Late Effects of Treatment on the Heart

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Disclosures

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None
Outline

• A growing population of survivors
• What are the late effects of treatment?
• What signs and symptoms should I be aware of?
• Seeking care for late effects
A Growing Population of Survivors

*The public health perspective*
Growing Population of Older Survivors

Signifies the year at which the first baby boomers (those born 1946-1964) turned 65 years old
Lifespan is Increasing in Survivorship

![Graph showing the increase in lifespan with years](image-url)
Survivors have Poorer Health Status

Burden of Illness in Cancer Survivors: Findings From a Population-Based National Sample

K. Robin Yabroff, William F. Lawrence, Steven Clauser, William W. Davis, Martin L. Brown

• Comparison of cancer survivors and age-matched individuals from the National Health Interview Survey in 2000

• Multiple measures of burden asked
Survivors have Poorer Health Status

CANCER SURVIVORS (N=1817)
- Excellent
- Very Good
- Good
- Fair
- Poor

31% Fair or Poor

NON-CANCER CONTROLS (N=5465)
- Excellent
- Very Good
- Good
- Fair
- Poor

18% Fair or Poor

• 1\textsuperscript{st} generation of AYA survivors now entering 4\textsuperscript{th} and 5\textsuperscript{th} decades of life

• Childhood Cancer Survivor Study
  • N= 14,359 childhood cancer survivors
  • N= 4,301 siblings

• Classified health conditions with NCI CTCAE
Earlier Chronic Health Conditions in Childhood Survivors

![Graph showing cumulative incidence of all conditions over age (years). The graph compares survivors and siblings.](image)
More Frequent Chronic Health Conditions in Childhood Survivors

B

Survivors

C

Cumulative Incidence (%)  

Age (years)

Cumulative Incidence (%)  

Age (years)

1st condition  
2nd condition  
3rd condition  
4th condition

1st condition  
2nd condition  
3rd condition  
4th condition

GT Armstrong et al. JCO, 2014.
What are the late effects of treatment?

Understanding cardiovascular side effects
Cardiac Effects of Cancer Therapies

Screening and intervention
- Pre-treatment phase
  - Cardiotoxicity risk assessment:
  - pre-treatment cardiac imaging
  - biomarkers
  - patient characteristics
  - genetic screening
- Cardiovascular risk factor modification
- Prophylactic treatment if needed

Early/acute phase
- Early detection of cardiotoxicity:
  - imaging
  - biomarkers
- Additional follow-up in high-risk groups

Post-acute phase
- Continued monitoring in high-risk groups

Late phase
- Continued monitoring for groups with high risk of late onset
- Early treatment initiation after detection of adverse cardiac effects
The Snowball Effect

1. Age-related changes in cardiovascular physiology
2. Age-related factors that influence pharmacokinetics
3. Pre-existing cardiac disease
4. Cardiac risk factors
5. Metabolic and lifestyle changes
6. Polypharmacy related to cancer treatment
7. Direct cardiotoxic effects of cancer treatment

Snowball set into motion by the diagnosis of cancer
Baseline risk factors
Cancer-related risk factors
Cancer treatment
Effects of cancer treatment
Cardiovascular morbidity and mortality
Side Effects of Cancer Therapies

Myocarditis: Immune Checkpoint Inhibitors?
Anthracycline Chemotherapies

- Daunorubicin (Cerubidine)
- Doxorubicin (Adriamycin)
- Doxorubicin liposome injection (Doxil)
- Epirubicin (Ellence)
- Idarubicin (Idamycin PFS)
- Valrubicin (Valstar)

Regimens
- AC
- TAC
- ABVD
- CHOP
- R-CHOP
- EPOCH
- R-EPOCH
- FAC

Known Risk Factors:
- Age (children, >65 years)
- Pre-existing heart disease
- Cumulative dose
- Combination chemotherapy
- Mediastinal radiation

Incidence of Heart Failure by Cumulative Dose

<table>
<thead>
<tr>
<th>Cumulative dose</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>400 mg/m²</td>
<td>5%</td>
</tr>
<tr>
<td>500 mg/m²</td>
<td>16%</td>
</tr>
<tr>
<td>550 mg/m²</td>
<td>26%</td>
</tr>
</tbody>
</table>

Targeted Therapies

- Trastuzumab (Herceptin)
- Bevacizumab (Avastin)
- Iapatinib (Tykerb)
- Sunitinib (Sutent)
- Sorafenib (Nexavar)
Androgen Deprivation Therapy for Prostate Cancer

Cardiovascular Effects of Androgen Deprivation Therapy for the Treatment of Prostate Cancer

| Table 2. Pathophysiology of Adverse Cardiovascular Effects of GnRH Agonists |
|-----------------------------|-----------------------------|-----------------------------|
| Indirect Effects            | Direct Effects              | Low Testosterone            |
| ▲Fat mass                   | ▼Cardiac contractility      | ▼Vasodilation               |
| ▼Lean body mass            | ▼T-cell activation and      | ▼HDL                       |
|                            | destabilization of fibrous cap/ plaque rupture |                  |
| ▲Insulin resistance/hyperinsulinemia |                  | ▲Visceral obesity          |
| ▲LDL, ▼HDL, and ▲triglycerides |                  | ▲Prothrombotic state       |
| ▲Diabetes mellitus          |                            |                            |
| ▲Metabolic syndrome         |                            |                            |
| ▲Arterial wall thickness    |                            |                            |

GnRH indicates gonadotropin-releasing hormone; HDL, high-density lipoprotein; and LDL, low-density lipoprotein.
What are the signs and symptoms I should be aware of?

*Raising your level of awareness*
New Changes to Be Aware of:

• Fatigue
• Dyspnea or difficulty breathing
• Weight gain
• Edema or swelling
• “Coughing spells”
Chronic Symptoms in Adult Survivors

• Fatigue – persistent in 25%, related to intensity of prior treatments
• Cognitive difficulties – 15-20%, depending on the type of treatments
• Decreased physical functioning
• Insomnia
Seeking care for late effects

A growing field of cardio-oncologists
Cardio-Oncology

Prevention and Lifestyle Interventions

Epidemiology and Registry Research (Cancer Survivor and CV Disease Cohorts)

Basic, Translational, and Clinical Research (Mechanisms, Biomarkers, CV Imaging Markers)

Guidelines and Clinical Practice Standards

CV Health and CV Risk Factors

Host and Cancer/Treatment Interaction

Cancer Treatment Toxicities

Oncology Clinical Trials with Comprehensive CV Safety Data

Education and Training of Cardiology and Oncology Health Teams

Addressing Increased CV Risk

• Health promotion
  • Avoiding tobacco, alcohol, weight gain
  • Enhanced physical activity to maintain function
  • Monitor bone health

• Management of post-treatment symptoms so that they do not progress or inhibit function
  • Discuss your symptoms with your physician as they may warrant imaging or stress testing
### ABCDE Algorithm – Breast Cancer

<table>
<thead>
<tr>
<th>ABCDE</th>
<th>ABCDEs to Prevent Heart Disease in Breast Cancer Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Awareness of risks of heart disease</td>
</tr>
<tr>
<td></td>
<td>Aspirin</td>
</tr>
<tr>
<td>B</td>
<td>Blood Pressure</td>
</tr>
<tr>
<td>C</td>
<td>Cholesterol</td>
</tr>
<tr>
<td></td>
<td>Cigarette/Tobacco cessation</td>
</tr>
<tr>
<td>D</td>
<td>Diet and weight management</td>
</tr>
<tr>
<td></td>
<td>Dose of chemotherapy or radiation</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus prevention/treatment</td>
</tr>
<tr>
<td>E</td>
<td>Exercise</td>
</tr>
<tr>
<td></td>
<td>Echocardiogram</td>
</tr>
</tbody>
</table>

## ABCDE Algorithm – Prostate Cancer

### Table 3. ABCDE Algorithm for Prostate Cancer Survivors

<table>
<thead>
<tr>
<th>Letter</th>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Awareness</td>
<td>Increased awareness of patients of cardiovascular signs and symptoms</td>
</tr>
<tr>
<td></td>
<td>Aspirin</td>
<td>Aspirin 81 mg daily for primary or secondary prevention of cardiovascular events</td>
</tr>
<tr>
<td>B</td>
<td>Blood pressure</td>
<td>Goal blood pressure &lt;140/90 mm Hg</td>
</tr>
<tr>
<td>C</td>
<td>Cholesterol</td>
<td>High-intensity statin therapy for preexisting CVD or hyperlipidemia</td>
</tr>
<tr>
<td></td>
<td>Cigarettes</td>
<td>Smoking cessation counseling, therapy</td>
</tr>
<tr>
<td>D</td>
<td>Diabetes mellitus</td>
<td>Frequent blood glucose monitoring</td>
</tr>
<tr>
<td></td>
<td>Diet</td>
<td>Diet rich in fruits, vegetables, and whole grain and low in saturated fat with 600 IU vitamin D daily and adequate calcium (1200 mg/d)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Avoidance of excessive alcohol</td>
</tr>
<tr>
<td>E</td>
<td>Exercise</td>
<td>150 min/wk of moderate-intensity physical activity or 75 min/wk of vigorous exercise</td>
</tr>
</tbody>
</table>

CVD indicates cardiovascular disease.
Common Cardiovascular Imaging Tests

- Echocardiography
- Cardiac MRI
Cardiovascular Stress Tests
New Frontiers in Cardio-Oncology

• Improving baseline risk stratification
• Studies of imaging and biomarkers to monitor cardiovascular changes during and after treatment
• Current studies with common cardiovascular drugs to reduce cardiac side effects of cancer therapies
• Monitoring cardiovascular complications of new therapies
• Development of cardio-oncology education, physician training, clinics, and outreach
Thank you!