

## Mid-Cancer Left Ventricular Function Measures Predict Long-Term Post-Cancer Left Ventricular Ejection Fraction



This study was a secondary analysis of previously published results from a National Institutes of Health-funded cohort (R01CA167821) of patients scheduled to receive potentially cardiotoxic chemotherapy (1). We sought to determine the utility of mid-cancer treatment assessments of left ventricular (LV) volumes for forecasting 2-year post-cancer treatment measurements of LV ejection fraction (EF) in those <55 or  $\geq$ 55 years in age. This prospective cohort study was approved by the Institutional Review Board of the Wake Forest School of Medicine, and all participants provided written informed consent.

Seventy-one subjects completed pre-therapy, 3 months into therapy, and 24-month post-treatment assessments of previously published, reproducible measures of LV end-diastolic volume and LV end-systolic volume (LVESV) (2) and LVEF using cardiac magnetic resonance (1). Baseline to 24 months' decline in LVEF  $\geq$ 5% were identified along with assessments of heart failure (3).

Participants were 68% women, 82% White, and averaged  $54 \pm 15$  years in age. The weight and body mass index averaged  $84.2 \pm 19$  kg and  $30 \pm 6$  kg/m<sup>2</sup>, respectively. The percentage of individuals with hypertension, history of smoking, diabetes, and previously receiving radiation were 51%, 12%, 17%, and 35%. Of the 71 participants, 29 had a history of breast cancer, 37 of lymphoma, and 5 of sarcoma. Twenty-two participants took 1 cardioprotective drug, 9 participants took 2 cardioprotective drugs, and 3 participants took 3 cardioprotective drugs; these included angiotensin-converting enzyme inhibitors, beta-blockers, and statins.

Patients were categorized as receiving or not receiving anthracycline-based chemotherapy and whether they were younger or older than the median age of 55 years. Forty-two percent of patients experienced a >5% decline (average drop of 11.4%) in LVEF over 2 years. Patients age  $\geq$ 55 years receiving an anthracycline were more likely to experience a 24-month post-treatment decline in LVEF relative to those <55 years of age or not receiving an anthracycline (Fisher exact test;  $p = 0.022$ ). For those <55 years of age or those not receiving an anthracycline, after accounting for sex or the presence of hypertension, diabetes, smoking, coronary artery disease, or hyperlipidemia, 3-month adverse LV volume changes (that included previously published increases in LVESV >3 ml or 10 ml decline in LV

end-diastolic volume with no decline in LVESV [1]) forecasted a 24-month post-cancer treatment decline in LVEF >5% (Fisher exact test;  $p = 0.011$ ). There was no relationship between measurements of LV function 3 months into treatment and symptoms associated with heart failure ( $p = 0.22$ ).

In this study, those patients <55 years of age or not receiving an anthracycline received additional prognostic information from comparing a pre-treatment to 3 months into treatment assessment of LV function in terms of predicting a 24-month post-treatment more long-term decline in LVEF. As such, these data support several societies' recommendations regarding mid-treatment assessments of subclinical cardiac injury in those at risk for long-term decline in LV function (4,5). This includes younger individuals even though symptoms of heart failure associated with mid-cancer treatment may not be present.

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