Cardiotoxicity in practice:

From diagnosis to management

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The Cardio-Oncology Concept

Cardiotoxicity in practice

Outline

• Definition and pathophysiology
  • Assessment and monitoring
• Management
• Case
• Conclusions
Cardiotoxicity is only a part of the problem!

CV complications of cancer therapy

- Myocardial dysfunction and/or HF
- CAD
- Valvular disease
- Arrhythmias
- HTN
- Thromboembolic disease
- Peripheral vascular disease and stroke
- PH
- Pericardial disease
Cancer therapeutics-related cardiac dysfunction

Definition

- CTRCD is defined as a drop in LVEF of $\geq 5\%$ in symptomatic patients or a drop in LVEF of $\geq 10\%$ to an EF of $<53\%$ in asymptomatic patients.

- CTRCD is defined as a decrease in the LVEF of $>10\%$ to a value below the lower limit of normal (50%). A relative percentage reduction of GLS of $>15\%$ from baseline is considered abnormal and a marker of early LV subclinical dysfunction.
Pathophysiology of Cardiotoxicity

Chemotherapy
Radiotherapy

Non-reversible damage type I
Pathophysiology
Cell loss (necrosis/apoptosis)

Manifestation
Cardiomyopathy / heart failure
myocardial infarction
thrombosis

Diagnosis
Injury marker release
progressive contractile dysfunction
cardiac remodeling

Progressive cardiovascular disease

Cardiovascular risk factors
(presisting cardiac disease, hypertension, age)

Cancer therapy
(anthracyclines vs. non-anthracyclines)

Reversible dysfunction type II
Pathophysiology
cellular dysfunction
(mitochondrial/protein dysfunction)

Manifestation
Temporary contractile dysfunction
vasospastic angina
arterial hypertension

Diagnosis
No injury marker release
reversible contractile dysfunction
reversible arterial hypertension

Normalization of cardiovascular function

Suter et al, Eur Heart J. 2013 Apr;34(15)
Characteristics of type I and II CTRCD

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic agent</td>
<td>Doxorubicin</td>
<td>Trastuzumab</td>
</tr>
<tr>
<td>Clinical course and typical response to antiremodeling therapy (β-blockers, ACE inhibitors)</td>
<td>May stabilize, but underlying damage appears to be permanent and irreversible; recurrence in months or years may be related to sequential cardiac stress</td>
<td>High likelihood of recovery (to or near baseline cardiac status) in 2–4 months after interruption (reversible)</td>
</tr>
<tr>
<td>Dose effects</td>
<td>Cumulative, dose related</td>
<td>Not dose related</td>
</tr>
<tr>
<td>Effect of rechallenge</td>
<td>High probability of recurrent dysfunction that is progressive; may result in intractable heart failure or death</td>
<td>Increasing evidence for the relative safety of rechallenge (additional data needed)</td>
</tr>
<tr>
<td>Ultrastructure</td>
<td>Vacuoles; myofibrillar disarray and dropout; necrosis (changes resolve over time)</td>
<td>No apparent ultrastructural abnormalities (though not thoroughly studied)</td>
</tr>
</tbody>
</table>
Cardiotoxicity Categorization

Repeat study within 2 to 3 weeks after the baseline diagnostic study showing the initial decrease in LVEF can further categorize cardiotoxicity as:

- **Reversible:** to within 5 percentage points of baseline
- **Partially reversible:** improved by ≥10 percentage points from the nadir but remaining >5 percentage points below baseline
- **Irreversible:** improved by <10 percentage points from the nadir and remaining >5 percentage points below baseline
- **Indeterminate:** patient not available for re-evaluation

**Anthracycline cardiotoxicity**

- **Early onset chronic progressive:** within the 1st year after completion of chemotherapy
- **Late onset chronic progressive:** greater than 1 year from completion of therapy (can present as long as 1-2 decades after completion of chemotherapy)
Outline

- Definition and pathophysiology
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- Case
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Baseline risk factors for cardiotoxicity

The first step to identify patients at increased risk for cardiotoxicity consists of a careful baseline assessment of cardiovascular risk factors.

<table>
<thead>
<tr>
<th>Current myocardial disease</th>
<th>Demographic and other CV risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Heart failure (with either preserved or reduced ejection fraction)</td>
<td>• Age (paediatric population &lt;18 years; &gt;50 years for trastuzumab; &gt;65 years for anthracyclines)</td>
</tr>
<tr>
<td>• Asymptomatic LV dysfunction (LVEF &lt;50% or high natriuretic peptide)</td>
<td>• Family history of premature CV disease (&lt;50 years)</td>
</tr>
<tr>
<td>• Evidence of CAD (previous myocardial infarction, angina, PCI or CABG, myocardial ischaemia)</td>
<td>• Arterial hypertension</td>
</tr>
<tr>
<td>• Moderate and severe VHD with LVH or LV impairment</td>
<td>• Diabetes mellitus</td>
</tr>
<tr>
<td>• Hypertensive heart disease with LV hypertrophy</td>
<td>• Hypercholesterolaemia</td>
</tr>
<tr>
<td>• Hypertrophic cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>• Dilated cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>• Restrictive cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>• Cardiac sarcoidosis with myocardial involvement</td>
<td></td>
</tr>
<tr>
<td>• Significant cardiac arrhythmias (e.g. AF, ventricular tachyarrhythmias)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous cardiotoxic cancer treatment</th>
<th>Lifestyle risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Prior anthracycline use</td>
<td>• Smoking</td>
</tr>
<tr>
<td>• Prior radiotherapy to chest or mediastinum</td>
<td>• High alcohol intake</td>
</tr>
<tr>
<td></td>
<td>• Obesity</td>
</tr>
<tr>
<td></td>
<td>• Sedentary habit</td>
</tr>
</tbody>
</table>

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines. European Heart Journal (2016) 37, 2768–2801
Incidence of LV dysfunction associated with chemotherapy

<table>
<thead>
<tr>
<th>Chemotherapy agents</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anthracyclines (dose dependent)</strong></td>
<td></td>
</tr>
<tr>
<td>Doxorubicin (Abriamycin) 400 mg/m²</td>
<td>3–5</td>
</tr>
<tr>
<td>550 mg/m²</td>
<td>7–26</td>
</tr>
<tr>
<td>700 mg/m²</td>
<td>18–48</td>
</tr>
<tr>
<td>Idarubicin (&gt;90 mg/m²)</td>
<td>5–18</td>
</tr>
<tr>
<td>Epirubicin (&gt;900 mg/m²)</td>
<td>0.9–11.4</td>
</tr>
<tr>
<td>Mitoxantrone &gt;120 mg/m²</td>
<td>2.6</td>
</tr>
<tr>
<td>Liposomal anthracyclines (&gt;900 mg/m²)</td>
<td>2</td>
</tr>
<tr>
<td><strong>Alkylating agents</strong></td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>7–28</td>
</tr>
<tr>
<td>Ifosfamide &lt;10 g/m²</td>
<td>0.5</td>
</tr>
<tr>
<td>&gt;12.5–16 g/m²</td>
<td>17</td>
</tr>
<tr>
<td><strong>Antimetabolites</strong></td>
<td></td>
</tr>
<tr>
<td>Clofarabine</td>
<td>27</td>
</tr>
<tr>
<td><strong>Antimicrotubule agents</strong></td>
<td></td>
</tr>
<tr>
<td>Docetaxel</td>
<td>2.3–13</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>&lt;1</td>
</tr>
<tr>
<td><strong>Monoclonal antibodies</strong></td>
<td></td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>1.7–20.1²</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>1.6–4³</td>
</tr>
<tr>
<td>Pertuzumab</td>
<td>0.7–1.2</td>
</tr>
<tr>
<td><strong>Small molecule tyrosine kinase inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>Sunitinib</td>
<td>2.7–19</td>
</tr>
<tr>
<td>Pazopanib</td>
<td>7–11</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>4–8</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>2–4</td>
</tr>
<tr>
<td>Imatinib mesylate</td>
<td>0.2–2.7</td>
</tr>
<tr>
<td>Lapatinib</td>
<td>0.2–1.5</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>1</td>
</tr>
<tr>
<td><strong>Proteasome inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>Carfilzomib</td>
<td>11–25</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>2–5</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td></td>
</tr>
<tr>
<td>Everolimus</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Temsirolimus</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

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Factors associated with risk of cardiotoxicity following treatment with anthracyclines

Patients who have received a cumulative dose of $>250–300 \text{ mg/m}^2$ of doxorubicin or its equivalent are considered to be at high risk for CTRCD.

<table>
<thead>
<tr>
<th>Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cumulative dose</td>
</tr>
<tr>
<td>• Female sex</td>
</tr>
<tr>
<td>• Age</td>
</tr>
<tr>
<td>- $&gt;65$ years old</td>
</tr>
<tr>
<td>- Paediatric population ($&lt;18$ years)</td>
</tr>
<tr>
<td>• Renal failure</td>
</tr>
<tr>
<td>• Concomitant or previous radiation therapy involving the heart</td>
</tr>
<tr>
<td>• Concomitant chemotherapy</td>
</tr>
<tr>
<td>- alkylating or antimicrotubule agents</td>
</tr>
<tr>
<td>- immuno- and targeted therapies</td>
</tr>
<tr>
<td>• Pre-existing conditions</td>
</tr>
<tr>
<td>- Cardiac diseases associating increased wall stress</td>
</tr>
<tr>
<td>- Arterial hypertension</td>
</tr>
<tr>
<td>- Genetic factors</td>
</tr>
</tbody>
</table>
Baseline Assessment and Monitoring

1. Thorough medical history and physical examination
2. ECG
3. Cardiac imaging (echocardiography, strain)

Strengths and limitations of GLS

In the absence of GLS by STE, quantification of LV longitudinal function using mitral-annulus displacement by M-mode echocardiography, and/or peak systolic velocity (s’) of the mitral annulus by pulsed-wave DTI is recommended.

2014 Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging European Heart Journal: Cardiovascular Imaging 15 1063–1093
# Diagnostic tools for the detection of cardiotoxicity

<table>
<thead>
<tr>
<th>Technique</th>
<th>Currently available diagnostic criteria</th>
<th>Advantages</th>
<th>Major limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiography:</td>
<td>- 3D-based LVEF&lt;br&gt;- 2D Simpson’s LVEF&lt;br&gt;- GLS&lt;br&gt;• LVEF: &gt;10 percentage points decrease to a value below the LLN suggests cardiotoxicity.&lt;br&gt;• GLS: &gt;15% relative percentage reduction from baseline may suggest risk of cardiotoxicity.</td>
<td>• Wide availability.&lt;br&gt;• Lack of radiation.&lt;br&gt;• Assessment of haemodynamics and other cardiac structures.</td>
<td>• Inter-observer variability.&lt;br&gt;• Image quality.&lt;br&gt;• GLS: inter-vendor variability, technical requirements.</td>
</tr>
<tr>
<td>Nuclear cardiac imaging</td>
<td>(MUGA) &lt;br&gt;• &gt;10 percentage points decrease in LVEF with a value &lt;50% identifies patients with cardiotoxicity.</td>
<td>• Reproducibility.</td>
<td>• Cumulative radiation exposure.&lt;br&gt;• Limited structural and functional information on other cardiac structures.</td>
</tr>
<tr>
<td>Cardiac magnetic resonance</td>
<td>• Typically used if other techniques are non-diagnostic or to confirm the presence of LV dysfunction if LVEF is borderlines.</td>
<td>• Accuracy, reproducibility.&lt;br&gt;• Detection of diffuse myocardial fibrosis using T1/T2 mapping and ECVF evaluation.</td>
<td>• Limited availability.&lt;br&gt;• Patient’s adaptation (claustrophobia, breath hold, long acquisition times).</td>
</tr>
<tr>
<td>Cardiac biomarkers:</td>
<td>- Troponin I&lt;br&gt;- High-sensitivity Troponin I&lt;br&gt;- BNP&lt;br&gt;- NT-proBNP&lt;br&gt;• A rise identifies patients receiving anthracyclines who may benefit from ACE-Is.&lt;br&gt;• Routine role of BNP and NT-proBNP in surveillance of high-risk patient needs further investigation.</td>
<td>• Accuracy, reproducibility.&lt;br&gt;• Wide availability.&lt;br&gt;• High-sensitivity.</td>
<td>• Insufficient evidence to establish the significance of subtle rises.&lt;br&gt;• Variations with different assays.&lt;br&gt;• Role for routine surveillance not clearly established.</td>
</tr>
</tbody>
</table>

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Stress Echocardiography

- Detection and prognosis of with intermediate or high pretest probability for CAD who are undergoing regimens that may be associated with ischemia (fluorouracil, bevacizumab, sorafenib, and sunitinib)
- Evaluation of subclinical LV dysfunction
- Evaluation of contractile reserve

Outline of a proposed model for risk assessment, monitoring and management of patients undergoing chemotherapy

1. Risk assessment

**Medication-related risk**

**High (risk score 4):**
- Anthracyclines, cyclophosphamide, ifosfamide, clofarabine, herceptin

**Intermediate (risk score 2):**
- Docetaxel, pertuzumab, sunitinib, sorafenib

**Low (risk score 1):**
- Bevacizumab, dasatinib, imatinib, lapatinib

**Rare (risk score 0):**
- For example, etoposide, rituximab, thalidomide

**Tests:** TTE with strain, ECG, cTn

**Patient-related risk factors**

- Cardiomyopathy or heart failure
- CAD or equivalent (incl. PAD)
- HTN
- Diabetes mellitus
- Prior or concurrent anthracycline
- Prior or concurrent chest radiation
- Age <15 or > 65 years
- Female gender

**Overall risk by cardiotoxicity risk score (CRS)**

(risk categories by drug-related risk score plus number of patient-related risk factors: CRS >6: very high, 5-6: high, 3-4: intermediate, 1-2: low, 0: very low)
The precise timing and frequency of imaging and/or biomarker sampling will depend upon the specific cancer treatment, total cumulative dose of cardiotoxic chemotherapy, delivery protocol and duration and the patient’s baseline cardiovascular risk.
Outline of a proposed model for risk assessment, monitoring and management of patients undergoing chemotherapy.

Overall risk by cardiotoxicity risk score (CRS)
(risk categories by drug-related risk score plus number of patient-related risk factors: CRS >6: very high, 5-6: high, 3-4: intermediate, 1-2: low, 0: very low)

2. Monitoring recommendations

**Very high cardiotoxicity risk:** TTE with strain before every (other) cycle, end, 3–6 months, and 1 year; optional ECG, cTn with TTE during chemotherapy

**High cardiotoxicity risk:** TTE with strain every 3 cycles, end, 3–6 months and 1 year after chemotherapy; optional ECG, cTn with TTE during chemotherapy

**Intermediate cardiotoxicity risk:** TTE with strain mid-term, end, and 3–6 months after chemotherapy; optional ECG, cTn mid-term of chemotherapy

**Low cardiotoxicity risk:** Optional TTE with strain and/or ECG, cTn at the end of chemotherapy

**Very low cardiotoxicity risk:** None
Initiation of regimen associated with **Type I and II agents**

![Flowchart showing the assessment and monitoring process for patients receiving Type I and II agents.](chart.png)

*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.

Combination therapy (trastuzumab after anthracyclines)

Initiation of trastuzumab after regimen associated with Type I toxicity

Baseline evaluation of LVEF
3D (preferred) / 2D (consider contrast)
GLS, Troponin I

LVEF < 53%*
GLS < LLN**
+ Troponins

Cardiology consultation

LVEF > 53%
GLS > LLN**
-Tn I

F/U every 3 months during therapy, and 6 months later

* Consider confirmation with CMR.
** LLN = Lower limit of normal. Please refer to Table 5 for normal GLS values based on vendor, gender and age.
Monitoring of patients

Low versus high risk

- For **low-risk patients** (normal baseline echocardiogram, no clinical risk factors), surveillance should be considered with echocardiography
  - every 4 cycles of anti-HER2 treatment or
  - after 200 mg/m2 of doxorubicin (or equivalent) for treatment with anthracyclines.
- More frequent surveillance may be **considered for patients with abnormal baseline echocardiography** (e.g. reduced or low normal LVEF, structural heart disease) and those with **higher baseline clinical risk** (e.g. prior anthracyclines, previous MI, treated HF).

*2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines. European Heart Journal (2016) 37, 2768–2801*
Troponin levels have added prognostic value to GLS. If both are abnormal, the specificity for the prediction of CTRCD increases from 73% to 93%. If both are normal, the negative predictive value increases to 91%.

2014 Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular ImagingEuropean Heart Journal: Cardiovascular Imaging 15 1063–1093
Outline

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• Management

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### Strategies to reduce chemotherapy-induced cardiotoxicity

<table>
<thead>
<tr>
<th>Chemotherapy drug</th>
<th>Potential cardioprotective measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>All chemotherapy drugs</td>
<td>Identify and treat cardiovascular risk factors</td>
</tr>
<tr>
<td></td>
<td>Treat comorbidities (CAD, HF, PAD, HTN)</td>
</tr>
<tr>
<td></td>
<td>QTc prolongation and torsade de pointes:</td>
</tr>
<tr>
<td></td>
<td>- Avoid QT prolonging drugs</td>
</tr>
<tr>
<td></td>
<td>- Manage electrolyte abnormalities</td>
</tr>
<tr>
<td></td>
<td>Minimize cardiac irradiation</td>
</tr>
<tr>
<td>Anthracyclines and analogues</td>
<td>Limit cumulative dose (mg/m²):</td>
</tr>
<tr>
<td></td>
<td>- Daunorubicin &lt;800</td>
</tr>
<tr>
<td></td>
<td>- Doxorubicin &lt;360</td>
</tr>
<tr>
<td></td>
<td>- Epirubicin &lt;720</td>
</tr>
<tr>
<td></td>
<td>- Mitoxantrone &lt;160</td>
</tr>
<tr>
<td></td>
<td>- Idarubicin &lt;150</td>
</tr>
<tr>
<td></td>
<td>Altered delivery systems (liposomal doxorubicin) or continuous infusions</td>
</tr>
<tr>
<td></td>
<td>Dexrazoxane as an alternative</td>
</tr>
<tr>
<td></td>
<td>ACE-Is or ARBs</td>
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<td></td>
<td>β-blockers</td>
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<tr>
<td></td>
<td>Statins</td>
</tr>
<tr>
<td></td>
<td>Aerobic exercise</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>ACE-Is</td>
</tr>
<tr>
<td></td>
<td>β-blockers</td>
</tr>
</tbody>
</table>

**High baseline cardiotoxicity risk** (CVD, previous anthracycline chemotherapy or CVD risk factors) then:
1. a very stringent optimization of risk factor control has to be obtained and
2. a prophylactic cardioprotective medication regimen should be considered

**Low baseline risk** scheduled for high total cumulative anthracycline doses (250–300 mg/m² doxorubicin or equivalent) may also be considered for prophylactic cardioprotective medication

**Cardioprotection** in patients who have a troponin increase during treatment

**Pre-existing clinical HF or significant LV dysfunction**
1. selection of an alternative non-cardiotoxic chemotherapy,
2. anthracycline preparations with lower cardiotoxicity (e.g. liposomal doxorubicin), reduced-dose schedules and/or
3. additional cardioprotective drugs (e.g. ACE inhibitors, beta-blockers, aldosterone antagonists or dexrazoxane

**In LVEF reduction** initiating one or more guideline-based HF therapies should be considered

**In HF** discuss necessity and duration of any interruption of cancer treatment, with interruption of cancer treatment recommended until the patient is clinically stable.

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Overall risk by cardiotoxicity risk score (CRS)
(risk categories by drug-related risk score plus number of patient-related risk factors: CRS >6: very high, 5-6: high, 3-4: intermediate, 1-2: low, 0: very low)

3. Management recommendations

Very high cardiotoxicity risk: Initiate ACE-I /ARB, carvedilol, and statins, starting at lowest dose and start chemotherapy in 1 week from initiation to allow steady state, up-titrate as tolerated
High cardiotoxicity risk: Initiate ACE-I /ARB, carvedilol, and/or statins
Intermediate cardiotoxicity risk: Discuss risk and benefit of medications
Low cardiotoxicity risk: None, monitoring only
Very low cardiotoxicity risk: None, monitoring only
Established algorithm for the monitoring of patients undergoing anthracycline-based chemotherapy

1. **Initial evaluation**
   - **LVEF > 50%**
     - Reassessment at 250-300 mg/k2
       - No high risk
         - Reassessment at 450 mg/k2
         - Reassessment prior to each cycle
           - Discontinue if LVEF ↓ ≥ 10% and LVEF ≤ 50%
       - High risk
         - Reassessment at 400 mg/k2
         - Reassessment prior to each cycle
           - Discontinue if LVEF ↓ ≥ 10% or LVEF ≤ 30%
   - **LVEF < 50%**
     - Initiation of anthracycline therapy
     - Reassessment prior to each cycle

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Herrmann et al, Mayo Clinic Proceedings 2014 89, 1287-1306
Established algorithm for the monitoring of patients undergoing Herceptin chemotherapy

- **Initial evaluation**
  - **LVEF ≥50%**
    - Reassessment at 12 weeks
      - Asymptomatic and stable LVEF
      - Reassessment at prior intervals
  - **LVEF <50%**
    - Reassessment at 6 weeks
      - Asymptomatic and LVEF ↓ ≥10% or LVEF <40%
  - **Potential risk factors**
    - Risk-benefit assessment

- **Initiation of trastuzumab therapy**
  - Discontinue trastuzumab
  - Heart failure therapy
  - Reassessment at 4 weeks
  - Risk-benefit assessment
  - Resume trastuzumab

*Herrmann et al, Mayo Clinic Proceedings 2014 89, 1287-1306*
Management algorithm of patients after radiation therapy

Late Effects | Treatment | Signs and Symptoms | Screening and Diagnostic Tests | Management and Intervention
--- | --- | --- | --- | ---
Pericarditis | >53 Gray | Fatigue, dyspnea on exertion, chest pain, dyspnea, peripheral edema, hypotension, tachycardia, syncope, fatigue, fever, diaphoresis, peripheral edema, hypotension, tachycardia, syncope, fatigue, fever | Electrocardiogram, Chest x-ray, Echocardiogram | Pericardiocentesis, Pericarditisomy

Cardiac toxicity (Myocardial) | >53 Gray or >25 Gray and anthracycline | Fatigue, dyspnea on exertion, chest pain, dyspnea, peripheral edema, hypotension, tachycardia, syncope, fatigue | Electrocardiogram, Echocardiogram, Cardiac catheterization | Education regarding risks of alcohol, smoking, and other drug use, pregnancy, and immunosuppression

 Coronary artery disease | >50 Gray | Chest pain, dyspnea, diaphoresis, hypotension, pallor, syncope, arrhythmia | Exercise stress test with or without radiolabeled angiography, or dobutamine stress echocardiography | Risk factor modifications including diet and conditioning regimen, Cardiac medications and lipid lowering agents

 Vascular disease | > 40 Gray | Cough, weakness, dyspnea on exertion, new warmth, rash, peripheral edema or any other signs of congestion, heart failure | Echocardiogram, Cardiac catheterization | Ampicillin prophylaxis for dental or surgical procedures, Revascularization

 Arrhythmia | | Palpitations, light-headedness, syncope | Electrocardiogram and 24 hour ECG, Evaluation for other abnormalities | Pacemaker

Herrmann et al, Mayo Clinic Proceedings 2014 89, 1287-1306
Long-term surveillance

• Should be considered for patients:
  1. who developed evidence of cardiotoxicity during treatment
  2. in whom cardioprotective medication has been initiated and
  3. exposed to high cumulative anthracycline doses and/or chest radiotherapy

• Survivors who have completed higher-dose anthracycline-containing chemotherapy (≥300 mg/m² of doxorubicin or equivalent) or who developed cardiotoxicity (e.g. LV impairment) requiring treatment during chemotherapy may be considered for follow-up surveillance echocardiography at 1 and 5 years after completion of cancer treatment

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Case

- Female patient 32 years old (14/01/1987)
- Two previous pregnancies (11/2/2012, 17/10/2014)
- Hodgkin lymphoma (diagnosis on 1/2/2017)
  - Stage III and treated with 6 cycles of ABVD (8/3/2017 - 30/8/2017)
  - Total doxorubicin dose 300mg/m^2 (25mg/kg/m^2)
- Presented with progressive dyspnea after the completion of chemotherapy and was admitted with HF symptoms and hemodynamic instability (20/10/2017)
- Treated with inotropes and transferred to Hippokration Hospital (29/10/2017)
TTE
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SCAI Releases Expert Consensus for Cardio-Oncology Patients Treated in Cardiac Catherization Labs

January 12, 2016

Core Curriculum

SCAI Expert Consensus Statement: Evaluation, Management, and Special Considerations of Cardio-Oncology Patients in the Cardiac Catheterization Laboratory (Endorsed by the Cardiological Society of India, and Sociedad Latino Americana de Cardiología Intervencionista)

Cezar A. Iliescu, MD, FSCAI, FACCC, Cindy L. Grines, MD, FSCAI, FACCC, Joerg Herrmann, MD, Eric H. Yang, MD, FACCC, Mehmet Cilingiroglu, MD, FSCAI, FESC, FACCC, Konstantinos Charitakis, MD, FACC, Abdul Hakeem, MD, FSCAI, FACCC, Konstantinos P. Toutouzas, MD, FSCAI, FESC, Massoud A. Leesar, MD, and Konstantinos Marmagkiolis, MD, FSCAI, FACCC
Outline

- Definition and pathophysiology
- Assessment and monitoring
- Management
- Case
- Conclusions
Conclusions

• Maximizing the benefits of chemotherapy while reducing cardiac risks

• While primary prevention of cardiotoxicity is still in the research domain, secondary prevention has already entered clinical practice guidelines despite persistent unresolved questions.

• Future aims:
  
  • Refining the predisposing factors for the development of CVD related to cancer treatment,

  • Evaluating the rate of subclinical LV dysfunction and its transition to overt HF,

  • Defining the most reliable cardiac monitoring approach
Cardiotoxicity from Anthracyclines

RISK FACTORS FOR ANTHRACYCLINE CARDIOTOXICITY
- Cumulative anthracycline dose
- Extremes of age
- Female gender
- Cardiovascular comorbidities
- Adjuvant chemotherapies
- Adjuvant thoracic RT

ANTHRACYCLINE CARDIOTOXICITY
No cardiotoxicity
- Subclinical myocardial injury
- Asymptomatic LV dysfunction
- Symptomatic HF
- Refractory HF/Cardiogenic shock
- Death

DIAGNOSIS
- Cardiac biomarker abnormalities
- Myocardial strain imaging
- LVEF assessment
- Symptoms & signs

MANAGEMENT STRATEGIES
- ACE-I ± β blocker
- ± Change in cancer treatment
- ? Statin
- ? Dexrazoxane

TIME FROM ANTHRACYCLINE THERAPY
- REVERSIBLE
- PROGNOSIS
- IRREVERSIBLE

Croarke et al Circulation. 2015;131:1946-1949
Cardiovascular management of patients treated with tyrosine kinase inhibitors

- The potential hemodynamic burden of other tyrosine kinase inhibitors (sunitinib, sorafenib) should be considered in patients with known CAD and should be assessed according to perceived individual risk with appropriate close monitoring and treatment of blood pressure and symptoms in patients at high cardiovascular risk.

2014 Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular ImagingEuropean Heart Journal: Cardiovascular Imaging 15 1063–1093

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines.European Heart Journal (2016) 37, 2768–2801
Increasing Number of Publications