Cardiovascular Magnetic Resonance of the Area at Risk and Myocardial Salvage

Ingo Eitel, MD

University Leipzig – Heart Center – Germany
I have no financial relationships to disclose.

- and –

I will not discuss off label use and/or investigational use in my presentation.
Reperfusion and Myocardial Salvage
Reperfusion and Myocardial Salvage

- Myocardium at risk
- Final infarct size

40 minutes
3 hours
96 hours

Kloner et al *J Clin Invest* 1974
Reimer et al *Circulation* 1977
In animal studies small variations in the myocardium at risk accounted for >70% of the variability in the extent of myocardial necrosis.
Myocardial Salvage

Area at risk (white) - Infarct size (black) = Myocardial salvage (green)
Myocardial Salvage - SPECT

Schomig et al *NEJM* 2000
Kastrati et al *Lancet* 2002
Kastrati et al *JACC* 2004
Carlsson *JACC Img* 2009
SPECT - Limitations

- low spatial resolution;
- need for tracer administration;
- interfering with patient management in the acute setting;
- access to a gamma camera <3 h of the tracer administration;
- need of two scans;
- application of radiation dose in both scans;

Wagner et al Lancet 2003
Carlsson JACC Img 2009
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CMR – Area at Risk

Higgins et al Am J Cardiol 1983
Area at risk – Animal Studies

Dog
Day 2

Dog
Month 2

LGE  FISP-ED  T2W  DENSE

Aletras et al Circulation 2006
Area at risk – Animal Studies

- **Day 0**
  - Area at risk
  - T2W
  - Infarct (LGE)

- **Day 2**
  - Area at risk
  - T2W
  - Infarct (LGE)

**Comparisons:**
- T2W vs. Area at risk: **p=NS**
- Infarct (LGE) vs. Area at risk: **p<0.001**
- Infarct (LGE) vs. T2W: **p<0.001**

*Aletras et al, Circulation 2006*
Area at risk – Animal Studies

Myocardial Salvage – Humans

Healthy control

Patient with inferior myocardial infarction

Friedrich et al JACC 2008
Myocardial Salvage – Humans

T2 Imaging

Friedrich et al JACC 2008
CMR versus SPECT- Validation

Carlsson et al JACC Img 2009
CMR versus Angiographic Scores - Validation

\[ R = 0.77 \]

\[ n = 50 \]

Berry et al *Circ Cardiovasc Img* 2010
CMR versus Angiographic Scores - Validation

\[ R = 0.87 \]

\[ n = 197 \]

Fuernau, Eitel et al *JACC Img* 2011, in press
Myocardial Salvage - Reproducibility

Desch, Eitel et al *Int J Cardiovasc Img* 2011, epub ahead of print
Myocardial salvage is the principal mechanism by which patients with acute myocardial infarction benefit from reperfusion therapies.

CMR allows for quantifying the extent of the salvaged area after reperfusion as an important clinical parameter.

Clinical data?
Myocardial Salvage – Clinical studies

First in-vivo, clinical, non-invasive evaluation of the consequences of early and delayed coronary reperfusion on myocardial salvage

n=70 STEMI, primary PCI

Time-to-reperfusion

- ≤90min: n=19
- >90-150min: n=17
- >150-360min: n=17
- >360min: n=17
Myocardial Salvage – Clinical Studies

Francone et al JACC 2009

Time to reperfusion (min)

Myocardial Salvage (%)

≤90 min >90-150 min >150-360 min >360 min

Area at risk (T2)

Infarct Size (LGE)

Myocardial Salvage (%)

p=0.003

Time to reperfusion (min)

≤90 >90-150 >150-360 >360

Francone et al JACC 2009
Myocardial Salvage

Time from symptom onset to reperfusion (h)

Myocardial Salvage (%LV)

Gersh et al. JAMA 2005
### Myocardial Salvage – Clinical Studies

#### Baseline Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate OR (95% CI)</th>
<th>p Value</th>
<th>Multivariate OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI transmurally (%)</td>
<td>1.04 (1.01–1.07)</td>
<td>0.005</td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>AAR (% of LV)</td>
<td>1.04 (1.01–1.07)</td>
<td>0.003</td>
<td>1.04 (1.01–1.08)</td>
<td>0.001</td>
</tr>
<tr>
<td>MSI (for 0.10 increment)</td>
<td>0.58 (0.46–9.75)</td>
<td>&lt;0.0001</td>
<td>0.64 (0.49–0.84)</td>
<td>0.001</td>
</tr>
<tr>
<td>Presence of MO</td>
<td>6.79 (3.55–18.06)</td>
<td>&lt;0.0001</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Time to reperfusion (min)</td>
<td>1.00 (0.99–1.00)</td>
<td>0.588</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Age (for 10-yr increment)</td>
<td>1.22 (0.87–1.72)</td>
<td>0.241</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Anterior vs. nonanterior MI</td>
<td>2.27 (1.02–5.04)</td>
<td>0.044</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>0.92 (0.87–0.97)</td>
<td>0.003</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

AAR = area at risk; CI = confidence interval; LV = left ventricle/ventricular; MI = myocardial infarction; MO = microvascular obstruction; MSI = myocardial signal intensity.

Masci et al *JACC Img* 2010
## Myocardial Salvage – Clinical Studies

<table>
<thead>
<tr>
<th>Baseline Variables</th>
<th>Early ST-Segment Resolution (%)</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MI transmurality (%)</td>
<td>$-0.79$</td>
<td>$&lt;0.0001$</td>
<td>$-0.31$</td>
</tr>
<tr>
<td>AAR (% of left ventricle)</td>
<td>$-0.48$</td>
<td>$0.007$</td>
<td>—</td>
</tr>
<tr>
<td>MSI</td>
<td>$0.85$</td>
<td>$&lt;0.0001$</td>
<td>$0.61$</td>
</tr>
<tr>
<td>Presence of MO</td>
<td>$0.14$</td>
<td>$0.371$</td>
<td>—</td>
</tr>
<tr>
<td>Time to reperfusion</td>
<td>$-0.23$</td>
<td>$0.130$</td>
<td>—</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>$0.01$</td>
<td>$0.941$</td>
<td>—</td>
</tr>
<tr>
<td>Anterior vs. nonanterior MI</td>
<td>$-0.41$</td>
<td>$0.007$</td>
<td>$-0.16$</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>$0.45$</td>
<td>$0.011$</td>
<td>—</td>
</tr>
</tbody>
</table>

Masci et al *JACC Img* 2010
Eligible STEMI patients (n=267)

No inclusion:
- Prior myocardial infarction (n=29)
- No informed consent (n=3)
- Technical reasons (n=4)

No CMR:
- Claustrophobia (n=11)
- Death (n=7)
- Refusal (n=2)
- Dyspnea (n=2)
- Metallic implant (n=1)

CMR (n=208)

MSI < median (n=104)
- Lost to 6 month follow-up (n=0)
- Endpoint analysis (n=104)

MSI ≥ median (n=104)
- Lost to 6 month follow-up (n=0)
- Endpoint analysis (n=104)

Myocardial Salvage – Clinical Studies
Prognosis in STEMI

• Time-to-reperfusion

• ECG parameters (ST-resolution)

• Angiographic parameters (TIMI-flow)

De Luca et al Circulation 2004
Schröder et al Circulation 2004
Stone et al Circulation 2001
Myocardial Salvage and Infarct Location

$56 \pm 26$

$p = 0.02$

$47 \pm 26$

Eitel et al. JACC 2010
Myocardial Salvage and TIMI flow

![Graph showing TIMI flow 0-1 and TIMI flow 2-3 with MSI](image)

- TIMI flow 0-1: 44 ± 24
- TIMI flow 2-3: 59 ± 26

*p < 0.001*

Eitel et al JACC 2010
Myocardial Salvage and ST-resolution

Eitel et al JACC 2010
RESULTS: MSI and time to reperfusion

Symptom onset to reperfusion time (minutes)

Eitel et al JACC 2010
RESULTS: MSI and time to reperfusion

Symptom onset to reperfusion time (minutes)

- <120 minutes: 73 (59-98)
- 120-240 minutes: 53 (34-74)
- 241-360 minutes: 43 (28-66)
- 361-480 minutes
- 481-600 minutes
- 601-720 minutes

Eitel et al JACC 2010
RESULTS: MSI and time to reperfusion

Symptom onset to reperfusion time (minutes)

- <120: 73 (59-98)
- 120-240: 53 (34-74)
- 241-360: 43 (28-66)
- 361-480: 38 (21-69)
- 481-600: 25 (16-62)
- 601-720: 26 (10-55)

Eitel et al JACC 2010
Myocardial Salvage and Mortality

- Log-rank test $p=0.003$
- **MSI < median**
- **MSI ≥ median**

Eitel et al. JACC 2010
Myocardial Salvage and MACE

Log-rank test \( p < 0.001 \)

- MSI < median
- MSI ≥ median

Eitel et al JACC 2010
Eligible STEMI patients (n=267)

No inclusion:
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No CMR:
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- Refusal (n=2)
- Dyspnea (n=2)
- Metallic implant (n=1)

CMR (n=208)

18.5 (13.8 to 20.8) months

METHODS

LONG TERM FOLLOW-UP (n=102)

MSI < median (n=104)
- LOST to 6 month follow-up (n=0)
- LOST to long term follow-up (n=2)

MSI ≥ median (n=104)
- LOST to 6 month follow-up (n=0)
- LOST to long term follow-up (n=5)

LONG TERM FOLLOW-UP (n=99)
Myocardial Salvage and Long-term Mortality

Log-rank test $p=0.001$

Eitel et al. *Heart* 2011, in press
Myocardial Salvage and Long-term MACE

Log-rank test p<0.001

MSI < median

MSI > median

Eitel et al. *Heart* 2011, in press
Area at risk in NST-ACS

Mortality

Days after Infarction

0 50 100 150

Edema negativ

Edema positiv

Raman et al JACC 2010
Myocardial Salvage – Summary II

- Myocardial salvage assessed by CMR predicts LV remodeling and patient prognosis

- The prognostic value of myocardial salvage enables its use as a primary endpoint in clinical trials assessing the efficacy of reperfusion

- Limitations?
Myocardial Salvage: Limitations

T2-weighted CMR of the area at risk—a risky business?

W. Benjamin Wince and Raymond J. Kim

Wince and Kim Nat Rev Cardiol 2010
Myocardial Salvage: Limitations

- Low signal-to-noise ratio and the relatively small differences in contrast-to-noise ratios between injured and normal myocardium.

- Dark-blood preparation used in TSE T2-weighted imaging may introduce significant signal loss due to through-plane cardiac motion, typically most noticeable in the posterior wall.

- Incomplete dark-blood preparation sometimes leaves a bright rim blood artifact adjacent to the endocardium (“slow flow artefact”).

- Subjective nature of T2-weighted CMR image interpretation.

Wince and Kim *Nat Rev Cardiol* 2010
Eitel and Friedirch *JCMR* 2011
Myocardial Salvage: Dark versus bright blood

Table 5. Sensitivity and Specificity of Bright-Blood TSE-SSFP and Dark-Blood STIR MRI for Detection of Anterior Versus Nonanterior MI

<table>
<thead>
<tr>
<th></th>
<th>Bright Blood T2-Weighted MRI</th>
<th>Dark Blood T2-Weighted MRI</th>
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<tbody>
<tr>
<td></td>
<td>Anterior Edema</td>
<td>Nonanterior Edema</td>
</tr>
<tr>
<td>Anterior MI (n=28)</td>
<td>27</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sensitivity = 96%</td>
<td></td>
</tr>
<tr>
<td>Nonanterior MI (n=26)</td>
<td>0</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Specificity = 100%</td>
<td></td>
</tr>
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Payne et al *Circ Cardiovasc Img* 2011
Myocardial Salvage – T2 mapping

T2 mapping  T2 STIR  LGE

Girie et al *JCMR* 2010
Verheart *JACC Img* 2011
Myocardial Salvage: Other Methods

![Graph showing correlation between T2-weighted Area at Risk and Infarct Endocardial Surface Area with an r value of 0.77.]

Ortiz-Perez *Eur Heart J* 2007
Wright et al *JACC Img* 2009
Ubachs et al *JCMR* 2010
Myocardial Salvage: Other Methods

Aborted MI
> 90% Salvage
43% Salvage
3% Salvage

40% Salvage
27% Salvage
22% Salvage

Ubachs et al JCMR 2010
Myocardial Salvage: Other Methods

Matsumoto et al. *JACC Img* 2011
Myocardial Salvage: When to image?

Dell`Armellina et al. *Circ Cardiovasc Img* 2011

![Bar chart showing % LV Myocardial Oedema over time after revascularisation. The chart indicates statistical significance (P<0.01) for certain time points.](chart.png)
T2-weighted CMR of the area at risk and myocardial salvage is a validated, unique technique which allows for quantifying the extent of the salvaged area after reperfusion as an important clinical parameter.

Myocardial salvage assessed with CMR predicts LV remodeling and mortality in patients with acute reperfused myocardial infarction.

Myocardial salvage assessment has important implications for the design of future trials intended to test new reperfusion therapy efficacy.

Is CMR imaging of the area at risk and myocardial salvage imaging a new diagnostic target: YES!
Thank you for your attention

ingo.eitel@medizin.uni-leipzig.de
ingoeitel@gmx.de