Cardiac Imaging: What for Whom? Which Test and When?

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Disclosures

• Janssen, Takeda, BI, Amgen Advisory Boards
Cardiac Imaging - Purpose

• To help risk stratify patients prior to, during, and / or after completion of cancer therapy with the hope of intervening to prevent prognostically important CVD
Cardiac Imaging – When?

• Assessment of risk prior to cancer treatment
  – EF / strain

• Detection of progression from stage A to B HF
  – During treatment – EF / strain / tissue characterization
  – Survivors – EF / strain / tissue characterization
Baseline Assessment – Whom?

Risk-Imaging Mismatch in Cardiac Imaging Practices for Women Receiving Systemic Therapy for Early-Stage Breast Cancer: A Population-Based Cohort Study

Pualadinesh Thavendirathan, Husam Abdel-Qadir, Hadas D. Fischer, Ying Liu, Ximena Camacho, Eitan Amir, Peter C. Austin, and Douglas S. Lee

Abstract

Purpose
To assess prechemotherapy cardiac imaging practices in relation to patients’ heart failure (HF) risk.

Methods
We performed a population-based retrospective cohort study of women receiving chemotherapy for early-stage breast cancer in Ontario between 2007 and 2012. We surveyed for baseline cardiac imaging 6 months before chemotherapy or 30 days thereafter. The proportion of patients who...
Baseline Assessment – Whom?

• Patients at elevated risk – ASCO guidelines
  – Anthracycline dose / trastuzumab / radiation dose / cardiovascular risk factors

• Others (no clear guidelines)
  – Proteasome inhibitors, ICIs, MEK inhibitors, alkylating agents
Baseline Assessment – LVEF

Every 5% decrease in LVEF 38% relative increase in MACE (2D LVEF)

2285 Patients, BREAST, HEME, OTHER, Anthracycline (Doxo - 223mg/m²)
Wang L et al AJC 2015
Baseline Assessment – Strain

Patients with 2D LVEF 50-59%
N=158 Anthracycline Treated Breast and Heme, Outcome: NYHA3/4 HF

Mousavi et al, EHJCVI 2015
Strain – TomTec 2D CPA

Mohammed TA, et al JASE 2016
Strain TomTec (2D CPA)
During Treatment – Echo LVEF

Thavendiranathan et al, JACC 2013

Zhang KW et al, JACC Imaging 2018
During Treatment – Echo LVEF

Cardinale D et al, Circulation 2015

Cardinale D et al, JACC 2010

Death, acute pulmonary edema, HF hospitalization, life threatening arrhythmia, conduction abnormalities requiring PM
During Treatment – Echo Strain

N=43, 21% CTOX, AC followed by TZM
Sawaya H et al. Am J Cardiol 2011;107:1375

N=81, 30% CTOX, All trastuzumab, 40% A
Negishi K et al, JASE 2013, 26: 493-8
During Treatment – Echo Strain

EXPERT CONSENSUS STATEMENT

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

Juan Carlos Plana, MD, FASE, Chair, Maurizio Galderisi, MD, FESC, Co-Chair, Ana Barac, MD, PhD,

- **Drop of 10 points to LVEF <53%**
  - Yes → CTRCD
  - Relative drop of GLS as compared to baseline
  - < 8%
    - No evidence of subclinical LV dysfunction
  - > 15%
    - Subclinical LV dysfunction*
Strain Knowledge Gaps

• Is GLS the best marker? GCS?
• What is the optimal change threshold?
• Impact of hemodynamic on GLS?
• GLS directed treatment change outcomes?
During Treatment – Echo

**SUCCOUR Trial**  
Recruitment Completed Dec 2018
During Treatment – MRI EF

53 Patients, Breast and Heme, Low/mod dose anthracyclines
Drafts et al, JACC cardiovascular imaging; 2013. 6:877-85

Barthur A et al JCMR 2017, HER2+ BC (41)
During Treatment – MRI EF

Cardiac MRI, Anthracycline Treated (200-250mg/m2)
Jones DN et al, JACC: Heart Failure 2018
MRI Tissue Characterization

- EGE
- T2 Weighted Imaging
- T2 mapping
- T1 mapping

LGE
MRI Tissue Characterization - EGE

A RE > 5 on day 3 predicted drop in LVEF at 28 days

Wassmuth et al. Am Heart J 2001;141:1007-13
N=22
MRI Tissue Characterization – T2

- 46 breast cancer patients (A, T, or both)
- MRI baseline, 1, 4, 12
- 50% edema at 4 months
- Higher edema – lower RVEF at 12 months

## MRI Tissue Characterization T1/T2

<table>
<thead>
<tr>
<th></th>
<th>Anthracycline</th>
<th>Non-anthracycline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (N=40)</td>
<td>Baseline (N=16)</td>
</tr>
<tr>
<td></td>
<td>3 months (N=40)</td>
<td>3 months (N=16)</td>
</tr>
<tr>
<td>Native T1, ms</td>
<td>1,058 ± 100</td>
<td>1,036 ± 41</td>
</tr>
<tr>
<td></td>
<td>1,071 ± 85.2*</td>
<td>1,041 ± 38</td>
</tr>
<tr>
<td>T2, ms</td>
<td>50.8 ± 2.9</td>
<td>51.5 ± 2.2</td>
</tr>
<tr>
<td></td>
<td>51.6 ± 3.5</td>
<td>52.4 ± 2.9</td>
</tr>
<tr>
<td>ECV, %</td>
<td>26.9 ± 3.1</td>
<td>26.7 ± 3.3</td>
</tr>
<tr>
<td></td>
<td>28.6 ± 3.0*</td>
<td>27.7 ± 3.8</td>
</tr>
</tbody>
</table>

Melendez GC et al. JACC Imaging 2017
Myocarditis

Ferreira V et al JACC 2018
During Treatment – ICI Myocarditis

CMR in 31/35 patients
LGE in 74%

Mahmood et al JACC 2018
Survivors – Stage B HF?

Table 2 Standard echo-Doppler quantification of LV geometry and function

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Post-ANT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV1 (mm)</td>
<td>46.5</td>
<td>51.5</td>
<td>0.002</td>
</tr>
<tr>
<td>LVIDS (mm)</td>
<td>29.8</td>
<td>33.2</td>
<td>0.007</td>
</tr>
<tr>
<td>LVM/ht (g/m²)</td>
<td>31.8</td>
<td>39.4</td>
<td>0.001</td>
</tr>
<tr>
<td>RDIWV</td>
<td>0.32</td>
<td>0.39</td>
<td>0.004</td>
</tr>
<tr>
<td>EF (%)</td>
<td>62.6</td>
<td>55.7</td>
<td>0.030</td>
</tr>
<tr>
<td>EDV (mL/m²)</td>
<td>26.4</td>
<td>30.5</td>
<td>0.012</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.17</td>
<td>1.35</td>
<td>0.030</td>
</tr>
<tr>
<td>E velocity DT (ms)</td>
<td>204.1</td>
<td>208.3</td>
<td>0.004</td>
</tr>
<tr>
<td>E/e' ratio</td>
<td>6.9 ± 2.2</td>
<td>7.3 ± 2.1</td>
<td>0.006</td>
</tr>
<tr>
<td>GLS</td>
<td>-22.2 ± 2.3</td>
<td>-20.1 ± 6.6</td>
<td>0.004</td>
</tr>
</tbody>
</table>

ANT, anthracycline; DT, deceleration time; EF, ejection fraction; LAV, left atrial volume index; LV1, left ventricular internal end-diastolic diameter; LVIDS, left ventricular internal end-systolic diameter; LVM/ht, left ventricular mass indexed for height; RDIWV, relative diastolic wall thickness; GLS, global longitudinal strain.

Table 3 Real-time 3D echocardiographic quantitative analysis of the left ventricle

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Post-ANT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS (%)</td>
<td>-16.8 ± 2.8</td>
<td>-15.2 ± 2.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GAS (%)</td>
<td>-30.2 ± 4.5</td>
<td>-27.5 ± 5.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GRS (%)</td>
<td>47.4 ± 9.2</td>
<td>43.1 ± 10.7</td>
<td>&lt;0.002</td>
</tr>
</tbody>
</table>

ANT, anthracycline; CO, cardiac output; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; GAS, global area strain; GCS, global circumferential strain; GLS, global circumferential strain; GRS, global radial strain; LVM/ht, left ventricular mass indexed for height; SV, stroke volume.

Post anthracycline
2D LVEF <50% = 0.0%
3D LVEF < 50% = 6.0%

Santoro C et al, EHJ CVI 2017
Survivors – Stage B HF?

N=1820

Armstrong GT et al, JACC 2016
Survivors – Stage B HF?

Tham et al. JCMR 2013;15:48
Survivors – Prognosis ECV

Neilan T et al, AJC 2013
Summary

• Cardiac imaging plays an important role in risk stratification (before, during, after)
  – Trastuzumab / Anthracyclines, image all high risk patients
  – Important knowledge gaps – other treatments?

• Echo based LVEF and GLS
  – Baseline LVEF/strain and strain change predictive
  – 3D LVEF more reproducible, diagnostic accuracy?
  – GLS based intervention – impact?
Summary

• CMR
  – Reproducible LVEF, tissue characterization
  – To understand mechanisms
  – Verification of abnormalities (during, survivors)
  – Detection of myocarditis

• Future: Risk based cardiac imaging / impact of imaging based interventions on outcomes
59M, Multiple Myeloma, Carfilozomib + Dex. No CV risk factors, stress test recently negative. Baseline LVEF 58%, GLS 19.0%, upper normal LV mass. After 3 cycles – SOB, NYHA II-III. Echo – LVEF 51%, GLS 15%, Gr II DDF, E/e’ 12.5. Concerned about discrepancy in the change in LVEF vs GLS (21%). Unclear cause of SOB. What imaging test would you order for further assessment?.

- A. Exercise stress echocardiogram to rule out coronary ischemia.
- B. Radionuclide angiogram / MUGA to obtain a more accurate LVEF
- C. Cardiac MRI to obtain a more accurate assessment of LVEF and rule out cardiac amyloid
- D. Do nothing and assume that the dyspnea is related to Carfilzomib therapy