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Prognostic impact of real-world immunohistochemical changes in breast cancer treated with neoadjuvant chemotherapy

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Objective: To evaluate the rate and types of immunohistochemical (IHC) changes after neoadjuvant chemotherapy (NAC) and their influence on disease-free survival and overall survival in breast cancer patients, with a focus on conversions such as hormone receptor-positive and human epidermal growth factor receptor-type 2-negative (HR+/HER-) 2+ to HR-/HER- 2- and their implications for treatment adjustments. **Methods:** This retrospective cohort study included 369 female patients aged 18 years or older with non-metastatic breast cancer treated with NAC between January 2011 and January 2023. Patients who did not achieve complete pathological response were evaluated for changes in IHC profiles, including HR status, HER-2 expression, and Ki-67 index. Prognostic outcomes were assessed using Kaplan-Meier survival analysis and multivariate Cox regression models. This study was approved by the research ethics committee of the Hospital do Servidor Público Estadual (CAAE 80127724.1.0000.5463) through Plataforma Brasil. Due to its retrospective nature, the requirement for informed consent was waived, ensuring the confidentiality and anonymity of patient data through record anonymization. **Results:** IHC changes were observed in 41.7% of patients. Among those initially classified as HR-/HER- 2-, 50.9% gained HR expression, and 14.1% acquired HER-2 expression. In HR+/HER-2+ cases, 70.8% experienced a loss of HER-2 expression. Patients with HER-2+ tumors exhibited more frequent IHC changes compared to HER-2- cases ($p < 0.0001$). After a median follow-up of 47.7 months, local recurrences occurred in 10.3% of patients, distant metastases in 29.5%, and death occurred in 25.5% of patients. Patients with IHC changes demonstrated significantly worse disease-free survival and overall survival ($p = 0.002$), with the poorest outcomes associated with conversion to HR-/HER-2- ($p < 0.001$). **Conclusion:** Post-NAC IHC changes are common and associated with poor prognosis, especially in patients losing HR and HER-2 expression. Monitoring IHC shifts is critical for guiding personalized treatment and improving prognostic evaluation.

Keywords: breast cancer; neoadjuvant chemotherapy; immunohistochemistry; receptors, estrogen; receptors, progesterone; receptor, ErbB-2.