**Receptor Conversion after Neoadjuvant Chemotherapy in Breast Cancer Patients**

**Abstract**

BACKGROUND: The hormone receptor (estrogen and progesterone) (HR) status and human epidermal growth hormone receptor 2 (HER2) status of patients with breast cancer may change following neoadjuvant chemotherapy (NCT). A core needle biopsy (CNB) is commonly performed to confirm the diagnosis and determine the presence of immunohistochemical markers, such as HER2 and HR. This study aimed to evaluate the prognostic impact of receptor conversion in breast cancer patients treated with NCT.

HYPOTHESIS: NCT may convert HR and HER2 status, which may result in poor prognosis.

METHODS: Data regarding the expression of HR and HER2 were collected from CNBs and surgical resection specimens obtained from 423 patients (cohort 1) who received NCT after CNB and had residual disease as well as 536 patients (cohort 2) who did not received NCT. The Chi-square test evaluated the HR and HER2 alterations cohort 1 and cohort 2. Fisher's exact test was performed when necessary. Univariate and multivariate patient survival analyses were performed to evaluate the prognostic value of the conversion of their HR and HER2 statuses. Multivariate Cox proportional hazard analyses were performed by adjusting for possible prognostic variables ($P<0.05$ in univariate analysis). The results were considered statistically significant if the P was $< 0.05$.

RESULTS: Of the 423 patients who had residual disease in the breast after NCT (cohort 1), 78 patients (18.4%) had discordant HR status and 40 patients (9.4%) had discordant HER2 status after NCT. Among them, 55 (13.0%) changed from HR (+) to HR (-), 23 (5.4%) changed from HR (-) to HR (+), 27 (6.4%) changed from HER2 (+) to HER2 (-), and 13 (3.1%) changed from HER2 (-) to HER2 (+). A total of 54 (12.8%) changed to the triple-negative (TN) tumor phenotype. In cohort 2, only 17 patients (3.2%) changed HR status and 4 patients (0.7%) changed HER2 status after NCT ($P<0.001$ for the Chi-square test). These results demonstrated that NCT was the major factor of altered HR and HER2 status. The multivariate model included all variables that were statistically significant in the univariate analysis except for interactive variables. The loss of HR positivity was an independent prognostic factor for worse disease-free survival (DFS) [$P<0.001$ for HR (+) to (-) and $P=0.013$ for HR (-) to (+)] and worse overall survival (OS) [$P<0.001$ for HR (+) to (-) and $P=0.008$ for HR (-) to (+)] in

multivariate survival analysis. The loss of HER2 positivity alone had no prognostic significance. In addition, the switch to the TN phenotype after NCT was another independent prognostic factor for worse survival for both DFS ($P$<0.001) and OS ($P$=0.003). Taken together, our current research showed that patients might experience changes in HR status, HER2 status and tumor phenotype after NCT. The loss of HR positivity and the switch to the TN phenotype after NCT were associated with a worse patient outcome.