CMR Perfusion and Viability
A STICH Out of Time?

Sung A Chang

Department of Internal Medicine, Division of Cardiology, Sungkyunkwan University School of Medicine, Samsung Medical Center
Can Imaging Improve Patient’s Outcome?
Myocardial viability in ischemic heart disease

Myocardial Viability
dysfunctional myocardium subtended by diseased coronary arteries with limited or absent scarring that therefore has the potential for functional recovery
Myocardial Viability and Survival in patients with CAD and Severe LV Dysfunction

Group I: Viability(+) and revascularization

Group II: Viability(+) and medical Tx

Group III: Viability(-) and revascularization

Group IV: Viability(-) and medical Tx

P = 0.01 Group I vs rest

Myocardial Viability Testing and Impact of Revascularization

Meta analysis of 3088 patients (DSE/SPECT/ PET)

Allman et al. JACC Vol. 39, No. 7, 2002
Coronary Artery Bypass Graft Surgery in Patients with Ischemic Heart Failure

Eric J. Velazquez, MD
on behalf of the STICH Investigators
All-Cause Mortality
— As Randomized

HR 0.86 (0.72, 1.04)
P = 0.123

Cardiovascular Mortality — As Randomized

HR 0.81 (0.66, 1.00)
P = 0.050
Adjusted HR 0.77 (0.62, 0.94)
Adjusted P = 0.012

Myocardial Viability and Survival in Ischemic Left Ventricular Dysfunction

Robert O. Bonow, M.D., Gerald Maurer, M.D., Kerry L. Lee, Ph.D., Thomas A. Holly, M.D., Philip F. Binkley, M.D., Patrice Desvigne-Nickens, M.D., Jaroslaw Drozdz, M.D., Ph.D., Pedro S. Farsky, M.D., Arthur M. Feldman, M.D., Torsten Doenst, M.D., Ph.D., Robert E. Michler, M.D., Daniel S. Berman, M.D., Jose C. Nicolau, M.D., Ph.D., Patricia A. Pellikka, M.D., Krzysztof Wrobel, M.D., Nasri Alotti, M.D., Ph.D., Federico M. Asch, M.D., Liliana E. Favaloro, M.D., Lilin She, Ph.D., Eric J. Velazquez, M.D., Robert H. Jones, M.D., and Julio A. Panza, M.D., for the STICH Trial Investigators*
K-M analysis of the probability of death

Hazard ratio, 0.64 (95% CI, 0.48–0.86)
P=0.003

P=0.21 after adjusting for baseline variables

No. at Risk
Without viability 114 99 85 80 63 36 16
With viability 487 432 409 371 294 188 102

K-M analysis of CV mortality

P=0.21 after adjusting for baseline variables
### A Without Myocardial Viability

- **Medical therapy** (33 deaths)
- **CABG** (25 deaths)

<table>
<thead>
<tr>
<th>Years since Randomization</th>
<th>No. at Risk</th>
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<tr>
<td></td>
<td>Medical therapy</td>
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<tr>
<td>0</td>
<td>60</td>
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<tr>
<td>1</td>
<td>51</td>
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<tr>
<td>2</td>
<td>44</td>
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</tr>
<tr>
<td>5</td>
<td>14</td>
</tr>
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<td>6</td>
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</table>

### B With Myocardial Viability

- **Medical therapy** (95 deaths)
- **CABG** (83 deaths)

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<tr>
<td>1</td>
<td>219</td>
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<td>2</td>
<td>206</td>
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<td>179</td>
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<tr>
<td>4</td>
<td>146</td>
</tr>
<tr>
<td>5</td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>51</td>
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</table>

### C

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No.</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without viability</td>
<td>114</td>
<td>58</td>
</tr>
<tr>
<td>With viability</td>
<td>487</td>
<td>178</td>
</tr>
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</table>

**Hazard Ratio (95% CI)**

- **Without viability**
  - Medical therapy: 0.70 (0.41–1.18)
  - CABG: 0.86 (0.64–1.16)

**P Value for Interaction**: 0.53

- **CABG Better**
- **Medical Therapy Better**
Viability Testing for Myocardium

IT’S USELESS!
Cardiac Imaging for Viability

- **Echo**
- **Nuclear test**
- **Cardiac MR**
- **Cardiac CT**
by SPECT or dobutamine echo

Myocardial Viability and Survival in Ischemic Left Ventricular Dysfunction

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and Julio A. Panza, M.D., for the STICH Trial Investigators*
Limitations of the STICH viability substudy

Lack of randomization in viability substudy
Optional viability testing performed at clinician’s discretion
Only about one-half of eligible patients from the main trial
Significant differences in baseline characteristics between those with versus those without viability testing.

Acceptable viability tests do NOT have highest sensitivity or negative predictive value for identifying viable myocardium
Some cardiologists say .......

Results might be different if they used other imaging modality like CMR!
Viability imaging tests

Nuclear scan
Dobutamine/exercise stress

Which test is preferred?
CMR assessment of viability; DE-CMR

Area of delayed hyperenhancement = nonviable myocardium (Bright is dead!)

Kim RJ et al, Circulation 1999
Delayed Enhancement CMR

Physiological basis

Normal myocardium
Acute infarction
Scar

Intact cell membrane
Ruptured cell membrane
Collagen matrix
CMR assessment of viability; DE-CMR

1-25% DE

Left: 26-50% DE
Right: 51-75% DE

76-100% DE

Kim RJ et al., J Cardiovasc Magn Reson 2003
CMR assessment of viability; DE-CMR

Viability (%)

0% 1-25% 26-50% 51-75% 76-100%

Delayed enhancement

CMR
After CABG...
After CABG...
Advantages of CMR

Higher spatial resolution as compared with SPECT

- 42 year-old male with NSTEMI

Perfusion defect (-)
Advantages of CMR

Direct visualization of nonviable tissue

Strong images in small or shallow lesions
Comparison with SPECT in Three-vessel Diseases

Chung and Choi, AJR 2011
Extent of Left Ventricular Scar Predicts Outcomes in Ischemic Cardiomyopathy Patients With Significantly Reduced Systolic Function

A Delayed Hyperenhancement Cardiac Magnetic Resonance Study

Deborah H. Kwon, MD,* Carmel M. Halley, MD,* Thomas R. Berwald, MD, Victoria Zysek, DO,† Zoran B. Popovic, MD, PhD,* Randall C. Starling, MD, MPH,* Paul Schoenhagen, MD,*‡ Milind Y. Desai, MD*‡

Cleveland, Ohio

Segmental scar score
0 = absence of DHE
1 = DHE of 1% to 25% of LV segment
2 = DHE extending to 26% to 50%
3 = DHE extending to 51% to 75%
4 = DHE extending to 76% to 100%
Kaplan-Meier Curves Demonstrating Difference in Outcomes Among 4 Quartiles

automatically derived scar: >2SD above viable myocardium

Deborah H Kwon et al. JACC : Cardiovascular Imaging 2009;2;1
Kaplan-Meier Curves Demonstrating Difference in Outcomes Among 4 Quartiles

Total scar score: summed segmental scar scores/patient divided by 17

Deborah H Kwon et al. JACC : Cardiovascular Imaging 2009;2;1
Adenosine Stress Perfusion CMR
First pass perfusion CMR

Time-intensity curve at normal and pathologic myocardium after administration of contrast media.
CINE
- Cardiac function, volumes, mass
- Valvular morphology, stenosis, regurgitation
- Pericardium

MORPHOLOGY
- Dark and bright blood tomographic imaging of heart & great vessels
- T2 weighted imaging (or T1 or T2 mapping) of acute injury

STRESS PERFUSION
- Post MI risk stratification
- Ischemia evaluation

ADDITIONAL IMAGING
- Velocity/Flow imaging for valvular disease and cardiac output
- Whole heart coronary MRA (may be performed prior to contrast)
- Additional cine imaging

REST PERFUSION
- Improves specificity of stress perfusion imaging
- Quantification of myocardial blood flow reserve

DELAYED ENHANCEMENT
- 2D or 3D, Segmented (high resolution and high SNR)

Useful Additional Sequences
- Single Shot (rapid, no breath hold required, resistant to arrhythmias)
- Long inversion time (~600 ms)
  (useful for thrombus detection and “no-reflow” regions in acute MI)
- Post contrast T1 mapping for ECV measurement and serial quantification
Adenosine Stress Perfusion Protocol (SMC protocol)

- **Adenosine**
  - 140μg/Kg
  - 5-6min

- **Gd-DTPA**
  - 0.1mmol/Kg
  - 0min, 24min

- **Cine MRI**
- **Stress perfusion**
- **Flow Coronary MRA**
- **Rest Perfusion**
- **Delayed enhancement**

Timeline:
- 0min: Gd-DTPA 0.1mmol/Kg
- 4min: Adenosine 140μg/Kg
- 5min: Stress perfusion
- 8min: Flow Coronary MRA
- 12min: Rest Perfusion
- 20min: Delayed enhancement
- 24min: Gd-DTPA 0.1mmol/Kg
Perfusion MRI
Scanning protocol and Interpretation of CMR

• Assessment of wall motion abnormality

• Adenosine Stress Perfusion image

• Viability image (visualization of dead tissue)
a. Interpretation Algorithm

START

DE-MRI

+ → CAD

DE-MRI

- → Stress Perfusion

+ → CAD

Stress Perfusion

- → Rest Perfusion

“Reversible” defect → CAD

“Matched” defect → No CAD

No CAD

b. Examples

| Patient 1 | 70% stenosis in LCX marginal artery |
| Patient 2 | proximal 95% stenosis in LAD artery |
| Patient 3 | Normal coronary arteries |

DE-CMR | Stress Perfusion | Rest Perfusion | Coronary Angiography
MR-IMPACT: comparison of perfusion-cardiac magnetic resonance with single-photon emission computed tomography for the detection of coronary artery disease in a multicentre, multivendor, randomized trial


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Received 22 April 2007; revised 11 November 2007; accepted 13 December 2007; Online publish-ahead-of-print 21 January 2008
18-center multivendor study

N = 234

Comparison of Perfusion MR with SPECT and CAG
Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial


Summary
Background In patients with suspected coronary heart disease, single-photon emission computed tomography (SPECT) is the most widely used test for the assessment of myocardial ischaemia, but its diagnostic accuracy is reported to be variable and it exposes patients to ionising radiation. The aim of this study was to establish the diagnostic accuracy of a multiparametric cardiovascular magnetic resonance (CMR) protocol with x-ray coronary angiography as the reference standard, and to compare CMR with SPECT, in patients with suspected coronary heart disease.

Methods In this prospective trial patients with suspected angina pectoris and at least one cardiovascular risk factor or clinical evidence of coronary disease were recruited for CMR. SPECT testing was carried out on two occasions in patients CMR. Main primary end points were diagnostic performance of CMR and SPECT.
Flow-Independent Dark-blood DeLayed Enhancement technique (FIDDLE)
**T2-prep time**

- **301**: 90° (90° down)
- **303**: d/2
- **305**: number of refocusing pulses (example has 4)
- **307**: -90° (90° up)
- **309**: d/2

**Angles and Pulses**

- **d**: inter-pulse spacing
- **90°**: tip-down pulse
- **180°**: refocusing pulse
- **-90°**: flip-back pulse

**Spoiler Gradient**: 312
Flow-Independent Dark-blood Delayed Enhancement technique (FIDDLE)
Canine

Patient with Left Circumflex infarct involving the inferior and lateral wall and the inferior papillary muscle

Patient

Figure 1 (abstract Q6) DE-MRI (left), FIDDLE (center), and TTC (right) showing myocardial infarction of only the inferior papillary muscle (arrows). Bottom: patient example of left circumflex coronary artery infarction showing subendocardial hyperenhancement and papillary infarction.

SCMR 2016 presented, from DCMRC
<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
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<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIDDLE</td>
<td>97% (95/98)</td>
<td>92% (35/38)</td>
<td>96% (130/136)</td>
</tr>
<tr>
<td>DE-CMR</td>
<td>81% (79/98)</td>
<td>95% (36/38)</td>
<td>85% (115/136)</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt; 0.001</td>
<td>0.65</td>
<td>0.001</td>
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<tr>
<td><strong>Subendocardial MI (transmurality &lt; 25%)</strong></td>
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<tr>
<td>FIDDLE</td>
<td>98% (44/45)</td>
<td>92% (35/38)</td>
<td>95% (79/83)</td>
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<tr>
<td>DE-CMR</td>
<td>71% (32/45)</td>
<td>95% (36/38)</td>
<td>82% (68/83)</td>
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<td>p-value</td>
<td>&lt; 0.001</td>
<td>0.65</td>
<td>0.008</td>
</tr>
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</table>
• CMR is the only cardiac imaging to visualize the viable and non-viable myocardium.
• Resolution of CMR stress imaging and viability imaging is better than nuclear imaging.
• CMR is not a single image - interpretation of CMR is more integrated and summation of multiple imaging technique.
• Viability imaging in CMR is progressing.