Elevated myocardial extracellular volume (ECV) occurs independently of LVEF declines in pediatric cancer survivors

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Introduction

Left ventricular dysfunction or myocardial fibrosis can occur after receipt of anthracycline chemotherapy. Myocardial fibrosis can be assessed noninvasively with cardiovascular magnetic resonance (CMR) T1 mapping to measure extracellular volume (ECV). We sought to obtain CMR assessments of systolic function and ECV in a multicenter study of anthracycline-treated adolescent/young adult (AYA) cancer survivors and age matched comparators.

Methods

The Resonance Imaging trial for heart Biomarkers was a cross sectional study of AYA cancer survivors. Survivors and age matched healthy volunteers were recruited at 2 cancer centers from 2012-2015. A subset of the recruited cohort agreed to receipt of IV contrast (Prohance^{TM}) at the time of CMR to measure ECV. Cancer survivors (n=16) who were asymptomatic for cardiovascular history and comparators (n=13) had T1-mapping pre- and 12 minutes post-contrast administration for ECV calculation. Study groups were compared with Student's t- and chi-square tests, and Pearson's correlation coefficients were used to determine the association of ECV with LVEF.

Results

Survivors of childhood cancer had received anthracycline chemotherapy (mean 248, range 75-450 mg/m^2) 8.4 years prior (3.2-17.7 years) for hematologic malignancies or solid tumors (Table). ECV was elevated in cancer survivors vs comparators (p=0.0019, Figure). Survivors trended to have a lower LVEF than comparators (p=0.09). ECV did not correlate with LVEF (r=0.07, p=0.71).

Conclusions

Anthracycline chemotherapy may cause systolic dysfunction and/or myocardial extracellular remodeling. We observed elevated measures of myocardial fibrosis that did not correlate with the mild LVEF depression in AYA cancer survivors. These findings indicate the potential of an alternative pathophysiologic pathway in cardiotoxicity and thus ECV may be an important noninvasive imaging biomarker of cardiotoxicity.

Table:

	Survivors (n=16)	Comparators (n=13)	p-value
Current Age, yrs	22±3	20±4	0.30
Age at Diagnosis, yrs	12±6	-	-
Time since Treatment, yrs	8.4±3.8	-	-
Female, n	10	4	0.14
Race (white), n	13	11	1.0
LVEF, %	56±6	60±5	0.09
Native T1, ms	930±37	931±18	0.94
ECV, %	25.2±2.5	22.0±2.5	0.0019

Figure: