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Association for Academic Surgery

Omission of radiotherapy after breast conservation surgery in the postneoadjuvant setting

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ARTICLE INFO

Article history:
Received 22 May 2017
Received in revised form
28 June 2017
Accepted 1 August 2017

Keywords:
Segmental mastectomy
Breast neoplasms
Neoadjuvant therapy
Radiotherapy
Breast/surgery
Standard of care

ABSTRACT

Background: Breast conservation therapy (BCT) consists of breast conservation surgery (BCS) and radiotherapy (RT). Neoadjuvant chemotherapy (NACT) can downstage tumors, broadening BCS eligibility in patients requiring mastectomy. However, tumor downstaging does not obviate need for RT. This study evaluated factors that predict RT omission after NACT and BCS.

Methods: The National Cancer Database was queried for women with unilateral, clinical stage II-III breast cancer, treated with NACT and BCS between 2008 and 2012. Patients not receiving RT after NACT and BCS were identified. A subgroup analysis was performed eliminating patients for whom RT was recommended but not received.

Results: Among 10,220 patients meeting study eligibility, 974 (9.53%) did not receive RT after BCS. Predictors of RT omission included older age, insurance status, facility type, facility region, more recent year of diagnosis, receptor status unknown, human epidermal growth factor receptor 2 status positive or unknown, and positive margins. Factors increasing the likelihood of RT receipt included cN3 disease, receptor positivity, and primary downstaging. Race, Hispanicity, education, income, comorbidities, rural *versus* urban setting, histology, grade, and nodal stage change were not associated with RT omission. When excluding the 314 patients for whom RT was recommended but not received, age, Medicaid insurance, facility type, facility region, receptor status unknown, human epidermal growth factor receptor 2 status unknown, and positive margins were predictors of RT omission.

Conclusions: Race, comorbidities, and socioeconomic status were not predictors of RT omission. It remains unclear whether omission of RT in some cases is due to lack of physician knowledge. Further efforts are needed to ensure that physicians and patients recognize that RT is a vital and required part of BCT, even after NACT.

This article was presented, in part, at the 12th Annual Academic Surgical Congress, Las Vegas, NV, Tuesday, February 7, 2017.

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0022-4804/$ – see front matter
http://dx.doi.org/10.1016/j.jss.2017.08.008

Introduction

Breast cancer is one of the most common diseases in women today with an estimated incidence of 252,710 in the United States in 2017.[1] Over the past several decades, breast conservation therapy (BCT) has expanded as the standard of care for treatment for clinical stage I, IIA, IIB, or T3N1M0 invasive breast cancer[2] and is increasingly performed for tumors >5 cm.[3] The American College of Surgeons' National Accreditation Program for Breast Centers defines this as a standard of care, requiring it to be performed for 50% of all eligible patients with early stage breast cancer.[4]

BCT consists of two distinct modalities: breast conservation surgery (BCS) and radiotherapy (RT). Previous randomized clinical trials comparing total mastectomy, BCS, and BCT have demonstrated that BCS alone produces significantly higher recurrence rates than mastectomy or BCT. While the local rate of recurrence may differ for mastectomy and BCT, the overall survival is equivalent.[5] The Early Breast Cancer Trialists' Collaborative Group showed in more than 10,000 women from 17 randomized trials, with over a decade of follow-up, that RT is a critical component of BCT. Furthermore, the group noted that omission of RT increases local recurrence, noting a link between prevention of local recurrence and improved disease-specific survival.[6]

In patients deemed unresectable at diagnosis because of skin or chest wall involvement, neoadjuvant chemotherapy (NACT) has been shown to downstage the primary tumor, allowing for BCS by improving the chances of a resection with negative margins.[7] NACT can also increase the likelihood of successful BCS in patients for whom the primary tumor is initially felt to be too large relative to the breast size, an accepted indication for mastectomy.[8] In addition, NACT provides equivalent survival to adjuvant chemotherapy as shown in two prospective randomized trials.[9] However, NACT is not a substitute for RT or other adjuvant treatments.

Despite the efficacy of BCT, there may be a subgroup of patients for whom the benefit of RT is small and for whom the omission of RT does not compromise survival. (i.e., women aged >70 years with low-risk breast cancers).[10,11] These patients can be spared the side effects of RT. However, the delivery of NACT should not alter the indications for adjuvant radiation. As proof of this point, the National Comprehensive Cancer Network guidelines recommend that in patients treated with NACT, decisions regarding adjuvant RT and systemic therapy be based on the patient's stage at presentation.[2]

On reviewing the patterns of post neoadjuvant RT administration in the National Cancer Database (NCDB), we found that many BCT patients did not receive RT after NACT. This study was performed to determine which factors predicted for the omission of RT as we feel that it is important for surgeons and oncologists to be aware of this phenomenon and to identify which patients are at risk for substandard therapy. Establishment of such risk factors could improve the likelihood that RT is delivered appropriately in patients for whom there is a known benefit.

Methods

Study design

A retrospective analysis of the NCDB was performed after approval by the Intuitional Review Board at Fox Chase Cancer Center and after permission to use the NCDB dataset was obtained from the American College of Surgeons. The NCDB was reviewed for women having unilateral, invasive, noninflammatory, nonmetastatic, clinical stage II-III breast cancer, treated with NACT and subsequent BCS between 2008 and 2012.

In light of prior data of ours[12] noting significant impairment in survival after delays between diagnosis and surgery >90 d, as well as that of others noting significant survival impairment after delays of adjuvant therapy after surgery >90 d,[13] the cohort was limited to those starting NACT <90 d after diagnosis but 80-270 d preoperatively allowing for proper chemotherapy administration time. Similarly, only those having RT 0-20 wk postoperatively were included.[14]

Patients were limited to those having one surgical procedure because of the challenges in differentiating excisional biopsy from lumpectomy in the NCDB, to create a more homogeneous cohort and decrease potential confounding from

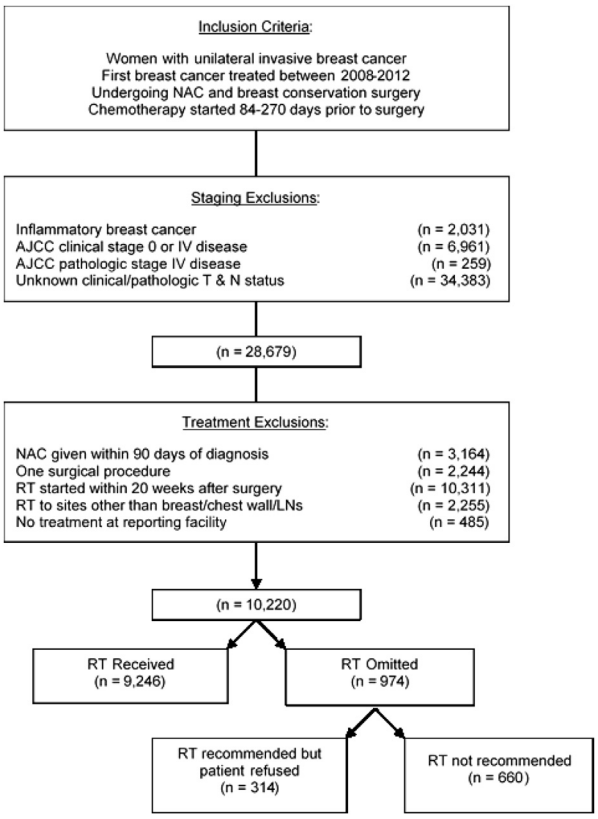

Figure – Exclusion and inclusion criteria. Numbers represent remaining patients after that set of exclusions. AJCC = American Joint Committee on Cancer; LNs = lymph nodes; N = nodal; T = tumor.