients with breast cancer. Ann Surg Oncol 16:2697–2704
21. Abbott A, Rueth N, Pappas-Varco S et al (2011) Perceptions of contralateral breast cancer: an overestimation of risk. Ann Surg Oncol 18:3129–3136
22. Black WC, Nease RF Jr, Tosteson AN (1995) Perceptions of breast cancer risk and screening effectiveness in women younger than 50 years of age. J Natl Cancer Inst 87:720–731
23. Alexander NE, Ross J, Sumner W et al (1996) The effect of an educational intervention on the perceived risk of breast cancer. J Gen Intern Med 11:92–97
24. Partridge A, Adloff K, Blood E et al (2008) Risk perceptions and psychosocial outcomes of women with ductal carcinoma in situ: longitudinal results from a cohort study. J Natl Cancer Inst 100:243–251
25. Rakovitch E, Franssen E, Kim J et al (2003) A comparison of risk perception and psychological morbidity in women with ductal carcinoma in situ and early invasive breast cancer. Breast Cancer Res Treat 77:285–293
26. Frost MH, Schaid DJ, Sellers TA et al (2000) Long-term satisfaction and psychological and social function following bilateral prophylactic mastectomy. JAMA 284:319–324
27. Montgomery LL, Tran KN, Heelen MC et al (1999) Issues of regret in women with contralateral prophylactic mastectomies. Ann Surg Oncol 6:546–552
28. Geiger AM, Nekhlyudov L, Herrinton LJ et al (2007) Quality of life after bilateral prophylactic mastectomy. Ann Surg Oncol 14:686–694
29. Altschuler A, Nekhlyudov L, Rolnick SJ et al (2008) Positive, negative, and disparate: women's differing long-term psychosocial experiences of bilateral or contralateral prophylactic mastectomy. Breast J 14:25–32
30. Herrinton LJ, Barlow WE, Yu O et al (2005) Efficacy of prophylactic mastectomy in women with unilateral breast cancer: a cancer research network project. J Clin Oncol 23:4275–4286
31. Fisher B, Anderson S, Bryant J et al (2002) Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 347:1233–1241
32. Veronesi U, Saccozzi R, Del Vecchio M et al (1981) Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancers of the breast. N Engl J Med 305:6–11
33. Early Breast Cancer Trialists' Collaborative Group (EBCTCG) (2005) Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 366:2087–2106
34. Freedman RA, He Y, Winer EP et al (2009) Trends in racial and age disparities in definitive local therapy of early-stage breast cancer. J Clin Oncol 27:713–719
35. Malin JL, Kahn KL, Adams J et al (2002) Validity of cancer registry data for measuring the quality of breast cancer care. J Natl Cancer Inst 94:835–844
36. Daroui P, Gabel M, Khan AJ et al (2011) Utilization of breast conserving therapy in stages 0, I, and II breast cancer patients in New Jersey: an American College of Surgeons National Cancer Data Base (NCDB) analysis. Am J Clin Oncol. doi:10.1097/COC.0b013e318209aa57
37. Hughes KS, Schnaper LA, Berry D et al (2004) Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. N Engl J Med 351:971–977
38. Tuttle TM, Jarosek S, Habermann EB et al. (2011) Omission of radiation therapy after breast-conserving surgery in the United States: a population-based analysis of clinicopathologic factors. Cancer. doi:10.1002/cncr.26505
39. Nattinger AB, Kneusel RT, Hoffmann RG et al (2001) Relationship of distance from a radiotherapy facility and initial breast cancer treatment. J Natl Cancer Inst 93:1344–1346
40. Abbott AM, Habermann EB, Tuttle TM (2011) Trends in the use of implantable accelerated partial breast irradiation therapy for early stage breast cancer in the United States. Cancer 117:3305–3310
41. Hologic. MammoSite. Available at: http://www.mammosite.com. Accessed Jul 6 2010
42. Gao X, Fisher SG, Emami B (2003) Risk of second primary cancer in the contralateral breast in women treated for early-stage breast cancer: a population-based study. Int J Radiat Oncol Biol Phys 56:1038–1045
43. Nichols HB, de González AB, Lacey JV Jr et al (2011) Declining incidence of contralateral breast cancer in the United States from 1975 to 2006. J Clin Oncol 29:1564–1569
44. Lostumbo L, Carbine N, Wallace J et al (2004) Prophylactic mastectomy for the prevention of breast cancer. Cochrane Database Syst Rev (4):CD002748
45. Peele PB, Siminoff LA, Xu Y et al (2005) Decreased use of adjuvant breast cancer therapy in a randomized controlled trial of a decision aid with individualized risk information. Med Decis Making 25:301–307
46. Sanghani M, Truong PT, Raad RA et al (2010) Validation of a web-based predictive nomogram for ipsilateral breast tumor recurrence after breast conserving therapy. J Clin Oncol 28:718–722
47. Bickell NA, Shastri K, Fei K et al (2008) A tracking and feedback registry to reduce racial disparities in breast cancer care. J Natl Cancer Inst 100:1717–1723
48. Whelan TJ, Pignol JP, Levine MN et al (2010) Long-term results of hypofractionated radiation therapy for breast cancer. N Engl J Med 362:513–520