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Prognostic impact of neoadjuvant chemotherapy-induced changes in immunohistochemical markers on survival outcomes in breast cancer: a systematic review and meta-analysis

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Objective: To evaluate the association between neoadjuvant chemotherapy (NAC)-induced alterations in immunohistochemical (IHC) marker expression and overall survival and disease-free survival in breast cancer patients. **Methods:** A systematic review and meta-analysis was conducted with searches performed on PubMed, Embase, and Cochrane Library databases to identify studies evaluating changes in IHC marker expression after NAC and their correlation with survival outcomes. Eligible studies comprised randomized controlled trials, cohort studies, and case-control studies involving breast cancer patients undergoing NAC. Data regarding changes in IHC markers and survival outcomes were extracted and analyzed utilizing a random-effects model to compute pooled odds ratios with 95% confidence intervals. The I^2 statistic was applied to assess heterogeneity, while publication bias was evaluated through funnel plot analysis and Egger's test. The study protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO), under CRD420250655833. **Results:** The meta-analysis included ten studies. The pooled analysis indicated that a transition from positive to negative hormone receptor status (estrogen and progesterone receptors) following NAC was linked to a notable reduction in overall survival and disease-free survival. In a similar manner, the conversion from positive to negative human epidermal growth factor receptor-type 2 (HER2) status was associated with decreased overall survival and disease-free survival. **Conclusion:** NAC significantly alters IHC marker expression, which correlates strongly with survival outcomes in breast cancer patients. The conversion of hormone receptors and HER2, reduction of Ki-67, and increase in tumor-infiltrating lymphocytes following NAC are significant prognostic indicators. The findings highlight the necessity for regular reevaluation of IHC status following NAC to guide personalized adjuvant therapy approaches and enhance patient outcomes. Additional prospective research is necessary to confirm these associations and investigate the underlying molecular mechanisms.

Keywords: breast cancer; neoadjuvant chemotherapy; immunohistochemistry; survival; lymphocytes, tumor-infiltrating.