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LETTER TO THE EDITOR

Limitations of locoregional and distant recurrence analysis after neoadjuvant chemotherapy

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Dear Editor,

We read with great interest the recent study by Brabender et al. on factors associated with locoregional recurrence after neoadjuvant chemotherapy (NAC) in a predominantly Hispanic cohort at a safety-net medical center [1]. While the study provides valuable insights into recurrence patterns, we would like to highlight several limitations that were not sufficiently acknowledged by the authors.

Firstly, the retrospective nature of the study introduces inherent selection and information biases. Despite multivariable analysis, the study does not fully account for confounding variables, such as socioeconomic disparities and access to post-treatment surveillance, which may influence recurrence rates and survival outcomes. Additionally, variations in chemotherapy regimens over the study period (2015–2023), including evolving HER2-targeted, BRCA-targeted, and immunotherapy with checkpoint inhibitors strategies, were not stratified in the analysis [2].

Secondly, the study does not adequately address the potential limitations of using radiographic and pathologic complete response (pCR) as surrogate markers for recurrence risk. Although pCR is associated with improved outcomes, it does not universally predict locoregional control, particularly in hormone receptor-positive disease, where late recurrences are common. The short median follow-up of 38.1 months may not capture late recurrences, particularly in estrogen receptor-positive/HER2-negative patients [3].

Thirdly, the study suggests that locoregional recurrences were uncommon after NAC, yet the reported recurrence rates (4% local, 2% regional, 18% distant). It should be noted that radical locoregional treatment itself may inadvertently create a microenvironment favorable for the reactivation of circulating and disseminated tumor cells, facilitating the development of metastatic niches in distant organs. Therefore, distant recurrence remains a crucial component of the success of multimodality therapy and should be more comprehensively analyzed in studies assessing treatment effectiveness [4].

Lastly, while the study emphasizes its focus on a largely Hispanic population, it does not provide subgroup analyses or comparisons with other racial/ethnic groups to determine whether these findings are generalizable beyond the safety-net setting. Given known disparities in breast cancer outcomes among racial and ethnic minorities, such comparisons would enhance the study's applicability.

We appreciate the authors' contributions to this important topic but encourage a more nuanced interpretation of the findings, considering the limitations outlined above.

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Data availability Datasets generated during this study are publicly available in this open access publication without any restrictions.

Declarations

Conflict of interest K.M. has received honoraria for offering academic and clinical advice to Merit Medical. The other authors declare no conflict of interest.

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