

## Comparing Trastuzumab-Related Cardiotoxicity between Elderly and Younger Patients with Breast Cancer: A Prospective Cohort Study

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**Abstract :** Introduction: Trastuzumab is a HER-2 targeted humanized monoclonal antibody that significantly improves the therapeutic outcomes of metastatic and non-metastatic breast cancer. However, it is associated with increased risk of cardiotoxicity that ranges from mild decline in the cardiac ejection fraction to permanent cardiomyopathy. Concerns have been raised in treating eligible older patients. This study compares trastuzumab outcomes between two age cohorts in the Kuwait Cancer Control Centre (KCCC). Methods: In a prospective comparative observational study, 93 HER-2 positive breast cancer patients undergoing different chemotherapy protocols + trastuzumab were included and divided into two cohorts based on their age (<60 and ≥60 years old). The baseline left ventricular ejection fraction (LVEF) was assessed and monitored every three months during trastuzumab treatment. Event of cardiotoxicity was defined as ≥10% decline in the LVEF from the baseline. The lower accepted normal limit of the LVEF was 50%. Results: The median baseline LVEF was 65% in both age cohorts (IQR 8% and 9% for older and younger patients respectively). Whereas, the median LVEF post-trastuzumab treatment was 51% and 55% in older and younger patients respectively (IQR 8%; p-value = 0.22), despite the fact that older patients had significantly lower exposure to anthracyclines compared to younger patients (60% and 84.1% respectively; p-value <0.001). 86.7% and 55.6% of older and younger patients, respectively, developed ≥10% decline in their LVEF from the baseline. Among those, only 29% of older and 27% of younger patients reached a LVEF value below 50% (p-value = 0.88). Statistically, age was the only factor that significantly correlated with trastuzumab induced cardiotoxicity (OR 4; p-value <0.012), but it did not increase the requirement for permanent discontinuation of treatment. A baseline LVEF value below 60% contributed to developing a post-treatment value below normal ranges (≤50%). Conclusion: Breast cancer patients aged 60 years and above in Kuwait were at 4-fold higher risk of developing ≥10% decline in their LVEF from the baseline than younger patients during trastuzumab treatment. Surprisingly, previous exposure to anthracyclines and multiple comorbidities were not associated with significant increased risk of cardiotoxicity.

**Keywords :** breast cancer, elderly, Trastuzumab, cardiotoxicity

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