Myocardial Viability: CMR

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Disclosures

- GE Healthcare: Consultant
- I will be talking about use of gadolinium contrast in a manner that is not FDA approved
- I may purposely take an extreme position
Outline

• Viability assessment with cardiovascular magnetic resonance (CMR) using late gadolinium enhancement (LGE)
• Superiority of CMR compared to PET
Gadolinium Contrast Kinetics in Myocardium

Kim et al, Circulation, Dec 1996; 94: 3318 - 3326
LGE Imaging Protocol

Determine TI Image

Gd

10 to 20 min
Late Gadolinium Enhancement
Prediction of Recovery of Function

Normal Myocardium
Anterior/Apical Scar
Ischemic CM with Viable Myocardium
Is CMR Superior to PET?

- Cost
- Safety
- Ease of implementation
- Accuracy
Is CMR Superior to PET?: Cost

• Cost
  – Medicare payment (rough estimate of cost to society)
    • CMR ~$750
    • PET ~$1400
  – Hospital margins/physician payments
    • PET > CMR

• Conclusion: CMR is superior
Is CMR Superior to PET?: Safety

• Safety
  – PET
    • Radiation
    • Hypoglycemia
  – CMR
    • NSF
    • Devices
      – ICDs typically implanted after revascularization
      – Can be imaged safely if appropriate steps are taken

• Conclusion: CMR and PET are both generally safe in this patient population
Is CMR Superior to PET?: Ease of Implementation

• Patient preparation for FDG PET is arduous
  – Hyperinsulinemic/euglycemic clamp
  – IV glucose loading +/- insulin
  – Oral glucose loading +/- insulin
  – (Acipimox is not FDA approved)
Patient Preparation Protocol for Myocardial Viability Imaging with FDG.

1. When the appointment is scheduled, obtain the following history:
   - Presence of diabetes
   - Presence of renal insufficiency
   - Presence of allergy to insulin (TRUE allergy only, not adverse reaction)

   If the patient is allergic to insulin, it is unlikely that imaging will be successful and an alternative imaging method should be suggested.

   If the patient has renal insufficiency, the pharmacokinetics of insulin may be altered. Please consult with the imaging physician to determine if this patient preparation protocol should be followed.

2. Instruct patient to fast overnight prior to the procedure. Patients may take their usual medication with the exception of their diabetes medications. Oral diabetes medications should not be taken the morning of imaging. Patients taking insulin should take no regular insulin and half the dose of their usual long-acting insulin.

3. Upon patient arrival on the day of imaging:
   - Place intravenous line
   - Check initial blood sugar (BS)

4. Give glucose according to the following protocol:

<table>
<thead>
<tr>
<th>Diabetes?</th>
<th>BS</th>
<th>Oral Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>≤150</td>
<td>50 g</td>
</tr>
<tr>
<td></td>
<td>151 to 250</td>
<td>25 g</td>
</tr>
<tr>
<td></td>
<td>&gt;250</td>
<td>None</td>
</tr>
<tr>
<td>Yes</td>
<td>≤150</td>
<td>25 g</td>
</tr>
<tr>
<td></td>
<td>151 to 250</td>
<td>12.5 g</td>
</tr>
<tr>
<td></td>
<td>&gt;250</td>
<td>None</td>
</tr>
</tbody>
</table>

   5. If the initial BS is >250, then give IV regular insulin according to the protocol below. If oral glucose is given, recheck BS in 30 minutes and then give IV regular insulin according to the same protocol.

<table>
<thead>
<tr>
<th>Give IV regular insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>BS 70 to 140</td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>BS 141 to 160</td>
</tr>
<tr>
<td>1 unit</td>
</tr>
<tr>
<td>BS 161 to 180</td>
</tr>
<tr>
<td>2 units</td>
</tr>
<tr>
<td>BS 181 to 200</td>
</tr>
<tr>
<td>3 units</td>
</tr>
<tr>
<td>BS 201 to 220</td>
</tr>
<tr>
<td>4 units</td>
</tr>
<tr>
<td>BS 221 to 240</td>
</tr>
<tr>
<td>5 units</td>
</tr>
<tr>
<td>BS 241 to 260</td>
</tr>
<tr>
<td>6 units</td>
</tr>
<tr>
<td>BS 261 to 280</td>
</tr>
<tr>
<td>7 units</td>
</tr>
<tr>
<td>BS 281 to 300</td>
</tr>
<tr>
<td>8 units</td>
</tr>
<tr>
<td>BS &gt;300</td>
</tr>
<tr>
<td>Notify Physician</td>
</tr>
</tbody>
</table>

6. Check BS every 15 minutes.
   - If BS is <140, inject FDG
     - If BS continues to rise, give IV regular insulin according to the protocol above and continue to check BS every 15 minutes
     - If BS is falling but remains elevated, give IV regular insulin at half the dose according to the protocol above and continue to check BS every 15 minutes
     - If BS remains elevated after 90 minutes, contact the imaging physician

7. Have the patient eat a light meal 15 minutes after injection of FDG.

8. Continue to check BS every 30 minutes after injection of FDG to monitor for hypoglycemia.

9. Begin imaging 60-90 minutes after injection of FDG.

10. After imaging, monitor patient for 30 minutes and obtain BS. If BS >70 then the patient can be discharged.

11. Upon discharge instruct the patient to:
   - Beware of hypoglycemia. Encourage the patient to have a meal soon after discharge.
   - Resume all prior medications.

   If at any time during the protocol there is a question about how to proceed, contact the imaging physician immediately.
PET Imaging Protocol

Glucose → Insulin → FDG → Image

Monitor for Hypoglycemia

2 to 3 hours
Failure of Patient Preparation
Is CMR Superior to PET?:
Superior Spatial Resolution/Scar Imaging

Wagner et al. Lancet. 2003;361:374
Is CMR Superior to PET?: Prediction of Recovery of Function

- 41 patients imaged before and ~80 days after revasc.
- 78% of segments with no LGE had recovery of function
- 92% of segments with >50% transmural LGE did not recover
- 36% of all segments had an intermediate probability of recovery
- Sensitivity 95%
- Specificity 72%

Is CMR Superior to PET?:
Direct Comparison of FDG PET and CMR

- Wu et al imaged 28 patients before and ~20 days after revasc.
- CMR (>50% transmural)
  - Sensitivity 92%
  - Specificity 45%
- PET/SPECT (>50% normalized uptake)
  - Sensitivity 99%
  - Specificity 60%
- ROC analysis showed no significant difference
Is CMR Superior to PET?:
Multicenter Trials

- Lenge et al imaged 183 patients before and ~6 months after revasc.
- 72% of segments with no LGE had recovery of function
- 83% of segments with >50% transmural LGE did not recover
- 21% of all segments had an intermediate probability of recovery
- Sensitivity 88%
- Specificity 62%

Lenge et al, SCMR 2008
Is CMR Superior to PET?: Multicenter Trials

- Gerber et al imaged 178 patients before and 2 to 6 months after revasc.
- Endpoint was >5% improvement in LVEF
  - RVG, echo, LV gram

![Graph showing sensitivity, specificity, and accuracy for the prediction of postoperative improvement of ejection fraction by more than 5% using different cut-off points, as determined by receiver operating curve analysis. Error bars indicate standard deviation of mean.](image-url)

*Figure 5* Sensitivity ■, specificity □, and accuracy □ for the prediction of postoperative improvement of ejection fraction by more than 5% using different cut-off points, as determined by receiver operating curve analysis. Error bars indicate standard deviation of mean.

Gerber et al, Eur Heart J 2001; 22, 1691–1701
Is CMR Superior to PET?: Comprehensive Evaluation

- Structure
- Function
  - With or without stress
- Flows
- Perfusion
  - With or without stress
- Scar/Viability
- Coronary Anatomy
Is CMR Superior to PET?

- Cost: CMR is superior
- Safety: Both are generally safe in this population
- Ease of implementation: CMR is superior
- Accuracy: CMR is superior
CMR 3.5

PET 0.5

Nephrogenic Systemic Fibrosis

- Potentially fatal sclerotic disease
- Epidemiologically linked to the administration of gadolinium to patients with severe renal failure
  - Typically on dialysis
  - Single agent (Omniscan) responsible for the vast majority of cases
    - No cases with ProHance
- Less than 300 reported cases worldwide

Garovic and Helgen, N Engl J Med 357;2
Intermediate Probability Segments: Dobutamine CMR

PET: Poor Specificity

- Gerber et al also assessed myocardial glucose uptake during hyperinsulinemic-euglycemic clamping
- Large overlap of normal and dysfunctional segments with wide intra- and inter-patient variation
- Probable large overlap of those segments that recover and those that do not recover (data not reported)

Figure 3: Histogram illustrating variations in absolute myocardial glucose uptake in normal (top) and dysfunctional (bottom) segments.

Gerber et al, Eur Heart J 2001; 22, 1691–1701
PET: Scar is More Important than Mismatch

- Beanlands et al evaluated 70 patients before and after revasc.
- “Scar” score was the most important predictor of recovery of function
  - Superior to mismatch score in both univariate and multivariate analyses

Table 2. Independent Predictors of Change in LV Function

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Coefficient Value Beta</th>
<th>SE</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scar score (%LV)</td>
<td>-0.451</td>
<td>0.097</td>
<td>0.001</td>
</tr>
<tr>
<td>Mismatch score (%LV)</td>
<td>-0.319</td>
<td>0.177</td>
<td>0.085</td>
</tr>
<tr>
<td>Tracer</td>
<td>-0.384</td>
<td>3.164</td>
<td>0.043</td>
</tr>
<tr>
<td>Tracer/mismatch interaction*</td>
<td>0.500</td>
<td>0.215</td>
<td>0.021</td>
</tr>
<tr>
<td>Time to OR (&lt;6 weeks)</td>
<td>0.286</td>
<td>1.969</td>
<td>0.008</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.237</td>
<td>1.878</td>
<td>0.029</td>
</tr>
<tr>
<td>Age</td>
<td>0.185</td>
<td>0.101</td>
<td>0.088</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>0.110</td>
<td>3.164</td>
<td>0.295</td>
</tr>
</tbody>
</table>

*Reflects the contribution of the interaction term.

CABG = coronary artery bypass graft; LV = left ventricle; OR = revascularization; SE = standard error.

Beanlands et al (PARR-1) JACC 2002;40:1735–43
PET Only Images Myocardium, Not Scar

$18$FDG-Uptake ($\%$)

Thickness viable tissue (mm)

- Match: $r = 0.84$
- Mismatch: $r = 0.72$

All data: $y = -0.18x^2 + 8.04x + 19.41$, $p < 0.0001$
PET: Fails to Improve Clinical Outcomes

- Beanlands et al randomized 430 patients to FDG PET guided revascularization or standard care
- Primary endpoint was a composite of cardiac death, MI or hospital stay for a cardiac cause at 1 year
- No significant difference in the primary endpoint or survival

Figure 3
Mantel-Haenszel test for differences between 2 survival curves; chi-square = 2.1, p = 0.14

Figure 4
"Survival" Curves (on the Basis of Time to Cardiac Death) for All Subjects
Mantel-Haenszel (log-rank) test for differences between 2 survival curves; chi-square = 1.3, hazard ratio = 0.72, 95% CI 0.4 to 1.3, p = 0.25. PET = positron emission tomography.
CMR is Superior to PET for Assessment of Myocardial Viability

- Affordable
- Easy to perform
- Safe
- Superior image quality
- Comprehensive cardiac assessment
- Superior accuracy for detection of scar and determination of viability
- Not yet proven to be clinically ineffective