Disclosures

- Janssen, Takeda, BI Advisory Board
Cardiovascular MRI Strengths
Role of CMR

1. Pre-treatment risk assessment
   - Treatment decision choices, follow-up plan

2. Early detection of CV injury during treatment
   - Promote intervention

3. Subclinical disease in survivors
   - Guide follow-up, risk factor management, prevention strategies

Hermann J et al, Circulation 2016; 133:1272-1289

Mariell Jessup and Susan Brozena
Early Detection of Myocardial Dysfunction

• N=53, breast and heme, Anthracycline (low / mod dose)
• MRI - LV volumes, LVEF, circumferential strain

¹Drafts et al, JACC cardiovascular imaging; 2013. 6:877-85
EMBRACE-MRI Study - HER2+ EBC

- Baseline CMR + echo
- Post Anthracycline, pre trastuzumab CMR + echo
- CMR + F/u echo
- CMR + F/u echo
- F/u echo

Time:
- Baseline
- 9-12 weeks
- 6 mos
- 9 mos
- 12 mos
- 15 mos

Therapies:
- Anthracycline Therapy
- Trastuzumab Therapy
Strain by ECHO vs LVEF MRI
**LVEF Reduction from Dehydration?**

From 112 participants receiving potentially cardiotoxic chemotherapy, 26 participants experienced baseline to 3 months LVEF drops of >10% or a decline to an absolute value of <50%.

\[
LVEF = \frac{LVEDV - LVESV}{LVEDV}
\]

- \(n=5\) ↓ EDV – ESV: Suggested Intravascular Volume Depletion (19.23%)
- \(n=1\) ↓ EDV ↑ ESV: Suggested Intravascular Volume Depletion + LV Systolic dysfunction (3.85%)
- \(n=15\) – EDV ↑ ESV: LV Systolic dysfunction (59.69%)
- \(n=5\) – EDV – ESV: Minor changes in either LV EDV or LV ESV (19.3%)

Melendez GC et al, AJC, 2017
Strain Reduction from Dehydration?

Jordan JG et al, Circulation 2017

No LVEF Decline
LVEF Decline: -EDV
LVEF Decline: +ESV
LVEF Decline: -EDV and +ESV
LVEF Decline: min volume changes
Impact of volume status LVEF/strain

No change in LVEF
What have we learned?

• Strain changes appear to follow LVEF changes seen with CMR
• Preload / afterload / inotropy are not independent - absence of reduction in ESV - ?marker of reduced inotropy
• Hemodynamics important consideration - LVEF/strain
• Given challenges of volume assessment by echocardiography – importance of repeated imaging at CTOX
Right Ventricular Function

Barthur A et al JCMR 2017, HER2+ BC
“Subclinical” Cardiac Injury

- 158 patients – various cancers, Adriamycin Rx
- Higher biopsy grades in pts with normal EF - even with moderate cumulative dose of Rx

Table 7. Comparison of Biopsy Grades With Ejection Fractions (EF)

<table>
<thead>
<tr>
<th>Biopsy Grade</th>
<th>Nuclear Scans (n = 173)</th>
<th>Echocardiogram (n = 146)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Patients</td>
<td>Mean EF</td>
</tr>
<tr>
<td>0</td>
<td>16</td>
<td>63%</td>
</tr>
<tr>
<td>0.5</td>
<td>50</td>
<td>66%</td>
</tr>
<tr>
<td>1.0</td>
<td>55</td>
<td>62%</td>
</tr>
<tr>
<td>1.5</td>
<td>21</td>
<td>58%</td>
</tr>
<tr>
<td>2.0</td>
<td>20</td>
<td>61%</td>
</tr>
<tr>
<td>3.0</td>
<td>11</td>
<td>61%</td>
</tr>
</tbody>
</table>

Fig. 2. Cardiac biopsy grade versus cumulative Adriamycin dose. The schedule of administration was by IV infusion over a 20-minute period every three to four weeks.
Tissue Characterization

EGE

LGE

T2 Weighted Imaging

The Promise of a Healthy Heart.
Myocardial Relaxometry

Thavendiranathan et al
JACC Imaging 2012

Wong et al, Circulation 2012
Myocardial Inflammation / Hyperemia

- Breast, lymphoma, sarcoma (n=22)
- MRI pre, day 3, 28, 6 mos (T1 weighted imaging)
- Doxo-67 ± 25 mg/m², Epi-76 ± 19 mg/m² first dose

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

Wassmuth et al. Am Heart J 2001;141:1007-13
Myocardial Inflammation / Hyperemia

HER2+ EBC - 17 v... Unpublished Data

<table>
<thead>
<tr>
<th>Baseline vs. post Baseline vs. post</th>
<th>AC CTOX</th>
<th>AC noCTOX</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value</td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td>0.003</td>
<td>0.003</td>
<td>0.42</td>
</tr>
<tr>
<td>0.06</td>
<td>0.08</td>
<td>0.27</td>
</tr>
<tr>
<td>0.5</td>
<td>0.1</td>
<td>0.41</td>
</tr>
<tr>
<td>0.03</td>
<td>0.02</td>
<td>0.09</td>
</tr>
</tbody>
</table>
Myocardial Edema

- 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

Myocardial Edema / Fibrosis?

<table>
<thead>
<tr>
<th></th>
<th>Anthracycline</th>
<th>Non-anthracycline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (N=40)</td>
<td>3 months (N=40)</td>
</tr>
<tr>
<td>Native T1, ms</td>
<td>1,058 ± 100</td>
<td>1,071 ± 85.2*</td>
</tr>
<tr>
<td>T2, ms</td>
<td>50.8 ± 2.9</td>
<td>51.6 ± 3.5</td>
</tr>
<tr>
<td>ECV, %</td>
<td>26.9 ± 3.1</td>
<td>28.6 ± 3.0*</td>
</tr>
</tbody>
</table>

Melendez GC et al. JACC Imaging 2017
Myocardial Edema – in HER2+ EBC
Myocarditis - Lake Louise Criteria

• In the setting of suspected myocarditis CMR findings c/w myocardial inflammation
  – Regional or global SI increase in T2 weighted images
  – Increase EGEr on T1 weighted images
  – Atleast 1 focal non-ischemic lesion on LGE images

1 criteria sens 88%, spec 48%
2 criteria sens 67%, spec 91%
? Better performance with quantitative methods

Myocarditis – ICIs

CMR in 31/35 patients
LGE in 74%

Mahmood et al JACC 2018
Vascular Disease

Hermann J et al, Circulation 2016; 133:1272-1289
Vascular Disease

Abdel-Qadir et al, JNCI, in press
Vascular Function

Kongbundansuk S and Hundley WG iJACC 2014, 7:824-38

Age associated aortic stiffness increase >15 years
Coronary Artery / Vascular Disease

Dynamic first-pass perfusion imaging (Adenosine)
Survivors
Left ventricular mass

- 91 patients, anthracycline CM (276 ± 82mg/m²)
- LVEF 36 ± 8%
- MACE – CV death, ICD therapy, decompensated HF
- 88 months post AC
- Followed for 27 months

Neilan et al. AJC 2012
Left ventricular mass

Jordan JH et al Circ HF 2018
Extracellular Volume Fraction

42AC Treated patients, 7 yrs prior
AC 282 ± 65mg/m²

Neilan T et al, AJC 2013

The Promise of a Healthy Heart
Extracellular Volume Fraction

- 30 childhood cancer survivors (15 ± 3 yrs)
- At least 2 years post anthracycline
- Hematological, sarcoma, wilm’s

Tham et al. JCMR 2013;15:48
## Tissue Characterization – LGE

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Chemo</th>
<th>%</th>
<th>Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fallah-Rad 2011</td>
<td>42</td>
<td>FEC-DH</td>
<td>25%</td>
<td>Lateral sub-epicardial in all 10 with CTX</td>
</tr>
<tr>
<td>Neilan et al 2012</td>
<td>81</td>
<td>Anthracycline, survivors</td>
<td>6%</td>
<td>Mid myocardial, RV insertion point, epicardial</td>
</tr>
<tr>
<td>Grover et al 2012</td>
<td>46</td>
<td>A or A + T, or T</td>
<td>2%</td>
<td>Subepicardial, lateral</td>
</tr>
<tr>
<td>Drafts 2013</td>
<td>53</td>
<td>A</td>
<td>0%</td>
<td>-</td>
</tr>
</tbody>
</table>
Other uses of CMR in the Oncology Patient

- Aortic stiffening increasing LV afterload
  - Increased AD
  - Decreased AD distensibility
  - Possible LGE or reduced LVEF

- Catheter-induced Thrombus
  - TIW imaging
  - No LGE or perfusion

- Pericardial inflammation and fibrosis
  - Septal shift with inspiration on real-time cine CMR
  - Fat/water separation to visualize pericardial space
  - Possible LGE

- Myocardial Contractile Dysfunction
  - Increased T2 or T2w signal
  - WMA and reduced LVEF

- Myocardial Injury / Myocardial Atrrophy
  - Declines in LV EF or myocardial strain
  - Possible diffuse LGE, increased T1 or ECV

- LV apical thrombus due to reduced contractility
  - TIW imaging
  - No LGE or perfusion

- Myocarditis
  - Non-ischemic LGE pattern with elevated T2 or T2w signal
  - Presence of LV dysfunction or pericardial effusion

- LV EF Decline due to Reduced Preload
  - LV EDV by SSFP cine stack

- Vascular Disease due to Radiation
  - Thickened valves on SSFP
  - Regurgitant flow on PC-CMR

- Microvascular Damage
  - Perfusion defect on stress CMR
  - Possible WMA

- Intermittent Myocardial Fibrosis
  - Increased T1, ECV
  - Possible focal LGE

- Infiltrative Diseases
  - Amyloidosis: Increased T1, ECV
  - Subendocardial or diffuse LGE
  - Concentric LV wall thickening with myocardial hypertrophy
  - Iron Overload: Reduced T2 and T2w

The Promise of a Healthy Heart.

UHN Peter Munk Cardiac Centre

TED ROGERS CENTRE FOR HEART RESEARCH

Jordan J et al, JACC Imaging 2018
Use of CMR in Cardio-oncology

• CMR imaging methods may potentially provide more sensitive measures of myocardial and vascular injury
  – More likely to identify myocardial and vascular functional changes
• Enhance pathophysiological understanding and how it relates to functional measures and serum biomarkers
• CMR - help improve the use of existing clinically available tools
• Existing data is quite limited – therapies, prognosis, intervention
• Opportunities for systematic studies / small sample sizes
Risk-Imaging Mismatch in Cardiac Imaging Practices for Women Receiving Systemic Therapy for Early-Stage Breast Cancer: A Population-Based Cohort Study

Palladinesh Thavendiranathan, 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...