Ann Surg Oncol (2022) 29:4019–4021
https://doi.org/10.1245/s10434-022-11788-7

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

EDITORIAL – BREAST ONCOLOGY

Immediate Breast Reconstruction in Inflammatory Breast Cancer: Are We There Yet?

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Inflammatory breast cancer (IBC) is a rare and aggressive cancer known for disproportionately poor outcomes compared with non-IBC.[1–3] The current standard of care is treatment with trimodality therapy consisting of neoadjuvant chemotherapy (NACT), followed by modified radical mastectomy (MRM) and post-mastectomy radiation therapy (PMRT) to the chest wall and regional nodal basins.[4,5] Up to 30% of patients present with metastases at diagnosis and breast cancer-specific survival (BCSS) is significantly worse when compared with locally advanced non-IBC (84% vs. 91%; hazard ratio [HR] 1.43, 95% confidence interval [CI] 1.09–1.85).[2] Due to these poor outcomes, immediate breast reconstruction (IBR) is often discouraged to avoid delaying curative therapy such as PMRT, as incomplete therapy is associated with worse survival.[6] Nonetheless, there has been interest in exploring the role of IBR in IBC, especially given modern advances in systemic therapy resulting in modest improvement in outcomes.[2,3,7] In this retrospective study using the National Cancer Database (NCDB), Hoffman and colleagues evaluated outcomes of IBC patients diagnosed between 2004 and 2016 treated with trimodality therapy.[8] Exclusion criteria included metastatic disease at presentation and incomplete or unknown therapy information. The authors examined trends in IBR use over time; overall survival (OS), defined as time from PMRT completion to death or last follow-up; and complications of 30-day readmission rates as well as mortality.

Of 27,019 cases of IBC identified in the NCDB, 6589 (24.4%) patients were included, of whom 635 (9.6%) underwent IBR. Median follow-up was similar between IBR and non-reconstructed patients (43 vs. 45 months) and receipt of IBR was associated with younger age, private insurance, higher income, and metropolitan residence. IBR use increased by 61% over the study period and was higher in academic settings compared with community centers. Autologous flap reconstruction was performed in 39.4% of IBR patients, while 26.9% of patients underwent implant-based reconstruction. With regard to treatment, total PMRT dose did not differ between groups and median time to PMRT was similar (8 weeks in the non-IBR group vs. 7 weeks in the IBR group). Pathological complete response or partial response rates did not differ between groups. Surgical outcomes were similar except for a longer length of stay in the IBR group (2.4 days vs. 1.4 days). In adjusted analysis using Cox regression, IBR was associated with improved OS but this association was absent when inverse probability weighting (IPW) statistical methodology was applied. A second survival analysis utilizing propensity score matching in 141 matched patients again demonstrated improved OS with IBR, suggesting residual selection bias despite statistical adjustment. The authors conclude IBR may be feasible in select patients without compromising oncologic outcomes.

First Received: 31 March 2022
Accepted: 6 April 2022;
Published Online: 26 April 2022

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In the US, IBR utilization in breast cancer patients has increased significantly over the last decade, and, similar to the study findings, IBR use is associated with younger age and private insurance status compared with public insurance.[9–11] Despite a lack of survival benefit in average-risk women, contralateral prophylactic mastectomy (CPM) has also mirrored this trend.[12–15] The psychosocial benefit of breast reconstruction in the immediate and delayed setting are well known and include greater patient satisfaction and improved quality of life.[16,17] In IBC, IBR is discouraged due to poor recurrence and survival outcomes as well as increased risk of complications that may significantly delay adjuvant therapy, including PMRT and further systemic therapy in patients with residual disease.[18–20] In a registry study, Nakhlis et al. evaluated recurrence patterns after IBR in 240 IBC patients who received trimodality therapy. In this cohort, 40 patients underwent reconstruction, and of 13 patients who underwent immediate reconstruction, 12 patients developed a locoregional and/or distant recurrence.[21] Of note, median time from surgery to PMRT was 56.5 days, similar to the current study, and 50% of patients recurred within the first 12 months after MRM. There is a higher likelihood of locoregional recurrence in IBC, with 5-year locoregional recurrence rates as high as 17% occurring over a shorter time period.[22] Omission of PMRT is also associated with inferior oncologic outcomes,[20,23] thus timely and complete locoregional therapy is essential. Furthermore, the reconstructed breast may pose significant challenges to optimal PMRT delivery, specifically to the ipsilateral internal mammary chain, which may have significant implications in high-risk disease such as IBC.[24] There is also concern that PMRT may worsen cosmetic outcomes and negatively impact patient satisfaction.[25,26]

We applaud the authors for investigating this important topic as their findings confirm a growing trend of IBR in IBC despite the paucity of data regarding oncologic safety. Nonetheless, the results of this study should be interpreted with caution for several reasons, including its retrospective nature with inherent selection bias, as demonstrated by superior survival in patients who underwent IBR despite statistical methodology to adjust for confounding. In addition, in this database study, it is unclear if all patients were truly diagnosed with IBC by meeting the clinical criteria needed for such a diagnosis. The diagnosis of IBC is clinical and is often challenging, therefore multidisciplinary assessment by oncologists familiar with presentation and treatment is recommended. Of note, only 24.4% of the entire cohort evaluated over the time period were included in the study, and an even smaller proportion of patients underwent IBR. Thus, this population is unlikely to be representative, and we support the authors' statement that firm conclusions regarding feasibility of IBR in IBC cannot be made. In IBC, surgical resection to negative margins, including the skin envelope, is recommended to avoid compromising local control and survival. The extent of skin resection typically required often results in a more complex reconstruction, and the autologous reconstruction technique is the usual approach in IBC. In this cohort, 37% of patients who underwent immediate reconstruction utilized the implant-based technique, which may suggest that reconstruction is achieved at the expense of adequate surgical therapy. It is highly concerning if the residual skin envelope is preserved in this cohort to facilitate implant-based reconstruction, as this is not the endorsed standard treatment for IBC.

Based on the study findings, it remains unclear which IBC patients are ideal candidates for IBR. Interestingly, tumor characteristics did not inform receipt of IBR, highlighting the challenges of identifying patients with improved prognosis in this aggressive cancer. In fact, socioeconomic variables such as insurance status impacted receipt of IBR, which speaks to known disparities that similarly impact IBR receipt in non-IBC.[27,28] While surgical outcomes, including OS, were similar between both groups, important oncologic outcomes such as locoregional recurrence and breast cancer-specific survival data are not routinely reported in the NCDB, and were unfortunately absent from this study. This information is essential to inform the feasibility of this operation, as salvage surgery is challenging in patients who recur.

CONCLUSION

It is encouraging that with modern therapy, locoregional outcomes for IBC are improving. In an analysis of 114 patients who received trimodality therapy, the reported 4-year probability of locoregional recurrence was 5.6% (95% CI 2.76–14.7%), comparable with non-IBC.[29] While IBR in IBC has the potential to improve patient satisfaction and quality of life, there is no strong evidence supporting the oncologic safety of this approach, and delayed post-mastectomy reconstruction with autologous flap is the current recommendation in IBC patients who have completed all recommended therapy and remain disease-free. Consensus guidelines also discourage routine CPM at the time of initial operation for IBC (to avoid any increased risk of complications and delay in adjuvant treatments), and, if desired, should be delayed until definitive reconstruction.[30] While increasing IBR utilization is noted in locally advanced non-IBC, even in the setting of radiation therapy,[31] we recommend caution extrapolating this approach to IBC. Further studies of feasibility are needed in a cohort with a confirmed diagnosis of IBC who receive trimodality therapy under an experienced multidisciplinary team.

ACKNOWLEDGMENT Institutional database supported by the Morgan Welch Inflammatory Breast Cancer Research Program, and State of Texas Rare and Aggressive Breast Cancer Research Program Grant.

DISCLOSURES Wendy Woodward discloses the following relationships: Exact Sciences (honoraria), DOD (contracted research agreement), Susan G. Komen (contracted research agreement), NIH R-01, Epic Science (honoraria).

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