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Impact of treatment intensity on cardiometabolic outcomes among high cardiovascular risk childhood cancer survivors: a report from CCSS-CHIIP

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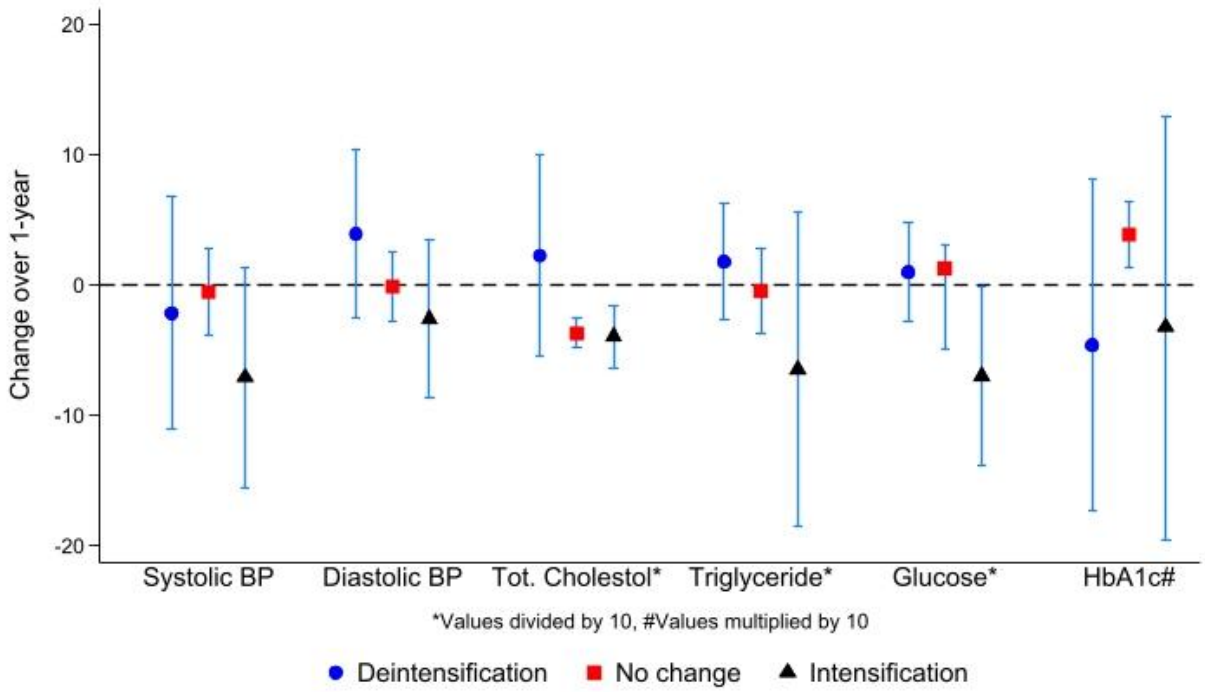
BACKGROUND: Childhood cancer survivors have an increased risk of cardiovascular disease (CVD) that is amplified by the presence of CVD risk factors like hypertension, dyslipidemia, and diabetes. However, among survivors with a history of cardiotoxic treatment exposures, the impact of CVD risk factor treatment intensity on these risk factors is unclear.

METHODS: Participants from the Childhood Cancer Survivor Study (CCSS) at an increased risk of future CVD due to prior cancer therapies, and with undertreated hypertension, dyslipidemia, or diabetes (per standard clinical definitions) were enrolled into a 1y randomized trial (CHIIP, NCT3104543) that tested the impact of a survivorship care plan-based counseling intervention to reduce CVD risk factor undertreatment. Resting blood pressures (BP) and a randomly timed blood draw (lipid profile, glucose, and hemoglobin A1c [HbA1c]) were obtained by a trained home examiner at baseline and 1y, with results shared with participants and their primary care providers. Medical records over the study period, including names of medications (and doses) used to treat any of the 3 CVD risk factors, were then abstracted, with changes in treatment intensity classified (blinded to risk factor outcomes) as no change, deintensified, or intensified. Changes in BP, total cholesterol, triglyceride, glucose, and HbA1c over 1y were compared by treatment intensity status using paired t-tests. Generalized estimating equations (GEE) evaluated the change in each risk factor measurement by treatment intensity status (no change as referent), adjusting for body mass index.

RESULTS: Of 347 randomized participants, 293 (84%) had evaluable medical records and were included in this analysis (mean age 40y, mean 31y since cancer diagnosis, 51% male, 76% anthracycline-exposed, 69% chest radiation). At baseline, 31%, 20%, and 11% of participants were on medications for hypertension, dyslipidemia, and diabetes, respectively; 40% were on at least one medication with 14% on ≥3 medications. Data were evaluable for 274 participants at 1y, with 35%, 25%, and 12% now on medications for the 3 risk factors, and overall, 46% receiving treatment. For each risk factor, rates of treatment intensification ranged from 16-19% of affected participants, and 4-12% of participants experienced treatment deintensification. In univariate analyses, intensification was generally associated with improvements in risk factors, with a borderline reduction in systolic BP (-7 mmHg [95%CI -15, 1] p=0.10), and significantly lower total cholesterol (-39 mg/dL [-63, -15]) and glucose (-69 mg/dL [-138, -1]; **Figure**). Participants who had no changes in intensity and those who had deintensification generally had similar values at follow-up versus baseline across all 3 risk factors. In GEE analyses, compared with no change, treatment intensification continued to be associated with significant glucose reduction (-90 mg/dL [-145, -34]). Although intensification was not associated with lower total cholesterol levels versus no change, deintensification was associated with significantly higher cholesterol levels (+45 mg/dL [2, 88]).

CONCLUSION: Treatment intensity influences CVD risk factor outcomes among long-term survivors exposed to anthracyclines and chest radiotherapy. More aggressive management of undertreated CVD risk factors may reduce CVD risk in this population.



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