https://doi.org/10.29289/259453942023V33S1028

Clinical and pathological differences between HER2 low and other cancer subtypes in breast cancer patients

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Objective: HER2 is a tyrosine kinase receptor belonging to the human epidermal receptor family and is considered an important proto-oncogene in the biology of breast carcinoma. HER2 overexpression is determined by a +3 score on the immunohistochemistry (IHC) assay. In addition, tumors with IHC results of +1 or +2 with ISH negative were defined as HER2-low. Recent studies have shown the clinicopathological characteristics of HER2-low tumors, pointing out potential differences regarding hormone receptor status. The objective was to assess clinicopathological differences between cancer subtypes, as well as the survival of these patients. **Methodology**: A total of 8,872 patients with breast cancer diagnosed between 2010 and 2019 included in the Pérola Byington Hospital database were eligible. Patients were excluded if they had bilateral disease, had participated in clinical studies, or had incomplete data. The primary endpoint was overall survival stratified by cancer subtype, and the secondary endpoints were clinicopathological differences between cancer subtypes and death probability. Both the t-test and the chi-square test were used to analyze the association of each variable between the groups. Multivariate analysis was used to calculate odds ratios and 95% confidence intervals for the death outcome. Cox regression was used for survival analysis, with the log-rank method, and the results were presented in a survival graph using the Kaplan-Meier method. The R software version 4.1.1 was used to perform all analyses, with a $p<0.05$ being considered statistically significant. **Results:** A total of 8,872 patients were included: 3,865 (43.65%) had luminal cancer subtype, 1,840 (20.74%) had HER2 low, 1,610 (18.156%) had triple-negative, and 1,557 (17.55%) had HER2 overexpression. In the multivariate regression (adjusted for the other evaluated characteristics), Her2 low had a median of 101 months of survival compared with 96 months for triple-negative. When comparing HER2 low with hormonal receptor positive versus negative, we saw better survival in hormonal receptor positive (90 vs. 101 $p<0.001$). These data did not differ among stages. As an additional finding, Ki67 is prognostic for survival and so is pCR. **Conclusion:** This study in breast cancer patients demonstrates significant differences between cancer subtypes, with a higher probability of progression to death for patients with triple-negative cancer. More studies are needed to clarify the impact of these differences between cancer subtypes on response to therapy.

Keywords: breast cancer.