Building a Cardio-Oncology Program

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Boston, MA
Cardio-oncology: an increasingly relevant issue

Czaja, Nat Acad Engin 2009, The bridge, 39:1
Associations cancer- cv disease

Cancer Incidence by Age

Cardiovascular Disease Incidence by Age

AHA statistical update; Circulation 2011

Merrill RM, Annals Epidemiol 2001

Patients with cancer have an increased risk of cv disease

Jones LW, JACC 2007
CV impact of cancer treatments: why is it relevant?

Estimated Number of Cancer Survivors in the U.S.

- Projections
- 2 Million at risk of Cardiotoxicity

Cardio-Oncology Program

The Massachusetts General Hospital Cardio-Oncology Program provides care at the intersection of heart and vascular disease, and cancer. The program focuses on improving the health of cancer patients and cancer survivors by providing comprehensive cardiac and vascular care.

Call 866-644-8910 to request a new patient appointment or to refer a patient
Request an appointment online
Request a second opinion

Coordinated, Patient-centered Approach to Treatment

The Cardio-Oncology Program at Massachusetts General Hospital is an initiative between the Corrigan Minehan Heart Center and the Mass General Cancer Center, two top-ranked centers at the forefront of patient care and research.

Patients with cancer may have a higher risk of developing cardiovascular disease, as cancer therapies may affect the heart and vascular systems. It is important to prevent, monitor and treat cardiovascular disease in cancer survivors and patients with cancer.
Patient-centered comprehensive cardiovascular care for the cancer patient

Cardio-Oncology Program

Survivorship

Pre-treatment risk assessment

Cardio-protective strategies

Management of complications of cancer treatment

Monitoring for complications from cancer therapies
Multidisciplinary Approach

Inside the cardiology department

Clinic
Echocardiography
CT Surgery
Cardiac MRI/CT
Heart Failure
Electrophysiology
Heart disease in pregnancy
Cardiac Performance Program

Outside cardiology

Oncologists
Surgeons
Neurologists
Nephrologists....
Advertisement, Outreach

• Inside the hospital
  – Multidisciplinary conferences
  – Cardiology clinics in the oncology department
  – Reserved echocardiography slots – machine in oncology

• Locally-regionally
  – Website
  – Lectures at nearby hospitals, practices
  – Training of nearby MDs by shadowing clinics

• Nationally-internationally
  – Raise the awareness of the field (lectures, research, consensus/guidelines etc..)
Cardio-oncologists education

• Cardio-oncology fellowships (MSKCC, UPenn, Toronto....) or “home-grown” shadowing program

• Clinical skills and imaging (echo +++)

• Importance of multidisciplinary meetings, journal clubs

• Online resources, including ACC.org, cardiooncology section

http://www.acc.org/clinical-topics/cardio-oncology?w_nav=MN#sort=%40foriginalz32xpostedz32xdate86069%20descending
Importance of Echocardiography

Clinically-indicated echocardiograms per year for cancer patients

- Increase in cancer cases seen at MGH
- Increase in cv follow-up
- Increase in echocardiograms vs MUGA

40% increase from 2002-2008 (2000 more cases)
Longer survival, more recognition of cv side-effects
ESC guidelines, push for echos

Tripled in 6 years
Indications for echocardiograms / cardio-oncology

1. Patients who have a cancer impacting the cv system
   Primary tumors (sarcomas) extremely rare (<0.1%)/ metastasis more frequent, (up to 20% of patients dying of cancer)

2. Patients who have cv disease and develop cancer

3. Patients who have received a cardiotoxic treatment and developed cv complications

4. Patients who will or are receiving a cardiotoxic treatment
Improve the value of LVEF

Have a good image quality

General Guidelines ASE/EAE

Contrast if 2 or more endocardial segments not visualized

3D decreases geometrical assumptions, improves detection of regional abnormality, decreases variability

Consensus

- Value of 3D LVEF if feasible

Min diff detect:
Bi-D10%
Tri-D 6%

Thavendiranathan P, JACC 2012
Otterstadt, Europ Heart J 1997
Monitoring using LVEF: is it enough?

2625 patients w. anthracyclines

9% cardiotox

- 11% totally reversible
- 71% partially reversible
- 18% irreversible

Cardiac events

- 8%
- 17%
- 46%

More sensitive indices needed!

Cardinale D, Circulation 2015
81 patients, 15 months FU

- Decrease in 10% peak longitudinal strain predictive

Consensus
- Incorporate strain
- Decrease > 15% = CTox

Prognostic value of biomarkers in chemotherapy-induced LV dysfunction

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Interval Change</th>
<th>HR (95% CI)*</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>TnI</td>
<td>1.38 (1.05–1.81)</td>
<td>0.020</td>
<td></td>
</tr>
<tr>
<td>NT-proBNP</td>
<td>1.11 (0.80–1.54)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>0.95 (0.52–1.73)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>GDF-15</td>
<td>1.33 (0.93–1.92)</td>
<td>0.118</td>
<td></td>
</tr>
<tr>
<td>MPO</td>
<td>1.34 (1.00–1.80)</td>
<td>0.048</td>
<td></td>
</tr>
<tr>
<td>PIGF</td>
<td>1.16 (0.77–1.73)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>sFlt-1</td>
<td>0.75 (0.51–1.10)</td>
<td>0.139</td>
<td></td>
</tr>
<tr>
<td>Gal-3</td>
<td>1.33 (0.86–2.05)</td>
<td>0.195</td>
<td></td>
</tr>
</tbody>
</table>

Ky B, J Am Coll Cardiol 2014
Putt M, Clin Chemistry 2015
Expert Consensus ASE/EACVI

**Initiation of regimen potentially associated with Type I toxicity**

1. Baseline evaluation of LVEF
   - 3DE (preferred) / 2DE (consider contrast)
   - GLS, Troponin I

2. LVEF < 53%*
   - GLS < LLN**
   - + Troponins

   - Cardiology consultation

3. LVEF > 53%
   - GLS > LLN**
   - - Troponins

   - F/U at completion of therapy, and 6 months later***

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**Initiation of trastuzumab**

1. Baseline evaluation of LVEF
   - 3DE (preferred) / 2DE (consider contrast)
   - GLS or Troponin I

2. LVEF < 53%*
   - GLS < LLN**
   - + Troponins

   - Cardiology consultation

3. LVEF > 53%
   - GLS > LLN**
   - - Troponins

   - F/U every 3 months during therapy

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* Consider confirmation with CMR.
** LLN = Lower limit of normal. Please refer to Table 5 for normal GLS values based on vendor, gender and age.
*** If the dose is higher than 240 mg/m² (or its equivalent), recommend measurement of LVEF, GLS and troponin prior to each additional 50 mg/m².

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*Plana et al., J Am Soc Echo 2014*
Non uniform recommendations for Monitoring

European Society of Medical Oncologists

Baseline cardiologic evaluation, ECHO

- Anthracycline-CTh
  - Tnl evaluation at each cycle
    - Tnl POS
      - Enalapril for 1 year
        - ECHO end CTh, 3-6-9 months
          - ECHO 12 m
    - Tnl NEG
      - ECHO 12 m

- Tnl not evaluated during CTh
  - ECHO at end CTh
    - No LVD
      - ECHO 3 months
        - No LVD
          - ECHO 6 months
            - No LVD
              - ECHO 9 months
                - No LVD
                  - ECHO 12 months
                    - No LVD
                      - ECHO ever year

ACE + BB

Clinical Follow-up

ECHO every 6 months for 5 years

ECHO every year
INITIAL CLINICAL ASSESSMENT FOR PATIENTS WHO HAVE RECEIVED PREVIOUS ANTHRACYCLINE THERAPY

- History and physical
  - Assess for signs and symptoms of heart failure
  - Assess patient’s ability to perform routine and desired activities of daily living
  - Look for signs of volume overload
- Evaluate for presence of heart failure risk factors
  - Hypertension
  - Dyslipidemia
  - Diabetes mellitus
  - Family history of cardiomyopathy
  - Age >65 years
  - History of other cardiovascular comorbidities (e.g., atrial fibrillation, known coronary artery disease [CAD], or baseline evidence of structural heart disease)
- Review other cardiovascular risk factors
  - Smoking
  - Alcoholism
  - Obesity
  - Family history of cardiomyopathy or other heart disease
- Review medications
- Review oncologic history
  - Review total cumulative dose of anthracycline
  - Other systemic therapy and/or chest radiation therapy

- Cardiovascular risk factor management
- Consider two-dimensional echocardiogram with doppler flow study for survivors with one or more cardiac risk factors within 1 year after completion of anthracycline therapy

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Management of cardiac health in trastuzumab-treated patients with breast cancer: updated United Kingdom National Cancer Research Institute recommendations for monitoring

A) Patient assessment

<table>
<thead>
<tr>
<th>LVEF value</th>
<th>LVEF decrease during trastuzumab</th>
<th>Signs or symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; LLN</td>
<td>&lt; 0.10</td>
<td>None</td>
</tr>
<tr>
<td>LLC ≤ 0.40</td>
<td>≥ 0.10</td>
<td>None</td>
</tr>
<tr>
<td>≤ 0.40</td>
<td>-</td>
<td>Any</td>
</tr>
</tbody>
</table>

LVEF = left ventricular ejection fraction
LLN = lower limit of normal

B) Pre-chemotherapy

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Start ACEi</th>
<th>Cardiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard CT</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Consider CT*</td>
<td>YES</td>
<td>REFER</td>
</tr>
<tr>
<td>Consider CT*</td>
<td>YES</td>
<td>REFER</td>
</tr>
</tbody>
</table>

*Consider non-anthraacyline chemotherapy (CT)

C) Post-chemotherapy

<table>
<thead>
<tr>
<th>Trastuzumab</th>
<th>Start ACEi</th>
<th>Cardiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start trastuzumab</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Defer until 'green'</td>
<td>YES</td>
<td>REFER</td>
</tr>
<tr>
<td>Not recommended</td>
<td>YES</td>
<td>REFER</td>
</tr>
</tbody>
</table>

*For patients with LVEF < LLN, cardiac function should be optimised and reassessed 3 months later

D) During trastuzumab

<table>
<thead>
<tr>
<th>Trastuzumab</th>
<th>Start ACEi</th>
<th>Cardiology</th>
<th>Additional monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue</td>
<td>NO</td>
<td>REFER</td>
<td>6–8 weeks after first amber End of treatment</td>
</tr>
<tr>
<td>Continue</td>
<td>YES</td>
<td>REFER</td>
<td>Within 6 weeks then as clinically indicated</td>
</tr>
<tr>
<td>STOP*</td>
<td>YES</td>
<td>REFER</td>
<td>*May restart if 'green' after consideration of risk vs benefit</td>
</tr>
</tbody>
</table>

Jones A, BJC 2009
Take home messages: cardio-oncology

Collaboration:
  often very complex patients, team work nowhere if the oncologists are not participating

Survivorship:
  Long follow up
  Need for Accuracy and reproducibility of techniques

New specialty, sparse guidelines, often case by case
Training in the Echo Lab

**Sonographers**
- Protocols for cardiac function monitoring in patients with cancer
  - Can be a limited echocardiogram (time/cost)
  - 3D LVEF
  - Strain

**Readers**
- Importance of optimization of the intra- and inter-observer variability
- Quality control interventions