Cardiac Stress MRI: Detection of Ischemia

Cardiac MRI in Today's Clinical Practice
Foundations of Cardiovascular Magnetic Resonance
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• Abbott Laboratories

Gadolinium-based contrast agents are not FDA approved for cardiac imaging.

Dobutamine Stress MR
Dobutamine Stress MR

- Protocol similar to echo: escalating doses of dobutamine at 3 minute intervals ± atropine to achieve target heart rate
- ECG ST segments not interpretable while in scanner, use wall motion assessment at each stage
- Cine imaging provides excellent image quality without contrast

Dobutamine Stress MR - accuracy

- 172 pts with DSE, DSMR, and Cath

<table>
<thead>
<tr>
<th></th>
<th>DSE</th>
<th>DSMR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient image-quality</td>
<td>18 (8.7%)</td>
<td>3 (1.8%)</td>
<td></td>
</tr>
<tr>
<td>Inadequate max heart rate</td>
<td>4 (1.9%)</td>
<td>2 (1.0%)</td>
<td></td>
</tr>
<tr>
<td>Severe obesity</td>
<td>...</td>
<td>3 (2.6%)</td>
<td></td>
</tr>
<tr>
<td>Claustrophobia</td>
<td>11 (5.3%)</td>
<td>1 (0.5%)</td>
<td></td>
</tr>
<tr>
<td>Metallic implants</td>
<td>...</td>
<td>1 (0.5%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>22 (10.6%)</td>
<td>22 (10.6%)</td>
<td></td>
</tr>
</tbody>
</table>


Dobutamine Stress MR - safety

<table>
<thead>
<tr>
<th></th>
<th>N=10001</th>
<th>N=16992</th>
</tr>
</thead>
<tbody>
<tr>
<td>Side Effects</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Sustained ventricular tachycardia</td>
<td>1 (0.1%)</td>
<td>2 (0.1%)</td>
</tr>
<tr>
<td>Non-sustained ventricular tachycardia</td>
<td>4 (0.4%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Paroxysmal atrial flutter/AF/T</td>
<td>16 (1.6%)</td>
<td>20 (1.2%)</td>
</tr>
<tr>
<td>Transient second degree AV block 2:1</td>
<td>2 (0.2%)</td>
<td>3 (0.2%)</td>
</tr>
<tr>
<td>Severe increase in BP (&gt;240/120 mmHg)</td>
<td>5 (0.5%)</td>
<td>3 (0.2%)</td>
</tr>
<tr>
<td>Decrease in systolic BP &gt;40 mmHg</td>
<td>5 (0.5%)</td>
<td>3 (0.2%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>31 (3.1%)</td>
<td>36 (2.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>64 (6.4%)</td>
<td>61 (3.6%)</td>
</tr>
</tbody>
</table>

Gebker et al. JCMR 2011; 13:46
Dobutamine Stress MR – clinical performance

Meta-Analysis of 14 studies (754 patients) undergoing MR wall motion imaging.

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.83 (0.79 - 0.86)</td>
<td>0.86 (0.81 - 0.91)</td>
<td>5.24 (3.28 - 7.21)</td>
<td>0.19 (0.15 - 0.24)</td>
</tr>
</tbody>
</table>

Cumulative Event 1y 2y 3y
- DSMR (-) 0.5% 0.8% 1.5%
- DSMR (+) 3.9% 4.9% 6.0%

Sensitivity Specificity LR+ LR- 0.83 (0.79 - 0.88) 0.86 (0.81 - 0.91) 5.24 (3.28 - 7.21) 0.19 (0.15 - 0.24)

Disease prevalence = 57.4%


Vasodilator Stress Perfusion MR

First-Pass Perfusion Imaging

N Northwester Medicine

First-Pass Perfusion Imaging
Two Phases of Myocardial Enhancement

Adenosine Perfusion

Stress

Rest

Adenosine Perfusion

Stress

Rest
Subendocardial perfusion

High spatial resolution of MRI enables measurement of gradients in transmural flow (from endo- to epicardium)


Syndrome X

- High spatial resolution enables assessment of blood flow across the myocardial wall
- Endo/Epi perfusion reserve index was lower in patients with Syndrome X than controls

Panting et al. NEJM 2002; 346(25): 1948
**Dark Rim Artifact**

- Transient subendocardial dark band, most prominent at peak blood pool enhancement, especially in phase encode direction
- Causes include Gibbs ringing, susceptibility, motion
- Solutions:
  - Increase resolution
  - Compare stress, rest, and LGE
    - Stress(+), rest (-), LGE(-) → ischemia
    - Stress(+), rest (+), LGE(-) → scar
    - Stress(+), rest (+), LGE(+) → artifact

Dilella et al. MRM 2005;54:1295-99
Elm et al. AJC 2002;47:1630-8

**Clinical Performance**

Meta Analysis of 24 studies (1516 patients) undergoing MR perfusion imaging.

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.91 (0.88 - 0.94)</td>
<td>0.81 (0.77 - 0.85)</td>
<td>5.10 (3.92 - 6.28)</td>
<td>0.11 (0.07 - 0.15)</td>
</tr>
</tbody>
</table>

Disease prevalence = 57.4%


**Cumulative Event Rate**

<table>
<thead>
<tr>
<th></th>
<th>1y</th>
<th>2y</th>
<th>3y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nl</td>
<td>0.7</td>
<td>0.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Abn</td>
<td>0.2</td>
<td>12.2</td>
<td>16.3</td>
</tr>
</tbody>
</table>

**MRI vs. SPECT perfusion**

CMR-IMPACT II: 533 pts; 46% CAD
33 SITES
CMR/SPECT, Cath order per MD
MR-IMPACT II: Only Rest/Stress Per interpreted

<table>
<thead>
<tr>
<th>CMR</th>
<th>SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>81.9%*</td>
</tr>
<tr>
<td>Specificity</td>
<td>85.9%</td>
</tr>
<tr>
<td>PPV</td>
<td>70.9%*</td>
</tr>
<tr>
<td>NPV</td>
<td>87.8%*</td>
</tr>
</tbody>
</table>

CE-MARC: 752 patients; 38% CAD
All imaging at one site
CMR/SPECT, Cath order per protocol
SPECT: Rest/Stress Perf, Card
CMR: Rest/Stress Perf, CF, Viability

<table>
<thead>
<tr>
<th>CMR</th>
<th>SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>75%*</td>
</tr>
<tr>
<td>Specificity</td>
<td>38%</td>
</tr>
<tr>
<td>PPV</td>
<td>70%</td>
</tr>
<tr>
<td>NPV</td>
<td>65%</td>
</tr>
</tbody>
</table>

### Multimodality Appropriate Use Criteria for the Detection and Risk Assessment of Stable Ischemic Heart Disease

<table>
<thead>
<tr>
<th>Indication</th>
<th>Stress RNI</th>
<th>Stress Echo</th>
<th>Stress CMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate/High prob CAD, unable exercise</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>High prob CAD, able to exercise</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Newly diagnosed systolic/diastolic heart failure</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Sustained VT, V5, Exercise VT, prior to antiarrhythmic</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Syncope with Intermediate/High CAD risk</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Abnormal rest ECG, Intermediate/high CAD risk</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Obstructive CAD on CCT/angiography</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Stenosis of unclear significance on CCT/angiography</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Ischemic symptoms post revascularization</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
</tbody>
</table>

### Comprehensive Cardiovascular Exam

- **Stress**
- **Cine**
- **Flow**
- **MRA**
- **Mapping**
- **LGE**

### Indications
- CAD
- Microvascular disease
- LV/RV ED/ES
- Congestive heart failure
- Valve disease
- Shunt
- Aortic aneurysm
- Pulmonary veins
- Iron overload
- Infiltrative disease
- Edema

### Limitations:
- Pharmacologic stress only – although hardware and procedures to perform exercise stress CMR are in development
- Limited slice coverage compared with nuclear
- Dark rim artifact
- Cardiovascular implantable electronic devices (PPM/ICD)
- Renal impairment - NSF
- Claustrophobia

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Wolk et al. JACC 2014;63:380-406

Kramer et al. Standardized cardiovascular magnetic resonance (CMR) protocols 2013 update. JCMR 2013, 15:91

Schulz-Menger et al. Standardized image interpretation and post-processing in CMR. JCMR 2013
Quantification of myocardial perfusion

- Perfusion assessment can be visual, semiquantitative (index), or fully quantitative (mL/min/g)
- Based on the principles of indicator-dilution, flow can be calculated by deconvolution of myocardial and blood signal intensity-time curves [1]
- Quantitative is more accurate than visual [2], semiquantitative [3]
- Pixelwise CMR perfusion quantification now possible [4,5]


Effect on Outcomes: CE-MARC2 Trial

- 1202 patients with chest pain and intermediate probability CAD randomized to:
  - CMR guided care
  - MPS guided care
  - UK NICE Guidelines based care
- Adjusted odds ratio of unnecessary angiography: CMR group vs NICE guidelines group, 0.21 (95% CI, 0.12-0.34, P < .001)

<table>
<thead>
<tr>
<th></th>
<th>NICE (n=240)</th>
<th>CMR (n=481)</th>
<th>MPS (n=481)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unnecessary invasive angiography</td>
<td>69 (28.8%)</td>
<td>36 (7.5%)</td>
<td>34 (7.1%)</td>
</tr>
<tr>
<td>Hard events (CV death or MI)</td>
<td>3 (1.3%)</td>
<td>5 (1.0%)</td>
<td>4 (0.8%)</td>
</tr>
</tbody>
</table>


Effect on Outcomes: MR-IMPACT

- 918 patients with
  - Stable angina CCS II-III
  - ≥2 risk factors
  - Positive exercise treadmill test
- Randomized to
  - MR guided
  - Invasive FFR guided
- Lower revascularization rate in MR-INFORMED
- MACE rate non-inferior
Summary:

- Dobutamine stress wall motion assessment and vasodilated myocardial perfusion imaging are the principle techniques for ischemia assessment by CMR
- Cardiac stress MRI techniques are safe, accurate, and predict prognosis
- Cardiac stress MRI can be combined with other techniques (MRA, LGE, parametric mapping, flow) for a comprehensive cardiovascular exam
- Future developments in acquisition, analysis (e.g. perfusion quantification), and clinical outcome trials

Thank you.