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Subtle cardiomyopathic changes in childhood cancers survivors on 10 year-follow-up

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Introduction:

Survivors of childhood cancer are at risk for anthracycline-induced cardiomyopathy. The aim of this study was to assess long-term cardiac natural history.

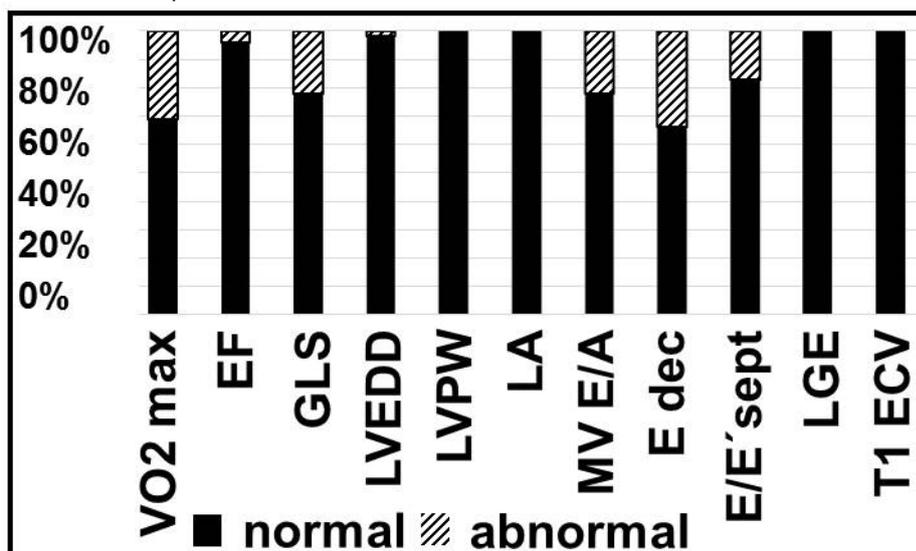
Methods:

Patients underwent cardiopulmonary exercise test (CPET), transthoracic echocardiography (TTE) with tissue doppler imaging (TDI) and speckle tracking, and cardiovascular magnetic resonance (CMR) with contrast. Findings were correlated to anthracycline and radiation dose, and compared to data from 27 gender- and age-matched patients with childhood onset hypertrophic cardiomyopathy (HCM).

Results:

Cardiac evaluation was performed in 55 patients (27 males) at 11.3 ± 4.4 years after cancer treatment. Oncologic diagnosis at a mean age of 10.3 ± 4.9 years was Hodgkin lymphoma in 13, sarcoma in 17, acute lymphoblastic or relapse leukemia in 18, and others in 7 patients. Cumulative anthracycline dose was more than 300 mg/m^2 in 24 patients. 25 patients also received radiation therapy. Decreased peak maximum respiratory oxygen uptake in % predicted ($\text{VO}_2 \text{ max}$) on CPET, increased global longitudinal strain (GLS) on TTE speckle tracking, and diastolic dysfunction on TDI were the most prominent findings (Figure: percentage of patients with normal (black bars) and abnormal (striped bars) values). Decreased CPET exercise capacity and increased septal E/E' ratio, respectively, correlated significantly with increased anthracycline dosing ($p < 0.001$, Pearson correlation). There was no correlation between radiation dose and abnormal cardiac findings.

In contrast to HCM patients, childhood cancer survivors did not show left ventricular hypertrophy (LVPW z-score 0.5 ± 0.6 vs. 2.8 ± 2 , $p < 0.001$), hyperdynamic systolic function on TTE (Ejection fraction (EF) $62 \pm 8 \%$ vs. $71 \pm 12 \%$, $p = 0.001$), or fibrotic myocardial changes on CMR (Late gadolinium (LGE) positive 0/13 vs. 12/20, $p = 0.001$; extracellular volume fraction (ECV) $22 \pm 2 \%$ vs. $28 \pm 4 \%$, $p < 0.001$) at time of follow-up.



Conclusions:

Long-term childhood cancer survivors exposed to cardiotoxic therapy show subtle cardiomyopathic changes best detected by CPET and TTE including TDI and speckle tracking. This underlines the importance of follow-up in specialty outpatient clinics for this patient population.