The Road to Improve Cardiovascular Health after Cancer

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June 2\textsuperscript{nd} 2018
Objective

- What are the cardiac complications in cancer survivors?
- Who is at risk for cardiac toxicity?
- When should my primary doctor refer me to Cardiology?
What are the Priorities in the Cardiovascular Care of Oncology Patients?

Prior to Cancer Therapy
- Identify high cardiovascular risk patients
- Mitigate cardiotoxicity risk

During Cancer Therapy
- Monitoring to identify cardiotoxicity
- Avoid dose interruptions
- Prevent CV events

After Cancer Therapy
- Decrease risk of late Cardiovascular events
- Improve long-term health

Armenian et al. J Clin Oncol 35:893-911
2012: 13.7 million adult cancer survivors alive

Overall survival:
Has clearly improved in the last decade

# Cardiovascular complication from cancer therapy

<table>
<thead>
<tr>
<th>Vascular conditions</th>
<th>Cardiac structural problems</th>
<th>Cardiac dysfunction and heart failure</th>
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<td>• Deep venous thrombosis /</td>
<td>• Problem in the cardiac rhythm</td>
<td>• Radiation</td>
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<td>pulmonary embolus</td>
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</table>
Where Cancer and Cardiovascular Disease are met?

Shared Common Risk Factors

Genetic predispositions
Cigarette smoking
Obesity
Hyperlipidemia
Sedentary lifestyle
Diabetes
Aging

Cardio-oncology (intersection between cancer and cardiovascular disease)

Development of cancer and cardiovascular disease

Cancer Treatment
- Radiation
- Traditional chemotherapies
- Targeted cancer therapies
- Other new cancer therapies

Cardiovascular Involvement from Tumor
- Cardiac amyloidosis from plasma-cell dyscrasia
- Cardiac metastasis
- Carcinoid heart disease from carcinoid tumors

Cardiac Tumors
- Myxoma
- Lipoma
- Papillary fibroelastoma
- Rhabdomyoma
- Sarcoma

Cancer-cell death

Vascular Toxic Effects
- Hypertension
- Venous and arterial thromboembolic events
- Peripheral-artery disease
- Pulmonary hypertension
- Vasospasm
- Proteinuria
- Accelerated atherosclerosis
- Metabolic derangements

Cardiac Toxic Effects
- Decline in left ventricular ejection fraction
- Congestive heart failure
- Arrhythmia
- Myocarditis
- Pericardial disease
- Pericardial effusion

Cardiovascular disease
Clustering of CVD and Cancer Rates

Heart Disease Death Rates, 2014-2016
Adults, Ages 35+, by County

Rates are spatially smoothed to enhance the stability of rates in counties with small populations.

Data Source:
National Vital Statistics System
National Center for Health Statistics
www.cdc.gov/nchs/maps

Rates of Cancer Deaths in the United States
All Types of Cancer, All Ages, All Races/Ethnicities, Both Sexes

Rate per 100,000 people
127.9 - 155.1
155.5 - 164.1
164.6 - 174.8
177.4 - 199.3
In fact, risk factors for cardiovascular disease are more prevalent in cancer survivors than in the general population.
Cardiovascular Complications

- Cardiac Dysfunction
- Atherosclerosis
- Arrhythmia
- Renal-vascular
CHEMOTHERAPY INDUCED CARDIOTOXICITY

- Normal Heart
- Heart Failure

Heart muscle pumps blood out of the left ventricle.

Weakened heart muscle cannot pump enough blood.
Defining cardiotoxicity

- Decrease of the left ventricular ejection fraction below the baseline after chemotherapy
- Normal LVEF ~50-70%

The risk of symptomatic HF is 1-2% at 10 years and 10-15% at 25 years and beyond

amount of blood pumped out
amount of blood in chamber

amount of blood pumped out.
The fraction or percentage helps describe how well the heart is pumping blood to the body.
Heart failure is a chronic, progressive condition in which the heart muscle is unable to pump enough blood through to meet the body's needs for blood and oxygen.

Basically, the heart can't keep up with its workload. 
  – this can be asymptomatic!
Symptoms of Congestive Heart Failure

- Shortness of breath
- Severe fatigue preventing exercise or normal play
- Very swollen feet or ankles (so swollen that if a finger is pressed firmly on the area for few seconds it leaves an indentation)
- Cough and wheezing that doesn’t go away
- Lack of appetite, nausea
- Increase heart rate
Drugs that can induced cardiotoxicity

- Trastuzumab
- Doxorubicin
- Daunorubicin (Cerubidine)
- Epirubicin (Ellence)
- Cyclophosphamide (Genoxal, Mitoxan)
- Osemertinib (Tagrisso)
Anthracycline cardiotoxicity

Doxorubicin dose | Incidence of LV dysfunction
---|---
400 mg/m² | 3-5%
550 mg/m² | 7-26%
700 mg/m² | 18-48%
Risk factors

- High doses anthracycline (≥ 250 mg/m² doxorubicin, ≥ 600 mg/m² epirubicin)
- High doses radiation therapy (> 30 Gy)
- Low doses anthracycline and radiation therapy
- Low doses anthracycline or trastuzumab + 2 CV risk factors

Age (U-Shape)
Female gender

Genetics factors

Low ejection fraction < 50%
Prior heart attack
At least moderate Valvular disease
Renal disease

Smoking
HTN
DM
Dyslipidemia
Obesity
Sedentary lifestyle

Which patients with cancer are at increased risk for developing cardiovascular disease?
AHA-proposed algorithm: Post-treatment

Following Therapy

Surveillance

Cardiac Risk Factors:
- History of MI/CAD
- Known LVD
- History of CHF
- Diabetes
- HTN
- Smoking
- HLD
- Family Hx CAD
- Female gender
- Age <15 or >75

No consensus exists on an optimal monitoring strategy

Hamo CE et al. Circ Heart Fail. 2016; 9:e002843
## Recommended Frequency of Echocardiogram or MUGA Scan

<table>
<thead>
<tr>
<th>Age at Treatment*</th>
<th>Radiation with Potential Impact to the Heart§</th>
<th>Anthracycline Dose†</th>
<th>Recommended Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt;200 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥200 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td>1-4 years old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;100 mg/m²</td>
<td>Every 5 years</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>≥100 to &lt;300 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
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</tr>
<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
<td>Any age with decrease in serial function</td>
<td></td>
<td></td>
<td>Every year</td>
</tr>
</tbody>
</table>

*Age at time of first cardiotoxic therapy (anthracycline or radiation [see fields below], whichever was given first)

§See Section 71

†Based on doxorubicin isotoxic equivalent dose [see conversion factors in Section 28 “Info Link (Dose Conversion)”]
Echocardiography is the modality of choice
Medium-high risk patients need surveillance: known your treatment and your risk factors!

If you have decrease of the function of your heart or symptoms of heart failure your doctor should referral you to see a cardiologist
Radiation Therapy and Cardiovascular Disease
<table>
<thead>
<tr>
<th>Structure</th>
<th>Abnormality</th>
<th>Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardium</td>
<td>Abnormality</td>
<td>Heart Failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fatigue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abdominal distention</td>
</tr>
<tr>
<td>Heart Muscle</td>
<td></td>
<td>Heart Failure</td>
</tr>
<tr>
<td>Cardiac Valves damage</td>
<td></td>
<td>Murmur/ Heart</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failure/Chest</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pain/Lightheadedness</td>
</tr>
<tr>
<td>Blockage of the arteries</td>
<td></td>
<td>Heart Attack/ Stroke</td>
</tr>
<tr>
<td>Electrical complications</td>
<td></td>
<td>Heart Block</td>
</tr>
</tbody>
</table>
Radiation therapy

Damage of the arteries and cardiac valves

Fibrosis

Coronary artery disease
Heart failure
Pericardial constriction
Valvular disease
Stroke

Risk factors:
Higher dose
Larger volume exposed
Younger age
Adjuvant chemo
Type of radiation source
CV risk factors

Chen-Scarabelli C et al. JNC 2016 May 25
Symptoms of Heart Attacks (coronary artery disease)

- Chest discomfort
- Discomfort in upper body
- Cold sweat
- Nausea
- Lightheadedness
Cardiac Valvular Disease and Radiation

Valves of the Heart

- Aortic valve
- Pulmonary valve
- Mitral valve
- Tricuspid valve
After Radiation

Electrocardiogram, echocardiogram, lipids and cardiac risk factors

Treat and known your Risk Factors (hypertension, lipids, diabetes, obesity, smoking, exercise)

Yearly follow up: Electrocardiogram and echocardiogram if clinically indicated

At 5 year: Electrocardiogram and echocardiogram

10 year f/u: Electrocardiogram, echocardiogram, stress test
What are the Risk Factors?

What You Can Change?

- Physical Activity
- Life Stress
- High Blood Pressure
- Obesity
- Diabetes
- High Cholesterol & Triglycerides
- Smoking
- Unhealthy Diet (HIGH in saturated fat & calories; LOW in fresh fruit, veggies, whole grains & fish)

What You Can’t Change?

- Age
- Gender
- Family History
Hypertension: Facts

- Its prevalence before chemotherapy is similar to that in the general population (29%)
- After the initiation of certain chemotherapeutic agents HTN increase significantly ~ 30%–80%

Drugs that target blood vessel formation (VEGF)

Bevacizumab (Avastin, Mvasi)
Sorafenib (Nexavar)
Sunitinib (Sutent)
## Always Know Your Numbers!

<table>
<thead>
<tr>
<th>Measure</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>&lt;200 mg/dl</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>&lt;150 mg/dl</td>
</tr>
<tr>
<td>Fasting Glucose</td>
<td>&lt;100 mg/dl</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>&lt;120/80 mmHg</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>&lt;25</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>&lt;35 inches</td>
</tr>
<tr>
<td>Exercise</td>
<td>Minimum 30 minutes most of the days</td>
</tr>
</tbody>
</table>
How often do discussions about CVD risk factors occur in cancer survivors?

One in three survivors with one or more risk factors for CVD did not report a health promotion discussion with their health care providers.
<table>
<thead>
<tr>
<th>Screening (condition)</th>
<th>US Preventive Services Task Force</th>
<th>COG</th>
<th>AAP / AHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>Annually for adults</td>
<td>Annually if treatment risk factors present</td>
<td>Check at every visit if &gt;3 yo</td>
</tr>
<tr>
<td>Fasting lipids</td>
<td>Males 20-34 yo / females 20-44 yo with CHD risk</td>
<td>2y after completing therapy and q2y</td>
<td>All cancer survivors</td>
</tr>
<tr>
<td>EKG / Echo</td>
<td>N/A</td>
<td>EKG 2y after therapy / Echo q1-5y depending exposures</td>
<td>NA</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>Only asymptomatic adults with BP&gt;135/80 mmHg</td>
<td>Q2y in cancer survivors exposed to specific treatments</td>
<td>Baseline for all cancer survivors</td>
</tr>
</tbody>
</table>
Full range of disease

Diagnostic Testing

Baseline ECG
Baseline LVEF assessment

Cancer Diagnosis

“Primordial Prevention”

Treatment/Prevention

Treat comorbidities
Lifestyle modification

Conclusions

- It is clear that both the disease (cancer) and the treatment itself carry risk.
- Known your cancer treatment
- Early detection and treatment of cardiotoxicity, even when asymptomatic, helps cardiac function to recovery and decrease cardiac events
- Management of risk factors is important not only during treatment and post treatment, but also in the prevention of these two diseases
Resources

- American Society of Clinical Oncology
- National Comprehensive Cancer Network
- American Cancer Society
- Children’s Oncology Group “Survivorship Guidelines”
- AHA website
Resources available at UW: Cardio-oncology

- Richard K. Cheng, MD (HF/transplant cardiologist): rkcheng@uw.edu
- Daniel Fishbein, MD (HF/transplant director): dfish@uw.edu
- Jim Kirkpatrick, MD (Echo director/imaging): kirkpatj@uw.edu
- Carolina Masri, MD (HF/transplant cardiologist): cmasri@uw.edu

- Patient care coordinators:
  Laura Yale: lauranne@uw.edu
  Kristelle Calma: kcalma@uw.edu
## Categories of BP in Adults*

<table>
<thead>
<tr>
<th>BP Category</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120 mm Hg</td>
<td>and &lt;80 mm Hg</td>
</tr>
<tr>
<td>Elevated</td>
<td>120–129 mm Hg</td>
<td>and &lt;80 mm Hg</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>130–139 mm Hg</td>
<td>or 80–89 mm Hg</td>
</tr>
<tr>
<td>Stage 2</td>
<td>≥140 mm Hg</td>
<td>or ≥90 mm Hg</td>
</tr>
</tbody>
</table>

BP indicates blood pressure (based on an average of ≥2 careful readings obtained on ≥2 occasions)

*BP: blood pressure

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**Notes:**

1. SBP: Systolic Blood Pressure
2. DBP: Diastolic Blood Pressure
3. SBP and DBP values are based on the average of ≥2 careful readings obtained on ≥2 occasions.
# Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension*

<table>
<thead>
<tr>
<th>Nonpharmacological Intervention</th>
<th>Dose</th>
<th>Approximate Impact on SBP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight loss</strong></td>
<td>Weight/body fat</td>
<td>Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.</td>
</tr>
<tr>
<td><strong>Healthy diet</strong></td>
<td>DASH dietary pattern</td>
<td>Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.</td>
</tr>
<tr>
<td><strong>Reduced intake of dietary sodium</strong></td>
<td>Dietary sodium</td>
<td>Optimal goal is &lt;1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.</td>
</tr>
<tr>
<td><strong>Enhanced intake of dietary potassium</strong></td>
<td>Dietary potassium</td>
<td>Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.</td>
</tr>
</tbody>
</table>
# Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension* (cont.)

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<th>Nonpharmacological Intervention</th>
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<tr>
<td><strong>Physical activity</strong></td>
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</table>
| Aerobic                        | ● 90–150 min/wk  
● 65%–75% heart rate reserve | -5/8 mm Hg  
-2/4 mm Hg |
| Dynamic resistance             | ● 90–150 min/wk  
● 50%–80% 1 rep maximum  
● 6 exercises, 3 sets/exercise, 10 repetitions/set | -4 mm Hg  
-2 mm Hg |
| Isometric resistance           | ● 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk  
● 8–10 wk | -5 mm Hg  
-4 mm Hg |
| **Moderation in alcohol intake** | Alcohol consumption | In individuals who drink alcohol, reduce alcohol† to:  
● Men: ≤2 drinks daily  
● Women: ≤1 drink daily | -4 mm Hg  
-3 mm |

*Type, dose, and expected impact on BP in adults with a normal BP and with hypertension.
†In the United States, one “standard” drink contains roughly 14 g of pure alcohol, which is typically found in 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), and 1.5 oz of distilled spirits (usually about 40% alcohol).
Cholesterol (Lipid) Recommendations You May Be Familiar With

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<tr>
<td>Total Cholesterol Goal:</td>
<td>&lt;200 mg/dL</td>
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<tr>
<td>“Bad Cholesterol” LDL Goal:</td>
<td>&lt;100 mg/dL</td>
</tr>
<tr>
<td>(Low Density Lipoprotein Cholesterol)</td>
<td></td>
</tr>
<tr>
<td>“Good Cholesterol” HDL Goal:</td>
<td>&gt;50 mg/dL</td>
</tr>
<tr>
<td>(High Density Lipoprotein Cholesterol)</td>
<td></td>
</tr>
<tr>
<td>Triglycerides Goal:</td>
<td>&lt;150 mg/dL</td>
</tr>
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Potential benefits of Cardio-Oncology

- Standardization of CV care
- Optimal cardiac imaging
- Improved communication and continuity of care
- Education: Patients, trainees, community
- Direct access w/ single contact
- Research collaboration

Improved patient outcomes
Cardiovascular complication from cancer therapy

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<tr>
<td>• Arterial Thrombosis</td>
<td>• Conduction system disease</td>
<td>• Radiation</td>
</tr>
<tr>
<td>• Deep venous thrombosis / pulmonary embolus</td>
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