Ann Surg Oncol (2018) 25:1786–1787
https://doi.org/10.1245/s10434-018-6415-8

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

EDITORIAL – BREAST ONCOLOGY

Delays in Adjuvant Chemotherapy Among Breast Cancer Patients: An Unintended Consequence of Breast Surgery?

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Use of adjuvant chemotherapy plays a crucial role in improving the outcomes of breast cancer (BC) patients.[1,2] In recent years, delays in administration of adjuvant chemotherapy have been associated with detrimental outcomes. The impact on outcomes is of significant magnitude, thus timeliness in chemotherapy administration has been proposed as a quality metric. Several studies have consistently identified that a delay in time to adjuvant chemotherapy (TTC) after definitive breast surgery was associated with adverse outcomes; patients receiving adjuvant chemotherapy 90 days after definitive breast surgery have worse overall and breast cancer-specific survival.[3,4] Of particular relevance is that the detrimental impact of such delays seems to be greater among patients with more advanced stages and among those with highly proliferative tumors, particularly patients with triple-negative breast cancer (TNBC).[5]

A large observational population-based study using data from the California Cancer Registry demonstrated an effect of TTC delays on survival outcomes in a contemporary cohort of patients[6] and identified factors associated with delays in TTC. Not surprisingly, the main determinants were either sociodemographic in nature, or related to the type of medical care received, specifically socioeconomic status, nonprivate insurance, Hispanic ethnicity or non-Hispanic Black race, mastectomy, and breast reconstruction. The article by Riba et al. in this issue of *Annals of Surgical Oncology* describes the factors related to definitive breast cancer surgery that correlated with a delay in TTC in a large cohort of patients using the National Cancer Database. This study adds to the body of evidence demonstrating that delays in TTC are associated with poor outcomes. Furthermore, this study shows that the proportion of patients experiencing delays is small, since only 4.3% of the included patients received chemotherapy > 90 days after definitive surgery, and that such percentage has slowly decreased over recent years.

The study by Rivas et al. also highlights the association between surgical factors and chemotherapy delays. Type of surgery was significantly associated with delays in TTC; patients undergoing mastectomy or mastectomy with reconstruction were at higher risk. These results have important implications in the current era, as evidence suggests that higher proportions of breast-conserving surgery (BCS)-eligible patients are undergoing mastectomy.[7–9] In addition, an important increase in bilateral mastectomies with associated reconstruction has been reported in recent years.[7] Reconstruction is a crucial component of patient care that has direct implications for the quality of life and psychosocial well-being of our patients. While reconstructive procedures are needed and should be offered to our patients, it is likely that, given their complexity, they are associated with longer recovery time, higher rate of postoperative complications, and therefore delays in TTC. Identifying patients at higher risk of such complications and recognizing the potential detrimental effect on survival caused by a delay in providing effective systemic treatment might be useful when counseling patients with regard to the surgical procedure of election and its optimal timing.

Unplanned postoperative readmissions had the strongest association with delays in TTC. While the reasons for readmission were not know, they were likely

First Received: 7 February 2018;
Published Online: 29 March 2018

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associated with postoperative complications. While the magnitude of the association was very important, it is likely underestimated by the fact that only readmissions to the same hospital were recorded. Presence of positive margins was also associated with delays in TTC; this observation is likely associated with the need to undergo subsequent surgical procedures to clear margins. Recent efforts have focused on establishing recommendations to define an adequate microscopic margin. Among patients undergoing BCS, current guidelines define a negative margin as no invasive cancer on ink.[10] In light of the high rates of reexcision observed in patients with early-stage invasive BC and the lack of data demonstrating a clear benefit in reducing local recurrence with wide margins,[11] it is of extreme importance to individualize patient management, and avoid unnecessary reexcisions to achieve wider margins.

Facility type and center volume were also associated with a delay in TTC. The correlation between high-volume hospitals and improved surgical outcomes has been established in studies in which the vast majority of procedures consisted of high-risk surgeries,[12] and evidence suggests that a survival benefit exists for patients treated in high-volume hospitals or by high-volume or specialized surgeons.[13,14] Although morbidity or mortality is considered low in breast surgery, it seems that center volume indeed mattered, as reported by Rivas et al. It is possible that patients treated at high-volume centers are less likely to have delays in chemotherapy, not because of differences in surgeon expertise, but because those centers have more efficient referral pathways and more rapid access to medical oncologists and other members of the multidisciplinary team, highlighting the importance of coordination of care.

Comorbidities, race/ethnicity, and type of insurance were associated with delayed TTC. Those factors may clearly interplay with surgical complications and may impact the interpretation of the reported findings. Disparities in delivery of care and in stage at diagnosis according to race/ethnicity have been extensively described.[15–18] Identifying groups of patients at higher risk for disparity of care is of foremost importance, and strategies should be developed to facilitate processes and avoid treatment delays in vulnerable populations.

These findings emphasize the importance of appropriately selecting patients prior to a surgical procedure and the relevance of implementing strategies aimed at preventing complications and decreasing disparities of care. Delays in TTC can be an unintended consequence of surgical procedures, and the multidisciplinary team should be aware of this risk. When cure and survival are the goals of care, all efforts should be concentrated on avoiding delays in treatment in order to preserve the survival benefit associated with adjuvant chemotherapy.

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