Cardiotoxic Effects of Chemotherapy on Pediatric and Adult Survivors of Cancer

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Cardiotoxic Effects of Cancer Therapies in Adult and Pediatric Survivors of Cancer
What’s New in Diagnosis and Treatment

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What is cardio-oncology?

• The prevention and management of heart disease in cancer patients
  
  – Primary focus is cardiovascular toxicity of cancer therapies
    • Assumes a standard definition of cardiotoxicity

  – Also important to remember that there may be other interactions between cancer and heart disease
    • Common risk factors for CV disease and many cancers
    • Different attitudes in the health care system towards cancer patients
    • Common disease pathways at cell and molecular level
Finally, the ACC predicted the continued growth of cardio-oncology. "This cardiology subspecialty is focused on the cardiovascular manifestations of cancer and complications of its treatment" and is offered at select US hospitals. In 2014, says the ACC, "look for it to expand rapidly to more hospitals across the country." A session devoted to this topic at the 2013 European Society of Cardiology meeting prompted one theheart.org blogger to say she had the "impulse to rush home to change my clinical practice."

heartwire, meanwhile, has its eye on several other cardiology tidbits. One, the long-awaited results from
Why is cardio-oncology so hot right now?

1. Cancer patients are now much more likely to survive their disease
Cancer survival

• Based on 2006–2008 estimates, the 5-year survival after a cancer diagnosis in Canada is 63%  
  – Between 1992–1994 and 2006–2008, survival rates increased from 56% to 63% for all cancers combined

• Many cancers can now be considered curable or manageable diseases, making management of comorbidities (e.g. CV disease) essential
Cardiovascular disease competes with breast cancer as the leading cause of death in older women diagnosed with breast cancer.
Prognostic importance of comorbidity in cancer patients

![Graph showing survival rates for different comorbidity levels: None, Mild, Moderate, Severe.](image)

- **HR 2.6**
- **Significant for all cancer types**

Stats Canada 2008
Why is cardio-oncology so hot right now?

1. Cancer patients are much more likely to survive their disease
2. The toxicity of conventional cancer treatments is greater than previously appreciated
Risk Factors for Doxorubicin-Induced Congestive Heart Failure

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Risk of CHF after cumulative dose 300 mg/m2: 1.5%
Congestive Heart Failure in Patients Treated with Doxorubicin

A Retrospective Analysis of Three Trials

Risk of CHF after cumulative dose 300 mg/m²: 1.7%
Risk of cardiac events after cumulative dose 300 mg/m²: 16.2%

Clinical heart failure

LV dysfunction
Why is cardio-oncology so hot right now?

1. Cancer patients are much more likely to survive their disease
2. The toxicity of conventional cancer treatments is greater than previously appreciated
3. New “targeted therapies” are being developed at a rapid pace, many of which have recognized or unrecognized cardiovascular toxicities
FDA-Approved Molecular Targeted Therapies

- Alemtuzumab
- Erlotinib
- Denileukin diftitox
- Dasatinib
- Crizotinib
- Cetuximab
- Carfilzomib
- Brentuximab
- Bevacizumab
- Ofatumumab
- Ipilimumab
- Imatinib
- Tositumomab
- Trastuzumab
- Vismodegib
- Bortezomib
- Bevacizumab
- Pertuzumab
- Imatinib
- Trastuzumab-DM1
- Pazopanib
- Panitumumab
- Ziv-aflibercept
- Regorafenib
- Temsirolimus
Change in LVEF on protocol sunitinib therapy

- 8% developed NYHA class III-IV HF
- 6% had LVEF reductions ≥20%
- 19% had LVEF reductions ≥15%
- 28% had LVEF reductions ≥10%
- 11% either developed CHF or had LVEF reductions ≥20%
Cardio-Oncology Clinics
What are the Key Components?

• (1) CV risk assessment and prevention in cancer patients
• (2) CV screening and monitoring of cancer patients
• (3) Active management of pre-existing CV disease
  • Enable the most effective cancer treatment while minimizing cardiovascular toxicities
• (4) Active management of treatment induced cardiotoxicity
  • Radiation therapy, traditional and targeted therapies
Practical Application of Cardio-Oncology

Example: Left Ventricular Dysfunction

1. Management of cardio-toxicity in patients receiving anthracyclines
2. Herceptin starting and stopping rules
3. CV evaluation before starting potentially toxic therapies
4. CV monitoring during/after cancer treatment
5. Treatment of LV dysfunction induced by cancer treatment
Algorithm for the management of cardiotoxicity in patients receiving anthracyclines
Conclusions

• The rapid growth of “targeted therapies” has seen a parallel growth in cardiovascular complications of cancer therapy
• Many of these agents are far more effective than their alternatives, so our job as healthcare providers is to give our patients the best chances to complete therapy
• The most common cardiovascular toxicities of novel agents so far have been LV dysfunction, heart failure and hypertension, but we must be prepared for new toxicities with new agents