Serial Echocardiographic Assessment of Diastolic Function in Women with Early-Stage Breast Cancer and Association with Cardiotoxicity

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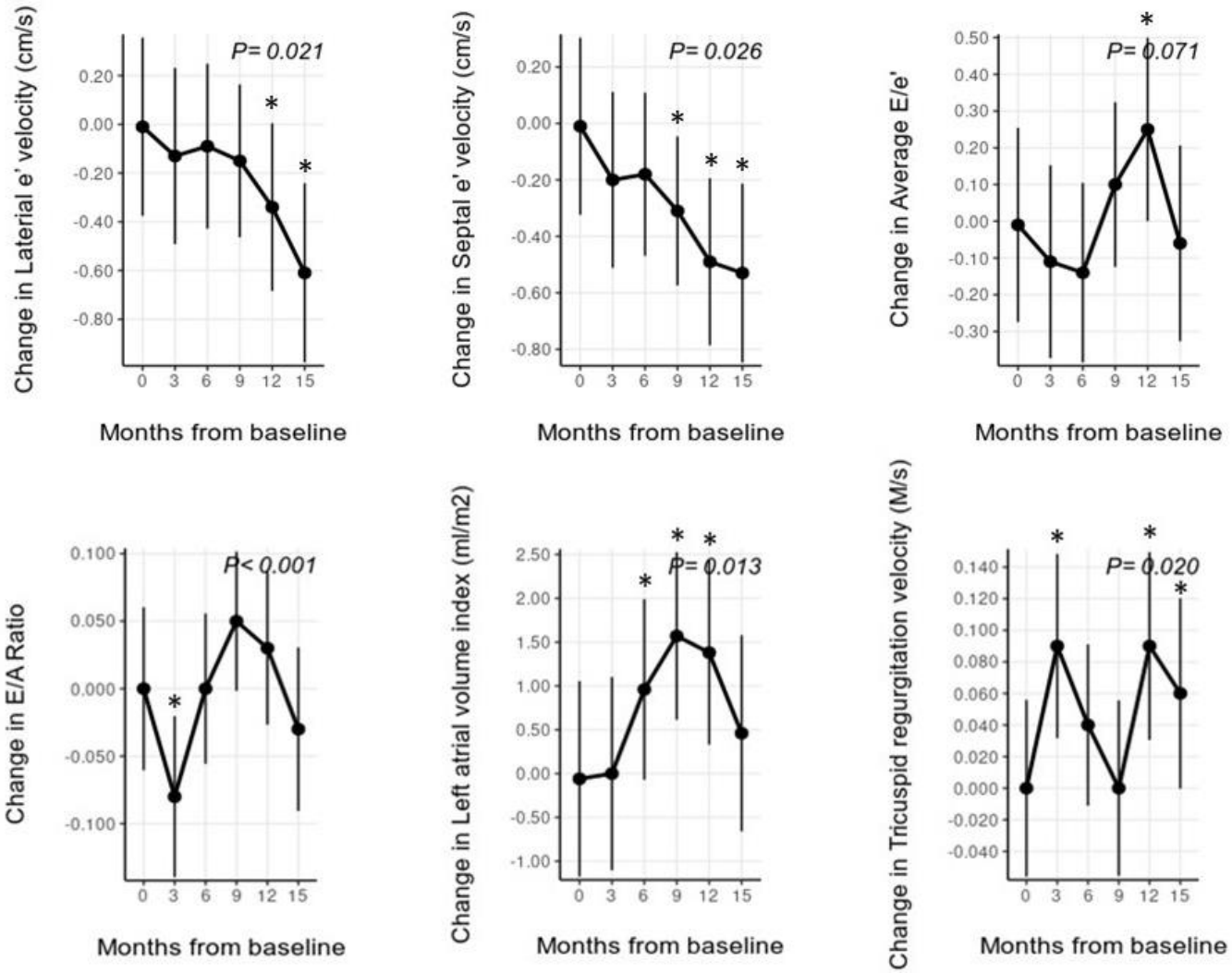
Background: Breast cancer patients receiving anthracyclines and trastuzumab are at risk of cancer therapy-related cardiac dysfunction (CTRCD). We aimed to assess the effect of these therapies on left ventricular diastolic function.

Methods: In this prospective cohort of 136 women with early-stage breast cancer receiving sequential anthracyclines and trastuzumab, echocardiography was performed at 6 timepoints: pre-anthracycline (baseline); post-anthracycline but pre-trastuzumab; 3, 6, and 9 months post-trastuzumab initiation; and within 6 weeks post-trastuzumab completion. Patients underwent cardiac magnetic resonance (CMR) imaging on the same day except at 9 months post-trastuzumab initiation. Diastolic parameters were measured on echocardiographic images as per American Society of Echocardiography (ASE) guidelines. Diastolic function was graded using 2016 ASE guidelines. We examined the association between diastolic dysfunction and subsequent risk of CTRCD, as defined by threshold changes in CMR-derived left ventricular ejection fraction (LVEF-CTRCD) and echocardiography-derived global longitudinal strain (GLS-CTRCD).

Results: At baseline, mean age was 51.1±9.2 years, LVEF by CMR was 63.2±4.0% and GLS by echocardiography was -20.4±1.7%. LVEF-CTRCD developed in 37 (27%) of 136 patients while GLS-CTRCD developed in 53 (42%) of 126 patients with analyzable GLS. Significant changes occurred in diastolic parameters starting at first follow-up with significant reduction in e' velocities persisting at end of therapy. Of 129 patients with baseline normal or indeterminate diastolic function, 24 (18.6%) developed incident diastolic dysfunction, 16 of whom developed grade 1 dysfunction. Patients with baseline abnormal diastolic function did not worsen. Diastolic dysfunction at any timepoint or worsening diastolic function from baseline was significantly associated with subsequent LVEF-CTRCD (OR 19.1; 95% CI 4.1 to 89.7; $p \leq 0.001$; OR 14.3; 95% CI 2.3 to 89.4; $p=0.005$, respectively). No significant association was observed between diastolic dysfunction and subsequent GLS-CTRCD.

Conclusions: Significant changes in diastolic parameters develop early during breast cancer therapy, resulting in incident diastolic dysfunction in nearly one-fifth of patients. Diastolic dysfunction is significantly associated with subsequent LVEF-CTRCD.

Figure 1: Mean predicted changes from baseline in echocardiographic diastolic parameters using linear mixed effects models with random patient-specific intercepts. Asterisk (*) indicate significant differences from baseline at each timepoint. P values represent overall significance for the entire group across all timepoints.



Abbreviations: A, atrial filling peak velocity; E, early filling peak velocity; e', early diastolic velocity by tissue Doppler imaging.