

## Top Ten Things To Know Long-term Cardiovascular Toxicity and Cancer Therapy in Children, Adolescents, and Young Adults

1. Cancer is diagnosed in over 12 000 children and adolescents in the United States each year. Because of progress in cancer treatments, survival rates for childhood cancers have improved. In the United States, this success translates into over 325,000 survivors of childhood cancer, of whom 24% are now >30 years from diagnosis. These numbers are expected to increase as incidence of pediatric cancer increases.
2. Cardiopulmonary diseases are the third-leading cause of death in survivors of childhood cancer, after only the recurrence of primary cancer and the development of second cancers. Death rates attributable to cardiac causes are 8 to 10 times as high among childhood cancer survivors as they are in age-matched control subjects.
3. In a report from the Children's Cancer Survivor Study, relative risk for strokes among survivors was almost 10 times as high as that of the sibling control group.
4. The evolution of pediatric cancer treatments has already changed the prevalence and spectrum of adverse treatment effects. Life-altering toxicities affecting endocrine, reproductive, musculoskeletal, and neurological function still occur after specific treatments (eg, infertility after high-dose alkylating agent chemotherapy or gonadal radiation). Of increasing concern are subclinical changes observed after cancer treatment that contribute to premature onset of common diseases associated with aging, such as obesity, diabetes mellitus, CVD, hypertension, and cancer.
5. Certain chemotherapeutic and biological agents, as well as radiation therapy (RT), independently and in combination, are well known causes of cardiotoxicity. Survivors of childhood cancers exposed to cardiac radiation intentionally or incidentally as a component of chest radiotherapy are at increased risk for ischemic CVDs, such as MI, as well as for other forms of cardiac dysfunction, including valvular disease, conduction abnormalities, pericarditis, and a restrictive-like cardiomyopathy, all of which can result in heart failure or death.
6. In the cardiovascular system, chemotherapeutic agents may cause adverse effects by compromising myocardial function or peripherally by changing vascular hemodynamics. These adverse effects may be predictable or unpredictable, set or cumulative, and potentiated or ameliorated by the use of concomitant antineoplastic agents.
7. Examples of pediatric chemotherapeutic agents associated with cardiotoxicity include:
  - Taxanes/paclitaxel: Bradycardia
  - Anthracyclines (doxorubicin): Arrhythmias/QT prolongation
  - Antimetabolites/5-fluorouracil: Myocardial ischemia
  - Anthracyclines (doxorubicin), Tyrosine kinase inhibitors (imatinib/sunitinib), Alkylating agents (cyclophosphamide/ifosfamide), Cisplatin: Left ventricular dysfunction/ CHF
8. *Standardization of follow-up care* can enhance opportunities to preserve cardiovascular health and facilitate assessing long term outcomes. As clinicians continue to learn about the cardiovascular effects of cancer treatment, *the importance of primary prevention* becomes abundantly clear.
9. The objective of effective monitoring is to identify signs of cardiac disease early enough to potentially prevent, reverse, or slow the deterioration of the structure and function of the heart.
10. There is a need for research to evaluate the impact of aging and health behaviors on health outcomes of adults treated for cancer during childhood. *Long-term prospective studies* are needed to better understand risks of cardiac events in this population and develop strategies to better treat patients.

ipshultz SE, et al; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young, Council on Basic Cardiovascular Sciences, Council on Cardiovascular and Stroke Nursing, Council on Cardiovascular Radiology and Intervention, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Council on Nutrition, Physical Activity and Metabolism. Long-term cardiovascular toxicity in children, adolescents, and young adults who receive cancer therapy: pathophysiology, course, monitoring, management, prevention, and research directions: a scientific statement from the American Heart Association. *Circulation*. 2013; published online before print September 23, 2013, 10.1161/CIR.0b013e3182a88099.  
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