

Childhood Cancer Survivorship, Late Cardiotoxicity, and CV Prevention



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The initial presentation in this session was a comprehensive outline of *Late onset cardiotoxicity: incidence, risk and individual risk prediction* by Dr Gregory Armstrong from St. Jude's Children's Hospital in Memphis, TN. He presented many primary studies from the Childhood Cancer Survival Study that indicated the extent and prognosis related to CV outcomes in long-term survivors of childhood cancer. He reported on the high quality data that has been systematically collected for the past 2 decades. The degree that cancer therapy, whether radiation or chemotherapy or the combination, can affect the CV outcomes of patients is profound [1, 2]. It is difficult to discern what exact profiles of patients are at highest risk but certainly the dose of radiation and chemotherapy is an important modifier of risk. Additionally, underlying CV risk factors that developed over time can have a major impact of overall outcomes [2]. Understanding what screening tests are most effective in detecting CV issues at a modifiable state is of paramount importance [3, 4]. These data inform our current strategies for optimal cancer survivorship cancer [5].

The second presentation in this session was *Genetic variants and the risk for cardiotoxicity* presented by Dr Smita Bhatia of the University of Alabama-Birmingham in Birmingham, AL. She is a recognized international leader in defining genetic determinants that may indicate those are risk for cardiotoxicity, especially associated with anthracycline treatment. Her presentation outlined many years of careful descriptive research attempting to detail those genetic variations that could be responsible for the susceptibility for cardiotoxicity [6]. This groundbreaking research has the potential to lead to the implementation of personalized cancer care, balancing the need for excellent cure rate with minimal long term cardiotoxicity [7].

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Next, Dr Saro Armenian, at City of Hope in Duarte, CA, presented a description and review of the data regarding *Screening and intervention for cardiomyopathy*. Early pharmacologic intervention, in the asymptomatic setting, has been shown to improve long-term cardiac outcomes in adults following myocardial infarction, or in children with progressive neuromuscular disorders at high risk for cardiac dysfunction such as Duchenne muscular dystrophy [8–11]. As a result, a number of clinical care Guidelines [12, 13] have recommend routine echocardiographic screening for cardiac dysfunction in asymptomatic childhood cancer survivors after completion of anthracycline-based therapy. However, there are gaps in knowledge pertaining to: how long should echocardiographic screening continue after completion of therapy, the reproducibility and validity of abnormal echocardiographic findings, and the utility of early intervention in childhood cancer survivors with asymptomatic cardiac dysfunction.

Two recently published cost-effectiveness analyses [14, 15] have utilized Markov modeling to demonstrate that screening for asymptomatic cardiac dysfunction can be cost-effective. However, the utility of screening is largely dependent on the relative effect size of the intervention. Co-administration of anthracyclines with dexrazoxane can ameliorate the acute cardiotoxicity asso-

ciated with anthracyclines [16, 17], but the long term efficacy of this approach has yet to be determined. Importantly, the growing numbers of childhood cancer survivors who have not been treated with dexrazoxane make it imperative that new approaches be investigated for long-term heart failure risk reduction. For this population, early initiation of an angiotensin-converting enzyme inhibitor or β -blocker may prevent the progression of chronic cardiac remodeling. This strategy is currently being investigated in an ongoing NCI-funded multi-institutional randomized double-blinded placebo controlled trial (NCT02717507) of low dose carvedilol in childhood cancer survivors at highest risk for developing heart failure. In the meantime, healthcare providers are asked to educate and counsel all survivors of childhood cancer about the importance of maintaining a heart-healthy lifestyle, and to aggressively screen for and manage modifiable cardiovascular risk factors such as hypertension, diabetes, and dyslipidemia [12].

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Authors' contributions:

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